



2006



**American Head And Neck Society  
Annual Meeting**

and

**Research Workshop on the Biology,  
Prevention and Treatment of Head and Neck Cancer**

**August 17 - 20, 2006**

Marriott Chicago Downtown

Chicago, Illinois

**The American Head & Neck Society (AHNS)**

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## General Information

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### **The American Head and Neck Society's 2006 Annual Meeting & Research Workshop on the Biology, Prevention and Treatment of Head and Neck Cancer**

**August 17 - 20, 2006**

**Marriott Chicago Downtown**  
540 North Michigan Avenue  
Chicago, IL 60611

### **On-site Registration Hours**

Wednesday, August 16, 2006:	1400 - 1800
Thursday, August 17, 2006:	0700 - 1700
Friday, August 18, 2006:	0700 - 1700
Saturday, August 19, 2006:	0700 - 1700
Sunday, August 20, 2006:	0700 - 1230

### **Exhibit Hall Hours**

<b>Thursday, August 17, 2006</b>	
<b>Welcome Reception</b>	1730 - 1900
<b>Friday, August 18, 2006</b>	
<b>Hall Open</b>	1000 - 1600
<b>Saturday, August 19, 2006</b>	
<b>Hall Open</b>	1000 - 1400

### **Accreditation Statement**

The American Head & Neck Society is accredited by the Accreditation Council for Continuing Medical Education (A.C.C.M.E.) to sponsor Continuing Medical Education for physicians. The American Head & Neck Society designates this Continuing Medical Education Activity for:

**24.5 credits**

in Category 1 of the Physicians Recognition Awards for the American Medical Association. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

### **Meeting Purpose and Goals**

The conference is designed to facilitate discussion regarding the approaches used in the diagnosis, treatment, and rehabilitation of head and neck neoplasms throughout the world. Our goals are:

- To bring together practicing surgeons, clinical investigators, geneticists, immunologists, and molecular and cellular biologists to share recent advances in head and neck cancer;
- To identify needed areas of future research;
- To disseminate this information to the larger community of investigators in related fields.

## AHNS Meeting Objectives

The conference is designed to facilitate discussion regarding the approaches used in the diagnosis, treatment, and rehabilitation of head and neck neoplasms throughout the world. Participants should accomplish the following at the conclusion of this event:

- Identify important basic science advances in head and neck oncology research;
- Develop an understanding of current issues in the diagnosis, evaluation, and treatment of head and neck neoplasms;
- Improve treatment strategies for head and neck patients;
- Facilitate discussion regarding the approaches used in the diagnosis, treatment, and rehabilitation of head and neck neoplasms;
- Recognize current research ideas in understanding the head and neck neoplastic process.

### Thanks to the 2006 AHNS Meeting & Research Workshop Supporters!

#### Platinum Level

**Bristol-Myers Squibb Company**  
**ImClone Systems Incorporated**  
**OmniGuide Inc.**  
**Sanofi-Aventis**

#### Silver Level

IRX Therapeutics, Inc.  
 Karl Storz Endoscopy

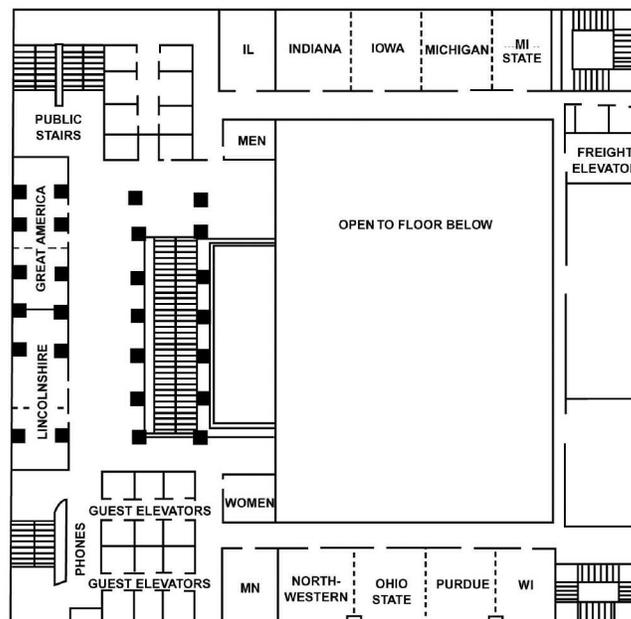
#### Bronze Level

Fanconi Anemia Fund  
 Gyrus ACMI- ENT Division  
 Stryker Leibinger  
 Vivential Biotech, Inc.  
 Xoran Technologies

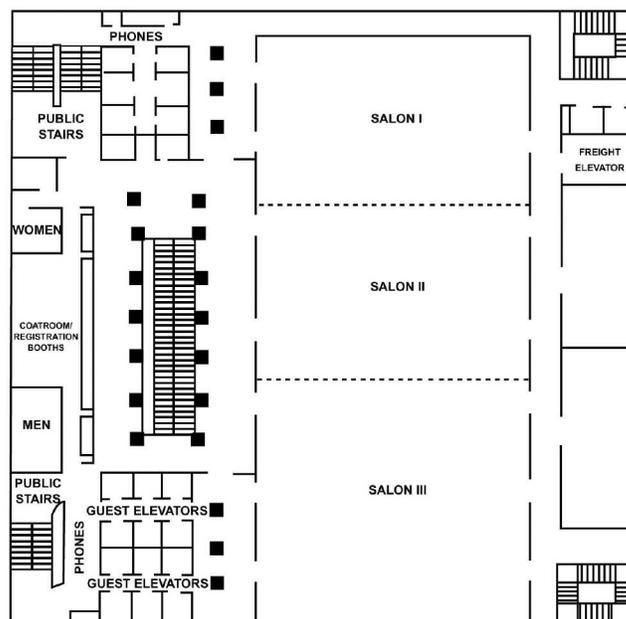
The American Head and Neck Society acknowledges the **National Institute of Dental and Craniofacial Research, National Institutes of Health** for its support of this meeting.

## Marriott Floorplans

### Sixth Floor



### Seventh Floor



# About the American Head & Neck Society

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## Mission Statement

The purpose of this society is to promote and advance the knowledge of prevention, diagnosis, treatment and rehabilitation of neoplasms and other diseases of the head and neck, to promote and advance research in diseases of the head and neck, and to promote and advance the highest professional and ethical standards.

## History of the Society

On May 13, 1998, The American Head and Neck Society (AHNS) became the single largest organization in North America for the advancement of research and education in head and neck oncology. The merger of two societies, the American Society for Head and Neck Surgery and the Society of Head and Neck Surgeons, formed the American Head and Neck Society.

The contributions made by the two societies forming the AHNS are significant in the history of surgery in the United States. Dr. Hayes Martin conceived the Society of Head and Neck Surgeons in 1954, a surgeon considered by many to be the “father of modern head and neck tumor surgery.” The purpose of the society was to exchange and advance the scientific knowledge relevant to the surgery of head and neck

tumors (exclusive of brain surgery) with an emphasis on cancer of the head and neck. Two years later, The American Society for Head and Neck Surgery was organized with the goal to “facilitate and advance knowledge relevant to surgical treatment of diseases of the head and neck, including reconstruction and rehabilitation; promote advancement of the highest professional and ethical standards as they pertain to the practice of major head and neck surgery; and to honor those who have made major contributions in the field of head and neck surgery, or have aided in its advancement”.

The new Society remains dedicated to the common goals of its parental organizations.

## Why Join the AHNS?

The American Head and Neck Society is an organization of physicians, scientists and allied health professionals dedicated to improving the understanding of Head and Neck Cancer and the care of patients afflicted with that disease. Membership is open to a wide variety of interested individuals in several categories that differ both in terms of responsibility and level of involvement in the society.

## AHNS President

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### John J. Coleman III, MD



John J. Coleman, III, M.D. was born in Boston, Massachusetts in 1947. He was educated at Thayer Academy, Harvard College and Harvard Medical School before beginning residencies in General Surgery and Plastic Surgery at Emory University Affiliated Hospitals in Atlanta, Georgia. He

completed a Surgical Oncology Fellowship at University of Maryland Hospitals and joined the faculty at Emory University School of Medicine in the Winship Clinic in the Division of Surgical Oncology in 1980 where he later became the Wadley Glenn Professor of Surgery.

In 1991, Dr. Coleman was appointed Chief of Plastic Surgery at Indiana University School of Medicine and is presently the

James E. Bennett Professor of Plastic Surgery and Chief of the Division of Plastic Surgery at IUSOM. A member of numerous surgical organizations, he has served as President of The Ohio Valley Society of Plastic Surgeons, Chairman of The American Board of Plastic Surgery and Chairman of the Residency Review Committee for Plastic Surgery.

Throughout his career, Dr. Coleman has studied the patient with cancer, particularly cancer of the head and neck. He has published numerous scientific articles, particularly on the effects of radiotherapy on the head and neck, and on reconstruction of the pharynx, mandible and mid-face with particular interest in microvascular surgery. He has served on numerous committees of The Society of Head and Neck Surgeons, The American Society of Head and Neck Surgeons and at present, The American Head and Neck Society.

Jack and his wife of forty years, Janice Ann Bianco Coleman, have four children, Angela Lee Munshi, John J. Coleman, IV, Maria Clarke Coleman, Patrick Carmine Coleman and five grandchildren

## Maurice J. Jurkiewicz, MD



Maurice John Jurkiewicz, MD was born September 24, 1923 and raised in Bellows Falls, Vermont. He graduated Magna Cum Laude from the University of Maryland in 1946 with a DDS degree and received his medical degree from the Harvard Medical School in 1952.

Dr. Jurkiewicz did his Residency in Plastic/Reconstructive Surgery and general surgery at Barnes Hospital Washington University. He was certified by the American Board of Surgery in 1960 and re-certified in 1980. He was also certified by the American Board of Plastic Surgery in 1963 and re-certified in 1978.

Dr. Jurkiewicz was the Chief of Plastic Surgery at the University of Florida from 1959-1971 and the Chief of Surgery at VAMC in Gainesville, Florida from 1968-1971. He became the Chief of Reconstructive/Plastic Surgery at Emory

University in 1971 and held that position until 1993. Since 1993, he has held the title of Professor of Surgery emeritus at Emory University.

He held many other positions including the Chief of Surgical Services at Grady Memorial hospital in Atlanta from 1972 to 1977 and the Chief of Surgery at VAMC Atlanta from 1989 to 1993. He acted as a Plastic Surgeon consultant at Walter Reed hospital in Washington DC from 1971 to 1991 and to the Shriners hospitals from 1995 to 2000. Dr. Jurkiewicz also served as a Scientific Councilor for the National Institution of Dental Research from 1966 to 1971.

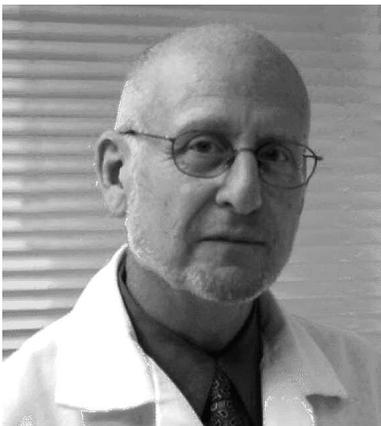
Dr. Jurkiewicz was a member-at-large of the National Board of Medical Examiners between 1985 and 1993 and is a member of the American Surgical Association joining in 1971.

Dr. Jurkiewicz served as the president of the American Society of Head and Neck Surgeons in 1989 as well as the president of the American College of Surgeons in 1989-1990. He also served as first vice-president on the Southern Surgical Association in 1993. In 1990, he became an Honorary Fellow of the Royal Australasian College of Surgeons and in 2004, became an Honorary Fellow of the Southern Surgical Association.

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## Hayes Martin Lecturer

## Keith S. Heller, MD



Keith S. Heller, M.D. was born in Brooklyn, New York, and grew up on Long Island, where he still practices. After receiving his undergraduate degree in Biophysics from Amherst College in Massachusetts, he returned to New York City where he graduated from the New York University School of

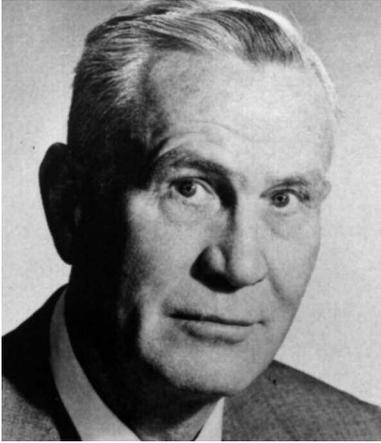
Medicine and then completed training in General Surgery at NYU and Bellevue Hospitals under Dr. Frank C. Spencer. In 1978 he began a Surgical Oncology fellowship at Memorial Sloan-Kettering Cancer Center where he was exposed to Head and Neck Surgery for the first time. In an era before formal Head and Neck fellowships, he was able to spend more than one year of his fellowship training with Drs. Elliot Strong, Ronald Spiro, and Jatin Shah all of whom inspired him to pursue a career in head and neck surgery and have continued to mentor him through the years. Following his fellowship, he was invited to return to Long Island to work with the late Dr. Joseph Attie at Long Island Jewish Medical Center.

Dr. Heller is Clinical Professor of Surgery at the Albert Einstein College of Medicine and Chief of the Section of Head and Neck Surgery at Long Island Jewish Medical Center where he has joint appointments in Surgery and Otolaryngology. He is actively involved in the education of residents in both specialties. He is a past president of the American Head and Neck Society and has been president of both the New York Head and Neck Society and the New York Cancer Society. He had been a member of the Society of Head and Neck Surgeons and the American Society for Head and Neck Surgery, and was one of the leaders of those societies who worked together to create the American Head and Neck Society. He is also a member of the American Association of Endocrine Surgeons and the American Thyroid Association.

He has published extensively on head and neck cancer surgery. Currently, his clinical research interest is the surgical treatment of diseases of the thyroid and parathyroid, an area in which he has a very large personal experience.

He was married in 1968 to his wife, Honey, who after a career as an international banker in Latin America now devotes her efforts to community activism and social justice. In 1997 they received the Allard Lowenstein Award of the American Jewish Congress for their work together. They recently moved to Manhattan after raising their two sons on Long Island. Jared, 28, is a law clerk in Federal District Court. Gregory, 20, is a student at Connecticut College in New London and a future TV producer.

## Hayes Martin, MD



Hayes Martin was born in Dayton, a small town in north central Iowa. He attended the University of Iowa at Iowa Falls before being accepted to the medical school in 1913 on the same campus, finishing 4 years later in a class of 20.

World War I began in April 1917 while Hayes was in his final year of

medical school. Many of his classmates at the medical school were in the Army ROTC units; however, Dr. Martin opted for the Navy, which he joined on the day America entered the war. He traveled to Europe on the USS Arkansas and was assigned to his permanent duty station at the U.S. Navy Air Station, La Trinite Sur Mer, France – a small seaside village on the southern coast of Brittany. The purpose of this base was antisubmarine warfare using blimps and kite balloons. Dr. Martin was made commanding officer of the air station for a brief period of time when the line officer in charge had become ill; it was a unique position for a medical officer in the Navy to take command during wartime.

After the war, Dr. Martin returned to the U.S and sought out an internship at the old Poly Clinic Hospital in New York City, which was temporarily made into a Veteran's Administration hospital. Part of his internship was spent at Bellevue in the fourth surgical division, where he felt he would have the best possible training in general surgery. The chief of the second division was John A. Hartwell, MD, the distinguished surgeon memorialized by the Fellow's Room in the library of the New York Academy of Medicine. Dr. Hartwell suggested that Dr. Martin go to Memorial Hospital to learn about cancer.

Dr. Martin received an internship at Memorial in the summer of 1922 and stayed on as a resident until 1923. He then had

two years at the second surgical service at Bellevue, where he operated to his heart's content and got the surgical education he so strongly desired. Once he finished his residency, Dr. Martin returned to Memorial where he joined as clinical assistant surgeon on the staff.

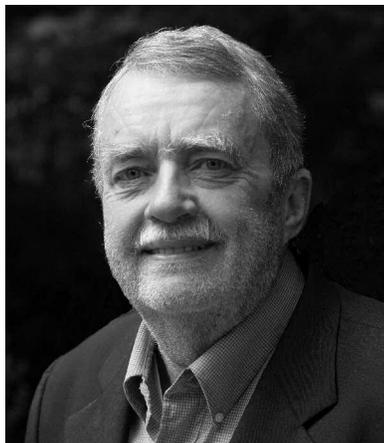
Dr. Martin made the use of aspiration biopsy on all solid tumors popular throughout Memorial. Now, this procedure is done throughout the world. Dr. Martin co-authored the first report on the subject published in the Annals of Surgery. Numerous other articles followed, including Dr. Martin's two most famous publications, "Cancer of the Head and Neck," published in two issues of the Journal of the American Medical Association in 1948, and "Neck Dissection," appearing in Cancer in 1951. These two papers were so extensively requested that the American Cancer Society made reprints by the thousands available to those who requested them as many as 20 years after publication. Dr. Martin's bibliography encompasses more than 160 articles.

In 1934, Dr. Martin was appointed Chief of the Head and Neck Service at Memorial Hospital. It wasn't until 1940 that surgery began to take over as the treatment of choice for the majority of cancers of the head and neck. In that year, the beginnings of improved anesthesia permitted advances in surgery. Later, during World War II, antibiotics became available and surgery began to dominate much of head and neck cancer management.

Dr. Martin wrote extensively on many subjects, most within the realm of head and neck surgery. His ideal was to be the complete head and neck surgeon and he treated a wide variety of head and neck abnormalities. His book, Surgery of the Head and Neck Tumors, was published in 1957.

Dr. Martin retired from active practice in 1957 at the age of 65. He performed his last operation at Memorial Hospital, assisted by Dr. Elliot Strong, in October 1959, but continued to see patients in his office until he passed away in 1977.

## John Stone, MD, MACP



John Stone is Professor of Medicine (Cardiology) Emeritus at Emory University School of Medicine. For 19 years he was Director of Admissions and Associate Dean. Prior to that, he worked in cardiology at Grady Hospital, where he founded the program in Emergency Medicine, now a full department in the School of Medicine.

He has taught often for Emory College through the years, including the British Summer Studies Program in Oxford, England (Creative Writing and Literature and Medicine).

Born in Jackson, Mississippi, Dr. Stone graduated from Millsaps College, then received his M.D. degree from Washington University School of Medicine. He trained in Medicine and Cardiology at the University of Rochester and Emory University, joining the Emory faculty in 1969. Dr. Stone has three times been selected Best Clinical Professor at Emory and has given the Graduation Address for the School of Medicine four times. He received the Thomas Jefferson Award from Emory (1983) and the Emory University Scholar / Teacher Award (1990). In 1987, he received the Theobald Smith Award, the highest academic award of Albany Medical College, for “distinguished service to mankind in the fields of science, medicine, and teaching.” In April 1996, he received the Nicholas E. Davies Memorial Scholar Award from the American College of Physicians for scholarly activities in the realm of the humanities. Dr. Stone received the Georgia Governor’s Award in the Humanities in 1992. In 2000, the Medical Alumni Association honored Dr. Stone with the Evangeline T. Papageorge Distinguished Faculty Award for excellence in teaching. Dr. Stone has received honorary degrees from Miami University, Northeastern Ohio Universities College of Medicine, and Albany Medical College. In April 2003, he received the Mastership designation (MACP) from The American College of Physicians.

Louisiana State University Press publishes Stone’s poetry: *THE SMELL OF MATCHES* (1972); *IN ALL THIS RAIN* (1980); *RENAMING THE STREETS* (1985); *WHERE WATER BEGINS* (1998). *MUSIC FROM APARTMENT 8: New and Selected*

*Poems*, was published by LSU in 2004. His work has twice received a Literature Award from the Mississippi Institute of Arts and Letters (1986 and 1999). (Former winners include Walker Percy, Ellen Gilchrist, and Barry Hannah.)

*IN THE COUNTRY OF HEARTS*, a book of new and collected essays, was originally published by Dell and reprinted by LSU Press (1996). Most of these essays appeared first in *The New York Times Magazine*, others in *Journal of the American Medical Association*, *Discover*, *MD Magazine*.

Stone is co-editor (with Drs. Richard Reynolds, Lois Nixon, and Delese Wear) of *ON DOCTORING*, an anthology of Literature and Medicine (Simon and Schuster). The book is presented annually as a gift from the Robert Wood Johnson Foundation to students entering U.S. medical schools; the book is now in its 3rd edition. More than 250, 000 copies of *ON DOCTORING* have been distributed.

Stone’s work has appeared in such publications as *Poetry*, *The American Scholar*, *The New York Quarterly*, *The Georgia Review*, *The Southern Review*, *New England Review*, *Five Points*, and *Poetry Northwest*. His work has been widely anthologized, including *The Norton Introduction to Literature*, *Contemporary Southern Poetry*, and *The Made Thing: An Introduction to Contemporary Southern Poetry*.

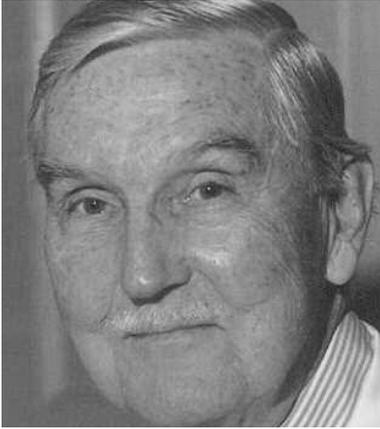
Stone has read and spoken at celebratory events at over 150 institutions in 40 states and given named lectures at such institutions as Yale, Stanford, Johns Hopkins, Virginia, American College of Physicians, Tulane, Vanderbilt, Brown, The Mayo Clinic, The Cleveland Clinic. Stone wrote the libretto for *CANTICLES OF TIME*, a choral symphony (music by Samuel Jones) that won the Music Award of the Mississippi Institute of Arts & Letters (1991). In February 2001, Stone and the pianist, William Ransom, performed a program called “The Poet and The Pianist” at Carnegie Recital Hall, New York. The Inaugural Poem for Emory’s new President, James Wagner, was commissioned to and read by Dr. Stone in April 2004.

Articles about John Stone appear in the following journals: *The Lancet* (Vol. 349, p. 275, January 25, 1997) and *The American Journal of Medicine* (Vol. 101, No. 4, p. 447, October 1996). His work was a front-page feature in the *Wall Street Journal* on March 3, 1998. Most recent reviews of his work: *The Lancet* Vol. 364, p. 833, Sept. 4, 2004; and *Annals of Internal Medicine*, Vol. 141, Sept. 21, 2004; *JAMA* 292 (14), Oct. 13, 2004.

# John J. Conley Biography

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## John J. Conley, MD



Although he looked and sounded like an English nobleman, Dr John Conley was born in Carnegie, Pennsylvania, a small steel mill town just outside of Pittsburgh. He graduated from the University of Pittsburgh and later its school of medicine. He interned at Mercy Hospital in Pittsburgh. During that year, the

nuns who ran the hospital suggested that Dr. Conley take a residency in cardiology and come back to Mercy as their cardiologist. He went to Kings County Hospital in Brooklyn, a very busy city hospital with a huge patient population. Shortly after he began his training, he had an arrhythmia diagnosed as paroxysmal atrial tachycardia. Little was known about this benign condition at that time. Dr. Conley was told that cardiology was too stressful and that he should go into an easier, less-stressful field with better working hours, like ENT. He did an otolaryngology residency at Kings County Hospital. This was followed by four years of military service during World War II, which included experience in otolaryngology and plastic and reconstructive and maxillofacial surgery in the U.S. Army Medical Corps, both in this country and in the South Pacific theater. Exposure to the reconstruction of war wounds would prove invaluable to him later on in applying these principles to reconstruction following ablative head and neck surgery.

Dr. Conley returned to New York City after the war. He became an assistant and then an associate of Dr George T. Pack, a technically superb general oncologic surgeon at Memorial Hospital who taught Dr. Conley major ablative surgery of the head and neck. They worked day and night catching up with the backlog of surgery that was neglected during

the war years. The combination of his training in otolaryngology, the exposure to ablative surgery, and the World War II experience in reconstructive surgery set the stage for Dr Conley to evolve his unique approach to head and neck surgery.

Ironically, despite the admonition of the cardiologists about hard work, Dr. Conley did a prodigious amount of major head and neck reconstructive surgery. This proved to be more than ample to provide training to many fellows. His commitment to education is further attested to by the position he held for many years as Clinical Professor of Otolaryngology at the College of Physicians and Surgeons at Columbia University. He loved his appointment at Columbia and particularly his involvement in teaching the residents.

Dr. Conley's vast surgical experience, together with active research interests, led to the authorship of almost 300 contributions to the scientific literature, and eight books. As a result of his productivity and rhetorical eloquence, he was very much in demand as a speaker in this country and abroad. He gave many prestigious eponymous lectures in our field and received many awards for his work, including the Philip H. Hench Award as the Distinguished Alumnus of the University of Pittsburgh School of Medicine, and the DeRoaldes and Newcomb Awards of the American Laryngological Association.

Dr. Conley's contributions to the scientific literature, many technical innovations and surgical experience placed him in the position to receive many honors and important leadership positions, such as President of the American Academy of Otolaryngology and Ophthalmology, member of the Board of Governors of the American College of Surgeons, founding member of the Society of Head and Neck Surgeons, and founding member and first President of the American Society for Head and Neck Surgery. During those years, Dr Conley used, to the great benefit of us all, his wisdom and diplomacy in carrying out such high-level responsibilities.

## Jatin P. Shah, MD



The AHNS would like to express its gratitude to Jatin P. Shah, MD, Chief of the Head and Neck Service and Elliot W. Strong Chair in Head and Neck Oncology at Memorial Sloan-Kettering Cancer Center, and Past-President of the Society of Head and Neck Surgeons, for his extraordinary contribu-

tion to the AHNS Research and Education Foundation. In recognition of this contribution, the AHNS announces the first “Jatin P. Shah Symposium on Clinical Controversies in Head and Neck Surgery” to be held during the AHNS 2006 Annual Meeting & Research Workshop in August. The symposium entitled “Management of Complex Issues In Thyroid Cancer” will take place on Saturday, August 19th from 1500 – 1600 and is chaired by Ashok R. Shaha, MD, also from Memorial Sloan-Kettering Cancer Center. The Jatin P. Shah Symposium will be a permanent part of the AHNS annual meeting whether that meeting is freestanding, international or part of a combined effort.

Professor Jatin P. Shah graduated from the Medical College of MS University in Baroda, India. He completed his post-graduate training at that Institution, followed by Fellowships at Memorial Sloan Kettering Cancer Center in New York. He is Professor of Surgery, and Chief of the Head and Neck Service, and Leader of the Head and Neck Disease Management Team, and holds The Elliott W. Strong Chair in Head and Neck Oncology at Memorial Sloan-Kettering Cancer Center in New York City.

Professor Shah is a national and international leader in the field of head and neck surgery, having served as President of The New York Cancer Society, The New York Head and Neck Society, The Society of Head and Neck Surgeons and The North American Skull Base Society. He is currently Director of

The International Federation of Head and Neck Oncologic Societies and President of The International Academy of Oral Oncology, and Chairman of the AJCC task force on Head and Neck. He was Chairman of the Joint Council for advanced training in head and neck oncologic surgery in the USA. He was also Chairman of The 4th International Conference on Head and Neck Cancer in Toronto in 1996. He has served in varying capacities for The American Board of Surgery, and The American College of Surgeons.

Professor Shah has been the recipient of numerous awards from various parts of the world, and is the recipient of honorary fellowships from The Royal College of Surgeons of Edinburgh, London and Australia. He has been elected as an honorary member of several head and neck societies in Europe, Asia, Australia, Africa and Latin America. He has been continuously listed in the “Best Doctors in America” directories for several years. He serves on the Editorial and Review Boards of 18 scientific journals and has over 300 peer-reviewed publications, 50 book chapters and 7 books. His textbook of Head and Neck Surgery and Oncology won First Prize from The British Medical Association and The Royal Society of Medicine and was awarded the George Davey Howells Prize from the University of London, for the best published book in otolaryngology in the last five years.

He is a much sought after speaker who has delivered over 800 scientific presentations including keynote addresses, named lectureships, and visiting professorships in the United States, Canada, United Kingdom, Scotland, Sweden, Belgium, Germany, Italy, Spain, Poland, Russia, Croatia, Turkey, Egypt, South Africa, India, China, Korea, Japan, HongKong, Singapore, Australia and all the countries in South America. He was the recipient of The Royal Society of Medicine Visiting Professorship for 1997.

In recognition of his outstanding contributions, and World Leadership in Head and Neck Surgery, Memorial Sloan Kettering Cancer Center, has established an endowed Chair in his name. The “Jatin Shah Chair in Head and Neck Surgery and Oncology”, which will support a Surgeon Scientist at the Professor level, at MSKCC.

# Distinguished Service Award

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## John Andrew “Drew” Ridge, MD, PhD



John Andrew “Drew” Ridge was born in 1950. After attending the University of Chicago he received the Ph.D. in Biochemistry from Stanford University in 1978 and the M.D. in 1981. He pursued residency training in General Surgery at the University of Colorado and both Surgical Research and Surgical

Oncology fellowships at the Memorial Sloan-Kettering Cancer Center.

From 1989 to 1991 he was Assistant Professor in Residence at the University of California at San Francisco before moving to the Fox Chase Cancer Center in Philadelphia when presented with an opportunity to limit his practice to head and neck surgery. At Fox Chase, he became chief of the Head and Neck Surgery Section and rose to the rank of Senior Member. A surgical oncology fellowship position has been endowed in his name.

Dr. Ridge has devoted his academic career to multidisciplinary treatment of head and neck cancer, with a strong commitment to clinical research. He has been influential in the design and execution of several clinical trials evaluating “organ preservation,” the non-surgical management of advanced squamous cancers of the head and neck. He serves as Co-Chair of the Head and Neck Committee of the Eastern Cooperative Oncology Group and is a member of the Head and Neck Steering Committee of the Radiation Therapy Oncology Group. He has been a member of the NCCN Head and Neck and Thyroid panels since their inceptions and has been a writing member of both committees.

After they met at Sloan-Kettering, he married Elin Sigurdson in 1989. An academic surgical oncologist interested primarily in colorectal cancer, she too works at Fox Chase. Their son, Lukas, and twin daughters, Kelsey and Hannah, are nearing college. A fencer, Drew holds an “A” classification in Epee and competes nationally in Division I.

Active in many professional organizations, he was part of the first Council of the American Head and Neck Society, and currently serves as Secretary of the AHNS.

# Presidential Citation

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## Marc D. Coltrera, MD



Marc D. Coltrera was born in New York City. He graduated from Brown University in Chemistry (ScB, 1977), Yale Medical School (1981), and trained in Otolaryngology-Head and Neck Surgery at the Massachusetts Eye and Ear Infirmary (1986). He then left the East Coast for the Great Northwest for a two-year research

and clinical Head and Neck Surgery Fellowship at the University of Washington (1988). He has been there ever since and is currently Professor and Vice-Chairman at the University of Washington in the Department of Otolaryngology-Head and Neck Surgery.

While his clinical interests have concentrated on head and neck cancer, his basic science research, for which he has

held several NIH grants, has taken him far a field. He has focussed on mechanisms of cell proliferation and growth control while finding ways of studying the mechanisms in both malignant and normal cells. Dr. Coltrera’s biologic basic science studies include the first description of the parathyroid hormone receptor.

In the past several years he has come to believe that the involvement of the clinician membership of societies such as the American Head and Neck Society is crucial to the study of disease and clinical trials. To help further the involvement of all members, Dr. Coltrera has devoted himself to creating database tools which allow clinicians at multiple sites to control their own data while sharing subsets of the data for consortium trials in a confidential, verifiable manner which protects the data integrity. Customized versions of these database tools are being used to study head and neck cancer, sarcomas, and respiratory papillomatosis by the AHNS and other organizations.

## **Diane Horner, RN**



Diane K. Horner, RN, BSN, CNOR, CPSN was born in Gary, IN. She received her Baccalaureate degree in Nursing from Indiana University and is currently pursuing her Master's of Education in nursing through the University of Indianapolis and will graduate this December. During her undergrad

education, she enrolled in Introduction to Perioperative elective class, which she loved and still practices. She quickly found a love in Plastic and Reconstructive Surgery and became coordinator of Plastic, Oral and Dental services, working closely with ENT also. The combination reconstructive cases with ENT and Plastics are some of her favorites.

Diane became a member of the Association of Operating Room Nurses and certified operating room nurse, CNOR, since 1996. She has also been a member of the American Society of Plastic and Reconstructive Nurses and a certified plastic surgery nurse, CPSN since 1992. She has become president of the American Society of Plastic Surgical Nurses

of Greater Indianapolis Chapter, which she still maintains. She also holds a certificate in the CITI Course in the Protection of Human Research Subjects. Diane has been a member of Sigma Theta Tau, Alpha Chapter, International Honor Society in Nursing since 1989.

Diane has volunteered as chairperson for the Midwest Region/Ohio Valley Meeting in both 1997 and 2003. She organized academic and social activities, including vendors for 200 doctors and nurses. She is already in the midst of organizing the next meeting in May of 2007.

She has gone on a medical mission trip to India in 1997 and assisted on numerous operations and education in this country. She hopes to go to India again this January. Diane has given many educational presentations and participated in various research projects. She was also a representative for Indiana Nurses in Washington D.C. in 2004.

Diane has also been very active in Race for the Cure, being team captain and participant.

Diane has worked at Indiana University for 17 years. She is also working at Clarian West Hospital and Wishard Hospital. She has received a Gold Performance Award for Excellence in Education as preceptor of the year in 1997 and again in 2003.

Diane is married to Michael and has two boys, Mark, 6 and Adam, 4.

# Presidential Citation

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## Fred M.S. McConnel, MD



Fred M.S. McConnel, MD received his medical degree from the University of North Carolina at Chapel Hill. He completed an internship at the University of Iowa, a otolaryngology residency and a head and neck fellowship at Northwestern University, Chicago IL, under the direction of Dr. George Sisson.

While at Northwestern, Dr. McConnel and Dr. Jeri Logemann developed a prosthetic speech device for usage after total laryngectomy. Dr. Mark Singer also worked on this project, later developed the Bloom-Singer voice prosthesis.

After serving two years in the Air Force, Dr. McConnel joined the otolaryngology division at Emory University to practice head and neck surgery. While at Emory, Dr. McConnel emphasized the team approach for the care of head & neck cancer patients. The team was composed of components from otolaryngology, plastic surgery, nursing, speech & swallowing pathology, radiation therapy and social services. With this team, a large series of free micro vascular jejunal grafts were performed for total laryngopharyngectomees, which established this method as an efficient reconstruction.

For oral and oropharyngeal defects, several reconstruction alternatives were being used: primary closure, skin grafts, distal flaps and free micro vascular flaps. Dr. McConnel worked with Dr. Logemann to develop a National Cancer Institute

(NCI) dealing with prospective multiple institutional study of speech and swallowing after reconstruction of surgical defects. This study examined post surgical function by using objective testing criteria for evaluating speech and swallowing. The results of reconstructions were analyzed in terms of the function instead of success of defect closure. With matched defects, many times primary closure functioned as well as flap reconstructions. This study redirected the focus of surgery toward more functional reconstruction.

Dr. McConnel developed a new method of swallowing analysis, Manofluorography, to give objective data. With this method, one could determine what forces are applied to the bolus during swallowing by each structure. This data supported a new concept of pharyngeal swallowing proposing a synergistic two-pump mechanism verses a peristaltic propulsive mechanism. The oral-pharyngeal pump was recognized to be the primary propulsive force generator for the pharyngeal swallow. Reconstructions, which interfered with propulsive force generation yielded impaired swallowing. With the tongue being under voluntary control, this gave a rationale for swallowing therapy.

Dr. McConnel was the principle investigator for three NCI five-year research grants, co-investigator for two NCI grants and one V.A. grant. The Manofluorography projects were supported by a five-year private grant funded by the Calvin & Marisa Allen Cancer Fund. He also has 64 publications, 130 invited presentations and two United States patents. He obtained the academic rank of Professor of Otolaryngology at Emory Medical School, Atlanta GA in 1989.

Dr. Fred McConnel is married to Marianne Roddenbery McConnel and has three children: Hunt, Mary Anne and Fred.

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## The American Head and Neck Society

K. Thomas Robbins, MD	1999
Ashok R. Shaha, MD	1999
Jesus E. Medina, MD	2000
Ernest A. Weymuller, Jr., MD	2001
Keith S. Heller, MD	2002
Paul A. Levine, MD	2003
Jonas T. Johnson, MD	2004
Patrick J. Gullane, MD	2005

## The American Society for Head and Neck Surgery

John J. Conley, MD*	1959-61
Paul H. Holinger, MD*	1961-63
Joseph H. Ogura, MD*	1963-65
John F. Daly, MD*	1965-67
W. Franklin Keim, MD*	1967-69
George A. Sisson, MD	1969-70
John S. Lewis, MD	1970-71
Burton J. Soboroff, MD*	1971-72
Edwin W. Cocke, Jr., MD	1972-73
Charles M. Norris, MD	1973-74
Daniel Miller, MD*	1974-75
Emanuel M. Skolnick, MD*	1975-76
George F. Reed, MD*	1976-77
John A. Kirchner, MD	1977-78
William M. Tribble, MD*	1978-79
Loring W. Pratt, MD	1979-80
J. Ryan Chandler, MD	1980-81
Douglas B. Bryce, MD	1981-82
Jerome C. Goldstein, MD	1982-83
Paul H. Ward, MD	1983-84
Hugh F. Biller, MD	1984-85
Robert W. Cantrell, MD	1985-86
John M. Lore, Jr., MD*	1986-87
Charles J. Krause, MD	1987-88
Eugene N. Myers, MD	1988-89
Willard N. Fee, Jr., MD	1989-90
Helmuth Goepfert, MD	1990-91
Michael E. Johns, MD	1991-92
Bryon J. Bailey, MD	1992-93
James Y. Suen, MD	1993-94
Gary L. Schechter, MD	1994-95
Charles W. Cummings, MD	1995-96
Nicholas J. Cassisi, MD	1996-97
Dale H. Rice, MD	1997-98

## The Society of Head and Neck Surgeons

Hayes Martin, MD*	1954
Hayes Martin, MD*	1955
Hayes Martin, MD*	1956
Hayes Martin, MD*	1957
Grant Ward, MD *	1958
Danely P. Slaughter, MD*	1959
Arnold J. Kremen, MD	1960
Arnold J. Kremen, MD	1961
H. Mason Morfit, MD	1962
H. Mason Morfit, MD	1963
Calvin T. Kloop, MD*	1964
Harry W. Southwick, MD*	1965
Edgar L. Frazell, MD*	1966
Oilver H. Behars, MD*	1967
Arthur G. James, MD	1968
William S. MacComb, MD*	1969
Ralph R. Braund, MD*	1970
Harvey W. Baker, MD*	1971
Charles C. Harrold, MD	1972
Robin Anderson, MD	1973
Alfred Ketcham, MD	1974
Richard H. Jesse, MD*	1975
Condict Moore, MD	1976
Donald P. Shedd, MD	1977
William A. Maddox, MD	1978
John C. Gaisford, MD	1979
Robert G. Chambers, M.D.*	1980
Elliot W. Strong, MD	1981
John M. Moore, MD	1982
Alvin L. Watne, MD	1983
Darrell A. Jaques, MD	1984
Alando J. Ballantyne, MD*	1985
Frank C. Marchetta, MD*	1986
William R. Nelson, MD	1987
Robert D. Harwick, MD	1988
James T. Helsper, MD	1989
M.J. Jurkiewicz, MD	1990
Jatin P. Shah, MD	1991
Oscar Guillamondegui, MD	1992
Stephen Ariyan, MD	1993
J. Edward M. Young, MD	1994
Michael B. Flynn, MD	1995
Robert M. Byers, MD	1996
John R. Saunders, Jr., MD	1997
Ronald H. Spiro, MD	1998

\*Deceased

## Past Hayes Martin Lecturers

William S. MacComb, MD	1972
Oliver H. Beahrs, MD	1973
Arthur G. James, MD	1974
Charles C. Harrold, MD	1975
Edgar L. Frazell, MD	1976
Harry W. Southwick, MD	1977
Harvey W. Baker, MD	1978
Edward F. Scanlon, MD	1979
Condict Moore, MD	1980
Richard H. Jesse, MD	1981
Milton Edgerton, MD	1982
John J. Conley, MD	1983
William A. Maddox, MD	1984
Alfred S. Ketcham, MD	1985
Donald P. Shedd, MD	1986
Elliot W. Strong, MD	1987
M.J. Jurkiewicz, MD	1988
George A. Sisson, MD	1989
Alando J. Ballantyne, MD	1990
Ian Thomas Jackson, MD	1991
John M. Lore, MD	1992
Ronald H. Spiro, MD	1993
John G. Batsakis, MD	1994
Helmuth Goepfert, MD	1995
Joseph N. Attie, MD	1996
Blake Cady, MD	1997
Jatin P. Shah, MD	1998
Jean-Louis H. LeFebvre, MD	1999
Robert M. Byers, MD	2000
William Wei, MS	2001
Eugene Myers, MD	2002
Michael Johns, MD	2003
Christopher J. O'Brien, MD	2004
Richard K. Reznick, MD, MEd	2005

## Past John J. Conley Lecturers

Edward Hughes, MD	2001
Rabbi David Saperstein	2002
Jonathan D. Moreno, MD	2003
David C. Leach, MD	2004
James F. Battey Jr., MD	2005

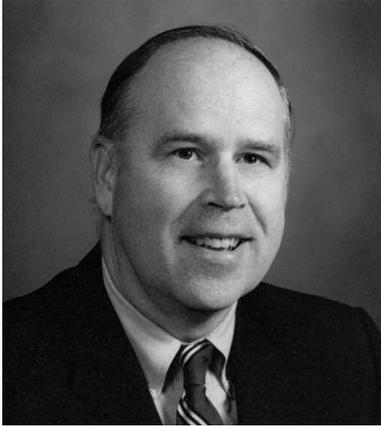
## Distinguished Service Awards

Jatin P. Shah, MD	1989
Stephan Ariyan, MD	1990
Ashok R. Shaha, MD	1991
Elliot W. Strong, MD	1995
John J. Coleman, III MD	1999
David L. Larson, MD	1999
Harold J. Wanebo, MD	1999
Jonas T. Johnson, MD	2001
Helmuth Goepfert, MD	2003
Mark D. Coltrera, MD	2004
Wayne Koch, MD	2005

## Special Recognition Awards

Paul B. Chyetien, MD	1984
John M. Lore, Jr., MD	1985
William S. MacComb, MD	1986
Calvin T. Klopp, MD	1987
Edgar L. Fazell, MD	1988
Harvey W. Baker, MD	1989
Vahram Y. Bakamjian, MD	1991
Jean-Louis Lefebvre, MD	1995

## Robert Maxwell Byers, MD



The Robert Maxwell Byers Award, in the amount of \$1000, is for the best clinical or basic science research paper submitted for presentation at the annual meeting of the American Head and Society.

Robert Maxwell Byers, M.D. was born in Union Hospital, Baltimore, Maryland on September 24, 1937. He grew up

on the Eastern Shore of Maryland in the small town of Elkton. Very active in the varsity sports of baseball, basketball and track during his high school years, he continued his athletic participation at Duke University along with his pre-med studies. He entered the University of Maryland Medical School in Baltimore in 1959, where he excelled in his medical studies and received membership in AOA and the Rush Honor Medical Society. The highlight of his sophomore year was his 1961 marriage to Marcia Davis, a high school sweetheart. During his junior year, he was commissioned an Ensign in the United States Naval Reserve and later rose to the rank of Captain in 1986.

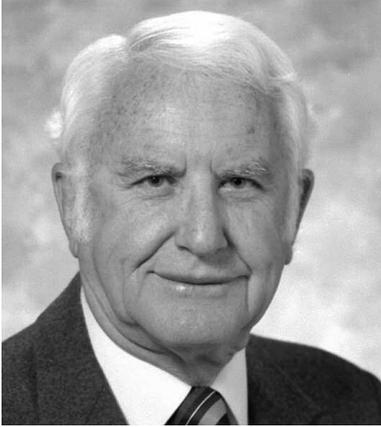
In 1963, Dr. Byers began his general surgical residency with Dr. Robert Buxton at the University Hospital in Baltimore. Five years later, as a fully trained general surgeon, he went to the Republic of Vietnam with the 1st Marine Division where he received a unit commendation medal and a combat action ribbon. On return to the United States, he spent a year at Quonset Point, Rhode Island Naval Hospital as Chief of Surgery. In 1969, he was certified by the American Board of Surgery. After discharge from the Navy in 1970, Dr. Byers and his family moved to Houston, Texas where he began a fellow-

ship in Surgical Oncology at the University of Texas M.D. Anderson Cancer Center under the guidance of Drs. R. Lee Clark, Richard Martin, Ed White, William MacComb, Richard Jesse and Alando J. Ballantyne. This move proved to be a decisive event, as he never left. His career in Head and Neck Surgical Oncology was born, nurtured, and matured during the 31 years of his academic/clinical practice at the University of Texas M.D. Anderson Cancer Center.

During his tenure at M.D. Anderson Cancer Center he rose through the ranks from Assistant Professor in 1972 to Associate Professor in 1976 and, finally, Professor and Surgeon in 1981. In 1998, he was honored with the Distinguished Alando J. Ballantyne Chair of Head and Neck Surgery. He is the author or co-author of over 200 published papers, book chapter and monographs. He has given invited lectures all over the world. Most recently (1999), he was selected to give the Hayes Martin Memorial Lecture at the 5th International Conference on Head and Neck Cancer. He has been President of the American Radium Society and President of the Society of Head and Neck Surgeons both in 1995 – 1996. His research interests and his expertise have been focused on cancer of the oral cavity, head and neck cancer in young people and treatment of the neck involved with metastatic cancer with a particular interest in various neck dissections. Dr. Byers is a member of many prestigious societies, of which the Southern Surgical Association, the Texas Surgical Society, the American College of Surgeons and the Society of Surgical Oncologists are but a few. He is a peer reviewer for many medical journals and on the Editorial Board of three. During his 31 years at the University of Texas M.D. Anderson Cancer Center, he has participated in the surgical education of over 300 residents and fellows, many of who have gone on to become prominent members of the specialty. The youth community of Houston has benefited from his coaching expertise in baseball and basketball while he has indulged in the hobbies of hunting, travel, and collecting toy soldiers.

# Alando J. Ballantyne Resident Research Pilot Grant

## **Alando J. Ballantyne, MD**



Alando J. Ballantyne, M.D., a giving teacher, dedicated surgeon, and a devoted husband and father, is memorialized by the Alando J. Ballantyne Resident Research Pilot Grant. This award, in the amount of \$10,000, is for the best grant application by a resident.

Alando, known simply as Jay, grew up in a lov-

ing Mormon home that taught him the values of family, excellence, integrity and hard work. Jay graduated Phi Beta Kappa from the University of Arizona and was then awarded a scholarship to Columbia Medical School. During World War II, Jay served as an army captain and medical doctor and had the good fortune to meet his wife, Maria, in San Antonio. In 1947, Dr. Ballantyne became the first resident at the new M.D.

Anderson Hospital in Houston. After his year-long residency, he went for further training at the Mayo Clinic in Rochester, Minnesota. He returned to the Anderson staff in 1952, where he quickly advanced from Assistant Surgeon in the Head and Neck Service to Associate Surgeon, and then from 1974 until his retirement in 1994, held the title of Surgeon and Professor of Surgery in the Department of Head and Neck Surgery as well as the title of Ashbel Smith Professor.

Dr. Ballantyne is credited as the first surgeon in the United States to pioneer modified radical neck dissection. His contri-

butions to his subspecialty, the result of an undying curiosity and uncanny powers of observations, have been published in numerous scientific papers and book chapters. Jay lectured at local, national, and international forums and loved his travels. He held memberships in many distinguished medical and surgical societies and served as President and Hayes Martin Lecturer of the Society of Head and Neck Surgeons and President of the Texas Surgical Society.

To honor the contributions of this world-renowned surgeon, the Cynthia and George Mitchell Foundation established the Alando J. Ballantyne Distinguished Chair in Head and Neck Surgery at the University of Texas M.D. Anderson Cancer Center.

Dr. Ballantyne's contributions to the subspecialty of Head and Neck cancer surgery have been the result of an undying curiosity and uncanny powers of observation. He was the father of conservative surgery, removing the cancer while preserving the function. He had a relentless desire to eradicate his patients' disease, yet was able to balance this fervor with a desire to maintain quality of life for all his patients.

Always an advocate of reconstruction and preservation of cosmesis as well as function, those fortunate enough to have worked with him and been taught by him are forever indebted to his wisdom, surgical expertise, and devotion to his patients. He was beloved by his patients, admired by his peers and idolized by his family.

The Alando J. Ballantyne Resident Research Pilot Grant is funded by the generous contributions of members of the Ballantyne family, including Dr. Gilchrist L. Jackson, a respected member of the American Head and Neck Society.

<b>Thursday, August 17, 2006</b>			
0800 – 0810		Welcome and Introduction	
0810 – 0900		Keynote Lecture – The Discovery of the Phosphoinositide 3-Kinase (PI3K) Pathway	
0915 – 1015	Instructional Courses I	0915 – 1030	Targeted Molecular Therapy in Head and Neck Cancer
1030 – 1130	Instructional Courses II	1045 – 1145	Scientific Session/Abstracts
1300 – 1400	Instructional Courses III	1300 – 1400	Instructional Courses III
1415 – 1515	Instructional Courses IV	1415 – 1515	Instructional Courses IV
1530 – 1630	Instructional Courses V	1530 – 1630	Instructional Courses V
1730 – 1900		Welcome Reception in the Exhibit Hall	
<b>Friday, August 18, 2006</b>			
0630 – 0745		Breakfast Satellite Symposium – “Integrating Targeted Therapy: Multidisciplinary Perspectives”	
0800 – 0930		Plenary Papers	
0930 – 1015		John J. Conley Lecture – Watchful Heart: Notes of a Doctor-Writer	
1040 – 1200	Scientific Session/Abstracts	1040 – 1200	Scientific Session/Abstracts
1400 – 1500		Panel: Quality of Life: How Best to Preserve It?	
1500 – 1515		AHNS Awards Ceremony	
1545 – 1645	Scientific Session/Abstracts	1545 – 1645	Scientific Session/Abstracts
1645 – 1715		AHNS Business Meeting	
1715 – 1830		Poster Tours	
1830 – 1915		Information Session on Head and Neck Fellowships	
<b>Saturday, August 19, 2006</b>			
0630 – 0800		Breakfast Satellite Symposium – “Photonic Band Gap Fiber Assembly CO2 Laser System”	
0800 – 0900		Translational Therapeutic Clinical Trials: Role of Working Group and SPORES	
0900 – 0930		Presidential Address	
0930 – 1010		Hayes Martin Lecture – Do All Cancers Need to be Treated? The Role of Thyroglobulin in the Management of Thyroid Cancer	
1040 – 1200	Scientific Session/Abstracts	1040 – 1200	Molecular Biology of Thyroid Cancer
1400 – 1500	Scientific Session/Abstracts	1400 – 1500	Scientific Session/Abstracts
1500 – 1600	Management of Complex Issues in Thyroid Cancer	1500 – 1600	Scientific Session/Abstracts
1600 – 1700	Scientific Session/Abstracts	1600 – 1700	Scientific Session/Abstracts
1700 – 1830		Poster Tours	
1930 – 2200		Main Social Event	
<b>Sunday, August 20, 2006</b>			
0800 – 0930	Scientific Session/Abstracts	0800 – 0930	Scientific Session/Abstracts
1000 – 1040		Keynote Lecture – Targeting COX-2 and EGFR in Oral Carcinogenesis	
1040 – 1200	Scientific Session/Abstracts	1040 – 1200	Scientific Session/Abstracts
1200 – 1210		Final Remarks	

## 0800 - 0810 Welcome and Introduction

John J. Coleman, III, MD, Dennis H. Kraus, MD, Carol R. Bradford, MD and Jean Louis Lefebvre, MD  
**Location: Salon I/II**

## 0810 - 0900 Keynote Lecture

### The Discovery of the Phosphoinositide 3-Kinase (PI3K) Pathway

Introduction by Carol R. Bradford, MD

**Keynote Speaker:** Lewis C. Cantley, PhD, Harvard Medical School, Boston, MA

**Location: Salon I/II**

#### CLINICAL PROGRAM

##### 0915 - 1015 Instructional Courses I

- C1. Paragangliomas and Carotid Body Tumors -**  
Dennis H. Kraus, MD and James L. Netterville, MD  
**Location: Indiana**
- C2. Advanced Non-melanoma Skin Cancer -**  
Christopher J. O'Brien, MD and Randal S. Weber, MD  
**Location: Iowa**
- C3. Management of Non-well Differentiated Thyroid Cancer -**  
James I. Cohen, MD, PhD and William B. Farrar, MD  
**Location: Michigan**
- C4. Surgical Approaches in the Head & Neck -**  
Guy J. Petruzzelli, MD, PhD and Karen T. Pitman, MD  
**Location: Michigan State**
- C5. Recent Advances in Management of Melanoma -**  
Grant W. Carlson, MD and Jesus E. Medina, MD  
**Location: Northwestern**
- C6. Endoscopic Sino-nasal -**  
Daniel M. Fliss, MD and Carl H. Snyderman, MD  
**Location: Ohio State**
- C7. How I Do It: Antero Lateral Thigh Flap -**  
Keith E. Blackwell, MD and Gerry F. Funk, MD  
**Location: Purdue**
- C8. Sarcomas of the Head and Neck -**  
Brandon G. Bentz, MD and Erich M. Sturgis, MD  
**Location: Wisconsin**

*AHNS gratefully acknowledges a generous educational grant in support of this session from OmniGuide, Inc.*

##### 1015 - 1030 BREAK

##### 1030 - 1130 Instructional Courses II

- C9. Tumors and Surgery of the Parapharyngeal Space -**  
Kerry D. Olsen, MD and David J. Terris, MD  
**Location: Indiana**
- C10. How I Do It: Parathyroid Surgery -**  
Jeremy L. Freeman, MD and Keith S. Heller, MD  
**Location: Iowa**
- C11. Salvage Surgery in Chemo radiation Era -**  
Jonas T. Johnson, MD and Pierre Lavertu, MD  
**Location: Michigan**
- C12. Head and Neck Ultrasound (Office-Based Neck Ultrasound) -**  
Marc D. Coltrera, MD and David L. Steward, MD  
**Location: Michigan State**
- C13. Sentinel Lymph Node Biopsy for Clinical Node Negative Squamous Cell Carcinoma of the Oral Cavity -**  
Ann M. Gillenwater, MD and Thom R. Loree, MD  
**Location: Northwestern**

#### RESEARCH PROGRAM

##### 0900 - 1030 Targeted Molecular Therapy for Head and Neck Cancer

**Panel Chair:** Carter Van Waes, MD, PhD  
**Location: Salon I**

- 1) Epidermal Growth Factor Receptor in Head and Neck Cancer -** Paul M. Harari, MD
- 2) Stress and Mitogen Activated Protein Kinases: Regulators of Cancer Invasion -** Christian Simon, MD
- 3) Targeting STAT3 as a Treatment Strategy for Head and Neck Cancer -** Jennifer R. Grandis, MD
- 4) Targeting the mTOR Pathway for Minimal Residual Disease in HNSCC -** Cherie-Ann Nathan, MD
- 5) NF- $\kappa$ B in the Pathogenesis and Therapy of Head and Neck Cancer -** Carter Van Waes, MD, PhD

At the conclusion of this event, the participants would be able to:

- Identify key receptor and signal pathways that contribute to pathogenesis of head and neck cancer
- Describe molecular targets that have been investigated in preclinical or clinical studies
- Describe current results and status of agents in clinical trials
- Discuss developments that affect future directions of research

##### 1030 - 1045 BREAK

##### 1045 - 1145 Scientific Session/Abstracts

**Moderators:** Jeffrey S. Moyer, MD and Duane A. Sewell, MD

**Location: Salon I**

- S001: Autocrine Chemokine Receptor 7 (CCR7) Activation in Squamous Cell Carcinoma of the Head and Neck**  
J.Wang<sup>1</sup>, A.Lokshin<sup>2</sup>, B.Gooding<sup>3</sup>, M.R.Shurin<sup>2</sup>, R.L.Ferris<sup>1</sup>  
<sup>1</sup>Department of Otolaryngology, University of Pittsburgh School of Medicine, Pittsburgh, PA; <sup>2</sup>Department of Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA; <sup>3</sup>University of Pittsburgh Cancer Institute, Pittsburgh, PA
- \*S002: Squamous Carcinoma (SCC)-Monocyte-Endotoxin Interactions Affect Monocyte Phenotype, Function and SCC STAT3 Activation**  
A.-Lam-ubol<sup>1</sup>, D.-Hopkin<sup>1</sup>, Z.-Kurago<sup>1</sup>  
<sup>1</sup>The University of Iowa, Iowa City, IA
- \*S003: Identification of a Novel HLA-A\*0201-Restricted T-Cell-Defined Antigen in Human SCCHN**  
C.Visus<sup>1</sup>, T.L.White<sup>1</sup>, A.B.DeLeo<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA

##### Discussion

\* Abstract was published in the *Archives of Otolaryngology*

**CLINICAL PROGRAM**

- C14. Endoscopic Laryngeal Surgery –**  
Bruce H. Haughey, MD and Wolfgang Steiner, MD  
**Location: Ohio State**  
*AHNS gratefully acknowledges an educational grant in support of this course from Karl Storz Endoscopy.*
- C15. How I Do It: Scapula Flaps –**  
John J. Coleman, III, MD and Mark L. Urken, MD  
**Location: Purdue**
- C16. Laryngeal Reconstruction –**  
Ara A. Chalian, MD and Ralph W. Gilbert, MD  
**Location: Wisconsin**  
  
*AHNS gratefully acknowledges a generous educational grant in support of this session from Karl Storz Endoscopy.*

**1130 – 1300 Lunch on Your Own**

**1300 – 1400 Instructional Courses III**

- C17. Reimbursement for Head and Neck Surgeons: Working Within the System –**  
Wayne M. Koch, MD and William M. Lydiatt, MD  
**Location: Northwestern**
- C18. Chemoradiation Organ Preservation –**  
David M. Brizel, MD and Jean Louis Lefebvre, MD  
**Location: Ohio State**
- C19. Mid-Facial Reconstruction –**  
Joseph J. Disa, MD and Neal D. Futran, MD, DMD  
**Location: Purdue**
- C20. Transnasal Esophagoscopy –**  
Christine G. Gourin, MD and Henry T. Hoffman, MD  
**Location: Wisconsin**
- C21. Lip Reconstruction –**  
Patrick J. Gullane, MD and Theodoros N. Teknos, MD  
**Location: Indiana**

**1400 – 1415 BREAK**

**1415 – 1515 Instructional Courses IV**

- C22. Head and Neck Transplantation –**  
Robert R. Lorenz, MD and Robert L. Walton, MD  
**Location: Iowa**
- C23. How I Do It: Neck Dissection –** David W. Eisele, MD and Eugene N. Myers, MD  
**Location: Northwestern**
- C24. PET: When to Use It –**  
Russell B. Smith, MD and Richard J. Wong, MD  
**Location: Ohio State**
- C25. Pharyngeal Reconstruction –**  
Brian B. Burkey, MD and Peter C. Neligan, MD  
**Location: Purdue**  
  
*AHNS gratefully acknowledges a generous educational grant in support of this session from IRX Therapeutics, Inc.*

**RESEARCH PROGRAM**

- \*S004: HPV-Infected Cancers Process and Present HLA-A2-p53(264-272) Peptide Complexes: Implications for p53-Based Immunotherapy**  
H.Kim1, X.Zhu2, A.Lopez-Albaitero1, N.Sirianni1, H.C.Wong2, R.L.Ferris1  
1Department of Otolaryngology at University of Pittsburgh Cancer Institute, Pittsburgh, PA; 2Altor BioScience Corporation, Miramar, FL
- S005: Immune Escape of Head and Neck Cancer by Functionally Altered Myeloid Dendritic Cells Can Be counteracted by CpG-ODN**  
C.Brocks1, R.Pries1, H.Frenzel1, M.Ernst2, B.J.H.Wollenberg1  
1University of Schleswig Holstein, Luebeck Germany; 2University of Schleswig Holstein, FZ Borstel Germany
- S006: T helper Type 2 Anti-tumor Immunity Induced by Mutant p53 Peptides and Immune Escape in Head and Neck Cancer Patients**  
R.Ferris1, J.Brennan2, W.Koch3, D.Sidransky3, M.Couch4  
1University of Pittsburgh, Pittsburgh, PA; 2Wilford Hall, San Antonio, TX; 3Johns Hopkins Hospital, Baltimore, MD; 4University of North Carolina, Chapel Hill, NC

**Discussion**

**1145 – 1300 Lunch on Your Own**

**1300 – 1400 Instructional Courses III**

- R1. Getting Your Grant Funded –** Thomas E. Carey, MD, PhD and Bhuvanesh Singh, MD, PhD  
**Location: Iowa**
- R2. Genomic Proteomic Profiling of Head and Neck Cancer –** Christine H. Chung, MD and Wendell G. Yarbrough, MD  
**Location: Michigan**
- R3. Mouse Models in Head and Neck Cancer –** Bert W. O'Malley, Jr., MD and Michiel van Den Brekel, MD, PhD  
**Location: Michigan State**

**1400 – 1415 BREAK**

**1415 – 1515 Instructional Courses IV**

- R4. Smoking Cessation, Alcohol and Depression Intervention –** Janice A. Blalock, PhD and Sonia A. Duffy, PhD, MS, RN  
**Location: Indiana**
- R5. Markers of Outcome and Response to Therapy –** Carol R. Bradford, MD and Joseph A. Califano, MD  
**Location: Michigan**
- R6. Immunotherapy for Head and Neck Cancer: Developing Cancer Vaccine Trials and Translating Basic Immunology into the Clinic –**  
Robert L. Ferris, MD, PhD and Duane A. Sewell, MD  
**Location: Michigan State**  
  
*AHNS gratefully acknowledges a generous educational grant in support of this session from IRX Therapeutics, Inc.*

\* Abstract was published in the *Archives of Otolaryngology*

# Scientific Program: Thursday, August 17, 2006

## CLINICAL PROGRAM

### 1515 - 1530 BREAK

#### 1530 - 1630 Instructional Courses V

- C26. How I Do It: Partial Laryngectomy** – Christopher H. Rassekh, MD and Jatin P. Shah, MD  
**Location: Northwestern**
- C27. Management of the Eye in Head and Neck Cancer**  
– Peter E. Andersen, MD and Ehab Y. Hanna, MD  
**Location: Ohio State**
- C28. Dilemmas in Reconstruction of the Head and Neck**  
– Daniel G. Deschler, MD and Mark K. Wax, MD  
**Location: Purdue**
- C29. Nasal Reconstruction** – Gary C. Burget, MD and Jeffrey S. Moyer, MD  
**Location: Wisconsin**

## RESEARCH PROGRAM

### 1515 - 1530 BREAK

#### 1530 - 1630 Instructional Courses V

- R7. A Scientific Approach to Voice, Olfactory, and Swallowing Rehabilitation in Head and Neck Cancer Patients** – Alfonsus J. Balm, MD and Jerilyn A. Logemann, PhD, CCC-SLP  
**Location: Indiana**
- R8. Molecular Methods of Detection and Prediction of Metastases** – Ruud H. Brakenhoff, PhD and Barbara Wollenberg, MD  
**Location: Michigan**

**1730 - 1900 WELCOME RECEPTION IN THE EXHIBIT HALL**  
**Location: Salon III**

**0630 – 0745 Breakfast Satellite Symposium**

**Integrating Targeted Therapy:  
Multidisciplinary Perspectives**

**Location: Salon I/II**

- 0630 – 0640 **Introduction and Welcome** – David G. Pfister, MD
- 0640 – 0655 **Anti-EGF Receptor Therapy for Head and Neck Cancer: An Update** – David G. Pfister, MD
- 0655 – 0725 **Case Challenges: Exploring Opportunities to Optimize Outcomes** – Erza W. Cohen, MD  
A case-led discussion of cross-disciplinary management opportunities for head and neck cancer.
- 1) Surgical Options and the Selection of Patients** – Jeffrey N. Myers, MD, PhD
- 2) Identifying Appropriate Medical Interventions** – Ezra W. Cohen, MD
- 0725 – 0740 **Integrating Approaches: How to Achieve the Best Patient Care** – Faculty and Audience
- 0740 – 0745 **What's Next: Highlights of Ongoing Research** – All
- 0745 **Closing Remarks** – David G. Pfister, MD

*This activity is jointly sponsored by Strategic Consultants International and Medical Education Collaborative (MEC).  
MEC is a non profit organization that has been certifying quality educational activities since 1988.*

*This activity was made possible by an educational grant from Bristol-Myers Squibb Company.*

**0800 – 0930 Plenary Papers**

**Moderators:** Jean Louis Lefebvre, MD and Johan Wennerberg, MD

**Location: Salon I/II**

**\*S007: Multi-institutional Prospective Study on the Prevalence of Sublevel IIB Metastases in Head and Neck Cancer**

A.Bolzoni<sup>1</sup>, C.Piazza<sup>1</sup>, G.Peretti<sup>1</sup>, L.Calabrese<sup>2</sup>, R.Pellini<sup>3</sup>, F.Chiesa<sup>2</sup>, G.Spriano<sup>3</sup>, P.Nicolai<sup>1</sup>

<sup>1</sup>University of Brescia, Brescia Italy; <sup>2</sup>European Oncologic Institute, Milano Italy; <sup>3</sup>Oncologic Institute Regina Elena, Roma Italy

**S008: Chronic Periodontitis and the Risk of Oral Cancer: Preliminary Findings**

M.Tezal<sup>1</sup>, M.A.Sullivan<sup>2</sup>, M.E.Reid<sup>2</sup>, J.R.Marshall<sup>2</sup>, E.Hausmann<sup>1</sup>, A.Hyland<sup>2</sup>, J.Wactawski-Wende<sup>1</sup>, T.Loree<sup>2</sup>, N.R.Rigual<sup>2</sup>, F.A.Scannapieco<sup>1</sup>

<sup>1</sup>State University of New York at Buffalo, Buffalo, NY; <sup>2</sup>Roswell Park Cancer Institute, Buffalo, NY

**\*S009: Sentinel Lymph Node Biopsy for Oral Cancer: A Multi-Institutional Validation Trial**

F.J.Civantos<sup>1</sup>, R.Zitsch<sup>2</sup>, D.Schuller<sup>3</sup>, A.Agrawal<sup>3</sup>, R.Smith<sup>4</sup>, R.Nason<sup>5</sup>, G.Petruzelli<sup>6</sup>, C.Gourin<sup>7</sup>, W.Yarbrough<sup>8</sup>, J.Myers<sup>9</sup>

<sup>1</sup>University of Miami School of Medicine, Miami, FL; <sup>2</sup>University of Missouri, Columbia, MO; <sup>3</sup>Ohio State University, Columbus, OH; <sup>4</sup>University of Iowa, Iowa City, IA; <sup>5</sup>University of Manitoba, Manitoba, MB Canada; <sup>6</sup>Loyola University, Chicago, IL; <sup>7</sup>Medical College of Georgia, Augusta, GA; <sup>8</sup>Vanderbilt University, Nashville, TN; <sup>9</sup>MD Anderson, Houston, TX

**Discussion**

**S010: Predictive Parameters for the Detection of Neck Metastases**

J.E.Meyer<sup>1</sup>, M.Bienemann<sup>2</sup>, J.Hedderich<sup>3</sup>, U.Schulz<sup>3</sup>, S.Lang<sup>1</sup>, M.Laudien<sup>3</sup>, J.Quetz<sup>3</sup>, B.Wollenberg<sup>1</sup>, S.Maune<sup>3</sup>

<sup>1</sup>Universitaetsklinikum Schleswig-Holstein, Luebeck Germany; <sup>2</sup>Universitaetsklinikum Schleswig-Holstein, Luebeck Germany; <sup>3</sup>Universitaetsklinikum Schleswig-Holstein, Kiel Germany

**\*S011: Vocal Fold Immobility After Thyroidectomy With Intraoperative Laryngeal Nerve Monitoring**

I.P.Netto<sup>1</sup>, J.G.Vartanian<sup>1</sup>, P.RR.Ferraz<sup>1</sup>, P.Salgado<sup>1</sup>, J.BM.Azevedo<sup>1</sup>, A.L.Carvalho<sup>1</sup>, E.C.Angelis<sup>1</sup>, L.P.Kowalski<sup>1</sup>

<sup>1</sup>Hospital do Cancer A.C.Camargo, Sao Paulo Brazil

**\*S012: Dendritic Cell (DC)-Based Vaccine for Patients With SCCHN Using Autologous Tumor Cells as Immunogens**

T.L.Whiteside<sup>1</sup>, R.L.Ferris<sup>1</sup>, E.N.Myers<sup>1</sup>, M.Tublin<sup>1</sup>, J.Kiss<sup>1</sup>, R.Johnson<sup>1</sup>, J.T.Johnson<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Pittsburgh, PA

**Discussion**

\* Abstract was published in the *Archives of Otolaryngology*

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# Scientific Program: **Friday, August 18, 2006**

**S013: Array Comparative Genomic Analysis of Oral SCC**

B.L.Schmidt<sup>1</sup>, A.M.Snijders<sup>1</sup>, R.CK.Jordan<sup>1</sup>, D.G.Albertson<sup>1</sup>

<sup>1</sup>University of California San Francisco, San Francisco, CA

**\*S014: Methylation Status of Genes in Papillary Thyroid Carcinoma**

J.A.Smith<sup>1</sup>, M.Kokoska<sup>1</sup>

<sup>1</sup>University of Arkansas for Medical Sciences, Little Rock, AR

**S015: Discovery and Development of DNA Methylation Based Diagnostic and Prognostic Biomarkers in Head and Neck SCC**

S.Ghoshal (Gupta)<sup>1</sup>, P.Mojica<sup>1</sup>, J.Frustino<sup>1</sup>, N.R.Rigual<sup>1</sup>, R.T.Cheney<sup>1</sup>, M.E.Reid<sup>1</sup>, M.Sullivan-Nasca<sup>1</sup>, T.R.Loree<sup>1</sup>,

D.J.Smiraglia<sup>1</sup>

<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY

**Discussion**

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**0930 – 1015 John J. Conley Lecture****Watchful Heart: Notes of a Doctor-Writer**

Introduction by John J. Coleman, MD

**Keynote Speaker: John Stone, MD, Emory University, Atlanta, GA**

**Location: Salon I/II**

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**1015 – 1040 Break with Poster and Exhibit Viewing**

## CLINICAL PROGRAM

### 1040 – 1200 Scientific Session/Abstracts

Moderators: Alfonsus J. Balm, MD and  
Jonathan Irish, MD

#### Location: Salon II

#### S016: Intra-Arterial Versus Intravenous Chemoradiation for Advanced Head and Neck Cancer, Early Results of a Phase III Trial

C.Rasch1, A.Balm1, R.Kroger1, J.Buter2, D.Rietveld3, R.Wiggenraad4, M.Jameson5, W.Heemsbergen1, F.Hoebers1, J.Schornagel1  
1NKI/AvL, Amsterdam The Netherlands; 2Free University Medical Center, Amsterdam The Netherlands; 3RIF/H&N cancer working group Groningen, Leeuwarden The Netherlands; 4Westeinde Hospital / H&N working group Leiden, The Hague The Netherlands; 5Waikato Hospital, Hamilton New Zealand

#### S017: Re-Irradiation Combined With Chemotherapy After Salvage Surgery in Head and Neck Carcinoma: A Randomized Trial

F.Janot1, D.de Raucourt 2, M.Castaigne1, E.Bardet3, G.Dolivet4, J.Bensadoun5, M.Hamoir6, P.Marandas1, G.Mamelle1, J.Bourhis1  
1Institute Gustave Roussy, Villejuif France; 2Centre François Baclesse, Caen France; 3Centre René Gauducheau, Nantes France; 4Centre Alexis Vautrin, Nancy France; 5Centre A Laccassagne, Nice France; 6Cliniques Universitaires St Luc, Bruxelles Belgium

#### \*S018: Validation of a Voice Prosthesis Questionnaire to Assess Valved Speech and Its Related Issues in Patients Following Total Laryngectomy

R.Kazi1, A.Singh1, J.DeCordova1, A.Al-Mutaery1, L.O'Leary1, C.Nutting1, P.Clarke1, P.Rhys-Evans1, K.Harrington1  
1Royal Marden Hospital, London United Kingdom

#### \*S019: Superselective Neck Dissection Following Chemoradiation: Feasibility Based on Clinical and Pathological Comparisons

K.T.Robbins1, K.Shannon2  
1Southern Illinois University, Springfield, IL; 2Sydney Head and Neck Cancer Institute, Sydney Australia

#### Discussion

#### \*S020: Significance of Viable Tumor in Postchemoradiation Neck Dissections

J.M.Bocker1, M.C.Coleman1, D.L.Carlson1, N.Lee1, D.G.Pfister1, J.O.Boyle1, A.R.Shaha1, D.H.Kraus1, J.P.Shah1, S.G.Patel1  
1Memorial Sloan-Kettering Cancer Center, New York, NY

#### S021: Is Neck Dissection Necessary for Nodal Metastases in Patients Treated with Radical CRT?

H.M.Mehanna1, N.Umapathy2  
1University Hosp Coventry & Warwickshire, Coventry United Kingdom; 2UHCW, Coventry United Kingdom

#### \*S022: Is Planned Neck Dissection Necessary for Head and Neck Cancer Treated with Intensity-Modulated Radiotherapy?

M.Yao1, H.T.Hoffman1, R.B.Smith1, G.F.Funk1, K.Chang1, G.H.Clamon1, K.J.Dornfeld1, J.M.Buatti1  
1University of Iowa, Iowa City, IA

#### \*S023: Deferring Planned Neck Dissection After Chemoradiation Therapy in Stage IV Head and Neck Cancer: The Utility of PET/CT

J.V.Nayak1, N.Daamen1, R.L.Ferris1, B.F.Branstetter1, J.T.Johnson1  
1University of Pittsburgh, Pittsburgh, PA

#### Discussion

## RESEARCH PROGRAM

### 1040 – 1200 Scientific Session/Abstracts

Moderators: Thomas E. Carey, MD, PhD  
and Amy Chen, MD

#### Location: Salon I

#### \*S024: Expression of p53 and Bcl-xL as Predictive Markers for Larynx Preservation in Advanced Laryngeal Cancer

B.Kumar1, K.G.Cordell1, N.D'Silva1, M.E.Adams1, S.G.Fisher2, G.T.Wolf1, T.E.Carey1, C.R.Bradford1  
1University of Michigan, Ann Arbor, MI; 2University of Rochester, Rochester, NY

#### \*S025: Biomarkers of Invasiveness in Oral Squamous Cell Carcinoma: A Cell Proteomic Approach

A.M.Mlynarek1, R.L.Balys1, M.P.Hier1, M.J.Black1, M.A.Alaoui-Jamali 1  
1McGill University, Montreal, PQ Canada

#### S026: A Murine Model of HPV16 Related Tonsil Squamous Cell Carcinoma

W.C.Spanos1, A.Hoover1, G.Harris1, J.H.Lee1  
1University of Iowa, Iowa City, IA

#### \*S027: Molecular Markers of Oral Squamous Cell Carcinogenesis - From Gene Chips to Tissue Microarrays

P.Choi1, C.D.Jordan1, L.Enriquez1, E.Mendez1, J.Houck2, B.Yueh1, G.Farwell3, C.Chen2  
1University of Washington, Seattle, WA; 2Fred Hutchinson Cancer Research Center, Seattle, WA; 3University of California, Davis, Sacramento, CA

#### Discussion

#### S028: Suppression of PKCepsilon Inhibits Cell Invasion and Motility Through Inactivation of Rho GTPases in HNSCC

Q.Pan1, L.Bao1, T.N.Teknos1, S.D.Merajver1  
1University of Michigan Health System, Ann Arbor, MI

#### S029: Cisplatin-DNA Adduct Formation in Normal Tissue and Tumor in Patients Treated With Cisplatin-based Chemoradiation

F.J.P.Hoebers1, D.Pluim1, M.Verheij1, A.J.M.Balm1, J.H.M.Schellens1, G.Fons1, L.J.A.Stalpers2, C.R.N.Rasch A.A.M. Hart1, H.Bartelink1, A.C.Begg1  
1The Netherlands Cancer Institute, Amsterdam The Netherlands; 2Academic Medical Centre, Amsterdam The Netherlands

#### S030: Cyclin A Overexpression in Oral Dysplasia

R.Tandon1, D.K.White1, J.L.Ebersole1, M.Li1, L.L.Cunningham1  
1University of Kentucky, Lexington, KY

#### \*S031: Survivin in Cisplatin-Induced Cell Death in Head and Neck Squamous Cell Carcinomas (HNSCC)

J.Chad.Brenner1, J.A.Bauer1, L.M.Saunders1, K.M.O'Connell1, C.R.Bradford1, T.E.Carey1  
1University of Michigan, Ann Arbor, MI

#### Discussion

## **1200 – 1400 Complimentary Lunch in the Exhibit Hall for Attendees and Exhibit Viewing**

**Location: Salon III**

### **Poster Viewing – Location: 6th Floor Breakout Rooms**

(Indiana/Iowa, Michigan/Michigan State, Northwestern/Ohio State and Purdue/Wisconsin)

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## **1400 – 1500 Quality of Life: How Best to Preserve It?**

Panel Chair: Jay Piccirillo, MD

**Location: Salon I/II**

1) **How to Interpret QOL Studies** – Jay Piccirillo, MD

2) **Pre-treatment and Treatment Predictors of QOL Outcomes** – Jeffrey E. Terrell, MD

3) **Treatment Options, QOL Challenges, Available Data and Type of Studies that are Needed To Fill Gaps for Both Early and Late Disease** – David G. Pfister, MD and Bevan Yueh, MD

At the conclusion of this event, the participants would be able to:

- Better understand QOL studies and how they can be used to assess treatment effectiveness
- Better understand factors that affect QOL
- Better understand the current status of QOL literature applicable to larynx preservation therapies (ASCO LP guideline experience)
- Understand why inclusion of QOL assessment is relevant in cancer research

*AHNS gratefully acknowledges an educational grant in support of this session from OmniGuide Inc.*

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## **1500 – 1515 AHNS Awards Ceremony**

**Location: Salon I/II**

Jay O. Boyle, MD, Maisie Shindo, MD and Marilene B. Wang, MD

1515 - 1545 Break with Poster and Exhibit Viewing

**CLINICAL PROGRAM**

**1545 - 1645 Scientific Session/Abstracts**

**Moderators:** Douglas B. Chepeha, MD &  
M. Boyd Gillespie, MD, MS

**Location: Salon II**

**\*S032: Randomized Placebo-Controlled Trial of Citalopram Demonstrating Depression Prevention During Treatment for HN Cancer**

W.M.Lydiatt<sup>1</sup>, D.Denman<sup>1</sup>, W.J.Burke<sup>1</sup>  
<sup>1</sup>University of Nebraska Medical Center, Omaha, NE

**S033: Correlations Among Patient-Reported, Observer Rated, and Objective Swallowing Function After Chemo-Irradiation**

T.Lyden<sup>1</sup>, M.Haxer<sup>1</sup>, F.Feng<sup>1</sup>, D.Chepeha<sup>1</sup>, H.Kim<sup>1</sup>, M.Feng<sup>1</sup>,  
A.Eisbruch<sup>2</sup>  
<sup>1</sup>University of Michigan, Ann arbor; <sup>2</sup>University of Michigan,  
Ann Arbor, MI

**\*S034: Intensity-Modulated Radiotherapy (IMRT) Aiming to Reduce Dysphagia: Early Dose-Effect Correlations**

A.Eisbruch<sup>1</sup>, T.Lyden<sup>2</sup>, F.Feng<sup>2</sup>, M.Haxer<sup>2</sup>, H.Kim<sup>2</sup>, M.Feng<sup>2</sup>,  
D.Chepeha<sup>2</sup>  
<sup>1</sup>University of Michigan, Ann Arbor, MI; <sup>2</sup>University of Michigan,  
Ann Arbor

**Discussion**

**\*S035: Driving Performance in Patients With Head and Neck Cancer: A Pilot Study**

H.K.Yuen<sup>1</sup>, T.A.Day<sup>1</sup>, M.B.Gillespie<sup>1</sup>  
<sup>1</sup>MUSC, Charleston, SC

**\*S036: The Pattern of Acute Mucosal Reactions in Pts with Head and Neck Cancer Treated by Conventional and Accelerated Irradiation**

A.Wygoda<sup>1</sup>, K.Skladowski<sup>1</sup>, W.Sasiadek<sup>1</sup>, M.Sygula<sup>1</sup>,  
B.Pilecki<sup>1</sup>, M.Hutnik<sup>1</sup>, T.Rutkowski<sup>1</sup>  
<sup>1</sup>Center of Oncology Maria sklodowska-Curie Institute, Gliwice  
Poland

**\*S037: Advanced T Stage Is Associated With Improved Swallowing Following Concurrent Chemoradiotherapy in Head and Neck Cancer Patients**

J.K.Salama<sup>1</sup>, E.E.Vokes<sup>1</sup>, M.A.List<sup>1</sup>, L.K.Mell<sup>1</sup>, K.M.Stenson<sup>1</sup>,  
E.MacCracken<sup>1</sup>, E.E.Cohen<sup>1</sup>, E.Blair<sup>1</sup>, D.J.Haraf<sup>1</sup>  
<sup>1</sup>University of Chicago, Chicago, IL

**Discussion**

**RESEARCH PROGRAM**

**1545 - 1645 Scientific Session/Abstracts**

**Moderators:** Susanne M. Gollin, MD  
and Marilene B. Wang, MD

**Location: Salon I**

**\*S038: Characterization of TMEM16A In Squamous Cell Carcinoma of the Head and Neck**

U.U. Duvvuri<sup>1</sup>, B.J.Henson<sup>1</sup>, X.Huang<sup>1</sup>, J.S.White<sup>1</sup>,  
R.A.Parikh<sup>1</sup>, R.Seethala<sup>1</sup>, J.R.Grandis<sup>1</sup>, S.M.Gollin<sup>1</sup>  
<sup>1</sup>University of Pittsburgh School of Medicine, Pittsburgh, PA

**\*S039: Activation of the Gain-of-Function p53R172H Allele Predisposes to Oral Cancer Progression**

S.Acin<sup>1</sup>, G.Lozano<sup>2</sup>, D.Roop<sup>1</sup>, C.Caulin<sup>1</sup>  
<sup>1</sup>Baylor College of Medicine, Houston, TX; <sup>2</sup>M.D Anderson  
Cancer Center, Houston, TX

**S040: Genetic Polymorphisms of Alcohol and Aldehyde Dehydrogenases in Japanese Men with Head and Neck Cancer**

T.Asakage<sup>1</sup>, T.Haneda<sup>2</sup>, M.Yamazaki<sup>2</sup>, T.Yokoyama<sup>2</sup>,  
A.Yokoyama<sup>2</sup>, Y.Kumagai<sup>2</sup>, M.Muto<sup>2</sup>, H.Kato<sup>2</sup>, T.Tsujinaka<sup>2</sup>,  
H.Igaki<sup>2</sup>  
<sup>1</sup>University of Tokyo, Tokyo Japan; <sup>2</sup>Japanese Research Group  
of Head and Neck Cancer and Alcohol-Metabolizing Enzymes,  
Tokyo Japan

**Discussion**

**\*S041: Identification of the Mechanism of 11q13 Amplification Leads to Detection of DNA Repair Defects in HNSCC Cell Lines**

S.M.Gollin<sup>1</sup>, R.A.Parikh<sup>2</sup>, J.S.White<sup>2</sup>, X.Huang<sup>2</sup>, R.Baskaran<sup>3</sup>,  
W.S.Saunders<sup>4</sup>, C.J.Bakkenist<sup>5</sup>, S.C.Reshmi<sup>2</sup>  
<sup>1</sup>University of Pittsburgh Graduate School of Public Health,  
Pittsburgh, PA; <sup>2</sup>Human Genetics, University of Pittsburgh  
Graduate School of Public Health, Pittsburgh, PA; <sup>3</sup>Molecular  
Genetics & Biochemistry, University of Pittsburgh School of  
Medicine, Pittsburgh, PA; <sup>4</sup>Biological Sciences, University of  
Pittsburgh, Pittsburgh, PA; <sup>5</sup>Radiation Oncology, University of  
Pittsburgh Cancer Institute, Pittsburgh, PA

**S042: WIF1, an Inhibitor of the WNT Pathway, Is Recurrently Inactivated in Salivary Gland Tumors**

D.Obeso<sup>1</sup>, A.M.C.Reis<sup>2</sup>, M.D.Hatfield<sup>1</sup>, L.Queimado<sup>1</sup>  
<sup>1</sup>Otorhinolaryngology Department, Oklahoma University Health  
Sciences Center, Oklahoma City, OK; <sup>2</sup>Dermatology  
Department, Oklahoma University Health Sciences Center,  
Oklahoma City, OK

**\*S043: Galanin Receptor Type 1 Inhibits Cell Proliferation in Squamous Carcinoma Cells Via Erk1/2 Activation**

T.Kanazawa<sup>1</sup>, P.Kommareddi<sup>2</sup>, T.Nair<sup>2</sup>, K.Misawa<sup>2</sup>, Y.Misawa<sup>2</sup>,  
Y.Ueda<sup>2</sup>, T.E.Carey<sup>2</sup>  
<sup>1</sup>Omiya Medical Center, Saitama Japan; <sup>2</sup>Laboratory of Head  
and Neck Cancer Biology, The University of Michigan, Ann  
Arbor, MI

**Discussion**

1645 – 1715 **AHNS Business Meeting**

Location: Salon II

1715 – 1830 **Poster Tours**

Location: 6th Floor Breakout Rooms

**POSTER TOUR: CLINICAL 1**

**Tour Leader: David W. Eisele, MD**

**Location: Northwestern/Ohio State**

**\*P001: Phase I Study of Erlotinib, Docetaxel and Radiation in Locally Advanced Squamous Cell Cancer of the Head and Neck**

P.S.Savvides<sup>1</sup>, S.S.Agarwala<sup>2</sup>, J.Greskovich<sup>1</sup>, A.Argiris<sup>2</sup>, J.Bokar<sup>1</sup>, N.Pagedar<sup>1</sup>, C.Hoppel<sup>1</sup>, D.W.Stepnick<sup>1</sup>, S.Remick<sup>1</sup>, P.Lavertu<sup>1</sup>

<sup>1</sup>CASE Comprehensive Cancer Center, Cleveland, OH; <sup>2</sup>University of Pittsburgh Medical Center, Pittsburgh, PA

**\*P002: Endoscopic CO2 Laser Supraglottic Laryngectomy**

G.LAWSON<sup>1</sup>, J.B.Watelet<sup>2</sup>, M.E.Debaty<sup>1</sup>, V.Beate<sup>1</sup>, H.Vermeersch<sup>2</sup>, M.Remacle<sup>1</sup>

<sup>1</sup>Louvain University Hospital at Mont-Godinne, YVOIR Belgium; <sup>2</sup>Gent University Hospital U Z De Pintelaan, 185, GENT Belgium

**\*P003: Survival and Prognostic Factors in Squamous Cell Carcinoma of the Retromolar Trigone Treated With Primary Surgery**

D.Lai<sup>1</sup>, G.J.Petrucelli<sup>1</sup>

<sup>1</sup>Loyola University Medical Center, Maywood, IL

**\*P004: Dental Patient Attitudes Toward Alcohol Screening for Oral Cancer Risk Reduction**

P.M.Miller<sup>1</sup>, M.C.Ravenel<sup>1</sup>, S.Thomas<sup>1</sup>, A.Shealy<sup>1</sup>

<sup>1</sup>Medical University of South Carolina, Charleston, SC

**\*P005: Reconsideration of the Indications for Neck Dissection After Chemoradiation for Oropharyngeal Squamous Cell Carcinoma**

T.Mau<sup>1</sup>, D.W.Eisele<sup>1</sup>, S.J.Wang<sup>1</sup>

<sup>1</sup>University of California, San Francisco, San Francisco, CA

**P006: Multimodal Therapy Improves Outcome in Recurrent Medullary Thyroid Cancer**

T.A. James<sup>1</sup>, T.R.Loree<sup>2</sup>, W.L.Hicks, Jr.<sup>2</sup>, J.R.Marshall<sup>2</sup>, N.R.Rigual<sup>2</sup>

<sup>1</sup>University of Vermont, Burlington, VT; <sup>2</sup>Roswell Park Cancer Institute, Buffalo, NY

**\*P007: False Negative Cases of Touch Smear Cytology in Thyroid Tumor**

S.Takebayashi<sup>1</sup>, H.Mineta<sup>2</sup>, S.Iwasaki<sup>2</sup>, N.Ashimori<sup>3</sup>, K.Misawa<sup>4</sup>

<sup>1</sup>Shizuoka Saiseikai General Hospital, Shizuoka Japan; <sup>2</sup>Hamamatsu University School of Medicine, Hamamatsu Japan; <sup>3</sup>Numadu City Hospital, Numadu Japan; <sup>4</sup>Seirei Mikatabara General Hospital, Hamamatsu Japan

**\*P008: Preoperative Imaging Diagnosis of the Nerve of Origin in Schwannomas of the Parapharyngeal Space**

D.M.Saito<sup>1</sup>, C.Glastonbury<sup>1</sup>, I.El-Sayed<sup>1</sup>, D.Eisele<sup>1</sup>

<sup>1</sup>University of California, San Francisco, San Francisco, CA

**P009: Efficacy of COX-2 Inhibitors on Tumor Anorexia-cachexia Syndrome in Patients With Head and Neck Cancer**

V.Lai<sup>1</sup>, J.George<sup>1</sup>, L.Richey<sup>1</sup>, T.Cannon<sup>1</sup>, H.Kim<sup>1</sup>, C.Shores<sup>1</sup>, M.Couch<sup>1</sup>

<sup>1</sup>University of North Carolina, Chapel Hill, NC

**\*P010: The Correlation of Clinical to Pathologic Neck Response After Radiation or Chemoradiation of N2-N3 Head and Neck Cancer**

B.J.Park<sup>1</sup>, J.M.Hsu<sup>1</sup>

<sup>1</sup>SUNY Upstate Medical University Department of Otolaryngology, Syracuse, NY

**\*P011: Clinical and Histopathological Correlation With Skip Metastases in Oral Cavity Cancer: How Important Is This Issue?**

C.T.Chone<sup>1</sup>, R.C.Silva<sup>1</sup>, A.Altamani<sup>2</sup>, A.N.Crespo<sup>1</sup>

<sup>1</sup>Department of Otolaryngology Head and Neck, State University of Campinas, Campinas Brazil; <sup>2</sup>Department of Surgical Pathology, State University of Campinas, Campinas Brazil

**\*P012: Fine-Needle Aspiration Biopsy of the Thyroid: Atypical Cytopathology**

M.N.Yehuda<sup>1</sup>, R.M.Seaberg<sup>1</sup>, R.J.Payne<sup>1</sup>, J.L.Freeman<sup>1</sup>, C.Macmillan<sup>1</sup>

<sup>1</sup>Mount Sinai Hospital, Toronto, ON Canada

**P013: Carotid Body Tumors**

M.Evasovich<sup>1</sup>, S.Patel<sup>2</sup>, R.Wong<sup>2</sup>, B.Singh<sup>2</sup>, A.Boyle<sup>2</sup>, D.Kraus<sup>3</sup>, A.Shaha<sup>2</sup>, J.Shah<sup>2</sup>

<sup>1</sup>University of Minnesota, Minneapolis, MN; <sup>2</sup>Memorial Sloan Kettering Cancer Center, New York, NY; <sup>3</sup>Memorial Sloan Kettering Cancer Center, New York

**\*P014: Determination of the Function of the Internal Branch of the Superior Laryngeal Nerve After Thyroidectomy**

J.M.Wasserman<sup>1</sup>, K.Sundaram<sup>1</sup>, A.E.Alfonso<sup>1</sup>, R.M.Rosenfeld<sup>1</sup>, G.Har-El<sup>1</sup>

<sup>1</sup>SUNY Downstate Medical Center, Brooklyn, NY

- \*P015: Phase I: Update of Weekly Docetaxel, Cisplatin, Daily Celecoxib, Concurrent Radiotherapy in Advanced Head and Neck Cancer**  
R.S.Axelrod<sup>1</sup>, M.Machtay<sup>1</sup>, P.R.Anne<sup>1</sup>, A.Dicker<sup>1</sup>, K.Sidhu<sup>1</sup>, M.Jacobs<sup>1</sup>, M.Rosen<sup>1</sup>, W.Keane<sup>1</sup>  
<sup>1</sup>Thomas Jefferson University, Philadelphia, PA
- \*P016: Oxaliplatin, Folinic Acid and 5-Fluorouracil (OFF) in Recurrent Advanced Head and Neck Cancer: A Phase II-Trial**  
J.D.Raguse<sup>1</sup>, J.Bier<sup>1</sup>, H.Oettle<sup>2</sup>  
<sup>1</sup>Clinic for Oral & Maxillofacial Surgery, Berlin Germany; <sup>2</sup>Clinic and Policlinic for Haematology and Oncology, Berlin
- P017: The Prevalence of Depression in Head and Neck Cancer Patients at the Time of Diagnosis**  
M.E.Sebelik<sup>1</sup>, E.Kruger<sup>1</sup>, D.Gerth<sup>1</sup>  
<sup>1</sup>University of Tennessee-Memphis, Memphis, TN
- P018: Parotid Gland Epithelial Malignancies: A Retrospective Analysis of 116 Patients**  
D.Lombardi<sup>1</sup>, G.Spriano<sup>2</sup>, L.Oscar.Redaeli de Zinis<sup>1</sup>, R.Roselli<sup>3</sup>, P.Nicolai<sup>1</sup>  
<sup>1</sup>Department of Otorhinolaryngology, University of Brescia, Brescia Italy; <sup>2</sup>Department of Otorhinolaryngology, Istituto dei Tumori "Regina Elena", Roma Italy; <sup>3</sup>Department of Otorhinolaryngology, University of Varese, Varese Italy
- \*P019: Is Lateral Neck Dissection the Choice for Planned Neck Dissection After Larynx/Hypopharynx Organ Preservation Protocol?**  
A.L.Carvalho<sup>1</sup>, A.Y.Carvalho<sup>1</sup>, U.R.Nicolau<sup>1</sup>, B.C.Araújo<sup>1</sup>, J.G.Vartanian<sup>1</sup>, J.Magrin<sup>1</sup>, M.K.Ikeda<sup>1</sup>, C.A.Pinto<sup>1</sup>, O.Feher<sup>1</sup>, L.P.Kowalski<sup>1</sup>  
<sup>1</sup>Hospital do Cancer A.C.Camargo, Sao Paulo Brazil
- \*P020: Total Nasal Reconstruction Using a Forearm Free Flap, Titanium Mesh and a Paramedian Forehead Flap**  
R.D.Hart<sup>1</sup>, J.Harris<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada
- \*P021: Regional Recurrence Rate of Squamous Cell Carcinoma of the Anterior Nasal Cavity: A Systematic Review and Meta-Analysis**  
W.Scurry<sup>1</sup>, F.G.Fedok<sup>1</sup>, D.Goldenberg<sup>1</sup>, E.L.Lengerich<sup>1</sup>  
<sup>1</sup>Penn State University, Hershey, PA
- P022: Neck Management During Salvage Laryngeal Surgery for Recurrent/Persistent Laryngeal Cancer After Radiation Therapy**  
T.Y.Farrag<sup>1</sup>, F.R.Lin<sup>1</sup>, J.Broussard<sup>1</sup>, G.Bajaj<sup>1</sup>, R.P.Tufano<sup>1</sup>  
<sup>1</sup>Johns Hopkins University School of Medicine, Baltimore, MD
- P023: RTOG 0421, A Phase III Trial For Recurrent, Previously Irradiated Head and Neck Cancer: Re-RT and CT vs CT Alone**  
S.J.Wong<sup>1</sup>, M.Machtay<sup>2</sup>, C.Langer<sup>3</sup>, C.J.Schultz<sup>1</sup>, J.A. Ridge<sup>3</sup>, M.List<sup>4</sup>, A.Konski<sup>3</sup>, T.F.Pajak<sup>5</sup>, K.Ang<sup>6</sup>  
<sup>1</sup>Medical College of Wisconsin, Milwaukee, WI; <sup>2</sup>Jefferson Medical College/Bodine Cancer Center, Philadelphia, PA; <sup>3</sup>Fox Chase Cancer Center, Philadelphia, PA; <sup>4</sup>Univ. of Chicago Cancer Research Center, Chicago, IL; <sup>5</sup>American College of Radiology, Radiation Therapy Oncology Group, Philadelphia, PA; <sup>6</sup>MD Anderson Cancer Center, Houston
- P024: Oral SCCMargin Shrinkage Following Resection and Specimen Processing**  
A.C.Cheng<sup>1</sup>, B.L.Schmidt<sup>2</sup>  
<sup>1</sup>University of California San Francisco, San Francisco, CA; <sup>2</sup>University of California, San Francisco, San Francisco, CA
- P025: The Incidence and Management of Postoperative Alcohol Withdrawal Syndrome in Head and Neck Cancer Patients**  
T.N.Teknos<sup>1</sup>, C.D.Lansford<sup>1</sup>, C.Guerrero<sup>1</sup>, M.Kocan<sup>1</sup>, M.Ebersold<sup>1</sup>, P.Abrahamse<sup>1</sup>, V.Bahl<sup>1</sup>  
<sup>1</sup>University of Michigan Health System, Ann Arbor, MI
- \*P026: MR in the Postoperative Assessment of Oral-Oropharyngeal Cancer: Is There a Role?**  
R.Maroldi<sup>1</sup>, I.Moraschi<sup>1</sup>, A.Bolzoni<sup>2</sup>, P.Nicolai<sup>2</sup>  
<sup>1</sup>Department of Radiology, University of Brescia, Brescia Italy; <sup>2</sup>Department of Otorhinolaryngology, University of Brescia, Brescia Italy
- P027: Transoral Laser Microsurgery of Occult Primary Lesions in Metastatic Squamous Cell Carcinoma of the Head and Neck**  
R.J.Karni<sup>1</sup>, B.H.Haughey<sup>1</sup>  
<sup>1</sup>Washington University School of Medicine, St. Louis, MO
- \*P028: Effectiveness of Supracricoid Partial Laryngectomy in Locally Advanced Laryngeal Cancer**  
M.Kim<sup>1</sup>, C.Bang<sup>1</sup>, Y.Joo<sup>1</sup>, K.Cho<sup>1</sup>, D.Sun<sup>1</sup>, S.Cho<sup>1</sup>  
<sup>1</sup>The Catholic University of Korea, Seoul Republic of Korea
- P029: WITHDRAWN**
- P030: Patterns of Failure on a Phase IB/II Trial of Celebrex with Chemoradiation for Head and Neck Cancer**  
J.Caudell<sup>1</sup>, P.Prellop<sup>1</sup>, G.Peters<sup>1</sup>, W.Carroll<sup>1</sup>, L.Nabell<sup>1</sup>, J.Bonner<sup>1</sup>, R.Ove<sup>2</sup>, S.Spencer<sup>1</sup>  
<sup>1</sup>University of Alabama-Birmingham, Birmingham, AL; <sup>2</sup>Mid-South Imaging & Therapeutics, Memphis, TN

**POSTER TOUR: CLINICAL 2**

**Tour Leader: Elizabeth Blair, MD**

**Location: Purdue/Wisconsin**

**P031: Utility of F-18 FDG PET-CT in Head and Neck Cancer After Segmental Reconstruction with Osteocutaneous Free Flaps**

C.L.Oliver<sup>1</sup>, A.Muthukrishnan<sup>1</sup>, J.Mountz<sup>1</sup>, J.Johnson<sup>1</sup>, F.Deleyiannis<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA

**\*P032: Differential Protein Expression Patterns of p53, NF-KB and NF- KB Regulated Genes in Head and Neck Squamous Cell Carcinoma**

P.Duggal<sup>1</sup>, Z.Chen<sup>1</sup>, C.Van Waes<sup>1</sup>  
<sup>1</sup>NIH/NIDCD Tumor Biology Section / Head & Neck Surgery Branch, Bethesda, MD

**\*P033: Analysis of Intratumoral Concentration of S100 Protein in SCC of Lower Lip, Predicting Metastasis and Survival**

L.R.Medina Santos<sup>1</sup>, M.R.Loretto<sup>2</sup>, A.R.Ferraz<sup>2</sup>  
<sup>1</sup>Hospital das Clinicas University of S. Paulo Medical School, Florianopolis Brazil; <sup>2</sup>Hospital das Clinicas USPMS, São Paulo Brazil

**P034: Phase I Study of Erlotinib With RT or Erlotinib With Cisplatin/RT in Patients with SCCHN**

J.Gilbert<sup>1</sup>, L.Nedzi<sup>2</sup>, G.Bajaj<sup>3</sup>, M.Rudek<sup>3</sup>, N.Tsottles<sup>3</sup>, S.Bienvenu<sup>4</sup>, A.Forastiere<sup>3</sup>, M.Gillison<sup>3</sup>  
<sup>1</sup>Louisiana State University Stanley S. Scott Cancer Center, New Orleans, LA; <sup>2</sup>Tulane University School of Medicine, New Orleans, LA; <sup>3</sup>Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; <sup>4</sup>Louisiana State University Stanley S. Scott Cancer Center, New Orleans, LA

**\*P035: Post-Thyroidectomy Supraglottoplasty: Laryngomalacia From Massive Goiter**

C.B.Franzese<sup>1</sup>  
<sup>1</sup>University of Mississippi Medical Center, Jackson, MS

**\*P036: Is the Dissection of Level IV Necessary in Squamous Cell Carcinoma of Larynx With NO Neck?**

C.T.Chone<sup>1</sup>, H.F.Kohler<sup>1</sup>, R.Magalhães<sup>1</sup>, M.Navarro<sup>1</sup>, A.Altemani<sup>2</sup>, A.N.Crespo<sup>1</sup>  
<sup>1</sup>Department of Otolaryngology Head and Neck, State University of Campinas, Campinas Brazil; <sup>2</sup>Department of Surgical Pathology, State University of Campinas, Campinas Brazil

**P037: Trans Oral Robotic Surgery (TORS) for Base of Tongue Neoplasms**

B.W.O'Malley<sup>1</sup>, W.Snyder<sup>1</sup>, N.Hockstein<sup>2</sup>, G.Weinstein<sup>1</sup>  
<sup>1</sup>The University of Pennsylvania, Philadelphia, PA; <sup>2</sup>Family Ear, Nose, and Throat, Wilmington, DE

**P038: Refeeding Syndrome - The Effect of Evidence Based Guidelines for Its Prevention and Treatment**

H.M.Mehanna<sup>1</sup>, J.Moledina<sup>2</sup>, R.Srinivasan<sup>2</sup>  
<sup>1</sup>University Hosp Coventry & Warwickshire, Coventry United Kingdom; <sup>2</sup>UHCW, Coventry United Kingdom

**\*P039: PNL2 Melanocytic Marker in Immunohistochemical Evaluation of Primary Malignant Mucosal Melanoma of the Head and Neck**

Y.Hanna.Wen<sup>1</sup>, L.G.Morris<sup>1</sup>, D.Nonaka<sup>1</sup>, D.I.Kutler<sup>1</sup>, Y.Huan<sup>2</sup>, B.Y.Wang<sup>1</sup>  
<sup>1</sup>New York University School of Medicine, New York, NY; <sup>2</sup>Mount Sinai Medical Center, New York, NY

**\*P040: Post Operative Monitoring Using an Implantable Doppler Device in Free Flap Reconstruction of the Head and Neck**

J.R.Harris<sup>1</sup>, J.Guillemaud<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada

**P041: WITHDRAWN**

**P042: Adenoid Cystic Carcinoma of the Larynx**

R.V.Moukarbel<sup>1</sup>, D.P.Goldstein<sup>1</sup>, L.Dawson<sup>1</sup>, R.W.Gilbert<sup>1</sup>, P.J.Gullane<sup>1</sup>, D.H.Brown<sup>1</sup>, J.C.Irish<sup>1</sup>  
<sup>1</sup>Princess Margaret Hospital, Toronto, ON Canada

**\*P043: Upfront Submandibulosalivaryglandulopexy (SMSGP) for Radiotherapy in Oro-Hypopharyngeal Cancer (for Radiation Compliance)**

R.L.Bhalavat<sup>1</sup>, A.Badrukar<sup>2</sup>, K.A.Pathak<sup>1</sup>, M.S.Deshpande<sup>1</sup>, B.L.Malpani<sup>1</sup>, S.R.Deasi<sup>1</sup>  
<sup>1</sup>Tata Memorial Hospital, Mumbai India; <sup>2</sup>Tata Memorial Hospital, Mumbai India

**\*P044: Prediction of Recurrence in Parotid Gland Carcinoma**

J.F.Carrillo<sup>1</sup>, R.Vazquez<sup>1</sup>, F.J.Ochoa<sup>1</sup>, L.F.Ocate-Ocana<sup>1</sup>  
<sup>1</sup>Instituto Nacional de Cancerologia, Mexico City Mexico

**\*P045: Reconstruction of Total Scalp Defects With Cranial Involvement: An Evolving Paradigm**

A.O.Mitchell<sup>1</sup>, J.D.Hornig<sup>1</sup>, E.R.Oliver<sup>1</sup>, M.B.Gillespie<sup>1</sup>, R.Kline<sup>1</sup>, M.Dunn<sup>1</sup>, T.A.Day<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**P046: Juvenile Angiofibroma: An Update of Treatment Trends**

V.V.Reddy<sup>1</sup>  
<sup>1</sup>Osmania Medical College, Koti, Hyderabad, A.P., Hyderabad, India India

**P047: Rhabdomyosarcoma of the Larynx in Adults**

N.N.Shah<sup>1</sup>, M.D.Williams<sup>2</sup>, J.S.Lewin<sup>2</sup>, A.S.Garden<sup>2</sup>, L.Ginsberg<sup>2</sup>, A.Hessell<sup>2</sup>, A.K.El-Naggar<sup>2</sup>, A.M.Gillenwater<sup>3</sup>  
<sup>1</sup>Univ. of Chicago Medical School, Chicago, IL; <sup>2</sup>Univ. of Texas MD Anderson Cancer Center, Houston, TX; <sup>3</sup>Univ. of Texas MD Anderson Cancer Center, Houston, TX

# Scientific Program: Friday, August 18, 2006

- \*P048: The Risk Factors Associated With Psychological Distress in Patients With Head and Neck Cancer**  
M.Schultze<sup>1</sup>, G.Robins-Sadler<sup>1</sup>, K.L.Clark<sup>1</sup>, J.Zabora<sup>2</sup>, R.Weisman<sup>1</sup>, M.Loscalzo<sup>1</sup>  
<sup>1</sup>University of California, San Diego, La Jolla, CA; <sup>2</sup>Johns Hopkins University, Baltimore, NH
- \*P049: Acute Morbidity of Chemoradiation for Locoregionally Advanced (Stage IV) Oropharynx Cancer: IMRT vs 3D Conformal RT**  
J.M.Holland<sup>1</sup>, K.M.Patel<sup>1</sup>, L.DePaula<sup>1</sup>, H.C.Chan<sup>1</sup>, C.R.Thomas<sup>1</sup>  
<sup>1</sup>Oregon Health & Science University, Portland, OR
- \*P050: PET-CT in Recurrent Head Neck Squamous Cancer**  
B.C.Shah<sup>1</sup>, A.K.D'cruz<sup>1</sup>, S.Shah<sup>2</sup>, V.Rangarajan<sup>2</sup>, A.C.Kakade<sup>1</sup>, M.S.Deshpande<sup>1</sup>, K.A.Pathak<sup>1</sup>, G.Pantvaidya<sup>1</sup>, N.Purandare<sup>2</sup>  
<sup>1</sup>Tata Memorial Hospital, Mumbai India; <sup>2</sup>Bioimaging unit, Tata Memorial Hospital, Mumbai India
- P051: WITHDRAWN**
- \*P052: Phase II Study: Concurrent Gemcitabine-Radiotherapy With Cetuximab in Locally Advanced Head and Neck Cancer (LAHNC)**  
M.Granados<sup>1</sup>, J.Luis.Aguilar<sup>1</sup>, A.J.Lavin<sup>1</sup>, M.Frías<sup>1</sup>, F.Maldonado<sup>1</sup>, K.Luna<sup>1</sup>, J.C.Cruz<sup>1</sup>, A.Morán<sup>1</sup>, J.L.Martínez<sup>1</sup>, J.de la Garza<sup>1</sup>  
<sup>1</sup>National Cancer Institute Mexico City, México D.F Mexico
- \*P053: Proper Capsular Incision Can Avoid Hoarseness After Enucleation of Schwannoma From the Cervical Vagus Nerve**  
Z.Wang<sup>1</sup>, H.Wang<sup>1</sup>, D.Li<sup>1</sup>  
<sup>1</sup>Cancer Hospital of Fudan University, Shanghai China
- P054: Concurrent Preoperative Chemoradiation of Resectable Stage III/IV Oral Cancer: 6-year Results of a Phase II Study**  
A.M.Eckardt<sup>1</sup>, C.Hofe<sup>2</sup>, B.Sinikovic<sup>3</sup>, J.H.Karstens<sup>3</sup>  
<sup>1</sup>Hannover Medical School, OE 7720, Hannover Germany; <sup>2</sup>University of Heidelberg, Heidelberg Germany; <sup>3</sup>Hannover Medical School, Hannover Germany
- P055: Juvenile Angiofibroma: An Update of Treatment Trends**  
V.V.Reddy<sup>1</sup>, r.--s<sup>2</sup>  
<sup>1</sup>Osmania Medical college, Koti, Hyderabad, A.P., Hyderabad, India India; <sup>2</sup>Osmania Medical College, Kothi, Hyderabad, Hyderabad India
- \*P056: Minimally Invasive Thyroid Surgery: The Delivery Technique**  
E.M.Genden<sup>1</sup>, B.Malkin<sup>2</sup>, S.Seo<sup>3</sup>  
<sup>1</sup>Mount Sinai School of Medicine, New York, NY; <sup>2</sup>Mount Sinai School of Medicine, New York, NY; <sup>3</sup>Mount Sinai School of Medicine, New York, NY
- P057: Outcomes of Esthesioneuroblastoma: The UCSF Experience 1971-2001**  
I.H.El-Sayed<sup>1</sup>, A.Ding<sup>1</sup>, E.Y.Wang<sup>2</sup>, M.J.Kaplan<sup>3</sup>, N.J.Fischbein<sup>3</sup>, R.C.Jordan<sup>1</sup>, M.W.McDermott<sup>1</sup>  
<sup>1</sup>University of California, San Francisco, San Francisco, CA; <sup>2</sup>University of California, Los Angeles, Los Angeles, CA; <sup>3</sup>Stanford University Medical Center, Stanford, CA
- P058: Concurrent Chemoradiotherapy and Gefitinib for Squamous Head and Neck Cancer: Preliminary Compliance Data**  
D.J.Adelstein<sup>1</sup>, J.P.Saxton<sup>1</sup>, L.A.Rybicki<sup>1</sup>, R.R.Lorenz<sup>1</sup>, B.G.Wood<sup>1</sup>, M.Strome<sup>1</sup>, R.M.Esclamado<sup>1</sup>, M.A.Carroll<sup>1</sup>  
<sup>1</sup>Cleveland Clinic Foundation, Cleveland, OH
- \*P059: Drain Removal After Neck Dissection Varies With Peri-operative Fluid Balance**  
J.M.Hsu<sup>1</sup>  
<sup>1</sup>SUNY Upstate Medical University, Syracuse
- \*P060: Significance of Insulin like Growth Factor Receptor I in the Development of Anaplastic Thyroid Cancer**  
G.Chakravarty<sup>1</sup>, Y.D.Yazici<sup>1</sup>, Z.Wang<sup>1</sup>, A.A.Santillan<sup>1</sup>, S.A.Jasser<sup>1</sup>, A.K.El-Naggar<sup>1</sup>, J.N.Myers<sup>1</sup>  
<sup>1</sup>The University of Texas M. D. Anderson Cancer Center, Houston, TX

## POSTER TOUR: OUTCOMES/QOL

**Tour Leader: Bevan Yueh, MD**

**Location: Indiana/Iowa**

- \*P061: Postoperative Survival and Number of Lymph Nodes Examined During Surgery for Node-Negative Oral Tongue Cancer**  
A.Y.Chen<sup>1</sup>, M.Sreevatsava<sup>1</sup>, M.Goodman<sup>1</sup>, J.Liff<sup>1</sup>, K.Ward<sup>1</sup>  
<sup>1</sup>Emory University, Atlanta, GA
- \*P062: Postoperative Swallowing Function in the Surgical Treatment of Tongue Base Cancers: Prospective Functional Outcomes**  
D.A.O'Connell<sup>1</sup>, J.Rieger<sup>2</sup>, P.Dziegielewski<sup>1</sup>, J.Zalmanowitz<sup>2</sup>, A.Sytsanko<sup>2</sup>, S.Li<sup>2</sup>, R.D.Hart<sup>1</sup>, J.R.Harris<sup>1</sup>, H.Seikaly<sup>3</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>COMPRU, Edmonton, AB Canada; <sup>3</sup>University of Alberta, Edmonton, AB Cameroon

**\*P063: Surgical Treatment for Head and Neck Paragangliomas: Is it Possible to Minimize the Postoperative Complications?**

P.A.Andrade<sup>1</sup>, E.N.Myers<sup>1</sup>, R.L. Carrau<sup>1</sup>, R.L.Ferris<sup>1</sup>, R.S.Andrade<sup>1</sup>, M.Tedla<sup>1</sup>, J.Johnson<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Pittsburgh, PA

**\*P064: Estimates and Analysis of Oral Cancer Incidence Rates Worldwide**

E.D.Gorham<sup>1</sup>, W.E.James<sup>2</sup>, S.B.Mohr<sup>1</sup>, S.Karahatay<sup>3</sup>, S.G.Reed<sup>4</sup>, M.B.Gillespie<sup>3</sup>, A.Chi<sup>4</sup>, M.Ravenel<sup>4</sup>, T.A.Day<sup>3</sup>, C.F.Garland<sup>1</sup>

<sup>1</sup>Behavioral Sciences and Epidemiology Program, Naval Health Research Center, San Diego, CA; <sup>2</sup>Medical University of South Carolina, Charleston, SC; <sup>3</sup>Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; <sup>4</sup>College of Dental Medicine, Medical University of South Carolina, Charleston, SC

**P065: WITHDRAWN**

**P066: Annexin V Scintigraphy for Imaging of Apoptosis in Tumor and Normal Tissue in HNSCC Patients Treated With RADPLAT**

E.J.P.Hoebbers<sup>1</sup>, M.Kartachova<sup>1</sup>, M.W.van den Brekel<sup>1</sup>, J.de Bois<sup>1</sup>, M.van Herk<sup>1</sup>, C.R.N.Rasch<sup>1</sup>, R.A.Valdes Olmos<sup>1</sup>, M.Verheij<sup>1</sup>

<sup>1</sup>The Netherlands Cancer Institute, Amsterdam The Netherlands

**P067: Genes Gone Silent: Transcriptional Down-Regulation of Genes in Head and Neck Squamous Cell Carcinoma**

T.J.Belbin<sup>1</sup>, N.F.Schlecht<sup>1</sup>, L.R.Adrien<sup>1</sup>, N.Kawachi<sup>1</sup>, C.Sarta<sup>2</sup>, M.Brandwein-Gensler<sup>1</sup>, G.Childs<sup>1</sup>, M.B.Prystowsky<sup>1</sup>, R.V.Smith<sup>2</sup>

<sup>1</sup>Albert Einstein College of Medicine, Bronx, NY; <sup>2</sup>Montefiore Medical Center, Bronx, NY

**P068: Life After a Total Laryngectomy: Is There Any? A Measure of Long Term Survival, Functional, and Quality of Life Outcomes**

T.D.Woodard<sup>1</sup>, A.Oplatek<sup>1</sup>, G.Petruzzelli<sup>1</sup>

<sup>1</sup>Loyola University Medical Center, Maywood, IL

**\*P069: The Effect of Second Hand Smoke in Patients With Squamous Cell Carcinoma of the Head and Neck**

H.Seikaly<sup>1</sup>, J.Chau<sup>1</sup>, C.H.Karen<sup>2</sup>, J.R.Harris<sup>1</sup>

<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>University of Columbia, Columbia, MO

**\*P070: Why Are Head and Neck Cancer Clinicians Not Measuring Quality of Life?**

H.M.Mehanna<sup>1</sup>, R.P.Morton<sup>2</sup>

<sup>1</sup>University Hosp Coventry & Warwickshire, Coventry United Kingdom; <sup>2</sup>Auckland regional head and neck centre, Auckland New Zealand

**\*P071: Assessment of Response Using Fluorodeoxyglucose F 18 Positron Emission Tomography and Computed Tomography to Evaluate Patients With Head and Neck Cancer After Definitive Radiation Therapy: Preliminary Results**

R.S.Andrade<sup>1</sup>, D.E.Heron<sup>1</sup>, P.A.A.Filho<sup>2</sup>, B.F.Branstetter<sup>2</sup>, R.R.Seethala<sup>2</sup>, R.L.Ferris<sup>2</sup>, N.E.Avril<sup>3</sup>, J.Johnson<sup>4</sup>

<sup>1</sup>University of Pittsburgh Cancer Institute, Pittsburgh, PA; <sup>2</sup>University of Pittsburgh, Pittsburgh, PA; <sup>3</sup>Barts and the London School of Medicine, Queen Mary United Kingdom; <sup>4</sup>University of Pittsburgh, Pittsburgh

**\*P072: Multivariate Analysis of Multidomain Quality of Life Predictors Among Head and Neck Cancer Patients**

L.Q.Rogers<sup>1</sup>, J.Malone<sup>1</sup>, T.Robbins<sup>1</sup>, K.Rao<sup>1</sup>, K.S.Courneya<sup>2</sup>, A.Seiz<sup>1</sup>

<sup>1</sup>Southern Illinois University School of Medicine, Springfield, IL; <sup>2</sup>University of Alberta, Edmonton, AB Canada

**P073: Deciphering the Distinct Molecular Signatures of Head and Neck Squamous Cell Carcinomas**

N.F.Schlecht<sup>1</sup>, R.V.Smith<sup>2</sup>, N.Kawachi<sup>1</sup>, Q.Chen<sup>1</sup>, H.Qian<sup>1</sup>, C.Sarta<sup>2</sup>, M.Brandwein-Gensler<sup>1</sup>, G.Childs<sup>1</sup>,

M.B.Prystowsky<sup>1</sup>, T.J.Belbin<sup>1</sup>

<sup>1</sup>Albert Einstein College of Medicine, Bronx, NY; <sup>2</sup>Montefiore Medical Center, Bronx, NY

**P074: Predictive Value of Response to Induction Chemotherapy in Head and Neck Cancer**

M.Stephen<sup>1</sup>, D.Huo<sup>1</sup>, E.Cohen<sup>1</sup>, D.Haraf<sup>1</sup>, K.Stenson<sup>1</sup>, B.Brokstein<sup>1</sup>, E.Vokes<sup>1</sup>

<sup>1</sup>University of Chicago, Chicago

**P075: Feasibility of Single Level Dissection for the N+ Neck Following Treatment With Radiation With or Without Chemotherapy**

J.E.Medina<sup>1</sup>, N.A.Vasan<sup>1</sup>, G.A.Kremp<sup>1</sup>

<sup>1</sup>University of Oklahoma, Oklahoma City, OK

**\*P076: International Variation in Age-Adjusted Nasopharyngeal Cancer Incidence Rates Among 175 Countries**

E.D.Gorham<sup>1</sup>, J.Ken.Byrd<sup>2</sup>, S.B.Mohr<sup>1</sup>, A.K.Sharma<sup>3</sup>, N.Sutkowski<sup>3</sup>, L.K.Yen<sup>4</sup>, U.Chaudhary<sup>3</sup>, T.A.Day<sup>3</sup>, C.F.Garland<sup>1</sup>

<sup>1</sup>Behavioral Sciences and Epidemiology Program, Naval Health Research Center, San Diego, CA; <sup>2</sup>Medical University of South Carolina, Charleston, SC; <sup>3</sup>Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; <sup>4</sup>College of Public Health, University of South Carolina, Columbia, SC

**\*P077: Swallowing Outcomes following Supracricoid Partial Laryngectomy in the Setting of Adjuvant Therapy**

J.S.Lewin<sup>1</sup>, F.C.Holsinger<sup>1</sup>, D.A.Barringer<sup>1</sup>, A.K.May<sup>1</sup>, K.A.Hutcheson<sup>1</sup>, O.Laccourreye<sup>2</sup>, E.M.Diaz, Jr.<sup>1</sup>

<sup>1</sup>The University of Texas M.D. Anderson Cancer Center, Houston, TX; <sup>2</sup>Hopital Europeen Georges Pompidou, Paris, France

**\*P078: Quality of Life Priorities in Kenyan Versus American Head and Neck Cancer Patients**

S.A.Omor<sup>1</sup>, J.R.Fann<sup>1</sup>, E.A.Weymuller<sup>1</sup>, I.M.Macharia<sup>2</sup>, B.Yueh<sup>1</sup>

<sup>1</sup>University Of Washington, Seattle, WA; <sup>2</sup>University of Nairobi, Nairobi

- \*P079: Swallowing Recovery and Chronic Aspiration After Supracricoid Partial Laryngectomy (SCPL)**  
M.Simonelli<sup>1</sup>, G.Ruoppolo<sup>2</sup>, M.de Vincentiis<sup>2</sup>, I.Habib<sup>3</sup>, M.Di Mario<sup>1</sup>, C.Pizzoli<sup>1</sup>, C. Vitello<sup>2</sup>, V.Manciocco<sup>4</sup>, A.Gallo<sup>2</sup>  
<sup>1</sup>Santa Lucia Hospital, Rome Italy; <sup>2</sup>"La Sapienza" University, Rome Italy; <sup>3</sup>"La Sapienza" University, Rome; <sup>4</sup>"La Sapienza" University, Roma Italy
- \*P080: Soft Palate Reconstruction Using the CAP Modification of the Radial Forearm Flap: An Assessment of Functional Outcomes**  
H.Seikaly<sup>1</sup>, J.Rieger<sup>1</sup>, R.Hart<sup>2</sup>, J.Wolfaardt<sup>2</sup>, J.R.Harris<sup>2</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>University of Alberta, Edmonton, AB Canada
- \*P081: Minimally Invasive Parathyroidectomy Under Local Anesthetic: Patient Satisfaction and Outcome**  
J.R.Harris<sup>1</sup>, J.Chau<sup>1</sup>, B.Tsui<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada
- \*P082: Questionnaire Analysis of the Swallowing Related Quality of life Following Total Laryngectomy**  
R.Kazi<sup>1</sup>, V.Prasad<sup>1</sup>, R.Venkitaraman<sup>1</sup>, C.Nutting<sup>1</sup>, P.Clarke<sup>1</sup>, P.Rhys-Evans<sup>1</sup>, K.Harrington<sup>1</sup>  
<sup>1</sup>Royal Marden Hospital, London United Kingdom
- P083: Interactions of ATF2 and ERK Result From Treatment with P38 Inhibitors in HNSCC Cell Lines**  
S.M.Dolgilevich<sup>1</sup>, D.C.Duffey<sup>2</sup>  
<sup>1</sup>The Mount Sinai School of Medicine, New York, NY; <sup>2</sup>The Mount Sinai School of Medicine, New York, NY, New York, NY
- P084: Longitudinal Oncology Registry of Head and Neck Carcinoma (LORHAN): A New National Cancer Registry**  
A.Y.Chen<sup>1</sup>, W.Curran<sup>2</sup>, P.Harari<sup>3</sup>, B.Murphy<sup>4</sup>, S.Wong<sup>5</sup>, L.Bellm<sup>6</sup>, D.Gamber<sup>6</sup>, D.Dawson<sup>7</sup>, K.Ang<sup>8</sup>  
<sup>1</sup>Emory University, Atlanta, GA; <sup>2</sup>Thomas Jefferson University, Philadelphia, PA; <sup>3</sup>University of Wisconsin, Madison, WI; <sup>4</sup>Vanderbilt University, Nashville, TN; <sup>5</sup>Medical College of Wisconsin, Madison, WI; <sup>6</sup>MedNet Solutions, Minnetonka, MN; <sup>7</sup>ImClone Systems, New York City, NY; <sup>8</sup>M. D. Anderson Cancer Center, Houston, TX
- P085: The Patient's Experience of Choice in Cancer Treatment Decision Making**  
L.Davies<sup>1</sup>, L.Rhodes<sup>2</sup>, D.Grossman<sup>3</sup>  
<sup>1</sup>White River Junction VA Medical Center, White River Junction, VT; <sup>2</sup>University of Washington, Seattle, WA; <sup>3</sup>Group Health Cooperative, Seattle, WA
- \*P086: Production of Proinflammatory Cytokines in Larynx Cancer**  
L.C.Conti-Freitas<sup>1</sup>, R.CM.Mamede<sup>1</sup>, M.C.Foss-Freitas<sup>1</sup>, D.LA.Figueiredo<sup>1</sup>, N.T.Foss<sup>1</sup>  
<sup>1</sup>Faculty of Medicine of Ribeirao Preto-Sao Paulo University, Ribeirao Preto Brazil
- \*P087: Quality of Life in Patients Treated of Oral, Pharyngeal and Laryngeal Cancer in São Paulo: Multicentric Study**  
C.Lemos.Furia<sup>1</sup>, L.Paulo.Kowalski<sup>2</sup>, J.Goes<sup>3</sup>, M.Abrahão<sup>4</sup>, O.Cervantes<sup>4</sup>, L.Fava<sup>5</sup>, L.Sennes<sup>6</sup>, A.Lopes.Carvalho<sup>2</sup>  
<sup>1</sup>Oncologia FMUSP, São Paulo Brazil; <sup>2</sup>Hospital do Câncer ACCamargo, São Paulo Brazil; <sup>3</sup>Instituto Arnaldo Vieira de Carvalho, São Paulo Brazil; <sup>4</sup>Hospital São Paulo UNIFESP, São Paulo Brazil; <sup>5</sup>Hospital do Servidor Público Estadual, São Paulo Brazil; <sup>6</sup>Hospital das Clínicas FMUSP, São Paulo Brazil
- P088: Knowledge and Attitudes About the Consequences of Tobacco Use in Relation to Head and Neck Cancer Within 8-18 Year Olds**  
J.K.Byrd<sup>1</sup>, D.Sinha<sup>1</sup>, J.C.Goddard<sup>1</sup>, A.O.Mitchell<sup>1</sup>, H.P.Upadhyaya<sup>1</sup>, S.Karahatay<sup>1</sup>, A.J.Alberg<sup>1</sup>, T.A.Day<sup>1</sup>  
<sup>1</sup>Hollings Cancer Center, Medical University of South Carolina, Charleston, SC
- P089: Sentinel Lymph Biopsy of Head and Neck Melanoma**  
J.Young<sup>1</sup>, R.Hundal<sup>1</sup>  
<sup>1</sup>St. Joseph's Healthcare, Hamilton, ON Canada
- P090: The Effect of Platelet Rich Plasma and Fibrin Sealant on Facial Nerve Regeneration in a Rat Model**  
T.Y.Farrag<sup>1</sup>, M.Lehar<sup>1</sup>, P.Verhaegen<sup>1</sup>, K.Carson<sup>1</sup>, P.J.Byrne<sup>1</sup>  
<sup>1</sup>Johns Hopkins University School of Medicine, Baltimore, MD

## POSTER TOUR: BASIC SCIENCE

**Tour Leader: TBD**

**Location: Michigan/Michigan State**

**P091: Salivary Oral Cancer Transcriptome Biomarkers (SOCTB) for Clinical Detection**

J.Wang<sup>1</sup>, S.Henry<sup>1</sup>, Y.Li<sup>1</sup>, D.A.Elashoff<sup>1</sup>, D.T.Wong<sup>1</sup>  
<sup>1</sup>UCLA, Los Angeles, CA

**P092: FAK-Related Non-Kinase (FRNK) Blockade of FAK Changes Malignant Properties of the SCC VII/SF Cell Line**

C.M.Bier-Laning<sup>1</sup>, C.Bien<sup>2</sup>, A.T. M.Vaughan<sup>3</sup>  
<sup>1</sup>Loyola University Medical Center, Maywood, IL; <sup>2</sup>Hines VA Hospital, Maywood, IL; <sup>3</sup>University of California-Davis, Davis, CA

**P093: MMS19, a Modulator of Transcription and Nucleotide Excision Repair, Is Overexpressed in Human Cancer**

M.D.Hatfield<sup>1</sup>, D.Obeso<sup>1</sup>, A.M.C.Reis<sup>2</sup>, L.Queimado<sup>1</sup>  
<sup>1</sup>Otorhinolaryngology Department, Oklahoma University Health Sciences Center, Oklahoma City, OK; <sup>2</sup>Dermatology Department, Oklahoma University Health Sciences Center, Oklahoma City, OK

**\*P094: Phenotypic and Functional Profiles of Natural Regulatory T Cells in the Circulation of Patients With Head and Neck Squamous Cell Carcinoma**

L.Strauss<sup>1</sup>, J.T.Johnson<sup>1</sup>, T.L.Whiteside<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA

\* Abstract was published in the *Archives of Otolaryngology*

- \*P095: Investigation of the Mismatch Repair Genes hPMS1, hPMS2 and hMLH1 in Young Patients With Oral Squamous Cell Carcinoma**  
J.Machado<sup>1</sup>, P.Pintor dos Reis<sup>2</sup>, N.Naranjo Galloni<sup>2</sup>, Y.Wang<sup>3</sup>, W.Xu<sup>3</sup>, C.MacMillan<sup>4</sup>, B.Perez-Ordóñez<sup>3</sup>, P.Gullane<sup>3</sup>, J.Irish<sup>3</sup>, S.Kamel-Reid<sup>1</sup>  
<sup>1</sup>Ontario Cancer Institute and University Health Network, University of Toronto, Toronto, ON Canada; <sup>2</sup>Ontario Cancer Institute and University Health Network, Toronto, ON Canada; <sup>3</sup>University Health Network, Toronto, ON Canada; <sup>4</sup>Mount Sinai Hospital, Toronto, ON Canada
- \*P096: Cytoglobin: A Candidate Tumour Suppressor Gene Epigenetically Silenced in Head and Neck Cancer**  
R.J.Shaw<sup>1</sup>, T.Liloglou<sup>2</sup>, J.K.Field<sup>3</sup>, J.M.Risk<sup>4</sup>  
<sup>1</sup>Head & Neck Surgery Unit, Liverpool United Kingdom; <sup>2</sup>University of Liverpool Cancer Research Centre, Roy Castle Lung Cancer Research, Liverpool United Kingdom; <sup>3</sup>University of Liverpool Cancer Research Centre, Liverpool United Kingdom; <sup>4</sup>Molecular Oncology & Genetics, School of Dental Sciences, University of Liverpool, Liverpool United Kingdom
- P097: Prognostic Significance of Intratumoral Dendritic Cells in Oropharyngeal Head and Neck Squamous Cell Carcinoma**  
C.Haddad<sup>1</sup>, Y.Wang<sup>1</sup>, M.Brose<sup>1</sup>, D.A.Sewell<sup>1</sup>  
<sup>1</sup>University of Pennsylvania, Philadelphia, PA
- P098: The Unique Autofluorescence of Human Buccal Cells Defined by High-Throughput Multispectral Flow Cytometry**  
M.Sullivan<sup>1</sup>, G.Paszkiwicz<sup>1</sup>, M.C.Mahoney<sup>1</sup>, T.R.Loree<sup>1</sup>, N.R.Rigual<sup>1</sup>, J.L.Pauly<sup>1</sup>  
<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY
- \*P099: Laryngotracheal Injury After Percutaneous Dilation vs Open Tracheostomy in Fresh Cadaver Specimens**  
J.R.Harris<sup>1</sup>, J.Krepelka<sup>1</sup>, J.Chau<sup>1</sup>, J.Tse<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada
- \*P100: Genetic Alterations in p53 in Head and Neck Cancer Cell Lines Change Cisplatin Sensitivity**  
J.A.Bauer<sup>1</sup>, J.Brenner<sup>1</sup>, M.J.Sikora<sup>1</sup>, C.R.Bradford<sup>1</sup>, T.E.Carey<sup>1</sup>  
<sup>1</sup>University of Michigan, Ann Arbor, MI
- P101: IL-6 Antisense Treatment of Human Head and Neck Cancer Cells Decreases Tumor Cell Proliferation and Angiogenic Activity**  
F.Riedel<sup>1</sup>, I.Zaiss<sup>1</sup>, D.Herzog<sup>1</sup>, K.Goette<sup>1</sup>, R.Naim<sup>1</sup>, K.Hoermann<sup>1</sup>  
<sup>1</sup>Dept. of ORL-HNS, Mannheim Germany
- \*P102: Induction of IL-10+ Tr1-Like Regulatory T Cells in the Microenvironment of COX-2+ Head and Neck Squamous Cell Carcinoma**  
C.Bergmann<sup>1</sup>, L.Strauss<sup>1</sup>, S.Lang<sup>2</sup>, R.Zeidler<sup>3</sup>, T.L.Whiteside<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA; <sup>2</sup>University of Schleswig-Holstein Campus Lubeck, Lubeck Germany; <sup>3</sup>LMU Medical Center, Munich Germany
- P103: Apoptosis Signaling Causes Genomic Instability Leading to Loss of Heterozygosity (LOH) in Cell Lines**  
C.M.Bier-Laning<sup>1</sup>, C.Bien<sup>2</sup>, A.T.M.Vaughan<sup>3</sup>, M.O.Diaz<sup>1</sup>  
<sup>1</sup>Loyola University Medical Center, Maywood, IL; <sup>2</sup>Hines VA Hospital, Hines, IL; <sup>3</sup>University of California-Davis, Davis, CA
- \*P104: Radioimmunotherapy of Head and Neck Cancer Xenografts Using 131I-L19-SIP for Selective Targeting of Tumor Vasculature**  
B.M.Tijink<sup>1</sup>, D.Neri<sup>2</sup>, M.Budde<sup>1</sup>, C.R.Leemans<sup>1</sup>, L.M.Dinkelborg<sup>3</sup>, M.Stigter-van Walsum<sup>1</sup>, L.Zardi<sup>4</sup>, G.A.M.S.van Dongen<sup>1</sup>  
<sup>1</sup>VU University Medical Center, Amsterdam The Netherlands; <sup>2</sup>Institute of Pharmaceutical Sciences, Swiss Federal Institute of Technology, Zurich Switzerland; <sup>3</sup>Research Laboratories of Schering AG, Berlin Germany; <sup>4</sup>Istituto G Gaslini, Genova Italy
- P105: Role of Slug (SNAI2) in Head and Neck Squamous Cell Carcinoma (HNSCC)**  
K.J.Patel<sup>1</sup>, D.Patel<sup>1</sup>, P.L.Lytle<sup>1</sup>, R.L.Griffin<sup>1</sup>, F.G.Ondrey<sup>1</sup>, P.M.Gaffney<sup>1</sup>  
<sup>1</sup>University of Minnesota, Minneapolis, MN
- \*P106: Expression of Nerve Growth Factor and Tyrosine Kinase A Receptor in Oral Squamous Cell Carcinoma**  
A.Kolokythas<sup>1</sup>, D.P.Cox<sup>1</sup>, N.Dekker<sup>2</sup>, R.C.K.Jordan<sup>1</sup>, B.L.Schimdt<sup>1</sup>  
<sup>1</sup>University of California, San Francisco, CA; <sup>2</sup>University of California, San Francisco, CA
- P107: Role of Antigen-Processing Machinery in the Resistance of SCCHN Cells to Recognition by CTL**  
A.Lopez Albaiteiro<sup>1</sup>, J.Nayak<sup>1</sup>, T.Ogino<sup>2</sup>, W.Gooding<sup>1</sup>, A.De Leo<sup>1</sup>, S.Ferrone<sup>2</sup>, R.L.Ferris<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA; <sup>2</sup>Roswell Park Cancer Institute, Buffalo, NY
- \*P108: Formation of Thanatosomes in Oral Cancer Cells: Insights Into the Early Stages of Apoptosis**  
P.Parashar<sup>1</sup>, N.G.Nikitakis<sup>2</sup>, M.A.Reynolds<sup>1</sup>, J.J.Sauk<sup>2</sup>, J.C.Papadimitriou<sup>3</sup>  
<sup>1</sup>University of Maryland Dental School, Baltimore, MD; <sup>2</sup>University of Maryland Dental School, Greenebaum Cancer Center, Baltimore, MD; <sup>3</sup>University of Maryland Medical School, Baltimore, MD
- P109: Increased Apoptosis in Head and Neck SCC Using Chemotherapy and E1b-19kD-deleted p53-expressing Replicating Adenovirus**  
D.I.Kutler<sup>1</sup>, H.Sauthoff<sup>2</sup>, J.Cheng<sup>2</sup>, Y.Huang<sup>2</sup>, S.Heitner<sup>2</sup>, W.N.Rom<sup>2</sup>, J.G.Hay<sup>2</sup>  
<sup>1</sup>Weill Cornell Medical College, New York, NY; <sup>2</sup>NYU School of Medicine/ Veterans Administration, New York, NY

**P110: Concomitant Inhibition of Epidermal Growth Factor Receptor and Insulinlike Growth Factor Receptor I in Cutaneous SCC**

C.L.Corey<sup>1</sup>, Z.Wang<sup>2</sup>, Y.D.Yazici<sup>2</sup>, F.Gomez-Rivera<sup>2</sup>, S.A.Jasser<sup>2</sup>, C.D.Bucana<sup>2</sup>, A.Ei-Naggar<sup>2</sup>, R.S.Weber<sup>2</sup>, J.N.Myers<sup>2</sup>  
<sup>1</sup>Baylor College of Medicine, Houston, TX; <sup>2</sup>The University of Texas M.D. Anderson Cancer Center, Houston, TX

**P111: Head and Neck Cancer Triggers the Internalization of TLR3 in Natural Killer Cells**

L.Xie<sup>1</sup>, R.Pries<sup>2</sup>, S.Wulff<sup>3</sup>, R.Kesselring<sup>2</sup>, B.J.H.Wollenberg<sup>2</sup>  
<sup>1</sup>Zhejiang University, Hangzhou China; <sup>2</sup>University of Schleswig Holstein, Luebeck Germany; <sup>3</sup>University of Schleswig Holstein, Luebeck Germany

**P112: Reduced Expression of 15-Lipoxygenase 2 in Human Head and Neck Carcinomas**

D.Wang<sup>1</sup>, S.Chen<sup>1</sup>, Y.Feng<sup>1</sup>, Q.Yang<sup>1</sup>, B.H.Campbell<sup>1</sup>, X.Tang<sup>1</sup>, W.B.Campbell<sup>1</sup>  
<sup>1</sup>Medical College of Wisconsin, Milwaukee, WI

**\*P113: Evidence for a Role of the Insulinlike Growth Factor (IGF) System in Head and Neck Squamous Cell Carcinoma (HNSCC)**

M.G.Slomiany<sup>1</sup>, L.Black<sup>1</sup>, M.M.Kibbey<sup>1</sup>, T.A.Day<sup>1</sup>, S.A.Rosenzweig<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**\*P114: Vitamin D Inhibits Carcinogenesis in the Hamster Cheek Pouch Model**

J.D.Meier<sup>1</sup>, D.J.Enepekides<sup>1</sup>, J.Albala<sup>1</sup>, C.Bradley<sup>1</sup>, R.Yunis<sup>1</sup>, D.G.Farwell<sup>1</sup>  
<sup>1</sup>UC Davis School of Medicine, Sacramento, CA

**\*P115: Hyaluronan-CD44 Interaction Influences Topoisomerase II Activity and Etoposide Cytotoxicity in Head and Neck Cancer**

S.J.Wang<sup>1</sup>, K.Peyrollier<sup>1</sup>, L.Y.Bourguignon<sup>1</sup>  
<sup>1</sup>University of California, San Francisco, San Francisco, CA

**P116: Stat3 Up-Regulates VEGF Production and Tumor Angiogenesis in Head and Neck Squamous Cell Carcinoma**

M.Masuda<sup>1</sup>, H.Ruan<sup>2</sup>, T.Nakashima<sup>2</sup>, S.Toh<sup>2</sup>, Y.Kutratomi<sup>3</sup>, S.Komune<sup>2</sup>, I.B.Weinstein<sup>4</sup>  
<sup>1</sup>Kyushu Koseinenkin Hospital, Kitakyushu Japan; <sup>2</sup>Kyushu University, Fukuoka Japan; <sup>3</sup>Saga University, Saga Japan; <sup>4</sup>Columbia University, NY, NY

**\*P117: Immunologic Effects of Combined Docetaxel and Radiation Therapy**

M.D.Ghegan<sup>1</sup>, M.RI.Young<sup>2</sup>, J.Clark<sup>3</sup>, L.M.Veatch<sup>2</sup>, D.M.R.Lathers<sup>2</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC; <sup>2</sup>Ralph H. Johnson VAMC and Medical University of South Carolina, Charleston, SC; <sup>3</sup>University Stritch School of Medicine and Cardinal Bernadin Cancer Center, Maywood, IL

**P118: Survivin Expression in Medullary Thyroid Carcinoma: Identification and Preliminary Signaling Mechanisms**

C.L.Noel, D.O.<sup>1</sup>, P.K.Pellitteri, D.O.<sup>1</sup>, D.J.Carey, Ph.D.<sup>2</sup>, P.C.Barth, M.D.<sup>1</sup>, T.L.Lindemann, M.D.<sup>1</sup>, W.L.Riefkohl, M.D.<sup>1</sup>, J.M.Winstead, M.D.<sup>1</sup>, K.K.Masker<sup>2</sup>, E.J.Harlor, MSII<sup>2</sup>  
<sup>1</sup>Geisinger Medical Center, Danville, PA; <sup>2</sup>Weis Center for Research, Danville, PA

**\*P119: CD24 Expression Correlates With Response to Cisplatin in Head and Neck Squamous Cell Carcinoma Cell Lines**

A.Kaczorowski<sup>1</sup>, M.Clay<sup>1</sup>, C.Brenner<sup>1</sup>, J.Bauer<sup>1</sup>, T.E.Carey<sup>1</sup>, C.R.Bradford<sup>1</sup>, M.E.Prince<sup>1</sup>  
<sup>1</sup>University of Michigan, Ann Arbor, MI

**P120: Withdrawn/TBD**

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## 1830 - 1915 Information Session on Head and Neck Fellowships

### Location: Salon II

The American Head & Neck Society cordially invites you, your Otolaryngology Residents & other Residents to come and learn about the typical fellowship, meet fellowship program directors, and converse with former fellows over cocktails.

**0630 – 0800 Breakfast Satellite Symposium**

**The Use of CO<sub>2</sub> Laser Photonic Gap Band Fibers for Head and Neck Surgical Oncology**

**Speakers: Yoel Fink, PhD and Chris Holsinger, MD**  
**Location: Salon I/II**

This is a non-CME event presented and supported by OmniGuide, Inc.

**0800 – 0900 Translational Therapeutic Clinical Trials:  
Role of Working Group and SPORES**

**Panel Chair: Jennifer R. Grandis, MD**  
**Location: Salon I/II**

- 1) **Efforts to Promote Correlative Biomarker Studies: RTOG Perspective** – Kie-Kian Ang, MD, PhD
- 2) **Identification of New Agents in Patients with Recurrent Disease in ECOG** – Arlene A. Forastiere, MD
- 3) **Progress with the Integration of Novel Medical Therapeutics for the Treatment of SCCHN** –  
Merrill S. Kies, MD
- 4) **ACOSOG: Opportunities and Obstacles in Surgical Research** – Jeffrey N. Myers, MD, PhD
- 5) **Locally Advanced Head and Neck Cancer: ECOG Trials** – John A. Ridge, MD, PhD
- 6) **Translational SPORE Research: The Challenges of Moving Phase II to  
Cooperative Group Phase III Trials** – Gregory T. Wolf, MD

At the conclusion of this event, the participants would be able to:

- To describe the role of working groups in translational clinical trials for head and neck cancer
- To describe the role of SPOREs in translational clinical trials for head and neck cancer
- To identify areas for collaboration between working groups and SPOREs
- To define translational clinical trials in head and neck cancer

**0900 – 0930 AHNS Presidential Address**

Introduction by Randal S. Weber, MD

**John J. Coleman, III, MD, AHNS President**  
**Location: Salon I/II**

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**0930 – 1010 Hayes Martin Lecture**

**Do all Cancers Need to be Treated? The Role of  
Thyroglobulin in the Management of Thyroid Cancer**

Introduction by John J. Coleman, III, MD

**Keynote Speaker: Keith S. Heller, MD**  
**Long Island Jewish Medical Center, New York, NY**  
**Location: Salon I/II**

**1010 – 1040 Break with Poster and Exhibit Viewing**

## CLINICAL PROGRAM

### 1040 – 1200 Scientific Session/Abstracts

Moderators: Daniel G. Deschler, MD &  
Roman M. Esclamado, MD

#### Location: Salon II

#### S044: Does Positron Emission Tomography Improve Our Ability to Detect Residual Neck Node Disease After Chemoradiotherapy?

A.Tan<sup>1</sup>, D.J.Adelstein<sup>1</sup>, R.M.Esclamado<sup>1</sup>, L.A.Rybicki<sup>1</sup>,  
J.P.Saxton<sup>1</sup>, B.G.Wood<sup>1</sup>, R.R.Lorenz<sup>1</sup>, M.Strome<sup>1</sup>, M.A.Carroll<sup>1</sup>  
<sup>1</sup>Cleveland Clinic Foundation, Cleveland, OH

#### S045: Management of N2A Cervical Lymph Node Metastases: Is Selective Neck Dissection Enough?

M.G.Moore<sup>1</sup>, D.G.Deschler<sup>1</sup>  
<sup>1</sup>Massachusetts Eye and Ear Infirmary, Boston, MA

#### \*S046: Sentinel Node Biopsy in N0 SCC of the Oral Cavity and Oropharynx in the Previously Operated or Irradiated Patient

R.D.Hart<sup>1</sup>, J.G.Nasser<sup>2</sup>, E.Henry<sup>2</sup>, J.Trites<sup>2</sup>, S.M.Taylor<sup>2</sup>,  
M.Bullock<sup>2</sup>, D.Barnes<sup>2</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>Dalhousie University, Halifax, NS Canada

#### \*S047: Value of Sentinel Lymph Nodes in Predicting Regional Lymph Nodes: A Comparison with Proliferation Marker PCNA

G.M.LAWSON<sup>1</sup>, M.Liu<sup>1</sup>, T.Van der Borgh<sup>1</sup>, M.Delos<sup>1</sup>,  
M.C.Nolleaux<sup>1</sup>, J.Jamart<sup>1</sup>, M.Remacle<sup>1</sup>  
<sup>1</sup>Louvain University Hospital at Mont-Godinne, YVOIR Belgium

#### Discussion

#### S048: Detection of Occult Bone Metastases From Head and Neck Squamous Cell Carcinoma: Impact of PET/CT Imaging

D.Basu<sup>1</sup>, B.A.Siegel<sup>1</sup>, B.Nussenbaum<sup>1</sup>  
<sup>1</sup>Washington University, St. Louis, MO

#### \*S049: Role of Routine Posttreatment Surveillance in Squamous Carcinoma of the Oral Cavity

A.K.Hsu<sup>1</sup>, M.C.Coleman<sup>1</sup>, P.Chu<sup>1</sup>, J.O.Boyle<sup>1</sup>, D.H.Kraus<sup>1</sup>,  
A.R.Shaha<sup>1</sup>, B.Singh<sup>1</sup>, R.J.Wong<sup>1</sup>, J.P.Shah<sup>1</sup>, S.G.Patel<sup>1</sup>  
<sup>1</sup>Memorial Sloan-Kettering Cancer Center, New York, NY

#### S050: The Role of Panendoscopy in the Staging of High Risk Head and Neck Squamous Cell Carcinoma Prior to Therapy

T.Bhandari<sup>1</sup>, C.Taneja<sup>1</sup>, J.Koness<sup>1</sup>, H.J.Wanebo<sup>1</sup>  
<sup>1</sup>Roger Williams Medical Center, Providence, RI

#### \*S051: Efficacy of a Selective Policy of Observation in Patients With Clinically Node-Negative T1-2 Carcinoma of the Tongue

S.Ghirardo<sup>1</sup>, P.Chu<sup>1</sup>, J.Boyle<sup>1</sup>, M.Coleman<sup>1</sup>, B.Singh<sup>1</sup>,  
R.Wong<sup>1</sup>, D.Kraus<sup>1</sup>, A.Shaha<sup>1</sup>, J.Shah<sup>1</sup>, S.Patel<sup>1</sup>  
<sup>1</sup>Memorial Sloan-Kettering Cancer Center, NY

#### Discussion

## RESEARCH PROGRAM

### 1040 – 1200 Molecular Biology of Thyroid Cancer

Panel Chair: Bhuvanesh Singh, MD, PhD

#### Location: Salon I

#### 1) Molecular Basis for Thyroid Cancer Progression and Treatment – Bhuvanesh Singh, MD, PhD

#### 2) Molecular Characterization of Differentiated Thyroid Cancer – Thomas J. Giordano, MD, PhD

#### 3) Molecular Approaches to Differentiation of Benign from Malignant Thyroid Neoplasms – Ronald A. Ghossein, MD

#### 4) Targeted Therapy in the Management of Aggressive Thyroid Cancers – Jeffrey N. Myers, MD, PhD

At the conclusion of this event, the participants would be able to:

- Define thyroid cancer as a progressive genetic malady
- Define the role of BRAF mutation in the pathogenesis of thyroid cancer
- Discuss novel targeted approaches that may play a role in thyroid cancer management

## 1200 – 1400 Complimentary Lunch in the Exhibit Hall for Attendees and Exhibit Viewing

Location: Salon III

### Poster Viewing

Location: 6th Floor Breakout Rooms

(Indiana/Iowa, Michigan/Michigan State, Northwestern/Ohio State and Purdue/Wisconsin)

\* Abstract was published in the *Archives of Otolaryngology*

**CLINICAL PROGRAM**

**1400 – 1500 Scientific Session/Abstracts with Emphasis on Endocrine**

**Moderators:** Claudio R. Cernea, MD  
and Richard V. Smith, MD

**Location: Salon II**

**\*S052: Head and Neck Melanoma in the Sentinel Node Era**  
D.Agnese MD<sup>1</sup>, R.Maupin BA<sup>1</sup>, B.Tillman MD<sup>1</sup>, R.D.Pozderac MD<sup>1</sup>, C.Magro MD<sup>1</sup>, M.J.Walker MD<sup>1</sup>  
<sup>1</sup>Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH

**\*S053: Epidemiology and Prognostic Factors of Cutaneous Head and Neck Melanoma: Population-based Study**  
A.Golger<sup>1</sup>, D.S.Young<sup>2</sup>, D.Ghazarian<sup>1</sup>, P.C.Neligan<sup>3</sup>  
<sup>1</sup>University of Toronto, Toronto, ON Canada; <sup>2</sup>University of Alberta, Edmonton, AB Canada; <sup>3</sup>University of Toronto, Canada, ON Canada

**S054: Recurrence and Survival of Patients With Melanoma of the Head And Neck Whose Treatment Included Sentinel Node Biopsy**  
F.Gomez-Rivera<sup>1</sup>, A.A.Santillan-Gomez<sup>1</sup>, A.B.McMurphy<sup>2</sup>, G.Paraskevopoulos<sup>1</sup>, D.B.Roberts<sup>1</sup>, V.G.Prieto<sup>1</sup>, J.N.Myers<sup>1</sup>  
<sup>1</sup>MD Anderson Cancer Center, Houston, TX; <sup>2</sup>MDAnderson Cancer Center, Houston, TX

**Discussion**

**S055: Utility of Sentinel Lymph Node Biopsy in the Management of Scalp Melanoma**  
M.Merzianu<sup>1</sup>, O.H.Iwenofu<sup>1</sup>, T.R.Loree<sup>1</sup>, R.T.Cheney<sup>1</sup>, N.R.Rigual<sup>1</sup>  
<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY

**S056: Clinical And Pathological Predictors of Cervical Node Metastases to Level V in Patients with WDTC**  
M.E.Kupferman<sup>1</sup>, A.Mishra<sup>1</sup>, A.A.Santillan-Gomez<sup>1</sup>, D.Roberts<sup>1</sup>, G.L.Clayman<sup>1</sup>, R.S.Weber<sup>1</sup>  
<sup>1</sup>MD Anderson Cancer Center, Houston, TX

**\*S057: Absorption Spectroscopy Potentially Identifies Carcinoma on Fine-Needle Aspiration Biopsy of Thyroid Nodules**  
O.Parise<sup>1</sup>, D.M.Zezel<sup>2</sup>, F.G.Albero<sup>3</sup>, N.D.Viera Jr<sup>2</sup>, R.Kuhbauche<sup>1</sup>, M.Takenaka<sup>1</sup>, L.VG.Tarelho<sup>2</sup>  
<sup>1</sup>Sirio-Libanes Hospital, Sao Paulo Brazil; <sup>2</sup>Centro de Lasers e Aplicações - IPEN/CNEN, Sao Paulo Brazil; <sup>3</sup>UNESP - Botucatu / Centro de Lasers e Aplicações - IPEN/CNEN, Sao Paulo Brazil

**Discussion**

**RESEARCH PROGRAM**

**1400 – 1500 Scientific Session/Abstracts with Emphasis on Thyroid**

**Moderators:** Gerard M. Doherty, MD and  
Christine G. Gourin, MD

**Location: Salon I**

**S058: Dual EGFR and VEGFR Inhibition with NVP-AEE788 for the Treatment of Aggressive Follicular Thyroid Cancer**  
M.N.Younes<sup>1</sup>, Y.D.Yazici<sup>1</sup>, S.Kim<sup>1</sup>, S.A.Jasser<sup>1</sup>, A.K.El-Naggar<sup>1</sup>, J.N.Myers<sup>1</sup>  
<sup>1</sup>UT MD Anderson Cancer Center, HOUSTON, TX

**S059: Gene Expression Profile of Complete Clinical Response Following Platin-based Induction Chemotherapy**  
F.C.Holsinger<sup>1</sup>, S.Temam<sup>2</sup>, K.R.Coombes<sup>1</sup>, L.Mao<sup>1</sup>  
<sup>1</sup>University of Texas M.D. Anderson Cancer Center, Houston, TX; <sup>2</sup>Institut Gustave-Roussy, Villejuif France

**\*S060: Serum Protein Profile Analysis in Patients With Papillary Thyroid Carcinoma**  
W.H.Moretz III<sup>1</sup>, C.G.Gourin<sup>1</sup>, D.J.Terris<sup>1</sup>, Z.Xia<sup>1</sup>, Z.Liu<sup>1</sup>, P.M.Weinberger<sup>1</sup>, B.Adam<sup>1</sup>  
<sup>1</sup>Medical College of Georgia, Augusta, GA

**Discussion**

**S061: Comparative Genomic Instabilities of Thyroid and Colon Cancers**  
D.L.Stoler<sup>1</sup>, N.J.Nowak<sup>1</sup>, S.Matsui<sup>1</sup>, T.R.Loree<sup>1</sup>, N.R.Rigual<sup>1</sup>, W.L.Hicks, Jr.<sup>1</sup>, S.N.Sait<sup>1</sup>, G.R.Anderson<sup>1</sup>  
<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY

**\*S062: Nuclear, Cytoplasmic Expression of Galectin-3 Is Associated with B-Catenin/Wnt-Pathway Activation in Thyroid Carcinoma**  
P.M.Weinberger<sup>1</sup>, B.Adam<sup>1</sup>, C.G.Gourin<sup>1</sup>, W.Moretz<sup>1</sup>, R.J.Bollag<sup>1</sup>, J.R.Lee<sup>1</sup>, D.J.Terris<sup>1</sup>  
<sup>1</sup>Medical College of Georgia, Augusta, GA

**S063: Incidence of B Type RAF kinase (BRAF), in Papillary and Follicular Subtype Papillary Thyroid Carcinoma**  
B.T.Miller<sup>1</sup>, J.Bentz<sup>2</sup>, R.Leslie<sup>3</sup>, B.Bentz<sup>4</sup>  
<sup>1</sup>University of Utah, Salt Lake City, UT; <sup>2</sup>University of Utah, Department of Pathology, Salt Lake City, VA; <sup>3</sup>University of Utah, Salt Lake City, VA; <sup>4</sup>University of Utah, Division of Otolaryngology, Salt Lake City, UT

**Discussion**

**CLINICAL PROGRAM**

**1500 – 1600 Jatin P. Shah Symposium on Clinical Problems in Head and Neck Surgery**

**Management of Complex Issues in Thyroid Cancer**

**Panel Chair:** Ashok R. Shaha, MD

**Location:** Salon II

Gerard M. Doherty, MD, Thomas V. McCaffrey, MD, PhD and R. Michael Tuttle, MD

- To discuss complex issues in the management of thyroid cancer such as locally advanced thyroid cancer
- The role of PET scan in the follow-up of patients with difficult thyroid problems
- The role of external radiation therapy
- Management of recurrent medullary thyroid cancer
- Management of advanced anaplastic thyroid cancer
- To discuss the issues related to poorly differentiated thyroid cancer

**RESEARCH PROGRAM**

**1500 – 1600 Scientific Session/Abstracts**

**Moderators:** TBD and  
J. Trad Wadsworth, MD

**Location:** Salon I

**S064: Gene Expression Profiles in HPV Infected Head and Neck Cancer**

N.F.Schlecht<sup>1</sup>, R.D.Burk<sup>1</sup>, H.Qian<sup>1</sup>, A.Dunn<sup>1</sup>, N.Kawachi<sup>1</sup>, G.Childs<sup>1</sup>, R.V.Smith<sup>2</sup>, T.J.Belbin<sup>1</sup>

<sup>1</sup>Albert Einstein College of Medicine, Bronx, NY; <sup>2</sup>Montefiore Medical Center, Bronx, NY

**\*S065: Serum Protein Profile Analysis Following Definitive Treatment in Patients with Head and Neck Squamous Cell Carcinoma**

C.G.Gourin<sup>1</sup>, W.H.Moretz III<sup>1</sup>, P.M.Weinberger<sup>1</sup>, Z.Xia<sup>1</sup>, Z.Liu<sup>1</sup>, D.J.Terris<sup>1</sup>, B.Adam<sup>1</sup>

<sup>1</sup>Medical College of Georgia, Augusta, GA

**S066: Amplification and Overexpression of HER-2/neu Gene and Protein in Salivary Duct Carcinomas**

G.Cornolti<sup>1</sup>, D.Lombardi<sup>2</sup>, M.Ungari<sup>1</sup>, M.Morassi<sup>1</sup>, F.Facchetti<sup>1</sup>, P.Nicolai<sup>2</sup>

<sup>1</sup>Department of Pathology, University of Brescia, Brescia Italy;

<sup>2</sup>Department of Otorhinolaryngology, University of Brescia, Brescia Italy

**Discussion**

**\*S067: Successive Aberrations in Protein Expression From Healthy Mucosa to Invasive Head and Neck Cancer**

E.X.Bosch<sup>1</sup>, M.Roesch-Ely<sup>2</sup>, U.Warnken<sup>3</sup>, M.Schnoeizer<sup>4</sup>, M.Nees<sup>5</sup>

<sup>1</sup>Molecular Biology Laboratory, Dep. Of Otolaryngology, Head & Neck Surgery, Unive, Heidelberg Germany; <sup>2</sup>Molecular Biology Laboratory, Dep. Head & Neck Surgery, University of Heidelberg, Heidelberg Germany; <sup>3</sup>Protein Analysis Facility, German Cancer Research Center, Heidelberg Germany; <sup>4</sup>Protein Analysis Facility, German Cancer Research Center, Heidelberg Germany; <sup>5</sup>VTT Biomedical Research Center, 20521 Turku Finland

**S068: High-Resolution Copy Number and Gene Expression Microarray Analyses of Two Sites for Head and Neck Squamous Cell Cancer**

A.K.Jarvinen<sup>1</sup>, R.Autio<sup>2</sup>, S.Haapa-Paananen<sup>3</sup>, M.Wolf<sup>3</sup>, M.Saarela<sup>4</sup>, R.Grénman<sup>5</sup>, O.Kallioniemi<sup>3</sup>, I.Leivo<sup>6</sup>, O.Monni<sup>1</sup>, A.A.Mäkitie<sup>7</sup>

<sup>1</sup>Biomedicum Biochip Center and Institute of Biomedicine, University of Helsinki, Helsinki Finland; <sup>2</sup>Institute of Signal Processing, Tampere University of Technology, Tampere Finland; <sup>3</sup>Medical Biotechnology, VTT Technical Research Centre of Finland, Turku Finland; <sup>4</sup>Institute of Signal Processing, Tampere University of Technology, Tampere Finland; <sup>5</sup>Department of Otorhinolaryngology, Turku University Central Hospital, Turku Finland; <sup>6</sup>Department of Pathology, Helsinki University Central Hospital, Helsinki Finland; <sup>7</sup>Department of Otorhinolaryngology, Helsinki University Central Hospital, Helsinki Finland

**\*S069: Saliva Array-Based Gene Expression Changes in Oral Squamous Cell Carcinoma: Presurgery and Postsurgery**

V.Nabili<sup>1</sup>, T.Yu<sup>2</sup>, X.Zhou<sup>2</sup>, N.Park<sup>2</sup>, B.Brinkman<sup>2</sup>, N.Pungpravat<sup>2</sup>, E.Abemayor<sup>1</sup>, D.T.Wong<sup>2</sup>

<sup>1</sup>Division of Head and Neck Surgery - Otolaryngology, UCLA Medical Center, Los Angeles, CA; <sup>2</sup>Yip Center for Head and Neck Oncology Research, UCLA School of Dentistry, Los Angeles, CA

**Discussion**

\* Abstract was published in the *Archives of Otolaryngology*

**CLINICAL PROGRAM**

**1600 – 1700 Scientific Session/Abstracts with Emphasis on Endocrine**  
**Moderators:** Timothy M. McCulloch, MD and Maisie Shindo, MD

**Location: Salon II**

**\*S070: Phase II Study of Combretastatin A4 Phosphate (CA4P) in Patients With Advanced Anaplastic Thyroid Carcinoma (ATC)**

P.S.Savvides<sup>1</sup>, M.Cooney<sup>1</sup>, S.S.Agarwala<sup>2</sup>, D.Wang<sup>1</sup>, N.Pagedar<sup>1</sup>, F.Johnson<sup>1</sup>, S.Bhakta<sup>1</sup>, P.Lavertu<sup>1</sup>, J.Ortiz<sup>1</sup>, S.C.Remick<sup>1</sup>  
<sup>1</sup>CASE Comprehensive Cancer Center, Cleveland, OH;  
<sup>2</sup>University of Pittsburgh Cancer Institute, Pittsburgh, PA

**\*S071: Is There a Role for FDG-PET/CT in Cytologically Indeterminate Thyroid Nodules?**

N.W.Hales<sup>1</sup>, G.A.Krempf<sup>1</sup>, J.E.Medina<sup>1</sup>  
<sup>1</sup>The University of Oklahoma Health Sciences Center, Oklahoma City, OK

**\*S072: Pre-operative FDG-PET Imaging to Assess the Malignant Potential of Follicular Neoplasms of the Thyroid**

R.B.Smith<sup>1</sup>, R.A.Robinson<sup>1</sup>, H.T.Hoffman<sup>1</sup>, M.M.Graham<sup>1</sup>  
<sup>1</sup>University of Iowa Hospital and Clinics, Iowa City, IA

**Discussion**

**S073: Incidence of Vocal Cord Paralysis With and Without Recurrent Laryngeal Nerve Monitoring During Thyroidectomy**

N.Chheda<sup>1</sup>, M.Shindo<sup>1</sup>  
<sup>1</sup>S.U.N.Y. @ Stony Brook, Stony Brook, NY

**\*S074: Risk Factors for Well-Differentiated Thyroid Carcinoma in Patients With Thyroid Nodular Disease**

S.N.Raza<sup>1</sup>, C.E.Palme<sup>1</sup>, F.T.Hall<sup>1</sup>, S.Eski<sup>1</sup>, J.L.Freeman<sup>1</sup>  
<sup>1</sup>University of Toronto, Toronto, ON Canada

**\*S075: Aggressive Detection and Resection of Recurrent or Persistent I-131-Resistant Papillary Thyroid Cancer**

O.H.Al-Saif<sup>1</sup>, W.B.Farrar<sup>1</sup>, M.B.Bloomston<sup>1</sup>, M.D.Ringel<sup>1</sup>, R.T.Kloos<sup>1</sup>  
<sup>1</sup>Ohio State University, Columbus, OH

**Discussion**

**RESEARCH PROGRAM**

**1600 – 1700 Scientific Session/Abstracts**  
**Moderators:** Ellie Maghami, MD and Kopal N. Patel, MD

**Location: Salon I**

**\*S076: Epigenetics of Head and Neck Cancer: The Role of Pyrosequencing**

R.J.Shaw<sup>1</sup>, T.Liloglou<sup>2</sup>, S.Rogers<sup>3</sup>, J.Brown<sup>3</sup>, D.Lowe<sup>4</sup>, J.K.Field<sup>2</sup>, J.M.Risk<sup>5</sup>  
<sup>1</sup>Head & Neck Surgery Unit, Liverpool United Kingdom;  
<sup>2</sup>University of Liverpool Cancer Research Centre, Roy Castle Lung Cancer Research, Liverpool United Kingdom; <sup>3</sup>Head & Neck Surgery, University Hospital Aintree, Liverpool, UK, Liverpool United Kingdom; <sup>4</sup>Medical Statistics, Head & neck Surgery, University Hospital Aintree, Liverpool, Liverpool United Kingdom; <sup>5</sup>Molecular Oncology & Genetics, School of Dental Sciences, University of Liverpool, Liverpool United Kingdom

**\*S077: An Epigenetically Derived Monoclonal Origin for Recurrent Laryngeal Papillomas**

M.J.Worsham<sup>1</sup>, L.E.Vaught<sup>1</sup>, K.Chen<sup>1</sup>, V.Shah<sup>1</sup>, J.Kunjoonju<sup>1</sup>, V.P.Schweitzer<sup>1</sup>, G.Gardner<sup>1</sup>, M.S.Benninger<sup>1</sup>  
<sup>1</sup>Henry Ford Hospital, Detroit, MI

**\*S078: Promotor Methylation Status of Tumor Suppressor and Cell Adhesion Genes In Oral Squamous Cell Carcinomas**

J.Houck<sup>1</sup>, P.Lohavanichbutr<sup>1</sup>, B.Yueh<sup>2</sup>, E.Mendez<sup>2</sup>, N.Futran<sup>2</sup>, M.Upton<sup>2</sup>, S.M.Schwartz<sup>1</sup>, C.Chen<sup>1</sup>  
<sup>1</sup>Fred Hutchinson Cancer Research Center, Seattle, WA;  
<sup>2</sup>University of Washington, Seattle, WA

**Discussion**

**\*S079: Methylation of Multiple Genes as Diagnostic and Therapeutic Markers in Primary HNSCC**

R.Sawhney<sup>1</sup>, K.Chen<sup>1</sup>, M.Khan<sup>1</sup>, M.S.Benninger<sup>1</sup>, M.J.Worsham<sup>1</sup>  
<sup>1</sup>Henry Ford Hospital, Detroit, MI

**\*S080: Tumor Cells Adapt More Quickly to High Levels of Nitric Oxide (NO) and Become More Malignant in High NO Environment**

K.Elseth<sup>1</sup>, B.G.Bentz<sup>2</sup>, B.J.Vesper<sup>1</sup>, M.Yao<sup>3</sup>, K.Haines III<sup>4</sup>, K.Altman<sup>5</sup>, J.Radosevich<sup>1</sup>  
<sup>1</sup>Center for Molecular Biology of Oral Diseases, University of Illinois at Chicago, Chicago, IL; <sup>2</sup>Department of Surgery, University of Utah, Salt Lake City, UT; <sup>3</sup>Department of Otolaryngology-Head and Neck Surgery, University of Illinois at Chicago, Chicago, IL; <sup>4</sup>Department of Pathology, Northwestern University, Chicago, IL; <sup>5</sup>Department of Otolaryngology-Head and Neck Surgery, Mt. Sinai School of Medicine, New York, NY

**\*S081: Loss of Imprinting of PEG1/MEST, IGF2 in Head and Neck Cancer**

H.Kataoka<sup>1</sup>, S.Nakano<sup>1</sup>, M.Oshimura<sup>1</sup>, Y.Kunimoto<sup>1</sup>, H.Kitano<sup>1</sup>  
<sup>1</sup>Tottori University, Yonago Japan

**Discussion**

1700 – 1830 **Poster Tours**

**Location: 6th Floor Breakout Rooms**

**POSTER TOUR: CLINICAL 3**

**Tour Leader: Nestor R. Rigual, MD**

**Location: Northwestern/Ohio State**

**P121: The Use of Microvascular Tissue in Reconstruction of the Lateral Skull Base**

D.J.Arnold<sup>1</sup>, D.T.Weed<sup>2</sup>, F.J.Civantos<sup>2</sup>

<sup>1</sup>University of Miami, Coral Gables, FL; <sup>2</sup>University of Miami, Miami, FL

**P122: Electroglottography-Based Videostroboscopic Assessment of Laryngectomy Prosthetic Speech**

R.Kazi<sup>1</sup>, A.Singh<sup>2</sup>, G.Mullan<sup>1</sup>, R.Venkitaraman<sup>1</sup>, C.Nutting<sup>1</sup>, P.Clarke<sup>1</sup>, P.Rhys-Evans<sup>1</sup>, K.Harrington<sup>1</sup>

<sup>1</sup>Royal Marsden Hospital, London United Kingdom; <sup>2</sup>Royal Marsden Hospital, London

**\*P123: Proteomic Screening of Saliva in Head and Neck Squamous Carcinoma: A Potential Diagnostic and Screening Applications**

K.Ohshiro<sup>1</sup>, R.Kobayashi<sup>1</sup>, G.L.Clayman<sup>1</sup>, D.I.Rosenthal<sup>1</sup>, R.S.Weber<sup>1</sup>, A.K.El-Naggar<sup>1</sup>

<sup>1</sup>The University of Texas M.D. Anderson Cancer Center, Houston, TX

**\*P124: Cost Savings of Patients With a MACIS Score Lower Than 6 When Radioactive Iodine is Not Given**

P.Pace-Asciak<sup>1</sup>, R.J.Payne<sup>1</sup>, J.S.Eski<sup>1</sup>, P.Walfish<sup>1</sup>, M.Damani<sup>1</sup>, J.Freeman<sup>1</sup>

<sup>1</sup>Mount Sinai Hospital, Department of Otolaryngology, Toronto, ON Canada

**P125: Bone Anchored Mucosal Flap for Reconstruction of Floor of Mouth and Gingiva: A Pilot Study**

J.A.Akervall<sup>1</sup>, L.Greif<sup>2</sup>

<sup>1</sup>Rontal Clinic, Farmington Hills, MI; <sup>2</sup>Dept of ENT, University Hospital, Lund Sweden

**P126: Quality of Life Is Acceptable in Locally Advanced Head and Neck Cancers Treated With Aggressive Regimen of Chemoradiation**

C.Taneja<sup>1</sup>, P.Somasundar<sup>1</sup>, O.Nadeem<sup>1</sup>, E.Carroll<sup>1</sup>, K.Radie-Keane<sup>2</sup>, H.J.Wanebo<sup>1</sup>, S.Stager<sup>1</sup>

<sup>1</sup>Roger Williams Medical Center, Providence, RI; <sup>2</sup>Northmain Radiology, Providence, RI

**\*P127: Radical Radiation for Unknown Primary Squamous Cancer Yields High Control But Has Major Toxicity Suggesting Need for a New Treatment Paradigm**

H.J.Wanebo<sup>1</sup>, T.Bhandari<sup>1</sup>, K.Radie-Keane<sup>2</sup>, R.Brotman<sup>3</sup>, R.Rathore<sup>1</sup>

<sup>1</sup>Roger Williams Medical Center, Providence, RI; <sup>2</sup>NorthMain Radiation Oncology, Providence, RI; <sup>3</sup>NorthMain Radiation Oncology, Providence, RI

**\*P128: Impact of Preepiglottic Space Tumor Involvement on Concurrent Chemoradiation Therapy for Squamous Cell Carcinoma**

M.Rizzi<sup>1</sup>, W.T.Lee<sup>1</sup>, R.R.Lorenz<sup>1</sup>, B.G.Wood<sup>1</sup>, M.Strome<sup>1</sup>, J.P.Saxton<sup>1</sup>, D.J.Adelstein<sup>1</sup>, R.M.Esclamado<sup>1</sup>

<sup>1</sup>Cleveland Clinic, Cleveland, OH

**\*P129: Toxicity Outcomes in Intensity-Modulated Radiation Therapy vs 3-Dimensional Conformal Radiotherapy for Head and Neck Squamous Cell Carcinoma With Unknown Primary**

J.A.Call<sup>1</sup>, D.Wang<sup>1</sup>, S.Firat<sup>1</sup>, R.W.Byhardt<sup>1</sup>, S.Wong<sup>2</sup>, B.H.Campbell<sup>3</sup>, C.J.Schultz<sup>1</sup>

<sup>1</sup>Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; <sup>2</sup>Department of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, WI; <sup>3</sup>Department of Otolaryngology, Medical College of Wisconsin, Milwaukee, WI

**P130: Safety Initiative for Surgically Altered Airways: The Bedside UCSF Emergency Airway Access Form**

I.H.El-Sayed<sup>1</sup>, S.Ryan<sup>1</sup>, P.Kelly<sup>1</sup>, J.Barba<sup>1</sup>, J.Petryk<sup>1</sup>, R.Rosanne<sup>1</sup>, H.Schell<sup>1</sup>

<sup>1</sup>University of California, San Francisco, San Francisco, CA

**\*P131: Rehabilitation Exercises Improve Cancer Treatment Outcomes**

P.S.Malhotra<sup>1</sup>, D.Reiter<sup>1</sup>

<sup>1</sup>Thomas Jefferson University Hospital, Philadelphia, PA

**P132: WITHDRAWN**

**\*P133: Pectoralis Major Flap for the Reconstruction of Composite Lateral Temporal Bone Defects: Reaching the Temporal Line**

V.A.Resto<sup>1</sup>, D.G.Deschler<sup>2</sup>

<sup>1</sup>University of Texas Medical Branch, Galveston, TX; <sup>2</sup>Massachusetts Eye and Ear Infirmary, Boston, MA

**\*P134: Combined Transoral Laser Microsurgery and Intensity Modulated Postoperative Radiation Therapy for Head and Neck Cancer**

W.L.Thorstad<sup>1</sup>, B.Nussenbaum<sup>1</sup>, D.R.Adkins<sup>1</sup>, B.H.Haughey<sup>1</sup>

<sup>1</sup>Washington University Medical Center, Saint Louis, MO

**\*P135: Oropharyngeal Cancer Associated With Oncogenic Human Papilloma Virus Is Clinically Unique and Portends Improved Survival**

J.A.Ernster<sup>1</sup>, C.Sciotto<sup>2</sup>, M.O'Brien<sup>3</sup>, L.Robinson<sup>2</sup>, T.Wilson<sup>2</sup>

<sup>1</sup>Colorado Otolaryngology Associates, Colorado Springs, CO; <sup>2</sup>Penrose-St. Francis Health Care System, Colorado Springs, CO; <sup>3</sup>University of Colorado Health Sciences Center, Denver, CO

- \*P136: Free Jejunal or Ileocolic Flap Transfers as a Method of Reconstruction Following Hypopharyngeal Tumor Resection**  
S.Nazarewski<sup>1</sup>, J.Szmdt<sup>1</sup>, T.Grochowicki<sup>1</sup>, Z.Galazka<sup>1</sup>, E.Osuch-Wojcikiewicz<sup>2</sup>, T.Jakimowicz<sup>1</sup>, J.Nyckowska<sup>2</sup>, A.Bruzgielewicz<sup>2</sup>, P.Checinski<sup>2</sup>  
<sup>1</sup>Dept. of General, Vascular & Transplant Surgery, The Medical Univ. of Warsaw, Warsaw Poland; <sup>2</sup>Dept. of Otorhinolaryngology, The Medical Univ. of Warsaw, Warsaw Poland
- \*P137: Validation of Our Histological Risk Assessment Model: An Interim Analysis**  
M.Brandwein-Gensler<sup>1</sup>, A.Thielken<sup>2</sup>, R.V.Smith<sup>1</sup>, A.Negassa<sup>3</sup>, C.Sarta<sup>1</sup>, R.Owen<sup>1</sup>, B.Schiff<sup>1</sup>, J.C.Smith<sup>1</sup>, M.Prystowsky<sup>1</sup>  
<sup>1</sup>Montefiore Medical Center, Bronx, NY; <sup>2</sup>Johannes Gutenberg, Mainz Germany; <sup>3</sup>Albert Einstein College of Medicine, Bronx, NY
- P138: Systematic Review and Meta-analysis of Follow-up Protocols and Cancer Progression of Oral Dysplasia**  
H.M.Mehanna<sup>1</sup>, T.Rattay<sup>2</sup>, J.Smith<sup>2</sup>, R.Srinivasan<sup>2</sup>, R.Sandhu<sup>2</sup>  
<sup>1</sup>University Hosp Coventry & Warwickshire, Coventry United Kingdom; <sup>2</sup>UHCW, Coventry United Kingdom
- \*P139: Paratracheal Node Dissection in the Management of Well-Differentiated Thyroid Cancer**  
C.M.Slough<sup>1</sup>, S.Weber<sup>1</sup>, K.Schuff<sup>1</sup>, M.Samules<sup>1</sup>, J.I.Cohen<sup>2</sup>  
<sup>1</sup>Oregon Health Sciences University, Portland, OR; <sup>2</sup>Oregon Health Sciences University, Portland, OR
- \*P140: Upper Aerodigestive Tract Venous Malformations**  
J.Y.Suen<sup>1</sup>, G.T.Richter<sup>2</sup>, L.M.Buckmiller<sup>3</sup>  
<sup>1</sup>University of Arkansas for Medical Sciences, Little Rock, AR; <sup>2</sup>University of Arkansas for Medical Sciences, Little Rock, AR; <sup>3</sup>University of Arkansas for Medical Sciences, Little Rock, AR
- P141: Outcome and Morbidity From Salvage Neck Dissection and Interstitial Brachytherapy for Recurrent Head and Neck Cancers**  
M.E.Kupferman<sup>1</sup>, W.Morrison<sup>1</sup>, D.Roberts<sup>1</sup>, R.S.Weber<sup>1</sup>  
<sup>1</sup>MD Anderson Cancer Center, Houston, TX
- P142: Merkel Cell Carcinoma of the Head and Neck Region**  
A.Popovtzer<sup>1</sup>, O.Purim<sup>2</sup>, B. BRENNER<sup>3</sup>, R. FEINMESSER<sup>4</sup>, M.FEINMESSER<sup>5</sup>, A.Sulkes<sup>6</sup>, E.Fenig<sup>7</sup>  
<sup>1</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel; <sup>2</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel; <sup>3</sup>campus Beilinson Rabin Medical center, Israel, PETAH TIKVA Israel; <sup>4</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel; <sup>5</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel; <sup>6</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel; <sup>7</sup>campus Beilinson Rabin Medical center, PETAH TIKVA Israel
- \*P143: Importance of Anterior Commissure in Recurrence of Early Glottic Cancer After Laser Endoscopic Resection**  
C.T.Chone<sup>1</sup>, E.Yonehara<sup>1</sup>, J.E.Martins<sup>1</sup>, F.M.Gripp<sup>1</sup>, A.Altemani<sup>2</sup>, A.N.Crespo<sup>1</sup>  
<sup>1</sup>Department of Otolaryngology Head and Neck, State University of Campinas, Campinas Brazil; <sup>2</sup>Department of Surgical Pathology, State University of Campinas, Campinas Brazil
- \*P144: Sebaceous Carcinoma of the Head and Neck: Outcome of 15 Consecutive Cases Treated in a Single Institution**  
U.B.Toscano<sup>1</sup>, F.L.Dias<sup>1</sup>, R.A.Lima<sup>1</sup>, R.A.Arcuri<sup>1</sup>, M.M.Barbosa<sup>1</sup>, I.S.Gisler<sup>1</sup>, F.G.Botelho, Jr<sup>1</sup>, J.Kligerman<sup>1</sup>, K.L.Fernandes<sup>1</sup>, A.L.C.Costa<sup>1</sup>  
<sup>1</sup>Brazilian National Cancer Institute/INCA, Rio de Janeiro Brazil
- P145: Swallowing Analysis Before and After Thyroidectomy**  
J.M.Carvalho<sup>1</sup>, F.N.Arakaki<sup>1</sup>, P.E.Ciocchi<sup>1</sup>, L.Arakawa-Sugueno<sup>1</sup>, D.M.Capobianco<sup>1</sup>, M.V.Kulcsar<sup>1</sup>, M.Sampaio<sup>1</sup>, L.G.Brandão<sup>1</sup>, A.R.Ferraz<sup>1</sup>, P.Michaluart<sup>1</sup>  
<sup>1</sup>University of São Paulo Medical School, São Paulo Brazil
- P146: Incidence and Survival Rates for Young Blacks With Nasopharyngeal Carcinoma in the US**  
L.M.Richey<sup>1</sup>, A.F.Olshan<sup>2</sup>, J.R.George<sup>1</sup>, C.G.Shores<sup>3</sup>, A.M.Zanation<sup>3</sup>, T.Cannon<sup>3</sup>, M.C.Weissler<sup>3</sup>  
<sup>1</sup>Doris Duke Clinical Research Fellow- UNC Chapel Hill School of Medicine, Chapel Hill, NC; <sup>2</sup>UNC School of Public Health, Chapel Hill, NC; <sup>3</sup>UNC Department of Otolaryngology- Head and Neck Surgery, Chapel Hill, NC
- \*P147: Analysis of Formant Frequencies in Patients With Oral or Oropharyngeal Cancers Treated by Glossectomy**  
R.Kazi<sup>1</sup>, V.Prasad<sup>1</sup>, J.Kanagalingam<sup>1</sup>, C.Georgalas<sup>1</sup>, R.Venkitaraman<sup>1</sup>, C.Nutting<sup>1</sup>, P.Clarke<sup>1</sup>, P.Rhys-Evans<sup>1</sup>, K.Harrington<sup>1</sup>  
<sup>1</sup>Royal Marden Hospital, London United Kingdom
- P148: WITHDRAWN**
- P149: Study of Inverted Papilloma in Rural Based Hospital in Eastern Nepal**  
S.Bhandary<sup>1</sup>, R.K.Singh<sup>2</sup>, A.Sinha<sup>3</sup>  
<sup>1</sup>BP Koirala Institute of Health Sciences, Dharan Nepal; <sup>2</sup>BP Koirala Institute of Health Sciences, Dharan Nepal; <sup>3</sup>BP Koirala Institute of Health sciences, Dharan Nepal
- P150: Photodynamic Therapy and the Treatment of Early Squamous Cell Carcinomas of the Larynx and Oral Cavity**  
M.A.Biel<sup>1</sup>  
<sup>1</sup>Ear, Nose and Throat SpecialtyCare of MN, Minneapolis, MN

**POSTER TOUR: CLINICAL 4**

**Tour Leader: Bruce J. Davidson, MD**

**Location: Purdue/Wisconsin**

**\*P151: Intraoperative Localization of the Marginal Mandibular Nerve: A Landmark Study**

H.Seikaly<sup>1</sup>, J.Krepelka<sup>1</sup>, C.Diamond<sup>1</sup>, R.Hart<sup>1</sup>, J.R.Harris<sup>2</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>University of Alberta, Edmonton, AB Canada

**\*P152: Treatment of Dysplastic Oral Mucosal Lesions With a New Cell-Cycle Inhibiting Agent**

M.Pandey<sup>1</sup>, R.Chih.Huang<sup>2</sup>, K.M.Nair<sup>3</sup>  
<sup>1</sup>Institute of Medical Sciences, Varanasi India; <sup>2</sup>Johns Hopkins University, Baltimore; <sup>3</sup>Regional Cancer Centre, Trivandrum India

**\*P153: Management of the NO Neck: Failure Rates and Salvageability After Surgery, Irradation, or Observation**

S.L.Collins<sup>1</sup>, K.Muzaffar<sup>2</sup>  
<sup>1</sup>Washington Univ. Sch. of Med - Dept Otol/HNS, St. Louis, MO; <sup>2</sup>Loyola Univ of Chicago Med Ctr - Dept Oto/HNS, Maywood, IL

**P154: Race As an Independent Factor for Advanced Oropharyngeal Cancer Outcomes for Treatment With Combined Chemoradiation**

K. Settle<sup>1</sup>, J.S.Wolf<sup>2</sup>, M.Suntharalingam<sup>2</sup>, R.J.Taylor<sup>2</sup>  
<sup>1</sup>University of Maryland School of Medicine, Baltimore, MD; <sup>2</sup>University of Maryland School of Medicine, Baltimore

**\*P155: Intensity-Modulated Radiation Therapy for Head and Neck Cancers: Acute Toxic Effects and Early Outcome Data**

J.M.Watkins<sup>1</sup>, A.K.Sharma<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**P156: Surgical Management of Lingual Arteriovenous Malformations**

G.T.Richter<sup>1</sup>, L.M.Buckmiller<sup>2</sup>, P.E.North<sup>3</sup>, C.A.James<sup>4</sup>, M.Waner<sup>5</sup>, J.Y.Suen<sup>2</sup>  
<sup>1</sup>University of Arkansas for Medical Sciences, Little Rock, AR; <sup>2</sup>University of Arkansas for Medical Sciences, Little Rock, AR; <sup>3</sup>Children's Hospital of Wisconsin, Milwaukee, WI; <sup>4</sup>University of Arkansas for Medical Sciences, Little Rock, AR; <sup>5</sup>Vascular Birthmarks Institute of New York, New York, NY

**\*P157: Intraoperative Frozen Section Analysis for Follicular Neoplasm of the Thyroid: Is It Worth the Effort?**

J.C.Nau<sup>1</sup>, D.Williams<sup>1</sup>, M.Fleming<sup>1</sup>, E.J.Lentsch<sup>1</sup>, J.M.Bumpous<sup>1</sup>, M.B.Flynn<sup>1</sup>  
<sup>1</sup>University of Louisville, Louisville, KY

**\*P158: Consequences of Chewing Habits in Gujrat, India**

G.J.Parmar<sup>1</sup>  
<sup>1</sup>Government Dental College and Hospital, Ahmedabad India

**\*P159: Salvage Surgery After Organ Preservation Therapy in Patients with Stage III or IV Head and Neck Squamous Cell Carcinoma**

F.L.Dias<sup>1</sup>, R.A.Lima<sup>1</sup>, K.L.Fernandes<sup>1</sup>, A.L.C.Costa<sup>1</sup>, T.P.Farias<sup>1</sup>, J.Kligerman<sup>1</sup>, D.Herchenhorn<sup>1</sup>, U.B.Toscano<sup>1</sup>  
<sup>1</sup>Brazilian National Cancer Institute/INCA, Rio de Janeiro Brazil

**\*P160: Frequency and Types of Human Papilloma Virus in Head and Neck Squamous Cell Carcinoma**

F.Gallegos-Hernandez<sup>1</sup>, D.Hernandez<sup>1</sup>, E.Paredes<sup>1</sup>, R.Flores<sup>1</sup>, G.Minauro<sup>1</sup>, H.Arias<sup>1</sup>, M.Hernandez<sup>1</sup>, J.Resendiz<sup>1</sup>, T.Apresa<sup>1</sup>, M.Aguilar<sup>1</sup>  
<sup>1</sup>Hospital de Oncologia, Mexico Mexico

**P161: Phase I Study of Intratumoral Injection of M.Leprae HSP-65 DNA in Patients With HNSCC Refractory to Standard Treatment**

P.Michaluart<sup>1</sup>, K.Abdallah<sup>1</sup>, F.Lima<sup>1</sup>, R.Smith<sup>1</sup>, R.A.Moyses<sup>1</sup>, C.Chammas<sup>1</sup>, R.Gomes<sup>1</sup>, A.R.Ferraz<sup>1</sup>, J.Kalil<sup>1</sup>, C.L.Silva<sup>2</sup>  
<sup>1</sup>University of São Paulo Medical School, São Paulo Brazil; <sup>2</sup>University of São Paulo, Ribeirão Preto Medical School, Ribeirão Preto Brazil

**P162: Lymphoscintigraphy and Sentinel Lymph Node Biopsy for Merkel Cell Carcinoma of the Head and Neck**

Y.Shnayder, MD<sup>1</sup>, A.Bared, MD<sup>1</sup>, F.J.Civantos, MD, FACS<sup>1</sup>, D.T.Weed, MD<sup>1</sup>, D.J.Arnold, MD<sup>1</sup>, W.J.Goodwin, MD, FACS<sup>1</sup>  
<sup>1</sup>University of Miami School of Medicine, Miami, FL

**P163: WITHDRAWN**

**\*P164: Extrathyroidal Extension in Well-Differentiated Thyroid Cancer as a Predictor of Outcome Measures**

A.Hu<sup>1</sup>, R.J.Payne<sup>1</sup>, J.Clarke<sup>1</sup>, S.Eski<sup>1</sup>, P.G.Walfish<sup>1</sup>, J.L.Freeman<sup>1</sup>  
<sup>1</sup>University of Toronto, Toronto, ON Canada

**P165: The Utility of Routine Thyroid Gland Evaluation Prior to Partial Laryngectomy: Why Is It Important?**

T.Y.Farrag<sup>1</sup>, F.R.Lin<sup>1</sup>, C.W.Cummings<sup>1</sup>, J.J.Sciubba<sup>1</sup>, W.W.koch<sup>1</sup>, R.P.Tufano<sup>1</sup>  
<sup>1</sup>Johns Hopkins University School of Medicine, Baltimore, MD

**\*P166: Histopathological Analysis of Cystic Metastasis in Head and Neck Squamous Cell Carcinoma**

F.Yao<sup>1</sup>, A.D.Francis<sup>1</sup>, J.Li<sup>1</sup>, G.Har-Ei<sup>1</sup>  
<sup>1</sup>SUNY Brooklyn, Brooklyn, NY

**P167: A Systematic Approach to the Reconstruction of the Chin and Lower-Lip Complex Following Ablative Surgery**

C.E.Stewart<sup>1</sup>, M.L.Urken<sup>2</sup>  
<sup>1</sup>Beth Israel Medical Center, New York, NY; <sup>2</sup>Beth Israel Medical Center, NYC, NY

\* Abstract was published in the *Archives of Otolaryngology*

- \*P168: Parathyroidectomy in Patients With Primary Hyperparathyroidism and Negative Findings on Technecium Tc 99m Sestamibi Localization Scan**  
K.Vasyukevich<sup>1</sup>, T.J.Ow<sup>1</sup>, R.C.Goldfarb<sup>2</sup>, D.K.Frank<sup>2</sup>  
<sup>1</sup>Montefiore Medical Center, Bronx, NY; <sup>2</sup>Beth Israel Medoc; Center, New York, NY
- P169: Influence of Tumor Grade on Patient Treatment and Outcome in Mucoepidermoid Carcinoma**  
M.A.Nance<sup>1</sup>, R.L.Ferris<sup>1</sup>, J.T.Johnson<sup>1</sup>, E.N.Myers<sup>1</sup>, D.E.Eibling<sup>1</sup>, S.Y.Lai<sup>1</sup>  
<sup>1</sup>University of Pittsburgh, Pittsburgh, PA
- \*P170: The Clavipectoral Osteomyocutaneous Free Flap in Oromandibular Reconstruction**  
H.Seikaly<sup>1</sup>, A.Moshaver<sup>1</sup>, J.Dumper<sup>1</sup>, J.Chau<sup>2</sup>, C.H.Karen<sup>3</sup>, J.R.Harris<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>University of Alberta, Edmonton, AB Canada; <sup>3</sup>University of Colombia, Colombia, MO
- \*P171: Stapler Application for Pharyngeal Closure After Total Laryngectomy**  
F.Walder<sup>1</sup>, C.N.Lehn<sup>2</sup>, F.D.Leonhardt<sup>1</sup>, R.M.Takimoto<sup>1</sup>, O.Cervantes<sup>1</sup>, M.Abrahão<sup>1</sup>  
<sup>1</sup>Federal University of São Paulo-Paulista School of Medicine, São Paulo Brazil; <sup>2</sup>Head and Neck Service of Heliópolis Hospital, São Paulo Brazil
- P172: Ambulatory Transoral Brush Biopsies for Nasopharyngeal Carcinoma Screening**  
R.Ng<sup>1</sup>, R.Ngan<sup>2</sup>, W.Wei<sup>3</sup>, W.Lau<sup>2</sup>, H.Dosch<sup>4</sup>, M.Gullane<sup>5</sup>  
<sup>1</sup>Centenary Health Sciences Centre, Markam, ON Canada; <sup>2</sup>Queen Elizabeth Hospital, Hong Kong Hong Kong; <sup>3</sup>Queen Mary Hospital, Hong Kong Hong Kong; <sup>4</sup>The Hospital for Sick Children, Toronto, ON Canada; <sup>5</sup>University Health Network, Toronto General Hospital, Toronto, ON Canada
- P173: Reconstruction of Oral Cavity With Radial Forearm Free Flap: Functional Aspects and Flap Design**  
M.Kim<sup>1</sup>, Y.Joo<sup>1</sup>, Y.Park<sup>1</sup>, D.Sun<sup>1</sup>, S.Cho<sup>1</sup>  
<sup>1</sup>The Catholic University of Korea, Seoul Republic of Korea
- P174: Laryngeal Papillomatosis: Clinico Epidemiologic Aspects- 24 Years Study**  
V.V.Reddy<sup>1</sup>, V.--k<sup>2</sup>  
<sup>1</sup>Osmania Medical college, Koti, Hyderabad, A.P., Hyderabad, India India; <sup>2</sup>Osmania Medical College, Kothi, Hyderabad, Hyderabad India
- \*P175: The Use of Medical Modeling in Head and Neck Reconstruction**  
H.Seikaly<sup>1</sup>, J.Wolfaardt<sup>1</sup>, R.Hart<sup>1</sup>, J.R.Harris<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada
- P176: Withdrawn**
- P177: Rapid Superselective High-Dose Cisplatin Infusion With Concomitant Radiotherapy for Advanced Hypopharyngeal Cancer**  
J.Furusawa<sup>1</sup>, A.Homma<sup>1</sup>, F.Suzuki<sup>1</sup>, Y.Furuta<sup>1</sup>, S.Fukuda<sup>1</sup>  
<sup>1</sup>Hokkaido University, Sapporo Japan
- P178: Management of Arterial Rupture After Upper Mediastinal Dissection**  
S.Hirano<sup>1</sup>, K.Nagahara<sup>2</sup>, S.Moritani<sup>2</sup>, M.Kitamura<sup>3</sup>, S.Takagita<sup>3</sup>  
<sup>1</sup>Kyoto University Graduate School of Medicine, Kyoto Japan; <sup>2</sup>Institute for Head and Neck Surgery, Kusatsu General Hospital, Kyoto Japan; <sup>3</sup>Department of Otolaryngology/Bronchoesophagology, NHO Kyoto Medical Center, Kyoto Japan
- P179: The Submental Flap: A Modified Technique for Training Residents**  
U.A.Patel<sup>1</sup>, S.W.Bayles<sup>2</sup>, R.E.Hayden<sup>3</sup>  
<sup>1</sup>University of Illinois, Chicago, IL; <sup>2</sup>Virginia Mason Medical Center, Seattle, WA; <sup>3</sup>Mayo Clinic, Scottsdale, AZ
- P180: Extratemporal Facial Nerve Schwannoma Mimicking Benign Parotid Tumors**  
Z.M.Soler<sup>1</sup>, D.D.Reh<sup>1</sup>, M.K.Wax<sup>1</sup>, P.E.Andersen<sup>1</sup>  
<sup>1</sup>Oregon Health & Sciences University, Portland, OR

## POSTER TOUR: TRANSLATIONAL RESEARCH

**Tour Leader: Wendell G. Yarbrough, MD**

**Location: Indiana/Iowa**

**\*P181: Combination Tumor Antigen-Targeted Immunotherapy in HPV-16-Positive Head and Neck Squamous Cell Carcinoma**

H.Kim<sup>1</sup>, J.Wang<sup>1</sup>, A.Lopez-Albaitero<sup>1</sup>, R.L.Ferris<sup>1</sup>

<sup>1</sup>Department of Otolaryngology at University of Pittsburgh Cancer Institute, Pittsburgh, PA

**\*P182: Clinical Application of Epigenetic Biomarkers in Head and Neck Cancer**

R.J.Shaw<sup>1</sup>, G.Hall<sup>2</sup>, T.Liloglou<sup>3</sup>, S.Rogers<sup>4</sup>, J.Brown<sup>5</sup>, J.K.Field<sup>3</sup>, J.M.Risk<sup>6</sup>

<sup>1</sup>Head & Neck Surgery Unit, Liverpool United Kingdom; <sup>2</sup>Department of Head & Neck Pathology, University of Liverpool, Liverpool United Kingdom; <sup>3</sup>University of Liverpool Cancer Research Centre, Roy Castle Lung Cancer Research, Liverpool United Kingdom; <sup>4</sup>Head & Neck Surgery, University Hospital Aintree, Liverpool United Kingdom; <sup>5</sup>Head & Neck Surgery, University Hospital Aintree, Liverpool United Kingdom; <sup>6</sup>Molecular Oncology & Genetics, University of Liverpool, Liverpool United Kingdom

**P183: Genetic Abnormalities Associated With Chemoradiation-Resistance of Head and Neck Squamous Cell Carcinoma**

G.Van den Broek<sup>1</sup>, V.Wreesmann<sup>1</sup>, M.Van den Brekel<sup>1</sup>, C.Rasch<sup>1</sup>, A.Balm<sup>1</sup>, P.Rao<sup>2</sup>

<sup>1</sup>Netherlands Cancer Institute, Amsterdam The Netherlands; <sup>2</sup>Texas Children's Cancer Center, Houston, TX

**P184: Gene Expression Profiling to Predict Outcome After Chemoradiation in HNSCC**

J.Pramana<sup>1</sup>, I.Hofland<sup>1</sup>, M.L.F.van Velthuisen<sup>1</sup>, C.R.N.Rasch<sup>1</sup>, M.W.M.van den Brekel<sup>1</sup>, A.C.Begg<sup>1</sup>  
<sup>1</sup>The Netherlands Cancer Institute, Amsterdam The Netherlands

**P185: The Effect of AlloDerm® on the Initiation and Subsequent Ingrowth of Human Neovessels**

J.Tenney<sup>1</sup>, S.Weiss<sup>1</sup>, E.Woltering<sup>2</sup>, P.Friedlander<sup>1</sup>  
<sup>1</sup>LSUHSC - Department of Otolaryngology - Head and Neck Surgery, Baton Rouge, LA; <sup>2</sup>LSUHSC - Department of Surgery, New Orleans, LA

**\*P186: p53 and Bcl-xL Expression Predicts Outcome in Patients with Oropharynx Cancer Treated with Chemoradiation**

B.Kumar<sup>1</sup>, J.S.Lee<sup>1</sup>, K.G.Cordell<sup>1</sup>, M.E.Prince<sup>1</sup>, G.T.Wolf<sup>1</sup>, S.G.Urba<sup>1</sup>, F.P.Worden<sup>1</sup>, D.B.Chepeha<sup>1</sup>, A.Eisbruch<sup>1</sup>, C.I.Tsien<sup>1</sup>, J.M.G.Taylor<sup>1</sup>, C.R.Bradford<sup>1</sup>, T.E.Carey<sup>1</sup>  
<sup>1</sup>University of Michigan, Ann Arbor, MI

**P187: Monoclonal Origin of Two Metachronous SCC - Evidence Of Implantation Metastasis as Mechanism Behind Second Primaries**

J.A.Akervall<sup>1</sup>, N.Goldstein<sup>2</sup>, P.Chen<sup>2</sup>  
<sup>1</sup>Rontal Clinic, Farmington Hills, MI; <sup>2</sup>Beaumont Hospital, Royal Oak, MI

**P188: Nuclear Survivin Is A Favorable Prognostic Marker in OSCC - Molecular Mechanism and Therapeutic Potential**

K.Engels<sup>1</sup>, S.K.Knauer<sup>2</sup>, W.Mann<sup>3</sup>, A.F.Kovacs<sup>4</sup>, R.H.Stauber<sup>2</sup>  
<sup>1</sup>Department of Pathology, Frankfurt Germany; <sup>2</sup>Georg-Speyer-Haus, Frankfurt Germany; <sup>3</sup>Department of Otorhinolaryngology, Mainz Germany; <sup>4</sup>Maxillofacial Plastic Surgery, Frankfurt Germany

**P189: The TKI, AZD2171, Inhibits VEGFR Signaling and Growth of Anaplastic Thyroid Cancer in an Orthotopic Nude Mouse Model**

F.Gomez-Rivera<sup>1</sup>, A.A.Santillan-Gomez<sup>1</sup>, S.Kim<sup>1</sup>, M.Gu<sup>1</sup>, M.Younes<sup>1</sup>, M.Zhao<sup>1</sup>, Z.Wang<sup>1</sup>, S.Jasser<sup>1</sup>, J.N.Myers<sup>1</sup>  
<sup>1</sup>MD Anderson Cancer Center, Houston, TX

**P190: Expression of LEKTI Correlates With Perineural Invasion in SCC of the Oral Tongue**

T.D.Shellenberger<sup>1</sup>, A.K.El-Naggar<sup>1</sup>, A.Jayakumar<sup>1</sup>, G.L.Clayman<sup>1</sup>  
<sup>1</sup>The University of Texas M. D. Anderson Cancer Center, Houston, TX

**P191: Restoration of 15-Lipoxygenase 2 Induces Apoptosis and Enhances Effect of Radiation on Head and Neck Carcinoma**

Q.Yang<sup>1</sup>, Y.Feng<sup>1</sup>, X.Qi<sup>1</sup>, X.Li<sup>1</sup>, C.J.Schultz<sup>1</sup>, D.Wang<sup>1</sup>  
<sup>1</sup>Medical College of Wisconsin, Milwaukee, WI

**\*P192: The Association Between Elevated EphB4 Expression, Smoking Status and Advanced Staged Disease in Patients With Head and Neck Squamous Cell Carcinoma**

U.K.Sinha<sup>1</sup>, K.Mazhar<sup>2</sup>, S.B.Chinn<sup>2</sup>, D.Vaninder<sup>2</sup>, L.Liu<sup>2</sup>, R.Masood<sup>2</sup>, D.H.Rice<sup>2</sup>, D.H.Rice<sup>2</sup>  
<sup>1</sup>Keck School of Medicine at University of Southern California, Los Angeles, CA; <sup>2</sup>USC, LA, CA

**\*P193: Short-Term Culture and In Vivo Modeling of Primary Head and Neck Squamous Cell Carcinoma**

A.S.Whigham<sup>1</sup>, J.L.Netterville<sup>1</sup>, B.B.Burkey<sup>1</sup>, R.J.Sinard<sup>1</sup>, C.H.Chung<sup>1</sup>, R.J.C.Slebos<sup>1</sup>, W.G.Yarbrough<sup>1</sup>  
<sup>1</sup>Vanderbilt University, Nashville, TN

**\*P194: A Systematic Review of Role of Biomarkers in Determining the Malignant Potential of Oral Dysplasia**

H.M.Mehanna<sup>1</sup>, J.Smith<sup>1</sup>, T.Rattay<sup>1</sup>, R.Sandhu<sup>1</sup>, R.Srinivasan<sup>1</sup>  
<sup>1</sup>University Hosp Coventry & Warwickshire, Coventry United Kingdom

**\*P195: Pulmonary Carcinoma Following Head and Neck Squamous Cell Carcinoma: Differentiation of Metastasis and Second Primary Tumors Using Loss of Heterozygosity and TP53 Analysis**

T.Geurts<sup>1</sup>, A.Balm<sup>1</sup>, T.Hoof van Huysduynen<sup>1</sup>, M.van den Brekel<sup>1</sup>, P.Nederlof<sup>1</sup>, R.Brakenhoff<sup>2</sup>, M.van Velthuisen<sup>1</sup>  
<sup>1</sup>The Netherlands Cancer Institute / Antoni van Leeuwenhoek Hospital, Amsterdam The Netherlands; <sup>2</sup>Free University Medical Center, Amsterdam The Netherlands

**\*P196: Inhibition of Sphingosine Kinase Potentiates Radiation Therapy in Head and Neck Squamous Cell Carcinoma**

S.B.Chinn<sup>1</sup>, K.Mazhar<sup>2</sup>, R.Masood<sup>1</sup>, U.K.Sinha<sup>1</sup>  
<sup>1</sup>USC, LA, CA; <sup>2</sup>USC, LA

**\*P197: Combining the Proteasome Inhibitor Bortezomib With Reirradiation in Patients With Recurrent Head and Neck Squamous Cell Carcinoma**

C.T.Allen<sup>1</sup>, Z.Chen<sup>1</sup>, C.Van Waes<sup>1</sup>  
<sup>1</sup>National Institutes of Health, Bethesda, MD

**\*P198: Ezrin and Moesin Cytoplasmic Mislocalization as Potential Predictive Biomarkers: A Tissue Microarray Validation Study**

M.Brandwein-Gensler<sup>1</sup>, N.Schlect<sup>2</sup>, D.Brouge<sup>1</sup>, H.Huang<sup>1</sup>, A.Thielken<sup>3</sup>, Q.Chen<sup>2</sup>, T.Belbin<sup>2</sup>, F.Gunn-Moore<sup>4</sup>, R.Smith<sup>1</sup>, M.Prystowsky<sup>1</sup>  
<sup>1</sup>Montefiore Medical Center, Bronx, NY; <sup>2</sup>Albert Einstein College of Medicine, Bronx, NY; <sup>3</sup>Johannes Gutenberg University, Mainz Germany; <sup>4</sup>University of St Andrews, Scotland United Kingdom

**\*P199: Securing Negative Margins at Surgery Using Conductive Interstitial Thermal Therapy**

P.M.Spring<sup>1</sup>, Y.Kaufman<sup>1</sup>, L.Hennings<sup>1</sup>, B.C.Stack<sup>1</sup>, J.Y.Suen<sup>1</sup>, G.Shafirstein<sup>1</sup>  
<sup>1</sup>University of Arkansas for Medical Sciences, Little Rock, AR

# Scientific Program: Saturday, August 19, 2006

**\*P200: Global Proteomic Analysis Distinguishes Biologic Differences in Head and Neck Squamous Cell Carcinoma Cell Lines**

S.Rajagopalan<sup>1</sup>, N.Kawachi<sup>1</sup>, P.Du<sup>1</sup>, A.Negassa<sup>1</sup>, E.Nieves<sup>1</sup>, R.H.Angeletti<sup>1</sup>, M.B.Prystowsky<sup>1</sup>  
<sup>1</sup>Albert Einstein College of Medicine, Bronx, NY

**P201: Environmental Carcinogens and Perspectives of Head and Neck Cancers**

V.V.Reddy<sup>1</sup>  
<sup>1</sup>Osmania Medical college, Koti, Hyderabad, A.P., Hyderabad, India India

**P202: Tonsil Cell Immortalization Requires HPV16 E6 and E7: The PDZ Binding Motif of E6 is Required for Efficient Immortalization**

M.E.Anderson<sup>1</sup>, W.Spanos<sup>2</sup>, J.Geiger<sup>3</sup>, R.B.Smith<sup>1</sup>, A.Klingelhutz<sup>1</sup>, J.H.Lee<sup>1</sup>  
<sup>1</sup>University of Iowa, Iowa City, IA; <sup>2</sup>University of Iowa, Iowa City, IA; <sup>3</sup>University of Iowa, Iowa City, IA

**P203: WITHDRAWN**

**P204: Expression of Cancer Testis Antigens in Head and Neck Cancers**

C.Cuffel<sup>1</sup>, Z.Yannick<sup>1</sup>, D.Rimoldi<sup>2</sup>, W.Seelentag<sup>1</sup>, P.Romero<sup>2</sup>, P.Monnier<sup>1</sup>, D.Speiser<sup>2</sup>, J.Cerottini<sup>2</sup>, D.Lienard<sup>2</sup>, L.P.Bron<sup>1</sup>  
<sup>1</sup>Centre Hospitalier Universitaire Vaudois, Lausanne Switzerland; <sup>2</sup>Ludwig Institute for Cancer Research, Lausanne Switzerland

**P205: Alteration of Methylation Profiles for Multiple Tumor Suppressor Gene Promoters in Salivary Gland Tumors**

W.K.Mydlarz<sup>1</sup>, M.O.Hoque<sup>1</sup>, W.H.Westra<sup>1</sup>, J.A.Califano<sup>1</sup>, P.K.Ha<sup>1</sup>  
<sup>1</sup>Johns Hopkins Medical Institutions, Baltimore, MD

**\*P206: Selection of Irrigation Fluid to Eradicate Free Cancer Cells During Head and Neck Cancer Surgery**

J.Hah<sup>1</sup>, Y.Jung<sup>1</sup>, S.Kwon<sup>1</sup>, K.Kim<sup>1</sup>, M.Sung<sup>1</sup>  
<sup>1</sup>Seoul National University Hospital, Seoul Republic of Korea

**\*P207: The Efficacy of Perioperative Aspirin in the Survival of Rat Microvascular Free Flap Following Preanastomotic Injury**

Y.Shnayder, MD<sup>1</sup>, M.B.Karakullukcu, MD<sup>1</sup>, A.Huang, BS<sup>1</sup>, S.Hart, BA<sup>1</sup>, F.J.Civantos, MD, FACS<sup>1</sup>  
<sup>1</sup>University of Miami School of Medicine, Miami, FL

**\*P208: A Molecular Study of Recurrent Respiratory Papillomatosis Undergoing Malignant Transformation**

W.Jeong<sup>1</sup>, J.Hah<sup>1</sup>, Y.Jung<sup>1</sup>, Y.Jeon<sup>1</sup>, Y.Song<sup>1</sup>, K.Kim<sup>1</sup>, M.Sung<sup>1</sup>  
<sup>1</sup>Seoul National University College of Medicine, Seoul Republic of Korea

**\*P209: Genetic Profiling of Oral Carcinomas and Surgical Resection Margins**

P.Pintor dos Reis<sup>1</sup>, N.Naranjo Galloni<sup>1</sup>, N.K.Cervigne<sup>1</sup>, I.Juriscica<sup>2</sup>, B.Perez-Ordenez<sup>3</sup>, M.Pintilie<sup>3</sup>, P.Gullane<sup>3</sup>, J.Irish<sup>3</sup>, S.Kamel-Reid<sup>2</sup>  
<sup>1</sup>Ontario Cancer Institute and University Health Network, Toronto, ON Canada; <sup>2</sup>Ontario Cancer Institute and University Health Network, University of Toronto, Toronto, ON Canada; <sup>3</sup>University Health Network, Toronto, ON Canada

**\*P210: Cancer-Supporting Factors Consistently Induced by Lipopolysaccharide-Squamous Cell Carcinoma-Monocyte Interactions**

Z.B.Kurago<sup>1</sup>, A.Lam-ubol<sup>1</sup>, B.Stone<sup>1</sup>, A.Stetsenko<sup>1</sup>  
<sup>1</sup>University of Iowa, Iowa City, IA

## POSTER TOUR: RESEARCH POTPOURRI

**Tour Leader: Theodoros N. Teknos, MD**

**Location: Michigan/Michigan State**

**\*P211: Salvage Neck Dissection in the Era of Combined Treatment Modality for Head and Neck Cancer**

K.J.Otto<sup>1</sup>, P.A.S.Johnstone<sup>1</sup>, A.Chen<sup>1</sup>  
<sup>1</sup>Emory University, Atlanta, GA

**\*P212: Impact of Preoperative Radiation Therapy on Wound Complications Following Total Laryngectomy: The Dartmouth Experience**

K.C.Deem<sup>1</sup>, N.P.Zwintcher<sup>2</sup>, J.A.Paydarfar<sup>1</sup>, B.J.Gosselin<sup>1</sup>, J.O.Donegan<sup>1</sup>, N.A.Geurkink<sup>1</sup>  
<sup>1</sup>Dartmouth-Hitchcock Medical Center, Lebanon, NH; <sup>2</sup>Dartmouth Medical School, Hanover, NH

**P213: A Retrospective Study of Voice Prosthesis Use Among Patients Undergoing Tracheoesophageal Puncture for Voice Restoration**

M.D.Trudeau<sup>1</sup>, A.Agrawal<sup>1</sup>, A.Lee<sup>1</sup>, K.Stroh<sup>1</sup>  
<sup>1</sup>The Ohio State University, Columbus, OH

**P214: Olfactory Neuroblastoma : A Long-Term Clinical Outcome in a Single Institute Between 1979 and 2003**

K.Nakao<sup>1</sup>, K.Watanabe<sup>1</sup>, Y.Fujishiro<sup>1</sup>, Y.Ebihara<sup>1</sup>, T.Asakage<sup>1</sup>  
<sup>1</sup>Graduate school of medicine, The University of Tokyo, Tokyo Japan

**\*P215: Systematic Review of Primary Treatment Modalities in Oropharyngeal Cancer**

J.R.Harris<sup>1</sup>, C.Diamond<sup>1</sup>, R.Hart<sup>1</sup>, P.Dziegielewski<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada

**\*P216: A Comparison of Drain vs NO Drain Thyroidectomy: A Randomized Prospective Clinical Trial**

J.R.Harris<sup>1</sup>, A.T.Morrissey<sup>1</sup>, J.Chau<sup>1</sup>, W.Yunker<sup>2</sup>, B.Mechor<sup>1</sup>, H.Seikaly<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada; <sup>2</sup>University of Calgary, Calgary, AB Canada

**\*P217: Retrospective Analysis of the Utility of a Low-Profile Locking Plate System in Major Head and Neck Reconstruction**

J.C.Goddard<sup>1</sup>, S.Karahatay<sup>1</sup>, J.Skoner<sup>1</sup>, M.B.Gillespie<sup>1</sup>, J.Hornig<sup>1</sup>, B.Davis<sup>1</sup>, P.O'Neill<sup>1</sup>, S.O<sup>1</sup>, J.Schnellmann<sup>1</sup>, T.Day<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**P218: Immunohistochemical Expression of Fatty Acid Synthase and ERBB2 in Oral Squamous Cell Carcinoma**

S.Silva<sup>1</sup>, I.da Cunha<sup>2</sup>, I.Nishimoto<sup>2</sup>, L.Kowalski<sup>2</sup>, E.Graner<sup>3</sup>  
<sup>1</sup>University of Campinas - UNICAMP, Piracicaba Brazil; <sup>2</sup>Hospital do Cancer A.C. Camargo, Sao Paulo Brazil; <sup>3</sup>University of Campinas - UNICAMP, Piracicaba Brazil

**\*P219: Health-Related Quality of Life in Head and Neck Cancer: A Review of Patient-Reported Outcome Measures**

A.L.Pusic<sup>1</sup>, J.Liu<sup>1</sup>, C.M.Chen<sup>1</sup>, S.Cano<sup>2</sup>, K.Davridge<sup>3</sup>, A.Klassen<sup>3</sup>, R.Branski<sup>1</sup>, S.Patel<sup>1</sup>, D.Kraus<sup>1</sup>, P.G.Cordeiro<sup>1</sup>  
<sup>1</sup>Memorial Sloan-Kettering Cancer Center, New York, NY; <sup>2</sup>University College London, London United Kingdom; <sup>3</sup>University of British Columbia, Vancouver, BC Canada

**\*P220: Transfusion as a Predictor of Recurrence and Survival in Head and Neck Cancer Surgery**

H.Seikaly<sup>1</sup>, J.Chau<sup>1</sup>, J.R.Harris<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada

**\*P221: Knowledge of Head and Neck Cancer Among Medical Students at 2 Chicago, IL Universities**

N.G.Mohyuddin<sup>1</sup>, A.Langerman<sup>2</sup>, C.W.Lehew<sup>1</sup>, L.M.Kaste<sup>1</sup>, D.Suskind<sup>2</sup>, K.Pytnia<sup>1</sup>  
<sup>1</sup>University of Illinois-Chicago, Chicago, IL; <sup>2</sup>University of Chicago, Chicago, IL

**\*P222: Functional Outcomes of Primary Reconstruction of Maxillary Defects**

H.Seikaly<sup>1</sup>, J.Rieger<sup>1</sup>, R.Hart<sup>1</sup>, J.Wolfaardt<sup>1</sup>, J.R.Harris<sup>1</sup>  
<sup>1</sup>University of Alberta, Edmonton, AB Canada

**P223: Distribution of Flow Cytometric Content in Non-Diploid Cell Populations Differ Between Glottic and Supraglottic Cancer**

G.Lindgren<sup>1</sup>, J.Wennerberg<sup>2</sup>, B.Baldetorp<sup>3</sup>, P.Wahlberg<sup>4</sup>  
<sup>1</sup>Department of Otorhinolaryngology, Lund University Hospital, S- 221 85 Lund Sweden; <sup>2</sup>Department of Otorhinolaryngology, Lund University Hospital, Lund Sweden; <sup>3</sup>Department of oncology, Lund Sweden; <sup>4</sup>Department of Otorhinolaryngology, Lund University Hospital, Lund Sweden

**P224: Induction of c-Myc Dependent Cell Proliferation by TLR3 in Head and Neck Cancer**

R.Pries<sup>1</sup>, L.Hogrefe<sup>1</sup>, C.Ditz<sup>1</sup>, L.Xie<sup>2</sup>, B.J.H.Wollenberg<sup>1</sup>  
<sup>1</sup>University of Schleswig Holstein, Luebeck Germany; <sup>2</sup>Zhejiang University, Hangzhou China

**\*P225: Genetic Analysis of Genes Involved in Signal Transduction Pathways in Oral Squamous Cell Carcinomas**

D.Thurnher<sup>1</sup>, P.Pintor dos Reis<sup>2</sup>, N.Naranjo Galloni<sup>2</sup>, J.Freeman<sup>3</sup>, D.Brown<sup>4</sup>, R.Gilbert<sup>4</sup>, P.Gullane<sup>4</sup>, J.Irish<sup>4</sup>, S.Kamel-Reid<sup>5</sup>  
<sup>1</sup>Princess Margaret Hospital, Toronto, ON Canada; <sup>2</sup>Ontario Cancer Institute and University Health Network, Toronto, ON Canada; <sup>3</sup>Mount Sinai Hospital, Toronto, ON Canada; <sup>4</sup>Princess Margaret Hospital and University Health Network, Toronto, ON Canada; <sup>5</sup>Ontario Cancer Institute and University Health Network, University of Toronto, Toronto, ON Canada

**\*P226: Lack of Exon 19 and 21 EGFR Mutations in Squamous Head and Neck Cancer Specimens and Cell Lines**

M.L.Carlson<sup>1</sup>, B.R.Wuertz<sup>1</sup>, J.Lin<sup>1</sup>, G.L.Adams<sup>1</sup>, R.S.Taylor<sup>1</sup>, F.G.Ondrey<sup>1</sup>  
<sup>1</sup>University of Minnesota, Minneapolis, MN

**\*P227: Tumor Origin and Molecular Profile of Microvesicles in Serum Samples of Patients With Head and Neck Squamous Cell Carcinoma**

E.U.Wieckowski<sup>1</sup>, J.T.Johnson<sup>1</sup>, T.L.Whiteside<sup>1</sup>  
<sup>1</sup>University of Pittsburgh Cancer Institute, Pittsburgh, PA

**P228: Gene-Expression-Analysis of Radiation-Induced Non-Healing Dermal Wounds of the Head and Neck**

U.R.Goessler<sup>1</sup>, P.Bugert<sup>2</sup>, K.Hormann<sup>1</sup>, F.Riedel<sup>1</sup>  
<sup>1</sup>Dept. of ORL HNS, University Hospital Mannheim, University of Heidelberg, Mannheim Germany; <sup>2</sup>Institute of Transfusiomedicine & Immunology, Mannheim Germany

**\*P229: The Role of Inhibitor of Differentiation (Id1) in the Angiogenesis of Head and Neck Cancers**

J.Lin<sup>1</sup>, Y.Hamajima<sup>1</sup>, M.Komori<sup>1</sup>, L.Feng<sup>1</sup>, E.Caicedo<sup>1</sup>, G.Adams<sup>1</sup>, B.Wuertz<sup>1</sup>, F.Ondrey<sup>1</sup>  
<sup>1</sup>University of Minnesota, Minneapolis, MN

**P230: Curcumin Suppresses IL-6 and IL-8 Production in Head and Neck Cancer Cell Lines via Inhibition of IκB Kinase (IKK)**

A.N.Cohen<sup>1</sup>, M.S.Veena<sup>1</sup>, E.S.Srivatsan<sup>1</sup>, M.B.Wang<sup>1</sup>  
<sup>1</sup>David Geffen School of Medicine at UCLA, Los Angeles, CA

**\*P231: The Identification of Epidermal Fatty Acid Binding Protein in Advanced Head and Neck Cancer Using a Proteomic Approach**

M.Gillespie<sup>1</sup>, J.Downie<sup>2</sup>, T.A.Day<sup>1</sup>, J.D.Hornig<sup>1</sup>, B.Oswald<sup>1</sup>, J.Arthur<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC; <sup>2</sup>Medical University of South Carolina, Charleston, SD

**P232: Up-Regulation of NK Cell Cytotoxicity Against Head and Neck Cancer in Response to ss-isRNA Requires TLR7**

R.Pries<sup>1</sup>, S.Wulff<sup>2</sup>, R.Kesselring<sup>2</sup>, L.Xie<sup>3</sup>, B.J.H.Wollenberg<sup>1</sup>  
<sup>1</sup>University of Schleswig Holstein, Luebeck Germany; <sup>2</sup>University of Schleswig-Holstein, Luebeck Germany; <sup>3</sup>Zhejiang University, Hangzhou China

\* Abstract was published in the *Archives of Otolaryngology*

**P233: Photodynamic Therapy for Local Persistent and/or Recurrent NPC's Development of a Light Application Device**

H.Nyst<sup>1</sup>, R.van Veen<sup>2</sup>, R.Peters<sup>2</sup>, S.Sapniol<sup>3</sup>, F.Stewart<sup>1</sup>, P.Levendag<sup>2</sup>, H.Sterenborg<sup>2</sup>, I.Tan<sup>1</sup>

<sup>1</sup>Netherlands Cancer Institute, Amsterdam The Netherlands; <sup>2</sup>ErasmusMC, Rotterdam The Netherlands; <sup>3</sup>Biolitec AG, Bonn Germany

**P234: Safety of PPAR Gamma Activation Strategies for Precancerous Leukoplakia**

N.Rhodus<sup>1</sup>, L.Hohberger<sup>1</sup>, K.Cole<sup>1</sup>, E.Szabo<sup>2</sup>, F.G.Ondrey<sup>3</sup>

<sup>1</sup>University of Minnesota, Minneapolis; <sup>2</sup>NCI/NIH, Bethesda, MD; <sup>3</sup>University of Minnesota, Minneapolis, MN

**P235: Withdrawn**

**\*P236: Tonsil Carcinoma Treated By Transoral Laser Microsurgery Part One: Previously Untreated Tumors**

M.L.Hinni<sup>1</sup>, D.G.Grant<sup>2</sup>, J.R.Salassa<sup>2</sup>, B.W.Pearson<sup>2</sup>, W.C.Perry<sup>1</sup>

<sup>1</sup>Mayo Clinic, Scottsdale, AZ; <sup>2</sup>Mayo Clinic, Jacksonville, FL

**\*P237: Tonsil Carcinoma Treated By Transoral Laser Microsurgery Part Two: Persistent, Recurrent and Second Primary Tumors**

D.G.Grant<sup>1</sup>, J.R.Salassa<sup>1</sup>, M.L.Hinni<sup>2</sup>, B.W.Pearson<sup>1</sup>, W.C.Perry<sup>2</sup>

<sup>1</sup>Mayo Clinic, Jacksonville, FL; <sup>2</sup>Mayo Clinic, Scottsdale, AZ

**\*P238: Quality Control Monitoring of a Cancer Database Using Visualization Software**

M.A.Nance<sup>1</sup>, C.H.Snyderman<sup>1</sup>, D.E.Eibling<sup>2</sup>, K.Sochats<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Pittsburgh, PA; <sup>2</sup>University of Pittsburgh, Pittsburgh, PA

**\*P239: Immunotherapy of Established Murine Squamous Cell Carcinoma Using Dendritic Cell-Tumor Fusion Hybrids**

W.T.Lee<sup>1</sup>, H.Tamai<sup>1</sup>, P.Cohen<sup>1</sup>, S.Shu<sup>1</sup>

<sup>1</sup>Cleveland Clinic, Cleveland, OH

**\*P240: Expression of Cell Cycle Regulators as Markers of Field Cancerisation and Second Primary Tumours in Larynx Squamous Cell Carcinoma**

R.D.Farhadieh<sup>1</sup>, R.Smee<sup>2</sup>, C.G.Rees<sup>3</sup>, L.Yang<sup>3</sup>, P.J.Russell<sup>4</sup>

<sup>1</sup>Prince of Wales Hospital, Sydney; <sup>2</sup>Prince of Wales Hospital, Sydney Australia; <sup>3</sup>UNSW, Sydney Australia; <sup>4</sup>UNSW, Oncology Research Center, Sydney Australia

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## 1930 – 2200 MAIN SOCIAL EVENT

**Location: Salon III**

### **An AHNS Taste of Chicago**

The Taste of Chicago is one of the largest food festivals in the country with 11 days of eating and entertainment in Grant Park. While it may be too late to celebrate with the rest of the city, it's never too late for the AHNS to have a celebration of their own! Dance to the blues rock of the Blooze Brothers while you indulge in some of the city's best, including tapas, deep dish pizza, Eli's Cheesecake and other delectable items.

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**CLINICAL PROGRAM**

**0800 – 0930 Scientific Session/Abstracts**

**Moderators:** Dan M. Fliss, MD and Peter C. Neligan, MD

**Location: Salon II**

**\*S082: Atypical Facial Access: An Unusually High Prevalence Among Patients With Skull Base Tumors Treated in 2 Centers**

C.R.Cernea<sup>1</sup>, F.L.Dias<sup>2</sup>, T.Farias<sup>1</sup>, U.BT.Mendonça<sup>3</sup>, E.Vellutini<sup>1</sup>, M.QT.Gomes<sup>1</sup>, J.Nogueira<sup>2</sup>, R.RG.Lorencetti<sup>1</sup>, L.G.Brandão<sup>1</sup>, L.RM.Dos Santos<sup>1</sup>  
<sup>1</sup>University of Sao Paulo Medical School, Sao Paulo Brazil; <sup>2</sup>National Cancer Institute, Rio de Janeiro Brazil; <sup>3</sup>National Cancer Institute, Sao Paulo Brazil

**S083: Paranasal Sinus Tumors: What to Expect From Neoadjuvant Chemotherapy and Lessons From Twenty-Two Years' Experience**

A.W.Ahamad<sup>1</sup>, A.Garden<sup>2</sup>, E.Hanna<sup>3</sup>, M.Kies<sup>4</sup>, L.Theriot<sup>5</sup>, I.Bristol<sup>2</sup>, P.Allen<sup>6</sup>, K.Ang<sup>7</sup>  
<sup>1</sup>University of Texas MD Anderson Cancer Center, Houston, TX; <sup>2</sup>Univ. of Texas MD Anderson Cancer Ctr. Div of Radiation Oncology, Houston, TX; <sup>3</sup>University of Texas MD Anderson Cancer Center, Dept. of Head and Neck Surgery, Houston, TX; <sup>4</sup>Univ of Texas MD Anderson Cancer Ctr, Div. of Head and Neck Medical Oncology, Houston, TX; <sup>5</sup>Univ. of Texas MD Anderson Cancer Ctr. Div. of Radiation Oncology, Houston, TX; <sup>6</sup>Univ of Texas MD Anderson Cancer Ctr, Div. of Radiation Oncology, Houston, TX; <sup>7</sup>Univ of Texas MD Anderson Cancer Ctr, Div. of Radiation Oncology, Houston, UT

**S084: A Pilot Study Assessing Surgical Exposure During Transoral Robotic Surgery (TORS) with the Da Vinci Robotic System**

G.S.Weinstein<sup>1</sup>, B.W.O'Malley<sup>1</sup>, W.Snyder<sup>1</sup>  
<sup>1</sup>The University of Pennsylvania, Philadelphia, PA

**Discussion**

**S085: Can Neck Dissection Be an Outpatient Procedure?**

G.A.Krempf<sup>1</sup>, J.E.Medina<sup>1</sup>  
<sup>1</sup>University of Oklahoma, Oklahoma City, OK

**\*S086: Liposarcoma of the Head and Neck: Experience at a Major Cancer Center**

E.C.Davis<sup>1</sup>, M.T.Ballo<sup>1</sup>, M.A.Luna<sup>1</sup>, S.R.Patel<sup>1</sup>, E.M.Sturgis<sup>1</sup>  
<sup>1</sup>The University of Texas M.D. Anderson Cancer Center, Houston, TX

**\*S087: Salvage Surgery After Loco-Regional Failure of Concomitant Radio-Chemotherapy in Advanced Head-and Neck Cancer**

R.Giger<sup>1</sup>, S.Temam<sup>1</sup>, F.Janot<sup>1</sup>, J.Bourhis<sup>1</sup>  
<sup>1</sup>Institut Gustave-Roussy, Villejuif Cedex France

**Discussion**

**S088: Periorbital Reconstructions After Orbital Exenteration: An Individualized Approach to Simplify Ocular Rehabilitation**

W.Cheung<sup>1</sup>, M.Cheng<sup>1</sup>, M.Leung<sup>1</sup>, Y.Mak<sup>1</sup>, V.Noronha<sup>1</sup>, C.Ho<sup>1</sup>  
<sup>1</sup>Kwong Wah Hospital, Hong Kong China

**S089: Optimizing Reconstruction of Composite Mandibular and Maxillary Defects Using Three Dimensional Models**

J.D.Hornig<sup>1</sup>, A.Redding<sup>1</sup>, B.Davis<sup>1</sup>, R.Beas<sup>1</sup>, B.Martin-Harris<sup>1</sup>, P.O'Neill<sup>1</sup>, S.O<sup>1</sup>, R.Kline<sup>1</sup>, M.B.Gillespie<sup>1</sup>, T.A.Day<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**\*S090: The Vessel Depleted Neck: Techniques for Achieving Microvascular Reconstruction**

A.S.Jacobson<sup>1</sup>, E.Park<sup>2</sup>, B.Roman<sup>2</sup>, E.M.Genden<sup>2</sup>  
<sup>1</sup>Mount Sinai Hospital, New York, NY; <sup>2</sup>Mount Sinai Hospital, New York, NY

**Discussion**

**RESEARCH PROGRAM**

**0800 – 0930 SCIENTIFIC SESSION/ABSTRACTS**

**Moderators:** Gerry F. Funk, MD and TBD

**Location: Salon I**

**S091: Factors Associated With Discontinuing Employment**

A.E.Buckwalter<sup>1</sup>, L.H.Karnell<sup>1</sup>, R.B.Smith<sup>1</sup>, G.F.Funk<sup>1</sup>  
<sup>1</sup>University of Iowa College of Medicine, Iowa City, IA

**\*S092: Defining the Clear Surgical Margin in Oral Cancer**

R.W.Nason<sup>1</sup>, A.Binahmed<sup>1</sup>, A.Abdoh<sup>2</sup>  
<sup>1</sup>CancerCare Manitoba, Winnipeg, MB Canada; <sup>2</sup>Department of Surgery, University of Manitoba, Winnipeg, MB Canada

**\*S093: Suicide Rates in Head and Neck Cancer Patients**

S.Misono<sup>1</sup>, J.Fann<sup>1</sup>, N.Weiss<sup>1</sup>, B.Yueh<sup>2</sup>  
<sup>1</sup>University of Washington, Seattle, WA; <sup>2</sup>VA Puget Sound Medical Center and University of Washington, Seattle, WA

**Discussion**

**\*S094: Oropharyngeal Swallowing: Functional Targets of Surgical Restoration**

B.Martin-Harris<sup>1</sup>  
<sup>1</sup>Medical University of South Carolina, Charleston, SC

**S095: Multi-Institutional Phase III Radplat IA Versus IV Trial in Advanced Head and Neck Cancer: 1st Year Quality of Life**

A.H.Ackerstaff<sup>1</sup>, C.RN.Rasch<sup>1</sup>, A.JM.Balm<sup>1</sup>, J.de Boer<sup>1</sup>, J.H.Schornagel<sup>1</sup>, R.Kröger<sup>1</sup>, D.HF.Rietveld<sup>2</sup>, R.Wiggenraad<sup>3</sup>, M.B.Jameson<sup>4</sup>, F.JM.Hilgers<sup>1</sup>  
<sup>1</sup>Netherlands Cancer Institute, Amsterdam The Netherlands; <sup>2</sup>Radiotherapy Institute Friesland, Leeuwarden The Netherlands; <sup>3</sup>Medical Center Haaglanden, Den Haag The Netherlands; <sup>4</sup>Waikato Hospital, Hamilton New Zealand

**\*S096: Nomogram for Predicting Locoregional Recurrence-Free Survival After Treatment of Oral Cavity Squamous Cell Carcinoma**

N.D.Gross<sup>1</sup>, S.G.Patel<sup>2</sup>, A.L.Carvalho<sup>3</sup>, P.Chu<sup>2</sup>, L.P.Kowalski<sup>3</sup>, J.O.Boyle<sup>2</sup>, J.P.Shah<sup>2</sup>, M.W.Kattan<sup>4</sup>  
<sup>1</sup>Oregon Health and Science University, Portland, OR; <sup>2</sup>Memorial Sloan-Kettering Cancer Center, New York, NY; <sup>3</sup>Centro de Tratamento e Pesquisa Hospital do Cancer AC Camargo, Sao Paulo Brazil; <sup>4</sup>The Cleveland Clinic Foundation, Cleveland, OH

**Discussion**

**S097: Association of Measures of General Health With Survival**

L.M.Grignon<sup>1</sup>, L.H.Karnell<sup>1</sup>, A.J.Christensen<sup>2</sup>, G.F.Funk<sup>1</sup>  
<sup>1</sup>University of Iowa College of Medicine, Iowa City, IA; <sup>2</sup>University of Iowa, Iowa City, IA

**S098: Chemoprevention of Head and Neck Cancer With Aspirin: A Case-Control Study**

V.Jayaprakash<sup>1</sup>, N.R.Figural<sup>1</sup>, K.B.Moysich<sup>1</sup>, T.R.Loree<sup>1</sup>, M.A.Sullivan Nasca<sup>1</sup>, R.J.Menezes<sup>1</sup>, M.E.Reid<sup>1</sup>  
<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY

**\*S099: The Effect of Health Insurance Status on Stage at Diagnosis for Laryngeal Cancer**

A.Y.Chen<sup>1</sup>, N.Schrag<sup>2</sup>, A.Stewart<sup>3</sup>, E.Ward<sup>2</sup>  
<sup>1</sup>Emory University/ American Cancer Society, Atlanta, GA; <sup>2</sup>American Cancer Society, Atlanta, GA; <sup>3</sup>American College of Surgeons, Chicago, IL

**Discussion**

0930 – 1000 **Break**

1000 – 1040 **Keynote Lecture**

## Targeting COX-2 and EGFR in Oral Carcinogenesis

Introduction by Jay O. Boyle, MD

**Keynote Speaker: Andrew J. Dannenberg, MD, Director of Cancer Prevention  
New York Presbyterian Hospital-Cornell, New York, NY**

**Location: Salon II**

### CLINICAL PROGRAM

#### 1040 – 1200 Scientific Session/Abstracts

Moderators: Amit V. Agrawal, MD and  
Piero Nicolai, MD

**Location: Salon II**

#### **S100: Prognostic Determinants Associated With Efficacy of Intra-Tumoral p53 Gene Therapy in Patients With Recurrent SCCHN**

R.E.Sobol<sup>1</sup>, J.Nemunaitis<sup>2</sup>, C.Bier-Laning<sup>3</sup>, G.L.Clayman<sup>4</sup>,  
D.Van Echo<sup>5</sup>, J.Hamm<sup>6</sup>, R.Dreicer<sup>7</sup>, G.H.Yoo<sup>8</sup>,  
K.B.Menander<sup>1</sup>, W.J.Goodwin<sup>9</sup>

<sup>1</sup>Introgen Therapeutics, Houston, TX; <sup>2</sup>Mary Crowley Medical Research Center, Dallas, TX; <sup>3</sup>Loyola University, Chicago, IL; <sup>4</sup>MD Anderson Cancer Center, Houston, TX; <sup>5</sup>University of Maryland School of Medicine, Baltimore, MD; <sup>6</sup>University of Louisville, Louisville, KY; <sup>7</sup>University of Iowa, Iowa City, IA; <sup>8</sup>Wayne State University, Detroit, MI; <sup>9</sup>University of Miami Sylvester Cancer Center, Miami, FL

#### **S101: Human Papillomavirus Contributes to Oral and Oropharyngeal Squamous Cell Carcinoma and to Recurrence After Treatment**

K.Rosenquist<sup>1</sup>, J.Wennerberg<sup>2</sup>, K.Annertz<sup>2</sup>, E.Schildt<sup>3</sup>,  
B.Hansson<sup>4</sup>, A.Bladström<sup>5</sup>, G.Andersson<sup>1</sup>

<sup>1</sup>Dept of Oral Surgery and Oral Medicine, Faculty of Odontology, Malmö Sweden; <sup>2</sup>Dept of Otorhinolaryngology, Head and Neck Surgery, Lund Sweden; <sup>3</sup>Dept of Oncology, University Hospital, Lund Sweden; <sup>4</sup>Dept of Lab Medicine, Section of Med Microbiol, University Hospital, Malmö Sweden; <sup>5</sup>Southern Swedish Regional Tumour Registry, University Hospital, Lund Sweden

#### **S102: Human Papillomavirus in Head and Neck Cancer - Is It Changing the Face of Our Patient Population?**

L.Davies<sup>1</sup>, H.Welch<sup>1</sup>

<sup>1</sup>White River Junction VA Medical Center, White River Junction, VT

#### **\*S103: The Association of BCL-2 and Survivin Expression to Disease Outcome in Head and Neck Cancer**

K.J.Otto<sup>1</sup>, M.Zapato<sup>1</sup>, S.Muller<sup>1</sup>, A.Chen<sup>1</sup>, S.Budnick<sup>1</sup>

<sup>1</sup>Emory University, Atlanta, GA

#### **Discussion**

#### **\*S104: Salvage Surgery After Radiotherapy for Laryngeal Cancer: From Endoscopic Resections to Partial and Total Laryngectomies**

C.Piazza<sup>1</sup>, G.Peretti<sup>1</sup>, A.Cattaneo<sup>1</sup>, F.Garrubba<sup>1</sup>, L.O.Redaeli de Zinis<sup>1</sup>, P.Nicolai<sup>1</sup>

### RESEARCH PROGRAM

#### 1040 – 1200 Scientific Session/Abstracts

Moderators: Eben L. Rosenthal, MD  
and Roland Stauber, MD

**Location: Salon I**

#### **\*S108: Proteasome Inhibition Reverses E6-Mediate p53 Degradation and Decreases Proliferation in Tonsil Epithelial Cells**

G.F.Harris<sup>1</sup>, J.H.Lee<sup>1</sup>

<sup>1</sup>University of Iowa, Iowa City, IA

#### **S109: Adenovirus Armed With Tissue Inhibitor Metalloproteinase-2 Potentiates Combined Chemoradiation Therapy of HNSCC in Vivo**

L.R.McNally<sup>1</sup>, E.L.Rosenthal<sup>2</sup>, D.J.Buchsbaum<sup>1</sup>

<sup>1</sup>University Alabama Birmingham, Birmingham, AL; <sup>2</sup>University Alabama Birmingham, Birmingham, AL

#### **\*S110: (-)-Gossypol, a BH3 Mimetic and Inducer of Apoptosis in Head and Neck Cancer Cells, Is Oxidized and Deactivated by ROS**

M.J.Sikora<sup>1</sup>, J.A.Bauer<sup>1</sup>, J.C.Brenner<sup>1</sup>, T.E.Carey<sup>1</sup>,  
C.R.Bradford<sup>1</sup>

<sup>1</sup>University of Michigan - Ann Arbor, Ann Arbor, MI

#### **S111: Recombinant Erythropoietin Beta Stimulates Growth of Squamous Cell Carcinoma in Vitro and in Vivo**

J.Wennerberg<sup>1</sup>, Y.Sasaki<sup>2</sup>, H.Mineta<sup>3</sup>, E.Kjellén<sup>4</sup>, L.Ekblad<sup>5</sup>,  
B.Zackrisson<sup>6</sup>

<sup>1</sup>Dept of Otorhinolaryngology, Head and Neck Surgery, Lund Sweden; <sup>2</sup>Dept of ORL/H&N Surgery Hamamatsu Medical School, Hamamatsu Japan; <sup>3</sup>Dept of ORL/H&N Surgery, Hamamatsu Medical School, Hamamatsu Japan; <sup>4</sup>Dept of Oncology, University Hospital, Lund Sweden; <sup>5</sup>Kamprad Research Lab, University Hospital, Lund Sweden; <sup>6</sup>Dept of Oncology, University Hospital, Umeå Sweden

#### **Discussion**

#### **\*S112: Assessment of Fluorescent Immunoguided Neoplasm Detection to Identify Microscopic Disease in Vivo**

E.L.Rosenthal<sup>1</sup>, B.D.Kulbersh<sup>1</sup>, R.Duncan<sup>1</sup>,  
J.Scott.Magnuson<sup>1</sup>, K.Zinn<sup>1</sup>

<sup>1</sup>University of Alabama at Birmingham, Birmingham, AL

#### **S113: Interactions of Dietary Factors in Oral Cancer**

J.R.Marshall<sup>1</sup>, M.E.Reid<sup>1</sup>, N.Natarajan<sup>1</sup>, J.L.Freudenheim<sup>2</sup>,  
T.R.Loree<sup>1</sup>, N.R.Rigual<sup>1</sup>

<sup>1</sup>Roswell Park Cancer Institute, Buffalo, NY; <sup>2</sup>State University of New York @ Buffalo, Buffalo, NY

## CLINICAL PROGRAM

<sup>1</sup>University of Brescia, Brescia Italy

**\*S105: Phase II Trial of CO2 Laser Supraglottic Laryngectomy and Irradiation: Experience of the Southwest Oncology Group**

A.Agrawal<sup>1</sup>, J.Moon<sup>2</sup>, R.K.Davis<sup>3</sup>, W.A.Sakr<sup>4</sup>, S.Giri<sup>5</sup>, J.Valentino<sup>6</sup>, M.LeBlanc<sup>2</sup>, J.M.Truelson<sup>7</sup>, J.F.Ensley<sup>4</sup>, D.E.Schuller<sup>1</sup>

<sup>1</sup>The Ohio State University, Columbus, OH; <sup>2</sup>Southwest Oncology Group, Seattle, WA; <sup>3</sup>University of Utah, Salt Lake City, UT; <sup>4</sup>Wayne State University, Detroit, MI; <sup>5</sup>Eastern Virginia Medical School, Norfolk, VA; <sup>6</sup>University of Kentucky, Lexington, KY; <sup>7</sup>University of Texas Southwestern, Dallas, TX

**\*S106: Retronasal and Orthonasal Olfactory Ability After Laryngectomy**

E.A.Veenker<sup>1</sup>, F.A.Catalanatto<sup>2</sup>, J.W.Werning<sup>2</sup>

<sup>1</sup>University of Florida, Gainesville, FL; <sup>2</sup>University of Florida, Gainesville, FL

**\*S107: Contact YAG Laser Assisted Endoscopic Supraglottic Laryngectomy**

R.V.Smith<sup>1</sup>, B.Schiff<sup>1</sup>

<sup>1</sup>Montefiore Medical Center, Bronx, NY

## RESEARCH PROGRAM

**S114: VEGF-C Expression Alters Tumor Cell Invasion in Squamous Cell Carcinoma of the Head and Neck**

J.M.Bock<sup>1</sup>, D.K.Trask<sup>1</sup>

<sup>1</sup>University of Iowa Hospitals and Clinics, Iowa City, IA

**\*S115: The Receptor Tyrosine Kinase C-MET Is Mutated in Head and Neck Cancer and Is a Promising Novel Target**

T.Y.Seiwert<sup>1</sup>, A.J.Klein-Szanto<sup>2</sup>, R.Jagadeeswaran<sup>1</sup>, M.Tretiakova<sup>1</sup>, L.Martin<sup>1</sup>, M.W.Lingen<sup>1</sup>, E.E.Cohen<sup>1</sup>, J.A.Ridge<sup>2</sup>, E.E.Vokes<sup>1</sup>, R.Salgia<sup>1</sup>

<sup>1</sup>University of Chicago, Chicago, IL; <sup>2</sup>Fox Chase Cancer Center, Philadelphia, PA

### Discussion

### Discussion

### 1200 - 1210 Final Remarks

John J. Coleman, III, MD, Dennis H. Kraus, MD, Carol R. Bradford, MD and Jean Louis Lefebvre, MD

**Location: Salon II**

## Future AHNS Annual Meeting Dates and Locations

### 2007

**American Head & Neck Society Annual Meeting  
during the Combined Otolaryngology Spring Meetings (COSM)  
April 28-29, 2007 in San Diego, CA**

### 2008

**7th International Conference on Head & Neck Cancer  
"Multidisciplinary Care in Head & Neck Cancer"  
San Francisco Marriott  
July 19-23, 2008 in San Francisco, CA**

# — Instructional Course Outlines and Objectives

## **C1: Paragangliomas and Carotid Body Tumors**

**Presenters:** Dennis H. Kraus MD and James L. Netteville MD

### **Course Outline:**

- I. Presentation
  - A. Symptoms
  - B. Physical Findings
  - C. Genetics
- II. Evaluation
  - A. Imaging
    1. CT
    2. MRI/MRA
    3. Angiography - Balloon Test
  - Occlusion/Spect
    4. Functional Imaging
  - B. Urine Catecholamines
- III. Treatment - Options and Indications
  - A. Observation
  - B. Radiation Therapy
  - C. Surgical Resection
    1. Surgical Access
    2. Management of Neurovascular Structures
    3. Reconstruction
  - D. Benign vs Malignant Disease
- IV. Outcome Measures
  - A. Recurrence
  - B. Quality of life
  - C. Sequelae
    1. Cranial Nerve Function
    2. Surgical Rehabilitation
    3. First Bite Syndrome

## **C2: Advanced Non-melanoma Skin Cancer**

**Presenters:** Christopher J. O'Brien MD and Randal S. Weber, MD

### **Description:**

This course will deal particularly with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). It will address the following issues in relation to the diagnosis, evaluation and treatment of advanced non-melanoma cutaneous cancer of the head and neck: Incidence, Epidemiology, Pathology, Perineural Invasion and Spread, Review of the Current TNM Staging, Locally Advanced Disease, Diagnostic Workup and Imaging, Orbital Involvement, Patterns of Lymphatic Spread, Metastatic Spread to the Parotid and Cervical Nodes, Reconstructive Options, The Role of Adjuvant Radiotherapy and EGFR Inhibitor Therapy and Outcome and Prognostic Factors.

At the conclusion of the Course the participants will have increased their knowledge in all these area and, in particular will have a thorough understanding of and be able to describe:

- How to identify and clinically evaluate a patient with an advanced high-risk local cutaneous of the head and neck;

- When to order imaging investigations and the appropriate use of CT, MRI and PET;
- How to treat locally advanced non-melanoma skin cancer, including indications for orbital exenteration;
- Useful reconstructive techniques including local, regional and free flaps;
- The indications for and the techniques employed for surgical management of nodal metastasis to the parotid and neck;
- Indications for adjuvant radiotherapy and the role of EGFR inhibition for treating aggressive cutaneous SCC;
- Limitations of the current TNM staging system.

## **C3: Management of Non-well Differentiated Thyroid Cancer**

**Presenters:** James I. Cohen MD, PhD and William B. Farrar MD

### **Description:**

Most patients seen with a malignant thyroid mass will have well differentiated thyroid cancer and while the debates that surround all aspects of the diagnostic workup, surgical management and use of adjuvant therapy for these patients are far from settled, they are well enough understood that most head and neck surgeons have developed a working strategy that allows them to manage these patients comfortably. By contrast the patient with medullary carcinoma, poorly differentiated thyroid carcinoma, or anaplastic carcinoma is a relative rarity and when encountered raises questions as to what changes in this “working strategy” may be necessary to manage these patients. This course will address these issues.

### **Course Outline:**

Using a case based format, the instructors will examine the evidence that supports the need for additional diagnostic testing, alterations in surgical strategies and the use of adjuvant therapies for a patient with medullary carcinoma, poorly differentiated thyroid carcinoma and anaplastic carcinoma. The intent of each of the case presentations will be to develop practical guidelines by answering the question “what do I need to do differently for this histology and why?”

Audience participation will be encouraged.

### **Objectives:**

At the conclusion of the course, attendees will be able to discuss, relative to well-differentiated thyroid cancer:

- How diagnostic strategies differ for medullary carcinoma, poorly differentiated thyroid carcinoma and anaplastic carcinoma;
- How surgical strategies differ for medullary carcinoma, poorly differentiated thyroid carcinoma and anaplastic carcinoma;
- How adjuvant therapies are applied differently for medullary carcinoma, poorly differentiated thyroid carcinoma and anaplastic carcinoma.

## **C4: Surgical Approaches in the Head and Neck**

**Presenters:** Guy J. Petruzzelli, MD, PhD and  
Karen T. Pitman, MD

### **Course Outline:**

1. Transcervical Approaches to the Pharynx
2. Endoscopic Techniques
3. Postoperative Complications
4. Modifications in Surgical Technique During Salvage Surgery

### **Objectives:**

At the completion of the course the following objectives will be met:

- Describe the indications, techniques and complications for several transcervical and endoscopic approaches to the pharynx;
- Discuss modifications to these techniques when operating on patients who have received prior chemoradiation therapy;
- Identify and treat postoperative complications.

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## **C5: Recent Advances in the Management of Melanoma**

**Presenters:** Grant W. Carlson, MD and Jesus E. Medina, MD

### **Description:**

Ten to 25 percent of malignant melanomas occur in the head and neck region. The lymphatic drainage in this region can be ambiguous, with multiple primary channels and the potential for multiple sentinel lymph nodes. Excisional biopsy in this area can be technically challenging, especially within the parotid gland and around the spinal accessory nerve. For these reasons, the use of sentinel lymph node biopsy in the management of head and neck melanoma has not been widely accepted.

Depending on tumor thickness, up to 35% of patients with melanoma of the head and neck will be found to have sentinel lymph node metastases. The extent of nodal dissection has not been clearly defined in this setting. Radiation therapy may reduce local-regional recurrence in patients with nodal involvement but a survival advantage has not been demonstrated.

### **Course Outline:**

- 1) Surgical margins in primary melanoma
- 2) Sentinel lymph node mapping and biopsy
  - a) Technique
  - b) Indications
  - c) Results
  - d) Management of the parotid gland

- 3) Therapeutic cervical lymphadenectomy
  - a) Gross vs. microscopically positive disease
  - b) Role of selective neck dissection
- 4) Role of adjuvant radiation therapy

### **Objectives:**

At the conclusion of this course, attendees will be able to discuss

- The surgical management of primary melanoma of the head and neck including surgical margins and wound closure;
- The indications for sentinel lymph node biopsy in melanoma. The problems inherent to node mapping in the head and neck area;
- Management of parotid gland in head and neck melanoma;
- The role of selective cervical lymphadenectomy in head and neck melanoma;
- The role of adjuvant radiation therapy in head and neck melanoma.

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## **C6: Endoscopic Sino-nasal**

**Presenters:** Daniel M. Fliss, MD and Carl H. Snyderman, MD

### **Description:**

Technological advances and increased appreciation of endoscopic anatomy now allow for the resection of many sinonasal tumors endoscopically. Although the surgical techniques are different, the oncological principles are similar. Surgical approaches to the ventral skull base are modular and extend from the sphenoid sinus in the sagittal and coronal planes. For high-grade malignancies, a completely endoscopic craniofacial resection of the skull base and dura is the gold standard. Challenges of the endoscopic approaches include instrumentation, hemostasis, and reconstruction of dural defects. In this course, the faculty will present the principles of endoscopic tumor management, review pertinent anatomical relationships, describe surgical techniques, and demonstrate endoscopic methods of hemostasis and dural reconstruction. Early outcomes data including complications and oncological results will be presented.

### **Objectives:**

- Understand the principles of endoscopic surgery for sinonasal malignancies;
- Recognize key endoscopic anatomy;
- Recall the steps of an endoscopic craniofacial resection;
- Recognize the risks and limitations of endoscopic techniques.

## **C7: How I Do It: Antero Lateral Thigh Flap**

**Presenters:** Keith E. Blackwell, MD and Gerry F. Funk, MD

### **Description:**

The anterolateral thigh flap has emerged recently as an extremely useful fasciocutaneous perforator flap in head and neck reconstruction. The flap has demonstrated utility in a number of head and neck applications including pharyngoesophageal reconstruction, oral cavity reconstruction, skin surface replacement, and many instances in which a relatively thin, easily conformable flap is needed. The flap is slightly thicker than a forearm flap, for instances in which additional bulk is not available with most forearm flaps and is available without turning the patient as would be needed for a subscapular system soft tissue flap. The donor site rarely requires more than primary closure unlike the forearm flap. The primary drawbacks to this flap have been the thickness of the flap in the North American population, and the variable anatomy encountered during harvest. This course will focus on the more common uses of this flap, the anatomy, and harvest techniques that render the variable anatomy less of an impediment.

### **Course Outline:**

- A. Anatomy: The anatomy of the pedicle and anterolateral thigh will be presented, and the variations will be discussed.
- B. Flap Utilization: Cases in which the flap are frequently used will be presented.
- C. Harvest: A video of a flap harvest will be presented with additional slides demonstrating anatomic and technique highlights.

### **Objectives:**

- In-depth understanding of the flap anatomy.
- Clear understanding of the harvest techniques.
- Appreciation for the head and neck reconstructive situations for which the flap is suited.

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## **C8: Sarcomas of the Head and Neck**

**Presenters:** Brandon G. Bentz, MD and Erich M. Sturgis, MD

### **Description:**

Sarcomas are a rare group of tumors, with those sarcomas arising in the head and neck region being even rarer still. Head and neck sarcomas are broadly classified as bony and soft tissue, and further subclassified by histologic appearance and grade. Both genetic and environmental risk factors exist for these tumors. Symptoms are often nonspecific and diagnosis is consequently delayed. Accurate imaging, staging, histologic classification and grading are critical to ultimate treatment planning. Complete surgical resection continues to be the primary treatment of choice if it can be accomplished

with acceptable morbidity. More recently, multimodality therapy is becoming the standard particularly for high-grade and pediatric sarcomas. Prognosis has been linked to age (child versus adult), grade, size, extension, margins, subsite, lymph node metastases, and distant metastases. Common potential pitfalls in the evaluation and treatment of these rare tumors include inappropriate biopsy, pathologic misdiagnosis, inadequate imaging, and the lack of a multidisciplinary evaluation and treatment.

This course will present an overview of sarcomas of the head and neck. The epidemiology, etiology, and histopathologic classifications will be discussed. Appropriate diagnosis and evaluation of these rare tumors will be reviewed along with potential pitfalls in their workup. Distinguishing clinical, radiographic, and histopathologic characteristics of the major subtypes will be discussed. Standard and emerging treatment paradigms for both children and adults will be presented. Recommended follow-up and prognosis will also be reviewed. Instructive cases will be presented.

### **Course Outline:**

#### **Epidemiology**

Incidence  
Mortality  
Prevalence

#### **Etiology**

Familial Syndromes  
Environmental Exposures

#### **Classification**

Histologic tissue of origin  
Grading  
Site

#### **Diagnosis and Evaluation**

Signs and symptoms  
Radiology  
Biopsy  
Staging  
Potential pitfalls

#### **Characteristics of the Four Leading Histologies**

Osteosarcoma  
Malignant Fibrous Histiocytoma  
Angiosarcoma  
Rhabdomyosarcoma

#### **Treatment**

Childhood  
Rhabdomyosarcoma  
Childhood Non-rhabdomyosarcoma  
Osteosarcoma  
Adult High-grade Soft Tissue Sarcomas  
Low-grade sarcomas

#### **Prognostic Factors/Outcomes**

#### **Instructive Cases**

### **Objectives:**

- To understand the epidemiology and classification of sarcomas of the head and neck;
- To be comfortable with the diagnosis and evaluation of these tumors;
- To understand the standard treatment paradigms for these tumors;
- To avoid the pitfalls in management of these tumors.

## **C9: Tumors and Surgery of the Parapharyngeal Space**

**Presenters:** Kerry D. Olsen, MD and David J. Terris, MD

### **Description:**

Tumors and surgery of the parapharyngeal space (PPS) present many challenges to the treating physician because of the varied tumor pathology encountered in this area. This course will review the pertinent anatomy of the parapharyngeal space and the clinical characteristics of its neoplasms. Special emphasis will be given to new and emerging technology in the evaluation and management of parapharyngeal space tumors. A number of tools have been developed that lend themselves to the surgical management of PPS tumors. Because these tumors are often well vascularized, hemostatic instruments such as the harmonic shears (based on frictional energy) and Shaw Hemostatix Scalpel (so called “hot knife”) can be used to minimize bleeding and improve visualization. Additionally, cranial nerve monitoring (facial and even accessory or vagal) may provide a further measure of safety for some surgeons. The surgical indications and technique for safely managing tumors in this area, the cervical parotid approach and the use of mandibulotomy, will be presented. The role of embolization for vascular PPS tumors is controversial but a balanced assessment of this and other adjunctive therapies will be presented. Illustrative case studies will also be presented for added audience participation.

### **Course Outline:**

- A. Parapharyngeal Space Anatomy
- B. Tumor Characteristics
- C. Evaluation and Decision Making
- D. Surgical Approach
- E. New and Emerging Technology
- F. Embolization and Other Adjuvant Therapies
- G. Case Discussion

### **Objectives:**

- The relationship between anatomic areas and tumor behavior.
- The current surgical approaches used to resect tumors of the parapharyngeal space.
- The role of new and emerging technology in the management of vascular lesions of the parapharyngeal space.

## **C10: How I Do It: Parathyroid Surgery**

**Presenters:** Jeremy L. Freeman, MD and Keith S. Heller, MD

### **Description:**

Over the last century the management of hyperparathyroidism has demonstrated a rich history with great strides having been made from the unsophisticated treatment of

patients in Europe and North America to world-wide high technological treatment.

Further, the profile of presentation of the hyperparathyroid patients has evolved from those who, in the past, have appeared with end stage tertiary hyperparathyroidism to the present where asymptomatic patients comprise the majority of the present cohort.

The status of localization studies has also changed over the last century with a more accurate battery of investigatory modalities now available. These will be discussed in detail.

The surgical indications as well as the surgical approach including intraoperative management with rapid assay PTH and/or the gamma probe will be discussed. In addition, the technique will be illustrated with a video presentation.

### **Objectives:**

At the end of this session the participants will be able to provide comprehensive management to patients presenting with hyperparathyroidism, including adenomatous disease both single and multiple as well as hyperplasia.

Further, step-by-step technical instruction will be provided by way of video surgical presentation.

## **C11: Salvage Surgery In The Chemo-radiation Era**

**Presenters:** Jonas T. Johnson, MD and Pierre Lavertu, MD

### **Objectives:**

- Identify modern issues which challenge the surgical team;
- Discuss current techniques to reduce post operative wound complications;
- Recognize the difficulty in planning surgery for the patients who has failed chemo/radiation.

We have entered another era of “Organ Preservation”, in which patients are given combination chemotherapy with irradiation in an attempt to enhance response, and improve local, regional, and distant control. Surgical management of these patients after therapy can be extremely challenging. The following issues facing the surgeon will be discussed.

#### **A. CAN AN UNRESECTABLE CANCER BE MADE RESECTABLE?**

Under some circumstances patients with truly unresectable cancer are treated with chemo/rads. Can these patients ever be considered for curative surgery?

#### **B. WHAT LEGITIMATE ALTERNATIVE EXIST FOR THE TRULY UNRESECTABLE PATIENT??**

Does further chemotherapy or re-irradiation offer these patients hope of a prolonged disease free interval? What is the “cost” of these therapies?

#### **C. HOW SHOULD THE NECK BE MANAGED POST THERAPY?**

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There is significant controversy regarding the need for a planned neck dissection following treatment of advanced neck disease. When should a neck dissection be performed? What should be the extent of the neck dissection. Modified radical, selective, or neck dissection?

## D. WHAT TECHNICAL MODIFICATIONS ARE CURRENTLY BEING USED TO REDUCE POST-SURGICAL MORBIDITY IN PATIENTS WITH PRIOR CHEMO/RADIATION?

Are wounds preferentially reconstructed with tissue which has not been irradiated?

## E. WHAT CAN BE DONE TO REDUCE THE INCIDENCE OF POST TREATMENT PHARYNGEAL STENOSIS AND DYSPHAGIA?

Does oral feeding during therapy reduce stenosis? Would early dilatation be beneficial? Can IMRT and other "focused" techniques reduce sequelae?

At the end of this presentation the listener will have a better understanding of the evolving role of surgery in this era of organ preservation.

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## **C12: Head and Neck Ultrasound (Office-Based Neck Ultrasound)**

**Presenters:** Marc D. Coltrera, MD and David L. Steward, MD

### **Course Outline:**

#### A. Utility of Office Based Neck Ultrasound

1. Best imaging for thyroid- sizing and malignant features
2. Better parathyroid localization
3. Optimize FNA of neck/thyroid masses- reduce non-diagnostic rate and sample error
4. Replacing radioiodine scans for thyroid cancer surveillance (coupled with Tg)
5. Endocrine surgery practice building

#### B. Ultrasound

1. Thyroid
2. Fine Needle Aspiration
3. Parathyroid

#### C. Conclusion: Ultrasound for parathyroid adenomas

1. Can be accurately performed by surgeon
2. More sensitive than sestamibi in this cohort
  - a. Larger multi-institutional study needed
  - b. Combined sensitivity 97%
3. Limitations
  - a. Very technical dependent: real-time vs. saved frames
  - b. Thoracic inlet/superior mediastinum: two false negatives, three true positive in this cohort

#### 4. Advantages

- a. Lower cost, office based procedure
- b. Greater anatomic detail than sestamibi

#### D. Ultrasound- Lymph Nodes

##### 1. Advantages of Office Ultrasound

- a. Extension of physical examination
- b. Best assessment of thyroid
- c. Comparison follow-up dimensions
- d. Accurate needle placement with FNA
- e. Better differentiation of mass structure
- f. Comprehensive node examination
- g. U/S analysis in real time
- h. Patient convenience

##### 2. Relative Disadvantages of Office Ultrasound

- a. Cost: \$25K outlay, cover in first year
- b. Time: Thyroid US takes < 5 minutes
- c. Learning Curve: Steep for thyroid > parathyroid > nodal mets
- d. Credentialing: AAO-HNS, ACS, AACE have accreditation courses
- e. Conflict with radiology: only an issue in hospital based practice

#### E. Ultrasound CPT Coding

1. Diagnostic neck ultrasound- 76536
2. Ultrasound for needle placement- 76942
3. Ultrasound guided FNA- 10022
4. Can code office visit and procedures: requires procedure note
5. Can code 76942/10022 multiple times for multiple biopsies performed.

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## **C13: Sentinel Lymph Node Biopsy for Clinical Node Negative Squamous Cell Carcinoma of the Oral Cavity**

**Presenters:** Ann M. Gillenwater, MD and Thom R. Loree, MD

### **Course Outline:**

1. The history of the development of SLNB of squamous cell carcinoma of the oral cavity.
2. Review of current literature and practice.
3. Presentation of case Material and Results.
4. Discussion of technical details and controversial issues.

### **Objectives:**

The first objective is to convey to the course participants the rationale of, indications for, and contraindications to performance of sentinel lymph node biopsy in patients with oral cavity squamous cell carcinoma;

The second objective is to convey techniques and pitfalls of sentinel lymph node biopsy for oral cavity cancer.

## **C14: Endoscopic Laryngeal Surgery**

**Presenters:** Bruce H. Haughey, MD and  
Wolfgang Steiner, MD

### **Description:**

Minimally invasive approaches to resection of malignant and benign diseases is now commonplace in many surgical disciplines and even the established standard of care. Although approaches to the larynx using laser endoscopy were developed in the 1970s, only in the last decade have these cost-effective techniques been extended to larger tumors. Several centers in Europe and more recently a few in the United States, have started to use transoral laser microsurgery (TLM) extensively for management of laryngeal tumors, including stage 3 and 4 malignant disease. With its potential for excellent oncologic and functional outcomes, minimal length of stay and low morbidity, it is not surprising that there is worldwide interest in the development of this field. Publications to date have supported the aforementioned advantages in a variety of subsites, including the larynx and hypopharynx. Data are also accruing that TLM is oncologically sound for selected salvage resections following failed radiation. The successful accomplishment of TLM resections, however, is a multifaceted exercise and requires the right equipment, an informed operating room team, pathologists who are sufficiently familiar with head and neck anatomy to generate a meaningful report from multi-part specimen, and surgeons who have mastered the “learning curve”.

### **Course Outline:**

This Instruction Course presents comparative data that underpin the oncologic effectiveness, rapid functional recovery and the low morbidity/toxicity of this method. How to approach tumors of the glottic, supraglottic larynx, and hypopharynx will be discussed. Specifically, the organ preserving potential of these procedures will be demonstrated, justified by statistical data. We will also present functional and quality of life outcomes. Case selection, equipment and technical pearls will be addressed, as well as advanced exposure techniques and indications for combined transoral and open resections.

### **Objectives:**

Upon completion of this course participants will:

- Understand selection process of cases for laryngeal endoscopic surgery;
- Understand endoscopic techniques for resection;
- Understand results of endoscopic laryngeal resections.

## **C15: How I Do It: Scapula Flaps**

**Presenters:** John J. Coleman, III, MD and Mark Urken, MD

### **Description:**

Contemporary head and neck reconstruction using free tissue transfer has an expanded array of donor sites from which to choose in order to achieve an optimal outcome for the patient and the particular disease process. There are 4 primary options for transferring vascularized bone for maxillo-mandibular reconstruction: the fibula, iliac, scapula and radial forearm donor sites. Each of these sites have unique features with respect to the bone and the soft tissue elements that can be harvested.

The subscapular system of flaps is perhaps the most versatile donor site with respect to the array of soft tissue flaps which can be transferred with the bone from the lateral scapular border. In addition to the vascularized bone and the traditional transversely oriented scapular flap, the vertically oriented parascapular flap and the latissimus dorsi muscle (or the musculocutaneous flaps) can be harvested. The serratus anterior muscle can also be incorporated in the composite flap if additional soft tissue is required. One additional feature which makes this donor site unique is the ability to harvest 2 segments of vascularized bone that are supplied by 2 different vascular pedicles which provide the freedom to move those 2 bone flaps in different directions in the inset process while still maintaining the perfusion to both segments. Modifications of the harvest technique will be shown including the use of free vascularized fascia and the reverse flow technique for revascularizing the flap in the vessel depleted neck.

### **Objectives:**

- To understand the anatomy of the posterolateral thorax and vascular anatomy of the subscapular artery system;
- To understand the technique of elevation of subscapular system flaps including the scapula osteocutaneous flap, the bipedicle scapula flap and other variations;
- To understand the clinical situations where these flaps are useful and the strengths and weaknesses of the various types of reconstruction.

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## **C16: Laryngeal Reconstruction**

**Presenters:** Ara A. Chalian, MD and Ralph W. Gilbert, MD

### **Description:**

Reconstruction of the larynx following tumor ablation has had a renaissance over the past decade with an increasing interest in organ preserving surgery in the primary treatment setting. In addition a number of centres have developed new techniques for reconstruction of segmental laryngeal defects following the failure of radiotherapy or concomitant chemoradiation. This course will review the current techniques for

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laryngeal resection in the primary surgery setting as well as for salvage of failure of non-surgical organ preservation strategies. It will use a case based approach to outline the treatment issues outlined below.

## Course Outline:

- A) Reconstruction in the primary surgery setting
  - 1) CHP and CHEP defects
  - 2) Horizontal supraglottic laryngectomy
  - 3) Vertical Segmental defects
  - 4) The post laser resection defect
- B) Reconstruction following failure of non-surgical approaches
  - 1) Overview of defect related problems following RT or ChemoRT
  - 2) Overview of reconstructive options
    - a. Delaere Procedure
    - b. Temporoparietal fascial flap
    - c. Forearm Flap
    - d. Other techniques
- C) Reconstruction of the Cricoid and Trachea

## Objectives:

At the conclusion of this course the attendees will be able to discuss

- The options for reconstruction of the supracricoid partial laryngectomy;
- The options for reconstruction of the segmental laryngeal defect in the primary surgical setting;
- The options for reconstruction of the larynx following segmental resection for salvage of non-surgical organ preservation strategies;
- The options for cricoid and tracheal reconstruction.

## C17: Reimbursement for Head and Neck Surgeons: Working Within the System

**Presenters:** Wayne M. Koch, MD and William M. Lydiatt, MD

### Objectives:

- Gain insight into the broader economic aspects of a head and neck practice such as down stream revenue and its implications for a hospital system;
- Understand several areas where the hospitals can assist in practice development;
- Understand the opportunities and limitations presented by the RUC process for CPT valuation;
- Recognize how proper coding can benefit individual practice and the community of head and neck surgeons.

## C18: Chemoradiation Organ Preservation

**Presenters:** David M. Brizel, MD and Jean Louis Lefebvre, MD

### Description:

Although total laryngectomy is an oncologically sound procedure, much clinical research has aimed to avoid removing the entire larynx. Organ preservation is a rational strategy to the extent that it adheres to the broader concept of function preservation without sacrifice of anti-tumor efficacy. Partial laryngectomies such as supracricoid partial laryngectomies and endoscopic laser CO2 surgery may constitute surgical alternatives in appropriately selected patients. Function preservation is now a major therapeutic aim in locally advanced, resectable head and neck cancer at many anatomic sites including but not restricted to the larynx. Radiotherapeutic strategies that incorporate better understanding of tumor biology (hyperfractionation, accelerated fractionation with concomitant boost, EGFR inhibition) and technical improvements in the ability to deliver radiation more precisely (intensity modulated radiotherapy, IMRT) have improved the therapeutic index. Chemotherapy has also played a definite role in head and neck organ preservation.

### Course Outline:

- A: FIRST GENERATION OF FUNCTION PRESERVATION STRATEGIES: SEQUENTIAL CHEMORADIATION  
That platinum-based chemotherapy protocols provided high response rates in previously untreated patients and that chemoresponsive tumors were also radioresponsive led to consider induction chemotherapy (ICT). After ICT good responders were considered for radiotherapy while poor responders were still candidates for radical surgery. This approach did not jeopardize survival or disease control and allowed preserving the larynx in 2/3 patients, but was never demonstrated to be superior to radiotherapy alone.
- B: SECOND GENERATION OF FUNCTION PRESERVATION STRATEGIES: CONCURRENT CHEMORADIATION  
Concurrent administration of chemotherapy and radiotherapy appeared as able to provide impressive response rates. Concurrent chemoradiation was compared to radiation alone and to sequential chemoradiation. Higher larynx preservation rates were achieved with concurrent therapy, but survival remained unchanged. Concurrent chemoradiation has improved survival compared to radiotherapy alone in advanced nasopharynx, oropharynx, and hypopharynx cancer. Both the incidence and duration of severe acute and chronic toxicity are exacerbated by concurrent therapy.
- C: THIRD GENERATION OF LARYNX PRESERVATION STRATEGIES: SEQUENTIAL AND CONCURRENT CHEMORADIATION  
ICT programs that utilize taxanes are superior to those that do not. This fact has reopened the discussion on the place of ICT in the armamentarium for organ/function preservation. ICT followed by concurrent chemoradiation vs concur-

rent chemoradiation is under active investigation in several prospective randomized trials.

## D: NEW PROSPECTS

Targeted therapies are under evaluation in head and neck cancers. One randomized trial has shown that EGFR inhibition with a monoclonal antibody improved local-regional disease control and survival without a significant increase in acute toxicity. Anti-angiogenic strategies are also under active evaluation.

### **Objectives:**

At the conclusion of this course, attendees will be able to discuss:

- The efficacy of chemoradiation for organ and function preservation in laryngeal and non-laryngeal primary sites;
- The limitations and morbidities of these strategies;
- Developmental strategies for the future.

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## **C19: Mid-facial Reconstruction**

**Presenters:** Joseph J. Disa, MD and  
Neal D. Futran, MD, DMD

### **Description:**

Loss of the maxilla and mid-facial structures secondary to tumor extirpation has significant functional and aesthetic consequences. The variable loss of both soft tissue and/or bone leading to collapse of the lip, cheek and periorbital soft tissues as well as palatal competence present a challenging dilemma for reconstructive surgeons. Efforts have been made to classify these mid-facial defects and provide appropriate algorithms for optimal reconstruction. Not only does the cavity need to be obliterated and mid-facial contours recreated, but the restoration of swallowing function, phonation and mastication is imperative for an ideal result. Traditionally these defects have been obturated by a maxillofacial prosthesis but advances in tissue transfers, particularly microvascular free flaps, have greatly expanded reconstructive options. The wide variety of both soft tissue and bone containing free flaps which offer unique properties applicable for each defect will be described. Combinations of free tissue transfer, local flaps, and/or maxillofacial prostheses may achieve a more ideal result than a single technique alone. Advances in the field of osseointegration have also enhanced the ability to achieve optimal function and form. It is clear that no single flap or technique is sufficient to reconstruct mid-face defects in all cases. The choices should be tailored to the bony and soft tissue needs of each specific defect, denture-bearing potential of the native tissues, and available prosthodontic support. This course will emphasize utilizing a multi-disciplinary approach to reconstruct these defects to yield optimal results.

### **Objectives:**

At the conclusion of this course, attendees will be able to:

- To identify relevant classification schemes for mid-facial defects;
- To describe the free flaps and local flaps available to reconstruct mid-facial defects;
- To discuss specific techniques appropriate to each mid-facial defect;
- To discuss the multi-disciplinary approach to this reconstructive challenge.

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## **C20: Transnasal Esophagoscopy**

**Presenters:** Christine G. Gourin, MD and  
Henry T. Hoffman, MD

### **Description:**

Chevalier Jackson and other otolaryngologists pioneered the use of rigid esophagoscopy years ago for examination, dilation, biopsy, and foreign body removal. Now, thin flexible transnasal esophagoscopy (TNE) endoscopes are available with distal-chip cameras for high-quality optics. A single channel extends along the length of this versatile endoscope to permit irrigation, suction, air-insufflation, topical delivery of anesthetics, and instrumentation for biopsy or injection of the larynx, pharynx, trachea and esophagus. TNE is particularly useful in the management of patients with head and neck cancer as a valuable adjunct in the evaluation of post-treatment dysphagia and may facilitate and in selected cases, replace routine panendoscopy in head and neck cancer patients. TNE is comparable with conventional endoscopy but offers the distinct advantage of performance in the office without sedation, which results in significant cost savings and improved patient care.

### **Course Outline:**

Transnasal esophagoscopy is safe and efficacious for the evaluation of head and neck cancer patients and has both a diagnostic and therapeutic role in the evaluation and treatment of the patient with head and neck cancer.

#### A. Diagnostic Applications of TNE:

- *Screening:* as a screening tool in high risk patients to evaluate for second primary malignancies
- *Staging:* as a panendoscopy tool in patients with suspected malignancy, that can be performed in the office under topical anesthesia without sedation
- *Biopsy:* TNE is a valuable biopsy tool for obtaining tissue specimens of the pharynx and larynx in patients with lesions suspicious for malignancy.
- *Expanded endoscopy:* the capacity to apply 4% lidocaine through the side port permits the application of topical anesthesia of the larynx to allow transglottic passage of the scope to examine the subglottis and trachea
- *Placement of pH probes*

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## B. Therapeutic Applications of TNE:

TNE has several therapeutic applications in head and neck cancer patients and in particular, facilitates the ability to perform the following procedures in-office:

- *Secondary tracheoesophageal puncture*
- *Assessment pre- and post- dilatation of esophageal stricture*
- *Excision/ablation of tissue*
- *Feeding tube placement*
- *Injection Laryngoplasty*
  - a. *Augmentation (collagen/hydroxyl apatite)*
  - b. *Chemodenevation (botulinum toxin)*

This instructional course will review the uses and technique of TNE in lecture format, with multiple case presentations used to illustrate the uses and limitations of TNE. Liberal use of video demonstrations will enhance this presentation.

### Objectives:

At the conclusion of this course, attendees will be able to discuss:

- Diagnostic and therapeutic uses of transnasal esophagoscopy in head and neck surgical oncology;
- Techniques and pitfalls associated with transnasal esophagoscopy;
- Indications for TNE in a robust head and neck surgical practice.

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## C21: Lip Reconstruction

**Presenters:** Patrick J. Gullane, MD and  
Theodoros N. Teknos, MD

### Description:

This lecture will address all of the surgical options in the repair of lip defects following resection. The content includes a brief review of the functional anatomy of the lip. Surgical techniques including rotation and transposition flaps will be discussed with particular emphasis on practical surgical detail. The choice of flap, its limitations, complications and outcome in partial, subtotal and total lip reconstruction will be discussed. Detailed schematic and intraoperative illustrations will be emphasized to provide a practical approach. Long-term follow-up of each technique will be presented.

The presentation will address the surgical options in the repair of lip defects following resection. It will include a brief review of the functional anatomy of the lip, surgical techniques, including rotation and transposition flaps. The choice of flap, its limitations, complications and outcome in partial, subtotal and total lip reconstruction will be compared.

Detailed schematic and intraoperative techniques will be presented, as well as the long-term follow-up of each technique.

### Course Outline:

1. Content
  1. Review the biology of carcinoma of the lip
  2. Review the clinical decision making process
  3. Present a treatment approach based on tumor extent
  4. Review the role of free-tissue transfer in lip reconstruction
2. Format
  - a) Minor Reconstruction
  - b) Medium Reconstruction
    - a. Small: up to 30%
    - b. Large: 30-80%
  - c) Total Reconstruction
3. Evaluation
  - A. Long-term patient outcome analysis
  - A. Total Composite reconstruction including mandible

### Objectives:

Learn a practical approach to lip reconstruction with application of various reconstructive options after lip ablation.

### References:

- Gullane PJ, Martin JF: Minor and Major Lip Reconstruction. *Journal of Otolaryngology* 12 (2) 75-82, 1983.
- Gullane PJ, Neligan PC: Modern Day Approaches to Lip Reconstruction. IN: *Advances in Otolaryngology- Head and Neck Surgery* Vol 15 ed: Mosby Inc 2001, 203-226

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## C22: Head and Neck Transplantation

**Presenters:** Robert R. Lorenz, MD and  
Robert L. Walton, MD

### Description:

Transplantation in Head and Neck took exciting leaps forward in the last 10 years. In 1998, the first successful composite laryngeal transplantation took place and the patient continues to thrive today with his transplanted larynx. More recently with the success of face transplantation, the entire field of reconstruction of the head and neck has become fertile ground for the development of transplantation options.

### Course Outline:

This course will be divided into two parts. The first will be discussing the field of laryngeal transplantation including historical interest and attempts, preliminary animal studies, and detailing the program which lead to the successful transplant in 1998. Details including the immunosuppressive regimen used and videostroboscopy of the transplanted organ will be shown. Other worldwide attempts and successes in laryngo-tracheal transplantation will be demonstrated. Subsequent research on immunosuppressive regimens which suppress malignant potentiation will be shown. The second portion of the course will cover the subject of composite facial recon-

struction through transplantation, including the ethical implications, technical considerations, and the ability to achieve tolerance via new immunosuppressive regimens. The successful French experience in facial transplantation will be highlighted.

## Objectives:

At the conclusion of the course, attendees will be able to discuss, relative to Head and Neck Transplantation:

- The historical interest and attempts at head and neck transplantation;
- The details surrounding the first successful laryngeal and face transplants;
- New immunosuppressive regimens, achieving tolerance between recipient and donor;
- New immunosuppression, which avoids malignant potentiation.

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## C23: How I Do It: Neck Dissection

**Presenters:** David W. Eisele, MD and Eugene N. Myers, MD

### Description:

Neck dissection is keystone in the management of cancer of the head and neck. Numerous modifications of neck dissection exist and different approaches to these procedures have been described. This course will present in a practical manner the presenters' methods for selective neck dissection and modified radical neck dissection.

### Course Outline:

The course will follow a "how I do it" format and will address the following topics for selective neck dissection and modified radical neck dissection:

1. Indications in neck dissection
2. Preoperative considerations
3. Incisions
4. Exposure of neck contents and nodal levels
5. Operative techniques with surgical "pearls"
6. Wound drainage and closure
7. Postoperative considerations
8. Complications: avoidance and management

### Objectives:

At the conclusion of the course, attendees should be able to discuss:

- The surgical technique of selective neck dissection;
- The surgical technique of modified radical neck dissection;
- The avoidance and management of complications of neck dissection.

## C24: PET-When to Use it

**Presenters:** Russell B. Smith, MD and Richard J. Wong, MD

### Description:

Introduction: FDG-PET imaging is frequently incorporated into the diagnostic evaluation of patients with head and neck cancer. It is most commonly utilized in patients with squamous cell carcinomas of the upper aerodigestive tract, but it can also be useful for other head and neck pathologies such as recurrent thyroid cancer as well as salivary gland malignancies. This imaging technique can play a critical role at many different time periods during cancer care including staging of new primary tumors, assessing the success of cancer directed therapy, as well as evaluating for recurrent disease. To optimally utilize PET imaging, a thorough understanding of image interpretation, as well as appropriate expectations and limitations of the study are required. This course will review the considerations for image interpretation as well as discuss the use of FDG-PET imaging for many clinical scenarios that are encountered in the management of head and neck cancers.

### Course Outline:

#### 1. FDG-PET IMAGING:

As with any radiographic examination, many factors play a role in obtaining a technically satisfactory exam. For PET imaging, the timing of imaging in relationship to therapy, the technique of examination performance, and the interpretation of the imaging are all critical to successful use of PET for head and neck cancer. The presenters will review considerations in PET imaging with examples of PET images to illustrate these issues.

#### 2. FDG-PET FOR UPPER AERODIGESTIVE TRACT CANCERS:

Most squamous cell carcinomas of the upper aerodigestive tract can be easily detected with PET imaging. Its greatest utility is for the detection of recurrent cancer in previously treated fields which can be extremely difficult to evaluate by both clinical exam as well as cross-sectional imaging. PET imaging can also be beneficial for initial staging and assessing treatment response after cancer therapy in certain scenarios. Incorporation of PET imaging in the management plan for both early as well as advanced stage cancers including the unknown primary will be discussed.

#### 3. FDG-PET FOR NON-SQUAMOUS CELL CANCERS OF THE HEAD AND NECK:

Despite PET imaging being most frequently utilized for squamous cell carcinomas, it may play a role in non-squamous cell malignancies of the head and neck. The use of PET in thyroid malignancies is potentially beneficial in recurrent well differentiated tumors that appear to no longer be iodine avid. PET can also play a role in salivary gland malignancies but the tumor behavior plays an important role in the utility of the exam. An algorithm for the use of PET imaging in non-squamous cell malignancies will be discussed.

# — Instructional Course Outlines and Objectives

## Objectives:

At the conclusion of the course, attendees will be able to discuss:

- Considerations in obtaining PET imaging which are requisite to maximizing its benefit in head and neck cancer. The timing of imaging, the technology aspects of imaging, and the interpretation of imaging should be understood;
- The role of PET imaging in staging, assessment of treatment response, and assessment for recurrent disease in upper aerodigestive tract cancers. Expectations of PET imaging in each clinical scenario for early and advanced stage disease should be understood;
- The role of PET imaging in the management of non-squamous cell cancers of the head and neck. An algorithm for appropriate use of PET imaging for thyroid malignancies should be understood.

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## C25: Pharyngeal Reconstruction

**Presenters:** Brian B. Burkey, MD and  
Peter C. Neligan, MD

### Description:

Resection of laryngopharyngeal cancers leads to significant defects in the upper aerodigestive tract. These defects primarily involve the pharynx, but also may involve all or part of the larynx and potentially the cervical esophagus. Repair of stenosis after chemoradiation treatment of similar cancers also creates significant mucosal defects. Although functional deficits are occasionally severe no matter the method of reconstruction, modern flap reconstruction of these defects can lead to an improvement in the quality of life for these unfortunate patients. This course will discuss the common defects encountered in the treatment of laryngopharyngeal cancers, the flaps used to reconstruct those defects, general guidelines important in the repair of these defects and expected functional outcomes in this type of reconstructive effort. An algorithm for pharyngeal defect repair will be presented as a summary of this discussion.

### Course Outline:

- I. Partial Pharyngeal Defect Reconstruction
  - a. Defining partial vs. total pharyngeal defects
  - b. Partial defect repair methods with regional and free flaps
    - i. Fasciocutaneous flaps
    - ii. Myocutaneous flaps
    - iii. Perforator flaps
  - c. Laryngeal preservation in partial pharyngeal reconstruction
  - d. Outcomes data
- II. Total Pharyngeal Defect Reconstruction
  - a. Total defect repair with regional flaps
  - b. Total defect repair with free tissue transfer techniques—general guidelines

- c. Flap selection for free tissue repair of total pharyngeal defects
  - i. Fasciocutaneous flaps
    1. Anterolateral thigh
    2. Radial forearm
  - ii. Enteral flaps
    1. Jejunal flap
    2. Gastro-omental flap
    3. Gastric pull-up
- d. The indication for gastric pull-up in pharyngeal reconstruction
- e. Outcomes data

## Objectives:

At the conclusion of this course, attendees will be able to discuss:

- The distinction between partial and total pharyngeal defects and the functional deficits related to their reconstruction;
- Methods useful in the repair of partial pharyngeal defects, and the resources necessary to complete the repair successfully;
- Methods useful in the repair of total pharyngeal defects, and the resources necessary to complete the repair successfully;
- The role of gastric pull-up in pharyngeal reconstruction.

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## C26: How I Do It: Partial Laryngectomy

**Presenters:** Christopher H. Rassekh, MD and  
Jatin P. Shah, MD

### Description:

Conservation surgery of the larynx is an important treatment option in patients who present with early staged supraglottic or glottic carcinoma and should be considered a treatment option in the selection of therapy amongst external irradiation and endoscopic resection. Conservation surgery of the larynx is also technically feasible in patients who have failed external radiation therapy and whose tumor meets the criteria required for successful completion of a partial laryngectomy.

For carcinomas of the supraglottic larynx, the selection criteria depend on patient factors and tumor factors. In general, the patient should have a good understanding of the operative procedure and the rigorous postoperative rehabilitation required following this surgery and should have an acceptable pulmonary status to handle varying degrees of aspiration of saliva and fluids postoperatively. In general, T1 and T2 tumors of the supraglottic larynx without fixation of vocal cords are suitable for a horizontal partial laryngectomy. Varieties of extensions of the standard supraglottic partial laryngectomy will be discussed during this presentation.

For carcinomas of the glottic larynx, the criteria for satisfactory performance of the operation relate to the local extensions

of tumor into the paraglottic and subglottic space. In general, patients with subglottic extension beyond 5 mm are considered not suitable for a standard vertical partial laryngectomy. Patients with reduced mobility of the vocal cord or even fixed vocal cord may still be suitable for a vertical partial laryngectomy as long as the disease is confined to the ipsilateral hemilarynx without any subglottic mucosal extension. Tumors that extend to the anterior commissure are not a contraindication and an anterolateral vertical partial laryngectomy can be safely performed. Finally, patients with tumors extending to both vocal cords are also considered for a conservation laryngeal operation through a supracricoid partial laryngectomy with cricohyoidoepiglottopexy. The technical variations of vertical partial laryngectomy including hemilaryngectomy, anterolateral vertical partial laryngectomy and supracricoid partial laryngectomy will be demonstrated during this presentation.

Finally, outcomes of conservation surgery in the patients who undergo these procedures primarily or for radiation failure persistent tumors will be shown in this presentation to show the feasibility and efficacy of conservation surgical procedures for recurrent carcinomas of the larynx.

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## **C27: Management of the Eye in Head and Neck Cancer**

**Presenters:** Peter E. Andersen, MD and Ehab Y. Hanna, MD

### **Description:**

Management of malignant and less commonly benign, neoplasms of the facial skin, nasal cavity, paranasal sinuses and anterior cranial fossa often require manipulation of the orbital contents. Orbital exenteration causes severe functional and cosmetic defects. Tumors that arise from or encroach upon the orbit can, in some circumstances, be resected without sacrificing vision, however, resection of the supporting structures of the eye such as the lids, bony orbital walls and lacrimal system may create functional problems that preclude good vision even with a functional eye.

The presenters will discuss the literature and their personal experience. Emphasis will be placed on practical matters often encountered when dealing with neoplasms of the orbit, facial skin, nasal cavity, paranasal sinuses and anterior cranial fossa. Algorithms for management of specific clinical scenarios will be presented and specific ancillary procedures designed to improve visual function if orbital preservation is chosen.

The course will be presented as a series of brief didactic discussions and case presentations with radiographic imaging. Discussion and audience participation is to be welcome at all points.

### **Objectives:**

At the conclusion of this course, attendees will be able to discuss:

- The anatomy of the orbit and the function and consequences of resection of supporting orbital structures such as the lids, bony orbital walls and lacrimal system;

- Clinical findings and imaging criteria useful for determining management of the eye in head & neck cancer;
- Intraoperative decision criteria for determining whether orbital preservation is possible;
- Orbital complications resulting from orbital preservation and their management;
- Management options for reconstruction when the supporting structures of the orbit require resection.

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## **C28: Dilemmas In Reconstruction Of the Head and Neck**

**Presenters:** Daniel G. Deschler, MD and Mark K. Wax, MD

### **Description:**

Reconstruction of defects of the head and neck following oncologic ablation has been shown to have a major impact on the rehabilitative potential of patients. While the ability to return to normal form and function following a large oncologic ablation is dependent to a great extent on what tissues have been removed, the reconstructive surgeon can certainly impact this return by their choice of composite tissue as well as their technique of reconstruction. It has been well documented that free tissue transfer of composite tissue is best considered for reconstruction of composite tissue defects. Over the years, a large number of free tissue donor sites have become available. This has made it possible to tailor the tissue to be transferred to closely mimic the donated tissue. Many authors have proposed algorithms for reconstruction of many areas of the head and neck. However, there still remains many times and circumstances where the exact or best reconstructive modality is undefined. This course will discuss a number of these more complex issues.

### **Course Outline:**

#### **A: LATERAL MANDIBULAR DEFECTS:**

Limited size defects of the lateral oral mandibular complex can be reconstructed using free bone flaps ranging from scapula, fibula, and radial forearm to soft tissue with a plate to no reconstruction and allowing for collapse. The course directors will present a number of cases discussing various options along with their benefits as well as drawbacks.

#### **B: MAXILLARY SINUS DEFECTS FOLLOWING MAXILLECTOMY:**

Either obturator and soft tissue, or a soft tissue bony free tissue transfer can effectively treat these. Morbidity of all of these modalities as well as potential benefits will be discussed.

#### **C: RECONSTRUCTION OF PATIENTS FOLLOWING FAILED CHEMO RADIATION PROTOCOLS:**

Chemoradiation is being used increasingly for organ preservation. Unfortunately, patients continue to develop a recurrence with this treatment modality. Surgical ablation is often the only form of salvage treatment available. The role

# — Instructional Course Outlines and Objectives

of free tissue transfer in patients who have failed organ preservation treated with chemoradiation will be discussed for various subsites.

All of the instruction course will take the format of case presentation with definition of the problem. The two instructors will then discuss their method of resolving the issue and audience participation is to be welcome at all points.

## **Objectives:**

At the conclusion of this course, attendees will be able to discuss:

- The current methods for reconstruction of lateral mandibular defects. The associated morbidity as well as functional outcomes to be expected with each of these treatment options;
- The morbidity associated with maxillectomy defects. A discussion of the methodology of rehabilitating these patients and expected functional outcomes;
- The morbidity of salvage surgery in patients who have failed organ preservation with chemoradiation. An approach and algorithm to reconstruction to decrease the morbidity and increase the functional and improve the functional outcomes should be understood.

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## **C29: Nasal Reconstruction**

**Presenters:** Gary C. Burget, MD and Jeffery S. Moyer, MD

### **Course Outline:**

1. Full thickness defect consideration (subunit principle)
2. Choice for internal nasal lining
3. Cartilage support
4. Choice for external lining
5. Management of adjacent subunit defects

### **Objectives:**

To gain a further understanding of complex nasal reconstruction by case examples and intraoperative video. Emphasis will be placed on full thickness defects requiring internal and external lining along with cartilaginous support.

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## **R1: Getting Your Grant Funded**

**Presenters:** Thomas E. Carey, MD, PhD and  
Bhuvanesh Singh, MD, PhD

### **Course Outline:**

- A. What grant options are available?  
Society vs. NIH grants
- B. What constitutes a good application?
  1. Important unanswered question.
  2. Testable hypotheses
  3. Strong preliminary data

4. Consider review criteria as you write

### **C. NIH Review Criteria**

Significance  
Approach  
Innovation  
Investigator  
Environment  
Budget  
Vertebrate Animals  
Human Subjects  
Hazards  
Plan for sharing access to new reagents

#### **Significance**

If this work is funded ...  
Everyone will live happily ever after  
Every child will grow up to be president  
Better than sliced bread

#### **Approach**

This will be an Aim by aim, sometimes even  
experiment by experiment  
Strengths of the approach

#### **Innovation**

How is this new and different?  
Novel approach, novel method, novel idea

#### **Investigator**

Do you have the experience and training necessary  
to carry out the work?

If not have you found collaborators with credibility  
on the areas that you are a novice?

Previous publications, preliminary data, show that all  
aims can be done

#### **Environment**

Is your institution a place that will foster this work?

Are there core facilities that will make it easier to  
carry out the proposed work?

Are there colleagues with special expertise that will  
make you more likely to succeed?

Are there intellectual and physical resources that  
facilitate your work?

Do you have access to animals or clinical specimens  
that are necessary?

#### **Budget**

Is the budget appropriate?

Is it well justified? Can you explain the role of each  
person and how they are necessary to the  
accomplishment of the aims?

For budgets greater than 10 modules you require  
careful and complete justification.

**Hazards-**Reviewers are asked to comment on potential  
hazards

Specific requirements for vertebrate animal use  
Must be followed as laid out in instructions

Specific Requirements for Human Subjects  
Must be organized as described in instructions

D. Grant organization that covers all important points  
Abstract- Mini paper-what, why. How. and significance  
Background and Significance  
Preliminary Data  
Research Design and Methods  
Hypothesis driven experiments  
Experiments can test the hypothesis  
Possible Pitfalls and Alternative strategies

E. Finish early and send out for external and internal review  
For outside reviewers- Select reviewers that will give good critique but don't use a friend who is on your study section because you don't want to eliminate the friend.

F. Get it to the right study section (if possible)

## Objectives:

Upon completion of the course the participant will have a strong over view of the grant organization and writing process. The participant will have knowledge of the important components of the review process and how this can affect the reviewer's impressions of your proposal. Specific guidelines on formatting, structure, and ideas for how to present aims and set up the proposal to help the reviewer will be suggested.

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## R2: Genomic Proteomic Profiling of Head and Neck Cancer

**Presenters:** Christine H. Chung, MD and  
Wendell G. Yarbrough, MD

### Course Outline:

- a) Genomics/Proteomics
- b) Platforms of analyses
- c) Discovery
- d) Prediction of tumor behavior
- e) Shortcomings
- f) Techniques for validation

### Objectives:

- Understand the techniques for discovery and validation of findings;
- Understand applications of these technologies to Head and Neck Cancer;
- Understand major shortcomings of data analyses.

## R3: Mouse Models for Head and Neck Cancer

**Presenters:** Michiel van den Brekel, MD, PhD and  
Bert W. O'Malley, Jr., MD.

### Description:

Genetic manipulation of mouse embryonic stem cells has enabled the generation of transgenic mice with a great variety of genetic alterations. Conditional knockout of genes has enabled to specifically alter gene expression at a certain site in the corps of the mouse. In addition to transgenic mouse models, there are syngeneic mouse models as well as human tumors in athymic mouse models that may be utilized to develop novel treatments for head and neck cancer. In this course, the current possibilities and future prospects of these mouse models and transgenic techniques as applied to head and neck squamous cancer will be discussed.

### Course Outline:

A: Generation of transgenic mice:

Several techniques can be used to modify the genome of the mouse. In the course some of these techniques will be shortly explained.

B: Systems for tissue specific and time controlled gene expression

The Cre-lox system and tetracycline controlled gene expression have enable to specifically target multiple tumor suppressor and oncogenes in organs of the mouse. In head and Neck cancer we have gained experience using the cre-lox system and tamoxifen inducible cre expression using the Cre-ERT construct.

C: Transgenic mouse models for head and neck squamous carcinoma:

In the course the currently available transgenic mice, developing oral squamous cell carcinoma's will be discussed. Promotors such as K14, ED-L2 or local switching of genes using Cre-ERT and tamoxifen in combination with knock-out for P53, P16, Rb, Ink4a and E-cadherin or upregulation of cyclin D1 or Ras have shown to produce oral squamous cell carcinomas. The prospects and limitations of these models will be discussed.

D. Syngeneic mouse models for developing treatments for head and neck cancer:

We will describe the SCCVII murine model for squamous cell cancer for both floor of mouth and flank tumor cell implantation and discuss the benefits and problems with each site. We will then describe how this model has been used to develop novel gene and molecular therapies for head and neck cancer and provide examples and data from key experiments.

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## E. Human tumor murine models:

When investigating and developing novel therapies for human head and neck cancer, there are theoretical advantages to studying actual human tumor responses using a mouse host. Given the species conflict, human tumors must be grown in immunocompromised mice, the most commonly used being the nu/nu athymic mouse. We will discuss how this model is created and used and provide examples of novel combination gene and conventional chemoradiation therapy experiments.

### Objectives:

At the conclusion of this course, attendees will be able to discuss:

- The current possibilities of transgenic mouse design;
- The common and available murine models and their advantages and disadvantages as applied to the development of novel therapies for head and neck cancer.

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## R4: Smoking Cessation, Alcohol, and Depression Intervention

**Presenters:** Janice Blalock, PhD and  
Sonia. A. Duffy, PhD, MS, RN

### Course Outline:

- I. Evidenced-Based Data
- II. Application to Clinic Settings
  - a. Clinical Trials vs. Reality
  - b. Medicare Reimbursement
- III. Smoking Assessment
  - a. 5 A's
  - b. Stages of Change
- IV. Pharmaceutical Intervention
  - a. 5 types of Nicotine Replacement Therapy
  - b. Zyban
- V. Behavioral Intervention
  - a. Brief Counseling
  - b. Cognitive Behavioral Therapy Cessation Workbook
  - c. Quitlines
  - d. Relapse Prevention
- VI. Comorbid Alcohol Use
- VII. Comorbid Depression
- VIII. Case Studies

### Objectives:

- To gain knowledge in evidence based smoking interventions, application of smoking cessation in clinic settings, smoking assessment, pharmaceutical and behavioral intervention, treating smoking along with comorbid alcohol use and/or depression;
- To apply knowledge to case studies.

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## R5: Markers of Outcome and Response to Therapy

**Presenters:** Carol R. Bradford, MD and  
Joseph A. Califano, MD

### Course Outline:

- I. Approach to biomarker identification/testing
  - a. cDNA microarrays
  - b. Tissue microarrays
- II. Importance of validation in independent datasets
- III. Importance of prospectively collected, previously untreated, uniform cohorts matched for site and stage
  - a. Examples of results obtained from large clinical trials
  - b. Examples of different results in non-uniform or unmatched datasets
- IV. Testing and confirmation of biomarker results
  - a. *in vitro* models
  - b. *in vivo* models
- V. Using biomarkers as tools to direct novel therapies
  - a. Examples
    - i. p53-mdm2 inhibitors
    - ii. Bcl-xL inhibitors
- VI. Current biomarkers for prognosis
  - a. Biomarkers in invasive disease, e.g. HPV, p53
  - b. Biomarkers in premalignant disease
    - i. Loss of heterozygosity
    - ii. Toluidine blue/vital staining
- VII. Biology of detection in body fluids
  - a. Field cancerization
  - b. Serum, blood, and bone marrow compartments
- VIII. Biomarkers for Staging using body fluids
  - a. Protein based
  - b. Cell based
  - c. Nucleic acid based
    - i. RNA
    - ii. DNA and epigenetic alterations
- IX. Biomarkers for Surveillance and Risk Assessment
  - a. Promoter Methylation

## **R6: Immunotherapy for Head and Neck Cancer: Developing Cancer Vaccine Trials and Translating Basic Immunology into the Clinic**

**Presenters:** Robert L. Ferris, MD, PhD and  
Duane A. Sewell, MD

### **Description:**

Major advances in our understanding of basic immunological responses to cancer have enabled the development of early stage clinical trials evaluating safety and immunogenicity of cancer immunotherapy. While therapeutic efficacy of cancer vaccination is the ultimate goal, the appropriate development and design of Phase I immunotherapy trials is crucial to the evaluation and future progress of cancer vaccination. Issues involve the selection of patient populations, selection of immunological endpoints, and plans for collection of tumor, lymphocyte and serum specimen for vaccinees. Experience with animal model systems maybe useful to identifying potential human toxicities that maybe avoided or monitored in the Phase I setting. The creation of parallel, correlative laboratory studies is also an important consideration to move human specimens from the clinical setting back to the laboratory, in order to identify biomarkers predictive of response. Ideally, serum biomarkers can be utilized to predict potential candidacy of selected patients and to design personalized regimens and follow individuals over time based on their responsiveness to the vaccination. The clinical trial should be designed to enable the design of second and third stage immunotherapeutic strategies to optimize the therapeutic success while minimizing toxicities. This presentation will provide an overview of the stages of preclinical and early, phase I clinical evaluation of cancer vaccines, using particular examples of current immunotherapy trials ongoing at the University of Pittsburgh Cancer Institute. Cancer vaccines by our group have utilized autologous tumor cells, tumor DNA, or tumor peptide-loaded dendritic cells (DC) to stimulate effective anti-tumor immunity. Clinical evaluation of head and neck cancer vaccines trials is yielding intriguing findings in clinical trials ongoing. The ultimate goal of reducing recurrence and development of second primary tumors is within reach due to these promising immunotherapeutic approaches.

### **Course Outline:**

- I. History of Immunotherapy in Head and Neck Cancer
  - A) Definition
    1. Manipulation of immune system to prevent or treat malignancies
  - B) Earliest trials
    1. BCG
    2. IL-2
    3. Autologous lymphocytes/tumor cells with GMCSF
  - C) Results of these trials

- II. Obstacles of Effective Immunotherapy
  - A) Lack of Tumor Antigens
  - B) Tolerance
  - C) Suppressive microenvironment
  - D) Lack of Immunogenicity of Vaccines
- III. Current Pre-clinical and Clinical Trials to Overcome Obstacles and Develop Effective Immunotherapies for HNSCC
  - A) Those using defined Tumor antigens
    1. p53 multipепitope trial UPMC
    2. HPV DNA and peptide trials JHU and U Maryland
  - B) Non-specific cytokines
    1. IRX trials
  - C) Non-specific costimulation
    1. TRICOM
  - D) Autologous tissue
    1. Autologous DCs – UPMC
- IV The Future
  - A) Preclinical In vitro Studies
    1. Identification of new tumor antigens
    2. Listeria
    3. Ferris In vitro work with APM
    4. Shibuya antibody coated suture
    5. Strome SCID mouse model

### **Objectives:**

To educate the participant on the current state of head and neck immunotherapy and to discuss the future of this important therapeutic modality.

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## **R7: A Scientific Approach to Voice, Olfactory, and Swallowing Rehabilitation in Head and Neck Cancer Patients**

**Presenters:** Alfonsus J. Balm MD and Jeri A. Logemann, PhD, CCC-SLP

### **Description:**

The disconnection of upper and lower airways as a result of total laryngectomy not only affects vocal function/communication and swallowing but also the respiratory and olfactory system. Comprehensive postlaryngectomy rehabilitation, therefore, should include all these aspects. Prosthetic vocal rehabilitation using TEP is presently the method most often selected by patients in discussion with their surgeon preoperatively. Relevant surgical and clinical issues and the treatment of adverse events in TEP will be discussed as will changes in swallowing resulting from total laryngectomy. An update will also be given on the essentials of airway protection and prevention/treatment of the frequent pulmonary problems with

# — Instructional Course Outlines and Objectives

heat and moisture exchangers. Procedures for evaluation and management of swallowing disorders in total laryngectomees will also be discussed. Finally, rehabilitation of the sense of smell, applying an easy to acquire nasal airflow inducing maneuver will be addressed.

## **Course Outline:**

After a scientific introduction to the various aspects of postlaryngectomy rehabilitation, clinical problems will be addressed. The two instructors will then discuss possible solutions in view of well thought-out algorithms. The audience is invited to contribute actively to the discussions.

## **Objectives:**

- Understand the rationale for prosthetic vocal rehabilitation as the gold standard for postlaryngectomy voice restoration and the basic surgical and clinical aspects of Tracheoesophageal puncture;
- Have insight in the most common adverse events of prosthetic voice restoration and in their solutions;
- Have a basic understanding of pulmonary and olfactory rehabilitation of laryngectomized individuals;
- Conduct a thorough functional assessment of swallow and speech in total laryngectomees.

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## **R8: Molecular Methods of Detection and Prediction of Metastases**

**Presenters:** Ruud H. Brakenhoff, PhD and  
Barbara Wollenberg, MD

## **Description:**

Metastatic dissemination both to the lymphatic and haematogenic compartment is one of the key capabilities of cancer cells, and largely determines survival. Reliable markers to predict metastases are still not available, but recent progress indicated that genomics profiling of the tumor as well as molecular diagnosis of residual cancer cells are promising to refine staging. The clinical problems are nonetheless somewhat different. Locoregional lymphatic dissemination is in principle well accessible by neck dissection, and the main

issue is selecting the patients for treatment as frequently occult metastases are present in the clinically N0 neck. The clinical problem for haematogenic metastases is more difficult, as there are no adequate therapies, and patients with distant disease have a bad prognosis. Notwithstanding, early detection of disseminated tumor cells to predict haematogenic metastasis has gained major attention like in many other solid tumors. Occult tumor cells can often be found in the bone marrow, and are likely to be key players in the metastatic process. Their presence is in almost all tumor models, including head and neck cancer, associated with outcome, and their molecular and phenotypic characterization should propel novel therapeutic approaches.

## **Course Outline:**

### 1. METHODS AND CLINICAL RELEVANCE OF MINIMAL DISEASE DETECTION

Various methods have been used to detect residual cancer cells, and the pro's and con's of all methods will be discussed in an interactive lecture. In addition the prognostic relevance of the studies on head and neck cancer patients will be discussed, and the way we should proceed.

### 2. THE METASTATIC CASCADE

Based on the clinical parameters predicting metastatic dissemination, the prognostic relevance of minimal disease detection and the phenotypic and genotypic characterization of DTC in bone marrow, a metastatic cascade model was proposed with either breast cancer and head and neck cancer as the extreme examples of the spectrum, and this model will be discussed in an interactive lecture. Also the results of published genomics profiling studies will be brought into perspective with this model and the future research directions outlined.

## **Objectives:**

At the conclusion attendees will be able to discuss:

- The state of the art in clinical metastatic research, and make decisions on the approaches to follow for future research;
- The current insights in metastatic progression models, and the methods to study these in future research.

# Faculty Listing

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**Lewis C. Cantley, PhD**

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**Thomas E. Carey, MD, PhD**

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## **S001: Autocrine Chemokine Receptor 7 (CCR7) Activation in Squamous Cell Carcinoma of the Head and Neck**

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Chemokine receptor (CCR) 7 expression, which mediates immune cell survival and migration to lymph nodes, has recently been associated with nodal metastasis of squamous cell carcinoma of the head and neck (SCCHN), through activation of the pro-survival, PI3K/Akt pathway. Here we show that this survival pathway is constitutively activated in metastatic SCCHN cells and is enhanced by CCR7 ligand and treatment. In the absence of exogenous ligand, blocking CCR7 reduced the activation of phospho-Akt and Bcl2 in metastatic SCCHN cells, suggesting that secretion of CCR7 ligands, CCL19 (MIP3&#223) and CCL21 (SLC) by tumor cells may be responsible for autocrine activation of CCR7. CCR7 blockade also decreased cell viability by MTT assay, and CCL19 induced-CCR7 activation protected metastatic SCCHN cells from cis-platinum induced apoptosis. ELISA assays confirmed that these cells secrete CCL19, whereas the autologous, non-metastatic CCR7- parental cells did not. This restricted pattern of CCR7 ligand secretion was also observed in vivo by measuring expression of CCR7 and its ligands in tumor specimens using quantitative RT-PCR and immunohistochemistry. In paucity of lymphoid T (plt) mice, which are deficient in CCR7 ligand secretion, significantly impaired growth of CCR7+ murine SCCHN tumors showed the in vivo importance of this receptor. We conclude that important pro-survival signals promote tumor progression of metastatic SCCHN cells, mediated through autocrine and paracrine CCR7 activation.

## **S002: Squamous Cell Carcinoma (SCC)-Monocyte-Endotoxin Interactions Affect Monocyte Phenotype, Function, and SCC STAT3 Activation**

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**Background:** Epithelial integrity in head and neck squamous cell carcinoma (HNSCC) is often disrupted, and microbial products and inflammation are potentially important in HNSCC pathogenesis. "Pro-inflammatory" CD16-positive monocytes expand in various malignancies, but their role in HNSCC is not known. Monocyte-lineage cells (MCs) are associated with HNSCC progression, potentially in part because MCs produce interleukin 6 (IL-6) in response to endotoxin (lipopolysaccharide, LPS), and IL-6 stimulates activation of STAT3, important in carcinogenesis. However, MC phenotypes and functions in HNSCC have not been characterized.

**Objective:** To determine impact of HNSCC-monocyte-LPS interactions on monocytes and HNSCC cells.

**Design:** HNSCC specimens were evaluated by immunohistochemistry for CD16-positive MCs. Healthy donor peripheral blood monocytes were cultured independently and together with HNSCC lines, with and without LPS. Expression of MC markers, including CD16 and DC-SIGN, as well as intracellular and secreted IL-6 were determined by flow cytometry and enzyme-linked immunosorbent assay, respectively. Effect of secreted soluble factors on HNSCC Y705-STAT3 phosphorylation (pY705-STAT3) was determined by Western blotting.

**Results:** Numerous CD16-positive MCs were found in HNSCC specimens. In vitro, CD16 and DC-SIGN expression consistently increased on monocytes cocultured with HNSCC cells. Unstimulated monocytes and most HNSCC lines produced little IL-6. However, in all HNSCC-monocyte cocultures stimulated by LPS, high levels of IL-6 were induced primarily in MCs, particularly in DC-SIGN- positive MCs. While HNSCC cells had little to no constitutive pY705-STAT3, supernatants from HNSCC-monocyte-LPS cocultures strongly induced HNSCC

Y705-STAT3 phosphorylation. Supernatant-induced STAT3 activation often decreased with IL-6 neutralization.

**Conclusions:** HNSCC-monocyte-LPS interactions affect monocyte phenotype and induce IL-6 and other soluble factors, consistently leading to HNSCC STAT3 activation.

## **S003: Identification of a Novel HLA-A\*0201-Restricted T-Cell-Defined Antigen in Human SCCHN**

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**Objective:** Few tumor-associated, immunogenic epitopes are available for anti-tumor vaccinations in SCCHN. Our antigen discovery program identified an aldehyde dehydrogenase 1 family member A1 (ALDH1A1) as a source of a CD8+ T-cell-defined HLA-A2-restricted peptide ALDH1A188-96 (LLYKL ADLI).

**Methods:** In vitro sensitization (IVS) of HLA-A2+ normal or patients' peripheral blood mononuclear cells (PBMCs) with peptide-pulsed dendritic cells was used to generate T-cell lines that were specific for ALDH1A1 peptides. We studied peptide messenger RNA expression, tumor specificity, and localization in tissues of the source protein using immunohistochemistry and Western blotting. Cytolytic T-lymphocyte (CTL) activity against squamous cell carcinoma of the head and neck (SCCHN) was tested in ELISPOT and cytotoxicity assays. Tetramers were used to assess the frequency of peptide-specific T cells in patients' PBMCs. Enzymatic activity was measured using Aldefluor by flow cytometry.

**Results:** ALDH1A188-96 peptide-primed CTLs generated from precursors in PBMCs recognized HLA-A2+ SCCHN targets in ELISPOT and cytotoxicity assays. Antibodies to major histocompatibility complex class I inhibited CTL reactivity. Transient transfection of ALDH1A1 complementary DNA into negative SCCHN targets resulted in their recognition by the CTLs. ALDH1A1 messenger RNA was overexpressed in SCCHN targets and detectable in normal mucosa and keratinocytes. Enzymatic activity correlated with ALDH1A1 protein expression in the tumor.

**Conclusions:** Aldehyde dehydrogenase activity is relevant to both ethanol and retinol metabolism. In SCCHN, the ALDH1A188-96 peptide is naturally presented, CTL defined, and immunogenic. It is a possible candidate for future vaccines in HLA-A2+ SCCHN patients. Supported by PO1-DE12321.

## **S004: HPV-Infected Cancers Process and Present HLA-A2-p53 (264-272) Peptide Complexes: Implications for p53-Based Immunotherapy**

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**Objective:** We have shown that the human papillomavirus (HPV) E6 oncoprotein in HPV-16+ head and neck squamous cell carcinoma (HNSCC) cells induces proteasomal degradation of p53, which leads to greater CD8+ T-cell lysis mediated by enhanced expression of HLA-A2-p53 (264-272) complexes on the tumor cell surface. By using a staining reagent capable of recognizing these complexes, we will be able to quantify and compare expression of HLA-A2p53 (264-272) complexes in HPV-infected HNSCC cells and what the effect of p53 destabilization has on this expression.

**Materials and Methods:** We used a multimeric, soluble T-cell receptor-like reagent to quantitate HLA-A2-p53 (264-272) complexes (264scTCR/multimer) and confirmed its specificity and sensitivity using T2 cells pulsed with various peptides. We then utilized the 264scTCR/multimer to directly measure tumor cell presentation of HLA-A2-p53 (264-272) complexes in HPV-infected cancer cells, which rapidly degraded p53. Various strategies are currently being used to improve staining of tumor cell lines by the 264scTCR, especially in cases where the cells are known to present HLA-A2-p53 (264-272) complexes.

**Results:** We observed enhanced staining of CaSki cells compared with other cell lines known to express the HLA-A2-p53 (264-272) complex, including several head and neck cell lines. Pretreatment with interferon gamma exhibited the strongest staining, likely due to up-regulation of HLA and antigen-processing proteins. HPV E6-transfected PCI-13 cells exhibited improved staining when staining with 264scTCR/multimer-PE followed by anti-PE antibody.

**Conclusions:** This novel tool, which can be improved upon, provides a method for selecting appropriate candidates best suited for immunotherapy, and also identifies those who may require further pretreatment before beginning an immunotherapeutic regimen.

## S005: Immune Escape of Head and Neck Cancer By Functionally Altered Myeloid Dendritic Cells Can Be Counteracted By CpG-ODN

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The influence of head and neck cancer (Head and Neck Squamous Cell Carcinoma, HNSCC) on various cellular functions of human myeloid dendritic cells (MDC) has been analyzed. We demonstrate that HNSCC massively affects the antigen processing machinery of MDCs and thus impairs an effective activation of T-cell responses. Analysis of MDC migration and cytokine secretion revealed that HNSCC triggers myeloid dendritic cells to produce increased amounts of tumorpromoting and immune suppressive cytokines IL-1 and IL-10 and results in an increased MDC migration activity. Our data indicate that CpG2216 is able to act contradictorily to HNSCC and stimulates an increased production of the proinflammatory cytokine IL-6 by human myeloid dendritic cells in the presence of the HNSCC microenvironment. Hence, the HNSCC microenvironment leads to significant functional alterations of human MDCs which participate in the immune escape of head and neck cancer.

## S006: T Helper Type 2 Anti-Tumor Immunity Induced By Mutant p53 Peptides and Immune Escape in Head and Neck Cancer Patients

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**Objective:** To determine if serologic recognition of p53 mutations depends upon the ability of p53 to express new epitopes that bind to human leukocyte antigen (HLA) complexes, we used anti-p53 antibody production as a marker for HLA class II-restricted T cell involvement in head and neck cancer patients. Our hypothesis is that p53 neoantigens bind to specific HLA class II molecules leading to a break in tolerance.

**Methods:** Sera and tumor specimens were collected for 43 head and neck cancer patients. The p53 gene was sequenced (exons 5 - 9) in the tumors. Immunoprecipitation and Western blot assays allowed identification of the p53 mutations that were associated with an immune response. Antibody response was correlated with the specific p53 mutations and the patients' HLA class II alleles and haplotypes. Competitive binding assays of p53 mutant peptides to the DQ7 molecule, DQ3.1, were performed. Interferon or interleukin 5 ELISPOT assays were performed to measure CD4+ T cell responses.

**Results:** Certain HLA-DQ and -DR alleles were frequently present in patients who produced serum anti-p53 antibodies. Selected mutated p53 peptides fit published allele-specific HLA class II binding motifs for the HLA-DQ7 or -DR1 molecules. Moreover, a mutant p53 peptide bound with a 10-fold greater affinity than the wild type p53 peptide to HLA DQ7 molecules. In vitro stimulation of HLA-DQ7+ peripheral blood mononuclear cells from 4 healthy donors with this mutant p53 peptide (p53 220C) induced secretion of interleukin 5 and lower levels of interferon-gamma by responding CD4+ T cells, as compared to in vitro stimulation using the wild type p53 210-223 peptide.

**Conclusions:** Our results support our hypothesis that p53 neoantigens bind specific HLA class II molecules, resulting in a break in tolerance. This may lead to skewing of the CD4+ T lymphocyte response toward a tumor-permissive T helper type 2 (Th2) profile in head and neck cancer patients, as manifested by seropositivity for p53. In this way, a form of immune escape mediated by p53 mutation may lead to presentation of a tumor antigen capable of shaping a tumor permissive immune response via HLA class II binding.

## S007: Multi-institutional Prospective Study on the Prevalence of Sublevel IIB Metastases in Head and Neck Cancer

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**Objective:** To evaluate the prevalence of sublevel IIB metastases and to identify patients in whom to avoid their dissection.

**Design:** Multi-institutional prospective study.

**Setting:** Two national cancer centers and 1 university hospital.

**Patients:** Between 2002 and 2004, 340 patients were operated on the primary and/or the neck (499 neck dissections). The sites were oral cavity (n=120), larynx (n=106), oropharynx (n=50), thyroid (n=23), scalp (n=16), hypopharynx (n=12), unknown primary (n=7), and parotid (n=6).

**Interventions:** Sublevel IIB lymph nodes (LNs) were separated from the others and processed apart.

**Main Outcome Measures:** The influence of primary site, pT and pN status on the prevalence of sublevel IIB metastases was evaluated by  $\chi^2$  test.

**Results:** cN0/pN0 were 28%; cN+/pN+, 49%; cN+/pN0, 7%; and cN0/pN+, 16%. The overall prevalence of sublevel IIB metastases was 5.4%. All 3 patients (0.6% of the dissected neck sides) who were cN0/pN+ at sublevel IIB had advanced T stage. The  $\chi^2$  test showed a higher risk for LNmetastases at sublevel IIB in parotid, scalp, and unknown primary tumors if a 10% of probability of having positive LNs was chosen as the threshold limit ( $P<.001$ ). The possibility of a cN0 neck with pN+ at sublevel IIB was lower than the probability of this finding in cN+ ( $P<.001$ ).

**Conclusions:** Sublevel IIB dissection is recommended for all cN+ patients and for those with parotid and scalp tumors, even if cN0. In all other settings, careful exploration of sublevel IIB should always be accomplished before avoiding its dissection.

## S008: Chronic Periodontitis and the Risk of Oral Cancer: Preliminary Findings

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**Objective:** Chronic infections have been implicated in the etiology of cancer. The aim of this study was to assess the association between chronic periodontitis and the risk of oral cancer. A case-control study design was employed.

**Methods:** The study population was derived from patients admitted to the Department of Dentistry and Maxillofacial Prosthetics at Roswell Park Cancer Institute (RPCI) between June 15, 1999 and January 10, 2005. All non-Hispanic white men newly diagnosed with primary squamous cell carcinoma of tongue were included as cases. The control group consisted of all non-Hispanic white men admitted to the department during the same time period but diagnosed with benign conditions. Edentulous, immunocompromised and those with prior history of any type of cancer and oral dysplasia were excluded. A total of 32 cases and 49 controls were included in the present analyses. Pathological confirmation of cancer cases were obtained from the RPCI Tumor Registry. Diagnoses of the controls as well as information on covariates were obtained from the RPCI Hospital Information System. History of periodontitis was represented by alveolar bone loss (ABL) measured on panoramic radiographs taken at the time of admission. ABL was measured on mesial and distal sites of all teeth using an operator-interactive program on digitized radiographic images by one trained and calibrated examiner blind to cancer status. The independent association of ABL and tongue cancer was estimated using multiple logistic regression analyses. Odds ratios (OR) and 95% confidence intervals (CI) are reported.

**Results:** After adjusting for age at diagnosis, smoking status and number of teeth present, each millimeter (mm) of alveolar bone loss was associated with a 5.69 fold increase in the risk of tongue cancer (OR=5.69, 95% CI=2.48-13.05). Mean alveolar bone loss was consis-

tently higher in cancer cases compared to controls in never (3.59 vs. 2.38 mm,  $p=0.004$ ), former (4.19 vs. 2.58 mm,  $p=0.001$ ) and current (5.37 vs. 3.29 mm,  $p=0.004$ ) smokers.

**Conclusions:** This study suggests an association between chronic periodontitis and the risk of tongue cancer in men independent of smoking status, age, race, ethnicity and number of teeth. If this association is confirmed with other studies, it has a potential impact on understanding the etiology of oral cancer and its prevention. Larger studies including other oral sites, women and subjects of other race/ethnicity with a more comprehensive control of confounding are needed to confirm this link. This study was supported by grant T32-DE07034 from the National Institute of Dental and Craniofacial Research.

## **S009: Sentinel Lymph Node Biopsy for Oral Cancer: A Multi-institutional Validation Trial**

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**Objective:** Validation of sentinel node (SN) biopsy technique for oral cancer.

**Methods:** Multi-institutional trial. One hundred sixty-one patients were enrolled with clinically invasive oral cancers, stage T1 and T2, N0. Patients underwent intralesional injection with radiocolloid, nuclear imaging, narrow-exposure sentinel lymphadenectomy, and immediate neck dissection. Training was provided to standardize technique. Fine sectioning and immunohistochemistry of the SNs and the largest nodes at each level of the neck are in progress. The performance of the SN marker is quantified using a measure similar to a negative-predictive value

(NPV), defined as the proportion of patients with negative SNs who also have no positive non-SNs.

**Results:** Interim analysis based on hematoxylin-eosin staining in 131 eligible patients. Of 100 clinically and pathologically negative gamma probe-guided neck explorations, 91 correctly predicted the status of the neck, an NPV of 0.91 (91%). By strict definition, 103 had negative SNs, and 91 of those had no positive non-SNs. This corresponds to a NPV of 0.88 (95% confidence interval, 0.81-0.94). Among the SN-negative patients, 25 were floor of the mouth tumors, while 77 were in other locations, an NPV of 0.80 and 0.91, respectively.

**Conclusions:** The floor of the mouth represented a less favorable site. Data acquisition, fine sectioning, and immunohistochemistry are in progress. We anticipate information regarding patterns of lymphatic drainage and stratification based on surgeon experience. For a group of formally trained but relatively inexperienced surgeons, the SN procedure was accurate and exceeded the projected success rate on interim hematoxylin-eosin evaluation.

## **S010: Predictive Parameters For the Detection of Neck Metastases**

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Head and neck squamous cell carcinoma (HNSCC) is now the fourth most common neoplasm in men and the eighth most common in women in the USA. Despite numerous advances in treatment, the long-term survival has remained the same over the past 40 years. Cervical lymph node metastases are one of the limiting events in HNSCC. The appearance of one or more cervical node metastases reduces the five years survival rate about 50%. Therefore, the knowledge on cervical lymph node stage is decisively important for the treatment planning. Ultrasound imaging is a reliable, fast and effective method for the scanning of cervical lymph node metastases, but still the predictive values of ultrasound criteria remains unclear. Most studies only employ single criteria and operate at small study cohorts. Here we present the data of 390 HNSCC patients, in which we investigated minimal, maximal transverse and the longitudinal diameter, ratios of both transverse and longitudinal to average transverse diameter, the volume of the lymph node. Additionally, the

echostructure of the lymph node was delineated, distinguishing between inhomogeneous and homogenous and appearance or absence of a hilum. The definitive histology following neck dissection was the gold standard for the discrimination between malignant and benign lesion. Only data sets of patients were involved, if all tested criteria were completely surveyed for one lymph node. Data were collected in an access data bank to allow a statistical analysis of the results and to clearly assign the results to the patient history. Limit values were defined by ROC curves and the predictive values of each criterion was estimated in terms of improved significance. Only the volume, the ratio of longitudinal to transverse and minimal transverse to maximal transverse diameter, the maximal longitudinal and the minimal transverse diameter elicited significant predictive information on the potential degeneration of the lymph node. Furthermore, we developed a one hundred point score scale for the daily clinical application in ultrasound investigation, in which a total score above 30 points indicates a probability for a malignant lesion with a sensitivity of 87% and specificity of 71%.

## **S011: Vocal Fold Immobility After Thyroidectomy With Intraoperative Laryngeal Nerve Monitoring**

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**Objectives:** To evaluate vocal fold mobility in patients who underwent thyroidectomy with intraoperative laryngeal nerve monitoring and to compare the results in patients without nerve monitoring.

**Design:** Prospective nonrandomized study.

**Setting:** Tertiary cancer center.

**Patients:** Previously untreated patients who underwent thyroid surgery using the intraoperative laryngeal nerve monitoring between November 2003 and January 2006.

**Interventions:** Videolaryngoscopic examinations were performed before surgery and 15 days, 1 month, and 3 months after surgery.

**Main Outcome Measures:** A descriptive analysis of vocal fold mobility was performed, and a comparison of the results with a previous series of similar patients without laryngeal nerve monitoring.

**Results:** A total of 107 patients were studied (median age, 49 years). A total thyroidectomy was performed in 56 patients. The duration of procedure varied from 105 to 310 minutes. The nodule size varied from 0.3 to 5.0 cm. Vocal fold immobility (total or partial) was detected in 12 patients (11.2%) at the first postoperative evaluation, and only 6 (5.5%) remained with vocal fold immobility 3 months after surgery. A previous series with 100 patients without nerve monitoring showed that 12% of patients presented with vocal fold immobility in the early examination, and just 5% maintained such immobility 3 months after surgery ( $P = .55$ ).

**Conclusion:** In this series, the use of laryngeal nerve monitoring in thyroid surgery did not decrease the rate of vocal fold immobility.

## **S012: Dendritic Cell (DC)-Based Vaccine for Patients With SCCHN Using Autologous Tumor Cells as Immunogens**

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**Objectives:** The primary objective of this clinical trial for patients with stage III/IV resectable squamous cell carcinoma of the head and neck (SCCHN) was to demonstrate the feasibility and safety of a vaccine prepared by feeding apoptotic autologous tumor (AuTu) cells to dendritic cells (DCs) and delivered intranodally under ultrasound guidance. The secondary objective was to demonstrate immune responses to the vaccine using interferon gamma (IFN- $\gamma$ ) ELISPOT assays.

**Methods:** Patients were eligible to receive 2 intranodal vaccines 6 weeks apart if they had positive delayed-type hypersensitivity to recall antigens and 1?107 sterile Tu cells banked. Immature DCs were generated from blood monocytes cultured with interleukin (IL)-4/granulocyte-macrophage-colony-stimulating factor. Peripheral blood was collected for immune studies before and after vaccines. Delayed-type hypersensitivity responses to the vaccine were measured after therapy. Correlative laboratory data were evaluated in relation to each patient's clinical course.

**Results:** Tu and/or Tu-involved lymph nodes from 30 patients were

processed. A total of 2?106 to 2?108 Tu cells were recovered. Nineteen (63%) of 30 were sterile; 10 (33%) of 30 had 1?107 sterile Tu cells; and 8 of 10 had positive delayed-type hypersensitivity. Five of 10 were leukapheresed to generate immature dendritic cells, which were cocultured with UV-B-treated apoptotic Tu cells (5:1 ratio). DC vaccines were evaluated for cell recovery (3?107-6 ? 107), viability (90%-100%), purity (80%-95%), and potency (IL-12p70) and delivered to 4 patients. No toxicities were observed. All 4 patients are alive with no evidence of disease. Peripheral blood mononuclear cell responses to AuTu and the vaccine (IFN- $\alpha$  ELISPOT) were measured.

**Conclusion:** Intranodal administration of DC-AuTu vaccines was safe. SCCHN patients generated immune responses to the vaccine, but AuTu sterility and cell number limited this vaccination strategy to few enrolled subjects. Supported by PO1-DE12321.

### **S013: Array Comparative Genomic Analysis of Oral SCC**

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Genomes of solid tumors are characterized by gains and losses of regions, which may contribute to tumorigenesis by altering gene expression. Often the aberrations are extensive, encompassing whole chromosome arms, which makes identification of candidate genes in these regions difficult. Array CGH detects and maps DNA sequence copy number variation throughout the entire genome. We performed CGH analysis on 89 formalin fixed paraffin embedded archival oral squamous cell carcinomas (SCC). The most commonly gained regions included 3q, 7p, 8q, 20p and 20q. Common regions of losses included 3p, 4p, 5q, 8p, 9p (including focal deletions of p16) and 18q. Frequent amplifications of genes previously associated with oral SCC, such as CCND1 at 11q13 and EGFR were also observed, as well as previously unreported amplicons. Using agglomerative hierarchical clustering of the array CGH data we found significant differences between tumors with mutations in TP53 and those in which mutations were not present. We also found a significant association of TP53 mutation with amplification of CCND1 ( $p = 0.009$ ) and amplification of EGFR ( $p = 0.036$ ). These results provide new higher resolution information on recurrent aberrations in oral SCC. We then focused our analysis of the array CGH data on narrow regions of gene amplification and used expression analysis to facilitate identification of genetic pathways important in oral SCC development. We found genes involved in integrin signaling (TLN1), survival (YAP1, BIRC2), and adhesion and migration (TLN1, LAMA3, MMP7), as well as members of the hedgehog (GLI2) and notch (JAG1, RBPSUH, FJX1) pathways to be amplified and over-expressed. Deregulation of these and other members of the hedgehog and notch pathways (HHIP, SMO, DLL1, NOTCH4) implicates cell fate misspecification in oral SCC development.

Finally, we used array CGH to perform a genome-wide analysis of patients with multiple oral SCC, clinically classified as second primary tumors because they occurred at a site >2 cm distant from the initial tumor and/or more than 3 years after the initial tumor (almost 17 years in one patient). We observed signature copy number alterations that were present in each of the multiple tumors from an individual patient, indicating that the tumors are clonally related. These observations, which are consistent with the tumors originating as second field tumors or by seeding from tumor cells from an earlier tumor, highlight the utility of molecular analysis for definition of second primary tumors in patients with multiple oral SCC and indicate the utility of molecular analysis for identification and management of patients at risk for second primaries.

### **S014: Methylation Status of Genes in Papillary Thyroid Carcinoma**

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**Objectives:** To determine methylation status of gene promoter regions using methylation-specific polymerase chain reaction (MS-PCR) for genes encoding for thyrotropin receptor (TSHR), E-cadherin (ECAD), sodium-iodine symporter (NIS-L), ataxia telangiectasia-mutated (ATM), and death-associated protein kinase (DAPK) proteins, and to correlate MSP results with patient variables, tumor factors, and outcome measures in patients with papillary thyroid carcinoma (PTC).

**Design:** Database query and retrospective chart review for patients with well-differentiated thyroid cancer treated at our institution (1996-

2004). MS-PCR was performed on surgical specimens, and results were compared with controls. Methylation status was then compared with patient variables, tumor factors, and outcome measures for patients with thyroid carcinoma and controls.

**Results:** Among 59 patients (32 PTC and 27 controls), all 5 genes were methylated more frequently in patients with PTC than in controls. NIS-L methylation correlated with a more advanced stage at presentation. When NIS-L was methylated in tumor cells, it was unmethylated in adjacent histologically normal thyroid tissue. Neither age nor gender impacted methylation status, and methylation status did not correlate with extent of the primary tumor or presence of nodal metastasis at diagnosis. Patients with methylated TSHR promoters had recurrences less frequently than patients with unmethylated TSHR promoter regions.

**Conclusions:** Promoter methylation may be a marker for malignancy in thyroid nodules. Our findings indicate that methylation for the promoter regions for TSHR, ECAD, ATM, and DAPK may be an early event in tumorigenesis, while NIS-L methylation may represent a late event. Furthermore, methylation status of tumors as determined by MS-PCR may help in determining patient prognosis.

### **S015: Discovery and Development of DNA Methylation Based Diagnostic and Prognostic Biomarkers in Head and Neck SCC**

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Head and neck squamous cell carcinomas (HNSCC) of the oral cavity, pharynx and larynx occur at a rate of approximately 500,000 new cases per year worldwide and are the sixth most common cancer. Some clinically relevant issues affecting survival and quality of life are early detection, proper staging, detection of sub-clinical lymph node metastases, local recurrence, and second primary tumor development. CpG island hypermethylation is a common occurrence in HNSCC and currently constitutes perhaps the most fruitful field for the identification of new molecular cancer biomarkers and has very high potential to significantly add to the panel of markers used to stratify patients. DNA methylation is an attractive candidate to use as a molecular cancer biomarker because it is a stable molecular alteration of the DNA that can be very sensitively detected with PCR based methodologies. Recent studies have used DNA methylation of genes known to be targets of genetic disruption in cancer as biomarkers for early detection of cancer, classification of malignancies, predicting response to drug treatment, and as markers predictive of outcome. We propose that CpG island methylation contributes to the molecular signature of squamous epithelial cells in various stages of malignant progression from pre-malignant to distant metastases and that the malignant behavior of these cells can be predicted by measuring the methylation of these CpG islands. To investigate this, we have used a CpG island genomic scanning method, Restriction Landmark Genomic Scanning (RLGS), to identify novel targets of CpG island hypermethylation in HNSCC. Using a set of 18 HNSCC this scanning method identified 125 RLGS fragments showing significant levels of aberrant CpG island methylation, with 18 of them exhibiting methylation in 6 or more cases. Based on these findings we have begun to develop highly sensitive and quantitative PCR based assays to detect and quantitate methylation of specific loci in clinically relevant and easily accessible tissues, as well as in archival sources of tissue. We have demonstrated the ability to sensitively detect aberrant methylation of known tumor suppressor genes as well as novel targets of CpG island hypermethylation in buccal cells, collected by oral rinses, of former HNSCC patients who have gone greater than 5 years with no evidence of disease. We have also demonstrated the same detection ability in formalin-fixed paraffin embedded tissues. Future work will expand the sample set in the initial RLGS screening phase to include 50 N0 and 50 N+ primary HNSCC thus allowing for the identification of CpG islands that are hypermethylated in any stage primary tumor at a non-random frequency, as well as methylation events that are specific for the more advanced N+ tumors. For each marker of interest based on the initial screening, we will develop the PCR based assays that can be applied to archival sources of tissue as well as buccal cells for further biomarker validation studies. Such markers will have the potential to stratify risk of HNSCC disease onset in smokers, predict the presence of occult metastases, and predict imminent development of second primary tumors.

## **S016: Intra-arterial Versus Intravenous Chemoradiation for Advanced Head and Neck Cancer, Early Results of a Phase III Trial**

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**Introduction:** Chemoradiation (CRT) is superior to radiation alone for advanced head and neck cancer. Mostly the chemotherapy is administered intravenously. The treatment is frequently associated with serious side effects often necessitating treatment interruption. Early results of intra-arterial CRT demonstrated very good results for stage III/IV head and neck cancer. We conducted a randomized trial to compare intra-arterial CRT to intravenous CRT.

**Patients and Methods:** From 2000 to November 2005 236 patients from 5 hospitals with (functionally) inoperable head and neck cancer of the oral cavity (19%), oropharynx (63%) and hypopharynx (18%) were randomly assigned to receive 70 Gy/35 fractions/7 weeks combined with either four courses of intra-arterial (IA) cisplatin (150 mg/m<sup>2</sup>) and intravenous Na-thiosulfate on days 2, 9, 16 and 23 (N=118) or intravenous (IV) cisplatin (100 mg/m<sup>2</sup>) on days 1, 22 and 43 (N=118). IA cisplatin was administered single-sided (33% oropharynx, 50% oral cavity, 68% hypopharynx) or double-sided. Tumor site, T and N-stage were equally distributed among the treatment arms, T2 2%, T3 31%, T4 67%, N0 20%, N1 12%, N2a 5%, b 28%, c 28%, N3 9%. The median follow-up was 17 months.

**Results:** One patient in the IV arm died before start of treatment and one patient in the IA arm received no CRT at all (not feasible). Ninety-five of 118 patients (81%) in the IA arm completed all planned cisplatin doses (1 no cisplatin, 11 IV cisplatin, 11 <4 courses) against 106 (83%) with IV treatment (including the patients where IA was not feasible: 22 of 128 <3 courses). Loco-regional complete response was achieved for 68% and 81% in the IA and IV arm respectively (chi square p=0.02). In 9% a neck dissection for residual disease was performed. The initial complete response for each site (IA vs IV) was: 68% vs 81% (oropharynx), 52% vs 70% (oral cavity) and 86% vs 91% (hypopharynx). At two years no significant difference was seen between IA and IV CRT in loco-regional control (62% and 68% respectively) or overall survival (61% and 63% respectively). Loco-regional control at 2 years was lower for oral cavity sites (50%) compared to hypopharynx (76%) and oropharynx (68%) (Logrank p=0.05). Eight patients died within three months after treatment, mostly of bacterial causes, 5 in the IA and 3 in the IV arm.

**Conclusion:** A difference in early response is seen between the treatment arms, favoring IV treatment. This difference disappears with two years FU. Severe renal, and skin toxicity is less frequent in the intra-arterial arm, but neurological toxicity and leucopenia are more common.

## **S017: Re-irradiation Combined With Chemotherapy After Salvage Surgery in Head and Neck Carcinoma: A Randomized Trial**

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**Background:** Full dose re-irradiation combined with chemotherapy has been shown to be feasible after salvage surgery with an "acceptable" toxicity (Cancer 2001; 91:2071-6). The GETTEC and GORTEC groups performed a prospective, multicentric, randomized study to assess its carcinologic value.

**Material/Methods:** Between 1999 and 2005, 130 head and neck cancer patients were treated with salvage surgery and then randomly assigned either to full dose re-irradiation combined with chemotherapy (arm A) or absence of post-operative treatment (arm B). Patients eligibility criteria were: recurrence or second primary in a previously irradiated area to at least 45 Gy, absence of distant metastasis, salvage surgery with macroscopic complete resection; possibility of starting adjuvant treatment within 6 weeks after salvage surgery.

Patients in arm A received 60 Gy in 12 weeks combined with concomitant 5FU, Hydroxyurea, as previously described (Ann Oncol 1996;7:913-8). Cox model was adjusted with stratification factors: tumor site, center, type of event (recurrence vs second primary).

**Results:** 65 patients were randomized in each arm, including 71% of local and/or regional relapse and 29% of second primary. There was no imbalance in the distribution of age, sex, tumor site, T and N re-staging, and histological gravity signs (N+ with ECE and/or positive margin). The most important acute toxicity related to re-irradiation and chemotherapy was mucositis with >= grade 3 in 29% of patients, and three toxicity-related deaths. An increase in > = grade 3 RTOG late toxicity was observed in arm A (trismus, mucosa, fibrosis), compared to arm B. Progression-free survival was significantly improved in Arm A with a hazard ratio of 1.6 (CI 95%, 1.1-2.4, p = 0.01), but overall survival was not statistically different.

**Conclusions:** This is the first randomized trial to evaluate the effect of full dose re-irradiation combined with chemotherapy after salvage surgery. The results showed that re-irradiation and chemotherapy were able to significantly improve progression-free survival with an increased acute and late toxicity, and without significant impact on overall survival. Supported by ARC.

## **S018: Validation of a Voice Prosthesis Questionnaire to Assess Valved Speech and Its Related Issues in Patients Following Laryngectomy**

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**Objective:** To establish the reliability and validity of a new self-administered questionnaire to assess valved speech and its related issues in patients who have undergone a total laryngectomy operation.

**Designs:** Retrospective cross-sectional psychometric validation study

**Methods:** We identified sixty-one total laryngectomy patients with no sign of recurrent disease and using voice prosthesis from the speech and language therapy database of the Royal Marsden Hospital. The patients were assessed using a postal self-administered voice prosthesis questionnaire (VPQ) that covered a wide range of issues such as the voice, valve leakage, quality of life, humidification, hands-free system. In addition, patients were also asked to complete the University of Michigan voice related quality of life (VRQOL) and University of Washington head and neck quality of life (UWQOL, version4) questionnaires.

Main Outcome measures: Test-retest and internal consistency reliability; content, criterion and construct validity.

**Results:** The internal consistency reliability using the Cronbach's alpha coefficient was 0.87 (range: 0.85 to 0.89). Test-retest reliability showed that more than 75% of patients had a score on re-test that was within 1 point of their original score. Content validity was ensured during the design process. The median Spearman correlation coefficient was 0.25 for convergent construct validity with the UWQOL and 0.64 for criterion validity on comparison with the VRQOL.

**Conclusions:** Standardized questionnaires that measure patient's outcome measures offer a means for demonstrating treatment impact and improving medical care. The VPQ is the first validated and reliable self-administered questionnaire designed specifically for evaluating valved speech and its related issues in patients who have undergone total laryngectomy. The VPQ has significant utility for audit, outcomes research and monitoring in these patients.

## **S019: Superselective Neck Dissection Following Chemoradiation: Feasibility Based on Clinical and Pathological Comparisons**

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**Objective:** To determine if superselective neck dissection (removal of 2 or fewer neck levels) is effective salvage surgery for patients with residual single level adenopathy following chemoradiation.

**Design:** Analysis of prospectively collected data.

**Subjects:** A total of 177 patients (239 hemi-necks) with N+ disease.

**Interventions:** Treatment: intra-arterial cisplatin 150 mg/m<sup>2</sup> on days 1, 8, 15, and 22, and radiation therapy 20 Gy/d 5 times per week over 7 weeks. Comparisons were made between neck-level-specific disease at restaging and pathological disease following neck dissection.

**Results:** Tumor sites included the oropharynx (n=81), hypopharynx (n=39), larynx (n=27), oral cavity (n=19), and others (n=11). Response of nodal disease based on clinical evaluation was as follows: complete remission (n=89 [50%]), partial response (n=81 [46%]), poorly differentiated (n=4 [2%]), and unevaluable (n=3 [2%]). Among the necks that were restaged as a partial response, 73 had clinical evidence of residual adenopathy involving only 1 neck level. Within this subset, 57 patients subsequently had a salvage neck dissection, and comparisons were made between the restaging evidence of residual adenopathy and the pathological findings specific for each neck level. Only 2 of the 57 evaluable patients had evidence of pathological disease extending beyond the single neck level, one of whom had disease in the contiguous neck level, and the other in a noncontiguous level. The use of superselective neck dissection with removal of only 2 neck levels would have encompassed all known disease in all except 1 patient.

**Conclusion:** Superselective neck dissection is feasible following this specific chemoradiation protocol for patients with persistent nodal disease confined to 1 level.

## S020: Significance of Viable Tumor in Postchemoradiation Neck Dissections

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**Objective:** To explore the reliability of clinical/radiologic examination in determining the presence of viable tumor in the neck after primary concurrent chemotherapy and radiation therapy (CTRT) for squamous cell carcinoma of the larynx and pharynx (SCCLP) and its prognostic significance.

**Design:** Retrospective review.

**Setting:** Tertiary care cancer center.

**Patients:** A total of 205 patients met the eligibility criteria for receiving CTRT for SCCLP at a single institution between 1995 and 2005. Fifty-three patients who received a comprehensive neck dissection (ND) after CTRT were included in this analysis.

**Interventions:** All patients had received primary concurrent, platinum-based CT and definitive-dose RT and a post-CTRT comprehensive ND.

**Main Outcome Measures:** Presence of viable tumor in the ND specimen; 2-year recurrence-free/disease-specific/overall survival rates.

**Results:** Forty percent of the ND specimens contained viable tumor. Twenty-two percent (2/9) of those with a complete response (CR) in the neck had viable tumor compared with 14% (1/7) with residual thickening and 50% (18/36) with a non-CR/major response. On contingency analysis, nodal response to CTRT did not correlate significantly to the presence of viable tumor in the ND specimen. Viable tumor in the ND specimen was associated with more adverse 2-year recurrence-free (45% vs 87%,  $P = .001$ ), disease-specific (75% vs 93%,  $P = .003$ ), and overall (65% vs 93%,  $P < .001$ ) survival rates.

**Conclusions:** In this study, clinical and radiologic examinations were imperfect predictors of viable tumor in post-CTRT ND specimens. The presence of viable tumor in ND specimens is associated with more adverse outcomes, and further research is necessary to clarify this observation with implications for selection of therapy.

## S021: Is Neck Dissection Necessary for Nodal Metastases in Patients Treated with Radical CRT?

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**Objectives:** 1. To determine the impact of neck dissection (ND) on disease specific survival and recurrence in the management of advanced (N2 or N3) nodal metastasis in patients with head and neck squamous carcinoma (HNSCC), treated with primary radical chemoradiotherapy (CRT). 2. To assess the feasibility and safety of a PET CT guided surveillance policy following radical CRT in the management of advanced (N2 or N3) nodal metastasis in patients with

head and neck squamous carcinoma (HNSCC), treated with primary radical chemoradiotherapy (CRT).

**Background:** Currently, there is no consensus regarding the indications for surgical treatment of advanced regional nodal disease in patients with HNSCC treated with CRT. Some follow a conservative surveillance policy, whilst others perform neck dissection pre-CRT, and others post-CRT as a planned procedure.

**Methods/Design:** Systematic review using criteria for identifying trials, data extraction and assessment of quality.

**Selection Criteria:** Randomised, case controlled, prospective trials or retrospective studies

**Interventions:** Neck dissection pre or post CRT, watch and wait policy

**Outcome Measures:** Overall and disease free survival, local neck recurrence rate

**Data Collection and Analysis:** Trials identified by electronic searches of MEDLINE, EMBASE, PubMed, Cochrane, CINAHL, and AMED using eligibility criteria. 2 authors independently quality assessed each trial and extracted data.

**Results:** Only 1 RCT was identified, comparing conservative follow-up to planned ND before CRT. It found improved disease specific survival following ND. However it was small and had several limitations. There were two level II studies, and 25 other level 3/4 studies were found. Several reported a significant benefit after neck dissection, and found that 30% patients who had ND following CRT had persistent histological tumour deposits in specimens, even after a clinically complete response. Others only found a benefit for ND in patients who had an incomplete response to CRT, and reported good control with CRT alone in patients achieving complete response following CRT. They reported recurrence rates of approximately 10%, which is similar to that of patients who had neck dissection. Furthermore, an experimental study using ki-67 proliferation marker found that residual disease found in pathological specimens was not viable.

**Conclusions:** The literature contains contradictory evidence and there is currently no strong evidence in the literature to support a particular treatment strategy. There is however sufficient evidence in the literature to support a policy of watch and wait versus planned neck dissection in the setting of a large multi-centre trial to elucidate this.

## S022: Is Planned Neck Dissection Necessary for Head and Neck Cancer Treated With Intensity-Modulated Radiotherapy?

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**Objective:** To determine the regional control of locoregional advanced head and neck squamous cell carcinoma (HNSCC) treated with intensity-modulated radiotherapy (IMRT).

**Design:** Retrospective study.

**Setting:** Academic center.

**Patients:** From December 1999 to July 2005, 100 patients with stage N2A or higher HNSCC were treated with definitive IMRT. Five patients who had neck dissection before radiation and 4 with nasopharyngeal cancer were excluded. One patient lost to follow-up 9 months after treatment was also excluded. The remaining 90 patients were analyzed. For IMRT, 3 clinical target volumes (CTVs) were defined and treated to 70 Gy (CTV1), 60 Gy (CTV2), and 54 Gy (CTV3), respectively. Neck dissection was performed for patients who had residual lymphadenopathy after IMRT and who were surgical candidates.

**Results:** The median follow-up for all patients was 29 months (range, 4-74). Two patients had persistent local and regional diseases. They refused surgery. Eleven patients underwent neck dissection after IMRT because of residual lymphadenopathy. Five of them contained residual viable tumor in the lymph nodes and 6 of them were pathologically negative. The remaining patients were observed without neck dissection. There was only 1 patient who had regional failure.

**Conclusions:** IMRT has excellent dose coverage for cervical lymph nodes. A high radiation dose can be safely delivered to the abnormal lymph nodes. There is a high complete response rate. Routine planned neck dissection for patients with N2A and higher stage after IMRT is not necessary. It is safe to reserve neck dissection only for those with residual lymphadenopathy.

## S023: Deferring Planned Neck Dissection After Chemoradiation Therapy in Stage IV Head and Neck Cancer: The Utility of PET/CT

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**Objective:** To determine whether combined positron emission tomography and computed tomography (PET/CT) could help to avoid unnecessary planned neck dissections in patients with advanced head and neck squamous cell carcinoma (HNSCC), we designed an observational study of patients with de novo cervical N2-N3 regional spread of HNSCC.

**Design:** We included all patients who underwent posttreatment PET/CT within 5 months of completing chemoradiation therapy. Thirty such patients were identified. The PET/CT was "positive" if the radiologist recommended tissue sampling or resection of cervical lymph nodes. Patients who had positive PET/CT underwent confirmatory biopsy given clinical suspicion for recurrent disease. Patients with 1 "negative" PET/CT were followed clinically and radiographically for a minimum of 9 months (median 20 months).

**Setting:** Tertiary care referral academic center

**Results:** Eight (27%) of the 30 posttreatment PET/CT studies were positive. Six (75%) of these 8 had histologically confirmed viable tumor. In the 22 patients with negative PET/CT, no recurrence was identified during the study. This corresponds to a sensitivity of 100% (6/6), specificity of 92% (22/24), positive predictive value of 75% (6/8), negative predictive value of 100% (22/22), and accuracy of 93% (28/30). Thus, 24 (80%) of 30 patients were spared neck dissection without evidence of recurrent disease in the neck. The other 6 patients underwent neck dissection and had histologically confirmed residual nodal disease.

**Conclusions:** Our results suggest that planned neck dissection after chemoradiation therapy may be deferred in favor of serial PET/CT imaging and that biopsy of suspicious fluorodeoxyglucose (F18)-avid regions may be considered prior to therapeutic neck dissection.

## S024: Expression of p53 and Bcl-xL as Predictive Markers for Larynx Preservation in Advanced Laryngeal Cancer

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**Objective:** To assess tumor markers in advanced laryngeal cancer.

**Design:** Marker expression and clinical outcome.

**Setting:** Laboratory.

**Patients:** Tissues from 112 patients of the Veterans Affairs laryngeal cancer trial were analyzed: 42 from the chemotherapy arm and 70 from the surgical arm of the study.

**Main Outcome Measures:** p53 and Bcl-xL expression in pretreatment biopsies was assessed for correlation with response to chemotherapy, laryngeal preservation, and survival.

**Results:** In the chemotherapy arm of the study, all patients with tumors having low p53 and low Bcl-xL (10/10) preserved their larynx compared with other combinations of p53 and Bcl-xL expression (24/32). Patients in this group had a 7.3-fold increased likelihood of larynx preservation relative to all others. No patient with tumor expressing low p53 and low Bcl-xL had a laryngectomy over a 10-year follow-up period ( $P = .08$ ). All 10 patients responded to chemotherapy (complete or partial response) vs 80% of patients in the other groups. A median survival of 48 months was observed in patients with low-risk biomarkers vs 25 months in patients with high-risk biomarkers ( $P = .18$ ).

**Conclusions:** In our data set of advanced laryngeal cancer patients, p53 and Bcl-xL together define groups with different risk profiles. Tumor expression of low p53 and low Bcl-xL is a strong predictor of larynx preservation in patients treated with induction chemotherapy followed by radiation therapy in responding tumors.

## S025: Biomarkers of Invasiveness in Oral Squamous Cell Carcinoma: A Cell Proteomic Approach

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**Objective:** To identify potential biomarkers of invasiveness in oral squamous cell carcinoma maintained in vitro and in vivo as an orthotopic model.

**Design:** A pilot proteomic study for the identification of cancer vs host protein biomarkers in head and neck carcinoma.

**Subjects:** Two cell lines were established from randomly picked oral squamous cell carcinoma tissues with distinct invasive phenotypes. The cell lines were implanted into the tongues of immunocompromised mice in order to understand the role of host-tumor microenvironment in tumor progression.

**Interventions:** Invasiveness was assessed clinically, histologically, as well as in the laboratory using the Boyden chamber and wound-healing assays. In parallel, cell lines with documented differences in invasion activity were grown in serum-starved and conditioned medium. The medium was then used to identify secreted proteins that emanate from cancer cells, using 2-dimensional gel electrophoresis and matrix-assisted-laser-desorption/ionization (MALDI), combined with tandem mass spectrometry (MS/MS).

**Results:** The invasion assays revealed a correlation between cell migration capacity through matrigel matrix and the aggressive phenotype seen in the clinical and histopathological assessments. Several proteins were identified as being differentially expressed in the more aggressive cell line forms and were found to be significant ( $P < .05$ ).

**Conclusions:** We report the first reliable and sensitive in vitro-in vivo approach to screen for oral squamous cell carcinoma invasiveness using proteomic technology. Both high and low abundant candidate proteins were identified. Ongoing validation studies will identify those markers that have potential to be translated into clinical applications.

## S026: A Murine Model of HPV16 Related Tonsil Squamous Cell Carcinoma

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**Objective:** Survival for Head and Neck Squamous cell carcinoma has not changed for the last 30 years. Improvement in survival will likely be linked to new therapies targeted at molecular mechanisms of carcinogenesis. Viral oncogenes, such as E6 and E7 from human papillomavirus (HPV) may contribute to transformation in up to 60% of tonsil squamous cell carcinomas. In an effort to develop a murine model of HPV related carcinogenesis mouse tonsil epithelial cells (MTEC's) were harvested and isolated in cell culture.

**Methods:** HPV16 oncogenes E6 and E7 were transduced with retroviruses into MTEC's. Clonal populations were isolated. Anchorage independent assays were performed, and cells were injected into subdermal and intraoral sites to determine neoplastic potential.

**Results:** MTEC's expressing E6 degraded p53 via proteasomal action, an established mechanism in human cells. E7 degraded pRb in MTEC's, also similar to human cells. The presence of E6 alone allowed for immortalization of MTEC's compared to senescence after 20 passages of primary MTEC's. E6/E7 MTEC's exhibited an increased growth rate compared to E6 MTEC's. E6 alone was sufficient to permit anchorage independent growth in MTEC's; however, the addition of E7 or Ras increased the percentage of seeded cells that exhibited anchorage independent growth. Metastatic tumor growth in mice was only noted with injection of MTEC's expressing Ras and E6. Tumor formation occurred at both the intraoral and subdermal locations with equal frequency.

**Conclusions:** The murine model of HPV related tonsil squamous carcinoma recapitulates the intracellular mechanisms of HPV oncogenes in human cells. Immortalization and anchorage independent growth occur in the presence of E6 or E6/E7. HPV oncogenes alone are not sufficient for neoplastic growth, but the addition of Ras results in a murine model of metastatic HPV tonsil carcinoma. This model will be valuable not only for preclinical testing of potential therapeutics but also a tool to better understand mechanisms of HPV mediated head and neck cancer.

## S027: Molecular Markers of Oral Squamous Cell Carcinogenesis—From Gene Chips to Tissue Microarrays

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**Objective:** To identify potential markers of oral squamous cell carcinoma (OSCC).

**Design:** By analyzing data from our laboratory, coupled with a systematic review of the literature, we selected 6 genes (CDH11, MMP3, POSTN, SPARC, TNC, and TGM3) to study via quantitative reverse transcriptase-polymerase chain reaction analysis (qRT-PCR) and tissue microarray (TMA) immunohistochemistry (IHC).

**Subjects:** All subjects were patients treated at the University of Washington Medical Centers. We performed qRT-PCR on OSCC samples from 6 patients and 6 normal oral tissue samples. For the IHC analyses, 70 tissue samples from 29 OSCC patients and 3 normal control patients were arrayed. Eighteen of the 29 OSCC patients presented with metastatic disease.

**Results:** Of the 6 genes selected for analysis, 4 (POSTN, SPARC, TNC, and TGM3) were validated by qRT-PCR, as evidenced both by significant differential expression between cancer and normal samples, as well as significant correlation of qRT-PCR data with gene microarray data. These genes also showed significant differences in protein expression between OSCC and normal tissues by TMA IHC. The up-regulated markers (POSTN, SPARC, and TNC) were expressed primarily within stromal cells and the extracellular matrix, and not in the epithelial cells. The

down-regulated marker, TGM3, was expressed only in epithelial cells. Decreased TGM3 expression in primary tumors was associated with increased metastasis at presentation ( $P < .03$ ).

**Conclusions:** TMA IHC is a useful validation tool for gene microarray data. Our TMA IHC results suggest that stromal elements may be important in OSCC carcinogenesis. Decreased TGM3 protein expression in primary tumors may be associated with an increased risk of OSCC metastasis.

## S028: Suppression of PKCepsilon Inhibits Cell Invasion and Motility Through Inactivation of Rho GTPases in HNSCC

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Over 70% of patients with head and neck squamous cell carcinoma (HNSCC) present with locoregionally advanced stage III and IV disease. In spite of aggressive therapy, locoregional disease recurs in 60% of patients and metastatic disease develops in 15-25% of patients causing a major decline in quality and length of life. Therefore, there is a need to identify and understand genes that are responsible for inducing an aggressive HNSCC phenotype prone to relapse and metastasize to allow for better clinical detection and management. Evidence has shown that protein kinase C? (PKCepsilon), a member of a family of serine/threonine protein kinases, is a transforming oncogene and may play a role in HNSCC progression. In this study, we determine the downstream signaling pathway mediated by PKCepsilon to promote an aggressive HNSCC phenotype. RNA-interference knockdown of PKCepsilon in UMSCC11A, an invasive and motile HNSCC cell line with high endogenous PKCepsilon levels, resulted in clones that were significantly less invasive and motile than the siRNA scrambled control transfectants; 51±5% (n=3, p<0.006) inhibition in invasion and 69±1% (n=3, p<0.0005) inhibition in motility, respectively. RhoA, Rac1, and Cdc42 GTPases are members of the small Rho GTPase family that are well-recognized modulators of cell invasion and motility. PKCepsilon-deficient UMSCC11A clones had reduced levels of activated GTP-bound and serine-phosphorylated RhoA, Rac1, and Cdc42. Moreover, PKCepsilon was demonstrated to directly phosphorylate RhoA but not Rac1 and Cdc42 *in vitro*. These results indicate that RhoA, Rac1, and Cdc42 are direct and/or indirect substrates in the PKCepsilon signaling cascade. Taken together, our work is the first report to demonstrate PKCepsilon as a global regulator of small Rho GTPases activation in HNSCC.

## S029: Cisplatin-DNA Adduct Formation in Normal tissue and Tumor in Patients Treated With Cisplatin-based Chemoradiation

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**Background:** Cisplatin-DNA adduct-formation has been studied as a predictive marker for outcome. The objectives of this study were to investigate cisplatin-DNA adduct-levels after 4 schedules of concurrent cisplatin-radiation and to explore relationships between adduct-formation in primary tumor and normal tissue.

**Methods:** Patients with advanced stage Head and Neck Squamous Cell Carcinoma were treated with 3 regimens of chemotherapy concurrently with radiation: daily low-dose (LD) (6 mg/m<sup>2</sup>) cisplatin intravenously (IV) (RADPLAT IV daily LD), cisplatin 100 mg/m<sup>2</sup> IV (RADPLAT IV 100), and cisplatin 150 mg/m<sup>2</sup> delivered intra-arterially (IA) (RADPLAT IA 150), with systemic rescue by sodium-thiosulphate. Patients with cervical cancer were treated with chemoradiotherapy with cisplatin IV 40 mg/m<sup>2</sup> (CERVIX IV 40). After the start of treatment, normal tissue (white blood cells (WBC) and buccal cells) and a tumor biopsy were obtained. Sampling times were 20-23 hours after the 1st course of chemotherapy in RADPLAT IV 100, RADPLAT IA 150 and CERVIX IV 40, 1 hour after the 5th daily dose in RADPLAT IV daily LD. 32P-postlabeling technique was used to quantify selectively the major forms of cisplatin-DNA adducts (i.e. intrastrand GG- and AG-adducts). The levels of adducts were analyzed by type of tissue (normal and tumor tissue) and by chemoradiation protocol, using multivariate analysis.

**Results:** Samples for cisplatin-DNA adduct determination were obtained from 77 patients: 27 from RADPLAT IV daily LD, 21 from RADPLAT IV 100, 14 from RADPLAT IA 150, and 15 from CERVIX IV 40. Normal tissue samples were taken from all patients, tumor biopsies from 28 patients. Adduct-levels in tumor were 2.5-5 times higher than those in WBC for all 4 treatment regimes for both GG- and AG-adduct formation ( $p < 0.001$ ). Analysis by schedule showed that increasing doses of cisplatin resulted in higher levels of GG-adducts in primary tumor (Spearman rank-correlation,  $r = 0.70$ ,  $p < 0.001$ ). For normal tissue (WBC and buccal cells) a similar pattern was seen for the IV schedules (CERVIX IV 40 and RADPLAT IV 100). However, the RADPLAT IA 150 schedule resulted in decreased GG-adduct formation in normal tissue compared to the RADPLAT IV 100 schedule, indicative of more systemic exposure to cisplatin after IV cisplatin compared to selective high-dose IA cisplatin administration. In multivariate analysis the relative contribution of cisplatin-dose and mode of administration (IV vs IA) were calculated separately in 3 schedules: RADPLAT IV 100, RADPLAT IA 150 and CERVIX IV 40. The level of GG-adducts was higher with higher cisplatin-dose (increase about 1.5% per mg cisplatin;  $p < 0.001$ ). Adduct-levels in normal tissue were lower after IA administration than expected from this dose effect (by about 65 - 70%;  $p < 0.001$ ). The effect of IA administration on primary tumor adducts showed a non-significant effect compared to IV treatment.

**Conclusions:** In concurrent chemoradiotherapy schedules cisplatin-DNA adduct-formation in normal tissue and tumor is mostly a cisplatin-dose dependent phenomenon. Selective high dose intra-arterial cisplatin-delivery results in decreased adduct-formation in normal tissue, but it does not result in increased intratumoral adduct levels.

## S030: Cyclin A Overexpression in Oral Dysplasia

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**Purpose:** Cell cycle dysregulation during S phase, which is caused by the overexpression of the cyclin A gene, has been implicated in the pathophysiology of oral dysplasia. The hypothesis tested in this study was that the prevalence of cyclin A-positive cells would be significantly increased in dysplastic oral squamous epithelium compared to normal tissue.

**Materials and Methods:** 41 samples of oral dysplasia and 10 samples of normal squamous epithelium that have been fixed and paraffin-embedded, and a diagnosis provided by the pathology diagnostic services of the University of Kentucky Oral Pathology division, were

used for this evaluation. Avidin-biotin staining kit, (Invitrogen Corp.), and cyclin A specific antibodies, (Santa Cruz Biotechnology, Inc.), were used to visualize and quantitate the presence of the cyclin A protein in cells. Three 1 mm areas (measured lengthwise) examined at 40X magnification, were examined in each sample, (a total length of 3 mm/tissues) and positive cells (brown staining) were determined.

**Results:** 37 dysplastic samples and 8 normal samples of oral squamous epithelium were available for final evaluation. 4 samples of dysplasia and 2 samples of normal epithelium showed ambiguous staining patterns, making conclusions indeterminate. In the dysplastic tissue, a mean of 39.3 cells/3 mm sample (95% CI: 31:48) stained positive for cyclin A. Positively stained cells were found throughout the epithelial layers. In the normal epithelium, a mean of 16.3 cells/3 mm sample (99% CI: 5 - 27) stained positive and were found in the basal and parabasal cell layers only. A rank sum analysis supported a statistical difference between the samples at  $p=0.003$ . Using a threshold positive cutoff of 31 cells/3 mm, the frequency of positive specimens was significantly elevated in the dysplastic tissue ( $p=0.0023$ ). A contingency analysis showed a Positive Predictive Value of 70.3%, Specificity of 38.1%, and an Accuracy of 86.5% for this descriptive characteristic of the dysplastic tissues.

**Conclusions:** These results supported a connection between a high incidence of cyclin A protein expression in oral squamous epithelial cells and oral dysplasia. This altered expression could occur independently or, more likely, in conjunction with other cellular growth dysfunctional changes. These preliminary results demonstrate a potential cellular marker of oral dysplasia that successfully identified 70% of the tissue samples with no false positives in normal specimens. More extended studies will be required to substantiate this finding, as well as determining if the cyclin A expression is limited to oral dysplasia or occurs in other forms of oral tissue lesions/changes.

### **S031: Survivin in Cisplatin-Induced Cell Death in Head and Neck Squamous Cell Carcinomas (HNSCC)**

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**Objective:** To study the role of the inhibitor of apoptosis protein (IAP), survivin, in cisplatin-induced head and neck squamous cell carcinoma (HNSCC) cell death.

**Design:** Parental and cisplatin-resistant HNSCC cells were evaluated for expression of survivin. The HNSCC cells were then transduced with lentiviral small interfering RNA (siRNA) expression vectors developed to express either a survivin-specific siRNA or a scrambled control siRNA. Infected cells were sorted using a green fluorescent protein marker to enrich for highly transduced cells. Cell viability was measured after a 48-hour exposure to cisplatin using trypan blue exclusion assays.

**Setting:** In vitro study of head and neck cancer cell lines UM-SCC-5, -5PT (cisplatin-resistant), -10B, and -10BPT (cisplatin-resistant).

**Results:** Western blotting revealed strong survivin expression in cisplatin-resistant lines (UM-SCC-5PT and -10BPT) but not in the parental lines (UM-SCC-5 and -10B). Infection of UM-SCC-5PT and -10BPT with a survivin siRNA virus resulted in a significant reduction of survivin expression in UM-SCC-5PT and a lesser reduction in UM-SCC-10BPT. Nevertheless, survivin siRNA infection sensitized both cell lines to cisplatin. Cisplatin (10  $\mu\text{mol/L}$  for 48 hours) induced 10% and 13% loss of viability, respectively, in uninfected and scrambled control infected

UM-SCC-5PT cells. Cisplatin-induced loss of viability increased to 29% in UM-SCC-5PT cells infected with the survivin siRNA (knockdown) construct. With 25  $\mu\text{mol/L}$  of cisplatin, uninfected and scrambled control infected UM-SCC-5PT cells still exhibited significant cisplatin resistance, with only 18% and 19% loss of viability, respectively, whereas 49% of the survivin siRNA (knockdown) UM-SCC-5PT cells were killed, indicating significant reversal of resistance. Similarly, cisplatin (10  $\mu\text{mol/L}$ ) killed 20% and 21% of uninfected and scrambled control infected UM-

SCC-10BPT cells, whereas 51% of the survivin siRNA infected cells were killed. In like fashion, the survivin knockdown increased the toxicity of 25  $\mu\text{mol/L}$  of cisplatin in UM-SCC-10BPT to 67% compared with the controls at 26% and 27% cell kill, respectively.

**Conclusions:** Our results indicate that survivin knockdown can sensitize cisplatin-resistant HNSCC cell lines to cisplatin. As such, survivin

expression may be an important factor corresponding to cisplatin resistance and may provide a potential target for therapeutic intervention.

### **S032: Randomized Placebo-Controlled Trial of Citalopram Demonstrating Depression Prevention During Treatment for HN Cancer**

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**Objective:** Prophylactic treatment with the antidepressant citalopram in patients with head and neck (HN) cancer could prevent depression and improve quality of life.

**Design:** Prospective, randomized, placebo-controlled trial.

**Setting:** Academic medical center.

**Patients:** Thirty-six subjects were initially randomized; 23 completed the study.

**Interventions:** Subjects received either 40 mg of citalopram or matching placebo for 12 weeks and a final visit at 16 weeks.

**Main Outcome Measures:** Psychiatric interview, the Hamilton Depression Rating Scale, the University of Washington Quality of Life (UWQOL) questionnaire, and the Clinician Global Index-Severity (CGI-S) scale.

**Results:** All measures of psychiatric well-being favored the group taking citalopram. The number of subjects who met criteria for clinically significant depression during the 12 weeks of active study was 6 (50%) of 12 in the placebo group (PG) and 2 (15%) of 13 in the citalopram group (CG) (Fisher exact test,  $P=.01$ ). No patients in the CG became suicidal, compared with 2 in the PG. At study end, the CGI-S scale was mildly ill or greater in 15% in the CG compared with 60% in the PG (Fisher exact test,  $P=.04$ ). At week 16, the UWQOL scores were 7 below baseline in the CG and 30 below in the PG (Wilcoxon statistic,  $P=.14$ ). Both the UWQOL and the CGI-S scores improved from the 12-week visit to the 16-week visit in the CG and continued to decline in the PG.

**Conclusion:** This study reports data from the first depression prevention trial in HN cancer and supports the concept that depression can be prevented and global mental health improved during the first 3 months following diagnosis.

### **S033: Correlations Among Patient-Reported, Observer Rated, and Objective Swallowing Function After Chemo-Irradiation**

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**Purpose:** to assess swallowing parameters and their correlations early after the completion of chemo- IMRT (intensity modulated radiotherapy), in which the planning of IMRT intended to reduce dysphagia and aspiration.

**Methods and Patients:** 36 patients with stage III-IV oropharyngeal (31) or nasopharyngeal (5) patients underwent definitive therapy with IMRT aiming at the sparing of the major salivary glands as well as the structures whose damage was found previously (IJROBP 2004;60:1425-39) to be a likely cause of dysphagia and aspiration: the pharyngeal constrictors (PC) and glottic +supraglottic larynx (GS). Gross tumor dose was 70 Gy and subclinical targets doses 64-60 Gy, all in 35 fractions. All patients received concurrent chemotherapy (Oropharynx: weekly carboplatin 1 AUC and paclitaxel 30mg/m<sup>2</sup>; nasopharynx: cisplatin 100mg/m<sup>2</sup> q. 3 weeks). Videofluoroscopy (VF), patient-reported swallowing questions from the Head and Neck quality of life (QOL) (HNQOL)(Terrell et al, Arch Oto HN Surg 123:1125-32) and the University of Washington QOL (UWQOL) questionnaires, and observer-rated swallowing toxicity scores according to CTC 2.0, were obtained before therapy and 3 months after the completion of therapy. The correlations between various VF end-points and patient-reported or observer-scored dysphagia were made using Spearman Rank tests.

**Results:** Worsening swallowing at 3 months compared to pre-therapy were noted in 66% of the patients according to UWQOL, in 53% (liquids) and 78% (solids) according to HNQOL, and in 30% according to CTC, respectively. VF-based strictures were observed in 3/36

patients and were not correlated with either HNQOL, UWQOL, or CTC. VF-based reduced base of tongue motion (14/36 patients) and reduced laryngeal elevation (16/36 pts) at 3 months were significantly correlated with difficulties swallowing liquids ( $p=0.05$ ) and solids ( $p=0.03$ ) according to HNQOL, and VF-based aspiration (16/36 patients) was significantly associated with swallowing solids ( $p=0.01$ ) but not liquids ( $p=0.4$ ) according to HNQOL. Reduced laryngeal elevation tended to correlate with the CTC ( $p=0.08$ ). None of the other VF parameter correlated or tended to correlate significantly with the CTC, and no parameter correlated significantly with WUQOL.

**Conclusions:** 3 months after IMRT, patient-reported swallowing according to HNQOL, but not UWQOL nor CTC, correlated significantly with major VF-based endpoints. The potential effect of IMRT in reducing dysphagia, compared with previous RT methods, will be discussed.

### **S034: Intensity-Modulated Radiotherapy (IMRT) Aiming to Reduce Dysphagia: Early Dose-Effect Correlations**

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**Purpose:** We have previously identified the pharyngeal constrictors (PC) and the glottic and supraglottic larynx (GSL) as structures whose dysfunction after intensive chemoradiation is a likely cause of dysphagia, and explored intensity-modulated radiotherapy (IMRT) strategies which spared these structures without compromising target doses (*Int J Radiat Oncol Biol Phys.* 2004;60:1425-1439). Early results of a clinical trial to validate these findings are presented.

**Patients and Methods:** Thirty-six patients with stage III-IV oropharyngeal ( $n=31$ ) or nasopharyngeal ( $n=5$ ) cancer underwent definitive therapy with IMRT aiming at the sparing of the major salivary glands as well as the PC, GSL, and esophagus. In all patients, the gross tumor volume (GTV) doses were 70 Gy, high-risk clinical target volume (CTV) doses 64 Gy, and low-risk CTV doses 60 Gy, all in 35 fractions. Inverse-plan IMRT optimization included cost functions for reducing the doses to the parts of the PC and GSL outside the planning target volumes (PTVs), without underdosage of the PTVs. All patients received concurrent chemotherapy (oropharynx, weekly carboplatin [1 area under the curve] and paclitaxel [30 mg/m<sup>2</sup>]; nasopharynx, cisplatin [100 mg/m<sup>2</sup> every 3 weeks]). Videofluoroscopy and patient-reported swallowing questions from the Head and Neck Quality of Life instrument

(*Arch Otolaryngol Head Neck Surg.* 1997;123:1125-1132) were obtained before and periodically after therapy. The correlations between the dysphagia end points and the doses received by the PC, GSL, and esophagus were assessed using dose-volume histograms of the whole structures (including the parts residing within the PTVs).

**Results:** Three months after the completion of therapy, videofluoroscopy-based strictures were observed in 3 patients (8%) and aspirations in 16 (44%). Statistically significant correlations were observed between aspiration risk and the partial volumes of the PC and the GSL (but not the esophagus) receiving doses between 50 and 65 Gy ( $P = .005$ ). Strictures were observed in 3 patients, and they had a threshold dose-volume relationship for the PC but not for the GSL or the esophagus. For the Head and Neck Quality of Life questionnaire scores, worsening liquid swallowing was significantly correlated with dose-volume parameters of the PC and the esophagus, but only the PC dose-volume parameters were correlated with worsening solid swallowing ( $P = .04$ ).

**Conclusions:** These dose-volume-effect relationships motivate efforts to further reduce the doses to the PC and GSL in order to reduce dysphagia and aspiration, and serve as the initial basis for setting relevant dose-volume goals for optimization of IMRT.

### **S035: Driving Performance in Patients With Head and Neck Cancer: A Pilot Study**

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**Purpose:** To investigate the driving performance of patients with head and neck cancer (HNC).

**Design:** Case-control.

**Setting:** Driving performance laboratory.

**Patients:** Ten patients with HNC participated in a laboratory evaluation of driving using a virtual reality driving simulator. Fifty community adults from the existing database served as comparison.

**Intervention:** Participants completed a 12-minute driving evaluation course.

**Outcome Measures:** (a) average speed, (b) steering variability, (c) mean brake reaction time, (d) number of collisions, and (e) scores of the Simulator Driving Performance Scale (SDPS) that evaluated how well the participant drove while in the simulator.

**Results:** The analysis of covariance indicated that the adjusted mean scores of the brake reaction time and steering variability (1/x) in the HNC group were significantly longer and larger than that of the control group ( $F_{1,55} = 5.005, P = .03$ ) and ( $F_{1,56} = 8.731, P = .005$ ), respectively. However, no significant difference between the 2 groups on the average speed and number of collisions was found ( $P_s > .05$ ). The safe driving practices of the HNC participants, as indicated by the scores of the Simulator Driving Performance Scale, were significantly inferior to those of the control group ( $F_{1,50} = 4.591, P = .04$ ).

**Conclusions:** Findings showed that HNC participants exhibited slower brake reaction time and more steering variability than the control group after adjusting for the difference in age and current medication use. In addition, the HNC group used fewer safe driving behaviors as rated by the observer than the control group.

### **S036: The Pattern of Acute Mucosal Reactions in Patients With Head and Neck Cancer Treated by Conventional and Accelerated Irradiation**

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**Purpose:** To evaluate acute mucosal reactions in head and neck cancer patients treated by conventional and accelerated irradiation, with particular consideration of appearance's and duration's time of morphological and functional parameters.

**Patients:** Sixty-six patients with head and neck cancer (oral cavity, oropharynx, hypopharynx, and larynx). Patients were irradiated by conventional (CF) and accelerated fractionation (AF): the distribution between groups was equal.

**Methods:** Acute mucosal reactions were evaluated by complex of clinical signs which include morphological and functional parameters. Functional parameters were collected everyday and morphological parameters at least 3 times per week during all the treatment time.

**Results:** A wide range of beginning of morphological and functional parameters for both type of fractionations were observed. Also, the healing time after completing of radiotherapy was in a wide range, but by 1 week shorter for CF than AF. Average time to onset of erythema and edema was observed significantly earlier for AF than CF, whereas the beginning of mucositis was equal for both type of fractionation. Confluent mucositis was observed in 73% of patients irradiated by CF and in 82% by AF.

**Conclusions:** 1. Wide range of morphological and functional parameters' appearance and duration suggests existence of individual radiosensitivity of mucosa in patients with head and neck cancer. 2. Despite more escalated reactions in patients irradiated by AF than CF, the total durations of reactions were similar for both types of fractionation. 3. Confluent mucositis was observed in almost three fourths of patients irradiated by CF, much more frequent than the percentage presented in the literature (50%), probably because of too rare clinical examination.

### **S037: Advanced T Stage Is Associated With Improved Swallowing Following Concurrent Chemoradiotherapy in Head and Neck Cancer Patients**

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**Objective:** Chemoradiotherapy is an integral component in the management of advanced head and neck cancer (AHNC) patients.

Dysphagia may manifest in these patients due to many factors. We sought to define factors that acutely influenced swallowing function prior to and during concurrent chemoradiotherapy.

**Methods:** From November 1998 to August 2002, 222 eligible AHNC patients were treated on a multi-institution phase II protocol. Ninety-five of 132 patients treated at the University of Chicago had swallowing function assessed via oropharyngeal motility (OPM) study prior to and within 1-2 months following the completion of chemoradiotherapy. The swallowing performance status scale (SPSS), a summary score on a scale of 1-7 of oral impairment, pharyngeal impairment, aspiration, and diet, was given by a single senior speech/swallow pathologist. Higher scores indicated worse swallowing. Generalized linear regression models were formulated to assess the effects of patient factors tumor factors and treatment-related factors on the differences between SPSS score before and after treatment.

**Results:** The mean pretreatment and posttreatment OPM scores were 3.09 and 3.7, respectively. Patients with T3/T4 tumors (odds ratio [OR], 0.38; 95% confidence interval [CI], 0.15-0.95;  $P = .04$ ) and ECOG performance status of 1-2 (OR, 0.37; 95% CI, 0.15-0.91;  $P = .03$ ) were less likely to have swallowing worsening after chemoradiotherapy. There was a trend for worse swallowing with increasing age (OR, 1.04; 95% CI, 0.99-1.09;  $P = .08$ ). Only T stage (T3/T4) was associated with improved swallowing after treatment (OR, 8.96; 95% CI, 1.9-41.5;  $P < .005$ ).

**Conclusions:** In patients undergoing concurrent chemoradiotherapy, improved swallowing function over baseline is associated with advanced T stage.

### S038: Characterization of TMEM16A in Squamous Cell Carcinoma of the Head and Neck

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**Background:** TMEM16A is a novel gene that we recently identified by high-resolution mapping of chromosomal band 11q13 in squamous cell carcinoma of the head and neck (SCCHN). The goal of the present study is to characterize the cellular distribution, expression profile, and function of this gene in SCCHN.

**Methods:** We prepared a polyclonal antibody against an immunogenic region of TMEM16A. The antibody was validated by epitope blocking and subsequently used for immunoblotting and immunofluorescence experiments. The expression profile of TMEM16A was evaluated in paired samples of SCCHN and normal adjacent mucosa by immunoblotting. The expression profile in SCCHN tumors was further investigated by immunohistochemical staining of a SCCHN tissue array (TMA). Small interfering RNA (siRNA) techniques were used to “knockdown”

TMEM16A in SCCHN cell lines. The effect of knockdown on cell proliferation was evaluated with a MTT assay.

**Results:** Immunoblotting of tumor cell lines with or without 11q13 gene amplification showed that TMEM16A protein levels were not directly correlated with amplification at the genomic level. By immunoblotting, TMEM16A was overexpressed in 80% of tumors, but not in normal mucosa. Tumors overexpress TMEM16A by 500% when compared with normal mucosa ( $P < .001$ ). The protein was found in multiple cellular compartments, including the nucleoplasm, nuclear membrane, and cytoplasmic membrane. Immunohistochemical analysis of the TMA showed 2 distinct tumor populations that were demarcated by the nuclear to cytoplasmic expression ratio. Tumors with a high nuclear to cytoplasmic ratio appeared to be more poorly differentiated. TMEM16A knockdown resulted in decreased cell viability based on the MTT assay. A higher percentage of TMEM16A-depleted cells were found in the G2 phase of cell cycle by flow cytometric analysis.

**Discussion/Conclusion:** TMEM16A is a novel gene mapped to chromosomal band 11q13 that is amplified in SCCHN with 11q13 amplification. This gene encodes a protein with an undiscovered function that is predicted to have 8 transmembrane domains. Our data indicate that TMEM16A can be found in the nucleus, despite the presence of transmembrane domains. Furthermore, siRNA knockdown studies indicate that TMEM16A may play a role in cell growth. The overexpression of TMEM16A observed in tumors vs normal tissue, when coupled with the nuclear to cytoplasmic expression profiles, suggests that TMEM16A may prove to be a novel therapeutic target. Further studies exploring the role of TMEM16A as a potential oncogene in SCCHN are currently under way.

### S039: Activation of the Gain-of-Function p53R172H Allele Predisposes to Oral Cancer Progression

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**Objective:** Mutations in the tumor suppressor gene p53 are found in more than 50% of the squamous cell carcinomas (SCC) that develop in the oral cavity. Most of these mutations are missense mutations that result in expression of altered versions of p53. We wanted to analyze the role of the mutant p53R172H in oral cancer development and determine whether p53R172H acquires gain-of-function properties.

**Methods:** We generated an inducible mouse model that allows the activation of oncogenes and/or tumor suppressor genes in the oral cavity. Using this model, we demonstrated that inducible activation of an oncogenic K-rasG12D allele in the oral cavity results in squamous cell papilloma formation (Caulin et al. *Cancer Res.* 2004;64:5054-5058). To determine whether activation of a mutant p53 allele can predispose to progression to SCC, we have now generated mice in which the p53R172H and K-rasG12D alleles can be activated in the oral cavity.

**Results:** We found that activation of the p53R172H allele results in increased oral tumor formation, suggesting that p53R172H contributes to oral cancer initiation. In addition, we also observed that activation of the p53R172H allele can induce progression to SCC.

**Conclusions:** These data support a gain-of-function role for p53R172H in oral SCC development and suggest that mutations in p53 not only contribute to late stages of tumor progression but also can cooperate with other genetic alterations in tumor initiation. We are currently analyzing expression profiles of p53R172H squamous cell papilloma in order to identify molecular mechanisms involved in mutant p53-mediated oral cancer progression.

### S040: Genetic Polymorphisms of Alcohol and Aldehyde Dehydrogenases in Japanese Men with Head and Neck Cancer

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Genetic polymorphisms of aldehyde dehydrogenase-2 (ALDH2), alcohol dehydrogenase-2 (ADH2), and alcohol dehydrogenase-3 (ADH3) influence the metabolism of alcohol and other carcinogens. The ALDH2\*1/2\*2 genotype, which encodes an inactive ALDH2, and the ADH2\*1/2\*1 genotype, which encodes a low-activity form of ADH2, enhance the risk of developing oropharyngeal and/or esophageal cancers. The present case-controlled study attempted to define the individual and combined roles of ALDH2, ADH2 and ADH3 gene polymorphisms on the risk of developing head and neck squamous cell carcinoma (HNSCC) in Japanese patients. One hundred thirteen Japanese men with HNSCC (43 cases of hypopharyngeal cancer and 70 cases of other site of HNSCC) and 642 cancer-free Japanese men who had undergone an annual health checkup were enrolled in this study. The ethics committee of each collaborating institution reviewed and approved the proposed study, and each of the participants provided their informed consent. The prevalence of the ALDH2\*1/2\*2 genotype was significantly higher among the patients with hypopharyngeal cancer (77.8%) than among the controls (39.4%). The prevalence of the ADH2\*1/2\*1 genotype was significantly higher among both cancer groups (hypopharynx, 29.2%; other sites, 16.5%) than among the controls (4.8%). The prevalence of the ADH3 (3\*2 allele carrier) genotype, which encodes a less-active form of ADH3, was significantly higher among patients with other site of HNSCC (21.4%) than among the controls (8.7%). Among hypopharyngeal cancer, the risk of moderate-to-heavy drinkers with an ALDH2\*1/2\*2 genotype was approximately 10 fold of that of moderate-to-heavy drinkers with an ALDH2\*1/2\*1 genotype, whereas no significant risk according to genotype was observed among never/rare-to-light drinkers (odds ratio [OR] = 10.08 vs. 0.51, respectively;  $P = .0005$  for the difference in ORs). As for the ADH2 genotype, only moderate-to-heavy drinkers with an ADH2\*1/2\*1 genotype had significantly higher risks of developing both hypopharyngeal cancers and other head and neck cancers (OR = 7.21 and 4.66, respec-

tively). The less-active form of ADH3 (ADH3\*1/3\*2+3\*2/3\*2) significantly increased the risk of cancer at other sites of HNSCC among moderate-to-heavy drinkers (OR= 3.88) but did not increase the risk of hypopharyngeal cancer in any of the drinking categories. In a multivariate analysis, the significant independent risk factors for the development of hypopharyngeal cancer were inactive ALDH2\*1/2\*2, less-active ADH2\*1/2\*1, frequent drinking of strong alcoholic beverages, and not eating green-yellow vegetables daily. The significant independent risk factors for the development of other site of HNSCC were less-active ADH2\*1/2\*1, frequent drinking of strong alcoholic beverages, smoking, not eating fruit daily, and notably, the presence of an ADH3\*2 allele. Education regarding these risks in connection with determining the ALDH2, ADH2 and ADH3 genotypes is vitally important in a new strategic approach aimed at preventing hypopharyngeal and other head and neck cancers in East Asians.

## **S041: Identification of the Mechanism of 11q13 Amplification Leads to Detection of DNA Repair Defects in HNSCC Cell Lines**

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**Objective:** To determine whether the initial step in 11q13 amplification, loss of distal 11q, including 3 critical genes involved in the DNA damage response pathway, *MRE11A*, *ATM*, and *H2AFX*, is associated with chromosomal instability.

**Design:** Eleven head and neck squamous cell carcinoma (HNSCC) cell lines were analyzed by fluorescence in situ hybridization (FISH) for copy number of *MRE11A*, *ATM*, and *H2AFX*; by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) and immunoblotting for RNA and protein expression; by quantitation of gamma-H2AX foci (a measure of the DNA damage response); and for survival and chromosomal instability after treatment with ionizing radiation (IR).

**Subjects:** In vitro analysis of HNSCC cell lines UPCI:SCC078, 084, 099, 104, 116, 122, 125, 131, 136, 142, and 182, derived in our laboratory.

**Intervention:** Cells were either treated with IR or untreated.

**Results:** FISH analysis revealed partial copy number loss of *MRE11A*, *ATM*, and *H2AFX* in 4 cell lines with 11q13 amplification and in 4 of 7 cell lines without 11q13 amplification. qRT-PCR and immunoblotting showed reductions in RNA and protein expression of *MRE11A*, *ATM*, and *H2AX* that correlated with the distal 11q loss. All cell lines with distal 11q loss demonstrated a decrease in the size and number of gamma-H2AX foci and increased chromosomal instability after treatment with IR. Unexpectedly, distal 11q loss was also correlated with reduced sensitivity to IR (radioresistance), regardless of 11q13 amplification status.

**Conclusions:** Although the literature attributes the poor prognosis in HNSCC to 11q13 gene amplification, our results suggest that distal 11q deletions lead to radioresistance and thus may be equally if not more important.

## **S042: WIF1, an Inhibitor of the WNT Pathway, Is Recurrently Inactivated in Salivary Gland Tumors**

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The Wnt signaling pathway controls many events during embryogenesis and oncogenesis. Activation of this pathway, mainly through mutations in the intracellular components or over-expression of WNTs, is a well-established oncogenic signal in several human and mouse tissues. In transgenic mouse models activation of the Wnt pathway leads to a high frequency of salivary gland benign and malignant tumors. Likewise, studies of human tumors suggest that activation of this pathway plays a role in human salivary gland cancer. However, the exact molecular nature of Wnt activation is unknown in this tumor type. Here we show that the Wnt inhibitory factor-1 (WIF1) gene, which encodes a secreted protein antagonistic to Wnt-dependent signaling, is targeted for rearrangement and loss in human salivary gland cancer. We have first identified the WIF1 gene as a novel

HMG2 fusion partner in a salivary gland pleomorphic adenoma. Then, using Southern blot and loss of heterozygosity analyses, we demonstrate that WIF1 rearrangements and deletions are a recurrent finding in carcinoma ex-pleomorphic adenoma. These data suggest that WIF1 is a salivary gland tumor suppressor gene. RT-PCR and northern blot analyses show that WIF1 is highly expressed in normal salivary gland tissue and down-regulated in cell lines derived from benign and malignant salivary gland tumors. Our results establish for the first time the WIF1 gene as a recurrent target for mutation in salivary gland tumors and provide a mechanistic link between the dysregulation of Wnt signaling and the development and/or progression of salivary gland pleomorphic adenomas.

## **S043: Galanin Receptor Type 1 Inhibits Cell Proliferation in Squamous Carcinoma Cells via Erk1/2 Activation**

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**Objective and Design:** We previously reported that loss of chromosome 18q develops with tumor progression and is associated with significantly decreased survival in head and neck cancer patients. Galanin receptor 1 (GALR1), a Gi-protein-coupled receptor, maps within the common region of 18q loss and is frequently inactivated by methylation, which is consistent with the possibility that it might be a tumor suppressor gene. To investigate effects of GALR1 and its signaling pathways, we stably expressed hemagglutinin-tagged GALR1 in a human laryngeal carcinoma cell line (UM-SCC-23-GALR1) that expresses no endogenous GALR1.

**Interventions and Results:** In UM-SCC-23-GALR1 cells but not in mock transfected cells, galanin induced the extracellular regulated protein kinase-1/2 (ERK1/2) activation and cell cycle arrest. Galanin also induced expression of the cyclin-dependent kinase inhibitors (CKI), p27Kip1 and p57Kip2, and decreased expression of cyclin D1. Pretreatment of UM-SCC-23-GALR1 cells with the ERK1/2-specific inhibitor U0126 prevents these galanin-induced effects. On the other hand, there was no significant difference in phosphatidylinositol 3-kinase (PI3K) pathway activation between UM-SCC-23-GALR1 and UM-SCC-23-mock cells after galanin treatment. In addition, using the Gi-protein-specific inhibitor pertussis toxin and the PI3K-specific inhibitor LY294002, we show that galanin and GALR1 induce ERK1/2 activation via the Gi pathway, not the PI3K pathway-linked to the G-beta and G-gamma subunits. Galanin and GALR1 also inhibit colony formation and xenografted tumor growth in vivo.

**Conclusion:** Our results identify a novel mechanism whereby GALR1, a Gi-protein-coupled receptor, inhibits cell proliferation by ERK1/2 activation.

## **S044: Does Positron Emission Tomography Improve Our Ability to Detect Residual Neck Node Disease After Chemoradiotherapy?**

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**Background:** The role of neck dissection in patients undergoing initial non-operative treatment for squamous cell head and neck cancer is controversial. This study details our experience at the Cleveland Clinic using the neck exam, computerized tomography (CT), and positron emission tomography (PET) to clinically evaluate patients for residual neck node disease after definitive chemoradiotherapy.

**Methods:** We retrospectively reviewed all PET-staged patients with squamous cell head and neck cancer who presented with N2-3 neck node disease, and who were treated with definitive concurrent chemoradiotherapy using 5-fluorouracil and cisplatin. Clinical restaging by neck exam, CT, and PET was accomplished 8-12 weeks after completion of treatment. Residual palpable nodes on exam; residual nodes larger than 1 centimeter or with central necrosis on CT; or any residual hypermetabolic lymph nodes on PET were considered to be clinical evidence of residual neck node disease. Persistent neck node disease was confirmed only if pathologic involvement was identified at the time of neck dissection, or if regional recurrence developed. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (Acc) were calculated for all three clinical assessment tools.

**Results:** The study included 48 patients with N2-3 disease, who had 72 positive necks, and who were followed for a median of 12.3 (range 3.9-40.7) months. All but 2 patients are still alive. After chemoradiotherapy, a planned neck dissection was performed in 33 necks, and was positive in only 5. Recurrent primary site or neck node disease prompted a delayed neck dissection in 5 necks, which was positive in 3. The utility of these clinical assessment tools and combinations thereof are detailed in the table.

**Conclusions:** In patients presenting with N2-3 squamous cell head and neck cancer, residual neck node disease after definitive chemoradiotherapy was infrequent and not well predicted by PET. A positive PET in this setting is of little utility. Although a negative PET was highly predictive for control of neck disease after chemoradiotherapy, it added little to the clinical neck exam and the CT.

## **S045: Management of N2A Cervical Lymph Node Metastases: Is Selective Neck Dissection Enough?**

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**Background:** In the current era of organ preservation and chemoradiation therapy, management of cervical lymph node metastases for patients with head and neck squamous cell carcinoma is in evolution. Historically, treatment of regionally advanced disease consisted of a comprehensive removal of all lymph nodes in cervical Zones I through V. Recent evidence suggests that selective nodal dissection may be as effective as comprehensive dissections in certain patients. This paper evaluates the actual extent of disease in patients with pre-operative nodal staging of N2A to determine if selective neck dissection would have resulted in removal of all pathologically positive lymph nodes.

**Methods:** A retrospective medical record review was performed on fifteen consecutive patients receiving comprehensive neck dissection by the same primary surgeon between January 2000 and June 2005 for pre-operative nodal staging of N2A. Patients underwent surgery prior to adjuvant radiation or chemoradiation therapy. Patient demographics and primary site tumor variables were recorded. Nodal variables included neck mass duration, size, and location. Pathology variables included the number of total lymph nodes, number of positive nodes, location of positive nodes, and presence or absence of extracapsular spread.

**Results:** There were 15 males and no females in the population with a mean age of 56.9 +/- 10 years. Two-thirds of the patients had an oropharyngeal primary tumor. Twenty percent of patients had cervical nodal disease with no known primary. The mean duration of the neck masses was 11.4 +/- 5.2 weeks, with the mean size of the largest node pre-operatively being 3.4 +/- 0.9 cm in largest dimension. Eighty percent of the neck masses were located in the level II nodal basin with all located between levels I through III. The mean nodal yield of the neck dissections was 37.9 +/- 12.7 lymph nodes with greater than one positive node found in 33.3% of the specimens. All positive lymph nodes were located in levels I, II or III, with 93.4% found in level II.

**Conclusions:** In this select group of N2A patients undergoing upfront comprehensive neck dissection of Zones I through V as part of their multidisciplinary treatment of SCCa of the oropharynx and unknown primary sites, all positive lymph nodes were found within cervical nodal levels I, II or III. Consequently, selective neck dissection with removal of Zones I through III would have resulted in complete removal of pathologically positive nodes and may be an appropriate option for upfront surgical management of select patients.

## **S046: Sentinel Node Biopsy in N0 SCC of the Oral Cavity and Oropharynx in the Previously Operated or Irradiated Patient**

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**Objectives:** To assess the feasibility of sentinel lymph node (SLN) localization and to determine the predictive value of sentinel node biopsy for occult neck metastases in the previously operated or irradiated patient with N0 squamous cell carcinoma (SCC) of the oral cavity or oropharynx.

**Design:** Case series.

**Setting:** Academic tertiary care hospital.

**Patients:** Eleven patients with T1-T4 N0 SCC of the oral cavity or oropharynx.

**Intervention:** All patients underwent preoperative peritumoral injection of technetium-99m followed by dynamic lymphoscintigraphy and operative localization of the SLN(s) with the use of a handheld gamma-probe.

**Main Outcome Measures:** Negative predictive value of the SLN(s) in N0 SCC of the oral cavity or oropharynx.

**Results:** One to 3 SLNs were identified by lymphoscintigraphy in all 11 patients. All SLNs identified by lymphoscintigraphy were successfully identified and removed with the use of an intraoperative gamma probe. In 10 of the 11 patients, the SLN(s) accurately predicted the presence or absence of occult neck metastasis. There was 1 instance of a negative SLN with a positive neck dissection. The overall negative predictive value of the study was 91%.

**Conclusions:** Sentinel lymph node biopsy in the previously operated or irradiated patient appears as effective as published SLN biopsy in previously untreated patients and warrants further study.

## **S047: Value of Sentinel Lymph Nodes in Predicting Regional Lymph Nodes: A Comparison With Proliferation Marker PCNA**

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**Objective:** The aim of the present study was to evaluate the efficacy of sentinel lymph node dissection in staging regional lymph nodes, which was compared with that of immunolabeling of PCNA.

**Design:** Multicentric prospective study.

**Setting:** Tertiary care center.

**Patients:** Fifty-four untreated patients with squamous cell carcinoma without detectable metastasis.

**Intervention:** All patients underwent a sentinel node radiolocalization with the peritumoral injection of technetium-99m colloid particles along with intraoperative gamma probe evaluation and primary site resection.

**Main Outcome Measures:** The percentage of PCNA-positive cancer cells was calculated. Sensitivity and specificity of both sentinel lymphadenectomy plus cytokeratin immunohistochemistry and PCNA index were calculated, and the efficacy of different methods in predicting lymph node metastasis was compared.

**Results:** Sentinel lymph nodes were identified in all cases. A total of 190 sentinel nodes were harvested. Twenty-three of 54 patients proved to have occult metastases on final pathological examinations. Lymphoscintigraphy and cytokeratin staining predicted in all but 1 occult metastatic patient, showing sensitivity and specificity of 96% and 100%, respectively. The mean percentage of immunolabeled cancer cells was 52%. The percentage of cancer cells immunolabeled for PCNA was much higher in the primary tumors associated with lymph node metastasis than in those without ( $P = .001$ ). Both sensitivity and specificity for PCNA index were only 74%.

**Conclusions:** Sentinel lymphadenectomy with cytokeratin staining is a promising and accurate method for predicting occult metastasis in head and neck cancer. The efficacy of proliferation marker PCNA was lower than that of sentinel lymphadenectomy with cytokeratin staining.

## **S048: Detection of Occult Bone Metastases From Head and Neck Squamous Cell Carcinoma: Impact of PET/CT Imaging**

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**Objective:** Bone metastasis of head and neck squamous cell carcinoma (HNSCC) is thought to be a clinical entity occurring in the setting of widespread metastases, portending very poor survival. Previously, these metastases were only detected through pain symptoms or abnormal laboratory serologies, both of which are insensitive for early lesions. The objective of this study is to define the role of positron emission tomography/computed tomography fusion (PET/CT) in early detection of skeletal metastases. Furthermore, this

study seeks to determine whether such earlier detection is impacting the management of these patients.

**Methods:** This study was performed through retrospective review of 650 PET/CT studies obtained in HNSCC patients from October 2002 until February 2006 at an academic tertiary care hospital. All individuals with PET/CT reports indicating previously undetected bone metastasis were selected for detailed chart review.

**Results:** PET/CT detected previously unrecognized bone metastasis in 16 patients, comprising 2.5% of all PET/CT exams in the HNSCC population. All 16 of these studies were performed to restage previously treated disease and comprised 3.7% of total restaging PET/CT studies. Most of the detected lesions were asymptomatic, and, in the 6 individuals in whom histologic confirmation was sought, only a single false positive was noted, conferring an 83% specificity. At the time of osseous lesion detection, 53% of individuals had no other identifiable distant metastatic disease. Furthermore, 20% of individuals were without detectable recurrent disease at any other site besides bone. The identification of bony metastases clearly impacted therapeutic management in at least 40% of the cases.

**Conclusions:** Restaging PET/CT frequently leads to earlier detection of skeletal metastases from HNSCC. This detection often occurs when the lesions are asymptomatic and would have gone undetected prior to the routine application of PET/CT for restaging. Given the poor prognosis associated with bone metastasis, PET/CT is shown significantly to impact clinical decision making in patients in whom such earlier detection is achieved.

## **S049: Role of Routine Posttreatment Surveillance in Squamous Carcinoma of the Oral Cavity**

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**Objective:** To assess the efficacy of routine surveillance in the diagnosis of recurrent and new primary head and neck cancers in patients treated for squamous cell carcinoma of the oral cavity (SCCOC).

**Design:** Retrospective chart study.

**Setting:** Tertiary cancer care center.

**Patients:** A total of 358 patients treated for SCCOC at 1 institution between 1990 and 1995.

**Interventions:** Primary surgery with posttreatment adjuvant radiotherapy as indicated.

**Main Outcome Measures:** Diagnosis of a recurrent or new primary tumor in the head and neck, mode of detection (routine or unscheduled). Other end points were overall survival (OS), disease-specific survival (DSS), and recurrence-free survival (RFS).

**Results:** Of the 178 recurrent or new primary tumors in 124 patients, 34% occurred in year 1, 16% in year 2, and 8% in year 3. Seventy-five percent of recurrences and 69% of new primary tumors were diagnosed on routine visits, 25% and 31% on unscheduled visits. With a median follow-up of 68 months (range, 1-187), the 5-year OS, DSS, and RFS were 61%, 80%, and 66%, respectively. The 5-year OS and DSS rates for patients whose recurrent tumors were detected on routine vs unscheduled visit were 56% vs 57% and 65% vs 69%, respectively ( $P = .90$ ).

**Conclusions:** Patient-initiated consultations were responsible for detection of some recurrences, but the majority of recurrent or new primary tumors after treatment of SCCOC were detected by the clinician during routine surveillance. This observation supports the need for prospective examination of the impact of better patient awareness in posttherapy surveillance for SCCOC.

## **S050: The Role of Panendoscopy in the Staging of High Risk Head and Neck Squamous Cell Carcinoma Prior to Therapy**

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**Background:** Panendoscopy has historically been advocated to adequately stage patients with head & neck squamous cancer, especially in the setting of neoadjuvant therapy. The role of panendoscopy in view of comparable information obtained by non-invasive radiological studies is still controversial.

**Objective:** The primary objective was to analyze the results of panendoscopy in a series of patients enrolled in a neoadjuvant chemo radiation protocol. The secondary objective was to assess whether the panendoscopy results changed the treatment plan.

**Methods:** We reviewed the results of 69 patients with stage III/IV head & neck squamous cell carcinoma (H&N cancer) treated with neoadjuvant chemo radiation at a single institution from 1996 to 2005. All patients underwent routine panendoscopy prior to protocol enrollment. This included detailed laryngoscopy/microlaryngoscopy with strategic biopsies, esophagogastroduodenoscopy (selected biopsies for Barretts) and placement of percutaneous gastrostomy (PEG) and bronchoscopy (washing for cytology). Patients were initially treated with chemo radiation (earlier protocols H & N 53, 67) whereas subsequent protocols utilized induction chemotherapy followed by chemo radiation (H & N 79, 86). Patients with persistent cancer on restaging biopsy underwent a surgical resection of primary tumor site. Evidence of nodal metastasis required a neck dissection at the completion of chemo-radiation or at the time of primary site resection.

**Results:** Of the 69 patients, 2 patients had bronchial cytology positive for malignant cells in absence of any lung findings (both were NED at 5 years). A radiologically occult bronchial cancer (primary) was found in an additional patient which excluded the patient from the treatment protocol. Two of 69 patients were diagnosed with Barrett's esophagus; another patient with oral cavity cancer also had a synchronous primary cancer of the cervical esophagus which excluded the patient from the treatment protocol. Nine of the 69 patients underwent panendoscopy for cervical metastases from an apparent unknown primary cancer at initial diagnosis. The primary cancer was documented in 6 patients at staging panendoscopy and in another patient at follow up panendoscopy. Detailed laryngoscopy was also helpful to assess the laryngeal extent of advanced primary cancers of posterior pharynx/hypopharynx and base of tongue.

**Conclusion:** Panendoscopy is overall a useful adjunct to staging high-risk H & N cancer patients prior to initiation of therapy. A detailed laryngoscopy (micro-laryngoscopy) with strategic biopsies is required for adequate staging of all cancers of oropharynx and larynx. A disciplined biopsy technique is essential for adequate assessment for unknown primary cancers. Esophago-gastro-duodenoscopy had a low but definable yield to find a second primary, but is also a necessary prerequisite to percutaneous gastrostomy prior to radiation therapy to ensure adequate nutrition during neoadjuvant therapy. Bronchoscopy has a limited role in the absence of radiologic chest findings.

## **S051: Efficacy of a Selective Policy of Observation in Patients With Clinically Node-Negative T1-2 Carcinoma of the Tongue**

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**Objective:** To audit our management policy of treatment of clinically N0 (cN0) early-stage squamous cell carcinoma of the oral tongue (SCCOT).

**Design:** Retrospective review of patients treated between 1986 and 1996.

**Setting:** Tertiary cancer center.

**Patients:** A total of 215 patients with previously untreated T1 (n=110) or T2 (n=105) cN0 SCCOT were identified. The median age was 59 years (age range, 14-88 years). Elective neck dissection (END) was performed in 51%, while the neck was observed in 49%. The END and surveillance groups differed significantly for the following features: clinical stage T2 (72% vs 28%), depth of invasion >2 mm (68% vs 32%), poorly differentiated grade (75% vs 25%), and postoperative radiation therapy (33% vs 1%).

**Main Outcome Measures:** 5-year overall survival (OS), disease-specific survival (DSS), and neck recurrence rate (NRR).

**Results:** With a median follow-up of 93 months (range, 1-236 months), 5-year OS and NRR for the END vs surveillance groups were 73% vs 83% and 23% vs 20% ( $P > .05$ ). The DSS for the END group was 78% vs 92% for the surveillance group ( $P = .009$ ). Tumor size >2 cm, depth of invasion >2 mm, and high histologic grade were significant predictors of pathologically positive nodes in the END group.

**Conclusion:** Our policy of selective observation in patients with cN0 T1-T2 SCCOT is effective. Selected patients with tumors <2 cm, <2 mm depth, and well-differentiated grade are suitable for observation of the cN0 neck.

## **S052: Head and Neck Melanoma in the Sentinel Node Era**

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**Objective:** In the sentinel node (SN) era, do head and neck melanomas (HNM) have a poorer outcome than other melanomas (OMs)?

**Design:** Prospective database 1994-2004. Characteristics, outcome of HNM vs OMs analyzed by Fisher exact test, *t* test, and  $\pm$  test.

**Setting:** Tertiary referral center.

**Patients:** A total of 755 melanoma SN biopsy patients.

**Main Outcome Measure:** Differences between HNM and OMs.

**Results:** There were 17.4% HNMs, 82.6% OMs. There was a male HNM preponderance: 68.7% vs 50.3% ( $P < .01$ ). HNM patients were older:  $57.1 \pm 16.6$  years vs  $53.3 \pm 16.2$  years ( $P < .01$ ). There were fewer cases of superficial spreading melanoma in HNM (29.0% vs 53.7%,  $P < .01$ ). There were more diagnoses in HNM of lentigo maligna (26.0% vs 1.9%,  $P < .01$ ). Mean thickness was  $2.32 \pm 1.9$  vs  $2.31 \pm 2.9$ ,  $P = .49$ . Fewer HNMs had Clark's level less than IV (13.3% vs 24.0%,  $P < .01$ ). More SN were harvested from HNMs ( $3.72 \pm 3.2$  vs  $2.89 \pm 2.6$ ,  $P < .01$ ), but a lower percentage of positive SNs were found (9.2% vs 16.0%,  $P < .05$ ). There was no difference in local, regional, or distant recurrence (5.3%, 6.9%, 5.3% HNMs and 3.4%, 5.5%, 6.7% OMs). The 2/5-year survival for HNM was 95.8%/57.1% vs 94.8%/71.3% (NS).

**Conclusions:** HNM patients are older males with more SNs harvested. They do not appear to have poorer outcome than patients with OMs.

## **S053: Epidemiology and Prognostic Factors of Cutaneous Head and Neck Melanoma: Population-Based Study**

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**Objective:** Study objective was to describe the epidemiology of cutaneous head and neck melanoma (CHNM), and to identify factors associated with mortality from this disease.

**Design:** Population-based cohort study.

**Setting:** Patients treated for CHNM in Ontario, Canada, between 1994 and 2002 were identified through provincial Cancer Registry. A Cox proportional-hazards regression model was used to analyze the data.

**Patients:** A total of 2218 patients with CHNM were identified, comprising 16% of all melanomas in Ontario. The average age of the cohort was 66 (SD, 16) years; 61% ( $n=1363$ ) were males.

**Main Outcome Measure:** Patients' vital status (dead/alive).

**Results:** The incidence of CHNM increased from 2/100 000 in 1996 to 2.7/100 000 in 2001, while mortality remained stable. The proportional hazards model showed that increased age (hazard ratio [HR], 1.06; 95% confidence interval [CI], 1.04-1.06) and male gender (HR, 1.31; 95% CI, 1.03-1.66) had significantly higher risk of death. Patients with lesions of the scalp and neck had 53% higher risk of death than those of the face. Nodular melanoma (HR, 1.61; 95% CI, 1.17-2.24) had the worst prognosis compared with other morphologic types. Increased tumor thickness (HR, 1.05; 95% CI, 1.03-1.07) and Clark level V (HR, 1.52; 95% CI, 1.01-2.22) compared with level I/II were significantly associated with increased mortality.

**Conclusions:** Our study demonstrated an increase in incidence in CHNM. Advanced age, male gender, nodular morphology, tumor thickness, and Clark level V carried significant risk of death, whereas facial melanomas had favorable prognosis.

## **S054: Recurrence and Survival of Patients With Melanoma of the Head And Neck Whose Treatment Included Sentinel Node Biopsy**

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**Introduction:** The prognostic utility of sentinel lymph node (SLN) biopsy for predicting survival outcomes has been demonstrated for patients treated for melanoma of the trunk and extremities. However, there is remaining controversy regarding the benefits of this staging procedure in the management of patients with cutaneous melanoma of the head and neck region (CMHN).

**Objective:** To determine the factors associated with recurrence rate and survival of patients treated at a single institution for CMHN whose management included sentinel nodes biopsy.

**Results:** One hundred-thirteen patients underwent SLN biopsy for head and neck melanoma. The median age was 51 years, distribution of tumors by depth of invasion was 16% T1, 33% T2, 41% T3 and 7% T4 tumors. All lesions <1 mm were Clark levels IV-V, or ulcerated. All but two patients had preoperative lymphoscintigraphy and 83 had blue-dye injections. One hundred nine patients (96%) had successful SLN identification, with a median of 3 sentinel lymph nodes identified per patient. Positive SLNs were identified in 23 patients (21%), and in 20 patients the SLNs were the only positive nodes identified. With a median follow-up of 34 months, 4/86 (4.6%) patients with (-) SLNs had a same basin recurrence, and of the 113 patients, 29% developed recurrent disease, with 6% local, 7% regional and 15% distant recurrences as the first site. Disease free and overall survival rates were 66% and 78% in SLN(-) and 39 and 62% in SLN(+) patients respectively. Factors significantly associated with a decreased 5-year actuarial disease-free survival (DFS) in univariate analysis were female gender, Breslow thickness 2-4 mm compared to less than 2 mm, Clark level IV or more and positive SLN. Five year overall survival (OS) was negatively impacted by age older than 60, Breslow thickness 2-4 mm, Clark level IV or more and a positive SLN. In multivariate analysis only Breslow stage affected 5-year DFS (44% for 2-4 mm vs. 63% for 1-2 mm thickness), while age more than 60 and Breslow stage affected 5-year DFS and OS. Patients older than 60 had a 56% 5-year DFS vs. 85% for patients younger than 60. The OS for Breslow 2-4 mm was 55% and for 1-2 mm was 82%. SLN positivity was not significantly associated with decreased OS and DFS.

**Conclusions:** Primary tumor thickness and age but not SLN status were associated with recurrence and decreased survival in patients treated for CMHN. Further prospective multi-institutional studies will be necessary to address the true value of SLN biopsy for CMM of the head and neck.

## **S055: Utility of Sentinel Lymph Node Biopsy in the Management of Scalp Melanoma**

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**Objectives:** Scalp melanomas (SM) are known to have a poor prognosis compared to cutaneous melanomas at other sites. Sentinel lymph node biopsy (SLNB) is routinely used in melanoma management. The scalp has rich and complex lymphovascular drainage and SLNB is critical to disease staging. The aim of this study was to assess lymphatic drainage patterns, examine the accuracy of SLNB in SM and to assess the best antibody panel for immunohistochemical (IHC) SLN evaluation.

**Methods:** The tumor registry was queried to identify all patients with scalp melanoma who had SLNB between 1996-2006. The SLNs were localized via lymphoscintigraphy, intraoperative Gamma probe and lymphazurin. Serial sections of the SLNs were alternately stained with hematoxylin-eosin and S100 and HMB-45. All SLNs were stained with 3 additional markers (Melan A1, microphthalmia transcription factor and tyrosinase) and the IHC yield was compared. For statistical analysis primary tumor sites were segregated into anterior and posterior scalp, defined by a virtual line through the vertex between the external ear canals. SLNs were also grouped as follows: cervical (levels 1-5) and extra-cervical (suboccipital, retroauricular and parotid).

**Results:** A cohort of 22 patients including, 4 women (18%) and 18 men (82%), age ranging from 11 to 79 years (median 61) was ana-

lyzed. 13 primary lesions were located posteriorly and 9 anteriorly. The first draining SLN of each group mapped in the extracervical region in 77% of posterior and 78% of anterior lesions. Number of SLNs identified per patient ranged from 1 to 5 (median 2). Ten patients had positive SLNs (45%). Of these, 6 underwent completion lymphadenectomy with no additional positive nodes identified. The remaining 4 patients had radiotherapy. The patients with positive SLN (PSLN) and negative SLN (NSLN) were compared in regard to histologic parameters, stage and outcome. No significant difference among the 2 groups (positive SLN vs. Negative SLN) was seen when compared by number of identified SLNs, presence or absence of tumor thickness, ulceration, or histologic regression and outcomes. The median follow-up ranged from 2 to 108 months (mean 28 mo.). No death from disease was recorded. 8 patients from PSLN group (80%) showed no evidence of disease (NED) while 11 patients from NSLN (92%) were NED at last follow-up. One distant metastasis was present in each group and one local recurrence was recorded in the PSLN group. No regional recurrences occurred.

Additional immunohistochemical studies did not detect further metastases.

**Conclusions:** SM is an aggressive tumor demonstrated by the high rate of nodal metastases. SLNB was found to be accurate and useful. We found no definitive histologic, anatomic or clinical predictor for regional metastases. Of the cases with positive SLNs 40% had multiple SLNs identified. Therefore, thorough SLNB sampling is necessary.

This limited experience raises the question whether additional regional treatment is necessary in SM patients with a positive SLN. An IHC panel including 2 standard melanocyte markers seems sufficient.

## **S056: Clinical And Pathological Predictors of Cervical Node Metastases to Level V in Patients with WDTC**

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**Objectives:** Cervical lymphadenectomy is frequently performed in patients with lateral cervical lymph node metastases to improve regional control of disease. However, there is no consensus regarding the appropriate levels of the neck that need to be dissected. Treatment options that have been advocated include the modified radical neck dissection, limited neck dissections and selective nodal excisions. In particular, the routine dissection of level V remains controversial due to the attendant morbidity to the spinal accessory nerve. To identify clinical and pathological predictors of cervical node metastases to level V in differentiated thyroid carcinoma, we reviewed our experience at MD Anderson Cancer Center for the management of metastatic WDTC.

**Methods:** Retrospective analysis of 71 patients who underwent thyroidectomy and neck dissection for WDTC at MD Anderson Cancer Center.

**Results:** In our series, 40 patients had lymph nodes dissected from level V, and 53% harbored metastatic thyroid carcinoma. Additionally, 13 level V contralateral neck dissections were performed, and 54% were found positive for metastases. Ipsilateral level V metastases were significantly associated with primary tumor with extracapsular spread ( $p=0.04$ ), perineural spread ( $p=0.04$ ), and ipsilateral level IV metastases ( $p=0.04$ ). Furthermore, ipsilateral involvement of level V was associated with contralateral lymph node metastases ( $p=0.006$ ). Age, gender, and size of primary tumor were not found to be associated with level V metastases.

**Conclusions:** In our series, cervical metastases from differentiated thyroid carcinoma were commonly present at level V. Patients harboring primary tumors with ECS, perineural spread and metastases in the ipsilateral level IV nodal station had a higher risk of harboring metastatic disease at level V. We believe that a comprehensive neck dissection, including level V, is necessary for locoregional control in patients with lateral cervical metastases from WDTC.

## **S057: Absorption Spectroscopy Potentially Identifies Carcinoma on Fine-Needle Aspiration Biopsy of Thyroid Nodules**

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**Objective:** Thyroid nodules are a common disorder. Although fine-needle aspiration biopsy (FNAB) is highly accurate to papillary thyroid tumor diagnosis, discrimination between benign and malignant follicular neoplasms is currently not possible. In this case, there is a lack of biological marker able to identify malignant transformation. The aim of this pilot study is to verify optical absorption differences on FNAB of thyroid carcinomas and goiters.

**Design:** Diagnostic test development.

**Subjects:** Samples of FNAB of thyroid nodules and corresponding normal surrounding gland, suspended in 2 mL of dimethyl sulfoxide, were surgically collected and frozen.

**Intervention:** The absorption spectra of samples were registered in Cary 17D-OLIS, from 200 nm to 1200 nm with 1-nm resolution. The spectra of each sample of thyroid nodule were normalized by the corresponding normal thyroid, as an internal control, determining the absorbance spectra.

**Results:** We evaluated 36 samples from 9 patients, including 6 adenomatous goiters, 2 carcinomas, and 1 Hashimoto's thyroiditis. All samples from carcinoma showed a lower absorbance among 520 nm and 560 nm, comparing with that of normal corresponding thyroid, contrasting with those curves from goiters or Hashimoto's thyroiditis, which presents many peaks of higher absorbance at this band.

**Conclusions:** Our preliminary results suggest that absorption spectroscopy may be useful to tell apart thyroid carcinomas from goiters or Hashimoto's thyroiditis. A further evaluation deserves to be done on FNAB of follicular thyroid pattern, as well as increase sample numbers.

## **S058: Dual EGFR and VEGFR Inhibition with NVP-AEE788 for the Treatment of Aggressive Follicular Thyroid Cancer**

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**Objective:** Patients with radioiodine-resistant follicular thyroid cancer (FTC) have a poor prognosis, if metastasized, with currently available treatment modalities. Epidermal growth factor (EGF) and vascular endothelial growth factor (VEGF) and their receptors (EGFR and VEGFR) have been reported to be overexpressed in FTC and have been implicated in FTC development. We hypothesized that inhibiting the phosphorylation of EGFR and VEGFR by treatment with NVP-AEE788 (AEE788), a novel dual specific EGFR and VEGFR inhibitor, either alone or in combination with paclitaxel, would inhibit the growth of FTC xenografts in an orthotopic nude mouse model.

**Methods:** To confirm previous reports, EGF and EGFR expression and vascularity were analyzed in human samples of FTC, Hürthle cell carcinoma, and normal thyroid tissues. EGFR expression in four FTC cell lines was measured using Western blotting. The antitumor effect of AEE788 on FTC cells in vitro was evaluated using MTT assays and Western blotting. The effect of AEE788, alone and in combination with paclitaxel, on FTC tumor growth in an orthotopic nude mouse model was also investigated. Immunohistochemical analysis of EGFR and VEGFR signaling status, cell proliferation, apoptosis, and microvessel density was performed.

**Results:** EGF, EGFR, and vascularity were increased in human thyroid tumor samples, and EGFR was increased in FTC cells. AEE788 inhibited FTC cell growth in vitro and reduced the phosphorylation status of EGFR, VEGFR, and two downstream targets, AKT and MAPK, in FTC cells. AEE788 alone and, to a greater extent, AEE788 plus paclitaxel suppressed FTC tumor growth in the thyroids of nude mice.

**Conclusion:** Dual inhibition of EGFR and VEGFR by AEE788 could represent a novel approach to the treatment of radioiodine-resistant FTC.

## **S059: Gene Expression Profile of Complete Clinical Response Following Platin-based Induction Chemotherapy**

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Concurrent chemoradiation is the standard of care for locally advanced laryngopharyngeal squamous carcinoma. As such, the role of induction chemotherapy remains controversial. Yet over the last years, there has been a re-emergence of interest in its use, as sequential therapy prior to chemoradiation. Others have suggested its role prior to conservation surgery. Numerous studies have suggested that complete responders to induction chemotherapy have a favorable outcome, both in terms of local control and overall survival. Yet there is no biomarker predictive of this favorable complete response. We hypothesize that there is a gene-expression profile associated with complete response to platin-based chemotherapy. 30 patients with locally advanced (T3-4) laryngopharyngeal carcinoma squamous cell carcinoma were treated in a prospective organ preservation trial with induction chemotherapy with 5-FU and CDDP. Pre-treatment fresh frozen tumor biopsies were obtained prospectively under an IRB-approved protocol from the Institut Gustave-Roussy (Villejuif, France) between 2000 and 2003. For each patient, total RNA was extracted from cells using the RNeasy Kit (Qiagen, Valencia, CA, USA) according to the manufacturer's protocol. Quality control was performed using the Agilent BioAnalyzer 2100 and spectrophotometry to determine concentration. Double-stranded cDNA was made mRNA. This cDNA was used to synthesize complementary RNA (cRNA). The cRNA was labeled and used for hybridization with the GeneChip U133Plus 2.0 Array, which contains 54,675 probe sets representing more than 46,000 transcripts derived from the entire human genome. Expression data from these arrays were then analyzed using DNA-Chip Analyzer software (dChip). Quantile normalization was then performed across all 30 samples, using only the PM signals with specified probe sequences. The perfect match (PM only model) was employed to calculate the expression values. To identify the differentially expressed genes using dChip, we set 100 as the average signal-intensity difference to avoid the effects of unreliable low intensity, and used the lower conB01 dence bound of fold change (LBFC; 90%) as the conservative relative change. Genes were filtered on the following three criteria. (1) Gene expression level must be greater than 20 in more than 50% of the samples. (2) Variation across samples:  $0.50 < \text{Standard deviation} / \text{Mean} < 1000.00$  (3) The % presence call must be at least 20%. After filtration, these 4,528 differentially expressed genes were then subjected to unsupervised clustering analysis. Using the R software environment, the BioConductor package, PerfectMatch intensity images were dissected using Positional Dependent Nearest Neighbor model. Twenty-five genes were identified to distinguish between those patients with complete clinical response and those with stable and/or progressive disease, with a fold change of greater than 1.2,  $p < 0.001$ . False discovery rate was calculated with 200 permutations.

**Conclusion:** We present a discovery set of 25 genes identified from a oligonucleotide microarray experiment using patient samples to predict response to platin-based chemotherapy. Future validation of this discovery set should be performed using separate patient samples from an independent data set in a prospective clinical trial to distinguish complete clinical response from no response to induction chemotherapy.

## **S060: Serum Protein Profile Analysis in Patients With Papillary Thyroid Carcinoma**

**W.H. Moretz, III**; C.G. Gourin; D.J. Terris; Z. Xia; Z. Liu; P.M. Weinberger; B. Adam

Medical College of Georgia, Augusta

**Objective:** To determine the sensitivity and specificity of surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS) for papillary thyroid cancer (PTC) detection.

**Design:** SELDI-TOF-MS protein profiles of patients with PTC, benign nodular disease (BND), and healthy controls were analyzed to determine the sensitivity and specificity of SELDI assay for PTC detection. Data analysis was performed using Ciphergen Biomarker Wizards and Biomarker Pattern Software to process the spectral data and classify the disease status of the patients.

**Subjects:** Serum samples were collected prospectively from 7 PTC patients, 8 BND patients, and 7 healthy control volunteers.

**Intervention:** All sample patients underwent thyroidectomy from October 2004 to January 2006.

**Results:** The majority of protein peaks resolved by the SELDI assay were in the range of 1 to 20 kDa. Classification tree analysis based on peak expression distinguished patients with PTC from BND with 85.7% sensitivity and 100%

specificity. Serum samples from PTC patients differed most significantly from BND by the underexpression of a protein peak at 11 101 Da.

**Conclusions:** This pilot study demonstrates that proteomic analysis of serum protein profiles distinguishes patients with PTC from patients with BND with a high degree of sensitivity and specificity. Further investigation into the clinical utility of this technology in PTC biomarker detection and surveillance is warranted.

## **S061: Comparative Genomic Instabilities of Thyroid and Colon Cancers**

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**Objectives:** Genomic instability facilitates tumor progression, resulting in tumor heterogeneity and the evolution of aggressive and metastatic subpopulations within the tumor. Measurements of genomic instability, by different methodologies, reveal that multiple independent forms of genomic instability can exist within a single tumor. The objectives of this study were to assess the forms and extent of genomic instability in thyroid cancers and colorectal neoplasms, and to determine if such measurements could explain the generally excellent prognosis of thyroid malignancies as compared to colon carcinoma.

**Methods:** Inter-simple sequence repeat polymerase chain reaction (ISSR-PCR) and Fractional Allelic Loss analysis (FAL) were utilized to quantify intrachromosomal genomic instability. ISSR-PCR tends to detect relatively small genomic alterations while larger events are revealed by FAL analysis. Chromosomal gains and losses were assessed by array-based Comparative Genomic Hybridization (aCGH), and Spectral Karyotyping (SKY) was used to visualize copy number and balanced alterations at the whole chromosome level.

**Results:** Genomic instability index (GII) of 32 thyroid carcinomas, 59 colon carcinomas and 11 colon polyps was determined by ISSR-PCR; no significant difference among the three groups was observed for instabilities detected by this method. Fractional Allelic Loss rates were comparable in thyroid cancers and colon polyps and significantly lower than FAL rates in colorectal cancers. Indolent papillary thyroid carcinomas were essentially diploid with no large-scale alterations in either chromosome number or structure when evaluated by aCGH or SKY. aCGH revealed striking chromosome alterations in the more aggressive anaplastic thyroid cancers. Colorectal carcinomas showed dramatic copy number changes and chromosomal rearrangements when analyzed by both aCGH and SKY.

**Conclusions:** Genomic alterations in papillary thyroid carcinoma, like benign colon polyps, are principally of the smaller event form detected by ISSR-PCR. With the evolution to more aggressive tumor types (i.e. anaplastic thyroid and colorectal carcinomas), larger events detected by FAL analysis, aCGH, and SKY, appear within tumor genomes. We hypothesize that mutations caused by smaller genomic alterations enable thyroid cells to achieve a malignant phenotype, but allow only minimal biological aggressiveness. Mutations for more aggressive tumor behavior remain unmanifested until larger genomic events generate more global disruptions.

## **S062: Nuclear, Cytoplasmic Expression of Galectin-3 is Associated With B-Catenin/Wnt-Pathway Activation in Thyroid Carcinoma**

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**Objectives:** Cytoplasmic galectin-3 is overexpressed in papillary thyroid carcinoma (PTC) and may activate the  $\beta$ -catenin/Wnt pathway, resulting in altered cyclin-D1 levels. Nuclear galectin-3 has not been well studied in PTC. We sought to characterize the localization of

galectin-3 in benign and malignant thyroid neoplasms and correlate this with alterations in  $\beta$ -catenin and cyclin-D1 expression.

**Study Design:** Immunohistochemical study of 116 paraffin-embedded archival specimens using tissue-microarray technique.

**Methods:** Thyroid tissue microarrays of 61 carcinomas (35 papillary, 13 follicular, 11 medullary, and 2 anaplastic), 48 adenomas, and 7 normal thyroids were stained by standard immunohistochemistry with monoclonal antibodies against galectin-3,  $\beta$ -catenin, and cyclin-D1. Nuclear and cytoplasmic expression of galectin-3 was correlated with clinical parameters,  $\beta$ -catenin, and cyclin-D1 expression.

**Results:** Both cytoplasmic (56%) and nuclear (42%) galectin-3 expression was observed in most malignant neoplasms but absent in benign thyroid specimens ( $P < .001$ ). Among carcinomas, cytoplasmic galectin-3 expression was observed in PTC (82%), follicular (33%), and medullary (9%), but absent in anaplastic carcinomas ( $P < .001$ ).

Galectin-3 nuclear expression was observed in PTC (62%) and follicular (33%) carcinomas, but undetectable in medullary, anaplastic carcinomas ( $P < .001$ ). Cytoplasmic but not nuclear galectin-3 was inversely correlated with TNM stage ( $P = .02$ ). There was a strong correlation between cytoplasmic/nuclear  $\beta$ -catenin expression and both nuclear ( $P = .04$ ) and cytoplasmic ( $P = .003$ ) galectin-3 expression. Similarly, there was a strong association between galectin-3 nuclear ( $P < .001$ ) and cytoplasmic ( $P < .001$ ) expression and cyclin-D1 expression.

**Conclusion:** Cytoplasmic and nuclear galectin-3 expression appears to be associated with activation of the Wnt-signaling pathway in well-differentiated thyroid neoplasms.

### S063: Incidence of B Type RAF kinase (BRAF), in Papillary and Follicular Subtype Papillary Thyroid Carcinoma

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**Introduction:** Several genetic rearrangements occur in thyroid cancer. Mutation of the B type RAF kinase (BRAF), represents the most common genetic alteration in thyroid cancer. Yet, very few investigations have examined the relative incidence of BRAF mutations in subtypes of papillary thyroid carcinoma.

#### Material and Methods:

A retrospective chart review of cases of garden-variety papillary and follicular-variant of papillary thyroid cancer was performed from the patient database at the Huntsman Cancer Institute of the University of Utah between the years of 1994 to 2004. Relevant clinical data was recorded to correlate with BRAF mutation status. Pathologic tissue from a small subset of both papillary and follicular-variants of papillary thyroid carcinoma was assessed for the BRAF mutational status using PCR and fluorescence melting curve analysis.

**Results:** Our 168 cases had a mean duration of follow-up of 24.6 months (range 1 to 75 months). One hundred twenty-three (73%) were female [mean age of 41.3, range: 11 to 77], while 45 (27%) were males [mean age of entire group was 50.6, range: 22 to 88]. At the time of diagnosis 44% were <45 years of age, while 55.6% were >45. No significant differences were found in the incidence of papillary carcinoma subtypes between males and females or subjects <45 years or >45 years of age. A significantly higher incidence of mutant BRAF was found in patients <45 years than >45 years [64.3% vs. 18.2% respectively,  $p = 0.01$ ]. One-hundred two patients (75%) were free of regional metastasis, whereas 34 (25%) presented with regional spread of disease. The presence of regional metastasis did not correlate with pathologic diagnosis of garden-variety or follicular-variant of papillary thyroid carcinoma or the presence or absence of BRAF mutation. Significantly higher percentage of patients >45 presented with advanced metastatic disease when compared to patients <45 years of age ( $p < 0.001$ ). Patients diagnosed with follicular-variant of papillary carcinoma had a significantly higher likelihood of being alive at final follow-up when compared to garden-variety papillary thyroid carcinoma ( $p < 0.001$ ). BRAF mutation was found to be significantly higher in papillary carcinomas when compared to follicular-variant of papillary thyroid carcinomas (55.6% vs. 14.3%,  $p = 0.05$ ).

**Conclusions:** Our study has found that the follicular-variant of papillary thyroid carcinoma demonstrated a significantly higher likelihood of being alive after the diagnosis of papillary thyroid cancer.

Moreover, a significant higher incidence of BRAF mutations was found in younger patients diagnosed with garden-variety papillary when compared to older patients and patients diagnosed with follicular-variant of papillary thyroid carcinomas. The presence of BRAF mutations may contribute to the relative impact each diagnosis has on survival. Further investigations into the biological consequences of BRAF mutations in well-differentiated thyroid carcinomas are warranted with the hope of discovering more targeted therapies for papillary thyroid carcinomas and its subtypes.

### S064: Gene Expression Profiles in HPV Infected Head and Neck Cancer

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**Objectives:** Overall 5-year survival rates for head and neck squamous cell carcinoma (HNSCC) are 50%, but there remains substantial variability in response to treatment and long-term prognosis that cannot be predicted on the basis of standard histopathology. Epidemiological and laboratory evidence now warrant the conclusion that, in addition to tobacco and alcohol, human papillomaviruses (HPV) play an etiologic and prognostic role in some HNSCC. To characterize the molecular profiles of HPV-positive head and neck cancer, we compared differences in gene expression patterns between HPV-negative and -positive HNSCC tumors using a 27,323 cDNA microarrays. **Methods:** Tumor samples were collected from histological confirmed HNSCC patients undergoing treatment for HNSCC at Montefiore Medical Center in the Bronx, a high-risk area of New York City, with a high incidence of HNSCC. HPV detection and genotyping was performed by PCR using the MY09/11 primer protocol. Total RNA was extracted and purified from frozen tumor samples and gene expression levels were assessed using a cDNA microarray chip compared to a universal human reference library of RNA. To identify genes that are differentially expressed between HPV+ and HPV- tumors, supervised clustering of tumor samples based on gene expression profiles was performed. Genes with similar expression profiles between HPV+ and HPV- tumors were identified and clustered using average linkage clustering, and the results visualized with TreeView.

**Results:** Collection and HPV testing of tumor samples from HNSCC patients has been completed for 49 patients. HPV analysis and typing by PCR using MY09/11 primers revealed an overall HPV prevalence of 29% (14/49) in the HNSCC tumors. Assessing HPV positivity by genotype, the majority of HPV+ tumors were found to harbor HPV16+ (93%). HPV prevalence was highest in pharyngeal tumors (41%), with the majority of HPV+ pharyngeal tumors originating from the oropharynx, including the base of tongue, soft palate, oropharynx, and palatine tonsil. Total RNA and gene expression analysis using microarray was available for 30 of the 49 tumor samples. Among cDNA clones assessed on the microarray chips, 165 were found to be differentially expressed with a median false discovery rate of <3%. Of these, 149 had higher average expression levels in the HPV+ tumors, whereas 16 clones were on average expressed at lower levels in the HPV+ tumors.

**Conclusions:** The molecular profile of HPV-positive HNSCC reveal a subset of distinct genes that appear to be differentially expressed from that of HPV-negative HNSCC. Some of the genes over-expressed in the HPV+ HNSCC tumors, such as carcinoembryonic antigen-related cell adhesion molecule 3 and ribosomal protein S6 kinase, have also been found to be over-expressed in cervical SCC. Analyses to identify gene expression signatures that correlate with HPV infection and survival in additional HNSCC patient tumors are ongoing.

### S065: Serum Protein Profile Analysis Following Definitive Treatment in Patients With Head and Neck Squamous Cell Carcinoma

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**Objective:** To determine the sensitivity and specificity of surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS) assay for head and neck squamous cell carcinoma (HNSCC) disease surveillance.

**Design:** SELDI-TOF-MS serum protein profiles of patients with HNSCC were analyzed to determine the sensitivity and specificity of the SELDI assay for HNSCC detection.

**Subjects:** Thirty-two patients with previously untreated HNSCC.

**Intervention:** Serum samples were collected prospectively at 3-month intervals following treatment over a 24-month follow-up period. A total of 93 serum samples were analyzed.

**Results:** SELDI-TOF-MS identified protein peaks in the range of 0 to 100 kDa. Classification tree analysis based on peak expression distinguished pretreatment from posttreatment samples with 87.5% sensitivity and 75.0% specificity. Samples collected at 3 months following treatment did not significantly differ from pretreatment samples or by disease status following treatment. Serum samples from patients who were disease free at 6 months or more following treatment differed from matched pretreatment samples by the overexpression of a protein peak at 6495 Da, while serum samples from patients with recurrence differed from matched pretreatment samples by the overexpression of a protein peak at 2439 Da.

**Conclusions:** Proteomic analysis of serum protein profiles distinguishes pretreatment and posttreatment samples from patients with HNSCC with a high degree of sensitivity and specificity. After 6 months, serum protein profiles appear to have distinct differences in peak expression based on disease status. Further investigation of the clinical utility of this technology in HNSCC detection and surveillance is warranted.

## **S066: Amplification and Overexpression of HER-2/neu Gene and Protein in Salivary Duct Carcinomas**

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**Background:** Salivary duct carcinoma (SDC) is an uncommon neoplasm, typically found in the parotid gland of elderly men. It is an aggressive neoplasm, with more than 60% of patients dying of their tumor within 5 years of diagnosis. Pathologically SDC resembles ductal in situ and invasive carcinoma of the breast; by immunohistochemistry, tumor cells regularly express androgen receptors, while estrogen and progesterone receptors are more variable. Recently, SDC has been found to express HER-2/neu protein in the majority of cases, raising the possibility that this neoplasm might respond to treatment with an anti-HER-2/neu monoclonal antibody (Herceptin).

**Patients and Methods:** We studied 13 cases of SDC, all arising in the parotid gland from elderly patients (10 males; 3 females; mean age: 66 years); 11/13 cases presented in an advanced stage (IV). Twelve patients were treated with surgery and radiotherapy. Seven patients died of causes directly related to the tumor (mean survival: 33 months), 3 patients were alive with disease and three were free of disease (mean follow-up: 39.7 months). On paraffin sections representative of the original tumors, the HER-2/neu protein expression and HER-2/neu gene amplification were evaluated using immunohistochemistry (IHC)(Hercept-test, Dakocytomation, Denmark) and fluorescence-in situ hybridization (FISH)(PathVysion Her2 DNA probe kit, Vysis, USA), respectively. Evaluation of positivity and grading were performed according to the manufacturers' indications.

**Results:** By immunohistochemistry, 10 cases showed overexpression (grade 3+) of HER-2/neu protein, while 3 cases were negative (grade 0/1+). On FISH analysis, amplification of HER-2/neu gene was found in 8 of the 10 grade 3+ cases, while all negative cases on IHC were also non-amplified. No correlations were found between HER-2/neu protein expression, gene amplification or survival.

**Conclusions:** This study demonstrates that HER-2/neu protein is frequently overexpressed in SDC and, in contrast to previous reports, it is associated with gene amplification in the majority cases. Treatment with Herceptin should be seriously considered as an adjuvant treatment in this aggressive neoplasm.

## **S067: Successive Aberrations in Protein Expression From Healthy Mucosa to Invasive Head and Neck Cancer**

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**Objective:** To further define the development of head and neck squamous cell carcinoma (HNSCC) by the process of field cancerization.

**Design:** Analysis of protein lysates by surface-enhanced laser-desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS) and identification of candidate biomarkers by MS. Validation of differential protein

expression by immunohistochemistry (IHC) on tissue microarrays.

**Subjects:** Biopsies of 113 HNSCC patients, and 73 healthy, 99 tumor-distant, and 18 tumor-adjacent squamous mucosae were studied.

**Results:** Among 48 protein peaks differentially expressed between healthy mucosa and HNSCC, several S100 proteins, the cysteine protease inhibitors cystatin A and B, acyl-CoA-binding protein, stratifin (14-3-3 sigma), a C-terminal fragment of beta-hemoglobin and the alpha-defensins 1-3 were identified. cDNA microarray analysis corroborated these data. Differential expression of some of these proteins already occurred in tumor-distant mucosa; others showed altered expression only in tumors. Supervised prediction analysis revealed excellent classification of healthy mucosa and tumor samples, and detected successive changes in tumor-distant and tumor-adjacent mucosa samples. Most of these biomarkers revealed very high diagnostic value (receiver operated characteristics and principal component analysis), but only stratifin was of possible prognostic significance in this patient cohort (Cox proportional regression analysis).

**Conclusions:** These data support the existence of genetically altered fields with inconspicuous histology. We conclude that proteomic profiling in conjunction with protein identification and biomarker validation greatly outperforms histopathological diagnosis and may have significant predictive power for clinical outcome and personalized risk assessment.

## **S068: High-Resolution Copy Number and Gene Expression Microarray Analyses of Two Sites for Head and Neck Squamous Cell Cancer**

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Molecular mechanisms contributing to initiation and progression of head and neck squamous cell carcinoma (HNSCC) are still poorly known. Numerous genetic alterations have been described, but molecular consequences of such alterations in most cases remain unclear. In this study, we integrated genome-wide data to achieve more accurate information about the target genes that are activated or inactivated by amplification or deletion because they could offer potential therapeutic targets in HNSCC. Here, we first performed an integrated high-resolution microarray analyses of gene copy number and expression in 20 laryngeal squamous cell carcinoma (LSCC) cell lines (UT-SCC) and primary tumors. Agilent's oligo and cDNA microarrays containing 17,000 and 12,000 genes served as a platform for these analyses. We utilized custom-developed bioinformatics tools to analyze and integrate our data. Our results show that high-level amplifications had a clear impact on gene expression in LSCC. Across the genome, overexpression of hundreds of genes could be attributed to gene amplification events including FADD and PPF1A1 at 11q13. The analysis of gene ontology and pathway distributions fur-

ther pinpointed genes that may identify potential targets of therapeutic intervention (manuscript submitted). After obtaining and analyzing microarray data from LSCC, we have collected a material from oral tongue squamous cell carcinoma (OTSCC). Similarly to that in LSCC, we have now profiled 20 OTSCC cell lines (UT-SCC and ATCC) on Agilent cDNA and oligo microarrays. We are comparing these two data sets obtained from two different HNSCC locations. Our aim is to investigate if same targets contribute to the oncogenesis of these two groups and if similar patterns of molecular profiles can be identified in LSCC and OTSCC. To identify potential HNSCC target genes, we are applying an integrated system level approach to combine different statistical tools and databases to analyze genome-wide gene copy number and expression data. With this approach, we aim to achieve new information about genetic alterations significant for tumor initiation and development in HNSCC.

## **S069: Saliva Array-Based Gene Expression Changes in Oral Squamous Cell Carcinoma: Presurgery and Postsurgery**

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**Objective:** Using a salivary transcriptome approach, we have already identified 7 potential human RNA biomarkers in oral cavity/oropharyngeal squamous cell carcinoma (OSCC). The objectives were to investigate whether these 7 or other gene(s) change their expression levels after surgery.

**Design:** RNA isolation and linear amplification from saliva followed by expression microarray analysis and quantitative polymerase chain reaction (qPCR) validation.

**Subjects:** Patients with stage I or II OSCC. Age- and sex-matched disease-free control patients.

**Interventions:** Collection of saliva from patients with OSCC before and 2 weeks after surgery (n = 10) and from control subjects (n = 10). Linear amplification of salivary RNA followed by expression microarray analysis. qPCR validation of genes with significant microarray expression difference ( $P < .05$ ) followed by comparison to control subjects.

**Results:** Transcripts of IL8, IL1B, DUSP1, HA3, OAZ1, S100P, and SAT remained elevated 2 weeks after surgery ( $P > .05$ ). Cytokeratin 14 (CK14) exhibited the greatest diminution in array expression pattern 2 weeks after surgery for OSCC and confirmed with qPCR. Using *t* test comparisons, postoperative CK14 gene expression was lower than before surgery ( $P < .05$ ) and no different vs control subjects. ( $P > .05$ ).

**Conclusions:** While IL8, IL1B, DUSP1, HA3, OAZ1, S100P, and SAT hold promise for detecting OSCC in saliva, salivary CK 14 mRNA can serve as a detection marker as well as a prognostic marker for therapeutic response to surgery in OSCC. Creating a saliva-based panel of these biomarkers could be used to diagnose and follow patients with OSCC.

## **S070: Phase II Study of Combretastatin A4 Phosphate (CA4P) in Patients With Advanced Anaplastic Thyroid Carcinoma (ATC)**

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**Background:** Combretastatin A4 phosphate (CA4P) is the first tubulin-binding vascular-disrupting agent tested in the clinic. Phase I studies demonstrated activity in anaplastic thyroid carcinoma (ATC).

**Methods:** Patients with metastatic ATC, good performance status, normal electrocardiographic and cardiac function, and no prior therapy for disseminated disease were eligible for study. CA4P at a dose of 45 mg/m<sup>2</sup> was administered as a 10-minute intravenous infusion on days 1, 8, and 15 every 28 days (1 cycle).

**Results:** A total of 18 patients (pts) (11M/7F), median age 62 years (range, 40-71 years), received a total of 55.67 cycles of treatment. Therapy was well tolerated, with mild to moderate nausea, vomiting, headache, and tumor pain (3 pts with grade 3), all of which essentially resolved within the first 24 hours. No objective responses were

seen; 6 pts with stable disease and 12 pts progressed. Median progression-free survival was 7.4 weeks (range, 2-84+ weeks); with 28% of pts progression free >3.0 months (12.0+, 14.3, 15.3, 25.6, and 84.0+ weeks). Fourteen pts have died; 4 are alive; and 2 are alive and on-study at 12.0+ and 84.0+ weeks. Median survival is approximately 20 weeks.

**Conclusions:** A quarter of patients treated with single-agent CA4P experience greater than 3 months of freedom from progression. Combined modality strategies with CA4P and either chemotherapy and other targeted agents or with radiation therapy are warranted. Supported in part by a clinical grant from OXiGENE, Inc, Waltham, Mass, and NIH grant M01 RR-00080.

## **S071: Is There a Role for FDG-PET/CT in Cytologically Indeterminate Thyroid Nodules?**

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**Objective:** To determine the accuracy of the 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) scan in the evaluation of thyroid nodules in which fine-needle aspiration (FNA) cytopathology is classified as "indeterminate," ie, either follicular or Hürthle cell lesion.

**Methods:** At an academic medical center, we conducted a prospective, pilot study of 15 patients with thyroid nodules in whom adequate FNA was diagnosed as "indeterminate." All patients underwent a whole-body FDG-PET/CT scan followed by thyroidectomy. Preoperative FDG-PET/CT results and the histopathology of the surgical specimen were compared and statistically analyzed.

**Results:** FNA demonstrated follicular cells in 11 patients (73%), Hürthle cells in 2 patients (13%), and both cell types in 2 patients (13%). Histopathology of the surgical specimen revealed thyroid cancer in 7 patients (47%). The FDG-PET/CT scan was positive in 7 patients; 4 (57%) were found to have cancer. The FDG-PET/CT scan was negative in 8 patients. Five of these patients had benign lesions and 3 had thyroid carcinoma. Thus, 3 patients (20%) had false-positive FDG-PET/CT scans, and 3 patients (20%) had false-negative studies. The sensitivity of FDG-

PET/CT to detect a malignant focus was 57% with a specificity of 63%. The positive and negative predictive values were 57% and 63%, respectively.

**Conclusions:** In this pilot study of patients with cytologically indeterminate thyroid nodules, FDG-PET/CT was not a predictable indicator of benign or malignant disease. While a larger series may elucidate a role for FDG-PET/CT, the relatively low predictability shown in this study should caution clinicians about utilizing FDG-PET/CT to consider forgoing thyroidectomy for cytologically indeterminate nodules.

## **S072: Preoperative FDG-PET Imaging to Assess the Malignant Potential of Follicular Neoplasms of the Thyroid**

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**Objective:** Fine-needle aspiration of a thyroid nodule may result in a diagnosis of a follicular neoplasm. Establishing a definitive diagnosis would allow the patient to undergo the appropriate initial thyroidectomy. This study evaluated the ability of positron emission tomography (PET) to assess the malignant potential of a follicular neoplasm.

**Method:** Prospective cases series.

**Setting:** Tertiary care academic center.

**Patients:** Twenty-one patients with a diagnosis of a follicular neoplasm.

**Interventions:** Patients underwent presurgical PET at 60, 90, and 120 minutes after injection of fluorodeoxyglucose F18 (FDG). Standard uptake value (SUV) was obtained at each time interval. Thyroidectomy was performed with comparison of the histopathology to the PET results.

**Main Outcome Measure:** PET can predict the malignancy in a follicular neoplasm.

**Results:** Five malignancies were identified (4 follicular thyroid cancers and 1 papillary thyroid cancer). The remaining cases were 10 follicular adenomas and 6 nonneoplastic disease. The SUV for the follicular neoplasms ranged from 0.9 to 44.8 (2.9-44.8 in the malignant cases

and 0.9-7.7 in the nonmalignant cases). The follicular thyroid cancers that exhibited only capsular invasion had an average SUV of 3.1, while those that exhibited vascular invasion had an average SUV of 39.9. The SUV increased from the 60-minute value in 80% of the malignant cases, while in only 44% of the nonmalignant cases.

**Conclusions:** Despite certain imaging patterns being suggestive of malignancy in follicular neoplasm, FDG-PET is not able to differentiate benign from malignant disease in many cases. Use of different radiotracers or combining PET with other tissue processing may allow more accurate diagnosis for follicular neoplasms.

## **S073: Incidence of Vocal Cord Paralysis With and Without Recurrent Laryngeal Nerve Monitoring During Thyroidectomy**

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In recent years, recurrent laryngeal nerve monitoring has been used with increasing frequency during thyroidectomy. Whether or not its use truly reduces the risk of recurrent laryngeal nerve (RLN) injury has yet to be proven. Very few studies with large sample size have compared the rate of postop RLN paralysis with and without RLN monitoring. One of the limitations of these previous studies is that data were compiled from the results of multiple surgeons. Variations in surgical technique of different surgeons could potentially affect the statistics. The purpose of this retrospective study was to compare the incidence of postop vocal cord (VC) paresis/paralysis with and without RLN monitoring in a large series of patients undergoing thyroidectomy by a single senior surgeon.

**Methods:** The medical records of 684 cases of thyroidectomy by the senior author (M.S.) in a single teaching institution were reviewed. A total of 1043 nerves were at risk, 671 in the monitored group and 372 in the non-monitored group. Continuous nerve monitoring was performed using the Xomed endotracheal tube with two channel electrodes connected to a nerve integrity monitor. All patients had pre- and postoperative laryngeal examination. Patients with postop VC paralysis/paresis resulting from intentional nerve sacrifice or dissection of a mass that was encasing or severely adherent to the RLN were excluded. The incidence of unexpected vocal cord paresis and complete paralysis was calculated based on nerves at risk.

**Results:** No patients experienced bilateral VC paralysis postop. The incidence of unexpected unilateral VC paresis was 2.1% (14 nerves) in the monitored group and 3.5% (11 nerves) in the non-monitored group. Ten patients with paresis were lost to long-term follow-up; the paresis resolved in all of the remaining ones. The incidence of unexpected complete unilateral VC paralysis was 1.6% in each group. Two of the 6 paralysis in the non-monitored group and 6 of the 11 paralysis in the monitored group had complete resolution. In those patients with long-term follow-up data, 4 patients had permanent paralysis (3 in the non-monitored group and 1 monitored group); thus the incidence of permanent paralysis was 0.2% in the monitored group and 0.1% in the non-monitored groups. In 3 of the patients with permanent paralysis, the injury was due to inadvertent transection.

**Conclusion:** RLN monitoring does not appear to reduce the incidence of complete nerve paralysis or prevent nerve transection. It may reduce the risk of temporary paresis resulting from neuropraxia. The details of the results, as well as utility and pitfalls of RLN monitoring will be discussed.

## **S074: Risk Factors for Well-Differentiated Thyroid Carcinoma in Patients With Thyroid Nodular Disease**

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**Objective:** To evaluate well-accepted risk factors in determining treatment approach in patients presenting with thyroid nodular disease.

**Study Design:** Retrospective analysis for the primary management of thyroid nodular disease.

**Setting:** Outpatient head and neck clinic in an academic institution (University of Toronto, Mt Sinai Hospital, Toronto, Ontario).

**Patients or Other Participants:** Individuals presenting with a thyroid nodular disease between 1990 and 2000. Three hundred patients

with benign thyroid nodular disease and a comparison group of 300 patients with well-differentiated thyroid cancer (WDTC) were randomly selected.

**Main Outcome Measures:** Patient, clinical, and investigational data were compared using univariate regression analysis. Multivariate regression analysis and individual sensitivity and specificity for factors significant on multivariate regression were determined.

**Results:** Regional lymphadenopathy (>1 cm in levels II-V), ipsilateral vocal cord palsy, solid nodule and/or calcification on ultrasound (US), and a fine-needle aspiration biopsy (FNAB) being malignant or suspicious all predicted for WDTC on univariate analysis (all  $P < .05$ ). Regional lymphadenopathy, solid and/or calcified nodules on US, and FNAB being malignant or suspicious were independent predictors for WDTC on multivariate regression (all  $P < .05$ ). A solid nodule on US was most sensitive (84%), while regional lymphadenopathy, calcifications, and

FNAB (malignant or suspicious) were highly specific for a diagnosis of WDTC (all >90%).

**Conclusions:** The recognition and evaluation of the importance of certain risk factors, as demonstrated by our study, are vital in choosing the most appropriate management approach in patients with thyroid nodular disease.

## **S075: Aggressive Detection and Resection of Recurrent or Persistent I-131-Resistant Papillary Thyroid Cancer**

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Ohio State University, Columbus

**Objective:** To determine the optimal detection and management of recurrent/persistent radioactive iodine-resistant papillary thyroid cancer (PTC) in the neck without distant metastases.

**Design:** Retrospective clinical study with institutional review board approval. Median follow-up was 31 months.

**Setting:** University based tertiary cancer hospital.

**Patients:** Between 1999 and 2005, 97 consecutive patients with recurrent/persistent PTC in the neck underwent exploration. Stimulated thyroglobulin (Tg) levels and high-resolution ultrasound were used to identify recurrent disease. All patients had previously undergone thyroidectomy (with or without lymph node dissection) and received radioactive iodine. Twenty-five patients with anti-thyroglobulin antibodies were excluded.

**Main Outcome Measures:** Undetectable stimulated Tg was considered as biochemical cure.

**Results:** Ninety-seven lymphadenectomies were undertaken in 72 patients. Median lymph node harvest was 9. Lymphadenectomy failed to identify PTC in 5 patients (7%). Biochemical cure was initially achieved in 13 patients (18%). Of the 54 patients with detectable postoperative Tg, 21 went on to reexploration, with biochemical cure being achieved in 4. In total, biochemical cure was achieved in 17 patients (24%). Patients in whom cure was not achieved after the first operation had significant reduction in Tg levels ( $P < .001$ ). Of variables analyzed, only undetectable preoperative unstimulated Tg was predictive of biochemical cure (odds ratio, 3.9; 95% confidence interval, 1.09-14.28;  $P = .04$ ). Hypocalcemia occurred in 2 patients (3%), while no patients suffered recurrent laryngeal nerve injury.

**Conclusions:** Aggressive resection of detectable recurrent I-131-resistant PTC in the neck is feasible and safe. Biochemical cure is possible in almost one quarter of otherwise incurable patients. In those not cured, Tg levels were significantly reduced.

## **S076: Epigenetics of Head and Neck Cancer: The Role of Pyrosequencing**

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**Introduction:** Promoter methylation of tumor suppressor genes has been investigated by a variety of means, recently including pyrosequencing.

**Method:** Fresh tumor tissue and normal tissue from resection margin were obtained from 79 patients undergoing resection for squamous

cell carcinoma. DNA was extracted and bisulphite treated. Polymerase chain reaction primers were designed to amplify 75- to 200-base pair regions of the CpG-rich gene promoters of p16, RAR-beta, E-Cad, CYGB, Cyclin A1, MGMT, ATM, hMLH1, STAT1, and TIMP3. Methylation status of 5-22 individual CpG sites per gene was determined by pyrosequencing. Reverse transcriptase-PCR was used to correlate these data with mRNA expression.

**Results:** Significant CpG methylation of gene promoters within tumor specimens was found in most genes studied; however, despite previous reports, there was no evidence in the mismatch repair genes ATM, STAT1, or hMLH1. Promoter methylation was in evidence in highly tumor-specific pattern for most genes; however, the quantitative nature of these data revealed that for RAR-beta and E-cadherin, the pattern was not tumor specific. Concordant methylation was demonstrated in this tumor series ( $P = .03$ ), but it was difficult to identify a true methylator phenotype (CIMP). Cyclin A1 promoter methylation showed an inverse trend with histological grade. Promoter methylation of CYGB is common in head and neck SCC.

**Conclusions:** Promoter methylation analysis using pyrosequencing reveals valuable quantitative data from several CpG sites. In contrast to qualitative data generated from methylation-specific PCR, our data clarify which genes are

methylated in a tumor-specific pattern. Cytoglobin is a novel candidate tumor suppressor gene highly methylated in upper aerodigestive tract squamous cancer.

### S077: An Epigenetically Derived Monoclonal Origin for Recurrent Laryngeal Papillomas

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**Objective:** Clonality, the property that the cells within a tumor are derived from a single parent cell, is often indicated by uniformity or relative uniformity of genetic aberrations contained within many or all cells of the tumor. The aberrations are assumed to confer or reflect biological distinctions relevant to tumor behavior, and thus to be relevant to tumor initiation and clonal expansion. We investigated the contribution of promoter methylation-mediated epigenetic events in recurrent laryngeal papilloma (RLP) tumorigenesis.

**Design:** Archival tissue DNA, extracted from microdissected papilloma lesions, was interrogated for methylation status using the novel multigene methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) assay.

**Subjects:** The cohort comprised 15 subjects, 3 females and 12 males, all adult onset, ranging in age from 23 to 73 years, except for 1 female juvenile onset (1-year-old) with a diagnosis of RLP.

**Results:** Promoter hypermethylation was recorded in 14 of 15 cases, and 21 of 22 methylation-prone cancer genes in the multigene panel had altered DNA methylation in at least 1 recurrent laryngeal papilloma biopsy. Identical abnormally methylated genes were found in 6 of 15 recurrent cases, of which the CDKN2B gene was common in 5 of 6 cases. Dissimilar epigenetic events were noted in the remaining 8 cases.

**Conclusions:** A clonal origin was derived for 6 of 15 RLP biopsies based on identical epigenetic events. The high frequency of epigenetic events, characterized by consistent promoter hypemethylation of multiple tumor suppressor genes, points to the utilization of gene-silencing mechanisms as a driving force behind the growth of RLP. Support: R01 NIH DE 15990.

### S078: Promoter Methylation Status of Tumor Suppressor and Cell Adhesion Genes in Oral Squamous Cell Carcinomas

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**Objective:** We sought to determine if promoter methylation in tumor suppressor and cell adhesion genes can be correlated with tumor stage, nodal metastasis status, or human papillomavirus (HPV) infection of oral squamous cell carcinoma (OSCC).

**Design:** We tested the methylation status of 27 tumor suppressor and cell adhesion genes, including ADAM23, APC, ATM, CDH13,

CDKN2A, CHFR, DAPK1, IGSF4, MLH1, PKP1, RARB, RASSF1, and TP73, and an additional gene, MAL, using the SALSA methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) tumor suppressor kit or methylation-specific polymerase chain reaction (MS-PCR) on bisulphite-treated DNA.  $\pm 2$  Tests were used to determine statistical significance.

**Subjects:** Sixty-one patients with primary OSCC and 7 patients without cancer were recruited from 3 University of Washington-affiliated hospitals under an institutional review board-approved study.

**Results:** RARB and ADAM23 were the most frequently methylated genes tested, when comparing OSCC tumors with normal oral tissue. However, we did not find a correlation with tumor stage, nodal metastasis status, or HPV presence for either gene. Methylation in more than 3 genes was more frequently observed in node-positive than node-negative patients (15/37, 41% vs 4/24, 17%;  $P < .05$ ). We also observed a correlation of methylation status of DAPK1 ( $P < .025$ ) and MAL ( $P < .025$ ) with HPV-16 positivity.

**Conclusions:** Overall, we found methylation to be infrequent for many of the genes tested: 20 (71%) of 28 genes showed methylation in 10% or fewer tumors within our sample set. Because of the small sample size, and a relatively small number of early-stage vs late-stage tumors, our findings need to be confirmed or refuted in additional studies.

### S079: Methylation of Multiple Genes as Diagnostic and Therapeutic Markers in Primary HNSCC

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**Objective:** Promoter methylation-mediated silencing is a hallmark of many established tumor suppressor genes. This study uses a novel, multigene approach to examine epigenetic events of aberrant promoter methylation as diagnostic markers in head and neck squamous cell carcinoma (HNSCC).

**Design:** DNA was interrogated for alterations in aberrant methylation status using the novel multigene (22 genes) methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) assay.

**Subjects:** Fresh-frozen primary head and neck tumor specimens from 29 patients (20 late stage [17 stage 4 and 3 stage 3], 6 early stage [stage 2], 3 stage missing) were examined.

**Results:** Genes RARB, APC, and CHFR were most frequently hypermethylated, occurring in more than 30% of cases for RARB, and 20% for APC and CHFR. Aberrant methylation of CDKN2B and DAPK1 was confined only to stage 2 tumors. Conversely, CHFR methylation was solely a late-stage event (6/20 stage 3 and 4 tumors).

**Conclusions:** Promoter methylation profiling of primary HNSCC using multiple target genes identified RARB, APC, and CHFR as frequent epigenetic events. The clinical implications of these genes as diagnosis and treatment biomarkers are highly relevant. The direct role of RARB in regulating gene expression and its retinoid-mediated antiproliferative, differentiative, immunomodulatory, and apoptotic-inducing properties may offer a therapeutic target in HNSCC. Treatment with the methyltransferase inhibitor 5-aza-2'-deoxycytidine induced reexpression of CHFR. Additionally, because cancer cells that lack CHFR expression have shown to be more susceptible to the microtubule inhibitor taxol, silencing of CHFR by methylation can serve as a marker for predicting sensitivity to particular chemotherapeutic agents. Support: R01 NIH DE 15990.

### S080: Tumor Cells Adapt More Quickly to High Levels of Nitric Oxide (NO) and Become More Malignant in High NO Environment

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**Objectives:** Nitric oxide (NO) plays an important role in cancer growth and metastases. Glutathione-S-transferase (GST-pi) is a protective mechanism against the free radical NO. Correlation between GST-pi and NO levels may indicate that cells can adapt to increasingly hostile NO environments. We hypothesize that tumor cells are better able to adapt and grow in high-NO environments.

**Methods:** Four human head and neck squamous cell carcinoma cell lines (SCC114, SCC056, SCC116, and CSS016), along with a human pulmonary adenocarcinoma cell line (A549) and a normal cell strain (WI-38), were adaptively grown in increasing concentrations of the NO donor, DETA NONOate, (Z)-1-[2-(2-aminoethyl)-N-(2-ammonioethyl)-amino]diazene-1-ium-1,2-diolate. Growth rates and cloning efficiencies on soft agar were assessed by a new 96-well method using MTT assays.

**Results:** Both normal and tumor cell lines were able to adapt to increasing levels of NO, but tumor cell lines adapted faster. Adapted cell lines grow faster than their untreated parent cells and clone more efficiently on soft agar. GST-pi was overexpressed in cells grown in high-NO environments.

**Conclusions:** We have found that tumor cells more easily adapt to increasing levels of NO and that cellular NO production is hypothesized to facilitate this adaptation. In a high-NO environment, this confers a distinct growth advantage over normal cells. Adaptation to an increasing NO level increased the cloning efficiency of tumor cells on soft agar, which is a measure of increased malignancy. Measurement of NO levels in formalin-fixed paraffin-embedded tumors may reveal the aggressiveness of tumors.

## **S081: Loss of Imprinting of PEG1/MEST, IGF2 in Head and Neck Cancer**

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**Objective:** The PEG1/MEST is an imprinted gene expressed from the paternal allele and located on chromosome 7q32. In this study, we examined the expression and imprinting status of PEG1/MEST and IGF2 in head and neck cancer.

**Methods and Procedures:** Tissue samples. Head and neck squamous cell cancers and adjacent normal tissues from 19 patients were analyzed. Six of these cases were able to analyze matched normal and cancer specimens.

**Subjects:** Cell lines. Seventeen oral squamous cancer cell lines were analyzed.

**Interventions:** Allelic expression of the gene has been determined by restriction fragment length polymorphism utilizing restriction enzymes. Allele-specific expression analysis with reverse transcriptase-polymerase chain reaction and digestions by restriction enzymes were performed under the same conditions as for detecting genomic polymorphisms.

**Results:** Loss of imprinting (LOI) showed 1 of 2 informative cases at IGF2 in both normal and tumor specimens; 4 of 4 informative cases were detected in tumor specimens; and 3 of 4 informative cases were detected even in normal specimens at PEG1/MEST. As for the cell lines, LOI showed 5 of 8 informative cases in PEG1/MEST and 6 of 10 informative cases in IGF2; LOI of both imprinted genes was observed in 2 cancer cells.

**Conclusions:** As a result of analyzing tissue samples and cell lines, frequent LOI of PEG1/MEST as well as IGF2 was observed. We identified the epigenetic changes at PEG1/MEST in head and neck cancer.

## **S082: Atypical Facial Access: An Unusually High Prevalence Among Patients With Skull Base Tumors Treated in 2 Centers**

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**Background:** In most series, the majority of skull base tumors are squamous cell carcinomas of the paranasal sinuses. Common facial approaches (FA) are lateral rhinotomy or Weber-Ferguson. In Brazilian series, most patients have very advanced skin cancers invading the skull base (ASCSB).

**Objective:** To analyze the influence of this unique proportion of ASCSB on the choice of FA.

**Design:** Multi-institutional retrospective analysis.

**Material and Methods:** Charts of all patients submitted to oncological craniofacial operations in 2 major tertiary care institutions from 1981 to 2005 were retrospectively reviewed. The following data were collected: demographics, tumor location, FA, histology, reconstruction, complications, and outcome.

**Results:** A total of 484 patients were operated on; 467 cases were available for analysis. The median age was 52.8 years (range, 4-88 years); the male/female proportion was 1.9/1. Tumor location was craniofacial skin (63.5%), ethmoid (10.8%), maxilla (2.3%), orbit (1.9%), and others, including endocranial origin (19.4%). Histology was basal cell carcinoma (42.0%), squamous cell carcinoma (29.5%), esthesioneuroblastoma (5.3%), adenocarcinoma (3.9%), adenoid cystic carcinoma (2.8%), and other types (16.5%). Due to this high prevalence of ASCSB, the most common FA was atypical, tailored to encompass all compromised skin and underlying tissues (55.5% of cases), followed by Weber-Ferguson, with all its variations (17.8%), lateral rhinotomy (12.2%), facial translocation (3.8%) and other FA (7.7%). No FAs were required in 1.5% of cases.

**Conclusion:** In this retrospective study, including a 25-year experience with skull base operations in 2 major Brazilian centers, the choice of the head and neck surgeon, in the majority of the situations, was an atypical FA, in order to properly resect all facial structures invaded by very advanced skin cancers.

## **S083: Paranasal Sinus Tumors: What to Expect From Neoadjuvant Chemotherapy and Lessons From Twenty-Two Years' Experience**

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**Objectives:** To evaluate the response to induction chemotherapy for advanced paranasal sinus tumors.

**Methods:** Data was collected for patients with advanced paranasal sinus cancers treated between 1982 and 2004 and the response to induction chemotherapy was assessed.

**Results:** Fifty-six patients with Stage T3- T4b tumors of the paranasal sinuses were treated with induction chemotherapy for cytoreduction prior to definitive local treatment at the University of Texas MD Anderson Cancer Center during this period. Twenty-two (39%) were female, and the median age was 51.9 years (range: 26 to 77.4 years). The histologies included twenty nine (52%) squamous cell, twelve (21%) undifferentiated, six (11%) sarcoma, three (5%) neuroendocrine carcinoma, two (4%) mucoepidermoid carcinoma, two (4%) adenoidcystic carcinoma, and one (2%) poorly differentiated carcinoma and one (2%) olfactory neuroblastoma. Forty-eight (86%) of patients were treated with a platinum based regimen. Of the eight nonplatinum treated patients, 5 were patients with a sarcoma. The responses were assessed after 2- 3 cycles of chemotherapy by cross-sectional imaging or earlier if there were signs or symptoms of progression. 38 (68%) proceeded to resection of tumor. Of the 58 patients, seven (13%) had a complete response (two of these are unconfirmed as they had radiotherapy as definitive local treatment); twenty-five (45%) had a partial response; twelve (22%) had stable disease and eleven (20%) had progressive disease following the induction regimen.

**Conclusions:** In light of the finding of 42% of patients experiencing either stable or progressive disease, it is recommended that if induction chemotherapy is administered, patients should be monitored carefully for signs of progression and re-imaging should be planned early in the course of treatment. The loco regional control will be presented and analyzed according to the response to induction therapy.

## **S084: A Pilot Study Assessing Surgical Exposure During Transoral Robotic Surgery (TORS) with the Da Vinci Robotic System**

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The aim of our prospective clinical trial was to determine that adequate exposure could be achieved in order to perform Trans Oral Robotic Surgery (TORS) on patients with oral and laryngopharyngeal benign and malignant lesions. This is the first large patient study examining a robotics approach to transoral surgery. We enrolled 50 patients on our protocol (44 males, 6 females). Utilizing the da Vinci® Surgical Robot (Intuitive Surgical, Inc., Sunnyvale, CA) we performed a total of 41 transoral robotic procedures (we have five patients awaiting surgery and four patients' surgeries were canceled). Only one patient's surgery was aborted due to inadequate exposure to perform the surgery robotically. The da Vinci Robotic Surgical System being evaluated in this pilot study consists of 3 basic components: a surgeon's console, articulated mechanical arms and sterilizable instruments. The console includes a computer, video monitor and instrument controls, and is located in the operating room. The console is connected via computer to the mechanical arms holding the endoscope and sterile surgical tools (e.g., forceps, electrocautery, etc.). The surgeon sits at the console and controls the position and movement of the arms and surgical tools. The design of these tools is based upon well-established, commonly used surgical instruments. The end of the surgical tools have miniaturized instruments which are "wristed" and mimic exactly the wrist movements of the surgeon at the console. Use of the da Vinci Robotic Surgical System in the aforementioned configuration facilitates an exact translation of the surgeon's hand and finger movements at the console to precise and tremor-free movements of the arms and miniaturized end effectors of the surgical instruments. Patient ages ranged from 39-76 with the average age of 60. Clinical staging ranged from T1 to T4 with and without neck disease. Neck dissections were completed separately, usually within two weeks of TORS. The three most common transoral cancer resections performed were radical tonsillectomy, tongue base resection and supraglottic laryngectomy. The average length of hospitalization was 4 days. To date there have been no intraoperative complications and only two postoperative non-life threatening complications. The study allowed for the development of techniques for effective exposure, hemostasis and resection and preservation of surrounding soft tissue, cartilaginous and neurovascular structures. TORS provided excellent three-dimensional visualization and instrument access that allowed successful surgical resections. Our results indicate that adequate exposure to successfully complete TORS has been possible in all but one patient. Moreover, the miniaturized end effectors of the surgical instruments are well suited for surgical procedures in the relatively confined space of the oral cavity, larynx and pharynx. Use of the Da Vinci Robot has also provided the surgeons with improved view of the operative field, improved dexterity, precision, and three-dimensional depth perception. TORS is a novel and minimally invasive approach to neoplasms of the upper aerodigestive tract which can be accomplished both safely and effectively. The outcomes will be compared to both traditional open surgical approaches as well as transoral laser approaches.

## **S085: Can Neck Dissection Be an Outpatient Procedure?**

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**Objective:** To examine the post-operative course of patients undergoing neck dissections to determine if hospitalization is necessary.

**Method:** A retrospective review of neck dissections performed at the University of Oklahoma from January 1998 through December 2005 was performed. Patients who underwent simultaneous laryngectomy, tracheostomy or free flap were excluded. Concomitant procedures, prior therapy, extent of neck dissection, length of hospital stay and complications were reviewed.

**Results:** One hundred eighty eight neck dissections performed in 184 patients were reviewed. Of those, 118 underwent neck dissection with or without endoscopy, while 66 underwent additional procedures simultaneously such as parotidectomy (35%), partial glossectomy (20%), thyroidectomy (17%), or skin excision (15%). Sixty-nine patients (38%) had undergone prior radiation therapy with or without chemotherapy. Seventy six percent (140/184) patients were hospital-

ized less than 24 hours. All but 1 patient was discharged with drains in place which were removed at an average of 6 days post-op. In the neck dissection alone group 56% had prior radiation therapy. Three patients were discharged the same day and 102 (87%) had hospital stays of less than 24 hours. Three patients (2.5%) were readmitted for wound problems, 2 after developing a chyle leak and 1 for facial swelling. All patients readmitted had been previously treated with radiation therapy and none were judged to have been potentially preventable by hospitalization. In the group of neck dissections with an additional procedure, 8% had previous radiation therapy. One patient was discharged the same day and 56% had a hospital stay of less than 24 hours. Of those discharged in less than 24 hours, 57% had undergone either parotidectomy or thyroidectomy. There were no readmissions in this group. Overall 36 patients (20%) developed a post-operative complication, however only 6 (3%) had a significant complication. Twenty-two patients (12%) had wound related complications, of whom only 3 (1.6%) required readmission. The most common complication was a late seroma, which occurred in 12 patients (6.5%), all but one of these had not been treated with prior radiation therapy. There was 1 post-operative hematoma which was small and evacuated in the ER. The wound complications differed between those who had pre-operative radiation therapy and those without, but the rate of wound complication in these two groups was identical. There were no returns to the operating room during the immediate post-operative period. Three patients were hospitalized more than 3 days, with contributing factors of urinary retention, post-operative pneumonia, and poor pre-operative pulmonary function.

**Conclusion:** Post-operative complications in patients undergoing neck dissection were not observed that required immediate return to the operating room, or were preventable by prolonged hospitalization. Prior treatment with radiation therapy or chemo/xrt did not appear to be associated with a higher risk for complications. Our data suggested, patients undergoing neck dissection alone could be considered for outpatient surgery, and most patient undergoing additional procedures such as parotidectomy, partial glossectomy, thyroidectomy or skin excision can be safely discharged after 23-hour observation.

## **S086: Liposarcoma of the Head and Neck: Experience at a Major Cancer Center**

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The University of Texas M. D. Anderson Cancer Center, Houston

**Objective:** To review the demographics, presentation, treatment, and outcomes of patients with liposarcoma of the head and neck region at a major cancer center, representing the largest review of such patients seen at a single institution reported to date.

**Design:** Retrospective chart review. Follow-up ranged from 5 months to 21 years.

**Setting:** Large tertiary comprehensive cancer center.

**Patients:** Forty charts were reviewed from a search of the institutional tumor registry from 1945-2005 for all patients with a pathological diagnosis of liposarcoma in the head and neck region. Ten patients were excluded due to different pathological diagnoses (lipoma [n=2], atypical lipomatous tumors [n=2]), non-head and neck primary sites (n=2), or insufficient information (n=4).

**Main Outcome Measure:** Disease-specific survival.

**Results:** Of the 30 patients, 10 (33%) were initially misdiagnosed. Local recurrences were common (52%), particularly for the young (80%) and patients with initial misdiagnoses (90%), while distant metastases were common for those with pleomorphic histology (27%) or large tumors (43%). Most patients (93%) were initially treated with either surgery alone (57%) or surgery with radiotherapy (37%). Decreased crude disease-specific survival was associated with younger patients (40%), large tumor size (43%), pleomorphic (46%) or unclassified (40%) histologic subtypes, and initial misdiagnosis (50%).

**Conclusions:** Local recurrence is common overall but is particularly frequent after initial misdiagnosis. Patients with well-differentiated or myxoid subtypes and older patients seem to have higher disease-specific survival rates than patients with pleomorphic or unclassified liposarcoma. Surgery with negative margins remains the treatment of choice and adjuvant therapies should be considered in patients with aggressive histologies or positive margins.

## **S087: Salvage Surgery After Loco-Regional Failure of Concomitant Radio-Chemotherapy in Advanced Head and Neck Cancer**

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**Objective:** To assess the feasibility, toxicity, and efficacy of salvage surgery for local or neck node recurrence after concomitant radiochemotherapy (CXRT) for locally and regionally advanced head and neck squamous cell carcinoma (HNSCC).

**Design:** Retrospective study with a follow-up of 2 to 8 years.

**Settings:** Referral center.

**Patients:** We reviewed the medical records of all patients with HNSCC treated at the Institut Gustave-Roussy from 1998 to 2003, using a CXRT regimen as initial therapy. Patients with initial second localization or distant metastasis had been excluded.

**Results:** Seventy (32%) of 222 patients initially treated by CXRT had local and/or neck node recurrence without distant metastasis. Thirty-six (51%) of these 70 patients underwent salvage surgery. Twenty-seven cases were initially classified as T3 and T4 tumors, and 27 patients had initially neck node involvement. After salvage surgery, 7 patients had a local recurrence; 1, neck node recurrence; 4, distant metastasis; 5, locoregional recurrence; and 3, locoregional recurrence with distant metastasis. Ten patients (28%) had major postoperative complications, and 3 of these patients died postoperatively.

**Conclusions:** After CXRT regimen for advanced HNSCC, about half of the patients with local and/or regional recurrence underwent salvage surgery. With a median follow-up of 20 months, only 36% of the operated patients were disease free. Major complication rate was high. Regarding the high major complication rate and the low overall survival rate, salvage surgery should be used only in carefully selected cases after CXRT.

## **S088: Periorbital Reconstructions After Orbital Exenteration: An Individualized Approach to Simplify Ocular Rehabilitation**

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This is a retrospective review of a consecutive series of 16 patients who had periorbital reconstructions after orbital exenteration between 1998-2005 in a regional hospital in Hong Kong. There were 15 male and one female patients. Age ranged between 22-88 years old (median 50). Indications for orbital exenteration included gross invasion of the orbital contents, involvement of orbital apex and periorbital by tumors that arose from orbit (2), skin (2), nasopharynx (3), paranasal sinus (8), and skull base (1). Squamous cell carcinoma was the commonest while meningioma, malignant oncocytoma, and haemangiopericytoma were the other uncommon tumors. 50% of this group of patients had received either surgery/radiation alone or combined treatments prior to the orbital exenteration. 11 tumors involved the cranial skull base and three had invaded the dura that required major craniofacial ablation resulted in complex craniofacial and extended exenteration defects. Six eyelids were spared whenever ablation was oncologically-sound. 15 defects were reconstructed by free vascularized tissue flaps in which four myocutaneous flaps were specially designed to seal the skull base and to house the ocular prosthesis so as to achieve ocular rehabilitation in one-staged orbital reconstruction. Minor secondary procedures to the eyelids were added whenever necessary to strengthen the holding ability of the ocular prosthesis. Six patients who had total exenteration without ocular rehabilitation were elected to wear an eye-patch or sun-glasses. There was no operative mortality in this series. Post-operative morbidity (31%) included wound infection (6.3%), chest infection (12.5%), and CNS-related (18.75%) complications. In the follow up period of 2-84 months (median 11), six patients died of disease recurrences (5 local regional and one distant) and ten patients remained well and alive (63%). In summary, we emphasized an individualized approach to this group of patients who had very aggressive tumors and complex craniofacial defects. Among the various approaches, we advocated a simplified one-staged orbital reconstruction that included an eyelid sparing exenteration and a versatile flap design that could seal the skull base and house the ocular prosthesis in one stage. This approach was aesthetically-superior in achieving ocular rehabilitation and was relatively affordable by this group of patients.

## **S089: Optimizing Reconstruction of Composite Mandibular and Maxillary Defects Using Three Dimensional Models**

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**Objective:** To examine the utility and usefulness of using a three dimensional patient derived model to assist the surgeon during the resection and the reconstruction of bony defects of the mandible and the maxilla.

**Methods:** A retrospective cohort study was performed of all patients undergoing reconstruction of the mandible and/or maxilla using a Three dimensional customized patient (CT Scan) derived model of the area at a single tertiary care institution during a three year period. All patients were evaluated by a multidisciplinary team including a head and neck oncologic surgeon, reconstructive surgeon, maxillofacial prosthodontist, speech pathologist, and head and neck radiologist. The inclusion criteria included: 1) treatment between 2000-2003, 2) use of preoperative 3D model in reconstruction, 3) at least one year of follow-up, and one or more of the following: outer periosteal involvement by cancer, osteoradionecrosis with mandibular defect, mandibular bone loss/fracture/malocclusion, maxillary defect with malocclusion, loss of condylar position, and/or external bone defect with cosmetic deformity. The eligible patients were evaluated along several parameters: speech and swallowing function, maxillofacial outcomes, cosmesis and usefulness of the model to both the ablative and reconstructive surgeon. A retrospective survey of the extirpative and reconstructive surgeon was analyzed to assess the utility, advantages, and disadvantages of the model in this patient population.

**Results:** There were a total of 26 patients who were eligible for this study. Two patients were excluded, one for the discovery of lung metastases preoperatively and the other after the patient refused to undertake surgery and opted for palliative treatment. From the 24 eligible patients, 70% were male, age ranged from 2-77, with the average age of 52 years old. The indications for the procedure and model included carcinoma in 22 and 2 with recalcitrant osteoradionecrosis requiring free tissue transfer. Of the cancer patients, 81% had a primary tumor stage T4 with 84% of the reconstructions performed primarily at the time of definitive tumor extirpation. There was a total of 25 3D models created utilizing the stereolithography technique. Of these models, 20 were mandible only, 1 was maxilla only, and 4 were both mandibular and maxillary. The results of the survey revealed significant and consistent advantages to the reconstructive surgeon and patient specific advantages to the extirpative surgeon. Overall advantages, disadvantages, complications, cost, and outcomes are presented.

**Conclusion:** The use of rapid prototyping is a useful adjunct to the surgeon in the reconstruction of complex mandibular and maxillary defects related to head and neck cancer. Their use has the potential to improve outcomes including occlusion, masticatory efficiency, and cosmesis. Additionally, it allows for improved communication with the patient, improved surgical planning, and shorter operating room time.

## **S090: The Vessel Depleted Neck: Techniques for Achieving Microvascular Reconstruction**

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**Objective:** To identify reliable alternatives for microsurgical donor vascular supply in the vessel-depleted neck.

**Design:** Retrospective chart review of patients with vessel-depleted necks who underwent microvascular reconstruction.

**Setting:** Faculty practice at a tertiary referral center.

**Patients:** All patients who underwent microvascular reconstruction between July 2001 and June 2005 were reviewed.

**Interventions:** None.

**Main Outcome Measures:** Donor vessels, vein grafts, and flap survival were examined to identify reliable alternative donor vessels.

**Results:** Fourteen (7%) of 197 patients had vessel-depleted necks. All patients had a prior neck dissection and radiation (100%) or chemoradiation (42%). Twenty-eight percent underwent 1 prior free flap; 35% underwent 2 prior free flaps; and 71% underwent at least 1 prior pedicled flap(s). Free flap revascularization was achieved using

the transverse cervical artery with a vein graft and a cephalic vein (4 cases), the thoracoacromial artery and cephalic vein (3 cases), the internal mammary artery and vein (3 cases), and the inferior thyroid artery and cephalic vein (1 case). In 3 cases, the reverse-flow thoracoacromial artery and cephalic vein were used to vascularize the scapular flap. In 7 cases, a lower extremity vein graft was used for the arterial anastomosis, while no cases required a vein graft for the venous anastomosis. The only complication was 1 cephalic venous thrombosis that was successfully salvaged.

**Conclusions:** The cephalic vein, transverse cervical artery, internal mammary vessels, and thoracoacromial vessels represent reliable alternatives in the vessel-depleted neck.

## S091: Factors Associated With Discontinuing Employment

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**Objective:** Loss of employment is a serious problem for cancer patients, influencing many aspects of their lives. Discontinuing employment is a prevalent problem among those diagnosed with head and neck cancer (HNC). The objective of this study was to evaluate self-reported reasons for discontinuing employment among patients with HNC.

**Methods:** This prospective, observational outcomes study included 666 patients with HNC who were enrolled in a longitudinal outcomes assessment project between January 1, 1998, and October 31, 2004. These patients were initially asked about the status of their employment prior to treatment, and were subsequently asked about any change in employment at each of their post-treatment follow-up visits from three months to one year after diagnosis. If their employment status changed due to their cancer or its treatment, patients were asked to rate the impact of five factors (eating, talking, appearance, pain, and fatigue) on their decision to discontinue employment. Ratings were provided on a 5-point, Likert-like scale with the end points labeled as not important (1) and very important (5).

**Results:** Of the 666 patients, 239 were employed (205 full-time and 34 part-time) at the time of their diagnosis. After treatment, 108 of the 239 (45.2%) reported having to discontinue work because of their cancer. Ninety-five of the 108 patients (88.0%) rated each of the five factors.

The areas with the highest percentage of very important ratings were talking and fatigue (37.9% each) and eating (34.7%). Pain and appearance were rated as very important by 23.2% and 8.4% of patients, respectively. The mean scores of all patients ranged from a high of 3.5 for fatigue to a low of 2.0 for appearance. Analysis by patient, disease, and treatment variables demonstrated that speech was an important reason for discontinuing work for patients with hypopharyngeal and laryngeal tumors (mean of 3.7), whereas eating was an important reason for patients with oral cavity and oropharyngeal tumors (means of 3.4 and 3.5, respectively). Patients who received chemoradiation therapy had a substantially higher mean fatigue score (4.4) than those receiving other types of treatment.

**Conclusions:** Patients with HNC rated speech and eating as important reasons for having to quit work, but appearance had little impact on their employment status. Less expected was the finding that fatigue was one of the primary reasons for having to quit work, especially in patients undergoing chemoradiation therapy. Efforts to enhance post-treatment functioning should include counseling patients about expected outcomes so that they can better prepare for and adjust to functional difficulties after treatment. Also, providing clinical intervention to reduce post-treatment fatigue, an often overlooked outcome, could be very beneficial to patients in their efforts to remain gainfully employed. Identification of the factors associated with the decision to discontinue work is a first step in providing focused solutions.

## S092: Defining the Clear Surgical Margin in Oral Cancer

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**Objective:** Microscopic tumor at the inked surgical margin has an adverse effect on outcome in oral cancer. This study examines the impact of the width of the close surgical margin on survival.

**Design:** Pathology reports were reviewed for the status of the surgical resection margin in an historical cohort of 277 patients with oral cancer. Cox proportional hazard models were used to determine the independent effect of the surgical margin, in millimeters, on survival.

**Results:** The 5-year absolute, disease-specific, and disease-free survivals were 60%, 73%, and 56%, respectively. Survival was significantly ( $P < .05$ ) impacted by age older than 65 years, male sex, and stage IV disease. After controlling for these prognostic factors, each 1-mm increase in the clear surgical margin decreased the risk of death at 5 years by 8% (hazard ratio, 0.92; 95% confidence interval, 0.86-0.99;  $P = .02$ ). Three groups were identified with similar survival probabilities. Patients with positive surgical margins had a 2.5-fold increase in risk of death at 5 years when compared with patients with clear ( $\geq 4$  mm) margins ( $P < .001$ ). Patients with close ( $\geq 3$  mm) margins had a 1.5-fold increase in risk of death compared with those with clear margins ( $P = .08$ ).

**Conclusions:** There is a step-by-step increase in survival with each additional millimeter of clear surgical margin. This systematic evaluation of surgical margins suggests that an adequate resection in oral cancer should affect a margin greater than or equal to 4 mm on permanent section.

## S093: Suicide Rates in Head and Neck Cancer Patients

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**Objective:** To quantify the incidence of suicide in US cancer patients.

**Hypotheses:** (1) cancer patients have a higher suicide rate than the US general population and (2) head and neck cancer (HNC) patients have a higher suicide rate compared with patients with other types of cancer.

**Design:** Retrospective cohort study.

**Setting:** National network of US population-based cancer registries in the Surveillance Epidemiology and End Results (SEER) program of the National Cancer Institute.

**Patients:** Patients with single primary cancer sites who were entered into SEER registries between 1973 and 2002. Head and neck cancer patients included those with cancers of the oral cavity, oropharynx, hypopharynx, and larynx. Figures provided by the US Bureau of the Census were used to derive suicide rates from 1969 through 2002 for the US populations represented in the SEER registries.

**Main Outcome Measure:** Suicide as cause of death.

**Results:** A total of 4732 suicides were identified among 2 860 156 people followed for 14 190 218 person-years, giving a suicide rate of 33.6 per 100 000 person-years. The suicide rate in the general US population was 15.8 per 100 000 person-years. The HNC suicide rate (50.5 per 100 000 person-years) was higher than that of both the general population and the overall cancer population. Among HNC patients, advanced disease was associated with higher suicide rates.

**Conclusions:** Cancer patients have twice the suicide rate of the general population. Head and neck cancer patients have a suicide rate that is higher than that of both the general population and cancer patients as a whole. Further examination of the psychological toll exacted by head and neck cancers is warranted.

## S094: Oropharyngeal Swallowing: Functional Targets of Surgical Restoration

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**Objective:** Lack of standardized methods to capture swallowing impairment has impeded our understanding of the functional results of restorative surgeries. This 3-year study sought empirical evidence for (1) physiologic components rated during a modified barium swallowing evaluation; (2) standard convention of grouping functional components into phases (ie, oral, pharyngeal, and esophageal); (3) relationships between components and redundancy of components; (4) scoring reliability; (5) the sensitivity of components to aspiration; and (6) sensitivity to health status and quality of life.

**Design:** Expert consensus was used to validate the swallowing components and scoring methods. Components and phases were organized into a measurement tool. Concordance measures determined rater reliability. Factor structure was tested using exploratory and confirmatory factor analysis.

**Setting:** Medical University of South Carolina, Charleston, and Saint Joseph's Hospital of Atlanta, GA.

**Patients:** Measurement model was tested in 320 patients, with a subset of 60 head and neck cancer patients.

**Intervention:** Modified barium swallowing.

**Main Outcome Measures:** Scoring reliability and construct validity of swallowing components and phases were described by their relationship to (1) aspiration, (2) diet, (3) nutrition, (4) health status, and (5) disease-specific quality of life.

**Results:** Eighteen components resulted. Rater reliability was 90%. Factor analysis revealed a parsimonious set of physiologic measures that were clinically meaningful, easily measured, and sensitive to change and outcome.

**Conclusions:** This standardized tool will enhance quantification of swallowing impairment and change in function over time. Components found critical to aspiration, optimal nutrition, health status, and quality of life should be targets when planning and testing restorative head and neck operations.

## **S095: Multi-Institutional Phase III Radplat IA Versus IV Trial in Advanced Head and Neck Cancer: 1st Year Quality of Life**

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**Introduction:** Quality of life (QoL) assessment is indispensable in organ preservation protocols to establish whether organ function can be preserved. Therefore it was integrated into a randomized, multi-institutional study in patients with functionally inoperable, stage IV head and neck squamous cancer treated with either targeted supra-dose cisplatin chemoradiation (IA) or systemic chemoradiation (IV).

**Patients and Methods:** 207 Patients, 152 male and 55 female, mean age 55 years, were randomized either into the IA arm (N=103) or into the IV arm (N=104) between December 1999 and November 2004. In the IA arm patients received weekly cisplatin 150 mg/m<sup>2</sup> as a targeted rapid IA injection with sodium thiosulphate IV rescue in weeks 1-4. In the IV arm patients received 100 mg/m<sup>2</sup> cisplatin as a 4 hour intravenous infusion on days 1, 22, and 43. Radiotherapy 70Gy in 35 fractions was administered over 7 weeks starting concurrently with chemotherapy. QoL assessment was performed prior to treatment, and 7 weeks, 3 months, 1, 2 and 5 years after its start, using the EORTC QLQ C30 and H&N 35 questionnaires and a trial-specific questionnaire. This first analysis concerns the 12 months follow-up data.

**Results:** During the first 12 months of follow-up, 60 patients died and 21 patients could not be interviewed (refusal 2, too ill 4, protocol violation 3, extensive salvage surgery 4, missing 8). Thus 126 patients were assessed (IA arm N= 59, IV arm N=67). All participating patients showed a clear deterioration in overall QoL at the end of the 7 week treatment period then a gradual improvement up till 12 months. The greatest difference between the two groups was twice as many patients in the IV group complaining of nausea and vomiting at 7 weeks ( $p<0.001$ ). At 3 months these complaints / differences almost disappeared. At 12 months 10 of 59 IA patients (17%) still had tube feeding, compared to 16 of 67 (24%) in the IV group (not statistically significant). The remaining patients returned to a more or less normal oral diet. Voice quality deteriorated by the end of treatment, but then improved over time, slightly exceeding the baseline values at 12 months. The majority (96%) of the patients had no problems with their appearance 12 months after treatment. Of the 62 patients who were employed before treatment, 42 were able to return to their job within 12 months. Xerostomia was reported by 70 patients (56%), with no statistically significant difference between the IA and IV group.

**Conclusion:** This preliminary analysis reveals significantly more problems with nausea and vomiting at the end of the treatment among patients in the IV group than those in the IA group. Problems with voicing and oral intake, clearly present at the second assessment point in both groups, improved during the 12 months follow-up, often exceeding baseline values.

## **S096: Nomogram for Predicting Locoregional Recurrence-Free Survival After Treatment of Oral Cavity Squamous Cell Carcinoma**

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**Objective:** To create and externally validate a nomogram for predicting, for individual patients, locoregional recurrence-free survival (LRFS) after primary surgical treatment of oral cavity squamous cell carcinoma (OCSCC).

**Design:** Cohort and validation cohort study. Median follow-up was 52.8 months for the primary cohort and 39.8 months for the validation cohort.

**Setting:** International, multi-institutional.

**Patients:** A nomogram for predicting LRFS after treatment of OCSCC was constructed from a cohort of 590 OCSCC patients treated with surgery ± postoperative radiation therapy at Memorial Sloan-Kettering Cancer Center

(MSKCC) in New York, NY, between 1985 and 1996. The nomogram was validated using a series of 417 OCSCC patients treated at Hospital do Cancer A. C. Camargo (HACC) in São Paulo, Brazil, during the same time period.

**Main Outcome Measures:** Locoregional recurrence-free survival (LRFS). Concordance index: measure of the predicted LRFS based on the nomogram compared with actual outcome.

**Results:** Substantial differences were noted between the MSKCC and HACC cohorts, including poorer LRFS among HACC patients ( $P<.001$ ). Despite these differences, the nomogram constructed using the MSKCC cohort was able to predict LRFS from OCSCC for the HACC cohort with a concordance index of 0.693. Of the variables used to construct the nomogram, only margin status ( $P = .006$ ) and pathologic N stage ( $P<.001$ ) were significant predictors of LRFS from OCSCC.

**Conclusions:** A nomogram with reasonable accuracy and discrimination has been constructed and externally validated to predict LRFS for individual patients treated surgically for OCSCC. This prognostic tool has practical utility in adjuvant treatment planning for OCSCC patients.

## **S097: Association of Measures of General Health With Survival**

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**Objective:** Previous research has shown that comorbidity present at the time of cancer diagnosis is a significant predictor of survival in the head and neck cancer (HNC) patient population. The purpose of the current study was to compare patient-reported general health status with comorbidity as independent predictors of survival. It was hypothesized that a patient-reported rating of general health, which has been shown to be associated with clinical ratings of comorbidity, would be a more accurate predictor of survival because it represents the physical and emotional effect of existing comorbidities as well as problems introduced by the HNC and its treatment.

**Methods:** In this prospective, observational outcomes study, self-reported pretreatment general physical and mental health scores (using the well-validated Medical Outcomes Study, Short Form 36 survey) were collected from 571 patients enrolled in this institution's longitudinal Outcomes Assessment Project. These physical and mental health scores were compared with the patients' pretreatment comorbidity ratings (assigned through chart reviews using the ACE-27 rating scheme). A Pearson's correlation was performed to determine the association between these health measures, and Cox regression analyses were performed to determine which of these measures was more predictive of observed and disease-specific survival.

**Results:** General physical health composite scores were significantly associated with the comorbidity ratings ( $p<0.001$ ), although the rather small correlation coefficient (-0.391) indicates that these two entities

measure different health aspects. General mental health composite scores were not associated with comorbidity. The results of the regression analyses that included these three health measures (comorbidity, physical health, and mental health) demonstrated that comorbidity and physical health were independently associated with five-year, observed survival (death from any cause), but that the impact of physical health was greater than that of comorbidity. Physical health was the only variable associated with five-year, disease-specific survival (death with cancer present). Subsequent regression analyses that included site and stage demonstrated similar results. In addition to stage, physical health was independently associated with observed and disease-specific survival. Comorbidity was associated only with observed survival, with less impact than physical health.

**Conclusions:** Factors that influence outcome need to be identified so that they can be incorporated into assessments of prognosis and evaluations of treatment efficacy. This study's findings suggest that a general measure of physical health may be a better predictor of survival than a general measure of comorbidity. Using a survey to have patients report their general health status might prove to be a more useful clinical and research tool than determining their comorbidity ratings. Such a survey would be especially useful if the shorter SF-12 was shown to provide similar results to the SF-36.

## S098: Chemoprevention of Head and Neck Cancer With Aspirin: A Case-Control Study

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**Objective:** To evaluate the chemo-preventive potential of aspirin against Head and Neck Cancer and to study this effect among smokers and alcohol drinkers.

**Design:** Hospital-based case-control study.

**Setting:** National Cancer Institute-designated Comprehensive Cancer Center.

**Subjects:** The subjects included individuals who received medical services at the Roswell Park Cancer Institute in Buffalo, New York, between the years 1982 and 1998, and who completed a comprehensive epidemiological questionnaire. This study examined aspirin use among 529 head and neck cancer cases and 529 hospital-based controls, matched by age, gender and smoking status.

**Results:** Our findings indicated that aspirin use was associated with a 25% reduction in the risk of all head and neck cancers [adjusted odds ratio (AOR) 0.75; 95% confidence interval (CI) 0.58-0.96; p-value 0.02]. Similar significant risk reduction was noted when tumor sites were examined separately. Risk reduction was observed across all primary tumor sites with Oral Cavity and Oropharynx exhibiting comparatively greater risk reduction. The results were adjusted for age, gender, packs of cigarettes per day and drinks of alcohol per week. Consistent risk reductions were also noted with frequent and prolonged aspirin use. Aspirin use of at least 7 (325mg) tablets per week was associated with 32% reduction in risk (p-value 0.04) and aspirin use for more than 20 years was associated with 33-35% reduction in risk (p-value 0.04), when compared to non-users. Further, a consistently decreasing trend in risk of head and neck cancer was noted with increasing duration of aspirin use (p=0.005). In addition, when analyzed by smoking and alcohol exposure levels, subjects with low to moderate exposure to either (< 1 pack of cigarette per day (and/or) ≤ 1 drink of alcohol per day) showed a statistically significant 33% risk reduction (AOR 0.67; 95% CI 0.50-0.91; p-value 0.009), whereas subjects exposed to both heavy smoking and alcohol use (? 1 pack of cigarette per day and >1 drink of alcohol per day), did not benefit from the protective effect of aspirin. The reduction in risk was more significant in females.

**Conclusion:** Aspirin use is associated with reduced risk of Head and Neck Cancer, with comparatively higher risk reduction for Oral cavity and Oropharyngeal tumors. This protective effect was greater in women than in men. The risk reduction was most pronounced in individuals with low to moderate exposure to cigarette smoke or alcohol consumption. Conversely, the protective effect was attenuated by heavy smoking and alcohol drinking. Additional clinical trials would be useful to confirm the strength of the association and to best define the target population for aspirin chemoprevention.

## S099: The Effect of Health Insurance Status on Stage at Diagnosis for Laryngeal Cancer

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**Introduction:** Stage at diagnosis not only dictates optimal treatment but also impacts prognosis. Early stage laryngeal cancer is treated with a greater than 80% chance of cure whereas late-stage laryngeal cancer has a five-year survival rate of less than 50%. As health insurance status may affect access to medical care and thus stage at diagnosis, this study was performed to determine the relationship between health insurance and stage at diagnosis for laryngeal cancer.

**Methods:** We examined data from 37 840 patients diagnosed with squamous cell laryngeal cancer between 1996 and 2001 using the National Cancer Database (NCDB), a hospital based US cancer registry. A total of 35 225 cases were available for analysis after excluding 2585 (6.8%) with missing insurance information. ±2 Analyses and odds ratios were calculated to determine the relationship between health insurance and stage of diagnosis.

**Results:** Among the NCDB cohort, 44% had Medicare coverage, 35% had managed care or other private insurance, 9% had Department of Veterans Affairs or other government insurance, 7% had Medicaid, and 5% were uninsured. Sixty percent of managed care participants and 59% of Medicare enrollees presented with early stage laryngeal cancer (stages I or II). In contrast, 64% of uninsured and 68% of Medicaid recipients presented with late-stage laryngeal cancer (stages III or IV). Compared with patients with Medicare or managed care, those who were uninsured or had Medicaid had a significantly increased odds of presenting with advanced stage, after controlling for race (odds ratio, 2.50; 95% confidence interval, 2.33-2.69).

**Conclusions:** Individuals lacking insurance coverage and those covered by Medicaid are at significantly increased risk of presenting with late stage laryngeal cancer.

## S100: Prognostic Determinants Associated With Efficacy of Intra-Tumoral p53 Gene Therapy in Patients With Recurrent SCCHN

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**Background:** We investigated the safety and prognostic factors influencing the efficacy of an adenoviral p53 gene therapy (contusogene) in patients with recurrent, SCCHN.

**Methods:** Two multicenter, open label phase II studies involving 173 patients were performed. Patients were treated with intratumoral injections of contusogene. The primary endpoint of this trial was the evaluation of the overall response rate by SWOG criteria. Duration of disease control, progression-free survival, and overall survival were secondary efficacy endpoints. Time to event data were analyzed using the Kaplan-Meier method. The significance of univariate associations was assessed using the logrank test, Pearson 063√ or Fisher exact tests, and the non-parametric Mann-Whitney U test as appropriate. Logistic regression and Cox regression analysis was employed to determine independent prognostic factors for dichotomized and time to event outcome variables, respectively.

**Results:** Prognostic factors defining sub-populations in which response rates up to 29% were observed included progression free interval (PFI) > 12 months from initial therapy, smaller tumor size (< 2.5 cm), and the absence of lesional pain and ulceration. Tumor response was an independent prognostic factor for survival with a statistically significant decreased risk of death for patients achieving response (HR 0.21, 95% CI, 0.07-0.61, p = 0.004) or durable tumor stabilization > 3 months (HR 0.48, 95% CI, 0.27-0.87, p = 0.015) compared to non-responders. In contrast with previous reports but consistent with known mechanisms of p53 action, prior DNA damag-

ing chemotherapy was an independent prognostic factor at baseline for increased survival. No long-term toxic effects were identified (median follow-up 15.9; range 2.3-46.6 months).

**Conclusion:** Intralesional administration of contusogene was well tolerated. Prognostic factors defining subpopulations of recurrent SCCHN most likely to benefit from intralesional p53 gene therapy were identified.

## **S101: Human Papillomavirus Contributes to Oral and Oropharyngeal Squamous Cell Carcinoma and to Recurrence After Treatment**

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**Objective:** The present study aimed to investigate the prevalence of high- and low-risk HPVs (human papillomavirus) in a consecutive series of oral and oropharyngeal squamous cell carcinoma (OOSCC) matched with population-based, healthy controls.

**Methods:** From 131 patients with OOSCC, samples taken from the surface of the tumour and from the tonsillar fossa by cotton tipped swabs were investigated together with exfoliated cells collected through a mouthwash. From 320 matched control persons, tonsillar fossa and mouthwash specimens were identically collected. All samples were tested for HPV DNA by nested PCR, and positive findings were HPV type-determined by DNA sequencing.

**Results:** Infection with high-risk HPV was shown to be a strong risk factor for OOSCC (OR= 63; 95% CI 14-480). Forty-seven (36%) of the cancer patients had one or more specimens positive for a high-risk HPV type (81% of which were HPV 16), while three (0.94%) of the control persons were positive for a high-risk HPV type. Seven (5.3%) of the cancer patients and 13 (4.1%) of the healthy controls were positive for one of the low-risk mucosal, muco-cutaneous, or cutaneous HPV types. In total, 128 patients had planned curative treatment. After a median follow-up time of 22 months (range 0:36 months), 30 patients experienced a recurrence, 2 had an SPT, 12 were lost to follow-up, and there were 21 DICD (death from intercurrent disease). High-risk HPV-positive cases had an almost threefold increased relative rate (RR) of recurrence/SPT, but a lower RR of DICD compared to high-risk HPV-negative cases. There was no increased RR of recurrence/SPT related to smoking, but there was an association between smoking and DICD.

**Conclusion:** These results demonstrate a strong association between infection with high-risk HPV types and OOSCC, suggesting that they have a key role in the carcinogenesis. The estimated proportion of OOSCC cases attributable to high-risk HPV infections was 35%. High-risk HPV-positive cases had an almost threefold increased RR of recurrence/SPT. However, since DICD, is a competing risk, the RR for high-risk HPV-negative cases might be underestimated due to DICD.

## **S102: Human Papillomavirus in Head and Neck Cancer - Is It Changing the Face of Our Patient Population?**

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**Objective:** To determine if the age distribution of human papillomavirus-associated head and neck squamous cell cancers has changed over time. The highest levels of HPV have been found in head and neck cancers located in the tonsil and oral cavity, but it has also been identified in the nasal cavity and the larynx. The prevalence of HPV infection is highest in persons under age 25, and is thought to clear 6-12 months later, although re-activation or re-infection has been observed after age 50-55.

**Methods:** Adults age 20 and over residing in one of nine areas participating in the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program were included. We studied the cancers at the two sites known to harbor high levels of HPV: palatine

tonsil, and oral mucosa – which includes the tongue and all mucosal surfaces of the mouth. Outcomes: age adjusted incidence, median age at diagnosis.

**Results:** Tonsil cancer incidence overall increased 16% between 1973 and 2002. Tongue cancer increased 13% during this time, but all other oral sites saw overall incidence fall. Site-specific estimates of HPV prevalence and trends in the age distribution of new cancers are shown below:

**Conclusions:** There has been a significant shift toward a younger age of incidence among head and neck cancers known to have the highest prevalence of HPV, which supports HPV as at least a partial causative factor. This is of particular interest because cancers linked to HPV may be biologically different from those caused by alcohol and tobacco use, which could lead to unexpected results from treatment regimens both old and new.

## **S103: The Association of BCL-2 and Survivin Expression to Disease Outcome in Head and Neck Cancer**

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**Objective:** Previous publications have reported the predictive utility of apoptotic proteins such as BCL-2 and survivin, in head and neck squamous cell carcinoma (HNSCCA) outcomes. BCL-2 has been described as a conveyor of altered sensitivity to radiotherapy. This study investigates the association between outcomes of patients with HNSCCA treated nonsurgically and the expression of BCL-2 and survivin.

**Design:** Retrospective review.

**Setting:** Tertiary care academic center.

**Patients:** Patients with HNSCCA, treated primarily nonsurgically. Patients were included if a pretreatment biopsy specimen from the primary tumor site was available.

**Interventions:** We used immunohistochemistry to detect the expression of BCL-2 and survivin in each of the primary tumor site specimens.

**Main Outcome Measures:** Patient charts were reviewed for the pretreatment disease stage, treatment modality used, and overall disease outcome. These results were compared with the expression of BCL-2 and survivin.

**Results:** Sixty patients were included for analysis 45 of 60 were disease-free at the last follow-up. Twenty-two of the 60 specimens stained positive for BCL-2. All specimens stained for survivin. Statistical analysis yielded no significant findings in the association of BCL-2 and survivin expression with treatment response or disease outcome.

**Conclusion:** Determining a marker for cancer outcome can help predict both response to treatment and success of treatment. Past publications have yielded conflicting evidence for the utility of BCL-2 in predicting outcomes for HNSCCA. In this study, no significant association between survivin or BCL-2 expression and disease outcome was detected, indicating that neither BCL-2 nor survivin are clinically useful predictors of outcomes.

## **S104: Salvage Surgery After Radiotherapy for Laryngeal Cancer: From Endoscopic Resections to Partial and Total Laryngectomies**

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**Objective:** To evaluate our experience in management of laryngeal cancer after radiotherapy failure by endoscopic resections, partial, and total laryngectomies.

**Design:** Retrospective study.

**Setting:** University hospital.

**Patients:** Between 1995 and 2004, 71 patients with recurrent laryngeal cancer after radiotherapy were managed by salvage surgery.

**Interventions:** Our treatment policy encompassed endoscopic resection for glottic rT1a, rT1b with limited anterior commissure involvement, and rT2 with normal mobility (group A, 22 patients). Supracricoid partial laryngectomies were performed for rT1 and rT2

with suboptimal endoscopic exposure, for rT2 with impaired mobility and/or transcommissural extension, and for rT3 for limited paraglottic space invasion or involvement of the inner portion of the thyroid (group B, 15 patients). Total laryngectomy was planned in patients not suitable to partial laryngectomy for general conditions, for rT3 with massive involvement of the paraglottic space, and for rT4 (group C, 34 patients).

**Main Outcomes Measures:** Survival curves were calculated by the Kaplan-Meier method and included 5-year determinate, disease-free, and laryngeal preservation rates for each group.

**Results:** The pT status after salvage surgery was pT1 in 12, pT2 in 20, pT3 in 20, and pT4 in 19. Five-year determinate, disease-free survival, and laryngeal preservation rates for the whole series were 72%, 61%, and 41% (group A: 95%, 63%, and 77; group B: 100%, 83%, and 80%; and group C: 48%, 51%, and 0%).

**Conclusions:** Survivals for the whole series are not different from those reported in the literature by using a more aggressive approach without any surgical organ preservation attempt. The laryngeal preservation rate observed justifies a conservative treatment in case of limited recurrent lesions.

## S105: Phase II Trial of CO<sub>2</sub> Laser Supraglottic Laryngectomy and Irradiation: Experience of the Southwest Oncology Group

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**Objective:** To evaluate feasibility, functional outcome, and disease control of treating patients with stage I, stage II, and selected stage III squamous cell carcinoma of the supraglottic larynx with endoscopic surgery and irradiation in a multi-institutional setting.

**Design:** Prospective, single-arm, phase II multi-institutional trial.

**Setting:** The Southwest Oncology Group trial S9709.

**Patients:** A total of 34 evaluable patients diagnosed with stage I, II, or selected stage III (T1/T2N1M0) supraglottic laryngeal carcinoma were enrolled.

**Interventions:** Transoral carbon dioxide laser supraglottic laryngectomy followed by planned postoperative radiation therapy.

**Main Outcome Measures:** Three-year progression-free survival, proportion of patients requiring tracheostomy as a result of surgery, and time to adequate oral intake.

**Results:** Thirty-two (94%) of 34 patients underwent adequate surgery and completed all planned postoperative radiotherapy without major deviation. Four patients (12%) required temporary tracheostomy prior to endoscopic resection. No subjects required tracheostomy as a direct consequence of surgery. Recovery of adequate oral intake occurred in the early postoperative period in 24 (71%) of 34 patients (median time point, 2 days; range, 1-7 days). Seven patients (21%) achieved recovery in delayed fashion (2.7-9.8 months). At the time of analysis, only 1 patient

(3%) experienced documented local disease recurrence. Estimated 3-year progression-free survival was 79%.

**Conclusions:** Transoral CO<sub>2</sub> laser excision of early supraglottic tumors (clinically T1/T2, N0/N1, M0) combined with postoperative radiotherapy appears to be feasibly carried out in a multi-institutional setting. Disease control appears to be reasonable with this approach, with uncommon need for adjunctive tracheostomy and early swallowing recovery observed in the majority of patients.

## S106: Retronasal and Orthonasal Olfactory Ability After Laryngectomy

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**Objective:** To characterize orthonasal and retronasal olfactory ability in patients who have had a total laryngectomy (TL).

**Design:** Prospective psychophysical evaluation of orthonasal and retronasal olfactory function.

**Setting:** Academic center outpatient clinic.

**Patients:** Volunteer sample of 36 laryngectomized subjects 0.5 to 25 years after TL (median, 3.5 years) and 36 age-, gender-, and smoking history-matched controls.

**Main Outcome Measures:** Scores on established psychophysical tests of orthonasal and retronasal olfaction and self-rating scores of smell using a visual analog scale.

**Results:** Assessment of orthonasal olfactory ability yielded a mean composite score (maximum score = 7) of 4.3 for the TL group and 5.3 for the control group ( $P = .002$ ). Evaluation of retronasal olfactory ability resulted in a mean score (maximum score = 20) of 11.0 for the TL group vs 14.3 for the control group ( $P < .001$ ). The mean self-rating scores of smell (maximum score = 10) were 2.9 and 6.6 for the TL and control groups, respectively ( $P < .001$ ). Self-ratings of smell positively correlated with orthonasal ( $rS = 0.42$ ;  $P < .001$ ) and retronasal ( $rS = 0.50$ ;  $P < .001$ ) olfactory ability.

**Conclusion:** Laryngectomy is associated with measurable decreases in olfactory function that are also subjectively perceived.

Quantification of decrements in orthonasal and retronasal olfactory function can be used to characterize the severity of hyposmia and to assess the potential for, and efficacy of, olfactory rehabilitation.

Although self-assessment with a simple visual analog scale successfully identifies many candidates for laryngectomy who have objective evidence of olfactory dysfunction, further investigation is necessary to evaluate and compare its validity and reliability with other available survey instruments that purport to measure olfaction.

## S107: Contact YAG Laser Assisted Endoscopic Supraglottic Laryngectomy

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**Objectives:** To assess the use of the Nd:YAG laser in performing endoscopic supraglottic laryngectomy.

**Design:** Retrospective review of a case series.

**Setting:** Academic tertiary care referral center.

**Patients:** Seventeen consecutive patients (mean age, 63 years; range, 37-81 years) with cT1-T4aN0 supraglottic tumors.

**Intervention:** Nd:YAG laser-assisted endoscopic supraglottic laryngectomy and selective neck dissection (SND) (levels 2, 3, and 4).

**Main Outcome Measures:** Locoregional control, survival, and swallowing function.

**Results:** The majority (71%) of patients had advanced T-stage disease (T4a-4 [24%], T3-8 [47%], T2-4 [24%], and T1-1 [6%]) at the time of the procedure. Fourteen (82%) of the 17 patients underwent concomitant bilateral SND (levels 2, 3, and 4), 1 underwent delayed bilateral SND, and 2 underwent unilateral SND. Five patients underwent postoperative radiotherapy, with 4 of 5 receiving chemotherapy to the neck, shielding the primary site in all but 1 patient. At a mean follow-up of 14 months (range, 1-45 months), 16 patients (94%) had no evidence of disease and 1

died of their disease. The tumors in 3 patients (18%) recurred (2 of 17) or persisted (1 of 17) locally. The single mortality was from distant metastasis. Two (67%) of the 3 patients who underwent total laryngectomy had undergone the endoscopic supraglottic laryngectomy for salvage of a radiation failure. All patients have resumed oral feedings (median of 5 days postoperatively; range, 2-150 days). Four patients (24%) required temporary gastrostomy tubes.

**Conclusions:** The use of the Nd:YAG laser for endoscopic supraglottic laryngectomy has demonstrated excellent functional and oncologic results. We believe this technique has advantages over the use of CO<sub>2</sub> laser excision and recommend its routine use.

## S108: Proteasome Inhibition Reverses E6-Mediated p53 Degradation and Decreases Proliferation in Tonsil Epithelial Cells

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**Objective:** A relatively new class of anticancer agents known as proteasome inhibitors is available for treatment of certain human malignancies. This study will determine whether proteasome inhibition will reverse E6-mediated p53 degradation *in vivo* and *in vitro* to predict the feasibility of treatment of human papilloma virus (HPV)-associated head and neck cancer.

**Design:** Molecular analysis.

**Subjects:** Primary mouse tonsil epithelium cell lines transduced with a retrovirus containing HPV16 E6 model human HPV-associated head and neck cancer. The E6-expressing mouse tonsil epithelium cell lines are immortal and form tumors when implanted in isogenic, immune-competent animals. Human tonsil epithelial cells are similarly isolated and transduced, followed by treatment and analysis.

**Intervention:** We have tested whether proteasome inhibition with MG132 will reverse E6-mediated p53 degradation and tumor growth in vivo and in vitro.

**Results:** In cells that express E6, proteasome inhibition with MG132 restores p53 protein levels and decreases proliferation in a dose-dependent fashion that is significantly more pronounced compared with controls. However, inhibition of proliferation occurs at a much lower dose compared with restoration of p53 expression. Inhibition of growth in cells lacking p53 (p53 knock out) and normal cells is identical. Animals treated with MG132 show various responses, which will be discussed in detail.

**Conclusions:** These findings suggest proteasome inhibition preferentially inhibits proliferation in cells expressing E6, but this occurs through a p53-independent mechanism. These results support the use of proteasome inhibitors in head and neck cancer associated with HPV, but the mechanism for their effectiveness appears to be independent of restored p53.

## **S109: Adenovirus Armed With Tissue Inhibitor Metalloproteinase-2 Potentiates Combined Chemoradiation Therapy of HNSCC in Vivo**

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**Background:** Previous clinical trials assessing anti-MMP monotherapies have not demonstrated significant benefit despite promising pre-clinical data. Recent studies suggest that molecularly targeted agents work best in combination with radiation therapy (XRT) with minimal added morbidity. We hypothesized that a treatment including a replicating adenovirus armed with tissue inhibitor metalloproteinase-2 (TIMP-2) in combination with XRT, and/or cisplatin would result in an augmented treatment response and reduce tumor growth in vivo of HNSCC xenografts. In vivo, TIMP-2 inhibits several matrix metalloproteinases (MMPs) that are involved in growth, invasion, and metastasis of tumor cells. In addition, TIMP-2 has anti-angiogenic and other MMP-independent anti-tumor effects.

**Methods:** Both single-agent (Ad-TIMP2, XRT, or cisplatin alone) and the combination therapies (Ad-TIMP2/XRT, Ad-TIMP2/cisplatin, XRT/cisplatin, or Ad-TIMP2/XRT/cisplatin) were evaluated in vitro and in vivo. Several endpoints were evaluated for SCC1 cells in vitro. These included cell growth curves, MMP expression, TIMP-2 expression, and apoptosis. The single-agent and combination therapy strategies were then evaluated against SCC1 tumor xenografts in nude mice (7 mice/group). The efficacy of both single agent and combination therapies in vivo was determined by tumor growth and survival analysis. TIMP-2, MMP-2, apoptosis, proliferation, and angiogenesis were evaluated by immunohistochemistry. At 14 days after SCC1 tumor cell injection (when tumors were 6-8 mm in diameter), mice received 3 mg/kg cisplatin 1 h prior to XRT treatment (2 Gy) every 4 days for 2 weeks. Mice received intratumoral injections of Ad-TIMP-2 (1 x 10<sup>8</sup> particles on days 2 and 9) after the first dose of cisplatin and XRT.

**Results:** In vivo expression of TIMP-2 in the Ad-TIMP-2 treated groups was confirmed by western blot analysis. Radiation, cisplatin, or Ad-TIMP-2 monotherapy produced minimal reduction in tumor growth rate of SCC1 subcutaneous HNSCC xenografts as compared to untreated control tumor growth. However, Ad-TIMP-2/XRT and Ad-TIMP-2/XRT/cisplatin resulted in a statistically significant tumor response with the combination therapies in the SCC1 xenograft nude mice compared to untreated controls and tumor treated with monotherapy.

**Conclusion:** These data indicate that Ad-TIMP-2 gene therapy potentiates therapy with either XRT or XRT and cisplatin. These data suggest that molecularly based anti-MMP therapies may require combined therapies.

## **S110: (-)-Gossypol, a BH3 Mimetic and Inducer of Apoptosis in Head and Neck Cancer Cells, Is Oxidized and Deactivated by ROS**

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**Objective:** To determine the contribution of reactive oxygen species (ROS) in (-)-gossypol-induced cell death in head and neck squamous cell carcinoma (HNSCC) cell lines.

**Design:** The HNSCC cell lines were treated with (-)-gossypol, and generation of ROS was measured by fluorescence microscopy and flow cytometry. Cells were treated with (-)-gossypol and/or antioxidant, or with (-)-gossypol that was pretreated with hydrogen peroxide. Following treatment, generation of ROS was measured, and cell survival was assayed.

**Results:** Treatment with (-)-gossypol induces generation of ROS in HNSCC cell lines. Concurrent treatment with antioxidant lowers ROS at early time points (12 hours) but increases ROS at 24 hours. Cell number after 24 hours of treatment with (-)-gossypol alone fell to 30% to 35% of control and dropped further to 8% to 15% of control with (-)-gossypol and antioxidant combination. Antioxidant alone is nontoxic (90%-110% vs untreated controls). Loss of viability as assessed by trypan blue exclusion assay indicate that concurrent antioxidant treatment increases the cytotoxic efficacy of (-)-gossypol. Pretreatment of (-)-gossypol with hydrogen peroxide, followed by peroxide inactivation, effectively protected HNSCC cells from induction of cell death by (-)-gossypol.

**Conclusions:** These results, combined with evidence in the literature regarding oxidation/metabolism of (-)-gossypol, suggest that intracellular ROS generated by (-)-gossypol (likely through redox cycling at the mitochondria) may act as a negative feedback loop to deactivate (-)-gossypol and inhibit its potent antitumor activity. Concurrent treatment with antioxidant may effectively increase efficacy of (-)-gossypol in vitro and in vivo in HNSCC.

## **S111: Recombinant Erythropoietin Beta Stimulates Growth of Squamous Cell Carcinoma in Vitro and in Vivo**

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**Objective:** Treatment of anaemia with recombinant human erythropoietin beta (rHuEpo) has been hypothesised to improve outcome of curative radiotherapy among patients with head and neck squamous cell cancer (HNSCC). However, Henke et al. (1) showed that rHuEpo does not improve cancer control. In fact, incompletely resected patients with HNSCC receiving radiation in combination with rHuEpo showed poorer loco regional progression-free survival than patients receiving radiation in combination with placebo.

Our objective was to examine the effect of recombinant erythropoietin beta (rHuEpo) on the growth of human squamous cell carcinoma under different conditions in vitro, as well as in vivo, alone and in combination with surgical trauma.

**Method:** In vitro an HNSCC-line without p53 mutation or cyclin D1 gene amplification was used. It expressed the EPO-receptor. The in vivo-effect of surgical trauma +/- rHuEpo on growth of the cell-line above was tested in two settings. I/ The effect on solid tumour growing as s.c. xenografts on nude mice was evaluated by measuring the tumour volume growth. The animals were divided into three groups; A/ control + NaCl, B/ surgery + NaCl and C/ Surgery + rHuEpo. The surgical trauma was inflicted through a s.c. transection of the tumour with a needle. rHuEpo / NaCl (0.2 ml / g b.wt.) was administered by s.c. injection every third day starting from day of transplantation, and the tumour size was measured in two dimensions three times/week. The tumour growth was followed for at least two doubling-times. II/ Four perforations of the abdominal wall was made with an injection needle, and through a fifth a cell suspension of the HNSCC-line was then administered i.p. The time to development of metastasis in the perforations were measured.

**Results:** Under FCS- (foetal calf serum) deficient conditions in vitro rHuEpo in high concentrations stimulated cell growth. rHuEpo alone had no effect on the growth of solid xenografted HNSCC. However, a significant increase ( $p=0.0074$ ) in the tumour growth was observed after surgical trauma in combination with rHuEpo as compared to surgery alone. rHuEpo also shortened the time to development of porthole metastasis.

**Conclusion:** 1) rHuEpo effects (in physiological concentrations) on HNSCC growth and might only be manifested in vivo and after cell trauma. 2) Correcting anaemia with rHuEpo might contribute to poor outcome after incomplete surgical resection. 1/ Henke et al. Erythropoietin to treat head and neck cancer patients with anaemia undergoing radiotherapy: randomised double blind, placebo-controlled trial. *Lancet*, vol 362, 1255, 2003

## S112: Assessment of Fluorescent Immunoguided Neoplasm Detection to Identify Microscopic Disease in Vivo

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**Background/Objective:** During ablative head and neck cancer procedures, a surgeon's assessment of tumor extent is dependent on subtle tissue changes and palpation. Accurate assessment of tumor extent by fluorescent optical imaging has the potential to provide surgeons real-time, intraoperative information about the local extent of tumor and the presence of residual disease.

**Study Design:** Orthotopically inoculated head and neck squamous cell carcinoma cells UM-SCC-1 ( $n = 6$ ), CAL 27 ( $n = 6$ ), or saline-injected controls were monitored for 14 days and then underwent mock surgical resections. Antiepidermal growth factor receptor antibody (cetuximab) was labeled with a near-infrared fluorochrome, Cy5.5. The cetuximab-Cy5.5 conjugate was systemically administered by tail vein injection 3 days prior to the resection. Near-infrared fluorescent monitoring was performed before resection and after partial and complete surgical excision of the tumors. After resection, the mandible and attached soft tissues were resected, paraffin embedded, and serial sectioned.

**Results:** After transcervical serial tumor resections, near-infrared stereomicroscopy was used to detect residual disease attached to the soft tissues or mandible in both cell lines. Histological analysis of serial sections of the mandible and floor of mouth after resection demonstrated that in every case negative fluorescence corresponded to the absence of residual tumor. The smallest residual disease that could be detected (SCC-1 cell line) was 0.7 mm. The location of residual disease visualized by fluorescence stereomicroscopy was confirmed on histological sections.

**Conclusion:** Near-infrared stereomicroscopy after systemic administration of cetuximab labeled with Cy5.5 may enable surgeons to visualize residual disease intraoperatively.

## S113: Interactions of Dietary Factors in Oral Cancer

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**Introduction:** The role of diet in cancer in general has been debated a great deal in the recent past. Case-control studies have suggested that diet could have an impact on the risk of oral cancer; a complication of these, however, is that a number of non-diet factors have also been identified: cigarette smoking, alcohol consumption, and compromised dentition.

**Methods:** A case-control study with 300 cases and age- and gender-matched controls, conducted in Western New York, collected data on diet by a food frequency questionnaire, along with a dental history questionnaire, along with questions on lifelong tobacco use and alcohol consumption.

**Results:** The findings confirmed that cigarette smoking, alcohol consumption and poor dentition increased oral cancer risk substantially: the relative risk associated with the second tertile of alcohol consumption was approximately 2 ( $p<.05$ ), and the relative risk associated with the third tertile was nearly 11 ( $p<.01$ ). A history of cigarette smoking was associated with a relative risk of nearly 4 ( $p<.05$ ). Compromised dentition, represented by the use of dentures, or by

teeth filled, or missing and not replaced, was associated with a doubling of relative risk ( $p<.05$ ). This study showed that, even with control for these risk factors, several dietary factors, including vitamin D, vitamin A, and dietary fiber, appeared to alter risk. Our analyses indicate that, with adjustment for tobacco, alcohol and dentition, dietary fiber is associated with an approximately 50% decrease in the risk of oral cancer; the relative risk associated with the top quartile of fiber intake was .54 ( $p<.05$ ). This pattern persists within strata of tobacco, alcohol and dentition, and it does not appear to be an artifact of cancer or cancer treatment.

**Conclusions:** In spite of evidence that vitamin D and vitamin A intake are protective against oral cancer, we find no evidence of protection in these data. The strongest dietary risk factor is fiber intake.

## S114: VEGF-C Expression Alters Tumor Cell Invasion in Squamous Cell Carcinoma of the Head and Neck

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**Objective:** Squamous cell carcinoma of the head and neck (SCCHN) is an aggressive disease, and lymphatic metastasis and local invasion are hallmarks of disease progression. Little is known about the biochemical factors that influence tumor cell invasion and metastasis. Vascular endothelial growth factor C (VEGF-C), a member of the VEGF family, has emerged as critical cytokine for normal lymphatic development, and recent studies have demonstrated that VEGF-C overexpression is associated with lymphatic metastasis in various human tumors. VEGF-C is also known to be highly expressed in peritumoral lymphatics of head and neck cancers. These studies were initiated to determine how VEGF-C levels affect SCCHN motility and invasion.

**Methods:** The entire human VEGF-C coding sequence was cloned into an expression plasmid, and a stable VEGF-C overexpressing SCCHN cell line was isolated, SCC116-VEGF-C. RNA levels were determined by quantitative real-time PCR, and protein expression was evaluated by western blot. Cellular invasion was evaluated by 24-hour semi-permeable membrane transit assay. RNA inhibition constructs were selected and designed for use with the Ambion pSilencer expression system. Adenoviral RNAi vector cloning was performed in conjunction with the University of Iowa Vector Core.

**Results:** SCC116-VEGF-C cells demonstrated increased expression of VEGF-C at the protein and RNA level compared to normal SCC116 controls. Using a semi-permeable membrane invasion assay, SCC116-VEGF-C cells demonstrated marked increases in cellular invasion and motility. We screened a panel of 5 different RNA inhibition (RNAi) sequences for the ability to block VEGF-C expression in SCCHN. We identified an RNAi sequence that would block VEGF-C expression more than 80% at the RNA and protein level, and cloned this sequence into a siRNA expression vector to determine the effects of VEGF-C knockout on SCCHN cellular invasion in vitro. Transfection of this VEGF-C siRNA expression vector into both SCC116 and SCC116-VEGF-C cells for 24 hours led to a 40-50% decrease in SCCHN invasion and motility as tested by membrane invasion assay. We developed an adenoviral expression system for this same VEGF-C RNAi sequence, and demonstrated a dose-dependent decrease in VEGF-C RNA expression and cellular invasion with increasing MOI adenoviral transfection, confirming the results from the previous DNA transfection experiments.

**Conclusions:** These studies demonstrate that intracellular VEGF-C levels are crucial for the progression of in vitro SCCHN motility and invasion. Further work is needed to clarify the specific receptors and signalling pathways that are involved in this phenomenon.

## S115: The Receptor Tyrosine Kinase c-MET Is Mutated in Head and Neck Cancer and Is a Promising Novel Target

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**Objective:** To determine mutations of the receptor tyrosine kinase c-MET in head and neck squamous cell carcinoma (HNSCC) and evaluate c-MET as a potential novel target using c-MET inhibitor SU11274.

**Design:** A total of 128 HNSCC, dysplastic, and normal tissues (using immunohistochemistry) and 7 HNSCC cell lines (using immunoblot) were evaluated for c-MET, phospho-c-MET, and hepatocyte growth factor.

**Interventions:** In 5 cell lines, c-MET was inhibited using SU11274/small interfering RNA (siRNA). Effects on signaling, viability, and motility were determined. Mutational analysis of HNSCC tumor tissue samples (n = 29) and cell lines (n = 7) was done.

**Results:** Eighty-four (66%) HNSCC tumor samples overexpressed c-MET/phospho-c-MET pY1003 (dysplasia, n = 30 [64%]). Normal tissue had the lowest rate of overexpression (n = 21 [23%]). pY1230/1234/1235 overexpression was less prominent. Cytoplasmic HGF expression was seen. All cell lines showed c-MET expression. Five HNSCC cell lines were treated with SU11274. Phospho-tyrosine immunoblots showed SU11274 dose-dependant effects. Specifically,

SU11274 lead to inhibition of c-MET signaling, with decreased levels of phospho-c-MET (pY1003 and pY1230/1234/1235), phospho-Akt (pT308), phospho-Erk1/2 (pTpY185/187), phospho-p70S6K (pT389), and phospho-SHP2 (pY542) at 2mM and complete abrogation at 5mM. Viability assays with SU11274 and siRNA decreased cell growth in 3 HNSCC cell lines (30%-75%). Hepatocyte growth factor stimulation had no effect consistent with autocrine HGF production. Mutational analysis of 29 tumor tissues and 7 cell lines revealed 2 novel mutations in the SEMA (T230M) and JM (T1010I) domains.

**Conclusions:** (1) c-MET is overexpressed in HNSCC. (2) Two novel c-MET mutations in HNSCC were identified. (3) Inhibition of c-MET leads to a marked decrease in cell growth. Accordingly, c-MET is a promising target in HNSCC.

## P001: Phase I Study of Erlotinib, Docetaxel and Radiation in Locally Advanced Squamous Cell Cancer of the Head and Neck

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**Background:** Epidermal growth factor receptor (EGFR) is highly expressed in squamous cell cancer of the head and neck (SCCHN), representing a promising therapeutic target. Erlotinib (E) is an EGFR tyrosine kinase inhibitor that may potentiate the efficacy of concurrent radiation (RT) and docetaxel (D). We sought to establish the maximum tolerated dose, toxicities, and preliminary efficacy of the combination of RT, D and E in patients with SCCHN.

**Methods:** Patients with previously untreated stage III-IVB SCCHN were enrolled in a phase I dose-escalating study with standard once-daily RT (70.2 Gy, 1.8 Gy/d), weekly D for the duration of RT, and daily E for 2 weeks prior, during, and up to 2 years following RT. Four dose levels were evaluated (D [mg/m<sup>2</sup>]/E [mg]: 15/50, 15/100, 20/100, and 20/150). A 3 + 3 escalation design was followed. Pharmacokinetic studies were performed.

**Results:** A total of 23 patients were enrolled. The primary site include the oral cavity (n = 1), pharynx (n = 15), and larynx (n = 7). Twenty patients (87%) had stage IV disease. In patients enrolled at dose level 13 (n = 18), postconcurrent chemoRT, best response was CR (n = 15), not evaluable (n = 2), death on study (n = 1). Three of 3 patients who underwent planned neck dissection had a pathologic CR. Three patients had relapsed. Significant interpatient variability of E peak plasma concentrations measured after the first dose was observed at all dose levels.

**Conclusion:** The combination of daily erlotinib with weekly docetaxel and RT for patients with stage III-IVB SCCHN is feasible and active. A phase II trial is planned. Supported in part by National Institutes of Health grants CA62502 and M01 RR-000080.

## P002: Endoscopic CO<sub>2</sub> Laser Supraglottic Laryngectomy

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**Objective:** The purpose of this study was to evaluate surgical complications and oncological and functional outcomes after endoscopic CO<sub>2</sub> laser epiglottectomy in patients with supraglottic carcinomas.

**Design:** Monocentric case series (mean follow-up, 48.3 months).

**Setting:** Tertiary care center.

**Patients:** This case series was composed of 31 patients suffering from epiglottis squamous cell carcinoma. The mean age was 65.2 years.

**Interventions:** The patients were operated on by an endoscopic approach with the use of a CO<sub>2</sub> laser.

**Main Outcome Measures:** The survival rate was correlated with demographic factors, tumor extension, locoregional dissemination, and metastasis statute.

**Results:** All cases but two were primary surgery. None of the patient had a tracheostomy. In 14 cases, the initial tumor was localized at the lateral of the epiglottis, while 7 cases were medially situated. The tumor was extended to the false vocal cord in 22 cases. Twenty-four cases were classified as T2, with 28 cases categorized as cN0 and 17 as pN0. The overall survival was 56% at 120 months. The mean postoperative hospitalization was 13 days. Two cases of pneumopathy and 2 cases of postoperative bleeding were reported. Age ( $P = .01$ ), associated laryngeal lesions ( $P = .03$ ), previous surgery ( $P = .003$ ), and previous treatment for their epiglottis diseases ( $P = .03$ ) were associated with a poor survival.

**Conclusions:** Endoscopic supraglottic laryngectomy is a validated alternative to external approach for epiglottis carcinomas. This technique is of particular interest for debilitated patients, considering the low rate of postoperative complications and the reduced hospitalization duration.

## P003: Survival and Prognostic Factors in Squamous Cell Carcinoma of the Retromolar Trigone Treated with Primary Surgery

**D. Lal**; G.J. Petruzzelli

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**Objectives:** To review our experience in treating squamous cell carcinoma of the retromolar trigone with primary surgery and to evaluate factors affecting locoregional control and survival.

**Design:** Retrospective study.

**Setting:** University hospital.

**Patients:** The charts of 51 patients with squamous cell carcinoma of the retromolar trigone who underwent surgery from October 1993 to March 2006 were reviewed. Ten patients had received prior treatment. Forty-one patients with previously untreated disease underwent primary surgery and were the focus of this study. They included 25 men and 16 women aged 40 to 83 years. Three had T1, 13 had T2, 11 had T3, and 14 had T4 lesions. Twenty-four patients had N0, 7 had N1, 10 had N2, and none had N3 disease. All patients had M0 disease. Two patients had stage I, 8 had stage II, 10 had stage III, and 21 had stage IV disease. Thirty-nine patients underwent neck dissection; nodal metastasis was present in 19 and extracapsular spread in 14. Twelve patients had bone invasion. Twenty-one patients underwent postoperative radiation.

**Outcome Measures:** Overall survival and locoregional control.

**Results:** The median follow-up was 45 months overall and 57 months for living patients. The median survival time was 62 months. The overall 2-year survival and 5-year survival were 83% and 54%, respectively, using the Kaplan-Meier method. Four patients had local, and 1 patient had regional recurrence. Two patients had delayed lung metastasis. The overall locoregional control rate was 76%.

**Conclusions:** Primary surgical treatment of squamous cell carcinoma of the retromolar trigone is effective in locoregional control and survival. Lower disease stage favors prognosis.

## P004: Dental Patient Attitudes Toward Alcohol Screening for Oral Cancer Risk Reduction

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Medical University of South Carolina, Charleston

**Objective:** To investigate dental patient attitudes toward the acceptability of alcohol screening and counseling by dentists to reduce oral cancer risk.

**Design:** All newly arriving clinic patients during an 8-week time period were asked to complete brief questionnaires.

**Setting:** University emergency walk-in dental clinic.

**Patients:** A convenience sample of 433 low-income patients.

**Interventions:** Participants completed the Alcohol Use Disorders Identification Test-C (AUDIT-C), a 3-item alcohol screening test, and a patient opinion survey consisting of 10 items related to attitudes about the acceptance of alcohol screening questions, emotional reactions to alcohol screening, and acceptance of advice to reduce alcohol use by dentists. Opinion statements were rated on a 5-point Likert scale from strongly agree to strongly disagree.

**Main Outcome Measure:** Total scores on an alcohol screening attitude questionnaire and the AUDIT-C.

**Results:** A total of 24% of patients screened positive for heavy alcohol use on the AUDIT-C. Younger patients (age, 18-49 years) scored significantly ( $P = .001$ ) higher on the AUDIT-C compared with older patients (age >50 years). The vast majority of patients (83%) moderately or strongly agreed that their dentist should inquire about their drinking habits, with over 90% in favor of dentists counseling patients about heavy drinking. Only 25% would be embarrassed by alcohol questions, with 23% reporting that they would be annoyed by alcohol screening.

**Conclusions:** These findings support the conclusion that the vast majority of patients would readily accept alcohol screening and counseling by their dentists.

## **P005: Reconsideration of the Indications for Neck Dissection After Chemoradiation for Oropharyngeal Squamous Cell Carcinoma**

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University of California, San Francisco

**Objective:** To analyze the pathological outcomes of neck dissections performed for clinical partial responders after chemoradiation for oropharyngeal squamous cell carcinoma with neck metastasis.

**Design:** Retrospective review.

**Setting:** Tertiary academic medical center.

**Patients:** Twenty-nine patients who underwent neck dissections after chemoradiation for oropharyngeal squamous cell carcinoma.

**Interventions:** Review of radiographic studies and pathology reports.

**Main Outcome Measures:** Presence of tumor cells in neck dissection specimen and association between pathological outcomes and postchemoradiation radiographic findings.

**Results:** Twenty-two (81%) of the 27 neck dissections for presumed partial response contained no residual tumor cells on pathologic analysis. Another 3 (11%) had rare tumor cells of questionable viability, and only 2 (7%) contained definite residual tumor. No association was found between the presence of tumor cells and the size of the residual neck node ( $P = .45$ ).

**Conclusions:** The vast majority of neck dissections carried out for patients with a clinical partial response to chemoradiation did not yield residual tumor cells on pathological analysis. This calls into question the adequacy of current patient selection criteria for post-radiation neck dissection, which rely heavily on post-radiation radiographic studies. While the data do not dispute the regional control benefit of post-radiation neck dissection for this patient population as a whole, it is likely there is a subset of clinical partial responders who in fact had a pathologic complete response and presumably may not have benefitted from a neck dissection. Our results suggest that a reconsideration of the indications for neck dissection following definitive chemoradiation treatment of oropharyngeal squamous cell carcinoma is warranted.

## **P006: Multimodal Therapy Improves Outcome in Recurrent Medullary Thyroid Cancer**

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**Introduction:** Despite seemingly appropriate treatment of Medullary thyroid carcinoma, recurrence rates occur in up to 30% of patients. Local and systemic therapies have been directed at treating recurrence with varying results. It is necessary to evaluate the outcomes of various treatment approaches in order to help develop strategies for optimizing patient care. The purpose of this study is to assess the effectiveness of re-operative surgery alone, and in combination with systemic therapy for the treatment of locoregional recurrent medullary thyroid cancer.

**Methods:** We reviewed our database of patients treated for medullary thyroid cancer over the past 35 years. Cases of recurrent disease were further examined to determine time to recurrence, site of initial disease recurrence, and management of recurrence. Additionally, serum calcitonin levels before, during, and following the treatment of recurrence were acquired when available. Calcitonin levels less than 150 pg/ml following treatment were considered 'normalized'. Mean, five, and ten-year survival rates were used as primary endpoints.

**Results:** Thirty patients treated for medullary thyroid cancer were identified. Twenty patients (67%) developed recurrence. Eight patients (40%) had recurrent disease limited to locoregional sites. The mean time to recurrence was 5.7 years (range 1-13 years), with 42% of patients recurring after 5 years, and 16% recurring after 10 years of follow-up. All cases of recurrent disease were associated with an elevated serum calcitonin. For all patients the serum calcitonin level remained elevated despite treatment of recurrent disease. The overall survival rate for locoregional disease recurrence was 29% with a mean survival of 6.3 years (5YS 43%, 10YS 14% respectively). Treatment with surgery alone resulted in a mean survival of 3.7 years (5YS 33%, 10YS 0% respectively). The use of surgery and chemotherapy (The most commonly used chemotherapeutic agent in

our series was Adriamycin, followed by 5-FU) yielded a mean survival of 8.3 years (5YS 50%, 10YS 25% respectively). There were no deaths observed in patients who remained disease free following initial therapy.

**Conclusions:** Recurrent disease associated with decreased survival. Nearly half of all recurrences occurred more than 5 years after initial treatment demonstrating the necessity of long-term surveillance. Following the treatment of recurrence, calcitonin levels remained elevated suggesting, the presence of occult residual disease. Combining systemic and local therapies may have a beneficial role in the treatment of local and regional recurrent MTC.

## **P007: False Negative Cases of Touch Smear Cytology in Thyroid Tumor**

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**Objective:** Cytological diagnosis, such as fine-needle aspiration (FNA), has been frequently used for the one of preoperative diagnosis. Touch smear cytology (TS) also has been used for the screening of gynecologic malignant tumor. We used this TS technique instead of the frozen section diagnosis. However, there are some false-negative cases that result to misdiagnosis. Therefore, the purpose of this study is to investigate the cause of false-negative cases.

**Patients:** The population investigated consisted of 234 pathologically confirmed thyroid tumor cases in which FNA was performed before operation or biopsy and TS were performed at the time of operation. Of these 234 cases, 150 cases are pathologically benign tumor and the remaining 84 cases are malignant tumor.

**Results:** There are 12 false-negative cases of 84 malignant cases by TS, whereas there are 38 false-negative cases of 143 by FNA. The diseases of these false-negative cases by TS consist of 8 follicular carcinoma cases of 15 and 4 papillary carcinoma cases of 63. There are no false-negative cases in other malignant tumors. Together with TS and FNA, the possibility of malignancy could not be suspected in only 3 (1 papillary and 2 follicular carcinoma) cases.

**Conclusions:** The sensitivity of TS in thyroid tumor is 85.7%, the specificity is 95.3%, and the accuracy is 91.9%. False-negative rate is reduced by a combination of the preoperative FNA and TS at time of operation. Touch smear cytology is a useful method to avoid misdiagnosis in thyroid tumor.

## **P008: Preoperative Imaging Diagnosis of the Nerve of Origin in Schwannomas of the Parapharyngeal Space**

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**Objective:** To determine if preoperative radiographic images can predict whether a schwannoma of the parapharyngeal space originates from the vagus nerve or the cervical sympathetic chain.

**Study Design:** A retrospective review of 12 patients who underwent surgical resection of schwannomas of the parapharyngeal space. The nerve of origin was identified based on operative findings and post-operative physical examinations. Eleven patients (11 of 12) had pre-operative magnetic resonance imaging (MRI) studies and 1 patient (1 of 12) underwent a contrast-enhanced computerized tomography scan. A neuroradiologist reviewed the imaging studies, blinded to the surgically determined nerve of origin. For each case, it was predicted whether the tumor arose from the vagus nerve or sympathetic chain based on the location of the schwannoma with reference to the carotid sheath vessels.

**Results:** Five patients (42%) had schwannomas from the cervical sympathetic chain and 7 (58%) had schwannomas of the cervical vagus nerve. By preoperative imaging, the nerve of origin was successfully determined in 4 (80%) of 5 cases of sympathetic chain schwannoma and in 7 (100%) of 7 cases of vagal nerve schwannoma. Schwannomas of the cervical sympathetic chain tend to displace the carotid and jugular vessels without separating them. Vagal nerve schwannomas tend to splay the carotid arteries from the internal jugular vein. A vagal schwannoma may also displace the sheath vessels posteriorly, without splaying them.

**Conclusions:** Vessel displacement produced by schwannoma growth in the parapharyngeal space can be useful to predict the likely nerve of origin. This determination allows for effective preoperative counseling regarding the expected sequelae of surgical resection.

## **P009: Efficacy of COX-2 Inhibitors on Tumor Anorexia-cachexia Syndrome in Patients With Head and Neck Cancer**

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**Objective:** Nonsteroidal anti-inflammatory drugs (NSAIDs) may palliate cachexia by maintaining muscle mass. A recent animal study demonstrated that cyclo-oxygenase-2 inhibitors (COX-2) reversed tumor-induced wasting in mice bearing human head and neck squamous cell carcinoma and colon carcinomas. Our hypothesis was that NSAIDs given to patients with cancer cachexia will stabilize or reverse their loss of lean body mass.

**Methods:** A prospective, randomized, double-blind, placebo-controlled clinical trial was designed to determine whether intervention with the COX-2 inhibitor celecoxib was effective at improving cancer cachexia in patients with cancer of the head and neck, and gastrointestinal (GI) tract. After the clinical diagnosis of cachexia was established, the following measurements were made: weight; body composition via dual X-ray absorptiometry; resting energy expenditure (REE) via indirect calorimetry; quality of life (QoL) surveys via Functional Assessment of Anorexia/Cachexia Therapy (FAACT) and performance status via Karnofsky Performance Scale (KPS). Patients were randomized to receive either celecoxib 200 mg po bid or placebo for three weeks. Three weeks later, each patient returned for the same evaluation as on day 1. In this pilot study, no nutritional intervention was made.

**Results:** Eleven patients have completed the study thus far. Seven have received placebo, while four have received active drug. Eight patients have head and neck cancers and three patients have cancer of the GI tract. All were male, with a mean age of 59.1 years. Interim unblinded analysis of the data reveals that, on average, patients taking celecoxib experienced weight gain of 1.0 kg (SE=1.33), body mass index (BMI) increase of 0.31 (SE=0.45), lean body mass percent (LBM%) increase of 0.28 (SE=2.81), and improvement of FAACT score of 10 points (SE=4). Those taking placebo experienced, on average, weight loss of 1.0 kg (SE=1.63), BMI decrease of 0.56 (0.68), LBM% drop of 0.04% (SE=1.60), and no improvement in FAACT score.

**Conclusions:** Promising initial trends were seen in the administration of celecoxib to patients with cancer cachexia in this study, including in weight gain, BMI, LBM%, and QoL score. Future studies may examine cytokine and C-reactive protein (CRP) levels and may include a nutritional intervention in studying the effect of anti-inflammatory therapy on cancer cachexia.

## **P010: The Correlation of Clinical to Pathologic Neck Response After Radiation or Chemoradiation of N2-N3 Head and Neck Cancer**

**B.J. Park**; J.M. Hsu

SUNY Upstate Medical University, Syracuse

**Objective:** To compare the incidence of residual pathologic disease in the neck between complete and incomplete responders after primary radiation or concurrent chemoradiation for N2 and N3 squamous cell carcinoma of the head and neck.

**Design:** Retrospective chart review.

**Setting:** Academic tertiary care medical center.

**Patients:** A consecutive series of 28 patients with previously untreated squamous cell carcinoma of the oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx with N2 or N3 nodal disease treated with definitive radiation followed by planned neck dissection between January 1998 and January 2006 at the SUNY Upstate Medical University Department of Otolaryngology. Twenty-six of the 28 patients also underwent concurrent chemotherapy. Patients treated with primary surgery were excluded.

**Main Outcome Measure:** Pathologic status of the neck.

**Results:** Seven (25%) of 28 patients had a complete clinical response in the neck, while 21 (75%) had an incomplete response.

After analysis of neck dissection specimens, 16 (57%) of 28 patients revealed a complete pathologic response, while 12 (43%) were incomplete. Of the 7 complete clinical responders, 3 (57%) had residual pathologic disease. Similarly, of the 21 incomplete responders, 9 (57%) had residual cancer.

**Conclusions:** Radiation with or without chemotherapy of bulky nodal disease in patients with head and neck squamous cell carcinoma did not leave an insignificant incidence of residual cancer in our study. Moreover, the incidence of pathologic disease was similar between complete and incomplete responders. Based on these data, we believe treatment should not differ between these 2 groups and should include planned neck dissection regardless of clinical response.

## **P011: Clinical and Histopathological Correlation With Skip Metastases in Oral Cavity Cancer: How Important Is This Issue?**

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**Objective:** To evaluate the rate of skip metastases according to clinical stage of primary lesion and determine the pattern of distribution of lymphatic metastases in oral cavity cancers.

**Design:** Retrospective nonrandomized trial.

**Setting:** Tertiary referral university center.

**Patients:** The charts of 50 patients with squamous cell carcinoma of oral cavity were studied.

**Intervention:** Supraomohyoid neck dissection was performed and each surgical specimen was marked denoting the dissected levels. Each neck dissection was considered individually. Skip metastases was considered isolated metastases to level IIB, III, IIIB, or IV.

**Main Outcome Measures:** The prevalence of histopathologically proven neck metastases for each neck level for neck dissections was related. The rate of skip metastases was calculated and correlated with clinical stage of primary lesion.

**Results:** Fifty-eight percent of patients presented at clinical stage I and II and 42% at stages III and IV. Unilateral neck dissection was performed in 38 patients and bilateral in 12, with a total of 62 sides dissected. Skip metastases were found in 8% of neck dissections. There was no statistically significant correlation between advanced stages and presence of skip metastases. Eleven percent of the metastases were located at level I, 13% at level II, 16% at level III, and 8% at level IV.

**Conclusions:** Skip metastases were found in 8% of all necks. There was no statistically significant correlation between advanced stages and presence of skip metastases. Eleven percent of the metastases were located at level I, 13% at level II, 16% at level III, and 8% at level IV.

## **P012: Fine-Needle Aspiration Biopsy of the Thyroid: Atypical Cytopathology**

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**Objectives/Hypothesis:** The objective of this study was to evaluate the positive predictive value of a thyroid nodule being malignant when described as atypical by the pathologist and to determine the usefulness of commonly reported cytopathological features in thyroid nodule fine-needle aspiration biopsy (FNAB).

**Methods:** This is a retrospective review of 111 consecutive patients who underwent thyroid surgery after presenting with a FNAB result categorized as atypical on cytopathological evaluation using Kini's criteria for the diagnosis of papillary carcinoma. An atypical FNAB result was designated when the specimen met 3 of the criteria or when the specimen had fewer than 3 but had other types of cytologic atypia.

**Results:** Between January 2000 and November 2005, 111 patients with FNAB categorized as atypical were included in the study. Of these, 62 patients (56%) were diagnosed with a thyroid malignancy postoperatively. The remaining 49 patients' FNAB samples (44%) were benign. Univariate analysis comparing cytological features between the 2 groups (malignancy vs benign) is as follows: micronucleoli (71% vs 49%;  $P = .01$ ), nuclear grooves (50% vs 30%;  $P = .03$ ), and powdery chromatin (37% vs 16%;  $P = .01$ ). Probability of malignancy

nancy was 83% if a combination of nuclear grooves, powdery chromatin and micronucleoli was present. If none of these cytologic features were present the probability drops to 32%.

**Conclusions:** At our institution, when a thyroid nodule FNAB is diagnosed as atypical, it is malignant 56% of the time. Moreover, the presence of micronucleoli, nuclear grooves and powdery chromatin, increases the likelihood that a specimen determined to be atypical is in fact malignant.

## **P013: Carotid Body Tumors**

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**Background:** Paragangliomas of the head and neck (HNP) are rare tumors of neural crest origin comprising 0.6% of head and neck tumors and 0.03% of all tumors. Carotid body tumors (CBT), a subset of HNP, are highly vascular, but rarely malignant tumors that can occasionally be familial and can recur. Surgery is the preferred treatment. However, there is therapeutic uncertainty regarding preoperative workup (specifically angiography and embolization), operative risk, and postoperative management should the tumor be malignant and/or recur. We describe our experience and management of these rare tumors.

**Methods:** Forty consecutive patients undergoing surgery for CBT over a ten-year period were identified from our institutional database. Demographics, pre operative work up, treatment and pathological diagnosis were entered into a computerized database. Only patients with pathological diagnosis of CBT were included in this study (Schwannomas and vagal or sympathetic chain paragangliomas were excluded). The primary endpoints analyzed included preoperative, imaging, including angiography and embolization, intraoperative estimated blood loss (EBL), operative complications and overall survival. Follow-up intervals were calculated from date of CBT resection.

**Results:** There were 24 females and 16 males with a median age of 48.7 years (range 19-72) who underwent resection of CBT. Four patients had a family history of CBT. Five patients had previous HNP (4/5 underwent prior surgery). 33/40 patients presented with a mass in the neck; four had cranial nerve deficits. Preoperative work-up included biopsy 15/31 (all at outlying hospitals) and imaging (14 CT Scan, 4 MR-angiogram, 21 MRI, 3 MRI/MRA). Of the 40 surgeries, only ten patients underwent preoperative angiogram (all at outlying hospitals), of which 2/40 (5%) CBT were embolized. The two CBT that were embolized extended well into the skull-base. Median operative time was 220 minutes with a median EBL of 100 ccs. Meticulous dissection with liberal use of bipolar cautery, was employed in all patients. Average length of stay was 4 days. Post operative complications included 3 patients with cranial nerve injuries (1 CN XII, 2 CN X). Three CBT were malignant based on tumor extension with local invasion and/or histopathological features. There were no post operative deaths.. One had unresectable residual disease (pathology confirmed malignancy, and patient underwent post-operative external beam radiation). No patients had recurrence of disease at the conclusion of this study.

**Conclusion:** Our data supports non-invasive preoperative work-up of CBT to include MRI +/- MRA, avoiding potential risks associated with angiography and embolization. Although highly vascular, if resected with meticulous surgical technique CBT surgery can be performed with minimal blood loss or complications and excellent outcome.

## **P014: Determination of the Function of the Internal Branch of the Superior Laryngeal Nerve After Thyroidectomy**

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**Objective:** To determine if the function of the internal branch of the superior laryngeal nerve is altered after thyroidectomy.

**Design:** Prospective cohort of patients undergoing thyroidectomy. All patients underwent preoperative and postoperative laryngopharyngeal sensory testing.

**Setting:** Academic medical center.

**Patients:** Thirty-three patients undergoing thyroidectomy were enrolled. Patients with a history of neurological disease or dysphagia unrelated to the thyroid were excluded.

**Interventions:** Patients were evaluated preoperatively and postoperatively. Patient characteristics and historical data were compiled. Flexible laryngoscopy with sensory testing was performed to determine laryngopharyngeal sensory thresholds.

**Main Outcome Measure:** Changes in laryngopharyngeal sensory thresholds were compared before and after surgery.

**Results:** Preoperatively, 16 patients (49%) reported dysphagia, 13 (39%) reported dyspnea, and 19 (58%) complained of globus sensation. Postoperatively, 24 patients (73%) complained of dysphagia, 1 complained of dyspnea, and 25 (76%) reported globus sensation. For all patients, preoperative sensory testing showed a mean threshold of  $2.79 \pm 0.51$  mm Hg. The mean change postoperatively was trivial ( $0.07 \pm 0.29$  mm Hg) and did not differ significantly from zero ( $P = .19$ ). One patient was found to have a postoperative ipsilateral vocal fold paresis; however, laryngopharyngeal sensory thresholds remained normal.

**Conclusions:** Many patients with thyroid disease complain of upper aerodigestive tract symptoms preoperatively and postoperatively. This is the first study to quantitatively measure and compare laryngeal sensory levels in patients undergoing thyroidectomy. There was no statistically significant change in laryngopharyngeal sensation before and after thyroidectomy. Based on our findings, thyroidectomy does not appear to alter the function of the internal branch of the superior laryngeal nerve.

## **P015: Phase I: Update of Weekly Docetaxel, Cisplatin, Daily Celecoxib, Concurrent Radiotherapy in Advanced Head & Neck Cancer**

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**Objectives:** Cyclooxygenase-2 (COX-2) overexpression in locally advanced head and neck cancer and preclinical benefit for COX-2 inhibitors with radiotherapy (RT) led us to study weekly doublet chemotherapy, daily radiotherapy, and celecoxib. Follow-up data on response and tolerability at median of 20.5 months are presented.

**Methods:** Eligibility: stage III or IV squamous cell cancer of oral cavity, oropharynx, hypopharynx, larynx; performance status 0, 1, 2; adequate hepatic, hematologic, renal function; and no prior radiotherapy/chemotherapy for this site. Treatment: weekly docetaxel (T), 12.5, and cisplatin (P), 20, intravenously, mg per M2, day 1 ? 6 weeks; RT single fraction, days 1-5 ? 7 weeks or to total standard dose (70 Gy); and celecoxib (C), 400 twice daily by mouth. Feeding tubes were placed prophylactically.

**Results:** Median age (7 patients), 52 years (36-69 years), 3 women. Sites: 4 tonsil, 2 base of tongue, and 1 supraglottic larynx. The study ended at cohort 1 as maximum tolerated dose had been achieved. Median time to completion of radiation therapy was 52 days (49-67 days). The response rate of the 6 evaluable patients was

100%. G-tube independence was achieved in 3 of 4 patients evaluable at 6 months (+1 death and 1 salvage surgery); the fourth was independent at 7 months. At the median follow-up of 20.5 months, 3 patients are alive in complete remission, 1 patient had surgical salvage at 6 months, 1 relapsed at 13 months, and 1 had response but noncancer death at 4.5 months. No patient developed metastatic disease.

**Conclusion:** Combination of the COX-2 inhibitor C with concurrent RT and weekly T and P was feasible with toxicity and response comparable to other concomitant therapies for locally advanced head and neck cancer.

## **P016: Oxaliplatin, Folinic Acid and 5-Fluorouracil (OFF) in Recurrent Advanced Head and Neck Cancer: A Phase II-Trial**

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**Objective:** The purpose of this phase II trial was to investigate first time the efficacy and toxicity of oxaliplatin combined with folinic acid (FA) and 5-fluorouracil (5-FU) in patients with recurrent squamous cell

carcinoma of the head and neck in advanced stage of disease.

**Design:** Thirty-six patients with recurrent/metastatic disease with a median age of 59 years were enrolled. Patients received oxaliplatin (85 mg/m<sup>2</sup>) and FA (200 mg/m<sup>2</sup>), followed by 5-FU (2000 mg/m<sup>2</sup>) as 24-hour continuous infusion on day 1 and 15 in a 4-week cycle. On days 8 and 22, FA (200 mg/m<sup>2</sup>) and 5-FU (2000 mg/m<sup>2</sup>) were administered without oxaliplatin, followed by 2 weeks without cytotoxic treatment.

**Results:** Toxic effects, survival, and response were assessable in 33 of 36 patients. The overall response was 60.6%, with 7 (21.2%) complete responders and 13 (39.4%) partial responders. Eight patients (24.2%) showed stable disease and 5 (15.2%) progressed. The median time to progression was 8.1 month (range, 2-14 months), and median overall survival was 10.8 months (range, 5-16 months). The 1-year-survival rate was 43.2%. Hematological toxicity was low, but mild paresthesias occurred in all patients who received more than 3 cycles of cytotoxic therapy, and dose reduction was necessary in 2 patients due to diarrhea grade 3.

**Conclusions:** In this small phase II study, the combination of oxaliplatin, FA, and 5-FU demonstrated, relative to the standard regimen of cisplatin and 5-FU, a high antitumoral activity in previously treated squamous cell cancer of the head and neck with a favorable toxicity profile.

## **P017: The Prevalence of Depression in Head and Neck Cancer Patients at the Time of Diagnosis**

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**Objective:** Head and neck cancer patients are often observed to become depressed during the management of their disease. This study is designed to establish the baseline characteristics of the patients with head and neck cancer at a single institution with reference to depression and other factors known to be correlated with depression.

**Methods:** 312 patients were diagnosed with head and neck cancer from January 1, 2000 to December 31, 2005 at the Veterans Administration Medical Center in Memphis. After appropriate institutional review board approval was obtained, the patients' charts were reviewed. Data with respect to patients' diagnosis by cancer site, stage at the time of diagnosis, age, presence of comorbidities, coexistence of diagnosis of depression, history of pharmacological treatment or psychological counseling, and presence of coexistent substance abuse at the time of cancer diagnosis were obtained.

**Results:** Mean age at the time of diagnosis was 63.6 years old, 12% of patients included in review had diagnosis of depression at the time of head and neck cancer diagnosis, slightly less than 12% of total patients were pharmacologically treated for their depression for the period of time ranging from 1 month to 3 years prior to cancer diagnosis. 76% had a history of alcohol abuse, 93% of patients had a history of tobacco use and 13% had a history of other substance use. The incidence of preexisting depression will be correlated with disease and treatment outcome as more survival data become apparent.

**Conclusions:** The patient treated for head and neck cancer is prone to the development of depression. Depression can significantly compromise quality of life, increase length of hospital stay and complication rates, and impact the patient's ability to remain independent. It may also affect survival. The baseline characteristics of the head and neck cancer population in this single institution with respect to depression will be used to design a prospective trial in which effective intervention strategies for the depressed head and neck cancer patient may be found to impact quality of life and survival.

## **P018: Parotid Gland Epithelial Malignancies: A Retrospective Analysis of 116 Patients**

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**Aim of the Study:** To review our experience with parotid gland epithelial malignancies and to define the role of different prognostic factors.

**Patients and Methods:** Between 1978 and 2002, 116 previously untreated patients (63 men, 53 women) with primary epithelial malignancy of the parotid gland underwent surgery at the Department of Otorhinolaryngology of the Universities of Brescia and Varese (Italy). Lesions were staged as follows (AJCC 2002): 35 pT1, 31 pT2, 14 pT3, 32 pT4a, 4 pT4b. In 53 patients a concomitant neck dissection was also performed. Postoperative radiotherapy was delivered in 77 patients. A minimum of 24-months follow up was available for all patients. Survival was estimated by Kaplan-Meier method. Log-rank test (univariate analysis) and Cox-regression test (multivariate analysis) were applied to predict impact of 11 prognostic factors on three end-points: disease specific survival (DSS), local recurrence free survival (LRFS), and distant metastasis free survival (DMFS).

**Results:** Estimated absolute survival at 5 and 10 years was 70.3±4.4% and 47.2±5.4%, respectively. Estimated DSS was 80.4±3.8% (5 years) and 69.2±5.0% (10 years). Estimated LRFS was 84.7±3.6% (5-10 years). Estimated DMFS was 81.8±3.8% (5 years) and 75.9±4.6% (10 years). When tested with the log rank test, all variables except age and facial nerve involvement significantly influenced DSS. The only variables significantly affecting LRFS were deep lobe involvement and extraparotid extension. For DMFS, only three variables were not significant: age, tumor size, and positive surgical margins. When multivariate analysis was performed on DSS, deep lobe involvement and presence of metastatic lymph nodes carried a significant higher risk of death. LRFS and DMFS were significantly influenced only by deep lobe involvement.

**Conclusions:** Our survival data are agreement with previous reports. Univariate analysis was of limited predictive value, since almost all the evaluated factors influenced both DSS and DMFS. LRFS was affected by deep lobe involvement and extraparotid extension. Multivariate analysis identified deep lobe involvement as a factor affecting all endpoints (DSS, LRFS, DMFS), whereas nodal metastasis was found to affect only DSS.

## **P019: Is Lateral Neck Dissection the Choice for Planned Neck Dissection After Larynx/Hypopharynx Organ Preservation Protocol?**

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**Introduction:** Planned neck dissection after organ preservation protocol for larynx and hypopharynx carcinoma is controversial. In this study we evaluate the clinical stage, clinical response, and pathological findings in the neck dissection specimen of patients submitted to an organ preservation protocol.

**Patients and Methods:** This study includes 46 patients with larynx or hypopharynx carcinoma submitted to an organ preservation protocol (paclitaxel and cisplatin concomitant with radiation therapy).

**Results:** Considering all patients submitted to neck dissection, 6 (33.3%) of them presented with pathological lymph node metastasis. When we stratified the analysis by initial clinical stage, we observed that among the 6 patients initially staged as N1, only 1 presented 1 pathologically positive lymph node metastasis. Among the N2 and N3 cases, 41.6% had pathological lymph nodes in the neck dissection specimen. According to the clinical response at the end of the protocol, the cN0 and cN1 cases presented 23.1% and the cN2 and cN3 presented 60.0% of pathological lymph nodes metastasis. Moreover, all cases found to be pathologically positive nodes had lymph node involvement at levels II, III, and IV.

**Conclusion:** The incidence of occult lymph node metastasis in patients with complete neck response after organ preservation protocol is low (23.1%), and it is even lower considering the cases initially staged as N1 (1 of 6 cases). In all cases submitted to neck dissection in which there was confirmed lymph node metastasis, the levels I and V were never involved; this result suggests that lateral neck dissection can be safely performed as planned neck dissection after organ preservation protocol.

## **P020: Total Nasal Reconstruction Using a Forearm Free Flap, Titanium Mesh and a Paramedian Forehead Flap**

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**Objective:** To evaluate the novel use of a radial forearm free flap, titanium mesh, and a paramedian forehead flap for the reconstruction of total or near total rhinectomy defects following oncologic nasal resection.

**Design:** Case series.

**Setting:** Academic tertiary care hospital.

**Patients:** Six patients with total or near total rhinectomy defects.

**Intervention:** Six consecutive patients underwent nasal reconstruction using a radial forearm free flap as nasal lining, titanium mesh as support and a paramedian forehead flap as cover.

**Main Outcome Measures:** Cosmesis, function, and flap survival.

**Results:** Good cosmesis and function were obtained in all patients. Satisfaction was reported as excellent by all 6 patients. In 2 of the 6 patients, a small portion of the titanium mesh became exposed and required a short revision surgery. There were no instances of infection or graft failure.

**Conclusions:** With careful attention to the principles of nasal reconstruction, excellent functional and esthetic results may be obtained with the use of a forearm free flap, titanium mesh, and paramedian forehead flap in reconstruction of total or near total rhinectomy defects.

## **P021: Regional Recurrence Rate of Squamous Cell Carcinoma of the Anterior Nasal Cavity: A Systematic Review and Meta-Analysis**

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**Objective:** To demonstrate by meta-analysis that the regional recurrence rate of squamous cell carcinoma of the nasal cavity may be higher than previously suspected.

**Data Sources:** Original articles, including a previously published series from our institution, were identified from a search of the MEDLINE database using both PubMed and Ovid search techniques.

**Study Selection:** Studies that analyzed tumors other than squamous cell carcinoma or tumors from sites other than the nasal cavity were excluded. Studies that did not report a regional recurrence rate were excluded.

**Data Extraction:** Identified studies were reviewed by a single reviewer (first author), and studies that were not excluded were reviewed for data extraction by 2 reviewers.

**Data Synthesis:** The average weighted percentage regional recurrence for squamous cell carcinoma of the nasal cavity from the 23 studies reviewed was 18.1%.

**Conclusions:** Currently, few authors advocate elective treatment of the necks in patients with squamous cell carcinoma of the nasal cavity. However, our review demonstrates that the regional recurrence rate of this specific entity may be higher than suspected. Because many studies include other histopathologies or analyze data from tumors of multiple subsites, a true regional recurrence rate for squamous cell carcinoma of the nasal cavity has not been firmly established. Now that a uniform staging system exists for nasal cavity cancers, better prospective analysis of these tumors will be available in the future. For now, we advocate aggressive management of the necks of certain patients with proven aggressive squamous cell cancer of the nasal cavity and very close monitoring of patients with early disease.

## **P022: Neck Management During Salvage Laryngeal Surgery for Recurrent/Persistent Laryngeal Cancer After Radiation Therapy**

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**Objective:** To help guide the management of cervical lymph nodes in patients with recurrent/persistent laryngeal cancer after primary radiation therapy undergoing salvage laryngeal surgery

**Study Design:** Retrospective chart review.

**Methods:** Charts of 34 patients who had a total or supracricoid laryngectomy with unilateral or bilateral neck dissection for recurrent/persistent laryngeal cancer after primary radiation therapy from 1995 to 2005 in our institution were reviewed. Reports of pre-radiation therapy and pre-salvage surgery staging of the primary tumor and the neck were recorded using the T,N,M staging system. Pathology reports for the excised laryngeal cancer and cervical lymph nodes were reviewed.

**Results:** Among the 34 patients, 32 (94%) patients were staged T-1 or T-2 prior to radiation therapy. 29 (85%) patients were staged T-3 or T-4 prior to salvage surgery, while 5 were T-2. 30 (88%) patients did not have evidence of nodal metastasis on final pathology. On comparing patients with and without nodal metastasis based on their final post-operative pathology, we found that the pre-salvage surgery neck staging, based on clinical neck examination and imaging (CT and/or MRI), was significantly associated with the negative/positive post-operative status of nodal metastasis [ $P=0.006$ ]. 28/29 (97%) patients staged pre-salvage surgery as N-0 did not have nodal metastasis on their post-operative final pathology [PPV=97%, CI: 82.2 : 99.9]. Pre-radiation therapy neck staging, pre-radiation therapy and pre-salvage surgery laryngeal tumor staging along with laryngeal subsite involvement (supraglottis, glottis, subglottis) did not significantly correlate with positive neck metastasis on final post-operative pathology [ $P=0.68, 0.78, 0.49$  and  $0.42$  respectively].

**Conclusion:** Patients undergoing salvage total or supracricoid laryngectomy for laryngeal cancer recurrence/persistence after primary radiation therapy are likely to have advanced laryngeal disease. Management of the neck should be based on the pre-operative clinical evaluation and radiographic (CT and/or MRI) imaging of the neck. Patients staged N-0 pre-salvage surgery are not likely to harbor occult nodal metastasis, and therefore do not require elective neck dissection.

## **P023: Postoperative Complications of Salvage Partial Laryngectomy**

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**Objective:** To report the incidence of postoperative complications for salvage partial laryngectomy (SPL) compared with primary partial laryngectomy (PPL) and to identify factors predictive of postoperative complications.

**Design:** Fourteen-year retrospective analysis.

**Setting:** Tertiary referral center specializing in head and neck cancer.

**Patients:** A total of 150 patients who had a partial laryngectomy were identified from an existing database of 662 patients treated for squamous cell carcinoma of the larynx from 1984 to 1998. Partial laryngectomy and SPL were performed in 129 and 21 patients, respectively. All SPL patients had radiotherapy as index therapy.

**Outcome Measures:** Postoperative complications were recorded for each group and categorized into local, swallowing, airway, and systemic complications. Postoperative complication rates for SPL were compared with those after PPL by univariate analysis. Patient and tumor related predictors of complications were identified by univariate and multivariate analyses.

**Results:** There was no postoperative mortality. Twenty percent of patients developed a postoperative complication following partial laryngectomy. Local complications, which were the most frequent complication, occurred in 17 patients (11%). Laryngocutaneous fistula occurred in 6 patients (4%). Statistical analysis showed that there was a greater number of patients with local wound complications (24% vs 8%;  $P = .05$ ) and fistula complications (14% vs 2%;  $P = .04$ ) in the SPL group when compared with PPL. Multivariate analysis

showed that primary radiotherapy was an independent predictor of local complications and laryngocutaneous fistula.

**Conclusions:** Salvage partial laryngectomy was more frequently associated with postoperative complications compared with PPL. Problems related to local wound healing, especially the development of laryngocutaneous fistula, constituted the most common postoperative complication in these patients.

## **P024: Oral SCC Margin Shrinkage Following Resection and Specimen Processing**

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**Background:** Resecting oral squamous cell carcinoma (SCC) with an appropriate margin of uninvolved tissue is critical in preventing local recurrence and making the decision regarding postoperative radiation therapy. This task can be difficult due to the discrepancy between margins measured intraoperatively and those measured microscopically by the pathologist following specimen processing. The goal of this study is to quantify and compare the amount of margin shrinkage observed based on tumor location and staging.

**Methods:** 47 patients who underwent resective surgery with curative intent for primary oral SCC were included in this study. All patients underwent resection of the tumor with a measured 1 cm margin by one attending surgeon. Specimens were then submitted to the UCSF Pathology Department for processing and review where histopathologic margins were measured. The closest histologic margin was compared to the intraoperative measured margin (1 cm) to determine percentage shrinkage. Percent shrinkages were grouped by locations (buccal mucosa, mandibular alveolar ridge and retromolar trigone in Group 1, maxillary alveolar ridge and palate in Group 2, and oral tongue in Group 3) and analyzed. Percent shrinkages grouped by stages T1/T2 or T3/T4 were compared. **Results:** The mean shrinkage for all patients was extremely significant ( $p < 0.0001$ ). The mean shrinkage was 70.95% for Group 1, 53.75% for Group 2, and 51.67% for Group 3 ( $p = 0.0336$ ). The mean shrinkage in T1/T2 tumors was 53.82% and T3/T4 tumors was 74.17% ( $p = 0.0170$ ).

**Conclusions:** Oral SCC margin shrinkage following resection and specimen processing is highly significant. Tumors located in the buccal mucosa, retromolar trigone, and mandibular alveolar ridge demonstrate significantly greater shrinkage than tumors of the maxilla or oral tongue. Late stage tumors also show significantly greater margin shrinkage. These findings suggest that it might be prudent to consider oral site and staging when outlining margins to ensure adequacy of resection.

## **P025: The Incidence and Management of Postoperative Alcohol Withdrawal Syndrome in Head and Neck Cancer Patients**

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**Objectives:** Alcohol consumption among patients with head and neck squamous cell carcinoma presents their caretakers with a distinct challenge in the post-operative setting. Alcohol withdrawal syndrome (AWS) occurs in a sizable percentage of these patients and often results in prolonged inpatient stays, frequent use of restraints, increased intensive care unit requirements and risk for serious adverse events. Furthermore, head and neck cancer patients' impaired ability to communicate post-operatively and a lack of standardized treatment paradigms may compound the effects of AWS. This paper describes an uncomplicated standardized protocol for the diagnosis and treatment of AWS applied prospectively on a large cohort of head and neck cancer patients and determines whether implementation of this protocol improves patient outcomes in this high-risk population.

**Methods:** Head and neck cancer patients treated at the University of Michigan between March 1, 2003 and January 1, 2005 were treated prospectively utilizing a standardized and validated alcohol withdrawal protocol. The care plan utilized the CAGE screening tool as part of the pre-operative intake exam. Post-operatively, nursing evaluations were conducted with a validated diagnostic scale, to identify symptoms of AWS and determine the appropriate use of benzodiazepines, sympatholytics, and/or neuroleptic agents. Patients were including in

the study group if they underwent a head and neck procedure and were admitted to the hospital for 48 hrs or longer. The control group for this study were patients with the identical inclusion criteria treated prior to the implementation of this standardized protocol from Jan 1, 2000 to Feb 28, 2003. Outcomes measured included hospital length of stay (LOS), postoperative complications, wound complications, transfers to the intensive care units (ICU), number of psychiatry consults, time in delirium, use of restraints, occurrence of falls, seizures, and violence and overall hospital variable direct costs.

**Results:** The overall incidence of AWS was 2.63% (42/1593) with an incidence of 4.15% (26/626) in the study population and 1.65% (16/967) in the control population. AWS patients had a significantly longer LOS than patients who did not undergo AWS (11.97 vs 6.62 days, respectively), higher variable direct hospital costs, and a larger percent of patients requiring ICU transfer. When comparing AWS patients in the study and control group, the LOS difference between patients in the control and study group was not significantly different (10.44 vs 12.92 days, respectively). However, the number of ICU transfers, days in the ICU, days in delirium (2.55 vs 0.88), number of violent episodes (43% vs 23%), number of respiratory arrests (14% vs 4%), hospital mortality (6.25% vs 0%) were significantly better for patients treated on the standardized regimen (all  $p$  values  $< 0.05$ ).

**Conclusion:** In this analysis, we report the incidence and treatment outcomes for head and neck cancer patients undergoing alcohol withdrawal syndrome postoperatively. The complications of this condition are illustrated and the utility and effectiveness of a standardized treatment algorithm for AWS are shown.

## **P026: MR in the Postoperative Assessment of Oral-Oropharyngeal Cancer: Is There a Role?**

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**Objective:** To analyze the magnetic resonance (MR) effectiveness in detection of oral-oropharyngeal cancer local recurrences.

**Design:** Retrospective study.

**Setting:** University hospital.

**Patients:** Thirty-six patients followed-up by MR (average, 38.2 months). The tumor stage was T1 (14%), T2 (30%), T3 (20%), T4a (28%), and T4b (8%).

**Interventions:** Surgery alone was performed in 61% of patients and multimodal treatment in 39%; 75% underwent reconstruction.

**Main Outcome Measures:** Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), posttest probability, and positive and negative likelihood ratios of MR in recurrence detection.

**Results:** Nineteen recurrences occurred in 16 patients. Magnetic resonance detected 14 of 16 first relapses. There were 2 false-negatives, 2 false-positives, and 18 true-negatives (sensitivity, 87.5%; specificity, 90%; PPV, 87.5%; and NPV, 90%). In 38% of first relapses, MR confirmed a clinical suspect, whereas in 50% the recurrence was detected by MR only. The prevalence of recurrences was lower among asymptomatic patients (36% vs 75%), and among them the posttest probability decreased from 36% to 11.1% with a negative MR result. Four of 8 patients with recurrence detected by MR were treated by surgery, whereas only 1 of 8 who had recurrence diagnosed by clinical examination underwent salvage treatment. Taking into account the entire number of examinations ( $n = 121$ ), the prevalence of recurrence was 11.6%; the sensitivity of MR, 87.5%; specificity, 98.1%; PPV, 87.5%; NPV, 98.1%; positive likelihood ratio, 45.93; and negative likelihood ratio, 0.127.

**Conclusions:** Clinical assessment may be hampered by scar formation or flap interposition. Because MR may detect up to 50% of subclinical recurrences, its use is recommended during the follow-up.

## **P027: Transoral Laser Microsurgery of Occult Primary Lesions in Metastatic Squamous Cell Carcinoma of the Head and Neck**

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**Objective:** To evaluate the efficacy of transoral laser microsurgery (TLM) in identifying and treating occult mucosal carcinoma in patients with malignant cervical lymphadenopathy from an unknown primary lesion.

**Methods:** Retrospective chart review of thirty patients with metastatic cervical squamous cell carcinoma who underwent rigid endoscopy under anesthesia to identify a primary lesion. We collected data on the use of TLM, neck dissection, discovery of an occult carcinoma, location of occult carcinoma, post-operative radiotherapy and disease-free survival. Data was analyzed using Chi-Square and Kaplan-Meier functions.

**Results:** All patients underwent rigid endoscopy under anesthesia and a neck dissection. Using TLM, an occult primary carcinoma was successfully identified in 17 of 18 patients. When TLM was not used during rigid endoscopy, an occult primary carcinoma was identified in 3 of 12 patients. Chi-Square analysis revealed a statistically significant increase in the occult primary discovery rate when TLM is added to rigid endoscopy under anesthesia ( $p < 0.001$ ). An occult primary carcinoma was identified in the oropharynx in nineteen patients. In one patient, synchronous primary lesions were identified in the nasopharynx and pyriform sinus. All seventeen occult primary carcinomas identified using TLM were resected to a negative margin. An occult primary lesion was not identified in ten patients; five of these patients developed local, regional and/or distant failure despite definitive radiotherapy. There were no local, regional or distant failures in patients who underwent TLM during endoscopy under anesthesia. TLM management of occult primary malignancies was associated with an improved disease-free survival ( $p < 0.001$ ). Median follow-up for patients with no evidence of disease was 2.3 years.

**Conclusions:** TLM is a very effective tool for identifying and treating an occult mucosal carcinoma during rigid endoscopy under anesthesia in patients with cervical squamous cell carcinoma from an unknown primary lesion. The oropharynx is the most common location for occult squamous cell carcinoma in our series. The successful identification and excision of occult primary lesions using TLM is correlated with improved disease-free survival. The routine application of TLM during rigid endoscopy may decrease the number of patients who are referred for large-field irradiation of an unidentified primary lesion.

## **P028: Effectiveness of Supracricoid Partial Laryngectomy in Locally Advanced Laryngeal Cancer**

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**Objective:** Supracricoid partial laryngectomy (SCPL) has been considered as a good surgical procedure for satisfactory results on oncological and functional aspects in locally advanced laryngeal cancer. The purpose of this study was to evaluate the oncologic and functional results to know the efficacy and safety of SCPL in locally advanced laryngeal cancer.

**Materials and Method:** Among 92 patients who underwent SCPL, 60 pathologically confirmed patients staged higher than T2b were investigated in oncologic and functional aspects. Local stages were T2b in 25 cases, T3 in 20 cases, and T4 in 15 cases. Average follow-up was 42 months.

**Results:** Among 60 cases staged T2b or higher, recurrence was noted in 11 cases (18.3%). Most of them were T3 ( $n = 4$ ) and T4 ( $n = 6$ ) cases. Among 11 patients, 7 were successfully salvaged by total laryngectomy, and the overall local control rate was 93.3% eventually. All patients had successful decannulation and oral diet except 3 patients (95.0%). In 20 patients, we could confirm the completely excision of the paraglottic space with involving tumor by special pathologic examination.

**Conclusion:** Supracricoid partial laryngectomy is considered as a safe and effective surgical modality in locally advanced laryngeal cancer, but careful case selection is needed in T4 cases.

## **P029: WITHDRAWN**

## **P030: Patterns of Failure on a Phase IB/II Trial of Celebrex with Chemoradiation for Head and Neck Cancer**

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**Background:** Inhibitors of cyclo-oxygenase 2 (COX-2) have shown promise as radio- and chemosensitizers in preclinical studies. We conducted a phase IB/II study to evaluate the toxicity and efficacy of celecoxib, a selective COX-2 inhibitor, administered concurrently with Carboplatin, paclitaxel, and radiation therapy for locally advanced squamous cell carcinomas of the Head and Neck, and herein report the patterns of failure.

**Methods:** Patients with recurrent, stage III or IV squamous cell carcinoma of the oropharynx, oral cavity, hypopharynx, or larynx were eligible. 28 patients were treated with weekly carboplatin (AUC=2.0), paclitaxel (30mg/m<sup>2</sup>) and concurrent radiotherapy (70.2 Gy) either with standard fields or with IMRT. Celebrex was started one week prior to initiation of radiation therapy and was given for a total of two years. In 12/2004, the study was interrupted due to concerns of cardiotoxicity with COX-2 inhibitors, and celecoxib was discontinued in all patients. The study was restarted in 5/2006 with the modification that celecoxib would be given only during radiation.

**Results:** Between 1/2003 and 11/2005 28 patients were enrolled, five of which entered after modification of the study. Three patients with recurrent disease at entrance, and one patient who expired before completion of therapy are excluded from the current analysis. At a median follow-up of 16 months (2-36 mo), 4 patients had failed; 3 were locally recurrent, 2 were distant, and 1 both local and distant. All local failures occurred within the high dose volume. Two patients with only local recurrences were salvaged, one with surgery alone, and one with surgery followed by concurrent chemotherapy and re-irradiation. Two year overall survival was 65%, freedom from distant metastasis was 83%, and 76% local control.

**Conclusion:** Although outcomes with the addition of celebrex are comparable to published series, local recurrence remains the primary mode of failure. Enrollment of further patients and continued follow-up are necessary.

## **P031: Utility of F-18 FDG PET-CT in Head and Neck Cancer After Segmental Reconstruction with Osteocutaneous Free Flaps**

**C.L. Oliver;** A. Muthukrishnan; J. Mountz; J. Johnson; F. Deleyiannis  
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**Objectives:** F-18 FDG PET-CT (PET-CT) scanning has emerged as an important tool in the surveillance of patients treated for head and neck malignancies. The purpose of this study was to investigate the value of early PET-CT scanning in patients who underwent segmental mandibular resection and reconstruction using an osteocutaneous free flap. In particular, the interpretability of PET-CT imaging in the presence of healing osteotomies and reconstruction hardware was analyzed.

**Methods:** Between January 2000 and December 2005, we identified 12 patients who underwent reconstruction of a segmental mandibular defect with an osteocutaneous free flap and postoperatively underwent F-18 fluoro-deoxy-glucose (F-18 FDG) PET-CT imaging within 18 months of surgery. Sixteen PET-CT studies performed using the standard UPMC dedicated combined PET-CT imaging protocol were reviewed jointly by radiologists and surgeons. The surgical sites, including adjacent tissue, reconstruction hardware, and a total of thirty-two osteotomies, were visually assessed for abnormal focal F-18 FDG uptake relative to uninvolved tissues. Focal F-18 FDG uptake was correlated with fused contrast-enhanced CT images. Based on both the intensity of F-18 FDG uptake and CT evidence of pathology, scans were classified as either positive or negative for abnormal uptake likely to represent malignancy. Scans interpreted as positive were characterized by F-18 FDG uptake which was focal, intense and could be correlated with CT anomalies. PET-CT scans interpreted as negative were characterized by F-18 FDG uptake comparable to uninvolved tissues, or areas of F-18 FDG uptake just above background not correlating with CT anomalies. Clinical follow-up was obtained for all patients, and PET-CT interpretation was compared to existing, or subsequently established, head and neck disease status.

**Results:** The mean interval from reconstruction to imaging was 193 days, with a range from 45 to 414. Unexpectedly, we observed no increase of F-18 FDG uptake at healing osteotomies in studies obtained as early as 1.5 months following reconstruction. The beam-hardening effects of reconstruction hardware limited full interpretability of adjacent anatomy on CT images. However, by examining both attenuation corrected and non-corrected images, reconstruction hardware did not hinder PET interpretability. PET-CT interpretation correctly identified the clinical cancer status in 15 of the 16 studies evaluated (94%). In none of the studies did the reconstruction hardware or osteotomy sites interfere with the ability to interpret the PET-CT.

**Conclusions:** F-18 FDG PET-CT imaging offers clear advantages over PET or CT imaging alone for surveillance of head and neck malignancies. The presence of reconstruction hardware and healing osteotomies at the site of an osteocutaneous free flap did not confound the interpretability of early postoperative PET-CT imaging when jointly reviewed by surgical and radiological physicians.

### **P032: Differential Protein Expression Patterns of p53, NF-KB, & NF-KB Regulated Genes in Head and Neck Squamous Cell Carcinoma**

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**Objective:** The current study examines the protein expression and activation of NF- $\kappa$ B (p65) and its regulated genes in head and neck squamous cell carcinoma (HNSCC) specimens based on p53 status.

**Design:** Head and neck squamous cell carcinoma tumor specimens were preserved in OCT and processed for frozen sections. Immunohistochemical staining of primary antibodies anti-p53 (DO1), phosphorylated NF- $\kappa$ B (p65), CA-9, YAP, c-IAP-1, ICAM-1, and HPV16-E6/18-E6 was carried out using the ABC-based method.

**Subjects:** Twenty-five tumor specimens were obtained from the tongue, larynx, pharynx, oral cavity, and tonsil of HNSCC patients without prior treatment, through Cooperative Human Tissue Network (CHTN), Midwestern Division, Columbus, Ohio, and National Institutes of Health clinical protocol #04C0104 and #04C0141.

**Results:** Head and neck squamous cell carcinoma with wild-type p53 (wt-p53) were found to display a reciprocal pattern of high phosphorylated NF- $\kappa$ B (p65) and low-negative p53 staining, in approximately 45% of all tumor samples examined. All tumors yielded staining of phospho-NF- $\kappa$ B (p65) and its downstream proteins (CA-9,

YAP-65, c-IAP-1, and ICAM-1). These downstream proteins coincided with p65 staining location, while varying in staining intensity, heterogeneity, and patterns. Tumors with wt-p53 status revealed a significantly stronger protein expression than mutant p53 (mt-p53) tumors for phospho-NF- $\kappa$ B (p65) and its downstream proteins.

**Conclusion:** The reciprocal relationship of immunostaining in phosphorylated NF- $\kappa$ B (p65) and p53 indicated the importance of the activation of NF- $\kappa$ B and its downstream genes in the malignant progression of HNSCC, especially in tumors with wt-p53.

### **P033: Analysis of Intratumoral Concentration of S100 Protein in SCC of Lower Lip, Predicting Metastasis and Survival**

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**Objective:** To study the relationship between intratumoral concentration of S100 protein and the development of metastasis in patients with squamous cell carcinoma of the lower lip and the impact on survival rates.

**Methods:** The charts of 66 patients with squamous cell carcinoma of the lower lip surgically treated at the Hospital das Clínicas University of São Paulo Medical School, Head and Neck Surgery Department, were retrospectively studied. Demographic, clinical and pathological variables (pT, thickness, grade, margins, invasions, inflammatory infiltrate, and lymph node involvement) were analyzed and compared with intratumoral concentration of S100 protein (dendritic cells), identified by immunohistochemical assay. The overall and disease-free survival were compared among pathological variables using the Kaplan-Meier curves.

**Results:** The mean number of dendritic cells counted in a microscopic field ranged between 1.7 to 74.2, with a median value of 20, which created 2 groups of patients: lower and higher concentration for S100 protein. Size of tumor (T1 and T2 vs T3 and T4) in centimeters was marginally statistical different ( $P = .06$ ), although keeping an inverted relation between tumor size and intratumoral S100 concentration. Thickness of tumor in millimeters showed a significant difference ( $P = .006$ ) in same inverted relation (the thicker the tumor, the lower the S100 concentration). Overall survival for N+ patients was significantly lower than that for N0 patients ( $P = .009$ ).

The same difference was found for thickness of tumor greater than 10 mm ( $P = .02$ ), perineural invasion ( $P = .006$ ), and intratumoral S100 concentration lower than 20 dendritic cells ( $P = .03$ ). The disease-free survival was significantly lower for patients with T3 or T4 tumors ( $P = .02$ ), with tumors greater than 4-cm extension ( $P = .03$ ), with a tumor thickness greater than 10 mm ( $P = .02$ ), and with presence of perineural invasion ( $P = .002$ ).

**Conclusions:** Low concentration of intratumoral S100 protein seems to be related with more metastasis and lower overall and disease-free survival for the analyzed patients. This can be helpful for the indication of elective neck dissection in patients with T2N0 stage, with a tumor thicker than 10 mm and low concentration of intratumoral S100 protein. Keywords: lip neoplasm; squamous cell carcinoma; metastasis; dendritic cells; biologic markers; prognostic.

### **P034: Phase I Study of Erlotinib With RT or Erlotinib With Cisplatin/RT in Patients with SCCHN**

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**Background:** The majority of squamous cell carcinomas of the head and neck (SCCHN) overexpress the EGFR. Activation of the EGFR results in numerous intracellular downstream signaling events that promote cancer cell growth and survival including proliferation, motility, adhesion, invasion and angiogenesis. Strategies that combine EGFR inhibition with standard therapy for SCCHN are warranted.

**Methods:** A phase I, dose-finding study of the small molecule tyrosine kinase inhibitor, erlotinib, in combination with RT (Group A-stage II or early stage III) or chemoRT (Group B-stage III or IV) was undertaken with curative intent in patients with SCC of the oral cavity or oropharynx. In both groups, the erlotinib dose was escalated in successive cohorts, with an initial starting daily dose of 50 mg. In both groups, RT was given to a total dose of 66-70Gy, 2 Gy/day fractions. Standard fractionation or IMRT was allowed. In Group B, cisplatin (CDDP) was given at a daily dose of 6 mg/m<sup>2</sup> concurrent with RT and erlotinib. Three patients were enrolled in each cohort. Patients who completed definitive therapy for the SCCHN were then given the option of daily erlotinib for two years and the safety and tolerability of this schedule was also determined. Erlotinib trough concentrations (C<sub>min</sub>) were evaluated when administered alone (lead-in) or in combination with RT or chemoRT. Erlotinib and the metabolite OSI-420 concentrations were determined by LC/MS/MS.

**Results:** Thus far, 16 patients have been enrolled on trial. In Group A, 3 patients on the first dose level had no dose limiting toxicities. Group A, dose level II (100 mg/day erlotinib/RT) is now accruing. For Group B, the combination of erlotinib/CDDP/RT, one patient in the first dose level (50 mg/day erlotinib) experienced a DLT of febrile neutropenia and erlotinib was dose reduced to 25 mg/day with no further DLT. This cohort was expanded to 6 patients with no DLT noted. Three patients have completed dose level II 100 mg/day erlotinib/CDDP/RT (Group B) with no DLT, and dose level III, Group B (erlotinib 150 mg per day/CDDP/RT) is now accruing. One patient has completed a two year course of chronic daily dosing of erlotinib at a dose of 25 mg with no significant toxicities. Thus far, MTD of the combination of agents has not been reached. Erlotinib and OSI-420 C<sub>min</sub> were not altered by the administration of chemoRT or RT (n=9). Erlotinib and OSI-420 C<sub>min</sub> were 599.2 ± 366.9 ng/mL and 51.5 ± 28.5 ng/mL (mean ± SD; n=6), respectively, at the 50 mg dose level. At 100 mg, Erlotinib C<sub>min</sub> was 375.5 and 1037.0 ng/mL while OSI-420 C<sub>min</sub> was 38.8 and 122.2 ng/mL (n=2).

**Conclusion:** The combination of erlotinib/RT and erlotinib/CDDP/RT is well tolerated so far. Further evaluation is ongoing.

## **P035: Post-Thyroidectomy Supraglottoplasty: Laryngomalacia from Massive Goiter**

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**Objective:** Airway management in patients with massive goiters can be challenging, potentially requiring fiberoptic intubation or tracheotomy. We present the case of a massive goiter with significant retropharyngeal, retrolaryngeal, and retroesophageal extension resulting in postthyroidectomy laryngomalacia. No other case has ever been reported.

**Design:** Case report.

**Setting:** Tertiary care center.

**Intervention:** A 58-year-old man presented with compressive symptoms from massive goiter. Preoperative flexible laryngoscopy revealed bilateral vocal cord paresis, with prolapse of the arytenoids and mucosa into the glottis with stridor. The patient was taken for total thyroidectomy and intubated orally without difficulty. Surgery was performed without intraoperative complication.

**Results:** After surgery, the patient was extubated but developed moderate stridor and respiratory distress. Flexible laryngoscopy demonstrated normal vocal cord motion and apparently edematous arytenoids with prolapse into the glottis. The patient was electively reintubated and given steroids for 48 hours. He returned to the operating room for direct laryngoscopy, and extensive amounts of redundant pharyngeal mucosa were discovered overlying the arytenoids and piriform sinuses with airway prolapse similar to laryngomalacia. Supraglottoplasty was performed, and the patient was extubated afterward with complete resolution of symptoms.

**Conclusion:** We present the first ever reported case of postthyroidectomy laryngomalacia. Massive goiters have the potential to expand the pharyngeal mucosa. After thyroidectomy, this excess mucosa has the potential to prolapse into the glottis, similar to laryngomalacia, causing stridor with symptoms of respiratory distress. Though massive goiters are less common, otolaryngologists should be aware of this potential unusual complication and be prepared to perform a supraglottoplasty to avoid an unnecessary tracheotomy.

## **P036: Is the Dissection of Level IV Necessary in Squamous Cell Carcinoma of Larynx with NO Neck?**

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**Objective:** To study the prevalence of lymphatic metastases to level IV in squamous cell carcinoma (SCC) of the larynx and compare this prevalence between clinically positive (cN+) and negative (cN0) necks and evaluate the possibility of isolated metastases to this level.

**Design:** Retrospective study.

**Setting:** Tertiary referral university center.

**Patients:** Thirty-one patients submitted to laryngectomies and neck dissections were enrolled in this study.

**Intervention:** Laryngectomy and neck dissection was performed, and each neck level was identified and marked for subsequent histopathological evaluation.

**Main Outcome Measures:** Calculation of the prevalence of lymphatic metastases to level IV in cN+ and cN0 necks and comparison of these prevalences with the correlation of positive metastases in level IV to positive metastases to other levels.

**Results:** Six percent (3 of 54) of the surgical specimens presented lymphatic metastases to level IV. All of the cN0 surgical specimens (n = 42) were exempted of histopathological metastases to level IV. Of the specimens that were cN+ necks (n = 12), 25% were histopathologically positive in level IV. This difference among clinically negative and positive necks was statistically significant ( $P = .009$ ). There were not isolated metastases to level IV; they were always related to metastases to level II or III ( $P = .002$ ).

**Conclusions:** The prevalence of lymphatic metastases to level IV in SCC of the larynx in cN0 necks was 0%. The prevalence of lymphatic metastases to level IV was correlated with clinically positive neck. Metastases to level IV were related to metastases to level II or III.

## **P037: Trans Oral Robotic Surgery (TORS) for Base of Tongue Neoplasms**

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The objective of this study was to develop a minimally invasive surgical technique for the treatment of base of tongue neoplasms using the optical and technical advantages of robotic surgical instrumentation.

Ten experimental procedures including tongue base exposure and dissections were performed on three cadavers and two mongrel dogs. Trans Oral Robotic Surgery (TORS) was then performed on three human patients with tongue base cancers in a prospective human trial. Utilizing the da Vinci® Surgical Robot (Intuitive Surgical, Inc., Sunnyvale, CA) we performed a total of ten base of tongue resections on edentulous and dentate cadavers as well as live mongrel dogs. In the cadaver models, exposure was evaluated using three different retractors, the Dingman, Crowe Davis, and FK retractors. The three human patients underwent TORS surgery of their tongue base cancers under an IRB approved prospective clinical trial. The ability to identify and preserve or resect key anatomic structures such as the glossopharyngeal, hypoglossal, and lingual nerves as well as techniques for identifying the lingual artery and achieving hemostasis were developed. The da Vinci® Surgical Robot provided excellent visualization and enabled removal of the posterior one-third to one-half of the oral tongue in cadavers, dogs, and human patients. Among the three retractors evaluated, the FK retractor offered the greatest versatility and overall exposure for robotic instrument maneuverability. Complete resection to negative surgical margins with excellent hemostasis and no complications was achieved in the live patient surgeries. TORS provided excellent three-dimensional visualization and instrument access that allowed successful surgical resections from cadaver models to human patients. Trans Oral Robotic Surgery is a novel and minimally invasive approach to tongue neoplasms that has significant advantages over classic open surgery or endoscopic transoral laser surgery.

## **P038: Refeeding Syndrome - The Effect of Evidence Based Guidelines for Its Prevention and Treatment**

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**Objectives:** To produce evidence based guidelines for detection and management of refeeding syndrome (RS).

To identify the incidence rate and complications due to refeeding syndrome (RS) in head and neck wards following introduction of guidelines.

**Background:** RS is a serious, well described, but often forgotten, phenomenon. Defined as potentially fatal fluid and electrolyte shifts which may occur in malnourished patients undergoing refeeding in any form. Its hallmark feature is hypophosphataemia. Consequently, patients can suffer a multitude of CVS, CNS and metabolic complications.

**Methods:** Part A: systematic review of the literature in RS

**Design:** Systematic literature review with set criteria for identifying studies and assessing quality of data.

**Selection Criteria:** Studies on epidemiology, diagnosis, prevention and management of RS

**Data Collection and Analysis:** Trials identified by electronic searches of MEDLINE, EMBASE, PubMed, Cochrane, CINAHL, and AMED using eligibility criteria. Part B: regional audit of the incidence and complications of RS.

**Study Design:** Prospective regional audit of head and neck wards for 6 months following introduction of evidence based guidelines for RS management.

**Setting:** 4 teaching and district general hospitals in the West Midlands, UK serving a population of 1.5m

**Patients:** All patients admitted to head and neck wards during 6-month period assessed to be at risk of RS.

**Interventions:** Guidelines introduced for diagnosis, prevention and management of RS

**Main Out come Measures:** Biochemical and clinical complications of RS.

**Results:** Part A: NO RCTs and 52 prospective and retrospective studies were identified. Most were level 3 or 4 evidence.

**Incidence:** True current incidence is not known.

**Aetiology:** Underlying causative factor is a period of undernourishment followed by rapid refeeding

**Risk factors:** include those chronically under-nourished, and those with diminished physiological reserve. ENT patients most at risk are those with head and neck cancer or chronic dysphagia.

**Diagnosis:** Monitor electrolytes daily over the first week of refeeding and then every two days in the second week.

**Prevention:** Most important factor in prevention is identifying those patients who are at high risk of developing RS, then the introduction of feeding according to a prescribed regimen with careful clinical and biochemical monitoring .

**Part B:** In total, 49 patients were assessed to be at risk of RS during the 6-month period. This was most commonly due to enteral refeeding following head and neck surgery. 35% patients were appropriately monitored during refeeding. 96% had refeeding at an appropriate rate. 100% developed severe hypophosphataemia. None developed clinical complications. In all, 35% of patients were managed according to guidelines.

**Conclusions** RS is not uncommon, and requires vigilance to prevent it. Increasing awareness of the condition, especially by junior medical staff, is needed, as are randomised controlled trials of management. Evidence based guidelines for prevention and management are presented, but still require increased awareness by medical staff.

### **P039: PNL2 Melanocytic Marker in Immunohistochemical Evaluation of Primary Malignant Mucosal Melanoma of the Head and Neck**

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**Objective:** Histologic diagnosis of mucosal melanoma of the head and neck can be difficult, requiring immunohistochemical stains. Our objective was to report staining characteristics of several antibodies, including a novel marker, PNL2, which has not been examined in mucosal melanoma.

**Design:** Pathologic specimens of primary mucosal melanomas of the head and neck were obtained, and immunohistochemical staining with 4 antibodies was performed.

**Subjects:** Eight surgical specimens.

**Intervention:** Formalin-fixed, paraffin-embedded tissue sections were used for immunohistochemical analysis with appropriate positive and negative controls, using the following antibodies: S-100, HMB-45, Melan A, and PNL2.

**Results:** A total of 8 cases were retrieved. All 8 cases arose from the sinonasal mucosa, 5 (62.5%) from the ethmoid sinuses, 2 (25%) from nasal polyps or masses, and 1 (12.5%) from maxillary lesion. Histologically, the tumor cells were epithelioid, with pleomorphism and high mitotic figures. The immunohistochemical profile is summarized in the Table.

**Conclusions:** We report the first characterization of PNL2 staining in head and neck mucosal melanoma. The positivity of melanocytic differentiation markers S- 100, HMB-45, and Melan-A in mucosal melanoma is comparable to that in their cutaneous counterparts. PNL2 also appears to demonstrate high sensitivity for mucosal melanoma and may be an important adjunctive marker in the evaluation of these lesions, especially in cases that immunoreactivity with HMB-45 and Melan-A is only focal or ambiguous.

### **P040: Post Operative Monitoring Using An Implantable Doppler Device in Free Flap Reconstruction of the Head and Neck**

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University of Alberta, Edmonton

**Objective:** To review our experience with the Cook-Swartz Doppler Flow Monitoring System for free flap monitoring in a large series of head and neck free flap reconstructions.

**Design:** Retrospective case series.

**Setting:** Tertiary care referral center.

**Patients:** All patients undergoing free flap reconstruction of head and neck defects with implantable Doppler monitoring.

**Intervention:** A consecutive sample of 407 patients requiring free flap reconstruction of head and neck defects and monitored by the Cook-Swartz Doppler Flow Monitoring System was identified through database analysis.

**Main Outcome Measures:** Flap compromise and flap salvage success rate.

**Results:** Early identification of the failed flap was achieved and resulted in a high percentage of successful salvage.

**Conclusions:** This is the largest reported series of implantable Doppler use in microvascular reconstruction. The advantages and disadvantages of this technique are discussed. Review of our experience would suggest that this is a reliable technique for postoperative monitoring in head and neck reconstruction. An algorithm for the assessment of the patient with an impaired Doppler signal is proposed to reduce the chance of unnecessary flap exploration surgery.

### **P041: WITHDRAWN**

### **P042: Adenoid Cystic Carcinoma of the Larynx**

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**Introduction:** Adenoid cystic carcinoma of the larynx is a rare malignancy with only few cases reported in the literature. It behaves quite differently from other primary laryngeal tumors. Our objective is to review the University of Toronto experience with this rare pathology and to try to define the characteristics of this disease and its outcome with current treatment modalities.

**Materials and Methods:** We conducted a retrospective chart review of the medical records of patients who were treated at the University Health Network between 1970 and 2004 for adenoid cystic carcinoma of the larynx. Patients with adenoid cystic cancer of the trachea were excluded. The data collected for each patient included: Age; Sex; Symptoms; Signs; Duration of Symptoms; Risk factors; Extent of the Tumor; Treatment strategy; Type of Surgical Intervention; Postoperative Complications; Radiation Regimen; Outcome and Survival. Descriptive statistical analyses were performed. Mean and median survival were reported and Kaplan-Meier curve constructed.

**Results:** Overall 32 patients were identified as having Adenoid Cystic carcinoma of the larynx or trachea. The larynx was the primary site of involvement in 10 patients. The mean age was 43.5 years with a range between 35 and 71 years. There was no sex predilection. Hoarseness and dyspnea were the most commonly reported symptoms. Half of the patients were smokers. Only one patient had regional metastasis and none had distant metastatic disease upon presentation. The treatment strategies included radiation therapy alone in 3 patients while the remaining 7 received combined modality treatment with surgery and radiation. The median follow up time was 98.5 months with a range of 25 to 252 months. The recurrence rate was 90%, with a local failure rate of 20% and a distal failure rate of 80%. The lungs were predominantly the site of distant metastasis. The median time until recurrence was 44.5 months. The 5 years overall survival rate was equal to 80% and the 10 years survival rate was equal to 40%.

**Conclusion:** Adenoid cystic carcinoma of the larynx is a rare disease. Adequate local control can be achieved, preferentially through a combined modality approach. Most patients recur often at a distant site. However, this disease shows a slow growth rate with many patients surviving for a prolonged period of time.

## **P043: Upfront Submandibulosalivaryglandulopexy (SMSGP) For Radiotherapy in Oro-Hypopharyngeal Cancer (for Radiation Compliance)**

**R.L. Bhalavat;** A. Badrukar; K.A. Pathak; M.S. Deshpande; B.L. Malpani; S.R. Deasi

Tata Memorial Hospital, Mumbai, India

**Introduction:** Protection of the salivary gland remains a key to preservation/retrieval of salivary function (SF) while treating head and neck cancers with radiotherapy (RT).

**Aim:** To estimate the influence of submandibular salivary gland transfer on SF and find out the incidence and level of xerostomia.

**Patients and Methods:** The contralateral submandibular salivary gland (SMSGD) of 44 patients with squamous cell carcinoma of the oro-hypopharynx was repositioned to the submental space and was blocked during the external beam RT (EBRT). Twenty-eight patients underwent radical EBRT (median, 66 Gy) and 16 patients underwent EBRT (median, 46 Gy) plus BRT (median, 30 Gy [range, 15-40 Gy]). Baseline SF was assessed through sialometry and scintigraphy and was repeated after the surgery and RT at subsequent follow-ups. Quantity and quality of saliva, xerostomia, mucositis, and dysphagia, etc. were recorded at 20 Gy, 40 Gy, and 60 Gy for radiation compliance during RT, and quality of life was assessed after radiation therapy.

**Results:** Quantity and quality of saliva remained practically normal in 53% at 20 Gy and deteriorated with increasing dose; saliva was thick, sticky, and reduced in 78% at a dose above 60 Gy. There was continual improvement in the amount and quality of saliva after RT, reflected by decrease in the intensity of xerostomia and improvement in swallowing to nearly normal by 1 year. Mean salivary output of transferred and untransferred SMSGD before and after surgery were comparable and was statistically significant ( $P<.001$ ) after RT at 6 months (Pathak KA, Bhalavat RL, Mistry RC, et al. *Oral Oncology*. 2004;40:960-963). Mean output after RT at 6 months is a reflection of transferred SMSGD and/or functioning gland (preserved/retrieved).

**Conclusion:** Upfront submandibular salivary gland transfer is a surgically feasible oropharyngeal dysphagia procedure. Upfront submandibulosalivaryglandulopexy as an adjunct to radical radiation leads to an improved radiation compliance during RT. Long-term improvement in quality of life is awaited.

## **P044: Prediction of Recurrence in Parotid Gland Carcinoma**

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**Objective:** To define recurrence prognostic factors in parotid gland carcinoma and develop a prognostic model.

**Design:** Retrospective study of medical records of patients with parotid gland carcinoma.

**Setting:** Tertiary cancer referral center.

**Patients:** A total of 127 patients with parotid gland carcinoma who completed treatment with a minimum 1-year follow-up.

**Interventions:** Surgery, radiotherapy, or combined treatment.

**Main Outcome Measures:** The logistic regression model was used to define factors associated with recurrence. This model was used to define risk groups. Disease-free and disease-specific survival were calculated using the Kaplan-Meier method and the log-rank test.

**Results:** Mean age was 52.92 years. Median follow-up was 2.7 years. Mean overall and median disease-free survival was 15.3 years (95% confidence interval, 13.2-17.5 years) and 8.3 years (95% confidence interval, 4.3-12.2 years), respectively. Univariate analysis demonstrated that gender, T and N classification, histology, grade, facial nerve dysfunction, vascular invasion, tumor size, surgical margins, neck dissection, and postoperative radiation therapy were recurrence predictors. Logistic regression analysis confirmed significance for T classification, surgical margins, differentiation grade, and histology. Consequently, we defined 3 risk groups: high, intermediate, and low risk, with 71.4%, 43.1%, and 8.8% recurrence frequencies, respectively ( $\pm 2$  test,  $P<.001$ ). Five-year disease-free survival for each one of these groups was 18.7%, 53.9%, and 99.9%, respectively (log-rank test,  $P<.001$ ).

**Conclusion:** T classification, histology, grade, and surgical margins were significant in multivariate analyses. A prognostic model for categorization of recurrence risk is proposed.

## **P045: Reconstruction of Total Scalp Defects With Cranial Involvement: An Evolving Paradigm**

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**Objective:** Reconstruction of large scalp defects that involve the skull pose a unique challenge for the head and neck reconstructive surgeon. Complete extirpation of tumor often leaves large tissue deficits, with exposure of dura or brain. This article details the outcomes of various reconstructive methods for patients with large oncologic total and near-total scalp defects that involve the cranium and/or dura.

**Design:** Prospective cohort study

**Setting:** Tertiary medical university.

**Patients:** A consecutive cohort of patients between 2005 and 2006 were selected with total or near total scalp defects with cranial involvement.

**Interventions:** The coverage methods included free tissue transfer (latissimus, anterolateral thigh, and abdominal perforator) and skin grafting. A new technique involving 3-dimensional modeling to construct a prosthesis for insertion into the cranial defect is described.

**Main Outcome Measures:** Patients were assessed for extent of scalp defect, adequacy and viability of tissue coverage, and cerebrospinal fluid (CSF) leakage. In addition, a classification scheme for the scalp defects and an algorithm for their treatment is outlined.

**Results:** For free flap patients, scalp coverage was 100%. In the skin-grafted group, initial coverage was 100%, with approximately 45% take overall. There were no incidences of CSF leakage or meningitis.

**Conclusions:** Microvascular free tissue transfer and advances in 3-dimensional modeling techniques have provided a new level of flexibility to the reconstruction of large scalp and skull defects. Dural coverage has been found to be excellent, with no CSF leakage or meningitis. Disadvantages included a somewhat long lead-in for prosthesis manufacture. The use of free tissue transfer, combined with custom-tailored implants, has become the preferred method of reconstruction.

## **P046: Juvenile Angiofibroma: An Update of Treatment Trends**

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**Introduction:** Nasopharyngeal angiofibromas are vascular tumors with different presentations, clinical courses and treatment options. The incidence is 0.05% of all head and neck tumors.

**Objective:** Various surgical approaches like transpalatal, lateral rhinotomy, Weber-Ferguson approach, endoscopic and combined approaches are established for management of NPAF. Recently less invasive endonasal approaches are being used, however at our institution endoscopic excision is in the beginning and angiography facilities are not widely available. To analyze the outcome of the different surgical procedures adopted in the last 24 years, a retrospective study was carried out.

**Materials and Methodology:** A total of 178 patients were examined from Government Ear Nose and Throat Hospital, Hyderabad, India. The histopathology slides of all these patients were thoroughly examined using a light microscope and few of the slides by electron microscope. The different surgical procedures, and treatment modalities adopted were analysed and conclusions drawn.

**Results:** Even though the number of nasopharyngeal angiofibroma cases per year are varying in number, on the whole it is showing a chronological increase. The common age group was 10-20 years. Transpalatal approach used in 89.33% case, lateral rhinotomy 3.93%, Endoscopic approach 1.69%, Weber-Ferguson approach 1.69%, and combined approach 0.56%, and polypectomy in 1.12% cases. The average blood loss was 1000ml to 1200 ml with minimal loss around 500 ml in enmass excision and a blood loss of around 2200 in situations where the tumor was removed piecemeal.

Around 4 –5 units of blood was transfused. The procedure was done under hypotensive anaesthesia. Two cases had intraoperative death due to profuse haemorrhage and they were extensive disease cases. Surgical pathology point of view the more the fibrous element the more recurrence rate. The average stay in the hospital was 7-10 days. Two cases were subjected to radiotherapy for uncontrolled bleeding postoperatively.

**Conclusions:** Transpalatal excision of tumor gave good results in stage I and II irrespective of availability of carotid angiography and embolisation. Lateral rhinotomy gave good exposure and the recurrence rates are less compared to transpalatal approaches. Overall Lateral rhinotomy approach is giving good results except for the scar on the face. Endoscopic excision may gain ground with specialized training.

## P047: Rhabdomyosarcoma of the Larynx in Adults

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**Background:** Adult rhabdomyosarcoma (RMS) is unusual, and presentation of RMS in the larynx is rare. Less than 25 cases of adult RMS of the larynx have been reported. Here we describe three cases of laryngeal rhabdomyosarcoma in adults, two of which occurred in women and compare this data with previously reported cases.

**Methods:** Retrospective chart analysis, case presentations, pathologic assessment and literature comparison.

**Results:** Three patients with laryngeal RMS aged 72, 56, and 29 are presented. The clinical presentation, physical and radiographic findings, and pathologic appearance of these cases are reviewed. One patient, with embryonal RMS, was treated successfully with definitive radiation therapy and is now five years without recurrence. The next two patients, both with the pleomorphic variant of RMS, were also treated non-surgically with different outcomes. One patient underwent aggressive induction chemotherapy combined with radiation and is now one year out in complete remission. In the third patient, induction chemotherapy did not produce a significant response; he refused further therapy, and died from disease. Data on clinical presentation, treatment and outcome from previously reported cases of adult laryngeal RMS are presented and compared.

**Conclusion:** We describe only the second and third cases of laryngeal RMS in adult women, the majority of reported cases having occurred in men. Although laryngectomy has historically been the preferred method of treatment for laryngeal RMS, two cases are presented where non-surgical therapy produced complete remissions. The description of three adult laryngeal RMS cases and a comparison to previously reported cases, adds substantially to the available data on this rare malignancy.

## P048: The Risk Factors Associated with Psychological Distress in Patients With Head and Neck Cancer

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**Objectives:** To study the prevalence of psychological distress in patients with head and neck cancers and to identify the specific stressors.

**Design:** In a cross-sectional study, patients in varying stages of the disease process completed the Basic Symptom Inventory (BSI) during outpatient registration.

**Setting:** Data were collected from adult outpatients undergoing cancer treatment from October 1998 to August 2002.

**Patients:** A total of 564 patients with head and neck cancer were recruited from Johns Hopkins Cancer Institute, Baltimore, Md. All new patients receiving cancer treatment participated. Sociodemographic characteristics were collected from patients' clinical files. The subsample included patients with head or neck cancer who had completed the BSI-53.

**Main Outcome Measure:** Because head and neck cancers can be uniquely disfiguring and disabling, there is an increased amount of

distress upon diagnosis and throughout treatment. The BSI measures distress, with the goal of improving patient care.

**Results:** Patients with head and neck cancers are at higher distress levels compared with patients with other cancers, reporting unique physical and psychological challenges in regard to diagnosis and treatment of their cancer. Patients at the highest risk for distress were either single, white, male, older than 50 years, or a combination of these factors. These patients had greater risk of many psychological conditions, including increased anxiety, hostility, and psychosis ( $P < .05$ ).

**Conclusions:** These findings will help clinicians focus on identifying at-risk patients and creating targeted interventions to incorporate into cancer management protocols for patients with head and neck cancers who are at risk for psychological distress during and following their treatment.

## P049: Acute Morbidity of Chemoradiation for Locoregionally Advanced (Stage IV) Oropharynx Cancer: IMRT vs 3D Conformal RT

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**Objective:** To compare acute morbidities of intensity-modulated radiation therapy (IMRT) with 3-dimensional conformal radiation (3D-CRT) in a uniform population of oropharynx cancer patients completing definitive chemoradiation.

**Design:** Retrospective case series.

**Setting:** University hospital referral center.

**Patients:** Thirty patients (15 IMRT and 15 3D-CRT) with nonmetastatic stage IV oropharynx squamous cell cancer.

**Interventions:** Median radiation dose was 70 Gy for both groups. All patients received concurrent chemotherapy, most (14 of 15 IMRT; 12 of 15 3D-CRT) with cisplatin-based regimens.

**Main Outcome Measures:** Acute morbidity in terms of weight loss, treatment break, and Radiation Therapy Oncology Group (RTOG) Acute Radiation Morbidity Scoring Criteria were assessed.

**Results:** Median weight loss was 23.2 lbs (range, 10.2-49.9 lbs) (10.44 kg [range, 4.59-22.46 kg]) after IMRT vs 21.4 lbs (range, 11.0-55.5 lbs) (9.63 kg [4.95-24.98 kg]) after 3D-CRT. Six (40%) of 15 in both arms required a treatment break (mean duration, 4 days for IMRT and 7.5 days for 3D-CRT). Overall, 29 (97%) of 30 patients developed RTOG grade 3 pharyngeal morbidity. A *t* test analysis failed to reveal a significant difference in RTOG worst score for mucous membrane ( $P = .47$ ), skin ( $P = .33$ ), or pharynx ( $P = .31$ ) between IMRT and 3D-CRT.

**Conclusions:** Morbidity of chemoradiotherapy is significant: 97% of patients develop RTOG grade 3 acute pharyngeal toxicity and median weight loss is greater than 20 lbs (9.00 kg). We could show no meaningful difference between 3D-CRT and IMRT in the development of acute morbidity.

## P050: PET-CT In Recurrent Head Neck Squamous Cancer

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**Objective:** To assess the role of positron emission tomography and computed tomography (PET-CT) fusion imaging in management of recurrent head neck squamous cancer in India.

**Design:** Retrospective cohort study of 1 year.

**Setting:** Specialized referral center.

**Patients:** Eighty previously treated patients with head neck squamous cancer underwent 85 whole-body PET-CT fusion scans during follow-up for recurrent disease that was clinically considered salvageable.

**Methods:** Nonsquamous cancers and clinically advanced and all nasopharyngeal tumors were excluded. PET-CT uptake was tested with gold standard positive histopathology.

**Results:** Sixty-six male and 14 female patients with a mean age of 55 years presented with recurrence at a median of 350 days. Thirty-four

(42.5%) had oral cancers; 11, base tongue lesions; 10, oropharyngeal; 16, hypopharynx; 6, larynx; and 3, other. At prior staging, 48 (60%) had stage IV; 16 (20%), stage III; and 16 (20%), stage II. Thirty-seven underwent combined surgery with radiation or chemoradiation; 21 received chemoradiation; 19 received radical radiotherapy; and 3 had undergone surgery only before PET-CT. Indications included 26 local and 28 regional recurrences; 21 suspected; 4 on follow-up; and 6 for abnormal imaging results.

**Main Outcome:** Of 18 patients with abnormal findings on endoscopy/examination under anesthesia prior to PET-CT, only 11 were salvageable. Of 47 patients with normal/equivocal endoscopy, 7 patients (17%) had nonsalvageable disease: 25 (31%) with local recurrence had change in plan; 11 (13%) change influenced by CT scan findings and 14 PET findings decisive. An extra investigation was avoided in 17. For PET-CT, sensitivity was 94.7% and specificity was 14.27%. The positive predictive value was 90%; negative predictive value, 25%; and accuracy, 85.94%.

**Conclusion:** Positron emission tomography and computed tomography fusion imaging has a definite role in management of recurrent head neck squamous cancers.

## P051: Management of Neck Disease Following Intensity-Modulated Radiation Therapy for Oropharyngeal Cancer

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**Objective:** The standard treatment at our institution for oropharyngeal squamous cell carcinoma (SCCA) is radiation (IMRT) or chemoradiation (chemo/IMRT) to the primary and neck. Our primary goal was to assess regional control between the 2 treatment modalities.

**Design:** Retrospective.

**Setting:** Tertiary care.

**Interventions:** Patients treated at our institution for oropharyngeal SCCA who have been treated with IMRT (70 Gy to primary, 50 Gy to both necks) or a combination of platinum-based chemoradiation (chemo/IMRT).

**Main Outcome Measures:** Clinical examination findings, before and 4-weeks after radiation therapy, and CT scan results were tabulated. Pathology records and operative notes of posttreatment neck dissections were reviewed, specifically recording whether a viable tumor was present and which neck levels were involved.

**Results:** Sixty-eight patients with oropharyngeal SCCA were treated over a 41-month period with a mean duration of follow-up of 19 months. Thirty-three patients were treated primarily with IMRT, and 35 patients were treated with chemo/IMRT. Of 68 patients, 43 underwent posttreatment neck dissections. Twelve patients in the IMRT group and 3 patients in the chemo/IMRT group had viable tumors in the neck specimens ( $P = .008$ ). Viable tumors were found most commonly in the ipsilateral level II. Based on the follow-up data, 3 of 33 (9%) patients treated with IMRT had regional recurrence, whereas 1 of 35 (2.8%) treated with chemo/IMRT had regional recurrence ( $P = .28$ ).

**Conclusion:** Specimens from the combined chemo/IMRT neck group were less likely to have a viable tumor than the IMRT group. The group with overall regional control with IMRT and the group with combined chemo/IMRT were not statistically different; however, those in the latter group had a more advanced pretreatment nodal stage.

## P052: Phase II Study: Concurrent Gemcitabine-Radiotherapy With Cetuximab in Locally Advanced Head and Neck Cancer (LAHNC)

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**Objective:** To evaluate efficacy and safety of a scheme using gemcitabine-radiotherapy plus cetuximab to treat LAHNC.

**Design:** Phase II study.

**Patients:** Nineteen patients (age range, 18 to 50 years) with LAHNC and 1 with recurrent cancer were enrolled, with confirmed of epidermoid carcinoma (Karnofsky performance score >70%; normal renal, hepatic and hematologic functions; without previous oncologic treat-

ment (CT, RT); or surgically inoperable disease; or patients with operable disease who did not consent to surgery. Assessment of expression of epidermal growth factor receptor was not evaluated. Radiotherapy was 200 cGy/d for 5 wk until 70 Gy were received. The initial dose of cetuximab was 400 mg/m<sup>2</sup>, followed by 250 mg/m<sup>2</sup> weekly until completion of radiotherapy. The dosage of gemcitabine was 50 mg/m<sup>2</sup> for weeks 1, 2, 4, 5, and 7.

**Results:** Twenty patients were enrolled from November 2004 to November of 2005 (16 men and 4 women; median age (range), 56 years (33-75 years)). The primary sites were the oral cavity (5 patients), oropharynx (5 patients), larynx (8 patients), hypopharynx (1 patient), and paranasal sinuses (1 patient). The tumor stages were III (7 patients), IVa (8 patients), and IVb (5 patients). One patient refused treatment. Nineteen patients were evaluable. Toxic effects were mucositis III-IV (8 of 19 patients; 42.1%) and rash III-IV (4 patients; 21%). Two patients (10.5%) did not complete treatment with chemotherapy owing to mucositis but did complete treatment with radiotherapy. Only 1 patient did not complete the radiotherapy. One patient (5.26%) developed leukopenia III-IV. Four patients developed dysphagia II. Seven patients (36.8) developed xerostomia II. Response rates were as follows: OR, 89.5% (17 of 19 patients); CR, 68.4% (13 of 19); PR, 21.1% (4 of 19); and NR, 10.5% (2 of 19). In the primary site 78.9% (15 of 19) had CR. The mean duration of follow up was 8 months, and 1 patient who did not respond to treatment died.

**Conclusion:** The scheme is safe and effective with tolerable toxic effects.

## P053: Proper Capsular Incision Can Avoid Hoarseness After Enucleation of Schwannoma From the Cervical Vagus Nerve

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**Objective:** Postoperative hoarseness is the major complication after enucleation of vagus nerve schwannoma. To improve the function of phonation, we compared the incidents of hoarseness after 2 different incisions of the tumor capsule after enucleation of schwannoma of the cervical vagus nerve.

**Design:** Cross-sectional study using self-administered questionnaire data and medical chart review.

**Setting:** Tertiary cancer referral center.

**Patients:** From January 1989 to December 2004, 19 cases of cervical vagus nerve were enucleated using 2 different capsular incisions.

**Interventions:** A postlateral capsular incision, usually posterior to the internal jugular vein, was used in 12 cases. The traditional method, an anterior capsular incision between the internal jugular vein and common artery, was used in 7 cases.

**Main Outcome Measures:** Postoperative phonation was measured by patient survey and laryngoscopic examination.

**Results:** Eight of 12 patients who underwent the postlateral incision had no hoarseness after the operation; the remaining 4 patients regained their good phonation after a short period of hoarseness. However, all 7 patients who underwent an anterior incision had postoperative hoarseness. After long follow-up periods (1-10 years), 6 of 7 patients still experienced hoarseness.

**Conclusions:** After correct diagnosis and a proper postlateral tumor-capsular incision, hoarseness in most SVN patients with cervical vagus nerve can be avoided.

## P054: Concurrent Preoperative Chemoradiation of Resectable Stage III/IV Oral Cancer: 6-year Results of a Phase II Study

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Preoperative radiochemotherapy in advanced oral and oropharyngeal cancer has been used frequently with the aim to improve local tumor control and survival. From 1998-2000 a non-randomized multicenter phase-II trial was performed including a total of 53 patients with stage III/IV cancer of the oral cavity and oropharynx. A combination of Paclitaxel (40mg/m<sup>2</sup>) and Carboplatinum AUC 1.5 was given

weekly, day 1 for 4 weeks. Conventional fractionated radiation was given simultaneously up to a total dose of 40 Gy. Surgery of the primary tumor and the neck nodes was performed after a recovery period of 2-3 weeks. 52 Patients were evaluable. Major acute toxicity was mucositis requiring intensive supportive care. Complete remission was observed in 31 patients (60%) and partial remission in 21 patients (40%). Complete histopathologic response was observed in 30 patients (58%). Overall survival after six years was 64%, recurrence free survival was 82%. Further analysis showed that complete remission after concurrent chemoradiation is an important prognostic factor with regard to survival. The present regimen was highly effective in advanced oral and oropharyngeal cancer with moderate toxicity. These phase II results are currently tested in a randomized phase III study comparing cisplatin vs paclitaxel/carboplatin as chemotherapeutic regimen.

## P055: WITHDRAWN

### P056 Minimally Invasive Thyroid Surgery: The Delivery Technique

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**Objective:** To review our experience with a new surgical approach, the delivery technique for minimally invasive thyroidectomy.

**Design:** Retrospective review.

**Setting:** Tertiary care hospital, head and neck surgery service.

**Patients:** Patients undergoing thyroidectomy.

**Interventions:** The delivery technique requires a 3- to 4-cm incision followed by ligation of the superior thyroid vessels, middle thyroid vein, and inferior thyroid vein, followed by delivery of the gland through the incision.

**Main Outcome Measures:** We reviewed 161 partial and total thyroidectomies over a 5-year period to identify indications, contraindications, complications, and outcomes of thyroidectomy using the delivery technique.

**Results:** The delivery technique was performed in 161 of 422 thyroidectomies (38.1%). Hemithyroidectomy was performed in 122 cases (75%), and total thyroidectomy was performed in the remaining 39 cases (25%). Twelve percent of cases required conversion to a standard open approach because of the need for lymph node dissection or the failure to accomplish the procedure using a minimally invasive technique. All of the surgical procedures were performed through an incision that was 4.0 cm or smaller (average length, 3.4 cm) without the use of videoendoscopy. All of the wounds were closed without a drain. There were no complications (including

hematoma, vocal cord paralysis, and excessive wound scarring). The most common contraindications included goiter (42%), substernal goiter (18%), and the presence of malignancy requiring paratracheal dissection (9%).

**Conclusion:** The delivery technique for minimally invasive thyroidectomy is a safe and effective surgical procedure for thyroid lobectomy; however, it is contraindicated in cases of malignancy that require paratracheal nodal dissection and in cases of goiter.

### P057: Outcomes of Esthesioneuroblastoma: The UCSF Experience 1971-2001

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**Objective:** Esthesioneuroblastoma (ENB) is a tumor of neural crest origin arising from olfactory epithelium. Nearly 1000 cases have been reported as small series or case reports. Recent improvements in diagnosis and management have improved outcomes, however, the optimal treatment is still uncertain. Published studies of single institution reports are complicated by heterogeneous treatment regimens consisting of variations of chemotherapy, radiation, and surgery. In the modern era of skull base surgery, at UCSF, this disease has generally been approached with craniofacial resection and post-operative radiation. The goal of this study is to report our experience and potentially provide further insight into the optimal management of this unusual malignancy.

**Methods:** This is a retrospective study at a single large academic institution. Thirty eight patients were identified with ENB from 1971-2001 at our institution by the Cancer Registry. Of these, 26 were treated with surgical resection and radiation therapy. Three patients with positive margins had additional chemotherapy. Demographics, tumor staging, histopathology, and treatment regimen was recorded. A single pathologist reviewed the pathology, and a single neuroradiologist reviewed films. Outcomes were analyzed with Kaplan-Meier survival curves. and analyzed for staging systems and pathologic characteristics.

**Results:** Median follow up was 62mo (range 6 -258mo). Median survival was 157 months with 84% alive at 5 and 76% at 10 years. Disease recurred in 34% (mean 54mo) with local recurrence in 15% (mean 106mo) of the patients, regional metastasis in 19% (mean 35mo) and distant metastases in 11% (mean 74mo). Two patients underwent successful salvage surgeries, and 3 patients remain alive with disease after salvage chemotherapy. The Hyams pathological grade and Kadish staging systems most accurately reflected outcomes.

**Conclusion:** Our results demonstrate that surgical excision followed by postoperative surgery provides excellent outcomes, and salvage after recurrence is possible.

### P058: Concurrent Chemoradiotherapy and Gefitinib for Squamous Head and Neck Cancer: Preliminary Compliance Data

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**Background:** Recent concurrent chemoradiotherapy programs for locoregionally advanced squamous cell head and neck cancer have produced an improvement in locoregional control and survival. Distant metastases have now emerged as a more frequent cause of treatment failure. We hypothesized that the addition of long-term maintenance gefitinib, an orally administered epidermal growth factor receptor inhibitor, might reduce this incidence of distant metastatic disease.

**Methods:** At the Cleveland Clinic, patients with stage III-IV squamous cell head and neck cancer are offered participation in a clinical trial employing hyperfractionated radiation therapy (7200-7440 cGy at 120 cGy bid) and two courses of concurrent chemotherapy using 5-fluorouracil, 1000 mg/m<sup>2</sup>/day and cisplatin, 20 mg/m<sup>2</sup>/day; both given as 96 hour continuous intravenous infusions during weeks 1 and 4 of the radiation. Gefitinib, 250 mg daily is begun on the first day of the radiation therapy and is to be continued for a total of two years. Primary site resection is reserved for residual or recurrent primary site disease after chemoradiotherapy. Neck dissection is considered for N2 or greater disease, irrespective of clinical response, and for residual or recurrent neck disease after chemoradiotherapy.

**Results:** Since April 2003, 42 patients have been entered on this study, and 35 have completed their chemoradiotherapy. These 35 patients have a median age of 59 (range 24-75) years; 34 were white; 30 were male; 8 had stage III and 27 had stage IV disease. Primary sites were in the oropharynx in 23 patients, larynx in 7, hypopharynx in 4, and oral cavity in 1. The toxicity experienced was significant and similar to our previously reported experience with this chemoradiotherapy regimen. It included grade 3-4 mucositis in 30 patients (86%), neutropenia below 1000/mm<sup>3</sup> in 24 patients (69%) and hospitalization for neutropenic fever in 20 patients (57%). Gefitinib skin reactions were grade 1 in 19 patients (54%), and grade 2 in 3 patients (9%). Diarrhea attributed to gefitinib was grade 1 in 6 patients (17%), grade 2 in 1 patient (3%), and grade 3 in 2 patients (6%). Excluding the 2 patients experiencing early (unrelated) death, and censoring the 8 patients taken off study for either progressive disease or second primary neoplasms, the Kaplan-Meier projected likelihood of remaining on gefitinib during the 6 weeks of chemoradiotherapy was 91%, for 3 months 85%, for 6 months 78%, and for 12,18 and 24 months 66%. Drug was discontinued prematurely in 6 additional patients because of one or several gefitinib-related toxicities, in 2 patients because of concerns about wound healing, and in 2 others because of patient refusal. Based on pill counts, patients continuing gefitinib took a median 92% (range 47-100%) of the prescribed doses while continuing on study.

**Conclusion:** Despite adequate compliance with daily oral dosing of gefitinib, long-term maintenance therapy with this agent proved sub-optimal in a patient population undergoing aggressive multi-modality treatment. This study continues to accrue patients, and is supported by AstraZeneca Pharmaceuticals.

## **P059: Drain Removal After Neck Dissection Varies With Perioperative Fluid Balance**

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**Objective:** To determine whether a relationship exists between perioperative fluid balance and time to drain removal.

**Design:** Retrospective review.

**Setting:** Tertiary care center.

**Patients:** The medical records of all patients who underwent unilateral neck dissection over a 3-year period were reviewed. Exclusion criteria were simultaneous resection of the primary tumor, postoperative hematoma and seroma, chylous fistula, or an incomplete medical record of drain output. A total of 33 patients were included in the study.

**Interventions:** Dissection of all 5 levels was performed on all patients. All wounds were evacuated by a closed suction system. Output was recorded every 8 hours. The drains were removed if the total output over 3 consecutive shifts totaled less than 30 cc.

**Main Outcome Measures:** Patient variables measured included removal of SCM, IJ, or CN XI; prior radiation or chemoradiation, extracapsular extension, and history of hypertension or diabetes mellitus. Patient age, serum osmolality, hematocrit, intraoperative blood loss, intraoperative fluid administration, 24-hour fluid balance, TNM stage, and the number of positive nodes were also compared with the length of time that drainage was required.

**Results:** Results from a *t* test showed a significant difference in mean number of shifts until drain removal if the sternocleidomastoid muscle was removed (11.8 shifts) or preserved (9.4 shifts) ( $P = .04$ ). The Pearson correlation coefficient showed that intraoperative fluid administration ( $R = 0.42$ ;  $P = .02$ ) and 24-hour fluid balance ( $R = 0.38$ ;  $P = .03$ ) correlated with the length of time until drain removal. None of the other variables measured were statistically significant.

**Conclusions:** A direct relationship exists between the amount of fluid administered during neck dissection and length of time required for adequate wound drainage.

## **P060: Significance of Insulinlike Growth Factor Receptor I in the Development of Anaplastic Thyroid Cancer**

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**Objective:** To determine if loss of expression of phospho-insulinlike growth factor (p-IGF) receptor IGF IR in human thyroid cancer specimens correlates with progression to anaplastic disease and responsiveness to anti-IGF-IR therapy.

**Design:** Retrospective histopathologic study with institutional review board approval

**Subjects:** Expression levels of IGF-I, pIGF-IR, IGF-IR, Akt, and pAKT were evaluated in 36 thyroid cancer specimens, 6 normal thyroid glands, and thyroid tissue arrays using an immunoperoxidase assay.

**Interventions:** Response to a small molecule kinase inhibitor of IGF-IR was tested using thyroid cell lines that either express or do not express detectable levels of pIGF-IR.

**Results:** All components of the IGF pathway were overexpressed in thyroid cancers. Specifically, immunoreactive IGF-I was present in all of the thyroid tissues examined; it was lowest in normal thyroid tissues and highest in all thyroid carcinomas studied. The mean staining intensity of IGF-IR was remarkably high in ATC, FTC, and PTC specimens compared with controls. However, none of the ATC samples retained pIGF-IR expression. Some FTC and PTC specimens retained moderate to low expression of pIGF-IR, respectively, and were also strongly positive for pAKT expression. Consistent with this model, FTC and ATC cell lines with detectable pIGF-IR levels responded well to anti-IGF-IR therapy.

**Conclusions:** Loss of IGF-1R phosphorylation correlates with anaplastic histologic findings in human thyroid tumor specimens. However, the intensity of pIGF-IR expression is variable, depending on the stage and type of the disease.

Further studies are required to demonstrate the prognostic value of IGF-IR and its phosphorylated form in thyroid cancer progression.

## **P061: Postoperative Survival and Number of Lymph Nodes Examined During Surgery for Node-Negative Oral Tongue Cancer**

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**Objective:** To examine the association between survival and the number of lymph nodes (LNs) examined among persons who underwent surgery for node-negative tongue cancer that was confirmed by pathologic findings.

**Design:** Data from the Surveillance Epidemiology and End Results (SEER) database were reviewed (1988-2002). The association between survival and the number of regional LNs evaluated during surgery among patients with tongue cancer was examined by constructing Kaplan-Meier curves. We also used multivariate Cox proportional hazard models to calculate age-, race-, sex-, grade-, and diagnosis year-adjusted hazard ratios (HRs) for different numbers of LNs. In these analyses, a hazard ratio of less than 1.0 indicates increased survival.

**Results:** A total of 1064 patients were included in the study. The unadjusted (Kaplan-Meier) survival analyses demonstrated that in comparison to the reference group (1-10 LNs), patients who had at least 11 LNs examined during surgery had a statistically significant increase in survival rate (log rank,  $P = .01$ ). This association persisted after adjustment for potential confounders (hazard ratio, 0.75; 95% confidence interval, 0.59-0.94). Similar analyses by LN tertile, using the lowest tertile (1-12 LNs) as reference, demonstrated that patients in the second tertile (13-25 LNs) had significantly improved survival (a hazard ratio, 0.68; 95% confidence interval, 0.52-0.89), but there seems to be no incremental improvement after evaluating more than 25 LNs (hazard ratio, 0.80; 95% confidence interval, 0.61-1.03).

**Conclusions:** These data suggest that an optimal staging should be between 10 and 25 regional LNs. Accurate staging of cervical lymphatics dictates appropriate adjuvant treatment.

## **P062: Postoperative Swallowing Function in the Surgical Treatment of Tongue Base Cancers: Prospective Functional Outcomes**

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**Objective:** To examine the association between swallowing outcomes and biomechanical properties of the tongue base (TB) and posterior pharyngeal wall in the reconstructed oropharynx after primary resection of oropharyngeal cancer.

**Design:** Prospective cohort study with minimum of 1-year follow-up.

**Setting:** Tertiary care facility.

**Patients:** Patients diagnosed with primary carcinoma of the oropharynx treated with primary surgical resection and reconstruction followed by radiotherapy. Inclusion criteria were the collection of video-fluoroscopic swallowing study data from before surgery and 1 year after surgery. Thirty-six patients were treated over a 5-year period, and we included 20 in the final analysis.

**Interventions:** Resection of more than 50% of the tongue base (TB), reconstruction with a beaver-tail radial forearm free flap, followed by postoperative radiation. Pudding consistency was used during the videofluoroscopic swallowing study.

**Main Outcome Measures:** These were (1) aspiration score, (2) pharyngeal residue score, and (3) biomechanical analysis of TB and posterior pharyngeal wall mobility performed using images from videofluoroscopic swallowing study. The TB and posterior pharyngeal wall positions measured from two static bony landmarks.

**Results:** (1) Ninety-five percent of patients were able to swallow safely at 1 year, (2) mobility of the TB following surgery was reduced in all

postoperative videofluoroscopic swallowing study ( $P < .05$ ), (3) antero-posterior dimension or bulk of the TB was preserved ( $P < .05$ ), and (4) there was no significant difference in PPW mobility ( $P < .05$ ).

**Conclusion:** The beaver-tail radial forearm free flap provides a good functional reconstructive option following resection of oropharyngeal cancers. Preservation of the bulk of the TB improves apposition of the base of tongue and posterior pharyngeal wall, allowing possible compensation by the lateral pharyngeal wall to enable swallowing. The bulk of the TB may protect the glottis by preventing aspiration.

## **P063: Surgical Treatment for Head and Neck Paragangliomas: Is It Possible to Minimize the Postoperative Complications?**

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**Introduction:** Surgery is usually the primary treatment but sometimes a more conservative policy such as "wait and scan" or radiation therapy may be preferred. The aim of this study was to review and analyze the surgical outcomes.

**Methods:** A retrospective review of 51 patients treated surgically by the Otolaryngology Department at the University of Pittsburgh, Pittsburgh, PA, was performed from 1994 to 2003. We identified 15 men and 36 women grouped according to the anatomical location. The mean ages at diagnosis for jugulotympanic paraganglioma (JP), carotid body tumors (CBT), vagal paraganglioma (VP), and thyroid paraganglioma (TP) were 56 years, 39 years, 44 years, and 40 years, respectively.

**Results:** All patients were diagnosed radiographically using computed tomographic scan or magnetic resonance imaging. Forty-three patients presented with sporadic paragangliomas, and 8 with familial paragangliomas; 12 patients had multicentric disease; and 2 had malignant familial paragangliomas. There were no cases of mortality related to the surgical procedures. Complete tumor resection was obtained in 49 patients. Two patients received adjuvant radiation therapy. Eighteen patients suffered sequelae from their treatment. The total (range) durations of follow-up was 28 months (1-26) and follow-up for jugulotympanic paraganglioma, carotid body tumor, and thyroid paraganglioma were, respectively, 25 months (2-82 months), 27 months (1-92 months), 53 months (9-126), and 11 months. Three deaths occurred that were not related to paragangliomas, and 1 local recurrence was salvaged by radiation therapy.

**Conclusions:** Surgical treatment for paraganglioma was effective. In the group with vagal paraganglioma, morbidity was higher owing to sacrifice of the vagus nerve. Complete resections for early cases may minimize the postoperative sequelae. Familial paragangliomas may be suitable for early detection owing to recommended follow-up of patients and members of their families.

## **P064: Estimates and Analysis of Oral Cancer Incidence Rates Worldwide**

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**Objective:** To obtain an accurate estimate of the incidence of oral cancer worldwide by assessing rates in 175 countries.

**Methods:** Age-adjusted incidence rates for oral cancer were obtained for 175 countries from the International Agency for Research on Cancer GLOBOCAN database. Data for 2002 are presented for oral (*International Statistical Classification of Diseases, 10th Revision*, codes C00 to 13, except C11) using the national cancer registries from available countries with analysis of the demographic data, rates per country, and total new cases combining available data.

**Results:** Rates were obtained for 175 countries from the International Agency for Research on Cancer using national registries to determine sex-specific incidence rates per 100 000 people. There were 274 289 new cases of oral cancer worldwide based on the registry data obtained. The highest incidence rates for cancer of the oral cavity occurred in Papua, New Guinea (42 of 100 000 people per year), the Solomon Islands (35 of 100 000 people per year), and Melanesia (33 of 100 000 people per year). These rates are far higher than in other countries and were highest in men. Preliminary analyses present data

graphically by latitude, gross domestic product, and percentage of urbanization.

**Conclusions:** There exists significant variation in rates of oral cancer among these 175 countries, although the direct relationship of geographic and lifestyle behaviors will require further study. Country-specific prevalence rates of behavioral risk factors, including reverse smoking and tobacco use, betel nut quid chewing, and alcohol use, as well as dietary risk factors and human papillomavirus infection, are being sought.

## **P065: Life After a Total Laryngectomy: Is There Any? A Measure of Long-Term Survival, Functional, and Quality-of-Life Outcomes**

**T.D. Woodard;** A. Oplatek; G. Petruzzelli

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**Objectives:** To analyze postoperative clinical, functional, and quality-of-life (QOL) outcomes in patients who have undergone a total laryngectomy (TL) and to determine the impact of preoperative variables on long-term survival and QOL.

**Design:** Retrospective cohort study.

**Setting:** Tertiary care facility.

**Patients:** One hundred forty-three patients who underwent a TL from 1994 to 2005 were identified. Ninety-one patients underwent a TL for primary carcinoma and 52 for recurrent cancer.

**Main Outcome Measures:** Baseline characteristics and preoperative clinical variables were collected. Follow-up data and functional and QOL outcomes were collected via the Head and Neck Cancer Inventory. Survival was estimated using the Kaplan-Meier method.

**Results:** Mean (SD) survival for the entire cohort was 50 (29) months, and 58 patients were alive at follow-up. Univariate analysis revealed 5 significant predictors of long-term survival: cancer site in the larynx, T3 stage, N0-1 stage, only 1 or no comorbidity, and absence of a previous cardiovascular comorbidity ( $P < .05$ ). Multivariate analysis revealed T stage as a significant predictor of survival ( $P = .03$ ). Functional and QOL outcomes ranged from intermediate to high categories. Patient-related factors that correlated with significantly higher functional and QOL outcomes were age older than 65 years, only 1 or no comorbidity, no history of chemotherapy or radiation therapy, and primary tracheoesophageal puncture.

**Conclusions:** Several pretreatment clinical variables have an impact on long-term survival after a TL. Despite common belief, many patients who have undergone a TL do maintain an overall good QOL. This study also demonstrates several patient-related factors that influence health-related QOL outcomes after a TL.

## **P066: Annexin V Scintigraphy for Imaging of Apoptosis in Tumor and Normal Tissue in HNSCC Patients Treated With RADPLAT**

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**Background:** The level of apoptosis is an important factor in the response of many malignant tumors and normal tissues to cytotoxic therapy. The purpose of this study was to determine the value of <sup>99m</sup>Tc Hynic-rh-Annexin V scintigraphy (TAVS) imaging, a non-invasive technique to demonstrate apoptosis, in patients with head and neck squamous cell carcinoma (HNSCC), treated with concurrent cisplatin-based chemoradiotherapy (RADPLAT). We wanted to evaluate patterns of Annexin-uptake in normal tissue and tumor.

**Material and Methods:** 16 patients treated with intravenous or intra-arterial RADPLAT were included. Baseline TAVS was performed in all patients. Follow-up scans within 48 hours after the 1<sup>st</sup> course of chemotherapy in week 1 of treatment were performed in 15 patients. Prescribed radiation dose given at the time of follow-up TAVS was 6 or 8 Gy. The TAVS-activity was corrected for radioactive dose administered and body weight. Scintigraphy SPECT data were co-registered to diagnostic imaging and planning CT-scan. This complete set of data was available in 12 patients. For each patient regions of interest (ROI) were delineated: primary tumor, involved lymph nodes and salivary glands. The actual radiation dose given at the time of follow-up TAVS was calculated 3-D in our radiation treatment planning system. The Annexin-uptake was determined in each ROI, and the difference between follow-up TAVS and baseline TAVS represented the

actual Annexin-uptake: Delta-uptake ( $\Delta U$ ). Correlations were calculated between  $\Delta U$  in salivary glands, tumor and radiation dose.

**Results:** In parotid glands an increase in  $\Delta U$  was observed in 22 of 24 glands. The level of mean  $\Delta U$  was significantly correlated with the mean radiation dose given to the parotid gland (Pearson's correlation coefficient  $r = 0.59$ ,  $p = 0.002$ ): Parotid glands that received higher doses showed more Annexin-uptake. The  $\Delta U$  in primary tumor and pathological lymph nodes showed large interpatient differences. No differences in primary tumor Annexin-uptake were seen between intravenous or intra-arterial RADPLAT, nor between radiation doses of 6 or 8 Gy. No relation was observed between primary tumor  $\Delta U$  and tumor volume. A positive correlation for maximum  $\Delta U$  in primary tumor and lymph nodes was observed on an inter-patient level ( $r = 0.71$ ,  $p = 0.006$ ). The level of Annexin-uptake in tumor will be correlated with clinical outcome (response and/or locoregional control) after obtaining appropriate follow-up.

**Conclusion:** Annexin V scintigraphy showed a radiation-dose-dependent uptake in parotid glands, indicative of early apoptosis during treatment. The interindividual spread in Annexin-uptake in primary tumors could not be related to differences in treatment schedule or tumor volume, but the Annexin-uptake in tumor and lymph nodes were closely correlated. This effect might represent a tumor-specific apoptotic response.

## **P067: Genes Gone Silent: Transcriptional Down-Regulation of Genes in Head and Neck Squamous Cell Carcinoma**

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**Objective of the Study:** Head and neck squamous cell carcinoma (HNSCC), as a neoplastic disease of multifactorial etiology and great variability in risk factors, is one of the most heterogeneous malignancies in the world. In many cancers, including HNSCC, aberrant DNA methylation of so called CpG islands, CpG-rich sequences frequently associated with promoters or first exons, is frequently associated with the inappropriate transcriptional silencing of critical genes. There is also a growing awareness that overall patterns of genomic DNA methylation play a critical role in the molecular characteristics of neoplastic disease. The objective of this study was two-fold. First, we sought to identify genes specifically down-regulated in HNSCC compared to normal adjacent mucosa from the same patient. Second, we utilized a global epigenomic approach to compare patterns of DNA methylation in HNSCC samples.

**Methods and Procedures:** Our group recruited 26 patients undergoing treatment for HNSCC at Montefiore Medical Center in the Bronx. The samples represented pharynx/hypopharynx (18), larynx (5) and oral cavity (3) SCC. First, we used a microarray containing 27,323 cDNA clones to compare gene expression between HNSCC primary tumors (Cy3) and normal adjacent mucosa (Cy5). Our goal was to select genes specifically down-regulated in HNSCC compared to adjacent normal tissue. Second, our group epigenomically profiled CpG island hypermethylation in genomic DNA from these HNSCC primary tumor specimens using a microarray of 12,288 CpG island clones. This new technique, known as methylation-specific restriction enzyme (MSRE) microarray hybridization, is a comparison of a single DNA sample's response to a methylation-sensitive restriction enzyme (HpaII) and its corresponding methylation-insensitive isoschizomer (MspI).

**Results:** With the cDNA microarray approach, we identified greater than 100 genes down-regulated in HNSCC, including such genes as epithelial membrane protein 1 (EMP1), apolipoprotein D (ApoD) and uteroglobin (UTG). We have also demonstrated the feasibility of the MSRE assay in generating genomic patterns containing hundreds of methylated CpG island loci per tumor sample. We evaluated its sensitivity and specificity using genomic DNA isolated from HNSCC cases. Estimation of the reproducibility of this microarray assay demonstrated that repeated assays achieved 87% concordance or greater for HNSCC samples after filtering of microarray data by fluorescence intensity. We utilized hierarchical clustering on this population of 26 HNSCC samples to cluster tumor samples into molecularly distinct groups based on similar DNA methylation profiles.

**Conclusions:** We have established a reproducible assay that measures, on a global scale, DNA methylation of CpG island clones.

Furthermore, we have identified more than 100 genes specifically downregulated in HNSCC. It is hoped that the combination of these techniques will identify genes specifically silenced by DNA hypermethylation. If correlations with patient outcomes can be established, such findings could be translated into new diagnostics for early detection of cancer using minimally invasive PCR-based screening techniques, and could enhance clinical care by identifying new therapeutic targets and expanding treatment options.

## **P068: Life After a Total Laryngectomy: Is There Any? A Measure of Long Term Survival, Functional, and Quality of Life Outcomes**

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**Objectives:** To analyze post-operative clinical, functional, and quality of life (QoL) outcomes in total laryngectomy (TL) patients, and determine the impact of preoperative variables on long-term survival and QoL.

**Design:** A retrospective cohort study on patients who underwent a total laryngectomy between 1994 and 2005.

**Setting:** Tertiary care facility.

**Patients:** Patients that underwent a TL were identified (n=143). Ninety-one patients had a TL for primary carcinoma and 52 for recurrent cancer.

**Main Outcome Measures:** Baseline characteristics and preoperative clinical variables were collected. Follow-up data, functional and QoL outcomes, was collected via the Head and Neck Cancer Inventory (HNCI). Survival was estimated using the Kaplan-Meier method.

**Results:** Mean survival for the entire cohort was  $50 \pm 29$  months and 58 patients were alive at follow-up. Univariate analysis revealed 5 significant predictors of long term survival: cancer site in the larynx, T3 stage, N0-1 stage, less than 2 comorbidities, and absence of a previous cardiovascular (CV) comorbidity ( $p < .05$ ). Multivariate analysis revealed T stage as a significant predictor of survival ( $p = 0.025$ ). Functional and QoL outcomes ranged from intermediate to high categories. Patient related factors that correlated with significantly higher functional and QoL outcomes were: age greater than 65, less than 2 comorbidities, no previous history of chemo-RT, and primary tracheoesophageal puncture.

**Conclusions:** Several pre-treatment clinical variables have an impact on long-term survival after a TL. Despite common belief, many patients that have undergone a TL do maintain an overall good QoL. This study also demonstrates several patient-related factors that influence health-related QoL outcomes after a TL.

## **P069: The Effect of Second-Hand Smoke in Patients With Squamous Cell Carcinoma of the Head and Neck**

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**Purpose:** To assess the effect of second-hand smoke on patients treated for head and neck squamous cell carcinoma.

**Design:** Prospective longitudinal cohort study.

**Setting:** Tertiary referral, teaching center.

**Patients:** One-hundred thirty-five patients were enrolled.

**Intervention:** Patients filled out an exhaustive smoking and alcohol questionnaire on presentation. They completed abbreviated questionnaires at each follow-up appointment. All patient data were collected prospectively by a dedicated research nurse. All patients had a minimum of 5 years of follow-up.

**Main Outcome Measures:** Survival and disease recurrence.

**Results:** One hundred twenty-seven patients completed the study, 74% of whom had been exposed to second-hand smoke. Exposure to second-hand smoke was associated with increased recurrence risk and decreased survival.

**Conclusions:** Smoking cessation in the home environment should be addressed with patients with head and neck cancer.

## P070: Why Are Head and Neck Cancer Clinicians Not Measuring Quality of Life?

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**Objective:** To quantify and qualify the use of quality-of-life (QOL) measures by head and neck cancer clinicians and to identify any impediments to their use.

**Design:** Questionnaire survey of members of the Australia and New Zealand Head and Neck Society.

**Setting:** Professional body of head and neck clinicians in Australasia.

**Main Outcome Measures:** Use of head and neck cancer QOL questionnaires, reasons for current use, and preferred characteristics of a consensus QOL questionnaire for patients with head and neck cancer.

**Results:** One hundred twenty-eight (68.5%) of 187 members responded. Only 43 (34%) had ever used a QOL questionnaire, and only 17 (13%) were currently using one. Impediments for use were that it was too time consuming to do so, lack of resource, and no proven benefit for clinical treatment. Nevertheless, 113 (88%) indicated willingness to use the minimum core QOL questionnaire for routine clinical use and for research but indicated a preference for a short (10-15 questions), quick (< 10 minutes) questionnaire.

**Conclusions:** This study highlights a gap between clinicians' practices and patients' stated preferences. Most head and neck cancer clinicians in Australasia do not use a QOL measure routinely, with impediments to routine use being mainly clinician based. Most respondents would use a minimum core QOL measure, especially if it were a short, quick consensus questionnaire. Comparisons with head and neck cancer clinicians from other countries are also made.

## P071: Assessment of Response Using Fluorodeoxyglucose F 18 Positron Emission Tomography and Computed Tomography to Evaluate Patients With Head and Neck Cancer After Definitive Radiation Therapy: Preliminary Results

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**Objective:** To evaluate the detection of persistent disease following definitive radiation therapy in patients with head and neck cancer using fluorodeoxyglucose F 18 positron emission tomography and computed tomography (FDG-PET/CT).

**Methods:** Posttreatment FDG-PET/CT was performed in 28 patients after completing definitive radiation therapy and was visually analyzed at 2 time points (4-8 weeks and >8 weeks after treatment). Pathological confirmation and clinical follow-up served as the reference standard.

**Results:** The overall specificity, sensitivity, and accuracy of FDG-PET/CT for detection of residual disease were 93.3%, 76.9%, and 87.5%, respectively. Posttreatment, the specificity, sensitivity, and accuracy of FDG-PET/CT performed more than 8 weeks after treatment were higher than those performed before treatment (100% for all vs 87.5%, 66.7%, and 76.5%, respectively). Follow-up data were collected at a mean time point of 17.6 months posttreatment (range, 4.5-33.6 months). Fifteen patients had persistent disease at an average of 3.6 months after treatment, and 1 patient experienced a recurrence at 11.6 months posttreatment. Twenty-one patients survived (mean duration of follow-up, 20 months), 12 of whom remain disease-free, and the disease of 6 patients remains locoregionally controlled by salvage therapy.

**Conclusions:** The assessment for treatment response using FDG-PET/CT was more accurate when performed 8 weeks after radiation therapy. Although PET/CT has not yet been established as a routine surveillance method, these encouraging preliminary results may advocate the effectiveness of this imaging modality in the detection of persistent or early failure after definitive radiation therapy. The opportunity for early salvage therapies prompted by a former diagnostic method may alter the long-term outcome for these patients with cancer.

## P072: Multivariate Analysis of Multidomain Quality-of-Life Predictors Among Head and Neck Cancer Patients

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**Objective:** To determine, among patients with head and neck cancer, factors predicting quality of life (QOL), depression, and fatigue more than 3 months after diagnosis.

**Design:** Survey study.

**Setting:** Academic oncology clinic.

**Patients:** Convenience sample of 39 patients with head and neck cancer (response rate, 92%). Most were men (82%) and white (92%) with a mean age (SD) of 59 years (13.3 years). The primary cancer sites were the oral cavity (26%), oropharynx (28%), and larynx (28%); 23% of tumors were stage I; 10%, stage II; 23%, stage III; and 44%, stage IV.

**Main Outcome Measures:** Chart audit and self-administered survey. The Functional Assessment of Cancer Therapy-Head and Neck (FACT H-N) measured the total QOL including physical well-being, social well-being, emotional well-being, functional well-being, and additional concerns. Physical, social, emotional, and functional well-being were summed for FACT-General (FACT-G). The Center for Epidemiological Studies Depression Scale assessed depression and the Likert-scale measured fatigue.

**Results:** Pearson correlations for QOL, depression, fatigue, age, sex, education, income, history of smoking, alcohol use, presence of comorbidity, body mass index, stage, node involvement, tumor size, and treatment type were followed by multiple linear regression for significant factors (ie,  $P < .05$ ). No factor was significantly associated with emotional well-being, social well-being, or depression. With multiple linear regression, less node involvement was the only independent predictor of better total QOL (ie, FACT H-N) ( $R^2 = 0.15$ ) and reduced fatigue ( $R^2 = 0.17$ ). Alcohol use predicted better physical well-being ( $R^2 = 0.17$ ) and functional well-being ( $R^2 = 0.18$ ). Prior radiation predicted poorer QOL related to additional concerns ( $R^2 = 0.18$ ) whereas alcohol use and less node involvement were independently associated with higher FACT-G scores ( $R^2 = 0.24$ ).

**Conclusions:** Although future research is needed for confirmation, node involvement may impair QOL and fatigue independent of treatment. Alcohol use is associated with improved QOL possibly owing to its use as a coping mechanism.

## P073: Deciphering the Distinct Molecular Signatures of Head and Neck Squamous Cell Carcinomas

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**Objective of the Study:** Head and neck squamous cell carcinoma (HNSCC), as a neoplastic disease of multifactorial etiology and great variability in risk factors, is one of the most heterogeneous malignancies in the world. Recent efforts by our group have focused upon analysis of global gene expression changes, in the hope of identifying changes in gene expression associated with head and neck carcinogenesis, and in identifying specific genetic signatures predictive of outcome in this disease.

**Methods and Procedures:** Our group has utilized a microarray containing 26,171 cDNA clones in order to generate individual gene expression profiles for 57 HNSCC patients undergoing treatment with curative intent at Montefiore Medical Center in the Bronx. Total RNA was extracted and purified from primary HNSCC tumor samples and compared to a universal human reference library of RNA. Tumor samples represented pharynx/hypopharynx, larynx and oral cavity SCC. Hierarchical clustering and supervised analysis methods were used to identify distinct gene expression signatures associated with clinical parameters such as anatomic site, grade of the disease including TNM status, and patient smoking exposure.

**Results:** The mean age at diagnosis of patients was  $62 \pm 12.2$  years of which approximately half (54%) were male. Three-fourths (75%) of

patients reported ever smoking. The majority of tumors (44%) originated in the pharynx, and 23% and 33% were from the oral cavity and larynx, respectively. Most tumors (84%) presented with advanced overall stage (III/IV) and metastatic lymph nodes (65%) at diagnosis. We identified approximately 156 cDNA clones that were differentially expressed between oral and pharyngeal or laryngeal tumors (Benjamini-Hochberg corrected  $p$ -value $<0.05$ ) including genes involved in cell metabolism and transport. Of these, 93 had higher average expression levels in oral tumors, whereas 63 were on average expressed at lower levels.

**Conclusions:** Gene expression profiling revealed differentially expressed gene profiles for tumors originating in the oral cavity, larynx or pharynx. Analysis by anatomic site also indicated somewhat distinct gene expression profiles for HNSCC tumors with respect to smoking exposure and disease grade. Efforts are ongoing to identify global gene expression changes associated with HNSCC carcinogenesis, and specific genetic signatures predictive of outcome in this disease.

## **P074: Predictive Value of Response to Induction Chemotherapy in Head and Neck Cancer**

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**Background:** Induction chemotherapy (IC) and concomitant chemoradiotherapy (CRT) is effective treatment for squamous cell carcinoma of the head and neck (SCCHN). While the majority of patients achieve a complete response after CRT, the responses to IC are variable. The purpose of this study was to assess the predictive value of initial response to IC with respect to disease relapse and survival.

**Methods:** Data from six multi-institutional clinical trials (from 11/89 to 11/04) involving IC/CRT regimens were combined and revised to conduct a retrospective analysis comparing patients with complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). The primary endpoint was progression-free survival (PFS); secondary endpoints included overall survival (OS), disease-specific survival (DSS), and site of relapse (local vs. distant). Kaplan-Meier and cumulative incidence curves were used to describe survival/event probabilities; log-rank tests and Cox models were used in univariate and multivariate analyses.

**Results:** 395 subjects were included in the analysis: 105 females and 290 males; mean age 55.9; and stage IV disease in 370 (94%). 352 of 395 (89.8%) subjects completed 75% of intended IC doses. The initial responses were 42% CR, 48% PR, 9% SD, and 2% PD. In PFS analysis, subjects with PR and SD had 66% and 225% increased risk, respectively, compared to patients with CR ( $p=0.001$ ). OS analysis showed patients with PR and SD had 50% and 146% increased risk of death over patients with CR ( $p=0.023$ ). In DSS analysis, compared to patients with CR, patients with PR and SD had 47% and 293% increased risk, respectively, of death due to primary cancer ( $p=0.012$ ), but the risk of dying from other causes was not predicted by initial response ( $p=0.56$ ). Initial response to IC appears to also better predict distant relapse than local relapse: compared to patients with CR, patients with PR and SD had 120% and 551% respectively increased risk of having distant relapse ( $p=0.002$ ), but 28% and 197% increased risk of having local relapse ( $p=0.17$ ).

**Conclusion:** Response to IC appears to be an effective predictor of PFS and OS. Differential effects of the response to IC in predicting site-specific relapse and DSS are also evident.

## **P075: Feasibility of Single Level Dissection for the N+ Neck Following Treatment With Radiation With or Without Chemotherapy**

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**Objective:** To determine the distribution of positive nodes in planned neck dissections performed for residual disease in the neck following definitive treatment of the primary with radiation + chemotherapy.

**Material and Methods:** Fifty-one patients with cancer of the larynx, oropharynx or hypopharynx and lymph node metastases, treated between January 1999 and March 2005 were studied. They underwent 55 planned neck dissections for clinically or radiologically apparent residual disease, after definitive treatment of the primary

tumor with radiation + chemotherapy. The neck was staged N1 in 19 (38%) patients, N2a in 8 (16%), 2b in 10 (20%), 2c in 6 (12%) and N3 in 7 (14%). The mean radiation dose was 7077 cGy and 5814 cGy to the primary and neck respectively. Twenty-one patients received chemotherapy. The neck dissections included lymph node levels II-IV in 32 (58%) of the cases, II-III in 16 (29%), I-IV in 4 (7.1%) and one each of I-IV, II-V and II only. Patients were followed for a minimum of 12 months (mean 16.6mo) or until death. The number and location of the positive lymph nodes prior to treatment and prior to neck dissection were mapped and compared with the number and location of the histologically positive nodes.

**Results:** 1) Histologically viable looking tumor was found in one or more lymph nodes in 15/55 neck dissections (27.2%) 2) Five patients had clinical or radiological evidence of metastases in Level II only; in all of them (5/5) histologically positive nodes were found only in Level II. Eight patients had clinical/radiological evidence of metastases in Levels II and III (1 patient also had a node in Level V); histologically positive nodes were found in different combinations in Level II, III and IV. Two patients had clinically/radiologically positive nodes in Levels I and II; histologically positive nodes were found in Levels I and II in one of them and in Level I and III in the other.

3) At the time of the analysis, 6 patients had died (Overall survival 87.2%). Four patients had died of disease and only 1 had recurrence in the neck and BOT. Only 2 (4%) patients had developed a recurrence in the neck, both occurring in the dissected area of the neck. No recurrence occurred in neck sites that were histologically negative or had positive nodes in only one Level of the neck. On the other hand, of the 5 patients with pathologically positive nodes in 2 or more levels, 2 (40%) developed a recurrence. With mean follow up of 25.9 months, there was only 1 recurrence in the neck (2.4%) and 4 at the primary site.

**Conclusions:** The data suggests that patients with clinical and radiologically positive nodes in Level II only could benefit from a single level dissection. As we do this in the future, the rate of recurrence in the neck observed in this study (4%) should serve as an efficacy benchmark.

## **P076: International Variation in Age-Adjusted Nasopharyngeal Cancer Incidence Rates Among 175 Countries**

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**Objective:** To obtain an accurate estimate of the incidence of nasopharyngeal cancer (NPC) by country using data obtained from 175 countries.

**Methods:** Using the national cancer registries from available countries during a recent single calendar year, we extracted the incidence of NPCs and analyzed the demographic data, rates per country, and total new cases, combining available data from these selected countries.

**Results:** Rates were obtained for 175 countries from the International Agency for Research on Cancer using national registries to determine sex-specific incidence rates per 100 000 people. There were 55 796 new cases of nasopharyngeal cancer worldwide. Incidence data for 2002 are presented for NPC by country. The highest rates of NPC were in Brunei (17 of 100 000 persons per year), Singapore (15 of 100 000 per year), and Malaysia (12 of 100 000 per year). These rates are far higher than in other countries and were highest in men. Data are presented graphically by latitude, gross domestic product, and percentage of urbanization. Latitude was statistically significantly inversely associated with NPC incidence in men ( $P$  value = .02) and women ( $P$  value = .03).

**Conclusions:** Current evidence suggests that NPC is an uncommon cancer worldwide and that variation in international age-adjusted incidence rates for NPC may provide clues to its etiology. The results may reflect a relationship between latitude and endemicity of the Epstein-Barr virus. Country-specific prevalence rates of known NPC risk factors, including Epstein-Barr virus infection, are being sought.

## P077: Swallowing Outcomes Following Supracricoid Partial Laryngectomy in the Setting of Adjuvant Therapy

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**Objective:** To evaluate swallowing recovery following supracricoid partial laryngectomy.

**Design:** Retrospective review.

**Setting:** Major comprehensive cancer center.

**Patients:** Twenty-seven patients treated with supracricoid partial laryngectomy for primary or recurrent larynx cancer.

**Intervention:** Functional swallowing strategies, maneuvers, and therapies based on objective modified barium swallow study results.

**Main Outcome Measures:** Hospital recovery (length of stay, decannulation rates, complications), swallowing outcomes (physiology, symptoms), and nutritional results (time to oral intake, tube dependency, final diet).

**Results:** Supracricoid partial laryngectomy included 1 arytenoid cartilage in 8 of 27 patients. The mean (SD) length of hospitalization was 8 days (9.23 days [median, 6 days; range, 3-53 days]) with a mean (SD) number of weeks to decannulation of 5 (8.23 weeks [median, 1 week; range, 1-30 weeks]). One patient required permanent tracheostomy. The most common complications were pneumonia and subcutaneous emphysema (7 [26%] of 27 complications). Pneumonia occurred more often in patients who had received radiation therapy ( $P = .02$ ). Twenty-two patients had MBS studies. Initially, all patients aspirated thin liquids and 55% (12 of 22) aspirated pureed consistencies owing to neoglottic incompetency. Diet modifications alone did not alleviate aspiration; 64% (14 of 22) of patients needed to use swallowing strategies. The supraglottic swallow maneuver was most effective in reducing or eliminating aspiration. Eighty-one percent (22 of 27) of patients returned to complete oral intake with mean (SD) time to feeding tube removal of 10 weeks (8.33 weeks [median, 6 weeks; range, 1-29 weeks]); 7 of these patients used swallowing strategies. Nineteen percent of patients (5 of 27) remained partially (4 of 27) or fully (1 of 27) tube dependent. Arytenoid resection did not significantly affect hospital course or swallowing outcomes.

**Conclusion:** Supracricoid partial laryngectomy initially produces severe swallowing dysfunction but most patients return to oral intake following targeted dysphagia intervention.

## P078: Quality-of-Life Priorities in Kenyan vs American Head and Neck Cancer Patients

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**Objective:** Observed differences in the quality of life of Kenyan and American patients with head and neck cancer may be related to cultural differences in illiteracy rates, diet, and social habits. To determine whether speech or swallowing is of higher priority to Kenyan vs American patients with head and neck cancer.

**Design:** Prospective, cross-cultural, cross-sectional study.

**Setting:** Tertiary head and neck cancer clinics at the University of Washington, Seattle, and the Kenyatta National Hospital, Nairobi, Kenya.

**Patients:** Long-term survivors of cancer of the oral cavity.

**Outcome Measures:** Validated English and Swahili versions of the University of Washington Quality of Life scale (head and neck cancer-specific quality of life) and the Patient Health Questionnaire-9 (depression).

**Results:** Nine Kenyan and 21 American patients were recruited. Despite similar T stage and treatment distributions, Kenyans had much worse scores for the University of Washington Quality of Life scale (42 vs 73;  $P < .05$ ). Although 56% of Kenyans rated speech as one of the 3 most important domains, only 24% of Americans did so. In contrast, 76% of Americans selected swallowing vs 44% of Kenyans. More Kenyans had depressive symptoms; 88% of Kenyan patients had at least moderate depression vs 21% of American patients.

**Conclusion:** We observed important cultural differences in priorities between patients with head and neck cancer in the United States and in Kenya. Speech seems to be more important to Kenyan patients, which may be related to higher rates of illiteracy. Swallowing seems more important to Americans, which may be related to the firmer textured diet and greater need to eat in public. Differences in depression were also observed. More data remain to be collected to confirm these initial impressions.

## P079: Swallowing Recovery and Chronic Aspiration After Supracricoid Partial Laryngectomy

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**Objective:** To evaluate the long-term swallowing status and the radiological manifestations of chronic aspiration in patients who have undergone supracricoid partial laryngectomy and to demonstrate that this procedure causes a mild and well-tolerated grade of chronic aspiration that does not require a nothing-by-mouth status.

**Design:** Cohort study. The follow-up period ranged from 3 to 13 years.

**Setting:** Referral medical center.

**Patients:** One hundred sixteen consecutive patients (mean age, 67 years) treated with supracricoid partial laryngectomy were analyzed. The patients included in the study were NED, followed up for more than 3 years, were without tracheal cannulae and nasogastric tubes and were able to feed orally. Twenty patients with chronic obstructive pulmonary disease and normal deglutition made up the control group.

**Intervention:** Evaluation of postoperative swallowing disorders included a careful observation of the patients by the physician, fiberoptic endoscopic evaluation of swallowing, and videofluoroscopy.

**Main Outcomes Measure:** Clinical grading of postoperative aspiration was assessed according to the Leipzig and Pearson scale. Radiologic manifestations of chronic aspiration were recorded using high-resolution computed tomographic scans.

**Results:** Higher incidences of bronchiectasis, lung cysts, and alveolar septal thickness were found in the patients affected by postoperative dysphagia compared with the control group. No significant differences were noted between the groups with reference to the remaining radiologic findings.

**Conclusion:** Supracricoid partial laryngectomy causes a mild and well-tolerated grade of dysphagia that does not require a nothing-by-mouth status. Patients with chronic aspiration showed pulmonary conditions similar to patients with chronic obstructive pulmonary disease.

## P080: Soft Palate Reconstruction Using the CAP Modification of the Radial Forearm Flap: An Assessment of Functional Outcomes

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**Objective:** To report prospectively collected aeromechanical, acoustical, and perceptual speech outcomes for soft palate reconstructions using the complete closure of the adynamic portion of the soft palate (CAP) modification of the radial forearm free flap.

**Design:** Prospective case series.

**Setting:** Tertiary referral teaching center.

**Patients:** Nine patients with soft palate defects of 75% or greater were included in the study.

**Intervention:** All the defects were reconstructed with a radial forearm free flap with the CAP modification.

**Main Outcome Measures:** Acoustical, aeromechanical, and perceptual speech data were collected at 3 evaluation times (before surgery and before and after radiation therapy).

**Results:** The soft palates of all patients were reconstructed with CAP modification. There were no significant differences at any of the evaluation times for VPO, nasalalance, or speech intelligibility. All patients resumed a normal oral diet, and none were gastric-tube dependent.

**Conclusions:** The CAP method of soft palate reconstruction provides good restoration of aeromechanical, acoustical, and perceptual speech outcomes.

## **P081: Minimally Invasive Parathyroidectomy Under Local Anesthetic: Patient Satisfaction and Outcome**

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**Objective:** To assess postoperative outcomes and overall patient satisfaction with minimally invasive single gland parathyroidectomy performed under local anesthesia.

**Design:** Prospective longitudinal cohort.

**Setting:** Tertiary level care referral center.

**Methods:** Twenty patients were enrolled. Patients filled out a patient satisfaction survey immediately after surgery, 4 hours after surgery, and at the time of discharge. Postoperative parameters measured were analgesic consumption, nausea, vomiting, headache, sore throat, and hospital stay. These were compared with historical controls who underwent parathyroidectomy under general anesthesia.

**Results:** Patients experienced less pain and fewer postanesthesia adverse effects than controls. Patients had an overall high rate of satisfaction with their surgical experience.

**Conclusions:** Minimally invasive single gland parathyroidectomy under local anesthesia is an excellent option for patients. They experience less pain and fewer postanesthesia adverse effects than with the general anesthesia method.

## **P082: Questionnaire Analysis of the Swallowing-Related Quality of Life Following Total Laryngectomy**

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**Objective:** To determine the effects of a total laryngectomy on the swallow and subsequent quality of life (QOL) in patients with head and neck cancer.

**Design:** Cross-sectional single center cohort study.

**Setting:** Head and Neck Oncology Unit and Tertiary Referral Unit.

**Patients:** Sixty-two patients of an initial cohort of 77 from the laryngectomy database who underwent total laryngectomy at our center.

**Methods:** Subjects were stratified by age, sex, tumor stage, and other procedures such as myotomy and nerve reimplantation. Pharyngectomy, glossectomy, flap reconstruction, neck dissection, and previous radiotherapy and chemotherapy were also assessed to see if they had affected swallow and subsequent QOL. Main outcome was measured using the M. D. Anderson Dysphagia Inventory (MDADI) questionnaire.

**Results:** Responses were received from 46 men and 16 women (response rate, 80.5%) with a median age of 63 years (range, 40-79 years). The mean (SD) MDADI total score in our series of patients was 77.7 (16.6). The MDADI global score was 79.4 (22.6), the emotional score was 77.7 (17.8), the functional score 81.3 (15.9), and the physical score was 74.1 (18). The MDADI global scores were significantly higher after cricopharyngeal myotomy but were significantly lower after chemotherapy. No significant correlation was seen between the subscale scores and the remaining treatment variables such as age, sex, site, tumor stage, PE segment closure, nerve implantation, radiotherapy, reconstruction, and major complications.

**Discussion:** The results of our questionnaire study, which to our knowledge is the largest of its type to date involving patients who have undergone a laryngectomy at a single center, revealed a very good swallow. This study shows that despite the loss of the larynx, patients do generally go on to establish good swallow after laryngectomy. Myotomy improves QOL while the toxic effects of chemotherapy should be borne in mind as a possible cause for reduced QOL. Further work is advised to assess the value of interventions to improve the swallow of patients who undergo laryngectomy.

## **P083: Interactions of ATF2 and ERK Result From Treatment with P38 Inhibitors in HNSCC Cell Lines**

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Activation of ATF2 results in regulation of genes involved in cell growth and proliferation and the ability to resist apoptosis. The p38 signaling pathway plays a key role in ATF2 signaling and response to treatment. Modulation of ATF2 activation has been shown to result in effects on TNF alpha signaling in a melanoma model. Melanoma shares with HNSCC a similar profile of transcription factors that are up-regulated including ATF2 and in previous studies we have demonstrated functional activity of ATF2 in HNSCC. Two distinct MAPK pathways for ATF2 phosphorylation and activation are known: 1. p38 MAPK pathway activated by cellular stress, e.g., UV light, osmotic and oxidative stress, and inflammatory cytokines; and, 2. JNK: stress-activated pathway, activated by some chemotherapy agents (e.g. cisplatin). The role of ERK1/2 in HNSCC downstream of cell surface receptor activation (e.g. EGFR or TNF alpha) is well-established and may have significance in p38-determined ATF2 effects.

**Objective:** In this study of HNSCC cell lines, we examine the interactions of these MAPK pathways and regulation of ATF2 activation in response to modulation of p38 activity using SB203580, a selective inhibitor of p38 MAPK. We also studied effects downstream of TNF alpha on this system.

**Methods:** The activation of ATF2, ERK1/2, p38, were determined by Western blot analysis using antibodies specific for phosphorylated and unphosphorylated forms of these proteins.

Cells proliferation was measured using MTT assay. Student's t-test was used for statistical verification of results.

**Results:** We demonstrate that UMSSC cells treated with high (50  $\mu$ M and 10  $\mu$ M) concentrations of SB203580 alone for 24 h showed toxicity while cells treated with lower concentrations

(5  $\mu$ M : 0.1 $\mu$ M) looked healthy. At drug concentration of 5  $\mu$ M, pATF2 and p44/42 were clearly increased although total ATF2 and total ERK expression were not changed. We also explored these changes downstream of TNF alpha stimulation. These results demonstrate that at a concentration of 5  $\mu$ M SB203580 increased pATF2 expression in parallel with pERK activation while total ATF2 and total ERK remained unchanged.

**Conclusions:** We show that ATF2 acts in tandem with ERK in response to p38 modulation and downstream of TNF receptor activation. This suggests that additive or synergistic effects may be seen as a result of treatment combinations that target these individual MAPK proteins. Further study will explore these combinations and their effects on cell survival and apoptosis.

## **P084: Longitudinal Oncology Registry of Head and Neck Carcinoma (LORHAN): A New National Cancer Registry**

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**Objective:** Registries are invaluable for describing care patterns and outcomes for a population of patients. Most cancer registries, however, lack sufficient breadth or depth to provide a comprehensive picture of clinical practice. Because management of head and neck cancer is increasingly treated with chemotherapy and radiation, we report the launch of LORHAN, a novel national registry of head and neck carcinoma (HNC) patients designed to examine contemporary patterns of care of HNC. LORHAN extends current cancer registries by providing detailed data on radiation and/or cancer drugs delivered to HNC patients, in addition to surgery, in all practice settings.

**Methods:** LORHAN is a prospective, multi-center, longitudinal, observational registry whose primary objective is to describe, in detail, patterns of care for HNC patients. Secondary objectives include documenting outcome by treatment regimen, incidence and severity of major toxicities and to identify supportive care received for

managing treatment-related complications. Patients participating in clinical trials are eligible for LORHAN. Patients with newly diagnosed HNC, scheduled to receive radiation or drug therapy with or without surgical resection, greater than or equal to 18 years of age and providing written informed consent are eligible for inclusion. In contrast to other cancer registries, detailed information regarding initial treatment and type of surgery, including curative, debulking and staging, performed either prior or subsequent to non-surgical therapy is captured. Patients are entered in LORHAN at time of initial diagnosis and are followed for a minimum of 2 years to a maximum of 10 years. Data entry is electronic, incorporating encrypted point-to-point data transfer via secure HTTP protocols. Participating practitioners can review and compare their data on a real-time basis to the broader registry database. Registry patients may be linked to the National Death Index to minimize lost to follow-up and obtain cause-specific survival rates. Analyses of data are primarily descriptive.

**Results:** LORHAN deployed Oct. 2005 and as of March 21 2006, 11 sites are approved to enroll. 19 patients have been enrolled to date. Sites are broadly distributed between academic sites and community-based practices. An additional 32 sites (24 academic, 8 community) are at various stages of participation. More than 100 physicians are anticipated to participate and approximately 26,000 patients will be eligible each year. Accrual status will be updated.

### **P085: The Patient's Experience of Choice in Cancer Treatment Decision Making**

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**Objective:** Describe the patient experience of head and neck cancer treatment decision-making. Surveys of cancer patients suggest that they want to participate in decisions for their treatment, and much of today's literature supports 'shared' decision making as the standard approach. However, we do not know the extent to which this paradigm of collaboration and debate of treatment choices fits the reality of head and neck cancer patients' decision-making process.

**Methods:** Prospective, longitudinal, qualitative study of 25 patients with a suspected or newly diagnosed head and neck cancer (mean age 58, 56% male). Data gathered: audiotapes of physician consultations, audio diaries kept by the patient on a portable cassette recorder prior to starting treatment, and a post treatment decision semi-structured interview several weeks later.

**Results:** Common choices identified in the transcripts were: radiation and/or chemotherapy vs. surgery vs. palliation (generally framed in passive terms: eg: 'let nature take its course'), or timing and type of surgery.

**Recall:** When interviewed, all patients who had been offered a choice of treatments were able to recall their choices and the associated risks when compared to transcripts of the physician consultations. They typically described themselves as having made their own decision about treatment.

**Choice of Treatments:** Half of patients who were offered choices, even after describing their choices, stated they felt they had 'no choice', either because they were facing death, or because the illness was cancer. Common characteristics of those feeling they had 'no choice' were a) one of the treatment choices offered was palliation (all patients offered palliation felt they had no choice), and b) severe pain (all but one described the presence of serious physical discomfort due to their cancer, either in their diaries or during their interviews). Major factors considered in decision making: not wanting to die, need for relief of pain due to the cancer, feeling of trust or confidence in the physician. Information about risk/complications was generally not used by people who perceived themselves to have 'no choice'.

**Conclusions:** In practice, decision making for head and neck cancer treatment did not fit the idealized concept of shared decision making. Patients remembered the details of their discussions with physicians, but made treatment decisions based on other factors, most notably a need for pain relief, and fear of death. Perhaps because of this, many patients felt they had no choices, although they still identified themselves as making their own decisions. These findings provide useful insight into the early patient experience, and will be helpful as outcomes data are formulated into decision aids for head and neck cancer treatment decision-making.

### **P086: Production of Proinflammatory Cytokines in Larynx Cancer**

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**Objectives:** The role of proinflammatory cytokines (IFN, TNF, IL-6, and IL-10) in the activity of cytotoxic CD 8+ T lymphocytes can interfere in the host's response to neoplastic cells. We quantified preoperative and late postoperative levels of IFN, TNF, IL-6, and IL-10 cytokines in supernatants of peripheral blood mononuclear cell cultures of larynx cancer patients to check the influence of the larynx carcinoma treatment on the immune response.

**Study Design/Methods:** Adherent and nonadherent cells cultures were stimulated with LPS and Con-A, respectively. Seventeen patients with larynx cancer were studied. Cytokine concentration was determined by enzyme-linked immunosorbent assay in supernatants of mononuclear cell cultures.

**Results:** In unstimulated cultures, patients with larynx cancer revealed lower IFN levels in the preoperative period ( $P = .003$ ) and LP ( $P = .02$ ) than controls, with lower levels of TNF cytokine in the late postoperative period ( $P = .01$ ) and decreasing preoperatively ( $P = .08$ ). IFN, TNF, and IL-6 exhibited high levels in cultures stimulated with Con-A and LPS during the late postoperative period, compared with the preoperative period ( $P = .001$ ;  $P = .01$ ;  $P = .004$ ; respectively).

**Conclusion:** It seems that patients with larynx cancer can present deficient cellular immune responses, expressed by the lower production of IFN and TNF associated with the tumor, whose removal seems to have a positive modulatory function, leading to the recovery of IFN, TNF, and IL-6 production capacity in the postoperative period.

### **P087: Quality of Life in Patients Treated for Oral, Pharyngeal, and Laryngeal Cancer in São Paulo: Multicentric Study**

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**Objective:** The objective of the multicentric study was to evaluate the quality of life of patients with oral, pharynx, and larynx cancer treated in São Paulo, Brazil, taking into account the sociodemographic, economic, and clinical factors.

**Methods:** Patients who had survived at least 1 year without disease were included. Selected patients were invited to answer a Portuguese version of the Functional Assessment of Cancer Treatment-Head and Neck (FACT-HN) questionnaire, which can be summarized in 3 global indices: TOI (physical and functional well-being); Functional Assessment of Cancer Treatment-General (FACT-G) (physical, functional, social-familial, and emotional well-being), and the FACT-HN, which include scores from all domains.

**Results:** We included 256 patients in this study. At multivariate analysis we observed that the sociodemographic and economic factors are more important for the definition of the global quality of life (FACT-G). The clinical-functional factors are more important for the definition of the functional quality of life (TOI). However, the sociodemographic and economic factors, as well as the clinical-functional factors, are equal influences on specific global quality life for patients with head and neck cancer (FACT-HN).

**Conclusion:** This study showed that factors related to the patient, to the professional, and to the treatment influenced the quality of life of patients with head and neck cancer. Thus, this study suggests that functional, social, and specific rehabilitation is very important for the improvement of the quality of life of these patients.

## **P088: Knowledge and Attitudes About the Consequences of Tobacco Use in Relation to Head and Neck Cancer Within 8-18 Year Olds**

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**Objective:** Tobacco is a major cause of morbidity and mortality in the United States, with nearly two-thirds of new smokers beginning their tobacco use prior to the age of 18. Head and neck cancers alone represent a significant portion of this morbidity and mortality, as they are associated with tobacco use in over 85% of cases and represent over 40,000 new cases per year in the United States. In an effort to further evaluate current knowledge surrounding the relationship between tobacco use and head and neck cancers, a population of 8-18 year olds was surveyed about their attitudes and beliefs regarding tobacco and head and neck cancer.

**Methods:** A ten question, computer-based survey was administered to 1207 youths aged 8-18 in February 2005 via the Harris Interactive® Youth Query<sup>SM</sup> service in advance of Oral, Head and Neck Cancer Awareness Week-2005. The survey group was representative of a general population of 8-18 year olds in the United States in terms of key demographic variables including age, gender, race, region, urbanicity, highest level of education, and parents' education level. The survey included questions surrounding patterns of parental tobacco use, specific disease relationship to tobacco use, concern for the health of their parents, whether they felt it important that their parents see a doctor, or if they would like their parents to stop using tobacco.

**Results:** Of 1207 subjects, 629 (52.1%) were male and 578 (47.9%) female. The average age for males and females was 12.96 and 13.46, respectively. Of the females, 232 (40.1%) were grouped as pre-teens (aged 8-12) and 346 (59.9%) as teens (aged 13-18). Among the males, 292 were pre-teens (46.4%) and 337 (53.6%) were teens. Sixty-four percent of subjects reported having a parent who used tobacco in the past, while 37% of this group acknowledged that their parents are current users. A majority (62%) of subjects whose parents had ever used tobacco worry to some extent about their parents' health and nearly all subjects (96%) whose parents currently use wished their parents would stop. Eighty-eight percent of teens and 79% of pre-teens were aware that tobacco use causes mouth and throat cancer (statistically significant,  $p < 0.05$ ). Meanwhile, 82% of children of parents who never used tobacco and 85% of those whose parents did use or currently use tobacco were aware of this linkage (not statistically significant,  $p > 0.05$ ). The majority of those surveyed knew that tobacco use causes mouth and throat cancer (84%), lung cancer (90%), gum disease (72%), and emphysema (66%).

**Conclusions:** Awareness that tobacco use can cause mouth and throat cancer is higher among teens than those aged 8-12. This awareness does not seem to be affected by whether a parent has or has not used tobacco. Among subjects whose parents previously used or currently use tobacco, the majority were concerned about their parents' health and almost all wished that their parents would stop using tobacco altogether. This survey may be useful to help programs that aim to prevent and decrease teenage smoking

## **P089: Sentinel Lymph Biopsy of Head and Neck Melanoma**

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**Background:** Sentinel Lymph Node (SLNB) biopsy is now recognised as standard investigation for cutaneous melanoma of the limbs and trunk. It is however, at least theoretically a more difficult procedure in the Head and Neck because of the complex lymphatic drainage and risk of complications, particularly in and around the parotid gland and underlying facial nerve.

**Methods:** A retrospective analysis was carried out on 76 Head and Neck melanomas treated by one Head and Neck Surgeon using standard SLNB biopsy technique from January 2000 to March 2006. All patients had lymphoscintigraphy using radioactive labeled sulphacolloid and where indicated Blue Dye injected intra operatively. Appropriate neck dissection was recommended for patients with positive sentinel lymph nodes.

**Results:** Of the 76 patients included in the study, 71 had successful SLNB, and 4 patients had positive sentinel nodes. Anatomic location of the primary was the face (35%), scalp (22%), neck (18%), ear (18%), nose (6%), and conjunctiva (1%). 10 (14%) patients had no sentinel lymph nodes identified with lymphoscintigraphy or dye. 51% of the patients had peri-parotid sentinel nodes which were harvested without injury to the facial nerve. 2 patients have developed recurrent disease (one in Lung; and one in-transit between primary site and previously positive sentinel node), 13% (9) patients had sentinel nodes detected surgically that had not been identified on lymphoscintigraphy.

**Conclusion:** SLNB of Head and Neck melanoma is feasible and safe in the hands of an experienced Head and Neck Surgeon. There are unique problems in the Head and Neck area. Older patients with scalp melanomas, sometimes don't have identifiable lymph nodes at lymphoscintigraphy or gamma-probe evaluation. This may be related to fibrosis of the lymphatics in the scalp in the aging population. On occasion the sentinel lymph node is so close to the primary site that it can not be identified at lymphoscintigraphy and sometimes not even at the time of the surgery when the primary site has been resected. Thus, tumour proximity to SLN, intra-parotid location and discrepancies between lymphoscintigraphy and gamma-probe evaluation make this technique more challenging in the Head and Neck area than elsewhere. Because of the many different sites in the Head and Neck area, ongoing evaluation to achieve larger series are necessary to establish suitable standards and "cure-rates" for the use of SLNB in Head and Neck melanoma.

## **P090: The Effect of Platelet Rich Plasma and Fibrin Sealant on Facial Nerve Regeneration in a Rat Model**

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**Objective:** To investigate the effects of platelet rich plasma (PRP) and fibrin sealant on facial nerve regeneration.

**Study Design:** Prospective, randomized and controlled animal study, with the behavioral and electro-myographic outcomes measured.

**Methods:** Experiments involved the transection and repair of facial nerve on 49 male adult rats. Seven groups were created dependant upon the method of repair: Suture; Platelet Rich Plasma (PRP) (with/without suture); Platelet Poor Plasma (PPP) (with /without suture); and Fibrin Sealant (FS) groups (with/without suture). Each method of repair was applied immediately after the nerve transection. The outcomes measured were: (1) observation of gross recovery of vibrissae movements within 8-week period following nerve transection and repair using a 4-point scale and comparing the left (test) side with the right (control) side. (2) Comparisons of facial nerve motor action potentials (MAP) between the recordings before, and 8 weeks after nerve transection and repair; including both the transected and control untreated nerves.

**Results:** (I) Vibrissae movements observation: the inclusion of suturing resulted in improved outcomes for many of the comparisons; this was true for comparisons involving the suture group with PRP group; PRP with/without suture groups; and PPP with/without suture groups ( $P=0.0002$ ;  $0.008$  and  $0.007$  respectively). We also found that the PRP group had a significantly greater degree of recovery than the PPP ( $p=0.04$ ). The recovery of the suture group was significantly better than FS group ( $P=0.014$ ). The recovery of function of the PRP groups was better than that of the FS groups, although this did not reach statistical significance ( $P=0.09$ ). (II) Electrophysiological testing: the PRP with suture group had the best results when compared to suture as well as PPP and suture groups in the duration and latency-2 of the action potentials ( $p<0.05$ ). There was a significantly better performance of the suture group when compared to PRP and PPP without suture groups in the nerve conduction velocity ( $p<0.05$ ). Similarly, FS with suture significantly differed from FS without suture in the area under the curve of the action potential ( $p<0.05$ ). We also found that the group of PRP with suture significantly showed the best performance in the latency-2 and the area under the curve of the action potentials when compared to the suture and FS with suture groups ( $p<0.05$ ).

**Conclusion:** The best results for the return of function in our rat facial nerve axotomy models occurred when the nerve ends were sutured together. The data is suggestive of improved outcomes when PRP is added to suture. There was a trend toward improved outcomes with the use of PRP in comparison to FS or no bioactive agents (PPP).

## **P091: Salivary Oral Cancer Transcriptome Biomarkers (SOCTB) for Clinical Detection**

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Saliva is an ideal diagnostic medium that meets the demands as an inexpensive, non-invasive and accessible bodily fluid. We have recently discovered a large panel of human RNA (~3000) could be detected in saliva (Li et al. *J Dent Res*, 2004; 83: 199-203). Seven salivary oral cancer transcriptome biomarkers (SAT1, S100P, OAZ1, IL1B, IL8, H3F3A and DUSP1) have been identified to distinguish oral cancer from normal controls (Li et al., *Clin Cancer Res*, 2004; 10: 8442-8450). Comparing the serum transcriptome from the same patients and control subjects revealed that the salivary transcriptome biomarkers are most predictive of oral cancer detection (Li et al., *J Clin Oncol*, 2006: in press). In order to implement the salivary transcriptome biomarkers for clinical applications, standardized assays are needed. We have discovered that there are technological variables inherent in DNA-based standard quantitative RT-PCR, as well as differential RNA degradation and RNA input created baseline shifts that prevented use of a cut-off threshold between experiments to segregate oral cancer from controls. The purpose of this study is to establish a genuine absolute quantitative PCR using RNA-based standard quantification, and using saliva internal control gene to normalize input RNA quantity, to make salivary RNA biomarker measurement more accurate and reproducible and solve the base-line shifting problem. The standardized assay will be used to further validate the SOCTB for oral cancer detection. For detecting each of the SOCTB, technology variance was explored by utilizing genuine absolute quantification. Primers for specific amplification of each of 7 SOCTB mRNAs with T7 promoter sequence fused to 5' end were designed and used to generate recombinant RNA (recRNA). Quantitation of recRNA was accurately measured with Nanodrop bioanalyser, and serial dilution was used to generate standard. Each set of standard was quantified by real time quantitative PCR (qPCR) parallel with saliva RNA samples. RNA input and degradation was explored by normalization to saliva internal reference (SIR) genes. Wilcoxon test and ROC analysis were used to judge the quality of makers. qPCR data showed that in seven independent detection studies, the 7 SOCTB gene expression levels are significantly elevated (> 1.5 fold, p<0.05) in all OSCC samples (n=266). S100A8 (S100 calcium-binding protein A8) is the most stably expressed SIR gene. The established absolute qPCR for oral cancer salivary mRNA biomarker measurement allows precise and reproducible measurements of each of the 7 SOCTB. The best prediction model is the DLDA model with an ROC value of 0.86 (sensitivity 0.85 and specificity of 0.81).

**Conclusion:** Salivary transcriptome markers can be used as clinical biomarkers for oral cancer detection. Standardized qPCR assays are in place to provide rapid quantitations of differential gene expressions, while absolute quantification together with normalization with a SIR gene provides an excellent tool for salivary mRNA biomarker prediction model building and validation. Supported by PHS grant RO1DE15970 and UO1DE16275.

## **P092: FAK-Related Non-Kinase (FRNK) Blockade of FAK Changes Malignant Properties of the SCC VII/SF Cell Line**

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**Objectives:** FAK occupies a pivotal role in transmitting signals about cellular processes key to the malignant phenotype, such as cellular invasiveness and cell cycle control. We have previously shown elevated levels of FAK in the motile and invasive murine squamous cell carcinoma cell line SCC VII/SF compared to normal murine keratinocytes. Others have shown decreased levels of caspase-3 activity after the induction of apoptosis in cells over expressing FAK (Sonoda et al, 2000). We hypothesize that blockade of FAK with FRNK (FAK-Related Non-Kinase) will reverse these malignant properties in the SCC VII/SF cell line.

**Methods and Procedures:** The murine squamous cell carcinoma cell line SCC VII/SF was grown in the usual manner. Cells were transfected with FRNK, the C-terminal, non-catalytic domain of FAK that blocks FAK activity. Transfected cells were then compared to sham transfected cells and untreated SCC VII/SF cells using in vitro measures of motility and invasion. After treatment with ionizing radiation,

cells were studied using immuno-histochemistry for active caspase-3.

**Results:** The FRNK transfected cells showed decreased cellular motility and invasion as compared to the native SCC VII/SF cells. In addition, the time course of apoptosis as measured by active caspase-3 activity was altered by transfection with FRNK.

**Conclusion:** Blockade of FAK activity using FRNK, the C-terminal, non-catalytic domain of FAK, reverses cellular processes such as motility and invasion that contribute to the malignant phenotype of the murine squamous cell carcinoma cell line SCC VII/SF. In addition, FRNK transfection of SCC VII/SF cells changes the time course of radiation-induced apoptosis. Regulation of FAK activity may represent a target for controlling the spread and survival of malignant cells.

## **P093: MMS19, a Modulator of Transcription and Nucleotide Excision Repair, Is Overexpressed in Human Cancer**

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MMS19 is required for efficient nucleotide excision repair (NER) and RNA polymerase II (Pol II) transcription. However, the precise molecular mechanism by which MMS19 participates in these essential cellular processes is unknown. We previously reported that the MMS19 primary transcript undergoes extensive processing in its translated and untranslated regions (UTRs). Processing in 5' and 3' UTRs can impact mRNA translatability and stability, while alternative splicing within translated regions makes possible the expression of different protein isoforms. In the present study we have identified and characterized five MMS19 splice variants which encode five distinct MMS19 polypeptides. We demonstrate that three MMS19 transcripts are conserved from mouse to human cells and are functionally distinct. Expression of each of these transcripts in yeast mms19-null cells leads to divergent responses to DNA damage or increased temperature, clearly establishing that MMS19 polypeptides lacking specific sequences have discrete roles in NER and RNA Pol II transcription. Our data suggest a model in which expression of distinct MMS19 polypeptides might lead to the alternate outcomes of DNA repair or transcription. Using northern blot and RT-PCR analysis we show that MMS19 is overexpressed in several human tumor samples. Furthermore, preliminary data indicates that the specific transcript up-regulated is incapable of repairing DNA, but might confer other advantages to cancer cells. We continue to study the effect of this dysregulated MMS19-expression in human salivary gland cancer.

## **P094: Phenotypic and Functional Profiles of Natural Regulatory T Cells in the Circulation of Patients With Head and Neck Squamous Cell Carcinoma**

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**Objective:** CD4+CD25 high T cells containing natural regulatory T cells (nTreg) are present in tumors and blood of patients with head and neck squamous cell carcinoma (HNSCC) and suppress immune responses. Pure populations of nTreg are necessary to define their phenotypic and functional profile in patients with cancer.

**Methods:** CD4+CD25+ PBMC of 12 patients with HNSCC were separated from CD4+CD25- cells using FACS sorting. Flow cytometry was used to determine phenotypes. Responder CD4+CD25- cells stimulated with OKT3 were coincubated with autologous Treg in CFSE-based assays. CD4+CD25+ and CD4+CD25- T cell subsets were expanded ± rapamycin (1 nM) with CD3/CD28-coated beads and IL-2. Annexin V binding was used to measure apoptosis of T cells.

**Results:** Compared with 12 normal donors (NDs), increased percentages of CD4+CD25 high T cells (1%-2% vs 6%-10%) and decreased percentages of CD8+CD25+ T cells (0.6%-2% vs 0.1%-0.3%) were found in patients with HNSCC. Phenotypic profiles of Treg in patients were distinct from those defined for ND. The nTreg expressed surface Fas and FasL but were resistant to apoptosis. Rapamycin-expanded CD4+CD25+ T cells were phenotypically and functionally similar to fresh nTreg. These Treg suppressed proliferation (85%-95%) of autologous sorted CD4+CD25- T cells at the 1:1 ratio. Comparable Treg fractions sorted from PBMC of NDs mediated lower suppression (0%-35%; P<.05) in CFSE assays.

**Conclusions:** The nTreg are significantly increased in the blood of patients and more immunosuppressive and phenotypically and functionally heterogeneous compared with CD4+CD25+ cells in NDs. Rapamycin expands pure populations of nTreg that are functionally comparable to fresh nTreg and are resistant to Fas-mediated apoptosis.

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## **P095: Investigation of the Mismatch Repair Genes *hPMS1*, *hPMS2*, and *hMLH1* in Younger Patients With Oral Squamous Cell Carcinoma**

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**Objectives:** To determine the involvement of mismatch repair (MMR) genes in oral squamous cell carcinomas (OSCCs) from younger (<45 years) and older patients.

**Design:** Complementary DNA microarrays were used to determine gene expression profiles. A quantitative real-time polymerase chain reaction (Q-RT-PCR) was used to measure the expression of the mismatch repair genes *hPMS1*, *hPMS2*, and *hMLH1*. The PMS1 protein expression was analyzed by immunohistochemistry.

**Subjects:** Fifty-seven patients younger than 45 years and 77 older patients with OSCC who underwent surgery as the primary mode of care were included. For microarray analysis, 23 tumors from older patients and 10 from younger patients were used. We performed Q-RT-PCR on samples from tumors and normal tissue from 14 older and 16 younger patients. Immunohistochemistry was performed on tumors from 40 older and 31 younger patients.

**Results:** The OSCC messenger RNA (mRNA) expression from younger and older patients clustered into separate groups on the microarray. Deregulated mRNA levels of *hPMS1*, *hPMS2*, and *hMLH1* were observed in tumors and adjacent normal oral mucosa of older and younger patients. Significantly lower PMS1 protein levels were detected in tumors of younger ( $P = .03$ ) compared with older patients and normal oral tissues. We also observed a decreasing trend of PMS1 expression from adjacent normal tissue to dysplasia to the tumor.

**Conclusions:** We suggest that differences exist in the genetics of younger vs older patients with OSCCs and that there is a possible role for the MMR genes in the development of OSCC in young patients. Differences between each age cohort will be further characterized so as to explain the mechanisms leading to early-onset OSCC.

## **P096 Cytoglobin: A Candidate Tumor Suppressor Gene Epigenetically Silenced in Head and Neck Cancer**

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**Introduction:** *CYGB* is a candidate tumor-suppressor gene on chromosome 17q and is the only gene completely contained within the 42.5-kb tylosis with esophageal cancer minimal region. This region is subject to frequent deletions in sporadic esophageal cancer; however, no coding mutations have been demonstrated in patients affected with tylosis. Cytoglobin is a recently described, intracellular globin whose role in cancer is as yet unclear but may be related to detoxification of oxygen-free radicals. Promoter methylation of *CYGB* in lung, head and neck, and sporadic esophageal cancer has recently become the focus of investigation within our group

**Method:** DNA was extracted from a series of snap-frozen head and neck squamous cell carcinoma (HNSCC) tumor and resection margin tissues. After bisulfite treatment, this was subjected to pyrosequencing-based quantitative methylation analysis. A methylation index was calculated as the mean percentage of methylation in each CpG site assayed. Real-time polymerase chain reaction quantitative assay of messenger RNA expression was carried out to determine the biological significance of these data.

**Results:** The *CYGB* promoter was found to be significantly methylated in 65% of HNSCC tumor specimens and significantly fewer normal controls ( $P = .002$ ).

**Conclusions:** The epigenetic data presented in this study add weight to the hypothesis that *CYGB* is a tumor suppressor gene highly methylated in upper aerodigestive tract squamous cancer.

## **P097: Prognostic Significance of Intratumoral Dendritic Cells in Oropharyngeal Head and Neck Squamous Cell Carcinoma**

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**Background:** Dendritic cells (DCs) are potent cells of the immune system that present foreign proteins to lymphocytes and stimulate them to eliminate cells that express the foreign antigen. It has been shown in a number of studies that the presence of DCs within malignant tumors is associated with improved survival in certain human cancers. However, no study to date has examined the prognostic significance of infiltrating dendritic cells within oropharyngeal squamous cell carcinomas.

**Hypothesis:** The presence of tumor infiltrating CD1a+ (immature) and CD83 (mature) dendritic cells is correlated with a decreased incidence of metastasis upon presentation and improved survival in oropharyngeal cancer patients.

**Methods:** Archived, paraffin-embedded oropharyngeal squamous cell carcinoma tissue samples were obtained from 52 patients. Immunohistochemistry was performed on slides prepared from each sample. The slides were stained with antibodies to CD1a and CD83. The number of CD1a+ and CD83+ cells per high-powered field was quantified. Clinical data was obtained from patient records and statistical correlations were calculated.

**Results:** 1) Two-year survival was improved in those patients with large numbers of CD1a dendritic cell infiltrates, although this benefit was lost at five years. 2) The number of dendritic cells within the tumor was not significantly correlated with the incidence of metastasis upon presentation.

**Conclusion:** Tumor infiltrating CD1a+ dendritic cells may have a short-term survival benefit in oropharyngeal squamous cell carcinoma patients.

## **P098: The Unique Autofluorescence of Human Buccal Cells Defined by High-Throughput Multispectral Flow Cytometry**

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**Objective:** To determine if a relatively purified population of human buccal cells obtained from different sites and tissues of the mouth can be analyzed for autofluorescence using flow cytometry.

**Design:** Research-based study conceived to identify by flow cytometry novel buccal cell surrogate biomarkers of oral cancer.

**Setting:** National Cancer Institute-designated Comprehensive Cancer Center.

**Subjects:** This study included healthy never smokers, former smokers and current smokers, and patients with oral cancer or pre-malignant lesions. This study was reviewed and approved by the Institutional Review Board (IRB) at the Roswell Park Cancer Institute in Buffalo, New York, and all study participants signed a consent statement.

**Results:** Our findings demonstrate that: (a) a flow cytometer (FACS), including a single laser (FACScan™) and an advanced three laser (FACSAria™) instrument, has been used successfully to analyze human buccal cells despite their large size (diameter, ~ 65 μm) and flake-like morphology; (b) a relatively large number of buccal cells (mean:  $12.9 \pm 7.1 \times 10^4$  cells; range:  $1.93 \times 10^4$  to  $36.6 \times 10^4$ ;  $n = 30$  subjects) were harvested with a toothbrush-based collection system; (c) buccal cells for FACS analysis were brushed from various locations of the mouth (e.g., cheek, tongue and gum) and from different tissue sites (e.g., normal mucosa and pre-malignant lesions); (d) a relatively pure population of buccal cells (> 97%) were obtained readily and reproducibly from different donors; (e) when compared to leukocytes, the autofluorescence of the buccal cells was remarkably

intense as defined using a purchased assay standard of fluorescent intensity Quantum™ microbeads; (f) the buccal cells fluoresced over a broad range ( $E_m$  range = 450 nm to 780 nm); (g) inter-assay reproducibility has been demonstrated in studies comparing fluorescent intensities of buccal cells harvested from the left and right cheek of a given donor; (h) buccal cell autofluorescence varied significantly from subject-to-subject (range: 65-fold); and (i) buccal cells exposed *in vivo* to tobacco smoke particulates ("tar") for one hour displayed a significant increase (~10-fold) in fluorescence.

**Conclusion:** This is thought to be the first report describing the analysis of human buccal cells by state-of-the-art flow cytometry. Populations of buccal cells suitable for cytometry were harvested successfully, and in a non-invasive manner, from different sites and tissues of the mouth. An investigation utilizing this technology has shown that buccal cells display a high level of autofluorescence that varies from donor to donor. It is reasonably anticipated that advantages afforded by the proposed high-throughput cytometry scheme will prove useful for screening high-risk populations of smokers for buccal cell alterations, some of which (e.g., micronuclei) have been reported elsewhere to be useful biomarkers of oral cancer.

### **P099: Laryngotracheal Injury After Percutaneous Dilatation vs Open Tracheostomy in Fresh Cadaver Specimens**

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**Objectives:** To compare injury patterns of the stoma and surrounding laryngotracheal structures following percutaneous dilatation tracheostomy (PDT) vs open tracheostomy (OT) that may contribute to decreasing rates of clinical tracheal stenosis.

**Methods:** A fixed (n = 40 + 16) and fresh (n = 20) cadaver study was performed in which human cadavers were randomly assigned to undergo either PDT or OT (40 fixed cadavers were first used to standardize the 2 surgical techniques, and 16 were then randomized) Stoma sites were surgically and endoscopically examined and graded for characteristic injury patterns using a previously described scale.

**Results:** Significant differences in grade of injury were found between the 2 groups. In the OT group, none of the 10 cadavers had mucosal or cartilaginous injury beyond that expected. In the PDT group, 5 of the 10 cadavers had injuries beyond expected in both the mucosal and cartilage damage analysis.

**Conclusions:** Laryngotracheal injuries found after OT had significantly lower injury grades when compared with PDT in fresh human cadavers. Implied lower rates of clinically significant tracheal stenosis favor the open technique

### **P100: Genetic Alterations in p53 in Head and Neck Cancer Cell Lines Change Cisplatin Sensitivity**

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**Objective:** To understand the role of p53 in head and neck squamous cell carcinoma (HNSCC) cells in response to cisplatin treatment.

**Design:** The HNSCC cells that contain mutant (nonfunctional) p53 and high levels of the prosurvival protein Bcl-xL were transduced with wild-type (WT) p53, and HNSCC cells containing WT p53, also over-expressing Bcl-xL, were transduced with short interfering RNA p53 constructs. These transduced cell lines were compared with parental cell lines for sensitivity to cisplatin treatment.

**Setting:** *In vitro* study of head and neck cell lines UM-SCC-14AxL (mutant p53) and UM-SCC-74BxL (WT p53).

**Results:** Exogenous expression of WT p53 in the mutant p53 cell line UM-SCC-14A resulted in an 11-fold decrease in cisplatin-induced cell kill compared with the vector control parental line as measured by trypan blue exclusion assay. The RNA interference of p53 (>90% efficiency in knockdown) in the WT p53 containing cell line UM-SCC-74B showed a 4-fold increase in cisplatin cell kill compared with parental control cells.

**Conclusions:** The functions of p53 and Bcl-xL expression are involved in resistance to cisplatin treatment in HNSCC cells. Tumor suppressor functions of p53 (such as cell cycle arrest and induction of DNA repair in the presence of high levels of Bcl-xL, which protect

the cells from apoptosis) are likely to contribute to resistance to cisplatin treatment in HNSCC cells. These data suggest that targeting p53 function may be an important therapeutic target in overcoming cisplatin resistance in HNSCC.

### **P101: IL-6 Antisense Treatment of Human Head and Neck Cancer Cells Decreases Tumor Cell Proliferation and Angiogenic Activity**

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The growth of tumor cells can be regulated by a variety of cytokines. To investigate the pathogenesis of head and neck cancer and explore a new therapeutic approach for the carcinoma, we examined the role of IL-6 in the growth of a human HNSCC cell line. We determined whether IL-6 is increased in HNSCC and whether IL-6 antisense oligonucleotide treatment can decrease proliferation and angiogenic activity of HNSCC cell lines. Established human HNSCC cell lines were screened for IL-6 expression at both mRNA and protein levels. By using a 15-mer antisense phosphorothioate oligonucleotide targeting a sequence in the second exon of the IL-6 gene, we examined modulation of IL-6 and VEGF expression in cell line supernatants by capture ELISA, and in cell lysates by RT-PCR. In addition, cell growth was determined by cell count. Endothelial cell (EC) migration was measured using a modified Boyden chamber. IL-6 was identified in the supernatant of the cell culture medium by enzyme-linked immunosorbent assay, indicating that these cells secreted IL-6. The mRNAs of IL-6 in this cell were shown to be present by reverse transcriptase polymerase chain reaction assay. IL-6 antisense oligonucleotide treatment resulted in a significant reduction of IL-6 protein expression compared to sense control. The antisense oligonucleotides targeting IL-6 mRNA, however, inhibited cell growth and IL-6 production as well as VEGF expression. The addition of conditioned medium from IL-6 antisense-treated tumor cells resulted in decreased endothelial cell migration and tube formation. Taken together, these findings indicate that endogenous IL-6 plays an important role in the growth of HNSCC, and it exerts its action by an autocrine growth mechanism. The results also suggest that the therapeutic trials with antisense oligonucleotides targeted to IL-6 mRNA may have some value for the treatment of HNSCC due to decrease of neovascularization.

### **P102: Induction of IL-10+ Tr1-Like Regulatory T Cells in the Microenvironment of COX-2+ Head and Neck Squamous Cell Carcinoma**

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**Objective:** Overexpression of COX-2 is associated with PGE2 production in head and neck squamous cell carcinoma (HNSCC) (Tu). This milieu promotes induction and accumulation of IL-10-/antigen-dependent regulatory T cells (Tr1).

**Methods:** A coculture system was established that consisted of COX-2+HNSCC (Tu) cell line, CD4+CD25+ or CD4+CD25- T cells obtained from normal donors and autologous immature dendritic cells (iDC). IL-2, IL-10, and IL-15 were added and cultures incubated for 7 days. The system was modified by addition of synthetic PGE2 (26 mM) in Tu absence or of rapamycin (1nM), which expands regulatory T cells (Treg). Flow cytometry for Treg phenotype (CD3, CD4, CD25, CD25, FOXP3, GITR, CTLA4, IL-10, IL-2R $\alpha/\beta$ , and Fas) and CFSE proliferation with CD4+CD25- autologous T cells as responders to measure Treg function were performed. Inhibition of responses  $\pm$  Treg to OKT3 and anti-CD28 Ab was determined.

**Results:** Most CD4+CD25- T cells plus COX-2+ Tu differentiated into CD25+FOXP3+GITR+CTLA4-IL-2R $\alpha$ +IL-2R $\beta$ + Treg with suppressive activity. PGE2 and cytokines in the absence of Tu induced IL-10 and GITR but no CD25 or FOXP3 expression on 50% to 80% of CD4+CD25- cells. These cells mediated suppression in CFSE assays. Rapamycin plus Tu selected for expansion of CD4+CD25+ IL-10+ cells, which were FOXP3-negative but strongly suppressed responses in CFSE assays.

**Conclusion:** In the microenvironment containing COX-2+ Tu, iDC, and cytokines, IL-10+ Tr1-like regulatory T cells are induced from CD4+CD25- precursors, which show considerable plasticity. PGE2 or

rapamycin led to induction of IL-10+ Treg with suppressive function but a distinct phenotype. Human Treg induced in the Tu are heterogeneous, depending on factors present in the microenvironment. Supported by Philip Morris USA Inc and Philip Morris International.

## **P103: Apoptosis Signaling Causes Genomic Instability Leading to Loss of Heterozygosity (LOH) in Cell Lines**

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**Objectives:** Loss of heterozygosity (LOH) leading to deletion of key regulator genes is an important component of tumor generation and progression. Current opinion is that the mechanism of LOH is a random consequence of chromosome non-disjunction during mitosis, or of somatic homologous recombination. We have previously shown in a variety of lymphoid cell lines that the process of apoptosis introduces specific DNA breaks at 11q23, a region commonly associated with LOH. Further, in specific cell systems, cells damaged in this way are apparently able to escape from an apoptotic cell death (Betti et al, 2003). We hypothesize that genomic instability caused by induction of apoptosis leads to LOH in cell lines representative of head and neck pathology.

**Methods and Procedures:** Three cell lines including a normal oral keratinocyte cell line that has been transformed with HPV (HOK-16B), a cell line derived from a lymph node metastasis of a pulmonary mucoepidermoid carcinoma with near-diploid chromosome counts (NCI-H292) and a cell line derived from a human hypopharyngeal squamous cell carcinoma (FaDu) were grown under usual conditions. Each cell line was treated with an LD99 dose of ionizing radiation and clonal populations were selected. The DNA was harvested and PCR was executed with specific primer sets recognizing locations along chromosome 11. Forward primers were labeled with 3B3-32P ATP. PCR products were then run on a sequencing gel and imaged.

**Results:** Depending on the cell line and its initial heterozygosity, LOH was noted at various sites along chromosome 11. Specific gels will demonstrate the location and frequency of LOH events in the 3 cell lines.

**Conclusion:** Treatment with ionizing radiation leads to LOH events, even in cell lines that show significant karyotypic abnormalities at baseline, at locations adjacent to those introduced by apoptotic nucleases. It is known that suppression of apoptosis is important both in the induction and the progression of cancer. If supported by further studies, apoptosis-linked LOH would represent a third key role for apoptosis in the development of neoplastic disease. In addition, it would represent a novel mechanism for the production of LOH.

## **P104: Radioimmunotherapy of Head and Neck Cancer Xenografts Using 131I-L19-SIP for Selective Targeting of Tumor Vasculature**

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**Objective:** The human monoclonal antibody L19-SIP is directed against the extra domain B of fibronectin (ED-B), a marker of tumor angiogenesis. The potential of radioimmunotherapy (RIT) with L19-SIP was evaluated, either alone or in combination with the anti-epidermal growth factor receptor (EGFR) antibody cetuximab, for treatment of head and neck squamous cell carcinoma (HNSCC).

**Design, Subjects and Interventions:** The HNSCC xenograft lines FaDu and HNX-OE were evaluated for ED-B and EGFR expression. L19-SIP was radiolabeled with 2 candidate radionuclides for RIT, 177Lu and 131I (or 125I as substitute). Biodistribution of coinjecting 177Lu-L19-SIP and 125I-L19-SIP was assessed in FaDu-bearing nude mice, while 131I-L19-SIP was evaluated in both xenograft lines. The efficacy of RIT with i.p. injected 131I-L19-SIP, either alone or in combination with unlabeled cetuximab (1 mg 2 times a week i.p. for 4 weeks), was evaluated in both xenograft lines.

**Results:** Xenograft lines showed similar EGFR expression, while ED-

B expression was highest in FaDu. Radioiodinated L19-SIP performed better than 177Lu-L19-SIP and was further exploited. Biodistribution of 131I-L19-SIP was most favorable in FaDu-bearing mice. RIT (74 MBq) caused significant tumor growth delay and improved survival in both lines. While FaDu was most sensitive for RIT, with size reduction of all tumors, HNX-OE was most sensitive for treatment with cetuximab. However, the best efficacy was obtained when RIT and cetuximab were combined.

**Conclusion:** Radioimmunotherapy with 131I-L19-SIP seemed to be efficacious in HNSCC xenografts. The efficacy of RIT was enhanced by combination with cetuximab without increase of toxicity.

## **P105: Role of Slug (SNAI2) in Head and Neck Squamous Cell Carcinoma (HNSCC)**

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**Objective/Hypothesis:** Head neck malignancies account for 6% of all cancers diagnosed in the United States and result in ~14,000 deaths annually. Our previous oligonucleotide microarray study (Ginos et al. Cancer Research 2004) identified Slug (SNAI2) overexpression in a signature associated with recurrent head and neck squamous cell carcinoma (HNSCC) following definitive treatment. Slug, a zinc finger transcription factor family member, is critical in mediating epithelial to mesenchymal transitions (EMT) in developing organisms and in modulating sensitivity to apoptosis. Since acquisition of an invasive phenotype and resistance to apoptosis are primary characteristics of human cancer we hypothesized that Slug overexpression would induce EMT, increase invasion and evade apoptosis in HNSCC cell lines.

**Methods:** Baseline levels of Slug and E-cadherin were determined using Real time PCR and Western blotting in a variety of HNSCC cell lines. A cell line with high E-cadherin expression and low Slug expression was selected for transfection studies. We overexpressed Slug in a HNSCC cell line (SCC-15) and probed for epithelial and mesenchymal markers (E-cadherin, Vimentin and 3B1-smooth muscle actin) using Immunofluorescence and Western blotting. Apoptosis evasion was tested using serum starvation and clonogenic assays.

**Results:** Epithelial marker, E-cadherin, expression was decreased significantly in the clones compared to mock transfectants. Increased mesenchymal markers Vimentin and 3B1-smooth muscle actin expression was observed using both Immunofluorescence and western blotting. Slug-transfected cells showed reduced cell death in a serum starvation assay. Preliminary data also suggested that Slug-transfected clones show increased resistance to radiation-induced apoptosis using clonogenic assay.

**Conclusion:** Slug induces EMT when overexpressed in SCC-15 cell line. EMT induction includes loss of E-cadherin and therefore loss of epithelial integrity. Epithelial integrity loss leads to an altered phenotype and increased expression of mesenchymal markers Vimentin and 3B1-smooth actin. Preliminary data from serum starvation and clonogenic assays suggest that Slug has a protective effect on the Slug-transfected clones when compared to the mock. The precise mechanism of this has yet to be explored in HNSCC cell lines. The above results suggest that Slug plays a strong role in recurrent disease through the malignant phenotype and evasion of apoptosis.

## **P106: Expression of Nerve Growth Factor and Tyrosine Kinase A Receptor in Oral Squamous Cell Carcinoma**

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**Objective:** Perineural invasion (PNI) in oral squamous cell carcinoma (SCC) is recognized as a significant predictor of outcome. Perineural invasion is associated with locoregional recurrence and decreased survival of patients with head and neck squamous cell carcinoma, independent of other factors. Nerve growth factor (NGF) may play a role in PNI in several malignancies such as breast, prostate, and pancreatic cancers. We investigated the hypothesis that NGF may be present or highly expressed in oral squamous cell carcinoma with histological evidence of PNI but not in those without PNI.

**Materials and Methods:** Archived oral tongue SCC specimens from an established database at the University of California, San Francisco, were retrieved. Group I consisted of T1 oral tongue SCC

with PNI. Group II included T1 oral tongue SCC without histological evidence of PNI. Forty specimens were included. Expression of NGF and TrkA was explored using immunohistochemistry in paraffin-embedded tissue specimens.

**Results:** Cancer cells in the tumors with PNI demonstrated significant immunoreactivity for NGF. The NGF was detected in the cytoplasm of the malignant cells. In group II, NGF was either not detected or was found in the stroma. All positive control specimens were found to be strongly positive for both antibodies.

**Conclusion:** We were able to demonstrate the presence of NGF in the cytoplasm of malignant squamous cells in tumors with histological evidence of PNI. Based on the results of this study, a link between PNI and NGF as well as TrkA expression may exist in oral cancers tumors that show early neurotropism.

## **P107: Role of Antigen-Processing Machinery in the Resistance of SCCHN Cells to Recognition by CTL**

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Squamous cell carcinoma of the head and neck (SCCHN) cells are poorly recognized in vitro by CTL despite expressing the restricting HLA class I allele and the targeted tumor Ag (TA). Several lines of evidence indicate that the lack of SCCHN cell recognition by CTL reflects defects in targeted TA peptide presentation by HLA class I Ag to CTL because of Ag-processing machinery (APM) dysfunction. First, lack of recognition of SCCHN cells by CTL is associated with marked down-regulation of the IFN-gamma inducible APM components LMP2, TAP1, TAP2, and tapasin. Second, SCCHN cell recognition by CTL is restored by pulsing cells with exogenous targeted TA peptide. Third, the restoration of CTL recognition following incubation of SCCHN cells with IFN-gamma is associated with a significant ( $p = 0.001$ ) up-regulation of the APM components TAP1, TAP2, and tapasin. Lastly, and most conclusively, SCCHN cell recognition by CTL is restored by transfection with wild-type TAP1 cDNA. Our findings may explain the association between APM component down-regulation and poor clinical course of the disease in SCCHN. Furthermore, the regulatory nature of the APM defects in SCCHN cells suggests that intralesional administration of IFN-gamma may have a beneficial effect on the clinical course of the disease, secondary to APM upregulation as demonstrated in vivo in a mice model. These effects will likely be beneficial for T cell-based immunotherapy of SCCHN.

## **P108: Formation of Thanatosomes in Oral Cancer Cells: Insights Into the Early Stages of Apoptosis**

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**Objective:** Thanatosomes were recently described as cytoplasmic structures that resemble hyaline globules and may be associated with cell death. Our aim was to assess and correlate the formation of thanatosomes and the induction of apoptosis in oral squamous cell carcinoma (SCC) cells treated with conventional chemotherapeutic drugs and apoptosis-inducing agents. The role of caspases in the formation of thanatosomes was also evaluated.

**Design:** Human oral SCC cells, including cisplatin-resistant SCC cells, were treated with the chemotherapeutic drugs cisplatin and doxorubicin. Also, staurosporine, a specific apoptosis-inducing agent, was used to treat SCC cells with or without preincubation with the pan-caspase inhibitor Z-VAD-FMK. Morphologic changes were assessed by light microscopic and electron microscopic examination.

**Results:** Treatment of SCC cells with cisplatin, doxorubicin, and staurosporine induced the formation of apoptotic bodies and thanatosomes. The latter appeared as eosinophilic cytoplasmic structures, either containing (nucleated) or devoid of (anucleated) basophilic/nuclear material. There was a significant correlation between exposure time and treatment-induced morphological alterations, independent of concentration ( $P = .002$ ): although short periods of treatment induced mainly anucleated thanatosomes, longer durations primarily caused the formation of nucleated thanatosomes

and apoptotic bodies. No significant morphological changes were seen in the cisplatin-resistant cell lines when treated with cisplatin. Pretreatment with caspase inhibitor did not abrogate the staurosporine-induced formation of thanatosomes but resulted in a significant reduction in apoptotic bodies.

**Conclusions:** Our findings support the time-dependent formation of 1 distinct category of thanatosomes in a caspase-independent manner; anucleated thanatosomes potentially participate in the onset of apoptosis, while nucleated thanatosomes may represent the immediate cytoplasmic precursors of fully formed apoptotic bodies.

## **P109: Increased Apoptosis in Head and Neck SCC Using Chemotherapy and E1b-19kD-deleted p53-expressing Replicating Adenovirus**

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**Objective:** The incidence and mortality associated with head and neck squamous cell carcinoma (HNSCC) is increasing despite multiple therapeutic and diagnostic advances. It is becoming quite evident that further improvements in outcome will only be achieved by developing novel therapies. A non-replicating p53-expressing adenovirus in combination with radiation has shown promising results for this disease and is the first approved gene therapy modality worldwide. An oncolytic virus (ONYX-015) in combination with chemotherapy has also shown encouraging results. Therefore, the application of a replicating p53-expressing virus in combination with chemotherapy may be a rational advancement of this strategy. One of the potential disadvantages of the wild-type replicating viruses is that the adenoviral E1b-19kD protein potently inhibits apoptosis and may compromise the therapeutic efficacy of a p53 thereby inhibiting the apoptotic effect of both p53 and chemotherapy. We hypothesized that an E1b-19kD gene deletion together with p53 expression in combination with chemotherapy could further improve the ability of a replicating adenoviral vector to kill head and neck cancer cells.

**Methods/Results:** In two head and neck cancer cell lines (1586 and SCC15), a p53-expressing E1b-19kD-deleted replicating virus (Adp53d19k) increased the amount of apoptosis by more than three-fold compared to a replicating control virus (Ad-co), and almost two-fold compared to a E1b-19kD-deleted virus that does not express p53 (Ad-d19k). In the presence of cisplatin, at a dose that does not induce apoptosis in these cells (2 $\mu$ M), the apoptotic effect of Adp53d19k was almost doubled, whereas Ad-co induced only minimal apoptosis. In the same two head and neck cancer cell lines, infection with Adp53d19k in combination with cisplatin also resulted in reduced cell viability, as compared to Ad-co or a p53-expressing but not E1b-19k-deleted virus (Adp53).

**Conclusion:** The presence of an E1b-19K-deletion can markedly enhance apoptosis and cancer cell death induced by a replicating p53-expressing virus in combination with chemotherapy. Therefore, deletion of the E1b-19kD adenoviral protein may be an important modification when designing new therapeutic strategies using replicating p53-expressing viruses.

## **P110: Concomitant Inhibition of Epidermal Growth Factor Receptor and Insulin-like Growth Factor Receptor I in Cutaneous SCC**

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**Objective:** Cutaneous squamous cell carcinoma (CSCC) is the second most common type of non-melanoma skin cancer. Even seemingly adequate treatment or excision of SCC can be complicated by recurrence, making it difficult to cure with standard approaches. Recent successes involving the therapeutic use of antibody inhibitors of tyrosine kinases has generated considerable interest in targeting these receptors in various types of tumors. In an attempt to improve the treatment of cutaneous SCC, we explore the effect of inhibition of two of these receptors, the epidermal growth factor receptor family (EGFR) and the insulin-like growth factor receptor I (IGF-IR), which have been implicated in tumorigenesis of various cancers, including SCC.

**Methods:** We analyzed the effect of targeted therapy on the growth and survival of CSCC cell lines using the anti-IGF-IR antibody, A12, alone or in combination with an anti-EGFR antibody, Erbitux, both in vitro and in a SCC athymic nude mouse model.

**Results:** Treatment with A12 and Erbitux inhibited the signaling pathways of IGF-IR and EGFR in vitro by reducing phosphorylation of IGF-IR, EGFR, and Akt. Treatment with A12 and Erbitux also limited proliferation and induced apoptosis of SCC cell lines in vitro. In addition, administration of A12, alone or in combination with Erbitux to a SCC athymic nude mouse model, inhibited the growth of tumors by 51% and 92% respectively, and significantly enhanced survival of treated animals over untreated animals ( $p=0.044$  and  $p<0.001$  respectively). Moreover, immunohistochemical staining revealed a decrease in proliferating cell nuclear antigen (PCNA) and microvessel density (MVD) as well as an increase in apoptosis within the treated tumor xenografts.

**Conclusions:** These data suggest that dual treatment with monoclonal antibodies to the EGFR and IGF-IR may be therapeutically useful in the treatment of CSCC.

### **P111: Head and Neck Cancer Triggers the Internalization of TLR3 in Natural Killer Cells**

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Natural killer (NK) cells play a dominant role in the network of the innate immunity. Via TLR3 NK cells can be efficiently stimulated by dsRNA. In head and neck squamous cell carcinoma (HNSCC) NK cells seem to be strongly impaired but the true mechanisms of immune escape are not sufficiently known to date. It is obvious that the microenvironment of head and neck cancer results in strongly affected immune functions. NK cells play a major role in the local immune response of HNSCC. In this work we show that TLR3 is predominantly expressed on the cell surface of native NK cells and gets rapidly internalized in response to the HNSCC microenvironment. These findings represent a novel immune escape mechanism of head and neck cancer. The internalization of TLR3 in response to HNSCC could as well be observed in fibroblasts expressing heterologous TLR3 protein. Specific stimulation of NK cell TLR3 with its ligand Poly I:C impairs the internalization of this Toll-like receptor and leads to activated NK cells within the HNSCC microenvironment.

### **P112: Reduced Expression of 15-Lipoxygenase 2 in Human Head and Neck Carcinomas**

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Nonsteroidal anti-inflammatory drugs (NSAIDs) have demonstrated cancer chemoprevention effects associated with their ability to modulate polyunsaturated fatty acid metabolism. In the present study, we report significant reduction of 15-lipoxygenase 2 (15-LOX-2) in seven carcinoma cell lines of human head and neck when compared with normal primary cultured keratinocytes, and 18 primary head and neck squamous cell carcinomas (HNSCC) when compared with matched normal mucosa. 15-LOX-2 is mainly expressed in the mature cells of the benign squamous epithelium, but not expressed in basal layer cells of benign epithelium, suggesting a role of 15-LOX-2 in cell differentiation. We further found that 15-lipoxygenase activity was reduced in carcinoma cells when compared with normal primary cultured keratinocytes. When the effects of NSAIDs were examined on cell proliferation and regulation of 15-LOX-2 in the carcinoma cells, NS398 treatment resulted in significant growth inhibition associated with upregulation of 15-LOX-2 and its major metabolite 15-S-HETE. Finally, restoration of 15-LOX-2 expression into these carcinoma cells significantly inhibited cell proliferation. Our results demonstrate that 15-LOX-2 expression is significantly reduced and this reduction may promote proliferation in human head and neck carcinoma. 15-LOX-2 may be a possible biomarker in human head and neck malignancy.

### **P113: Evidence for a Role of the Insulinlike Growth Factor (IGF) System in Head and Neck Squamous Cell Carcinoma (HNSCC)**

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**Objective:** It is widely recognized that the insulinlike growth factor (IGF) system is involved in cancer progression and tumorigenesis. To determine the contributions of this system in head and neck squamous cell carcinoma (HNSCC), we examined patient samples and established HNSCC cell lines for IGF system expression and activity.

**Design:** The HNSCC patient tumor/normal matched pair samples were assessed for IGF-1 receptor (IGF-1R) and IGF binding protein (IGFBP) expression by immunoblot analysis. Eight HNSCC cell lines were assayed for IGF-1, IGF-2, IGFBP, and IGF-1R expression. IGF-1-stimulated Erk and Akt activation was evaluated in the context of vascular endothelial growth factor (VEGF) secretion and cell proliferation. The VEGF was quantified in conditioned medium by immunoblot analysis and cell proliferation was assessed by flow cytometry.

**Results:** Seven of 12 tumor/normal matched pairs exhibited reduced IGFBP-2 levels. Little difference in IGF-1R expression or of the other IGFBPs was observed. All 8 HNSCC cell lines expressed IGF-1R, IGF-1/2, IGFBP-2, IGFBP-3, and IGFBP-5. IGF-1 stimulated Erk and Akt phosphorylation, HIF-1 alpha expression, VEGF promoter activity, VEGF secretion, and S-phase transition. Significantly, a VEGF autocrine loop was identified in SCC-9 cells that was attenuated by addition of the Flk-1 tyrosine kinase inhibitor, ZM323881. Treatment of cells with recombinant IGFBP-3-attenuated IGF-1 stimulated VEGF secretion and cell proliferation.

**Conclusions:** We identified decreased IGFBP-2 expression in tumor vs normal tissue, which may result in enhanced IGF-1R signaling and HNSCC tumorigenesis. These findings provide support for targeting the IGF system in HNSCC therapeutics.

### **P114: Vitamin D Inhibits Carcinogenesis in the Hamster Cheek Pouch Model**

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**Objective:** To investigate whether systemic vitamin D3 therapy prevents tumor formation in the hamster buccal pouch model.

**Design:** Randomized trial in which a known carcinogen, 7,12-dimethylbenz[a]anthracene (DMBA), was applied to the right buccal pouch of 20 golden Syrian hamsters 3 times per week. To evaluate vitamin D3 as a chemopreventive agent, animals were randomized to receive systemic vitamin D3 or no treatment. Animals were sacrificed at 14 weeks after the initiation of DMBA exposure.

**Subjects:** Twenty male golden Syrian hamsters, 5 to 6 weeks of age, were used.

**Interventions:** A total of 0.25  $\mu\text{g}/\text{kg}$  of vitamin D3 via intraperitoneal injection was given to 10 animals thrice weekly. Of the remaining 10 control animals, 5 received placebo vehicle injection, and 5 received no further treatment.

**Results:** The number of hamsters with visible lesions at 14 weeks was significantly decreased in hamsters treated with vitamin D3 (5 of 10 compared with 9 of 10 untreated hamsters;  $P = .05$ ). The total diameter of lesions in the vitamin D3-treated group was 1.20 mm compared with 6.75 mm in the control group ( $P = .02$ ). The time of onset to lesion formation was significantly delayed in those animals treated with vitamin D3, with an average time to lesion development of 13 weeks whereas those not treated with vitamin D3 developed lesions at an average of 11 weeks ( $P = .04$ ).

**Conclusions:** Systemic vitamin D3 therapy delays carcinogenesis in the hamster buccal pouch model. Further investigation into the mechanisms through which vitamin D3 inhibits carcinogenesis may lead to effective chemopreventive agents to combat head and neck cancer.

## P115: Hyaluronan-CD44 Interaction Influences Topoisomerase II Activity and Etoposide Cytotoxicity in Head and Neck Cancer

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**Objective:** Hyaluronan (HA) is a ligand for the CD44 receptor, which interacts with multiple signaling pathways to influence cellular behavior. We recently determined that HA-CD44 promotes phospholipase C (PLC)-mediated Ca<sup>2+</sup> signaling and cisplatin resistance in head and neck squamous cell carcinoma (HNSCC). The objective of this study was to investigate the downstream molecular targets of HA-CD44 and PLC-mediated Ca<sup>2+</sup> signaling in HNSCC.

**Design, Subjects, and Interventions:** HNSCC tumor cell proliferation and topoisomerase (Topo) II enzymatic activity, including DNA-cleavable complex formation and DNA decatenation, were analyzed in the presence or absence of HA, the Topo II poison etoposide (VP-16), and various inhibitors of PLC and Ca<sup>2+</sup> calmodulin kinase II (CaMKII) signaling.

**Results:** Hyaluronan treatment promoted Topo II phosphorylation, suggesting that HA can modulate Topo II activity. Topo II-mediated DNA-cleavable complex formation was increased by VP-16, and this increase was significantly enhanced by noncytotoxic doses of the PLC inhibitor U73122 and the CaMKII inhibitor KN-62,

implicating PLC and CaMKII in Topo II regulation. However, the drug- and inhibitor-mediated increase in DNA-cleavable complex formation was reduced with HA pretreatment. Phospholipase C and CaMKII inhibitors also enhanced VP-16 inhibition of Topo II-mediated DNA decatenation. Hyaluronan treatment reduced VP-16 cytotoxicity. On the other hand, U73122 and KN-62 enhanced VP-16 cytotoxicity and reduced the ability of HA to promote VP-16 resistance.

**Conclusion:** Our results suggest that HA, PLC, and CaMKII are upstream regulators of Topo II-mediated DNA metabolism in HNSCC and suggest that this signaling pathway could be a promising target for development of novel therapies against HNSCC.

## P116: Stat3 Up-Regulates VEGF Production and Tumor Angiogenesis in Head and Neck Squamous Cell Carcinoma

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Overexpression of vascular endothelial growth factor (VEGF) is associated with angiogenic phenotypes and poor prognosis of numerous tumors including head and neck squamous cell carcinoma (HNSCC). However, the precise mechanism that causes VEGF overexpression in HNSCC remains unknown. Since there is evidence that a transcriptional factor, Stat3, is constitutively activated in HNSCC and this activation is significantly associated with aggressive phenotypes of this disease, we investigated the roles of Stat3 activation on VEGF production and angiogenesis in HNSCC both in vitro and in clinical samples. VEGF promoter assays with YCU-H891 cells demonstrated that dominant negative Stat3 significantly inhibited VEGF promoter activity in the full length (-2279 to +54) and two truncated forms of VEGF promoter luciferase-reporter construct (-1179 to 54 or -1014 to +54), which retain the putative Stat3 responsive elements (-849 to +842). However, this was not seen in the shorter construct (-794 to +54), which lacks the putative Stat3 responsive elements. In the derivatives of YCU-891 cells that stably express dominant negative Stat3 protein, cellular levels of VEGF mRNA and VEGF protein were significantly inhibited. In the clinical samples obtained from the patients with tongue carcinoma, the expression levels of phosphorylated (activated) form of Stat3 protein were significantly correlated with VEGF ( $p < 0.05$ ) production and intra-tumor micro vessel density IMVD ( $p < 0.01$ ). These results strongly indicate that Stat3 directly up-regulates VEGF transcription and thereby promotes angiogenesis in HNSCC. Inhibition of Stat3 activity may provide a new anti-angiogenic therapy in HNSCC.

## P117: Immunologic Effects of Combined Docetaxel and Radiation Therapy

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**Objective:** Studies have demonstrated an advantage in locoregional control and overall survival when cisplatin, used as a radiosensitizer, was added to standard postoperative radiation therapy (RT) in patients with head and neck cancer. This combination therapy has also been associated with significant adverse effects. A newer chemotherapeutic agent, docetaxel, seems to be as effective with fewer adverse effects. In addition, this agent may stimulate the immune system. Our studies assessed whether treatment with combined docetaxel and RT stimulates the immune function in patients with head and neck cancer.

**Design/Subjects:** Blood samples from 7 patients with head and neck cancer, status post-surgical excision, were analyzed before, during, and after treatment with combined docetaxel and RT.

**Interventions:** Peripheral blood mononuclear leukocytes were immunostained and analyzed by flow cytometry.

**Results:** During the course of treatment, indicators of antigen-presenting cells significantly increased. This increase was observed predominantly in myeloid cell lineage populations as measured by the proportion of HLA-DR cells expressing CD11b and CD11c. Conversely, T-cell levels, including both CD4+ and CD8+ cells, diminished significantly during treatment. However, the levels of CD4 and CD8 did increase at the posttreatment assessment.

**Conclusions:** Although treatment with docetaxel and RT seems to cause some toxicity to T-cell populations, myeloid lineage cells, such as macrophages and myeloid dendritic cells, increased during the course of treatment.

## P118: Survivin Expression in Medullary Thyroid Carcinoma: Identification and Preliminary Signaling Mechanisms

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**Objectives:** Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor that shows resistance to both chemotherapy and radiotherapy treatments. Survivin, a member of the inhibitor of apoptosis protein (IAP) family, has been identified in a number of malignant adult neoplasms and is thought to play a role in preventing cancer cell death. The aims of this study were: 1) to determine if survivin is expressed in MTC cells, 2) to evaluate its mechanism of action in preventing MTC cell death, 3) to explore the hypothesis that modulation of survivin expression directly affects apoptotic pathways and cell death, and 4) to study the complex interaction between chemotherapeutic agents and survivin expression and function.

**Design:** Human MTC cell lines DRO81-1 and TT were investigated to determine survivin expression, and to evaluate the effect of modulating survivin expression on apoptosis and MTC cell death. Chemotherapeutic agents were administered to determine effects on survivin expression and corresponding MTC cell death.

**Methods:** Survivin mRNA and protein were identified by RT-PCR amplification and Western Blot analysis, respectively. A validated survivin siRNA with transfection was used to downregulate survivin levels. Infection with an adenoviral survivin expression vector was utilized to upregulate survivin levels. Analysis of apoptotic pathway components was performed using Western Blot and fluorescence methodologies. The effects of adding Paclitaxel, both separately and in conjunction with modulation of survivin levels, were analyzed via flow cytometry cell proliferation studies.

**Results:** Survivin expression was identified in MTC cell lines DRO81-1 and TT. Survivin mRNA was detected via RT-PCR amplification with survivin specific primers; survivin protein expression was confirmed by Western Blot analysis. siRNA transfection resulted in an 86% reduction in survivin levels versus controls. Survivin levels

were upregulated greater than 60% by adenoviral expression vector infection. MTC cell death was measured for baseline, upregulated and downregulated levels of survivin, the results of which corresponded with modulated levels of survivin expression. The addition of Paclitaxel resulted in upregulation of survivin expression, but was associated with arrested cell growth for the majority of MTC cells, with the remaining progressing to cell death.

**Conclusions:** This investigation represents the first to demonstrate the expression of survivin in human MTC cell lines. Modulation of survivin expression caused a corresponding change in MTC cell death. Cell death was not consistently noted to correlate with levels of caspase pathway activation, suggesting that survivin effects cell death via an alternate signaling pathway. The upregulation of survivin seen after treatment of MTC cells with Paclitaxel is paradoxically followed by growth phase arrest or cell death. Studies to further elucidate alternate pathways effected by survivin, as well as to identify long-term effects of Paclitaxel on MTC cell viability are ongoing. Continued research efforts to better understand the function of survivin and its effect on MTC cells may yield important clinical implications for targeted therapy.

## **P119: CD24 Expression Correlates With Response to Cisplatin in Head and Neck Squamous Cell Carcinoma Cell Lines**

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**Objective:** To evaluate the role of CD24 expression regarding cisplatin sensitivity in head and neck squamous cell carcinoma (HNSCC) cell lines.

**Design:** Cell line study involving University of Michigan Squamous Cell Carcinoma (UM-SCC) cell lines.

**Main Outcome Measures:** Expression of membrane-bound CD24 was measured by flow cytometry in molecules of equivalent standard fluorochrome (MESF) units. Tumor cell viability in response to cisplatin was measured by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay following CD24 RNA interference or CD24 up-regulation.

**Results:** Sixteen UM-SCC cell lines exhibited highly variable levels of CD24 (MESF, 5728.2-312 356.2). High levels of CD24 expression correlated with cisplatin resistance, whereas low levels of expression correlated with cisplatin sensitivity ( $R^2 = 0.72$ ). To further explore this relationship UM-SCC 10BPT, a cell line expressing high levels of membrane-bound CD24 and exhibiting cisplatin resistance was infected with a lentiviral vector containing a CD24 short interfering RNA construct. Knockdown of CD24 resulted in increased sensitivity compared with controls following a 72-hour exposure to cisplatin (IC50 = 91M compared with IC50 = 18 061M). Similarly, infection of UM-SCC 74B, a cisplatin-sensitive cell line expressing a low level of membrane-bound CD24, with a lentiviral expression containing CD24 complementary DNA resulted in increased resistance compared with controls following a 48-hour exposure to cisplatin (IC50 = 211M compared with 181M).

**Conclusion:** This is the first evidence that CD24 may play a role in cisplatin response in HNSCC cells, in vitro. If a similar relationship can be displayed in clinical specimens, CD24 may have value as a predictor of response to cisplatin in HNSCC patients.

## **P120: WITHDRAWN**

## **P121: The Use of Microvascular Tissue in Reconstruction of the Lateral Skull Base**

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The lateral skull base presents the modern head and neck surgeon with a variety of neoplastic disease. The majority of these tumors require resection and radiation. The resultant defects are often complex an inoperable for reconstructive tissue. It is crucial that bony coverage be achieved to avoid osteomyelitis. Free tissue transfer allows safe and reliable coverage for these defects. We present a series of 19 patients with lateral skull base resections, all of which were reconstructed with microvascular flaps. Short and long-term follow up is provided. The use of several different flaps and their advantages and disadvantages are reviewed.

## **P122: Electroglottography-Based Videostroboscopic Assessment of Laryngectomy Prosthetic Speech**

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**Objectives:** The primary purpose of this study was to assess for the first time the anatomical and morphologic characteristics of the pharyngoesophageal (PE) segment in tracheoesophageal (TO) speakers using an electroglottography (EGG) based videostroboscopy tool.

**Study Design:** Cross-sectional cohort study.

**Setting:** Head and Neck Oncology Unit, tertiary referral centre.

**Patients:** 52 patients following total laryngectomy with no recurrence and using prosthetic (Blom-Singer) speech.

**Intervention:** EGG based rigid videostroboscopy and perceptual evaluation.

**Main Outcome Measures:** Stroboscopic protocol included 9 subjective/visual parameters that were used to evaluate the neoglottis and study correlation with GRBAS and the overall voice quality (OVQ) as well with the treatment variables.

**Results:** We had 52 males and 10 females with a mean age of 63.4 years (10.5) in our study. Median time since TL was 2 years. There was excellent correlation between G and OVQ (Spearman rho, >0.9). We had equal number of patients (n=13) in both the G1 of the GRBAS and the good voice category of the OVQ. Statistically significant correlation was found between G1/good over all voice quality with saliva (p=0.03 & 0.02) and LVV (p=0.05 & 0.03). Using Pearson's chi-square tests, there was significant statistical correlation between saliva and sex (p=0.03), site (p=0.01) and reconstruction (p=0.009). Significant correlation was also seen between ROV and sex (p=0.04), site (p=0.01), PMV with pharyngectomy (p=0.05), primary cases (p=0.03) and finally between VSM and nerve implantation (p=0.02).

**Conclusions:** This study shows for the first time that useful data can be obtained even in TO speakers using prosthetic speech using an EGG based videostroboscopy protocol and tool. Our observations suggest that from a functional voice standpoint, the most fluid vibratory segment in laryngectomees may be one that is that has thin, floppy and redundant mucosa. EGG based videostroboscopy is an attractive concept and it can possibly provide the clinician with useful information in this unique set of patients. However, it still has its limitations most notably being that it cannot be used in all very irregular and highly variable TO speakers.

## **P123: Proteomic Screening of Saliva in Head and Neck Squamous Carcinoma: A Potential Diagnostic and Screening Applications**

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University of Texas M. D. Anderson Cancer Center, Houston

**Methods:** Saliva is a readily accessible secretion that may be used in the diagnosis and screening of patients with head and neck squamous cell carcinoma (HNSCC). Saliva from 5 healthy volunteers and 3 patients with oral squamous cell carcinomas were used for proteomic analysis; we first depleted major proteins by affinity column. Depleted saliva was then divided and analyzed by the following methods: (1) LC-MS/MS after in-solution digestion and peptide anion exchange chromatography, (2) peptide separation by chromatography, and (3) sodium dodecyl sulfate-polyacrylamide gel electrophoresis and in-gel digestion and by liquid chromatography/tandem mass spectrometry.

**Results:** Method 1 identified 14 to 44 proteins in all normal samples. Method 2 identified 21 to 118 proteins, and method 3 identified 64 to 163 proteins. Proteins present in all normal samples were 4, 11, and 26 for methods 1, 2, and 3 respectively. Unique proteins 33, 14, and 33 were identified in patients' saliva for each sample. Compared with normal saliva, the saliva of patients with SCC contained 2 unique proteins: alpha-1-B-glycoprotein and complement factor-B. These proteins can be targeted for future validation in clinical trials.

**Conclusions:** (1) A set of common proteins is identified among all normal salivars. (2) Intermethodological differences between specimens were noted. (3) Certain distinctive proteins distinguish normal from subjects with HNSCC. (4) Saliva is an easy and accessible source for diagnosis and screening of HNSCC.

## P124: Cost Savings of Patients With a MACIS Score Lower Than 6 When Radioactive Iodine Treatment Is Not Given

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**Objectives:** Previous studies have demonstrated that radioactive iodine (RAI) treatment in patients with well-differentiated thyroid carcinoma (WDTC) and a MACIS (metastases, age, completeness of resection, invasion, and size for prognostic measures) score lower than 6 does not decrease the rate of recurrence or impact on survival. The goal of this study is to assess the potential savings to the health care system of ceasing to treat patients with MACIS scores lower than 6 with radioactive iodine after total thyroidectomy.

**Methods:** A retrospective chart review involving 199 consecutive patients at a primary care center, over a 43-month period, who received radioactive iodine after total thyroidectomy for WDTC and who had MACIS scores lower than 6. Patient demographics were analyzed. Costs for the dose of RAI, hospital stay, and health insurance claims were included in calculations.

**Results:** Cost savings can be accrued by our institution by stopping iodine 131I treatment after total thyroidectomy in patients with MACIS scores lower than 6. For 199 consecutive patients the total cost for iodine 131I treatment amounted to \$161 587, and the total cost of the required 2-day stay in an isolation unit at a primary care center totaled \$764 558. Overall, the total cost to the health care system was \$934 106.

**Conclusions:** By following the recommendations of recent evidence-based studies and stopping RAI treatment following total thyroidectomy in low-risk patients (MACIS scores <6) with WDTC, a significant cost savings can be accrued by the health care system.

## P125: Bone Anchored Mucosal Flap for Reconstruction of Floor of Mouth and Gingiva: A Pilot Study

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**Objectives:** Defects after resections of T2 and limited T4 tumors of the anterior floor of mouth and gingiva, are often reconstructed with free forearm flaps or bilateral mesolabial flaps. These techniques are often associated with impaired sensation and unpredictable scar formation both intra orally and at the donor site. Patients may experience dysphagia, dysarthria and donor site cosmetic problems. We have developed a reconstructive alternative that allows for the reliable coverage of soft tissue and bone, preservation of local sensation and rapid recovery of oral functions.

**Study Design:** This is a prospective study of eight patients, six of which had T2 lesions of the anterior floor of mouth and two had T2 lesions of the gingiva. The defects measured 4-5 cm by 2.5-3 cm including partial mandibulectomy and up to nine teeth.

**Method:** A local mucosal flap was raised from the inferior aspect of the tongue. Multiple holes were drilled in the exterior cortex of the mandibular defect. The flap was being pulled forward and anchored to these drilled holes by 3-0 sutures. The anterior margin of the defect was also anchored to these drill holes to produce a water tight closure and to make the lip independent of the mucosal flap.

**Results:** The mucosal flap stretched and normalized into position within 2 weeks. After that 7/8 patients had normal or minimally decreased tongue mobility, and 7/8 normal speech (one patient developed osteoradionecrosis after postoperative radiation). Swallowing capacity was normal or minimally affected. Six patients had fully normal and two slightly impaired sensation in the flap.

**Discussion:** This local bone anchored mucosal tongue flap has the advantage of short operating room time and hospitalization, only one surgeon is needed, there is no donor site morbidity, and rapid return of oral function.

**Conclusions:** We propose this flap as a reconstructive alternative for defects up to the size of T2 and small T4 lesions of the anterior floor of mouth and gingiva.

## P126: Quality of Life Is Acceptable in Locally Advanced Head and Neck Cancers Treated With Aggressive Regimen of Chemoradiation

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**Background:** Patients with locally advanced head and neck squamous cell cancer (HNSCCA) have traditionally been treated with an aggressive regimen of concurrent chemo-radiation, or more recently, induction chemotherapy followed by concurrent chemo-radiation, to achieve high rates of local control at our institution. Despite a high initial acute toxicity, long-term quality of life (QOL) data was not available in these patients.

**Methods:** The study included 75 patients with stage III-IV HNSCCA treated with either concurrent chemo-radiation or induction chemotherapy followed by concurrent chemo-radiation at our institution. Patients had to be on long-term follow-up, at minimum of 3 months after completion of treatment, and with no evidence of disease at the time of survey. We were unable to complete the survey in 43 either due to a change in contact information, placement in assisted living, inability to answer or unwillingness to participate. In the remaining 32 patients, the University of Washington QOL survey could be completed over the telephone. Two patients were excluded due to current treatment for recurrent head and neck cancer. Additional information regarding acute toxicity during treatment was obtained from a review of records.

**Results:** There were 11 women and 19 men in this group. The median duration of follow up was 36 months (range 3-120 months) after completion of treatment. The complication rate associated with gastrostomy tube placement were 5 leaks and 6 infections (12/31 patients, 38.7%) and for the portacath were 2 deep vein thrombosis requiring port removal and anticoagulation (6.45%). No patients in this group were still dependent on their gastrostomy tube for nutrition at the time of follow up. Of note, 9% of patients were still smoking and drinking on a regular basis. The composite scores for the 9 domains ranged from 370-875, with a median score of 615/900. Major issues regarding QOL were reported as saliva 11/31 (35.5%) and swallowing 10/31(32.2%), followed by mood 6/31(19.3%), pain 5/31(16.12%), chewing 4/31(12.9%), pain 5/31(16.12%) and shoulder problems 5/31(16.12%).

**Conclusion:** Most patients had a good or acceptable quality of life after treatment for advanced HNSCCA.

## P127: Radical Radiation for Unknown Primary Squamous Cancer Yields High Control But Has Major Toxicity Suggesting the Need for a New Treatment Paradigm

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**Objective:** Radical radiation to the upper aerodigestive tree is associated with a high rate of tumor control but at the price of major quality-of-life impairment. A new treatment paradigm is under study.

**Methods:** Review of our database of patients with unknown primary head and neck squamous cell cancer (HNSCC) revealed 54 patients, 46 of whom had SCC nodal disease. Radical radiation with or without surgical resection was given to 39 patients (85%).

**Results:** Long-term survival was 54% (mean duration of follow up, 37 months). Local recurrence (tumor reappearances) occurred in 13% of patients, distant failure in 7%. Major complications of therapy occurred in 20%. The latter included xerostomia (5 patients); esophageal stricture (1 patient); carotid rupture (1 patient); and brachial, plexopathy/fibrosis of the shoulder (3 patients). We have initiated a pilot study of neoadjuvant chemotherapy (without primary radiation) with subsequent neck dissection and selective site radiation for extra nodal disease. One of 5 patients treated developed a recurrence of tumor at the base of the tongue at 16 months and responded to surgical resection and radiation to primary site. The patient had no evidence of disease at 26 months, and the 4 other patients were doing well at 6 to 18 months.

**Conclusion:** Although radical radiation to potential primary site(s) is considered the standard of care, we believe a new treatment paradigm is warranted. Neoadjuvant chemotherapy with neck dissection and selective radiation therapy and continued primary site observation seem to be a reasonable treatment alternatives.

## **P128: Impact of Preepiglottic Space Tumor Involvement on Concurrent Chemoradiation Therapy for Squamous Cell Carcinoma**

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**Objective:** To determine the prognostic impact of preepiglottic space involvement on tumor recurrence after concurrent chemoradiation therapy for patients with head and neck squamous cell carcinoma.

**Design:** Retrospective chart review.

**Setting:** Tertiary care center.

**Patients:** Patients who underwent concurrent chemoradiation therapy for stage T3 or T4 laryngeal carcinoma, stage T4 hypopharyngeal carcinoma, or stage T3 or T4 oropharyngeal squamous cell carcinoma from 1989 to 2005.

**Main Outcome Measure:** Local tumor control.

**Results:** A total of 102 patients were included in the study; 28 patients (27%) had documented preepiglottic space involvement as determined radiologically and/or clinically. The mean duration of follow-up for all patients was 46 months. A multivariate analysis was performed in the presence of recurrence using the following pretreatment variables: preepiglottic space involvement, tumor extent, pathological cell differentiation, lymph node involvement, age, and sex. Involvement of the preepiglottic space was not significantly associated with local tumor recurrence ( $P = .69$ ). No other variables had a significant impact on tumor recurrence. Major preepiglottic was defined as radiographic involvement with tumor palpable on examination under anesthesia. Minor preepiglottic involvement was defined as radiographic involvement without palpable tumor on examination. The extent of preepiglottic involvement did not have an impact on local control after concurrent chemotherapy treatment ( $P = .61$ ).

**Conclusion:** Preepiglottic space involvement does not have a negative impact on local tumor control or recurrence after concurrent chemoradiation therapy.

## **P129: Toxicity Outcomes in Intensity-Modulated Radiation Therapy vs 3-Dimensional Conformal Radiotherapy for Head and Neck Squamous Cell Carcinoma With Unknown Primary**

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Medical College of Wisconsin, Milwaukee

**Objective:** To evaluate toxicity outcomes for head and neck squamous cell carcinoma (HNSCC) with unknown primary treated with 3-dimensional conformal radiotherapy (3D-CRT) compared with intensity-modulated radiation therapy (IMRT).

**Design:** Retrospective review of records.

**Setting:** Medical College of Wisconsin Cancer Center.

**Patients:** Records were found for 27 patients treated with radiation therapy for HNSCC of unknown primary from 1991 to 2004. Median follow-up after treatment was 32 months (range, 4-108 months).

**Interventions:** Eleven patients (age range, 44-75 years) received 3D-CRT, and 16 (age range, 38-70 years) received IMRT. No patients received chemotherapy.

**Main Outcome Measures:** Toxicity scores were compared using a Fisher exact test. Weight changes and local, regional, and distant failures were compared.

**Results:** Percentages of patients with acute grade = 2 and = 3 xerostomia were 63.7% and 45.5%, respectively, in the 3D-CRT group compared with 18.8% and 0.0% in the IMRT group. These differences were statistically significant ( $P = .04$  and  $.006$ , respectively). One patient terminated therapy after receiving 16.2 Gy owing to acute toxic effects. When this patient was excluded, a significant difference in late xerostomia grade = 3 was noted, 0.0% in the IMRT group and 30.0% in the 3D-CRT group ( $P = .046$ ). A difference in late gastroin-

testinal toxicity grade = 2 was identified ( $P = .02$ ). A significant difference in acute pain grade = 3 ( $P = .001$ ) was identified that favored IMRT. No significant difference in weight loss or local, regional, or distant failure was identified.

**Conclusions:** Intensity-modulated radiation therapy may reduce acute pain and xerostomia as well as permanent (late) xerostomia and gastrointestinal toxicity.

## **P130: Safety Initiative for Surgically Altered Airways: The Bedside UCSF Emergency Airway Access Form.**

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Surgically altered airways present unique challenges during emergency situations in an inpatient hospital setting. Health care professionals responding to respiratory compromise in these patients face a potential knowledge deficit regarding the anatomy, confusion in terminology used by various staff, and possible difficulty communicating with primary surgical teams. As part of a safety initiative, we formed an airway committee and developed the Emergency Airway Access Form. The form is posted at the bedside of all patients with a surgically altered airway and specifically labels the type of airway present. Further it identifies possible routes of intubation, establishes a uniform terminology to be used in emergent settings, and allows for the primary surgeon to indicate unique features of each patient's airway. Prior to the introduction of the form, a written survey was distributed in a 12 hour time period to nurses and physicians at all levels of training throughout the medical center. The survey revealed that 10% of general surgeons and 40% of internists believed it was acceptable to oxygenate a laryngectomy patient by mouth. Only 30% of internists, 60% of anesthesiologists, and 65% of general surgeons could accurately identify the purpose of stay sutures. Compliance with use of the form was 43% at 2 months and 100% at 4 months after introduction of the form.

**Conclusion:** a significant knowledge deficit exists in medical professionals potentially responsible for emergent management of surgically altered airways. We introduce an airway form that is simple to use, easy to implement, and has a high rate of compliance with hopes of improving management of complex airways. This form is particularly important for patients with unusual airway alterations created in the population with head and neck cancer and should be considered for general use.

## **P131: Rehabilitation Exercises Improve Cancer Treatment Outcomes**

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**Objectives:** To introduce to otolaryngologists the evidence showing benefits of exercise in patients with cancer and other chronic diseases, to stimulate incorporation of exercise regimens into the treatment of patients with head and neck cancer and other chronic diseases of the head and neck, and to promote investigation into and development of dedicated physical therapy regimens for head and neck cancer.

**Study Design:** Comprehensive review and analysis of literature.

**Diseases Studied:** Cancers of multiple organs and systems and cognitive dysfunction.

**Interventions:** Rehabilitation exercise programs.

**Outcome Measurements:** Survival, tumor control, and quality of life.

**Statistical Methods:** Meta-analysis.

**Results:** Exercise has been shown to improve quality of life in patients with cancers of various organ systems with statistical significance using reported methods of analysis. Other beneficial effects have been suggested but seem to be tumor specific rather than universal. For example, survival benefit is suggested for patients with breast cancer in multiple studies. No study has reported any deleterious effect of exercise on outcomes in cancer management.

**Conclusions:** Exercise regimens are highly likely to benefit patients with head and neck cancer, both in tumor management and in quality of life. Appropriate regimens already published to be safe and effective should be employed more widely, with benefits investigated more fully.

**P132: WITHDRAWN****P133: Pectoralis Major Flap for the Reconstruction of Composite Lateral Temporal Bone Defects: Reaching the Temporal Line**V.A. Resto<sup>1</sup>; D.G. Deschler<sup>2</sup><sup>1</sup>University of Texas Medical Branch, Galveston; <sup>2</sup>Massachusetts Eye and Ear Infirmary, Boston

**Objective:** Reconstruction of lateral skull base defects remains a challenge. The pectoralis major myocutaneous flap (PMF) has been a true workhorse in head and neck reconstruction for decades, yet application to the reconstruction of lateral skull base defects has been restricted to defects below the external auditory canal because of perceived difficulty in achieving sufficient flap length to ensure flap viability as well as a tension-free, water-tight closure. We present our experience using the PMF for the reconstruction of composite lateral temporal bone defects extending beyond the temporal line.

**Methods:** Illustration of specific technical modifications that are important for the reliable application of this reconstructive method with retrospective review of outcomes.

**Results:** Between February 2001 and February 2006, 8 patients with composite lateral temporal bone defects after surgical ablation for tumor underwent reconstruction with the PMF. All patients underwent total or near-total auriclectomy, wide skin excision, and lateral temporal bone resection as part of the surgical ablation, thus requiring obliteration of the middle ear cavity as well as replacement of skin cover. All the patients received radiation. Patients had a median age of 80 years. Median duration of postreconstruction follow-up was 9 months. All cases achieved complete healing of the reconstructed surgical defect with no flap loss (partial or total).

**Conclusions:** This series demonstrates, that with specific technical modifications, the PMF can be reliably used for the reconstruction of composite lateral temporal bone defects extending up to and beyond the temporal line, making this flap an important alternative to free-flap reconstruction in selected cases.

**P134: Combined Transoral Laser Microsurgery and Intensity Modulated Postoperative Radiation Therapy for Head and Neck Cancer**

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**Objective:** To evaluate the locoregional control and functional results of transoral carbon dioxide (CO<sub>2</sub>) laser microsurgery (TLM) followed with intensity-modulated radiation therapy (IMRT) for treatment of locally advanced head and neck carcinoma.

**Design:** Retrospective review of patients treated with TLM followed by treatment with IMRT.

**Setting:** Tertiary care academic medical center.

**Patients:** Forty patients were treated from June 1997 to December 2004.

**Intervention(s):** Transoral CO<sub>2</sub> laser microsurgery followed with IMRT. Indications for radiation included close surgical margins, more than 1 positive lymph node metastasis, or extracapsular extension in any lymph node.

**Main Outcome Measure:** Locoregional control rate and quality of life as assessed by the functional outcome swallowing scale (FOSS).

**Results:** Although 79% of patients had T1-T2 primary tumors, 97% of patients had stage III/IV disease overall. Chemotherapy was delivered concurrently with radiation in 19% of patients. The ratio of men to women was 34:6; the median age was 58 years. The tumor subsites were the oropharynx, hypopharynx, and larynx. The locoregional control rate was 100% at a median follow-up time of 33 months (range, 7-98 months). Three patients developed second primary tumors, and 2 patients developed distant metastasis. The mean FOSS score was 0.73 (range, 0-5). Both the median and mode of the FOSS scores were zero.

**Conclusions:** Transoral CO<sub>2</sub> laser microsurgery and IMRT represent less invasive forms of surgical resection and radiation therapy, respectively. In our preliminary experience, the combination of these limited approaches resulted in excellent locoregional control in a group of patients with locally advanced squamous cell carcinoma of the head and neck. Functional status based on the FOSS scale is encouraging.

**P135: Oropharyngeal Cancer Associated With Oncogenic Human Papilloma Virus Is Clinically Unique and Portends Improved Survival**J.A. Ernster<sup>1</sup>; C. Sciotto<sup>2</sup>; M. O'Brien<sup>3</sup>; L. Robinson<sup>2</sup>; T. Willson<sup>2</sup><sup>1</sup>Colorado Otolaryngology Associates, Colorado Springs;<sup>2</sup>Penrose-St Francis Health Care System, Colorado Springs;<sup>3</sup>University of Colorado Health Sciences Center, Denver

**Objective:** To determine how the presence of the oncogenic human papilloma virus (HPV) genome affects the clinicopathologic features and survival of a group of patients with oropharyngeal cancer.

**Design:** Retrospective analysis of a cohort of patients identified over a 25-year period. Duration of follow-up ranged from 14 months to 22 years. The HPV status was determined by polymerase chain reaction.

**Setting:** Molecular biology laboratory in a tertiary community hospital.

**Patients:** Of a total of 114 patients, 72 had satisfactory clinical histories and pathologic material. Fifty patients were positive for HPV-16.

**Main Outcome Measures:** Features analyzed were age at diagnosis, sex, decade of diagnosis, stage, subsite, histologic findings, and smoking status. We determined the differences in each by HPV status. We determined the disease-specific survival by HPV status and sex.

**Results:** Significant differences were found in age at diagnosis ( $P < .001$ ) and decade of diagnosis ( $P < .008$ ). Survival was affected by HPV status ( $P < .001$ ). In the patients with 2-year follow-up, disease-specific survival was 50% (5 of 10) of the HPV-positive patients and 0% (0 of 7) of the HPV-negative patients. When those with 2- to 10-year follow-up were added, survival was 80% (32 of 40) and 17% (3 of 18). When those with greater than 10-year follow-up were added, survival was 83% (38 of 46) and 15% (3 of 20). Women who were HPV-positive had the best survival. Kaplan-Meier survival curves displayed the significant differences.

**Conclusions:** Human papilloma virus-positive oropharyngeal cancer is more common in younger individuals and is occurring more frequently in recent decades. Survival is significantly better when the HPV genome is identified.

**P136: Free Jejunal or Ileocolic Flap Transfers as a Method of Reconstruction Following Hypopharyngeal Tumor Resection**

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**Objective:** To compare the results between free jejunal and free ileocolic flap transfers for reconstruction following circumferential hypopharyngeal tumor resection.

**Design:** Retrospective clinical review.

**Setting:** Academic tertiary care medical center.

**Patients:** Twenty-four patients underwent microvascular free jejunal flap transfer, and 12 patients underwent free ileocolic autograft for immediate reconstruction after ablative surgery for advanced hypopharyngeal carcinoma.

**Main Outcome Measures:** The intraoperative and postoperative variables, complication rates, and success of early and late functional results were determined.

**Results:** The most common complication was autograft necrosis owing to vessel thrombosis. This resulted in graft removal in 3 patients. We observed no anastomotic fistulas in any patients. Patients started oral food intake on the 11th or 12th day after surgery. The length of hospital stay was 26 to 28 days. Two-year survival rates for jejunal and ileocolic transfers were 61.4% and 66.7%, respectively. Speech was restored in all patients with free ileocolic flap reconstruction due to Bauhini valve vibration, in contrast to the group of patients who underwent free jejunal flap reconstruction, none of whom reached these results.

**Conclusions:** No significant differences were found between patients' outcome in both groups of reconstruction in terms of early and late complications, start of oral food intake, and hospital stay. This study demonstrated that free ileocolic transfer could be considered as a better option for pharyngoesophageal reconstruction, offer-

ing immediate restoration of swallowing and good voice function. Although some patients with advanced hypopharyngeal squamous carcinoma have a poor prognosis, this technique allows a better quality of life for a probable short life span.

## **P137: Validation of Our Histological Risk Assessment Model: An Interim Analysis**

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**Background:** A novel histological risk assessment of squamous cell carcinoma (SCC) is predictive of overall survival (OS) in patients with cancer of the oral cavity. The purpose of the current study is to validate this risk scoring on a new cohort. Our target sample size is an estimated 344 patients. We present an interim analysis on 163 patients with primary upper aerodigestive tract SCC (UADT-SCC).

**Materials and Methods:** Patients were identified; 2 pathologists, blinded to outcome, reviewed resection slides; and the risk score was applied. Binary outcome and time-to-event analyses (date of first locoregional recurrence vs last known recurrence-free date, and date of death vs last known date alive) were performed using SAS statistical software.

**Results:** The distributions of risk categories were 21 patients in the low-risk group, 67 in the intermediate-risk group, and 75 in the high-risk group. The median follow-up time for all patients was 17.9 months. Median OS for all groups was 36.6 months; the low-risk group it was 60.0 months; for the intermediate risk group, 48.9 months; and for the high-risk group, 31.0 months. High-risk category was predictive of decreased OS compared with low risk ( $P = .007$ , hazard ratio [HR] 2.9) after adjusting for sex and tumor stage. After additional adjustment for treatment, high-risk classification was still predictive for decreased OS compared with low-risk ( $P = .02$ , HR 4.3).

**Conclusion:** This interim analysis suggests that our risk assessment is predictive of OS. We believe that the relatively short median follow-up time (17.9 months) and the relatively few locoregional recurrences do not allow us to see significant differences in locoregional recurrence between the risk categories.

## **P155: Intensity-Modulated Radiation Therapy for Head and Neck Cancers: Acute Toxicity and Early Outcome Data**

**J.M. Watkins**; A.K. Sharma

Medical University of South Carolina, Charleston

**Objectives:** To describe acute toxic effects and locoregional control for patients with head and neck cancers treated with intensity-modulated radiation therapy (IMRT).

**Design:** Prospectively collected database.

**Setting:** Academic radiation oncology clinic.

**Patients/Intervention:** Patients with head and neck cancers treated with IMRT.

**Main Outcome Measures:** Acute toxic effects and locoregional control.

**Results:** From August 2003 to December 2005, 85 patients with head and neck cancers were treated with IMRT either as definitive (55%) or postoperative (45%) therapy. Oropharyngeal (36%) and laryngeal (15%) sites were most common, and 83% of patients were American Joint Committee on Cancer stage III-IVA. Intensity-modulated radiation therapy doses of 450 to 800 Gy (median dose, 660 Gy) were delivered, and 70% of patients received concurrent chemotherapy. No patient experienced Radiation Therapy Oncology Group grade 4 or 5 radiotherapy-associated toxic effects. Grade 3 mucous membrane toxicity occurred in 27%, pharynx (9%), skin (5%), larynx (1%), and none in the salivary gland. Only 5% of patients experienced a toxic effects-related treatment delay of more than 3 days (maximum delay, 7 days). Median weight loss was 7% of pretreatment weight (range, +6% to -20%). Forty-nine percent of patients had percutaneous endoscopic gastrostomy (PEG) tubes placed (29% before treatment and 20% during treatment). The PEG tubes remained in place for a median duration of 105 days (range, 48-317 days). At a median follow-up of 12 months, 80% of patients

were alive without evidence of disease, 11% of patients were alive with disease, 8% had died with disease, and 1% had died of other causes. In 16 patients who experienced recurrent disease, 4 failed locoregionally, 3 at the field margin, 5 failed in-field and distantly, and 4 failed distantly only.

**Conclusions:** Intensity-modulated radiation therapy is well tolerated by patients and allows for completion of scheduled therapy without significant toxic effects-associated treatment breaks.

## **P138: Systematic Review and Meta-analysis of Follow-up Protocols and Cancer Progression of Oral Dysplasia**

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**Objectives:** To assess the cancer progression rates of oral dysplasia. To assess the effectiveness, safety, and acceptability of follow-up regimens for oral dysplasia. Based on results, we propose an evidence-based follow-up protocol.

**Study Design:** Systematic literature review with criteria for identifying studies, assessing quality and data extraction.

**Selection Criteria:** all studies reporting oral dysplasia

**Interventions:** Clinical follow-up and surveillance, surgical and non-surgical treatment, modification of aetiological factors.

**Outcome Measures:** Malignant transformation rate; clinical resolution, predictive value of clinical prognostic indicators.

**Data Collection and Analysis:** Using selection criteria, we identified published data by electronic searching. The validity of studies and extracted data was independently assessed by two authors. Metaanalysis of quantitative data is performed and compared and summarized in a table. Qualitative data is also discussed.

**Results:** There are no RCTs assessing follow-up strategies. 19 RCTs of non-surgical treatment reported follow-up. No RCTs of surgical treatment were found. A further 17 prospective or retrospective studies reported variable follow-up (mainly level III evidence). Overall 765 patients were identified as having dysplasia in the studies. The malignant transformation rate varies widely between studies (6.6 to 36.0%). There is a significant trend between mild and severe dysplasia for increased malignant progression rate (mean 14% vs 26% respectively) and mean duration to progression (5.6 vs 4.4 years respectively). Smoking status, site and histological grade of the lesion are associated with progression to cancer.

**Conclusion:** There is currently no evidence-based or consensus strategy for malignant risk quantification or follow-up of patients with oral dysplasia. We will present a follow-up protocol based on best evidence. Large level I trials are needed to assess the new strategies, including the use of molecular markers, for risk quantification, treatment and follow-up of these lesions.

## **P139: Paratracheal Node Dissection in the Management of Well-Differentiated Thyroid Cancer**

**C.M. Slough**; S. Weber; K. Schuff; M. Samules; J.I. Cohen

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**Objective:** To describe a specific technique of paratracheal node dissection in the reoperative situation and to report the clinical outcomes and complications of its use.

**Design:** Retrospective case series.

**Setting:** Tertiary referral academic medical center.

**Patients:** Sixty-five patients with recurrent, well-differentiated thyroid cancer treated surgically between January 2000 and September 2005 at Oregon Health Sciences University.

**Interventions:** Paratracheal node dissection.

**Main Outcome Measures:** Perioperative complications (recurrent laryngeal nerve injury and/or hypoparathyroidism).

**Interventions:** Twenty male and 45 female patients (average age, 45.2 years) underwent central compartment neck dissections for recurrent papillary thyroid cancer based on an elevated thyroglobulin level and/or anatomic evidence of nodal involvement. Twenty-eight patients underwent a bilateral central neck dissection, while 38

underwent a unilateral dissection (22 right and 15 left). This included 46 patients who also underwent a simultaneous cervical lymphadenectomy of at least levels III and IV.

**Results:** Fifty-five central compartment specimens yielded pathologically confirmed papillary thyroid carcinoma. Complications included temporary hypocalcemia in 15 patients (ionized serum calcium, <1.0), as well as a single patient each with shoulder dysfunction, temporary recurrent laryngeal nerve paralysis and hematoma. Significant hypocalcemia (ionized serum calcium, <0.8) was seen in only 6 cases. No patient had permanent hypocalcemia.

**Conclusions:** The central compartment is a common site of nodal metastasis and recurrence in well-differentiated thyroid carcinoma. An anatomically based systematic approach to the paratracheal region allows for effective clearance of this nodal station with a minimum of morbidity.

## **P140: Upper Aerodigestive Tract Venous Malformations**

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University of Arkansas for Medical Sciences, Little Rock, AR

**Objective:** To examine the experience of our vascular anomalies team with venous malformations (VMs) of the upper aerodigestive tract (UADT) and provide management recommendations for this disorder.

**Design:** Retrospective chart review.

**Setting:** University of Arkansas for Medical Sciences.

**Patients:** Twenty-six patients (15 female and 11 male), treated from 1992 to 2006, with clinical and radiographic evidence of UADT VM.

**Results:** All patients were diagnosed at childhood but often with a misdiagnosis as hemangioma. Current diagnosis was based solely on clinical and radiographic evidence. Presenting symptoms included upper airway compromise, speech problems, bleeding, and pain. Seven patients underwent previous treatment consisting of sclerotherapy and/or laser therapy. Areas involved were the nasal cavity, nasopharynx, lower lip, floor of the mouth, tonsils, tongue, palate, pharynx, hypopharynx, and supraglottic larynx. Two patients with intranasal VM involving dura underwent craniofacial resection. Tongue VMs were excised in 4 patients (3 with reconstruction) who have shown evidence of clinical cure. Twenty-two patients completed 1 or more Yag laser treatments with 25% to 75% disease improvement.

**Conclusions:** Significant morbidity results from VMs involving the UADT. Most physicians have little to no experience with UADT VMs and are unclear how to manage them. We present our experience with UADT VMs and offer management recommendations.

## **P141: Outcome and Morbidity From Salvage Neck Dissection and Interstitial Brachytherapy for Recurrent Head and Neck Cancers**

**M.E. Kupferman;** W. Morrison; D. Roberts; R.S. Weber

MD Anderson Cancer Center, Houston, TX

**Objectives:** Patients who develop regional neck recurrences after definitive treatment for head and neck cancer are not amenable to successful salvage. The role of interstitial brachytherapy (IBT) as an adjunct to surgical salvage for recurrent cancer has not been defined to date. We reviewed our experience utilizing IBT and surgical salvage in patients with regional recurrences to assess effectiveness on regional control and morbidity.

**Methods:** A retrospective chart review was performed on all patients treated with IBT for neck recurrences. Twenty-two patients were identified (M: 18, F: 4), of which 20 had SCCA and 2 had salivary gland malignancies. All patients underwent a radical or modified radical neck dissection, soft tissue reconstruction and intra-operative placement of after-loading catheters as part of the salvage treatment. Iridium 192 wires were loaded into the catheters five days post-operatively. The duration and dosage of salvage radiotherapy was reviewed, and the regional recurrence rate was determined. Early complications were classified as those occurring within the first 30 days after surgery. Late complications were classified as those occurring more than 30 days after surgery.

**Results:** All patients had been treated with external beam radiation therapy prior to recurrence to an average dose of 65 Gy. A neck dissection had been performed in 50% (11/22) of patients. The average

time to regional recurrence after definitive treatment was 18.4 months. IBT doses averaged 51.8 Gy for 4 days (range: 1-5 days) specified at 5 mm. Soft tissue coverage with a muscle flap, most commonly a pectoralis major myocutaneous flap, was necessary in 19 of 22 patients. Early complications occurred in 7 patients (32%), and were limited to local infection, donor site hematoma, and cardiopulmonary sequelae. Late complications occurred in 9 patients (41%) and were related to shoulder weakness and local wound complications. There were no perioperative deaths. Of those patients with more than 12 months of follow-up, 18% developed recurrences in the re-irradiated neck. Overall 1-year and 2-year survival rates were 80% and 60%, respectively.

**Conclusions:** The management of recurrent cervical metastasis after neck irradiation for head and neck malignancies remains a difficult clinical problem. As these patients have already received EBRT, they are generally not candidates for re-irradiation. In select patients, salvage neck dissection with IBT appears beneficial in the management of regional recurrences of upper aerodigestive tract carcinomas. Our preliminary report suggests that this approach is successful, with acceptable morbidity.

## **P142: Merkel Cell Carcinoma of the Head and Neck Region**

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**Introduction:** Merkel cell carcinoma (MCC) is an uncommon cutaneous malignancy therefore its natural history and treatment is undefined. However lately there is a threefold worldwide increased incidence in MCC. Almost half of them appear in the head and neck region (H&N). The purpose of this study is to report the natural history, and prognostic factors of MCC in the H&N region.

**Patients / Methods:** We retrospectively reviewed 25 files of patients diagnosed with H&N MCC between 1995 and 2005. A multivariate analysis was performed using Mann-Whitney test. Disease free survival (DFS) and overall survival were calculated with Kaplan-Meier survival curves.

**Results:** There were 16 males and 9 females. The median age was 72.7 (range, 30-91 years). The most common primary tumor location was the cheek (6) followed by the forehead (5). The average primary size was 12.5 mm (Range, 0-120 mm). In 2 the diagnosis was based upon metastatic lymph nodes without a primary tumor. Seventeen (68%) of the patients initially had a lesion without nodal involvement and 8 (32%) of them had clinical nodal disease; in 88% of them the primary echelon nodes were involved. Twenty-two (88%) patients underwent surgical excision; in eight a functional neck dissection was performed and in two a sentinel lymph node biopsy. Three patients received adjuvant chemotherapy and two chemoradiation. Three patients who were not operated due to inoperable tumors received chemo radiation and one medically inoperable received chemotherapy. Eleven (44%) patients had recurrence, 7 of them were locoregional and four distant (visceral, lung and bone). The median time to recurrence was 177 days all but one recurrence occurred in the first year. Among the recurrence patients five were treated with second line chemotherapy and four were treated with chemo radiotherapy, One by radiation and one with supportive care. The Average survival rate was 3.3 years with a median follow up of 3.15 years. The overall 2-year survival was 70% and the five-year survival 66.6%. Six patients died of disease 3 due to distant metastases and 3 Locoregional diseases all died within 1.5 years. Six patients with recurrence survived including 2 with distant metastases. In four of the surviving patients there is follow up over 7 years. According to a multivariate analysis Complete resection and lymph node involvement were found to be independent prognostic factors (p<0.05). Adjuvant treatments (chemotherapy, radiation and neck dissection) did not seem to have impact.

**Conclusions:** MCC is an aggressive skin cancer with a high tendency for early recurrence. However early survival rates suggest better outcome than previous reports. Initial Resectability and nodal status have an influence on survival. Patients who initially present with a favorable disease who have recurrences respond well to chemotherapy and radiation combinations.

## **P143: Importance of Anterior Commissure in Recurrence of Early Glottic Cancer After Laser Endoscopic Resection**

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**Objective:** To analyze the impact of anterior commissure involvement on local control, rate of recurrence, and larynx preservation in patients with early glottic cancer (pT1a-pT2a) treated with laser microsurgical resection.

**Design:** Prospective nonrandomized trial.

**Setting:** Tertiary referral university center.

**Patients:** Forty-eight patients with early glottic (T1-T2a) cancer treated with laser microsurgical resection with at least 2 years of follow-up were enrolled in this study.

**Intervention:** Laser microsurgical resection of early glottic lesions.

**Main Outcome Measures:** Data of local control and the larynx preservation rates were given according to presence or absence of a lesion in the anterior commissure, and both results were compared with a statistical proposal.

**Results:** Among 48 patients presenting with early glottic cancer, the anterior commissure was involved in 24 cases. Local control rate was 79%, and the larynx preservation rate was 96%. In the 24 cases without anterior commissure involvement, the local control rate was 96%, and the corresponding larynx preservation rate 100%. The rate of local recurrence in anterior commissure involvement was 21% and 4% when this site was not affected by the tumor ( $P = .08$ ). This difference had a tendency to statistical significance.

**Conclusion:** This study shows the tendency to greater tumor recurrence in lesions with anterior commissure involvement after laser microsurgery for early glottic cancer.

## **P144: Sebaceous Carcinoma of the Head and Neck: Outcome of 15 Consecutive Cases Treated in a Single Institution**

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Brazilian National Cancer Institute/INCA, Rio de Janeiro, Brazil

**Objectives:** To describe clinical features, management, and prognosis of sebaceous carcinoma of the eyelids and adjacent structures as well as of extraocular sites.

**Design:** A cohort study with all cases of SC of the head and neck from 1994 to 2002.

**Setting:** Head and Neck Service of the Brazilian National Cancer Institute/INCA.

**Patients:** From the original 44 reviewed cases of sebaceous carcinoma, 16 were confirmed after pathologic revision. All cases were reviewed by a senior pathologist (R.A.A.) to confirm the diagnosis of sebaceous carcinoma.

**Intervention:** All cases treated primarily by surgery.

**Main Outcome Measures:** A retrospective analysis of clinical features, management, pathologic characteristics, and outcome of SC was made to evaluate its biological behavior. The mean time of follow-up was 34 months

**Results:** The most frequent histologic differential diagnoses were squamous cell carcinoma in 20 cases and basal cell carcinoma with sebaceous differentiation in 9 cases. The median age was 68 years. The primary site was the orbital region in 3 cases, the face in 6 cases, skin of the neck in 3 cases, forehead in 2 cases, and ear in 2 cases. Seven patients had the primary treatment elsewhere. Six patients presented with associated skin tumor: 3 squamous cell carcinoma and 2 basal cell: 1jm[carcinoma]. Six patients had recurrences, and 5 patients died from the disease.

Four patients presented with neck metastasis and had the worst prognosis ( $P < .01$ ); none survive after 48 months. The 5-year disease-specific survival was 42%.

**Conclusions:** The occurrence of neck metastasis influenced adversely the prognosis. The aggressive behavior of this neoplasm in the head and neck was confirmed.

## **P145: Swallowing Analysis Before and After Thyroidectomy**

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**Introduction:** Alterations in voice functions, swallowing and breathing can happen after thyroidectomy. Dysphonia is the most but dysphagia is reported in paralysis of laryngeal nerve (BHATTACHARYYA et al., 2003; PÉRIÉ, S et al. 1998).

**Objective:** To analyze swallowing before and after thyroidectomy.

**Method:** Prospective study of 13 patients with thyroid gland's disease (61,53% non-malignant tumor and 38,46% papillar carcinoma). Removed nodule's volume: 4 between 14,25 to 19,1cm<sup>3</sup>, 4 between 120 to 189cm<sup>3</sup> and 3, 313 to 548cm<sup>3</sup>. There were 12 females and 1 male, aged 42 to 74 years. The patients were submitted to a clinical and flexible endoscope evaluation of swallowing with four consistencies: liquid (L), thickened liquid (TL), paste (P) and solid (S). They were submitted to evaluations in 2 moments: the first one was up to 15 days before surgery (PRE) and the second up to 7 days after surgery, recent post operator (RPO). A third valuation was performed in 7 of the 13 subjects, between 30 and 60 days after the surgery (LAT). Total thyroidectomy was performed in 9 and unilateral thyroidectomy in 4 patients. All had normal laryngeal mobility before the surgery. At the RPO 9 subjects presented unilateral mobility alteration and 3 in the LAT.

**Results:** At the PRE, three patients presented swallowing disorders: residue in region of vallecula with P consistence (n=1); residue in piriform sinus with TL (n=1) and residue in posterior wall of the pharynx with P (n=1). At the RPO, swallowing disorders were found in all subjects with larynx alteration mobility, except one. This group presented residue at tongue base with TL and S (30,77%, n=4); residue in region of vallecula with TL, P and S (46,15%, n=6); residue in piriform sinus with L, TL e S (38,46%, n=5); residue in posterior wall of pharynx with S e P (15,38%, n=2); premature escape with L e TL (7,69%), penetration and aspiration with L (15,38%). At the LAT, 5 among 7 patients had residue and premature escape, and 3 of them with larynx alteration mobility. All subjects that presented dysphagia during this period already had alterations at the RPO. The alterations were: residue at tongue base with L, TL and P (42,86%, n=3); residue in region of vallecula with L, TL and P (42,86%, n=3); residue in perform sinus with L, TL and P (42,86%, n=3); residue in posterior wall of pharynx with TL, P and S (28,57%, n=2); e premature escape with L, TL and S (28,57%, n=2).

**Conclusion:** Dysphagia may happen after thyroidectomy. Patients with vocal folds mobility alteration had abnormal exams in all of the evaluated aspects. These characteristics were not related only with larynx closure, but to other aspects from all of the swallowing process. The incidence of swallowing alterations was bigger at the RPO. Many patients did not come for the LAT evaluation at; which may suggest that they did not have a complaint about the swallowing.

## **P146: Incidence and Survival Rates for Young Blacks With Nasopharyngeal Carcinoma in the US**

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**Objective:** To compare the incidence rates of nasopharyngeal carcinoma (NPC) in blacks, whites and Asians in the US, with a focus on those diagnosed under 20 years of age and between 20 and 29 years of age. Our secondary objective is to determine differences in survival rates between blacks, whites, and Asians under 30 in the US with NPC.

**Methods:** Data from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) tumor registry system was used to determine incidence and survival rates for cases of NPC diagnosed in specified age groups in the US between 1973 and 2002.

**Results:** From 1973 to 2002, incidence rates per one million persons, adjusted to the 2000 standard population, for blacks, whites, and Asians/Pacific Islanders with NPC under 20 years of age were 1.61

(n=43), 0.61 (n=99), and 0.95(n=18), respectively. The incidence rate ratio of blacks relative to Asians under 20 was 1.69 (P=0.0741) while the rate ratio for blacks relative to whites was 2.66 (P<0.0001). From ages 20 to 29, rates increased slightly in blacks (1.87) and whites (0.96), while increasing dramatically in Asians/Pacific Islanders (7.18). The rate ratio of blacks relative to whites remained increased until age 45 and above, while the rate ratio of blacks to Asians decreased for all older ages. In a comparison of the time periods from 1973 to 1987 and 1988 to 2002, incidence rates remained constant for nearly all races and age groups. Among all blacks diagnosed with NPC between 1973 and 2002 in the SEER registries, 11% were under 20, while percentages of whites (4%) and Asians (1%) diagnosed under age 20 were less. Among all blacks in the SEER registries diagnosed with World Health Organization (WHO) Type III NPC, a higher percentage were under 30 (31%) relative to similar calculations for whites (15%) and Asians (8%). Two and five year relative survival rates in blacks under 30 were 84% and 64%, respectively, with little variation between races in this age group.

**Conclusions:** Blacks under 20 have increased incidence rates of NPC relative to whites, and may be the only group having a higher NPC incidence rate than Asians. The increased rate in blacks relative to whites declines in those diagnosed over age 45, while the increased rate relative to Asians declines in those 20 and above. Two and five year survival rates of blacks, whites, and Asians under 30 with NPC are similar.

### **P147: Analysis of Formant Frequencies in Patients With Oral or Oropharyngeal Cancers Treated by Glossectomy**

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**Objective:** To compare voice quality as defined by formant analysis using sustained vowel in patients who have undergone a partial glossectomy with a group of normal subjects.

**Design:** Single-center, cross-sectional cohort study.

**Setting:** Adult tertiary oncology referral unit.

**Patients:** Twenty-six patients (19 male) who underwent partial glossectomy and 31 healthy volunteers (18 male) participated in our study.

**Intervention:** Group comparisons using the first 3 formant frequencies (F1, F2, and F3) using linear predictive coding (Laryngograph Ltd, London, England) were performed.

**Main Outcome Measures:** The existence of any significant difference of F1, F2, and F3 between the 2 groups using the sustained vowel /i/ and the effects of other factors, namely age, first presentation vs recurrence, site (oral cavity or oropharynx), subsite (anterior 2/3 of the tongue or tongue base), stage, irradiation, complication, and neck dissection was determined.

**Results:** Formant frequencies F1, F2, and F3 were normally distributed. The F1 and F2 frequencies were significantly different in normal male vs female subjects. The F1, F2, and F3 frequencies were no different statistically between male and female patients who underwent glossectomy. Comparison of only women showed significant differences between healthy subjects and patients in F2 and F3 but none in F1. This was the opposite in men, for whom F1 was significantly different. Age, tumor presentation, site, subsite, irradiation, and neck dissection showed no significant difference. Postoperative complications significantly affected the F1 formant frequency.

**Conclusions:** This study found that the formant values in patients following a partial glossectomy were altered significantly compared with the control subjects. Only sex and complications and not the age, site, subsite, irradiation, and neck dissection were seen to influence the formant scores.

### **P148: WITHDRAWN**

### **P149: Study of Inverted Papilloma in Rural Based Hospital in Eastern Nepal**

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**Introduction:** Inverted papilloma (IP) is a true benign epithelial tumor that accounts from 0.5% to 4% of all neoplasms of the sinonasal tract. It is more common in elderly male patients and very rare in children younger than 10 years. It arises from the Schneiderian mucosa of the nasal cavity, which is of ectodermal origin and is embryologically different from the endodermally derived mucosa of the upper respiratory tract, characteristic features such as multicentricity, frequent association with squamous cell carcinoma (SCC), and high incidence of recurrence, IP is considered an aggressive lesion in that it is best treated with a medial maxillectomy by an external approach. However, in the early 1980s, endonasal surgery with a purely endoscopic or a micro-endoscopic approach was introduced, providing the head and neck surgeon with less invasive techniques for the management of IP. The results so far reported suggest that, when properly planned, endoscopic or micro-endoscopic assisted approaches can favorably compete with traditional external techniques in the surgical treatment of IP. Some authors still advocate the superiority of traditional techniques for advanced lesions and cast doubts on the possibility of obtaining adequate exposure of the entire sinonasal complex. Moreover, the need for long-term follow-up to establish the efficacy of a surgical approach in a disease presenting late recurrences has been emphasized.

**Material and Method:** This report analyzes prospectively for the first time a series of 22 patients with IP treated by external as well as combined Endoscopic and external approach at BP Koirala Institute of Health Sciences. We present and discuss the details of clinical profile of the cases along with surgical management, and outcome.

**Result:** Of the total 22 patients 27% were female and 73% were male with male female ratio of 2.7:1. The age group ranged from 17 to 73 years with maximum number of patient being elderly. Nasal obstruction was common presentation in all 22 cases followed by noticing of nasal mass or nasal deformity. Other symptoms were that of headache, anosmia, epistaxis and proptosis in 4 cases. Sixteen (72%) were patients belonging to Mongoloid race hailing from hilly areas while 6 (28%) were Indo-Aryans from the plains. All lesions were unilateral. Lateral nasal was the site of origin of tumor in all cases. In no cases was the contralateral nasal cavity involved. Nineteen (86.3%) had involvement of PNS. Four patients had orbital extension of the lesion. All patients underwent surgical treatment. Lateral rhinotomy and medial maxillectomy was performed in 18 cases, total maxillectomy in 2 whereas 2 patients required orbital exenteration in addition to the total maxillectomy. No major surgical complications were seen in any of the above cases.

**Conclusion:** Though rare, IP is not found uncommon in eastern Nepal as compared to the other part of the country. It should be included as a differential diagnosis of masses of nose and paranasal sinuses. In view of its malignant potential, timely diagnosis is required and adequate surgery is the treatment of choice.

### **P150: Photodynamic Therapy and the Treatment of Early Squamous Cell Carcinomas of the Larynx and Oral Cavity**

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Photodynamic therapy has been successfully used to treat various cancers of the head and neck. Three hundred thirty six patients with neoplastic diseases of the larynx, oral cavity and pharynx have been treated with PDT with followup to 179 months. Those patients with primary or recurrent carcinoma in situ and T1 carcinomas of the larynx and oral cavity obtained a complete response after one PDT treatment and 88% remain free of disease. Importantly, 100% of all treated patients were salvaged with additional therapy. Patients with T2 and T3 superficial carcinomas of the oral cavity were also successfully treated with PDT with a cure rate of 90%. This outpatient treatment has the benefit of less morbidity and improved healing as compared to radiotherapy or surgery. PDT is effective for the curative treatment of early carcinomas of the larynx and oral cavity and should be considered as a treatment option on par with radiotherapy and surgery.

## **P151: Intraoperative Localization of the Marginal Mandibular Nerve: A Landmark Study**

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**Objective:** To determine the surgical location of marginal mandibular branch of the facial nerve in vivo.

**Design:** Prospective in vivo study.

**Setting:** Tertiary referral teaching center.

**Patients:** Marginal mandibular nerves were examined in 52 consecutive patients undergoing neck or salivary gland procedures.

**Interventions:** All the nerves were identified anatomically and through electrical stimulation. Two measurements were then recorded: (1) the distance from the nerve to the inferior edge of the angle of the mandible and (2) the distance from the lowest point of the nerve to the inferior edge of the mandible.

**Results:** Eighty-five mandibular nerves were examined. The lowest point of the nerve was located an average of 3.4 mm above the inferior edge of the mandible, with a range of 13 mm above to 10 mm below. The location of the nerve on the right did not correlate with that on the left. The location of the nerve did not correlate with patient's age.

**Conclusions:** The in vivo location of the marginal mandibular branch of the facial nerve is significantly higher than previously reported.

## **P152: Treatment of Dysplastic Oral Mucosal Lesions With a New Cell Cycle-Inhibiting Agent**

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**Objective:** Oral cancer is associated with tobacco habit and is preceded in most cases by premalignant lesions. An approach to cancer control is to identify potentially malignant or premalignant lesions where treatment of these lesions may prevent transformation to cancer. The present study was carried out to evaluate the clinical and molecular response of intralesional tetra-O-methyl nordihydroguaiaretic acid in oral premalignant lesions.

**Design:** Single group.

**Setting:** Tertiary cancer center, India.

**Main Outcome Measures:** Toxic effects were monitored by World Health Organization criteria. Response was recorded as change in surface area, necrosis, pathologic response, molecular response (CDC2 and survivin), complications, and recurrences.

**Results:** All the four lesions were located on the buccal mucosa three lesions were excised while the fourth completely regressed with M4N alone. At the end of 27 months one patient developed a new lesion on the same side and at 33 months one patient developed a new lesion on the opposite side. Down regulation of cdc2 was seen in 3 and of survivin in 2 patients. Both the patients who developed new lesions showed cdc2 downregulation while one showed downregulation of survivin.

**Conclusions:** Intralesional tetra-O-methyl nordihydroguaiaretic acid appears to be well tolerated at doses of up to 100 mg (20 mg/d) with no evidence of acute or delayed toxic effects. The drug has demonstrated inhibition of cellular production of cdc2 and survivin, a strongly pro-apoptotic response. The advantage of present technique is in its simplicity of administration: these intralesional injections can be administered on day-care basis.

## **P153: Management of the N0 Neck: Failure Rates and Salvageability After Surgery, Irradiation, or Observation**

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**Objective:** To clarify optimal management of the N0 neck by comparing both initial failure rates and salvageability of evolving cancer in the neck after elective neck dissection (END), elective neck irradiation (ENI), or observation.

**Design:** Retrospective clinical data review.

**Setting:** University-affiliated, tertiary care Department of Veterans Affairs Medical Center.

**Patients:** Previously untreated patients with N0 necks (n = 425) with a single, controlled primary head or neck squamous cell carcinoma treated from 1983 to 1995.

**Interventions:** Three curative-intent management strategies: (1) END, (2) ENI, or (3) observation.

**Main Outcome Measures:** Initial failure rates and salvageability of neck failures. Comparisons between groups used  $\chi^2$  or Fisher exact test.

**Results:** With a median follow-up of 3 to 4 years, neck failure occurred in 11% of patients overall (range, 7%-18%). Salvage treatment was successful in 15% to 63%, yielding ultimate neck control rates of 84% to 97%. Management strategy ranked from most to least favorable was as follows: (1) observation, (2) END, and (3) ENI. There were statistically significant differences favoring observation over ENI in 4 oncologic domains ( $P = .03$  to  $P < .001$ ). Cancer evolving in the N0 neck could not be reliably salvaged after ENI with surgery plus brachytherapy.

**Conclusions:** Clinical guidelines are defined as follows for selecting N0 patients: (1) suitable for observation (low risk of initial failure and high salvageability) or (2) requiring treatment initially. Morbidity related to contemporary elective treatments are emphasized, including the now frequently reported sequelae of irradiation-induced carotid arteriosclerosis. To decrease elective treatment morbidity, nontraditional treatment sequencing is suggested in appropriate cases, such as performing END(s)—and necessary dental extractions—first, followed in 2 to 3 weeks by irradiation or chemotherapy/irradiation combination when nonsurgical treatment for the primary tumor is chosen.

## **P154: Race As an Independent Factor for Advanced Oropharyngeal Cancer Outcomes for Treatment With Combined Chemoradiation**

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**Objective:** To evaluate our recent institutional experience for African American (AA) and White patients treated with concurrent Chemoradiation for advanced head and neck cancer and assess factors contributing to worse observed clinical outcomes.

**Methods:** We performed a retrospective analysis of patients treated with a uniform Chemoradiation protocol at the University of Maryland School of Medicine in the Department of Radiation Oncology with advanced (stage III and IV) head and neck cancer. A weekly Carboplatin and Taxol regimen was used with definitive radiation doses (70.2 Gy) employed from 1997-2003. Complete demographic data were available for analysis for both patients and disease characteristics. Additionally, specifics regarding patient's response to treatment, disease status and patterns of failure were observed.

**Results:** One hundred and three patients were evaluated over this time period. AA (42%) and Whites (58%) were similar with respect to age, gender, clinical stage, tumor site, and duration of treatment. AA had a higher unadjusted disease recurrence rate than Whites (57% and 37%  $p=0.05$ , respectively) and failed distantly more often (27% and 12%  $p=0.06$ , respectively). Logistic regression analysis was performed to determine which factors contributed most to recurrence in our population. The multivariable model that best predicted recurrence (Chi-square 12.1,  $p=0.01$ ) included the following equation: Recurrence =  $-1.2 \times \text{race}$  ( $p=0.02$ ),  $-1.1 \times \text{clinical stage}$  ( $p=0.05$ ),  $-0.3 \times \text{tumor site}$  ( $p=0.12$ ) and  $0.25 \times \text{grade of mucositis}$  ( $p=0.58$ ). In essence, AA had a higher probability for recurrence than Whites and Stage IV disease more than Stage III. Oropharyngeal sites were more predictive of recurrence as was more extensive mucositis.

**Conclusions:** In our study, we observed that AA were more likely to recur than their White counterparts following concurrent Chemoradiation for advanced head and neck cancer (57% vs. 37%, respectively). When multivariable analysis was performed, AA independently had an increase probability for recurrence compared to Whites. Stage IV disease and oropharyngeal tumors also were important predictors for recurrence.

## P155: Intensity-Modulated Radiation Therapy for Head and Neck Cancers : Acute Toxic Effects and Early Outcome Data

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**Objectives:** To describe acute toxic effects and locoregional control for patients with head and neck cancer (HNCA) treated with intensity-modulated radiation therapy (IMRT).

**Design:** Prospectively collected database.

**Setting:** Academic radiation oncology clinic.

**Patients:** Eighty-five patients with HNCA treated with IMRT either as definitive (n = 47; 55%) or postoperative (n = 38; 45%) therapy between August 2003 and December 2005.

**Intervention:** Oropharyngeal (36%) and laryngeal (15%) sites were most common, and 83% of cases (n = 71) were American Joint Committee on Cancer stages III to IVA. Doses of IMRT ranging from 45 to 80 Gy (median dose, 66 Gy) were delivered and 70% of patients (n = 60) received concurrent chemotherapy.

**Main Outcome Measures:** Acute toxic effects and locoregional control.

**Results:** No patient experienced Radiation Therapy Oncology Group grade 4 or 5 radiotherapy-associated toxic effects. Grade 3 mucous membrane toxic effects occurred in 27% (n = 23); pharynx, 9% (n = 8); skin, 5% (n = 4); larynx, 1% (n = 9); and salivary gland, 0% (n = 0). Only 5% of patients (n = 4) experienced toxicity-related treatment delay of more than 3 days (maximum, 7 days). Median weight loss was 7% of pretreatment weight (weight change range, +6% to -20%). Forty-two (49%) of patients had percutaneous endoscopic gastrostomy tubes placed (29% before treatment and 20% during treatment, n = 25 and n = 17, respectively). The tubes remained in place for a median of 105 days (range, 48-317 days). At a median follow-up of 12 months, 80% of patients (n = 68) are alive without evidence of disease. Eleven percent of patients (n = 9) are alive with disease, 8% died from disease (n = 7), and 1% died of other causes (n = 9). In 16 cases of recurrent disease, 4 failed locoregionally, 3 at the field margin, 5 failed in field and distantly, and 4 failed distantly only.

**Conclusions:** Intensity-modulated radiation therapy is well tolerated by patients and allows for completion of scheduled therapy without significant toxicity-associated treatment breaks.

## P156: Surgical Management of Lingual Arteriovenous Malformations

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**Objective:** To examine our Vascular Anomalies Team's experience with tongue arteriovenous malformations (AVM) with specific emphasis on surgical management and the spectrum of disease.

**Design:** Retrospective chart review of 11 patients (10 female, 1 male), discovered from 1997-2005, with histologic, radiographic, and clinical characteristics consistent with tongue AVM.

**Results:** Four patients displayed advanced disease with malformations involving the tongue, floor of mouth and neck. Contributions from multiple feeding arteries were identified by angiography. Each patient had prior history of surgical and/or embolization procedures. In contrast, 7 patients had discreet and measurable tongue malformations with a single feeding lingual artery and no previous intervention. Patients with advanced disease required preoperative embolization, extensive resection with complex reconstruction (mean op time: 10.8 hrs). Two of which required additional tongue surgery and 1 had evidence of recurrent disease (mean f/u: 24.6 mos). Patients with focal tongue lesions required only one resection, had less operative time (mean: 2.5 hr) and have shown no evidence of recurrence (mean f/u: 9.3 mos).

**Conclusions:** This study suggests that tongue AVM can occur within a spectrum of disease with different clinical presentations and radiographic findings among patients with focal versus advanced lesions. Prior interventions create collateral blood flow and possible disease progression while focal lesions likely represent early AVM that are more amenable to surgical management.

## P157: Intraoperative Frozen Section Analysis for Follicular Neoplasm of the Thyroid: Is It Worth the Effort?

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**Objective:** The utility of frozen section analysis for follicular thyroid neoplasms has been debated in the literature and a broad range of sensitivities are reported for frozen section diagnosis of follicular malignancy (40-78%). In this study, we review our experience with intra-operative frozen section to determine the utility of this diagnostic tool for follicular neoplasms.

**Methods:** A retrospective review of 294 patients at two University of Louisville affiliated hospitals between 1993 and 2003 that underwent thyroid surgery with intra-operative frozen section analysis for follicular neoplasms.

**Results:** Follicular/hurthle cell carcinoma was identified in 6% (19/294) of patients on permanent section histologic tissue analysis. Of these 19 patients, 4 were diagnosed as carcinoma on frozen section. The remaining 15 required more detailed analysis, including external review in 5 (26%). The sensitivity, specificity, positive predictive value, and accuracy of frozen section for identifying follicular/hurthle cell carcinoma were 21.1%, 100%, 100%, and 82.1% respectively. The probability of recognizing follicular/hurthle cell carcinoma, by frozen section analysis, in this group of patients was 1% (4/294).

**Conclusions:** Based upon a low sensitivity of frozen section for follicular thyroid neoplasms and a very low probability of identifying follicular/hurthle cell carcinoma on frozen section, this study indicated that the intra-operative decision process was enhanced in less than 1-2% of patients with suspected follicular thyroid neoplasms. The routine use of intra-operative frozen section histologic tissue analysis for follicular thyroid neoplasms should be limited to tertiary referral centers that can demonstrate by volume, experience and quality parameters the value of this test in the intra-operative decision process.

## P158: Consequences of Chewing Habits in Gujarat, India

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**Objective:** To investigate the effect of chewing areca and/or betel quid with pan masala (tobacco) on oral hard tissue, oral submucous fibrosis (OSMF), and associated molecular impairment underlying the causation of oral precancerous disorders.

**Design:** 365 subjects [chewers (n = 168) and non-chewers (n = 197)], who attended the Out Door Patient Department of Government Dental College and Hospital, Ahmedabad: 380016, India were enrolled. Chewers had chewing habits of pan masala (tobacco), areca nut, betel quid and non-chewers without habit of chewing any products containing tobacco. Informed consent received. Clinical dental examination was conducted and biological samples (saliva, blood and urine) collected.

**Results:** Findings indicated that attrition and incidence of periodontal conditions were significantly higher in chewers ( $P < .001$ ); 21% of chewers had OSMF. The pH of chewers' saliva was slightly more alkaline than that of nonchewers. Kruskal-Wallis analysis of variance indicated that chewers had a high risk of producing micronuclei in buccal mucosa cells, and the duration of chewing had a significant impact ( $P < .05$ ;  $df = 3$ ). Chewers with OSMF had slightly higher level of copper in their serum and saliva, but serum zinc levels in chewers were significantly decreased ( $P < .05$ ). Data on serum IgG, IgA, and IgM levels indicated a nonsignificant rise in serum IgG and decline in IgA and IgM levels in chewers. Study indicated that low educational attainment, occupation as a physical laborer, and poor hygiene were associated with significantly increased risk.

**Conclusions:** The small sample size of this study limited the power to precisely estimate the tobacco-cellular interactions, but it nonetheless provides an important basis for diagnostic values for epidemiological work in smokeless tobacco exposure assessment.

## **P159: Salvage Surgery After Organ Preservation Therapy in Patients With Stage III or IV Head and Neck Squamous Cell Carcinoma**

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**Objectives:** To evaluate the outcome of patients with squamous carcinomas (SCC) of the upper aerodigestive tract (UADT) who required locoregional surgical salvage (SS) or planned neck dissection after chemoradiation therapy.

**Design:** A cohort study from 2001 to 2005 with a mean 24 months of follow-up.

**Setting:** Head and Neck Service, Brazilian National Cancer Institute/INCA.

**Patients:** Ninety-four patients with stage III or IV SCC of the UADT underwent concurrent cisplatin-based chemoradiation therapy as their primary treatment in our institution. Twenty-seven patients who had SS or planned neck dissection were included in this study.

**Intervention:** Salvage surgery or planned neck dissection.

**Main Outcome Measures:** A retrospective study.

**Results:** According to the 2002 International Union Against Cancer/American Joint Committee on Cancer staging system we classified 5 patients as stage III, 20 patients as stage IVA, and 2 patients as stage IVB. Twelve patients (44%) had laryngeal primary tumors, 9 had oropharyngeal primaries, and 6 had hypopharyngeal primaries. Fourteen patients (52%) underwent SS for persistent disease, 7 (26%) underwent SS for recurrent disease, and 6 (22%) underwent a planned neck dissection. Twelve patients had surgical complications, 5 major complications requiring surgical intervention, and 7 minor complications that resolved with conservative measures. Eleven stage-IVA patients had complications, 5 major complications and 6 minor complication. The 2-year disease-free survival rate for patients with complete response and partial response to chemoradiation treatment was 74% and 38%, respectively ( $P < .05$ ). No patient who had persistent neck disease survived after 8 months.

**Conclusion:** The occurrence of persistent disease in the neck adversely influenced the prognosis. Clinical response to the chemoradiation treatment was an important prognostic factor.

## **P160: Frequency and Types of Human Papilloma Virus in Head and Neck Squamous Cell Carcinoma**

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**Objective:** Over 400 000 cases of head and neck squamous cell carcinoma (HNSCC) were diagnosed in 2005 throughout the world, mainly in oral cavity and oropharynx. Alcohol and tobacco are the most important etiologic agents. Since 1983 it has been suggested that human papilloma virus (HPV) 16 might have a role in HNSCC carcinogenesis. Our objective was to determine HPV prevalence in patients with HNSCC.

**Design:** Presence of HPV was determined in fresh tumor tissue by polymerase chain reaction test and staged by hybridization in situ. We analyzed stage, tumor site, sex habits, alcohol and tobacco consumption. Multiple regression analysis was performed.

**Patients:** We included 118 patients with HNSCC (77 men and 41 women; (mean age, 64 years).

**Results:** The 3 most frequent tumor sites were larynx, oral cavity, and oropharynx. In 50 patients (42%), some type of HPV was identified; larynx and oropharynx cancers were the most common (50%) followed by oral cavity (25%);

HPV-16 was the most frequently isolated (70%); laryngeal cancer had the highest ratio of HPV-16 infection (69%). Univariate analysis showed the following factors to be associated with HPV infection: age greater than 50 years, tobacco or alcohol consumption, and male sex. Nevertheless, in multivariate analysis, none of the variables showed a statistically significant importance ( $P > .50$ ); Infection with HPV was more frequent in patients with a history of alcohol or tobacco consumption than in nonsmokers or nondrinkers ( $P = .60$ ).

**Conclusions:** We found HPV infection in 42% of patients with HNSCC, 70% of them high risk. The most affected sites were the lar-

ynx and oropharynx. No variable was associated with virus presence. Head and neck cancer has multiple etiologic factors, and HPV is one of them.

## **P161: Phase I Study of Intratumoral Injection of M.Leprae HSP-65 DNA in Patients With HNSCC Refractory to Standard Treatment**

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**Objective:** To test the safety of intratumoral injections of DNAHSP65 in patients with squamous cell carcinoma refractory to standard treatment and to define a maximum tolerated dose. We also aim to evaluate response to treatment by measuring tumor volume.

**Methods:** Patients with histologically proven and measurable recurrent head and neck squamous cell carcinoma after standard treatment that included radiotherapy, without any option for salvage surgery or any other treatment with curative intent, Karnofsky performance status greater than 70% and no organ failure were eligible for the protocol. We proposed three injections per patient with an interval of 21 days. CT scan was taken up to 5 days before the first injection and 7 days after the last. Seven to nine days after the last injection biopsy of the injected tumor was performed. We proposed 3 groups of 6 patients with escalating doses (150mcg; 600mcg; 1200mcg/dose). The injections were guided by ultrasound in order to avoid necrotic tissue. For toxicity assessment we used the CTCAE and for response evaluation we measured the lesion volume and applied the RECIST criteria.

**Results:** The first group that received 150mcg of DNAHSP65/injection consisted of 4 male and 2 female with median age of 58,3 years. One patient died due to bleeding before protocol completion. He had an ulcerated lesion and we considered the bleeding non related to the protocol treatment. All patients referred increase in pain with one grade 4; 5 presented edema grades 1/2 and 1 had grade 4 asthenia considered related. The second group received 600mcg/injection and consisted of 5 male and 1 female with median age of 58,5 years. Three patients died before the completion of the 90 day protocol, all considered non related to treatment. One died of gastrostomy complications, one had rapid progression of the tumor and had a fatal bleeding. The autopsy of the third showed pulmonary carcinomatosis. Probably related to the treatment, we had 2 patients with pain, one with edema and one with asthenia, all grade 4. Also, other 3 patients presented increase in pain up to grade 3 and four patients had edema grades 2 or 3. Due to this toxicity we decided to lower the dose of the third group to 400mcg. Three of the patients from this group also died before protocol completion, all due to cancer progression. We decided to add 3 more patients in this group, one is still on protocol. Three presented pain up to grade 3, 7 presented edema up to grade 3 and one grade 4 that required tracheostomy. Three patients presented infections grade 2. From the 14 patients that received the 3 doses and were studied for response, 8 had progression, 3 had stable disease and 2 had partial responses.

**Conclusions:** Intratumoral injections of DNAHSP65 may cause adverse events mainly pain and edema and is safe in the dose of 400mcg/injection for this group of patients. Measurement of the tumor volume suggests that the treatment may have had an impact on the disease growth in some patients.

## **P162: Lymphoscintigraphy and Sentinel Lymph Node Biopsy for Merkel Cell Carcinoma of the Head and Neck**

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**Introduction:** The natural history of Merkel cell carcinoma is often compared with that of intermediate thickness malignant melanoma. Lymphoscintigraphy and sentinel lymph node biopsy have an established role in the diagnosis and treatment of thin cutaneous melanoma. We hypothesized that the use of pre-operative lymphoscintigraphy and intra-operative sentinel lymph node localization for patients with early stage Merkel cell carcinoma of the head and neck may prove useful for identifying patients with occult cervical

metastases, and may prevent unnecessary morbidity of neck dissection or neck irradiation in patients without metastatic nodal involvement.

**Materials and Methods:** This study represents a retrospective review of medical records of 20 patients with previously untreated Merkel cell carcinoma of the head and neck area, presenting to a comprehensive cancer center between 1998 and 2005. Records were evaluated for the type of surgical treatment, including wide local excision (WLE), sentinel lymph node (SLN) biopsy, with or without formal neck dissection (ND), post-operative radiation therapy, as well as follow-up status, recurrence and clinical outcomes.

**Results:** Twelve patients with complete medical records, with the median age of 62 years (range, 54-85 years) were included in the study. Follow-up ranged from 3 to 84 months (median follow-up 57 months). Eight patients presented with previously untreated disease, and 4 patients presented with recurrent disease. All patients were staged NO by clinical and radiologic criteria.

Seven patients underwent WLE and SLN biopsy with or without ND. The combination of pre-operative lymphoscintigraphy and intra-operative gamma probe successfully localized SLN in all 7 patients. Metastatic SLN were identified in 3 out of 7 patients, and in the remaining 4 patients, SLN were negative. Two of the three patients with positive SLN, had also undergone neck dissections. In one patient, SLN as well as two other lymph nodes in the ND basin were positive by H&E. He received adjuvant radiation therapy, and remains free of disease. The other two patients had only one positive SLN each. One of these patients with a single positive SLN had no neck dissection, and subsequently recurred on the contralateral side, and the last patient with positive SLN had neck dissection and remains free of disease. The other four patients with negative SLN had no neck dissections. One recurred in the neck, and 3 remain free of disease.

The remaining 5 patients underwent WLE without SLN biopsy. One had WLE only, and 4 had WLE with neck dissections. All four of these patients presented with previously treated, recurrent Merkel cell lesions, and all four remain free of disease after WLE/ND. All 12 patients remain alive, including one patient who developed distant metastases.

**Conclusion:** Wide excision and SLN biopsy for primary Merkel cell carcinoma with NO neck is feasible for early stage, previously untreated lesions. The role for SLN biopsy in previously treated and recurrent lesions is hard to define due to a high risk of anomalous lymphatic drainage pathways. Therefore, the majority of those patients with recurrent Merkel cell cancer are still treated by an elective neck dissection.

## P163: WITHDRAWN

### P164: Extrathyroidal Extension in Well-Differentiated Thyroid Cancer as a Predictor of Outcome Measures

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**Objectives:** To examine the prognostic difference between gross and microscopic extrathyroidal extension (ETE) in well-differentiated thyroid cancer (WDTC).

**Design:** Retrospective study.

**Setting:** Tertiary care academic hospital

**Patients:** From a database of 582 patients who were surgically treated for thyroid cancer, we selected 55 (10.5%) with stage III WDTC and a minimum 5-year follow-up (17 men and 38 women; mean age, 53.1 years).

**Main Outcome Measures:** Overall survival (OS) and disease-specific survival (DSS) at 5, 10, and 20 years and recurrence rates.

**Results:** In univariate analysis, there was no difference in 5, 10, and 20-year OS, 5, 10, and 20-year DSS, and recurrence rates in the gross vs microscopic groups ( $P = .59$ ,  $P = 0.39$ ,  $P = 0.58$ ,  $P = 0.45$ ,  $P = 0.37$ ,  $P = 0.62$ , and  $P = 0.37$ , respectively). The only confounding factor was that more patients were treated with external-beam radiation therapy (RT) in the gross than in the microscopic ETE group ( $P = .007$ ). In multivariable analysis, RT, and not gross vs microscopic ETE, trended toward being a predictor of OS and DSS. In Kaplan-Meier curve analysis, gross vs microscopic ETE had no effect on OS

or DSS in the RT group. In the no-RT group, gross ETE had a strong trend toward decreased OS and DSS.

**Conclusions:** Gross vs microscopic ETE does not alter OS and DSS when the patient has received RT; however, gross ETE has a strong trend toward decreased OS and DSS when the patient has not received RT. In patients with gross ETE, we would recommend RT.

### P165: The Utility of Routine Thyroid Gland Evaluation Prior to Partial Laryngectomy: Why Is It Important?

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**Objective:** (1) To determine the incidence of synchronous thyroid pathology in a patient population undergoing partial laryngectomy. (2) To determine whether routine pre-operative evaluation of the thyroid gland prior to partial laryngectomy is useful to identify synchronous thyroid lesions in order to reduce the need for re-operation in this complex patient population.

**Study Design:** Retrospective chart review.

**Methods:** Charts of 67 consecutive patients with laryngeal tumors who have undergone partial laryngectomy from 1996 to 2005 have been reviewed for synchronous thyroid pathology. For all patients, reports of: (1) complete pre-operative examination findings, (2) inpatient course, (3) post-operative follow up, and (4) post-operative final pathology have been reviewed. For patients with synchronous thyroid pathology, reports of: (1) thyroid evaluation and imaging, (2) pre-operative (fine needle aspiration), (3) intra-operative (frozen section), and (4) post-operative (final) histo-pathologic results for the thyroid lesions have been reviewed.

**Results:** Eight of 67 (12%) patients with laryngeal tumors who underwent partial laryngectomy, had histo-pathologic evidence of synchronous thyroid pathology ( $P=0.006$ ). All 8 patients had squamous cell carcinoma of the larynx. All suspected synchronous thyroid lesions were incidentally detected. Four patients had papillary thyroid carcinoma, 1 had squamous metaplasia, and 3 had follicular thyroid tissue on final pathology. In 2 patients, the thyroid pathology was detected pre-operatively (prior to partial laryngectomy); in another 2 patients thyroid masses were detected intra-operatively; and in 4 patients the thyroid pathology was identified post-operatively in excised cervical lymph nodes. In 2 patients, thyroidectomy was performed as a second operation after the partial laryngectomy, and one of them had transient vocal fold paralysis for 2 months. Thyroid ultra-sonography was performed in 4 patients. Three of the patients had ultra-sonography performed after the partial laryngectomy final pathology report indicated metastatic thyroid disease in cervical lymph nodes. Ultra-sonography revealed intra-thyroidal lesions in all three patients.

**Conclusions:** Patients with laryngeal tumors undergoing partial laryngectomy might have occult synchronous thyroid lesions. Thyroid surgery in patients with previous partial laryngectomy may have an increased potential for complication due to post-surgical changes in the central neck region. Routine pre-operative evaluation of the thyroid gland with ultra-sonography to screen for occult synchronous thyroid lesions is recommended in all patients with laryngeal tumors undergoing partial laryngectomy. Eradication of any pre-operatively FNA detected thyroid cancer should be performed at the same time as partial laryngectomy. Pros and cons of total thyroidectomy for indeterminate thyroid nodules should be weighed with the patient.

### P166: Histopathological Analysis of Cystic Metastasis in Head and Neck Squamous Cell Carcinoma

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**Objective:** Branchiogenic carcinoma is a controversial entity. Some authors believe that the reported cases reflect cystic degeneration of metastatic lymph nodes rather than a primary tumor arising from cyst epithelium. In a previous study, we found evidence of normal epithelium within malignant cysts in 2 cases of possible branchiogenic carcinoma. In contrast, in the setting of a known primary tumor where cystic metastases are present, there is histologically highly dysplastic epithelium lining these degenerative cysts. Our goal was to analyze lymph nodes from patients with head and neck squamous cell carcinoma (SCC), with a documented primary focus, for the presence of normal epithelium within lymph nodes taken during neck dissection.

**Design:** Histologic review of neck dissection specimen slides for evidence of normal epithelium.

**Patients:** Thirty-five patients with known upper aerodigestive tract (UADT) SCC.

**Interventions:** Histopathologic slides from neck dissection specimens were reviewed for histologic evidence of normal squamous epithelium or epithelial lined cysts.

**Results:** Fifty neck dissection specimens with 902 lymph nodes were evaluated. Ninety-six nodes were positive for metastatic disease; 15% had evidence of cystic degeneration. None of the lymph nodes evaluated had any evidence of normal epithelium.

**Conclusions:** Cystic degeneration is a frequent phenomenon in metastatic lymph nodes in patients with UADT SCC, but in our study we found no evidence of normal epithelium in any of these cysts. Hence when combined with Martin's other 3 criteria, the presence of SCC in a normal epithelium-lined cyst is suggestive of branchiogenic carcinoma.

## **P167: A Systematic Approach to the Reconstruction of the Chin/Lower-Lip Complex Following Ablative Surgery**

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**Objectives:** Surgical resection of oral cavity carcinomas can lead to complicated defects of the chin/lower-lip complex that can leave the patient with significant postoperative morbidity. The reconstruction of this region to restore function and aesthetics is particularly challenging. We present our results from a small case series using both free-tissue transfer and regional flap reconstruction.

**Design:** Case series.

**Interventions:** Three patients underwent a combination of skin expansion, microvascular free-tissue transfer, and posterior scalping flap for reconstruction of postablative defects of the chin/lower-lip complex.

**Results:** This approach used a combination of skin expansion, microvascular free-tissue transfer, and the posterior scalping flap to reset lower-lip height, reestablish cheek contour, and achieve functional oral competence as well as provide excellent skin color match for the cutaneous defect.

**Conclusion:** We offer a systematic approach to the reconstruction of the composite defect of the chin/lower-lip complex in both the primary and secondary setting.

## **P168: Parathyroidectomy in Patients with Primary Hyperparathyroidism and Negative Findings on Technetium Tc 99m Sestamibi Localization Scan**

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**Objective:** To describe the findings at the time of neck exploration and to devise a surgical strategy when confronted with hyperparathyroid cases with negative findings on technetium Tc 99m sestamibi localization scan.

**Design:** All technetium Tc 99m sestamibi localization scans completed between the years 1996 and 2004 at a single institution were reviewed.

**Patients:** Nineteen patients with primary hyperparathyroidism and negative findings on technetium Tc 99m sestamibi scan were identified. These patients underwent parathyroid exploration and were selected for this study. The operative notes and surgical pathology reports were analyzed.

**Results:** Of the 19 patients who met the criteria for the study, 5 (26%) of 19 had multiple-gland disease. A single adenoma was found in 14 (74%) of the patients with primary hyperparathyroidism and negative localization scans. An inferior parathyroid adenoma was responsible for the hyperparathyroidism in 11 (58%) of the patients. A superior parathyroid adenoma was found in 2 (10%) of the patients. Only 1 adenoma (5%) was located in the mediastinum. No ectopic or intrathyroid lesions were identified.

**Conclusions:** A single-gland adenoma is responsible for hyperparathyroidism in the vast majority of patients who have negative

findings on preoperative technetium Tc 99m sestamibi localization scan. However, multigland disease can be expected to occur with much greater frequency in patients who have negative scan findings relative to the entire population of patients presenting with primary hyperparathyroidism. The analysis of our institutional data suggests that inferior parathyroid adenoma is the most common lesion in patients with hyperparathyroidism and negative findings on technetium Tc 99m sestamibi localization studies. These findings should be considered when planning a parathyroid exploration on such a patient.

## **P169: Influence of Tumor Grade on Patient Treatment and Outcome in Mucoepidermoid Carcinoma**

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**Background:** Histologic grade of Mucoepidermoid carcinoma (MEC) is a well-recognized predictor of prognosis and influences patient treatment. Tumor behavior is significantly more aggressive in high grade than in low grade MEC. This has led to a more intensive treatment protocol for high grade MEC. The clinical outcome of patients treated for intermediate grade MEC is less clear, and the treatment protocol for this group is not well defined.

**Objective:** To investigate the treatment protocol and survival outcomes of patients treated for intermediate grade MEC of the head and neck at our institution in comparison with outcomes of patients with low and high-grade disease

**Design:** Retrospective clinical review.

**Setting:** Tertiary care medical center.

**Patients:** From 1973 to 2004, 87 patients were treated at our institution for MEC of the head and neck. Sixty-two of these patients were available for retrospective clinical review.

**Results:** All patients underwent surgical resection. Sixty four percent of patients with high grade MEC were treated with adjuvant radiation therapy, while 45% of patients with intermediate grade and 11% a patients with low grade received post-operative radiation therapy. Median survival of patients with low grade MEC was 62 months, while median survival of patients with high grade MEC was 51 months. Patients with intermediate grade MEC had a median survival of 42 months. Overall and disease-free survival were significantly worse for intermediate grade patients than both high and low grade MEC patients ( $p < 0.001$ ).

**Conclusions:** Median survival for patients with intermediate grade MEC was worse than for patients with low grade and high grade MEC. Though survival was lowest for intermediate grade lesions, a lower percentage of these patients were treated with radiation therapy than for high grade MEC. This finding suggests that the malignant behavior of intermediate grade MEC was underestimated and should be treated more aggressively in these patients.

## **P170: The Clavipectoral Osteomyocutaneous Free Flap in Oromandibular Reconstruction**

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<sup>1</sup>University of Alberta, Edmonton; <sup>2</sup>University of Colombia, Colombia, MO

**Objectives:** Mandibular reconstruction continues to challenge most head and neck reconstructive surgeons despite the tremendous advances in surgical and fixation techniques. We have recently described the clavipectoral osteocutaneous flap for mandibular reconstruction. This flap encompasses the clavicle and clavicular head of pectoralis major with overlying skin. Our objective was to report our prospective clinical experience with the use of clavipectoral osteocutaneous flap in reconstruction of oromandibular defects.

**Design:** Prospective case series.

**Setting:** Tertiary referral teaching center.

**Patients:** Five patients undergoing mandibular reconstruction.

**Intervention:** Patients underwent mandibular reconstruction using the newly described clavipectoral flap.

**Main Outcome Measures:** Flap survival and patient shoulder function.

**Results:** All 5 flaps survived in total. The transferred clavicles demon-

strated good vascularity on the postoperative bone scans. The shoulder morbidity was minimal, and all patients resumed their preoperative levels of activity.

**Conclusions:** The clavipectoral flap has bone and soft tissue components that are especially suited for composite mandibular defects, but it should be used as a second-line flap owing to the short pedicle and the regular need for vein grafts.

## **P171: Stapler Application for Pharyngeal Closure After Total Laryngectomy**

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**Objective:** To study the use of linear stapler for pharyngeal closure after total laryngectomy.

**Design:** Cohort study with mean follow-up of 13 months.

**Setting:** Two referral centers of head and neck surgery.

**Patients:** Nineteen consecutive patients were analyzed, 18 men and 1 woman (age range, 44-80 years), all with squamous cell carcinoma transglottic tumors: 11 with T4, 7 T3, and 1 T2; 12 N0, 4 N1, and 3 N2; all M0.

**Interventions:** The patients underwent selective and/or radical neck dissection, depending on neck preoperative status. Two patients underwent laryngectomy after chemotherapy and irradiation failure, and 16 underwent adjuvant chemoradiation therapy. The follow-up time ranged from 8 to 31 months (average, 12.95 months). For all patients we used a linear stapler for pharyngeal closure after total laryngectomy, 18 with a 75-mm charge and of 80 mm; in each case we applied only 1 charge.

**Main Outcome Measures:** The evolution and prognosis of the disease were analyzed, with emphasis on salivary fistulae, hospitalization time, nasogastric intubation time, and the time of pharyngeal closure after total laryngectomy.

**Results:** One patient (5%) presented a salivary fistula, and the hospitalization time varied from 3 to 12 days. The nasogastric intubation time ranged from 8 to 10 days. The time to pharyngeal closure after total laryngectomy was decreased substantially, to only 5 to 10 minutes.

**Conclusions:** The mechanical sutures with the closed stapling technique are simply and quickly applied, providing watertight closure with good hemostasis, and preventing field contamination. Good speech and deglutition results were also achieved, with no increase in fistula or local recurrence rates.

## **P172: Ambulatory Transoral Brush Biopsies for Nasopharyngeal Carcinoma Screening**

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**Background:** It has been shown that Nasal Pharyngeal Cancer (NPC) has a near absolute association with the Epstein - Barr virus (EBV) with each tumor cell harboring copies of the same viral clone. This is already detectable in carcinoma-in-situ. Due to its remote retronasal location, NPC is usually diagnosed late with consequently poor prognosis. If diagnosed early, the prognosis is significantly improved.

**Objectives:** To assess the sensitivity and specificity of a new screening test kit (NP Screen®) for the identification of NPC in a high-risk population.

**Materials and Methods:** A new single use transoral brush biopsy kit was used to harvest epithelial cells from the nasopharynx. This kit includes preservation medium and shipping kit for remote, real-time PCR-base EBV quantitation (Advance Sentry Corporation, Los Angeles, CA). All consented study subjects were referred to ENT Clinics and underwent transoral brushing of the nasopharynx and nasoendoscopy. Standard biopsies for histopathology were obtained in subjects with abnormal endoscopic findings. Subjects with normal ENT examinations, including normal nasopharyngoscopy were classi-

fied as NPC negative if their initial status continued without evidence of NPC for two years after the initial examination. Those subjects with NPC-positive histopathology were considered to be NPC positive.

**Results:** Of the 271 specimens taken, 11 had insufficient DNA for PCR and 1 could not complete the procedure due to gag reflex. Of the 259 patients that had adequate brushings taken 70 patients had NPC positive pathology. Of these 70 patients who were histologically positive, 69 had EBV-positive brushings on PCR. There was therefore 1 false negative. Of the 189 NPC negative patients all had negative brushings. The sensitivity and specificity of the NP Screen® are respectively 98.6% (CI 92.3: 100%) and 100% (CI 98.1-99.8%) with a PPV=100% and a NPV=99.6%.

**Conclusion:** The NPC screening test kit fulfills the requirements for routine ambulatory NPC risk assessment in high-risk populations.

## **P173: Reconstruction of Oral Cavity With Radial Forearm Free Flap: Functional Aspects and Flap Design**

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**Background:** We evaluated the nature of flap and functional outcomes in 106 consecutive cases of radial forearm free flap (RFFF) for the reconstruction of oral cavity and oropharynx and analyzed the usefulness of the flap.

**Methods:** We retrospectively reviewed the clinical data of 106 patients who underwent reconstructive surgery for oral and oropharyngeal cancers using RFFF in last 11 years. Clinical factors and functional evaluation were analyzed by the modified barium swallow (MBS) test (n = 72) and speech-language assessment (n = 22).

**Results:** There were 90 men and 16 women and the average age was 56.2. The designs of free flap were unilobed shape in 25 cases and 52 bilobed, 13 trilobed, 15 tetralobed and 1 pentaloled shape according to the defects. The average size of flap was 61.0 cm<sup>2</sup>. MBS results showed 30 out of 72 patients (41.7%) had no aspiration, only two patients (2.7%) had maximum aspiration. Twenty patients (27.8%) had residue and 4 patients (5.6%) had velopharyngeal insufficiency. In speech evaluation, 20 out of 22 patients (91.0%) showed more than 50% accuracy of precise consonants. Five out of 22 patients (22.7%) had moderate to severe articulation disorder but, others (77.3%) had excellent speech intelligibility.

**Conclusion:** We could confirm that the RFFF by the various design is an excellent reconstructive method for the restoration of the function in the reconstruction of the oral and oropharyngeal defects.

## **P174: Laryngeal Papillomatosis: Clinico Epidemiologic Aspects- 24 Years Study**

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**Objective:** To study the clinical behaviour and to present the surgical concept and results

**Methods:** 279 patients of histologically confirmed laryngeal papillomatosis visiting Govt. Ear Nose Throat hospital from June 1982 to February 2006 were retrospectively analysed.

**Results:** There were 156 (55.91%) males, and 123(44.09%) females with mean age of years (range 1-55 years). Year wise distribution showed a peak in the year 2002, (24 cases 8.60%) followed by 1999 (18 cases,6.45%) and 1997 (15 cases,5.38%).Age wise distribution showed a preponderance(20.78%) in the 4-6 years, 12.90% in 7-9 years group, 12.18% in 10-12 age group followed by 8.24% in the 0-3 years group. Majority belonged to 6-10 year age group. The recurrences are more in males (62.86%) compared to females (37.14%). Recurrences in adults were more in the fourth decade. In children the recurrence was more in the 3-9 age group with maximum in a child of 3 years. The age distribution of affected showed a bimodal curve with the first peak around 6 years and the second in the fourth decade. As the sample size is small no statistical significance tests were applied. All the patients belonged to low socioeconomic group. All the patients were hoarse. 40% of patients were dyspnoeic at admission and required emergency tracheostomy. The predominant sites of the lesion were the true vocal cords and the anterior commissure.. All the cases underwent tracheostomy and periodic

microsuspension laryngoscopic removal using a cup forceps. In 20 cases adjuvant therapy (Thuja-a homeopathic antiviral) was used. We did not notice any deaths due to the disease. No malignant transformations were noted in our series

**Conclusion:** Different forms of treatment did not affect the rate of recurrence.

Removal of the mass by cup forceps showed reasonably good results as it can be used for bulkier lesions, sessile lesions and is free from thermal injury as seen in lasers. It is significantly less expensive than laser and microdebrider and training is easy. Laryngeal papilloma in children may have grave sequelae, hence a high index of suspicion is needed in all patients with progressive voice change exceeding six weeks and unresponsive to medical therapy.

## **P175: The Use of Medical Modeling in Head and Neck Reconstruction**

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**Objective:** Medical modeling technology generates 3-dimensional models from computed tomography data. This study was designed to evaluate utility of rapid prototyping models in head and neck reconstruction.

**Design:** Prospective case series.

**Setting:** Tertiary referral teaching center.

**Patients:** Thirty-six patients undergoing bony reconstructions.

**Intervention:** Medical models were obtained on all patient requiring bony reconstruction of the head and neck. These models were available in the operating room and were used to aid in the resection and reconstructive phases of the surgery.

**Main Outcome Measures:** Questionnaire regarding the utility of these models were obtained from the residents and staff surgeons at the end of the procedures.

**Results:** The availability of a 3-dimensional model in the operating room has numerous advantages, including allowing for a better understanding of the defect, an improved communication between surgeons, and a valuable teaching tool for residents.

**Conclusions:** Medical modeling is an excellent adjunctive tool in patients requiring bony reconstruction of the head and neck.

## **P176: Management of Salvage Laryngectomy Defects Following Organ Preservation Failure**

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**Objective:** Salvage laryngectomy to treat organ preservation failures results in significantly higher local wound complications. Even in the absence of extralaryngeal disease, primary closure of laryngeal defects results in protracted wound care problems. Our objective was to determine whether, in cases where sufficient mucosa is present to close the defect primarily, use of previously untreated vascularized tissue to close the wound may improve outcomes.

**Design:** A retrospective chart review (2000-2006).

**Setting:** Two tertiary care institutions.

**Patients:** Thirty-seven patients who underwent salvage surgery for laryngeal squamous cell carcinoma. Patients requiring laryngopharyngectomy or with pharyngeal involvement were excluded.

**Interventions:** There were 37 patients who underwent salvage laryngeal surgery: 17 underwent free-flap reconstruction (16 radial forearm flaps and 1 rectus flap), and 20 underwent primary closure. The median follow-up was 12 months (range, 4-60 months). Previous treatment consisted of chemoradiation therapy for 41% of the reconstruction group and 35% of the primary closure group; the remainder were treated with primary irradiation alone.

**Results:** The free flap reconstruction group had a significantly lower rate of fistula (18%) than the primary closure group (50%;  $P = .04$ ). The development of a fistula in either group resulted in a prolonged hospital stay (mean stay, 19 days vs 7 days) and additional procedures. There was also a higher rate of stricture formation (16% vs 25%) and feeding tube dependence (23% vs 45%) in the primary closure group.

**Conclusions:** Planned reconstruction of posttreatment laryngeal defects with vascularized tissue is associated with a lower complication rate and may improve long-term outcomes and reduce costs.

## **P177: Rapid Superselective High-Dose Cisplatin Infusion With Concomitant Radiotherapy for Advanced Hypopharyngeal Cancer**

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**Purpose:** Squamous cell carcinoma of the hypopharyngeal cancer (HPC) is an unfavorable disease, which frequently presents in advanced stages. The survival and functional outcome for HPC still remains poor despite aggressive standard treatment involving debilitating surgery and postoperative radiation therapy. Hence, we reviewed our experience in the management of advanced HPC using rapid superselective high-dose cisplatin infusion with concomitant radiotherapy (RADPLAT) as organ preservation chemoradiotherapy.

**Methods:** From April 2000 to December 2005, 20 previously untreated patients with locally advanced HPC were treated at Hokkaido University Hospital (Sapporo, Japan). All the patients either had disease for which radical surgery was contraindicated or had rejected radical surgery. All patients were given superselective intra-arterial infusions of cisplatin (100-120mg/m<sup>2</sup>/week) with simultaneous intravenous infusion of thiosulfate to neutralize cisplatin toxicity and conventional extra-beam radiotherapy (66Gy/33fr/6.6 weeks). The tumor-feeding arteries were decided after the distribution of bloodstream in the tumor and neck disease was investigated by digital subtraction angiography (DSA). About the latest 11 patients, we used not only DSA but also angio-CT. If lymph node metastases remained or recurred, patients with resectable neck disease were referred for neck dissection.

**Results:** Twenty patients were enrolled in this study and could be evaluated. Ages ranged from 46 to 74 years (median, 58.5 years). Among the 20 patients, 9 (45.0%) were considered to have unresectable disease, and the remaining 11 (55.0%) had refused radical surgery. All patients had stages IV disease except one patient (stages III). Seventeen patients (85.0%) completed therapy without interruption. Sixteen (80.0%) patients experienced grade III to IV toxicity, including mucositis (n=9), leukopenia (6), anemia (3), fever (3), dermatitis (3), nausea (3), thrombocytopenia (2), neurologic sign (1) and vomiting (1). During the median follow-up period of 14.7 months, the 2-year overall survival and preservation rates of larynx were 53.0% and 58.3%, respectively. Among the 18 patients with positive neck disease, the diseases of 14 (77.8%) were well controlled without surgery. Another 3 patients with persistent neck disease after RAD-PLAT were treated successfully by salvage neck dissection. There are 13 surviving patients without evidence of disease, all of them are able to have oral intake without feeding-tube support.

**Conclusion:** In this study, we found that RADPLAT is very effective and safe. Prospective studies should be required to determine which modality is more effective and safe, RADPLAT or systemic chemoradiation.

## **P178: Management of Arterial Rupture After Upper Mediastinal Dissection**

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**Objectives:** Successful control of upper mediastinal metastasis has a great impact on therapeutic outcomes for advanced head and neck cancer, namely, cervical esophageal cancer, hypopharyngeal cancer, laryngeal cancer and thyroid cancer. Although upper mediastinal dissection is important to achieve loco-regional control, postoperative breakdown of greater vessels is a severe life-threatening complication. The present retrospective chart study aimed at clarifying the cause and preventing further arterial breakdown.

**Materials:** Thirteen of 315 patients (4.1%) who underwent upper mediastinal dissection encountered postoperative rupture of the greater vessels. They were, 4 cervical esophageal cancer, 2 hypopharyngeal cancer, 2 laryngeal cancer, 4 thyroid cancer including 3 anaplastic cancer, and one malignant mediastinal tumor.

**Results:** The ruptured vessels were innominate artery (5), common

carotid artery (7), and vertebral artery (1). A high incidence of tumor invasion to neighboring organs was noticed, which led to considerable damage by surgical intervention to the greater vessels, the trachea, and the esophagus. Predisposing factors of the arterial rupture were tumor invasion to the vessels, postoperative tracheal necrosis, and inflammation. Eight of 13 patients were once successfully salvaged, while the remaining expired before taking any life saving procedure. The vessels were ligated in 6 patients. Four patients died of blood loss, and finally, four patients survived.

**Conclusion:** Prognosis of the arterial rupture after mediastinal dissection is still poor. Although only 4 of 13 patients (31%) were finally rescued, 8 patients had chance to recover. Highpoints to prevent arterial breakdown is to preserve the microvascular network around the innominate artery and trachea which prevents them worn thin, or to protect them by inserting thin vascularized tissue like omentum or free flap in between, around the continuously rubbed area following respiratory movement.

## **P179: The Submental Flap: A Modified Technique for Training Residents**

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**Background:** Training residents in the art of reconstruction is a difficult task. While the popularity of the submental artery flap increased since its introduction in 1993, it remains underutilized in head and neck reconstruction. The harvest of this flap generally requires a careful vessel dissection through the submandibular and submental triangles in order to preserve the perforating vessels. When training residents to raise this flap, the dissection off the mylohyoid muscle is particularly treacherous.

**Objective:** The objective of this study is to familiarize readers with a modified technique of submental flap harvest in order to teach residents to raise the flap with safety and confidence. The technique is discussed as is its use in seven consecutive patients treated at a teaching institution.

**Surgical Technique:** The conventional technique to harvest the submental artery flap is well-described. The submental artery and vein are identified at their respective takeoffs from the facial vessels. The submandibular gland and the peri-facial nodes are removed. The submental vessels are dissected distally over the mylohyoid towards the digastric muscle. The flap is then dissected distal to proximal. The perforating vessels that supply the flap are identified superficial to the mylohyoid and dissected off to connect with the earlier dissection and complete the flap harvest. While the experienced reconstructive surgeon is comfortable with such vessel dissection, the senior resident may not be. In the modified approach, the mylohyoid muscle is included as the deep aspect of the flap. After the submental vessels are dissected to the lateral border of the mylohyoid, the flap is raised distal to proximal with inclusion of the mylohyoid. The mylohyoid muscle is readily dissected from the geniohyoid with primarily blunt dissection, similar to elevation of a pectoralis major flap. Accordingly, the perforating vessels remain safely encased by the mylohyoid on the deep aspect and the digastric muscle superficially.

**Methods:** This modified technique was used for seven consecutive patients requiring submental flap harvest. These cases were performed at a teaching institution by the senior resident under the direct supervision of the attending surgeon. All cases involved reconstruction for cancer ablation and were combined with neck dissection.

**Results:** In all seven cases, the flap was elevated successfully. At the time of inset, all flaps had good capillary refill with no signs of arterial or venous insufficiency. On peri-operative follow-up, a previously radiated patient demonstrated a distal loss of 30%, with no long-term sequelae. In one other case, there was a transient palsy of the marginal mandibular nerve.

**Conclusion:** Incorporation of the mylohyoid muscle in the submental flap reduces the difficulty of vessel dissection required in the conventional method. With this modification, this flap can be taught to senior residents who are able to complete all necessary steps with safety. Accordingly, residents can gain sufficient confidence to add this highly versatile flap to their reconstructive armamentarium.

## **P180: Extratemporal Facial Nerve Schwannoma Mimicking Benign Parotid Tumors**

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Extratemporal facial nerve schwannomas are rare benign tumors accounting for 15% of all facial nerve schwannomas. These tumors often present as asymptomatic, slowly growing masses in the parotid region. Fine needle aspiration of these masses is not specific and often is mistaken for pleomorphic adenoma. Radiographic imaging is rarely helpful due to the lack of discriminating features. In most cases surgical resection leads to facial nerve paralysis necessitating nerve grafting to restore facial function. Intraoperative biopsy may also lead to permanent or temporary facial paralysis. The ability to identify these tumors intraoperatively and make adjustments in the surgical plan is essential in minimizing patient morbidity. We present 3 cases of extratemporal facial nerve schwannomas that were mistaken as pleomorphic adenomas prior to surgical resection. Preoperative pathology and imaging will be reviewed. Findings that should raise concern as to the possibility of facial nerve schwannoma will be discussed. We also review our algorithm in identifying and treating these tumors in order to minimize patient morbidity. Patients: KC mr: 1275775, KB mr: 1597307, CD mr: 1914901.

## **P181: Combination Tumor Antigen-Targeted Immunotherapy in HPV-16-Positive Head and Neck Squamous Cell Carcinoma**

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**Objective:** To show that E6-induced proteasomal degradation of p53 in human papillomavirus (HPV) 16-positive head and neck squamous cell carcinoma enhances cytotoxic T-lymphocyte recognition and lysis mediated by increased HLA-A2-p53 (264-272) complexes. By directly targeting E7 and p53, we can increase efficacy of adjuvant immunotherapy by avoiding viral mutation and the potential loss of a target.

**Design:** Adjuvant treatment was 5% imiquimod cream (Aldara) or aqueous imiquimod, a toll-like receptor 7 agonist and Food and Drug Administration-approved topical immunomodulatory treatment for HPV-associated warts. Initial in vivo work with murine H2-Kb and -Db restricted peptides, p53 (158-166) and E7(49-57), respectively, compared subcutaneous delivery with or without subcutaneous aqueous imiquimod. Current in vivo vaccination models use the HLA-A2 restricted peptides E7 (11-20) and p53(261-269), the murine homologue of human HLA-A2 restricted p53(264-272).

**Results:** Interferon gamma enzyme-linked immunospot assay showed enhanced antigen-specific recognition and reactivity after vaccinating with both Kb and Db peptides, which improved in the effect of imiquimod. The same regimen exhibited improved in vitro recognition and reactivity by splenocytes in mice vaccinated against an HLA-A2-positive HPV-16 E6 and E7-transformed murine carcinoma cell line, TC-1/A2. With the HLA-A2-restricted p53 and E7 peptides, improved tumor protection was observed from groups receiving Aldara with both peptides or p53(261-269) alone. Tumor protection with Aldara and p53(261-269) alone was greater than when vaccinating with both peptides and almost identical to that seen after vaccination with both peptides and montanide.

**Conclusions:** Our work supports the use of targeting this specific combination of peptides as well as the feasibility and efficacy of using a topical agent that can serve the dual role of vehicle and adjuvant.

## **P182: Clinical Application of Epigenetic Biomarkers in Head and Neck Cancer**

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**Objectives:** While the crucial role of epigenetics in cancer is now being realized, this field has not yet been exploited for clinical benefit in head and neck squamous cell carcinoma (HNSCC). Our objective was to evaluate the biomarker possibilities of DNA promoter methylation.

**Patients:** Seventy-nine patients with HNSCC undergoing surgical resection.

**Interventions:** Tissue samples were obtained from the patients. In addition, 320 longitudinally collected plasma specimens, as well as urine and saliva specimens, were collected from these patients. From fixed specimens, lymph nodes and sequential specimens from the invasive front and deep margins of resection were also prepared. Samples of DNA were extracted and bisulphite treated. The methylation status of several tumor suppressor genes was elucidated using existing and novel pyrosequencing-based assays.

**Results:** Promoter methylation of *P16INK4a*, *cyclin A1*, and *cytoblobin* was common (28%, 53%, and 65%, respectively) as well as tumor specific ( $P = .048$ ,  $P = .001$ ,  $P = .002$ ). Other genes ranged from frequently methylated (*RAR3B2* and *E-cadherin*) but not in a tumor-specific manner, rarely methylated (*MGMT*), or 100% unmethylated (*hMLH1* and *ATM*). Analysis of urine and plasma specimens, despite smaller published reports to the contrary, did not appear to show significant clinical potential as biomarkers. However, analysis of tumor margins and lymph nodes gave additional insight into the tumor biology and adequacy of resection. Assay of saliva-derived DNA correlated well with tumor and may be useful in premalignant conditions.

**Conclusions:** Novel assays of both tumor and surrogate tissue specimens have been developed. These assays exploit new technology using controlled and quantitative measures of DNA methylation. These technological improvements in epigenetic biomarkers form the basis of further research.

### **P183: Genetic Abnormalities Associated With Chemoradiation-Resistance of Head and Neck Squamous Cell Carcinoma**

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**Purpose:** Concurrent chemoradiation (CCRT) is presently treatment of choice in patients with advanced head and neck squamous cell carcinoma (HNSCC). Underlying mechanisms of chemoradiation-resistance of advanced head and neck squamous cell carcinoma (HNSCC) that may provide reliable predictors of treatment failure have remained obscure.

**Materials and Methods:** Twenty-six out of 104 consecutive patients with HNSCC had residue tumor after concurrent chemoradiation treatment or a recurrence during follow-up. We performed a matched-pair analysis of 20 chemoradiation-resistant (resistant) and matched 20 chemoradiation-sensitive (sensitive) HNSCC. We compared the global DNA copy number profiles derived from comparative genomic hybridization analysis of both groups to identify genetic factors associated with chemoradiation-resistance. Statistical analysis was performed to identify cytogenetic bands that were associated with treatment failure.

**Results:** Although sensitive and resistant groups were characterized by a similar total number of genetic aberrations, gains of 5q11-q12, 6p11-pter, 6q23-q27, 8p21-p23, 9, 10q11-q22, 15q13-q26, 18q21-q23, 22 and Xq and losses of 2p22-p25, 5p11pter, 7q11-q22 and 18p11-pter were found to differentiate both groups. A significantly higher number of high-level amplifications was observed among the resistant cases: 1p32, 3q24, 7p11.1, 7p11.2-12, 8p11.1, 8p11.1-12, 12q15, 13q21, 15q12, 18p11.3 and 18q11. Statistical analysis revealed that the presence of gains of 3q11-q13 ( $p = 0.017$ ), 3q21-q26.1 ( $p = 0.038$ ) and 6q22-q27 ( $p = 0.036$ ) and losses of 3p11-pter ( $p = 0.016$ ) and 4p11-pter ( $p < 0.001$ ) was significantly associated with chemoradiation treatment failure.

**Conclusions:** Sensitive and resistant HNSCC are characterized by divergent genomic profiles. These profiles are predictive factors for treatment failure.

### **P184: Gene Expression Profiling to Predict Outcome After Chemoradiation in HNSCC**

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**Objective:** To improve prediction of local-regional control after chemoradiation in head and neck cancer using gene expression

analysis. Background. Chemoradiation is the preferred treatment modality for organ-preservation in head and neck squamous cell carcinoma (HNSCC), but fails in 20-30% of the cases. Surgery, chemoradiation and radiotherapy alone are employed in larger tumors. The choice however between these different treatment options is often arbitrary. Clinical parameters have limited additional value for selection of optimal treatment. To date no reliable biological predictive markers are available for aiding treatment choice. Gene expression using microarrays are expected to reveal characteristics of tumor behavior relevant to chemotherapy and radiotherapy responses. Such expression profiles have proven their value in predicting outcome in other tumors, and are likely to help in choosing between different treatment options.

**Materials and Methods:** We collected 61 fresh frozen biopsies from previously untreated head and neck cancer patients subsequently given high dose cisplatin-based chemoradiation (RADPLAT) for stage 3-4 squamous cell carcinomas. Twenty-one patients developed a local-regional recurrence and 40 patients remained in complete remission for at least 1.5 years. RNA was extracted from the frozen biopsies, amplified, labeled using a fluorescent CyDye kit, and hybridized to a 35K oligo array manufactured by the NKI microarray facility. An aRNA-reference pool was constructed, consisting of 62 samples of patients with head and neck tumors. This enabled us to do a straight color, and a color reverse. Analyses were performed with bioinformatics software (Biometric Research Branch tools and Gene Set Enrichment Analysis).

**Results:** Hierarchical clustering and class prediction analysis yielded a 27-gene profile with a sensitivity and specificity of 62% and 84% respectively for local-regional control. The predictive profile could significantly split tumors into good and poor local-regional control as assessed by Kaplan-Meier analysis ( $p = 0.002$ ). Gene Set Enrichment Analysis on 311 gene sets revealed 6 sets with a nominal  $p$ -value  $< 0.05$  and a false discovery rate  $< 25\%$ . For these gene sets, Kaplan-Meier analysis showed significant differences in local-regional control for high and low expressing tumors. In addition, we tested two other published gene signatures, namely, those for the core serum response (wound signature) and hypoxia. Both were significant predictors of outcome.

**Conclusion:** Several gene sets were found with predictive potential for local-regional control after combined radiation and chemotherapy in HNSCC. We are confirming these findings on an independent patient group using oligo arrays, RT-PCR and tissue microarrays.

### **P185: The Effect of AlloDerm® on the Initiation and Subsequent Ingrowth of Human Neovessels**

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**Introduction:** Head and neck surgeons are often operating in chemoirradiated fields. We commonly employ AlloDerm® for reconstruction of ablative soft tissue and mucosal defects. Although devoid of growth factors, AlloDerm® may serve as an adhesive matrix for binding of growth factors. This may increase local angiogenesis and wound healing. We hypothesize that AlloDerm® will enhance angiogenesis and furthermore may be altered with autologous blood products to enhance initiation.

**Study Design:** In vitro investigation

**Materials and Methods:** We used a human placental vein angiogenesis model which analyzes endothelial growth from a centrally placed disc using inverted phase microscopy scoring. Four groups, human placental vein (HPVM) alone, HPVM with AlloDerm®, HPVM with AlloDerm® and platelet poor plasma (PPP), and HPVM with AlloDerm® and platelet rich plasma (PRP) were evaluated. Endothelial cell growth in the 2 groups was evaluated using semi-quantitative inverted phase microscopy. Selected hematoxylin and eosin staining as well as immunofluorescent staining for evaluation of endothelial growth within the AlloDerm® matrix were also performed. Two person scoring was employed and the experiment was repeated in triplicate. To assess sites of attachment of human umbilical vein endothelial cells (HUVEC) to AlloDerm®, we incubated HUVEC cells with AlloDerm® for a period of 2 weeks and assessed attachment with anti-factor 8 immunofluorescence.

**Results:** Statistical analysis performed for angiogenic initiation and angiogenic indices in the 4 groups was performed and revealed

decreased initiation in the combined placental vein with AlloDerm® group ( $p$ -value < .0001 at day 7, 14, 21). Additionally, initiation in the AlloDerm® + PPP group was significantly better than the AlloDerm® alone group when placentas 2 and 3 were compared ( $p$ -value < .0001). All treatment groups had significantly lower angiogenic indices compared to controls at Days 14 and 21 with  $p$  : value at least  $p$  < .03. AlloDerm + PPP vs. AlloDerm® alone had greater angiogenic indices but did not reach significance. On hematoxylin and eosin staining as well as immunofluorescent factor 8 staining, no endothelial ingrowth into the AlloDerm® was noted in the selected samples analyzed.

**Conclusions:** We conclude that in this in vitro model, AlloDerm® inhibits angiogenic initiation. Further research is needed to validate this observation, assess its clinical relevance, and modulate implementation of AlloDerm® with autologous blood products.

## **P186: p53 and Bcl-xL Expression Predicts Outcome in Patients With Oropharynx Cancer Treated With Chemoradiation**

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**Objective:** To assess tumor markers in oropharynx cancer.

**Design:** Marker expression and clinical outcome.

**Setting:** Laboratory.

**Patients:** Forty-two patients with advanced oropharyngeal cancer treated with chemoradiation therapy.

**Intervention:** Treatment with chemoradiation therapy.

**Main Outcome Measures:** Expression of p53 and Bcl-xL in tumor tissues was assessed for correlation with chemotherapy response and survival.

**Results:** Patients with low p53 and low Bcl-xL tumor expression enjoyed the best overall survival. Patients with low p53 and high Bcl-xL had the poorest overall and disease-free survival. Among patients with the same T stage and p53 expression, for each unit increase in subjectwise average of Bcl-xL proportion, the adjusted hazard of dying increased by an estimated 127% for overall survival (p53 and Bcl-xL interaction term,  $P = .01$ ) and by 139% for disease-specific survival (p53 and Bcl-xL interaction term,  $P = .05$ ) (Cox regression model). T stage ( $P < .001$ ) was the only significant factor associated with risk of recurrence or persistent cancer. Bcl-xL and p53 phenotype was significantly (p53 and Bcl-xL interaction term,  $P = .03$ ) related to initial chemotherapy response in combination with T stage ( $P = .047$ ).

**Conclusions:** Low p53 and low Bcl-xL tumor expression identifies patients with the best outcome, whereas low p53 and high Bcl-xL identifies those with the poorest survival. These findings are consistent with laboratory studies that show that the low p53 (wild type) high Bcl-xL phenotype is highly resistant to cisplatin, whereas the low p53 (wild type) low Bcl-xL phenotype is very sensitive to cisplatin.

## **P187: Monoclonal Origin of Two Metachronous SCC - Evidence Of Implantation Metastasis as Mechanism Behind Second Primaries**

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Since Slaughter's field cancerization theory in 1954, second primaries in the head and neck region have been suggested to be the result of exposure to carcinogenic substances, subsequently resulting in a cancer prone mucosa in which new cancers can develop independently of each other. However, over the last decade cytogenetic and genetic studies of single gene alterations have yielded data indicating a subset of synchronous and metachronous tumors to share a monoclonal origin, which counteracts the field cancerization theory. We report a case of a non smoking, non drinking woman with a left tonsil SCC, T2N0M0, who six months after radiation therapy with complete response developed a metachronous SCC of the posterior glottis with subglottic extension. The two tumors were analyzed by LOH for 9 genetic loci. Seven of the 9 microsatellite markers were identical in the two malignancies. The statistical likelihood for this to represent two independent tumors was 5.24E-06, and the likelihood of the tumors to be clonally related was 1.26E+03 higher. The localization of

the second primary in the posterior glottis rather than on the vocal cords, signaled the tumor not to represent an independent new primary, but possibly an implantation metastasis. This was confirmed by the LOH studies since the two tumors share the same clonal origin. A possible explanation is that manipulation by the endotracheal tube during intubation for biopsies of the first tonsil cancer resulted in exfoliated tumor cells that were implanted in the posterior glottis when the tube was placed. Exfoliated viable cells have previously been found on gloves and instruments after tumor resections, which further strengthen the hypothesis of local implantation as a mechanism for development of second primaries. This will argue for a no touch surgical technique in a similar fashion to what is standard care for colorectal cancers. It also favors the idea of development of a protecting tumor seal applied on the cancer prior to resections to prevent exfoliation of tumor cells.

## **P188: Nuclear Survivin Is A Favorable Prognostic Marker in OSCC - Molecular Mechanism and Therapeutic Potential**

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**Objective:** Local-regional relapse after therapy is a major cause of death in patients with OSCC. Consequently, identification of prognostic biomarkers that signal increased risk of treatment failure would have a major impact on treatment planning decisions, and may represent the basis for novel therapeutic intervention strategies.

Methods and

**Results:** Oncogenomic analysis identified the apoptosis inhibitor survivin as being overexpressed in OSCC cells. We next systematically examined the localization and prognostic value of survivin in the pathogenesis of 138 oral squamous carcinoma (OSCC) patients. Immunohistochemical analysis using multiple tissue arrays demonstrated cytoplasmic as well as nuclear survivin. Survival rates estimated by the Kaplan-Meier method revealed that patients with nuclear survivin responded significantly better to chemoradiation therapy.

We further show that the intracellular localization of survivin in OSCC cell lines is regulated by a Crm1-dependent nuclear export signal (NES) in survivin. Importantly, the integrity of the NES is required for the cytoprotective activity of survivin, because export deficient survivin fails to protect tumor cells against chemo- and radiotherapy-induced apoptosis. Moreover, expression of NES-deficient survivin in trans sensitizes tumor cells against cancer therapy. Finally, we developed cell based assays, which will be applied in chemical-genetic screens to identify survivin transport inhibitors.

**Conclusions:** Our study proposes nuclear survivin as a prognostic marker to stratify OSCC patients into groups with favorable or unfavorable responses to chemo/radiotherapy. We show that nuclear export is essential for the tumor promoting activity of survivin. We suggest chemical-genetic interference with the nuclear export of survivin as a potential anticancer strategy.

## **P189: The TKI, AZD2171, Inhibits VEGFR Signaling and Growth of Anaplastic Thyroid Cancer in an Orthotopic Nude Mouse Model**

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**Introduction:** Anaplastic thyroid cancer (ATC) accounts for a small proportion of all thyroid cancers (3%), however it is responsible for more than half of the 1200 annual deaths from the disease. It is a locally aggressive type of tumor with a high distant metastases rate. With the conventional treatment modalities the median survival for this disease ranges from 4 to 12 months. Therefore, targeted molecular therapy is an attractive approach. The tyrosine kinase inhibitor (TKI) AZD2171 is an angiogenesis inhibitor that targets selectively VEGFR-1, 2 and 3, expressed by endothelial cells. Furthermore, VEGFR-2 is also expressed by thyroid cancer cells.

**Objective:** To determine if AZD2171 can inhibit VEGFR-2 signaling, the main effector of the functions of VEGF in endothelial and/or tumor cells in vitro and decrease tumor growth and prolong survival of ATC in an orthotopic nude mouse model.

**Methods:** We examined the effects of AZD2171 on phosphorylation of VEGFR-2, MAPK and AKT on human umbilical vein endothelial cells (HUVEC) and the ATC cell lines DRO and ARO by western blotting. To check its anti-proliferative and anti-apoptotic effects we performed MTT and flow cytometry assays for hypodiploid cells respectively. We assessed the antitumor effects of AZD2171 in a xenograft model of ATC using four randomized groups of 10 animals each: control, AZD2171, paclitaxel and combination groups by measuring tumor size and survival.

**Results:** Treatment of AZD2171 led to dose-dependent inhibition of VEGFR-2 phosphorylation and its downstream signaling in both HUVEC and ATC cell lines. In endothelial cells, the IC50 for cell proliferation was found to be 500 nM. In the ATC cell lines DRO and ARO it was 5  $\mu$ M and 6.5  $\mu$ M, respectively. AZD2171 was also capable of inducing apoptosis in 50% of endothelial and ATC cells at 3 and 10  $\mu$ M concentrations respectively. Treatment of mice bearing ATC tumors led to significant differences in mean tumor size between the control (460 mm<sup>3</sup>), Paclitaxel (150 mm<sup>3</sup>), AZD2171 (150 mm<sup>3</sup>) and AZD2171/Paclitaxel treated mice (110 mm<sup>3</sup>) ( $p=0.006$ ). The median survival for the control, AZD2171, paclitaxel and combination groups were 17, 16, 23 and 23 days respectively. The difference between the 4 groups was statistically significant by log-rank test ( $p<0.001$ ). Moreover, survival was significantly higher among AZD2171 ( $p<0.001$ ) and combination ( $p<0.001$ ) groups compared to the control group. However, no difference was found between paclitaxel and the control group ( $p=0.676$ ).

**Conclusions:** AZD2171 effectively inhibits tumor growth and prolongs survival in an orthotopic model of ATC. We demonstrated that VEGFR-2 is also present in ATC cell lines. However the concentrations necessary to inhibit proliferation and induce apoptosis were much higher than those required for endothelial cells. Therefore the main effect of AZD2171 appears to be mediated through inhibition of angiogenesis. Further studies will be necessary to determine the function of VEGFR-2 in ATC cells. Acknowledgment: AZD2171 was a gift from AstraZeneca Pharmaceuticals and the National Cancer Institute, NIH.

## **P190: Expression of LEKTI Correlates With Perineural Invasion in SCC of the Oral Tongue**

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**Objective:** Invasion and metastasis may result from imbalance of proteinase enzymes and their inhibitors in the microenvironment that favors degradation of extracellular matrix (ECM). Lymphoepithelial kazal-type inhibitor (LEKTI) is an endogenous inhibitor of serine proteinases we identified by constitutive expression in normal oral mucosa and lost or downregulated expression in matched tumor specimens of patients with head and neck squamous cell carcinoma (HNSCC). Previously, we found that expression of LEKTI in HNSCC cell lines regulates the expression and secretion of matrix metalloproteinases critical to ECM degradation. Furthermore, using an orthotopic mouse model, we found increased perineural invasion (PNI) in tongue tumors derived from parental or vector OSC-19 cells compared to those derived from clones expressing LEKTI. Accordingly, we hypothesized that loss of LEKTI expression in primary tumors correlates with aggressive biologic behavior in patients with HNSCC. To determine the significance for the loss of LEKTI expression, we investigated the expression of LEKTI in primary tumor specimens of patients with SCC of the oral tongue and correlated pathologic findings and clinical outcomes.

**Methods:** To characterize the expression of LEKTI in primary tumors, we performed immunohistochemical analysis of paraffin-embedded, formalin-fixed specimens from 60 unselected patients with HNSCC from various primary sites and stages. Further, we assembled a retrospective, inception cohort of 81 consecutive, previously untreated patients who underwent surgery as initial treatment for SCC of the oral tongue with at least 18 months of follow-up. The primary tumor specimens were recut and stained with a purified mouse anti-LEKTI monoclonal antibody. Slides were reviewed and scored by two independent investigators. The surgical pathology reports were reviewed for histopathologic features of the primary tumor. Medical records were reviewed for covariate and clinical follow-up data. Time-to-event analysis was performed with the Kaplan-Meier method for patients stratified by LEKTI-staining pattern.

**Results:** LEKTI expression was negative in 31, intermediate in 44, and strong in 6 patients. PNI was present in 12 of 31 patients with LEKTI-negative tumors, in contrast to 6 of 50 patients with LEKTI-positive tumors. Therefore, the relative risk of PNI was 3.2 (95% CI from 1.2 to 8.9) in patients with LEKTI-negative tumors compared to those LEKTI-positive tumors ( $p = 0.007$  by Chi Square Test). Analysis of the covariates for disease recurrence and death found no significant differences in age, gender, T-stage, grade, N-stage, and postoperative treatment between patients with LEKTI-negative and LEKTI-positive tumors. Patients with LEKTI-negative expression had a 20% increased risk of disease recurrence (HR 1.2 and 95% CI 0.61 to 2.33,  $p = 0.23$  by Logrank test) and an 80% increased risk of death from all causes (HR 1.8 and 95% CI 0.34 to 9.41,  $p = 0.48$ ).

**Conclusions:** These data confirm our previous in vitro and in vivo findings that loss of LEKTI expression in HNSCC results in a cellular phenotype with locally aggressive behavior. Our findings shed new light on mechanisms of PNI, offer potential prognostic value, and may bring insight into patient selection for therapeutic approaches.

## **P191: Restoration of 15-Lipoxygenase 2 Induces Apoptosis and Enhances Effect of Radiation on Head and Neck Carcinoma**

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Our previous studies have demonstrated that 15-lipoxygenase 2 (15-Lox2) is significantly reduced in carcinoma cells of head and neck in vivo and in vitro, and restoration of 15-Lox2 expression results in inhibition of cell proliferation in carcinoma cells of head and neck. In this study, we further investigated if restoration of 15-Lox2 expression resulted in apoptosis and enhanced the effect of radiation on carcinoma cells of head and neck. To achieve this, we first performed transient transfection of carcinoma cells of head and neck with 15-Lox2 expression vector (pIRES-hrGFP-15lox2), and then investigated if the tumor cells developed apoptosis when compared with the tumor cells transfected with control vector (pIRES-hrGFP). We have found significant increase of the apoptotic cells containing Annexin-V fluorescence and immunoreactive Caspase 3 (apoptotic marker) in the carcinoma cells of head and neck transfected with pIRES-hrGFP-15Lox2. In addition, we subcloned the 15-Lox2 cDNA downstream a radiation inducible promoter pdelta7egr, and created a new construct called pdelta7egr-15lox2-hrGFP. Radiation induced expression and enzymatic activity of 15-Lox2 were observed in carcinoma cells of head and neck transfected with pdelta7egr-15lox2-hrGFP. Furthermore, we irradiated the carcinoma cells of head and neck containing pdelta7egr-15lox2-hrGFP with a dose of 4 Gy. Significant decrease of survival colonies was observed in the irradiated cells when compared with the control cells without irradiation. Results of this study suggest that restoration of 15-Lox2 expression results in cell apoptosis and sensitizes effect of radiotherapy on carcinoma cells of head and neck. 15-Lox2 may be important in radiation-induced gene therapy of head and neck cancer.

## **P192: The Association Between Elevated EphB4 Expression, Smoking Status, and Advanced- Staged Disease in Patients With Head and Neck Squamous Cell Carcinoma**

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**Objective:** To examine the expression of *EphB4* in cigarette-smoking and nonsmoking patients with head and neck squamous cell carcinoma (HNSCC) and to determine its role in tumor growth and metastasis, key factors associated with patient survival.

**Design:** Expression of *EphB4* was determined by Western blot, real time polymerase chain reaction, and immunohistochemical staining from fresh and archival tissues.

**Setting:** University medical center otolaryngology-head and neck surgery department.

**Patients:** Forty-eight patients were enrolled into this study with different cancer stages (I, II, III, and IV) by the staging system of the American Joint Committee on Cancer.

**Main Outcome Measure:** *EphB4* expression.

**Result:** *EphB4* expression was detected in all tumor specimens from HNSCC patients, with expression levels higher in the metastatic lymph nodes. Patients with advanced-stage disease (III or IV) showed higher *EphB4* expression compared than those with initial-stage disease (I or II). Patients who smoked showed a significantly higher expression of *EphB4* than patients who did not smoke. However, patients who drank alcohol showed no significant difference in *EphB4* expression.

**Conclusions:** Overexpression of *EphB4* is associated with advanced stages of HNSCC as well as with patients who smoke. To our knowledge, these data are the first to demonstrate the association of *EphB4* with advanced stages of disease and smoking in HNSCC and hence provide a strong rationale for targeting *EphB4* for HNSCC therapies.

### **P193: Short-Term Culture and In Vivo Modeling of Primary Head and Neck Squamous Cell Carcinoma**

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**Objective:** To develop techniques for isolation, short-term culture, and in vivo modeling of epithelial and stromal cells from head and neck squamous cell carcinoma (HNSCC).

**Design:** Xenograft model trial.

**Patients:** Specimens of HNSCC were obtained from 34 patients (20 incident, 14 persistent or recurrent).

**Interventions:** Primary HNSCC tissue was disaggregated with trypsin and collagenase 1A. Cells were seeded onto collagen IV coated tissue culture plates in keratinocyte growth media with fetal bovine serum, additives, and antibiotics. Serum was removed on day 3, and later media were switched to MEM/RPMI with fetal bovine serum. After short-term growth in culture, cells were transferred to denuded rat tracheas and implanted subcutaneously in nude mice.

**Results:** A 100-mg fragment yielded about 6 million cells that exhibited morphologic characteristics consistent with epithelial or stromal derivation. Ninety-one percent of cultures had viable cells at 10 days; 44% were maintained 30 days or longer; and 44% proliferated after passage. Preliminary data from the xenograft model revealed successful establishment of tumors in vivo from 67% of primary tumors. Immunostaining for Ku and cytokeratin confirmed human and epithelial origin, respectively.

**Conclusions:** The high success rate of these techniques indicates that selective pressures for short-term culture of HNSCC may be considerably less than for establishment of cell lines. Therefore, short-term cultures may better represent the diversity of HNSCC. The techniques permit tumor-derived epithelial and mesenchymal cells to be cultured simultaneously, which is ideal for examining tumor-stromal interactions. Preliminary data for the in vivo trachea xenograft model is promising. Once optimized, this model can be used to determine the response of a heterogeneous group of HNSCC to standard and novel therapies.

### **P194: A Systematic Review of Role of Biomarkers in Determining the Malignant Potential of Oral Dysplasia**

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**Objective:** To establish the role of biochemical and genetic markers in predicting the malignant potential of premalignant lesions of the oral cavity and oropharynx.

**Design:** Systematic literature review with set criteria for identifying studies and assessing quality of data. Studies were identified using MEDLINE, EMBASE, PubMed, Cochrane, CINAHL, and AMED. Studies were included if they assessed correlation between studied markers and histologic grade or clinical outcome.

**Main Outcome Measures:** Sensitivity, specificity, positive and negative predictive value for progression to cancer, correlation with histologic grade, and disease-free survival.

**Results:** A total of 155 articles were identified. Most commonly studied markers were those associated with enhancement of tumor growth and tumor suppression. Most studies demonstrated trends

between studied markers and either the grade of dysplasia or the development of squamous cell carcinoma. Few trends were found to be statistically significant when related to clinical outcome.

Sensitivity, specificity, and predictive values were poorly reported. Six studies demonstrated significant correlation between markers (p53, Ki67, TSP1, ST3, Bcl-2, and Bax) and dysplasia grade. Four studies of tumor markers (p53, pRb, Cyclin D1, p16, Ki67, VEGF, and Ets-1/ST3) demonstrated significance in predicting precancerous or malignant change and in disease-free survival. In a further 4 studies, DNA content and DNA ploidy was shown to be a significant predictor of future malignant behavior, but these last 4 studies should be interpreted with care.

**Conclusions:** Several markers show the potential to improve or augment the current histopathologic grading system in prediction of dysplasia and malignancy. Further prospective studies of accuracy and predictive value are needed to fully establish their role in prognostication.

### **P195: Pulmonary Carcinoma Following Head and Neck Squamous Cell Carcinoma: Differentiation of Metastasis and Second Primary Tumors Using Loss of Heterozygosity and TP53 Analysis**

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**Objective:** To differentiate distant metastasis (DM) from second primary tumors (SPTs) in patients with pulmonary carcinoma after curatively treated head and neck squamous cell carcinoma (HNSCC).

**Setting:** Ambulatory patients in an oncology referral center of institutional practice.

**Patients:** Forty-four patients with a histopathologically proven lung carcinoma.

**Interventions:** Clinical data (stage, tumor status, radiographic findings, and time interval) and histologic data were used to differentiate DM and SPTs. Loss of heterozygosity (LOH) analysis was performed using 12 microsatellite markers on 11 chromosome arms. Clonality was decided on the basis of concordant LOH of at least 2 loci. Analysis of *TP53* mutation was performed in 18 of the 44 patients.

**Results:** Clinical scoring showed 38 DMs and 6 SPTs. Histologic findings gave firm evidence in 1 case for DM and in another for SPT. The LOH analysis showed DM in 19 cases, and SPT in 24 cases. In 1 case, LOH analysis was inconclusive. For 25 patients, LOH findings supported the clinical criteria, and in 18 cases it did not. Analysis of *TP53* could differentiate in 8 cases. Five SPTs and 3 DMs were diagnosed. Six cases were diagnosed in accordance with the LOH analysis, and 2 revealed a different diagnosis.

**Conclusions:** Loss of heterozygosity analysis seems a useful tool to differentiate metastases and second primaries. A considerable number of SCC lung lesions (50% in this study), clinically interpreted as DMs, were suggested to be SPTs by LOH analysis. *TP53* mutation analysis confirms that the clinical criteria are of little use, and it shows that LOH analysis with the marker panel we now use is useful but can be further improved.

### **P196: Inhibition of Sphingosine Kinase Potentiate Radiation Therapy in Head and Neck Squamous Cell Carcinoma**

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University of Southern California, Los Angeles

**Objectives:** To examine the expression of sphingosine kinase (SPK) levels in patients with head and neck squamous cell carcinoma (HNSCC) at different clinical stages. To demonstrate that SPK inhibition leads to higher levels of ceramide in HNSCC cells, which enhances irradiation-induced apoptosis and also inhibits tumor invasion and migration.

**Design:** Expression of SPK was determined by Western blot, real-time polymerase chain reaction (RT-PCR), and immunohistochemical staining from fresh and archival tissues and HNSCC cell lines. Sphingosine kinase : 2µm[siRNA] was tested to block the tumor growth invasiveness and migration of HNSCC. Ceramide levels and effect of irradiation on tumor and normal cells were studied.

**Setting:** University Medical Center

**Patients:** Sixteen patients were enrolled in this study with different stage of cancers (stages I-IV) as graded by the American Joint Committee on Cancer staging system.

**Main Outcome Measure:** Expression of SPK.

**Results:** Higher levels of SPK expression were detected in all primary tumors and metastatic lymph nodes than were found in normal mucosa. Patients with advanced disease (stage III or IV) showed higher SPK expression than those with earlier disease stage (I or II). Four HNSCC cell lines showed high expression of SPK; SPK siRNA specifically blocked the expression of SPK and thus increased the ceramide levels. Blocking of SPK resulted in inhibition of cell growth, migration, invasion, and irradiation-induced apoptosis in a dose-dependent manner.

**Conclusions:** To our knowledge, these data are the first to demonstrate the higher expression of SPK in HNSCC than in normal mucosa. The radiation dose needed to cure HNSCC may be reduced by blocking SPK expression, which will improve quality of life for patients with HNSCC.

## **P197: Combining the Proteasome Inhibitor Bortezomib With Reirradiation in Patients With Recurrent Head and Neck Squamous Cell Carcinoma**

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**Objective:** The transcription factor nuclear factor 3BAB (NF-3BAB) promotes cell survival and radioresistance in head and neck squamous cell carcinoma (HNSCC). Our objective was to study bortezomib, a small-molecule inhibitor of proteasome activity that disrupts the degradation of inhibitor 3BAB (I3BAB) and activation of NF-3BAB, for potential cytotoxic and radiosensitizing activity in recurrent HNSCC.

**Design:** During a dose-escalation phase 1 clinical trial, clinical effects of proteasome inhibition and antitumor response were evaluated. Serial tumor biopsy specimens were collected before and 24 hours after bortezomib treatment alone, and immunohistochemical staining of p65NF-kB and other biomarkers was conducted.

**Patients:** Patients with recurrent HNSCC.

**Interventions:** Twice-weekly bortezomib administration (0.6-0.9 mg/m<sup>2</sup>) with irradiation up to 72 Gy.

**Results:** Eight of 19 patients exhibited tumor reduction of more than 30%. Variable nuclear localization of NF-3BAB was detected in 7 of 7 pretreatment biopsy specimens. Of 4 patients who underwent biopsy before and after treatment, 3 showed reduced nuclear NF-3BAB bortezomib treatment, with no change in nuclear Erk1/2 or STAT3; 1 had a dramatic tumor reduction; and 1 had stabilized disease. Two patients showed progressive disease with weak, heterogeneous NF-3BAB staining prior to treatment and no reduction of the staining after bortezomib treatment.

Increased apoptosis, decreased proliferation, and decreased expression of NF-3BAB-regulated genes were also observed in patients with tumor reductions.

**Conclusions:** Bortezomib can specifically inhibit NF-3BAB and target genes in vivo, and combined therapy with reirradiation shows evidence of clinical activity in a subset of patients with therapy-resistant HNSCC.

## **P198: Ezrin and Moesin Cytoplasmic Mislocalization as Potential Predictive Biomarkers: A Tissue Microarray Validation Study**

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**Objectives:** The band 4.1 (FERM) proteins, normally adjacent to the cytoplasmic membrane, are part of the molecular scaffolding involved in filamentous actin-based signaling modules. Another FERM protein, NF2 (merlin), has known tumor-suppressor activity. We have previously shown that FERM up-regulation is 1 of many changes seen in tumor progression. Here, our objective was to validate this by

immunohistochemical analysis (IHC) and tissue microarrays (TMAs) in a new prospective cohort.

**Design:** We constructed TMAs from patient tissue; IHC was performed with antibodies against ezrin, moesin, merlin, and willin, a newly described FERM protein.

**Patients:** Fifty-six consenting patients with primary upper aerodigestive tract squamous cell carcinoma (SCC).

**Results:** Mean  $\pm$  SD Cytoplasmic staining in primary SCC was highest for ezrin (1.7  $\pm$  0.8) vs moesin (1.0  $\pm$  0.9), merlin (1.2  $\pm$  0.6), and willin (1.3  $\pm$  0.8). Likewise, ezrin membranous staining was strongest (1.1  $\pm$  1.1) vs moesin (0.3  $\pm$  0.7), merlin (0.1  $\pm$  0.4), and willin (0.6  $\pm$  0.9). Only merlin and willin had nuclear localization. Sixteen patients developed locoregional recurrence (LRR) (median, 10 months). Strong tumor ezrin cytoplasmic localization was predictive of LRR ( $P = .02$ , log-rank test). Cytoplasmic tumor moesin expression was also predictive of LRR ( $P = .04$ , log-rank test).

**Conclusions:** Our results confirm our previous pilot data and the reports of others indicating that strong cytoplasmic mislocalization of ezrin and moesin in SCC may be predictive of LRR, and thus these markers have potential as predictive biomarkers. We continue to accrue patients and follow-up time in this study.

## **P199: Securing Negative Margins at Surgery Using Conductive Interstitial Thermal Therapy**

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**Objective:** We have developed the conductive interstitial thermal therapy (CITT) device as a means to deliver precision controlled energy to targeted tissues. Our objective was to use animal studies to demonstrate that CITT technology is a feasible adjunct to obtain negative surgical margins in head and neck cancer following primary tumor resection.

**Design:** A prototype CITT device was designed specifically for animal studies. The probe is inserted into the tumor itself and/or the excised tumor cavity. Initially, tumor ablation efficacy was assessed using the female rat model with mammary adenocarcinoma model flank tumors. Subsequently, human squamous cell carcinomas were ablated in the nude mouse model. The study consisted of 10 treated mice and 5 untreated control mice.

**Subjects:** Mice and rats.

**Interventions:** Insertion and application of the CITT device into the tumor xenografts in rodents.

**Results:** Coagulation of the tumors in the rat model was observed following CITT ablation at tissue temperature of 92°C for 15 minutes. Histologic evaluation revealed uniform deep thermal ablation of the cancer to a distance of 9 to 10 mm from the probe surface. Ablation of head and neck tumors in the mouse model using the same parameters as with the rat model resulted in uniform tumor ablation and margins.

**Conclusions:** The CITT technique effectively ablates surgical margins 9 to 10 mm beyond the resection site. Temperature control of the active probe and treatment time are essential variables to CITT technology. This CITT technology represents a promising therapeutic complement for surgical margin control in head and neck cancers.

## **P200: Global Proteomic Analysis Distinguishes Biologic Differences in Head and Neck Squamous Cell Carcinoma Cell Lines**

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**Objective:** To estimate technical variations due to protein extraction, digestion, and liquid chromatography (LC) with tandem mass spectrometry (MS) analysis and to validate this technique for proteomic analysis of head and neck squamous cell carcinoma (HNSCC).

**Design:** Proteins from 2 HNSCC cell lines, FADU and SCC-25, were isolated, cleaved with cyanobromide followed by enzymatic digestion with endoproteinase lysine and trypsin. Peptide mixtures were separated by ion exchange chromatography and analyzed using LC-MS. Extraction and digestion of proteins from each cell line was repeated 3 times, and each extract was analyzed 3 times, producing 9 data sets for each cell line. Data analysis was performed using in-house

software to build arrays with mass, retention time, and intensities. Statistical analysis was done to determine the technical and biological variations.

**Results:** Differences between the 3 replicates from each cell line reflect the technical variation. Preliminary data analysis showed that the technique is highly reproducible. As an example, nearly 100 peptides in 1 salt cut significantly differed between the 2 cell lines ( $P < .03$ ). Since multiple peptides from the same protein can be identified in each salt fraction, the 100-peptide difference could correspond to fewer than 100 proteins. These proteins can be identified by targeted MS/MS analysis of the differential peptides.

**Conclusions:** We found that LC-MS analysis is highly reproducible and can be used to study biological variations in HNSCC samples. Encouraged by the reproducibility of the methodology, we are currently testing the feasibility of LC-MS analysis to discriminate/classify HNSCC with different clinical outcomes.

## **P201: Environmental Carcinogens and Perspectives of Head and Neck Cancers**

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**Aims and Objectives:** To assess the probable cause of various carcinomas of head and neck region and investigate the Environmental risk factors and their mechanism on both disease prevalence & progression.

**Materials and Methods:** 202 cases of tumors on ear, nose, throat and neck diagnosed at Government Ear Nose and Throat Hospital, South India in the year 2004 and histologically confirmed with routine hematoxylin-eosin stain formed the subjects. Detailed information on epidemiological factors like medical history, socioeconomic status, age, sex and occupation was collected using a standard questionnaire.

Ambient air quality data from Andhra Pradesh pollution control boards publicly accessible data from their institutional web site.

**Observations and Results:** The increased incidence of head and neck cancers mostly attributed to environmental carcinogens and life style. Out of 202 cases males were 152 and 52 females. Frequency of carcinomas of tongue was more than post cricoid malignancies in females and the age of onset was early. The incidence of cancer in non-smokers is increasing suggesting the role played by environmental risk factors. Here we focus mostly on recent environmental factors that have shown the increase in levels in urban areas with the standing fact of increase in suspended particulate matter with any other known carcinogens under least consideration levels in the urban areas of Hyderabad (South India) in which the investigations have been carried out and also the anatomical incidence of the disease and the hold of correlation between two incidences. It is clearly shown that among the monitored factors of ambient air quality like NOX, SO<sub>2</sub>, that are beyond the standard levels might contribute a lot for disease prevalence or progression. The chemical nature of various constituents and their strength of carcinogenicity will be clearly focused in the presentation.

**Discussion:** Environmental risk factors along with life style aspects like smoking and occupational exposures to various potential chemicals either directly may lead to carcinogenicity or can be a common irritant which when acted upon benign tumors acts as a potential risk factor leading to malignant conversion of the area. This we can interpret through the physico chemical properties of chemical pollutants or toxins the skip of cancer cells accession to immune system which is needed to eradicate the mutated cells from the system makes the cells more prone to various small genotoxic factors which are enormous in environment We found the rise in suspended particulate matter among the ambient air quality as probable risk factor along with heavy metal like lead which we have for environmental risk assessment. We present the data of ambient air quality of present status even though we are following analysis quite a long time to discuss the present date risk assessment in our population.

## **P202: Tonsil cell immortalization requires HPV16 E6 and E7: The PDZ binding motif of E6 is required for efficient immortalization**

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Human papilloma virus plays a key role in the malignant transformation of tonsil epithelial cells. In order to better understand what role HPV plays in this multi-step process we have used normal tonsil cells isolated from non-diseased patients and expressed the HPV viral oncogenes to understand what viral genes are required for immortalization, which is a key component of carcinogenic transformation. These studies have increased understanding regarding HPV related HNSCC by providing the following evidence: 1) Although E7 slightly extends growth in culture, both E6 and E7 are required for tonsillar epithelial immortalization, 2) E6 efficiently degrades the cellular protein p53 and activates telomerase, 3) the PDZ c-terminal binding tail is required to efficiently immortalize tonsillar cells, and E7 degrades Rb in tonsil cells. The findings from these studies indicate that both HPV16 E6 and E7 are required for the immortalization of tonsil epithelial cells. They also strongly suggest that a mechanism related to the E6 PDZ motif plays a significant role in the transformation. Identification of the specific pathways affected by E6's interaction with PDZ containing proteins will further our understanding of how HPV causes HNSCC and provide potential targets for therapeutic intervention.

## **P203: WITHDRAWN**

## **P204: Expression of Cancer Testis Antigens in Head and Neck Cancers**

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Tumor-associated antigens (TAAs) have been shown to selectively stimulate antigen specific cytotoxic T cells, making them attractive targets for immunotherapy. Cancer-testis antigens (CTAs) are TAA comprising several families of genes, among which NY-ESO-1, MAGE-A and SSX families are the best studied. These antigens have been shown to generate potent immune responses and have been used in several vaccination trials, notably in melanoma. Profiling of TAAs expression and identification of specific tumor infiltrating lymphocytes (TILs) represent the first steps towards immunization protocols. The aim of our study was to determine the level of CTA expression of 12 CTA and 3 additional TAA (Prame, Herv-K-Mel, NA-17) in a panel of head and neck squamous cell carcinomas (HNSCC) from different sites in the upper aerodigestive tract. From December 2004 to December 2005, 46 fresh tumor specimens and 10 specimens from normal mucosa were collected from 41 previously untreated patients, presenting with HNSCC at the Otolaryngology and Head and Neck department of Lausanne University Hospital, Switzerland. Primary site, differentiation and staging of the tumor were prospectively recorded in an electronic database. Specimens collected during surgery were analysed using reverse transcriptase polymerase chain reaction (RT-PCR). Specific primers for 15 CTAs were used on each sample. Expression at the protein level of the most frequently expressed antigens was confirmed by immunohistochemistry (IH). Eighty nine percent of tumors expressed at least 1 of the 15 TAA tested and 34/46 (74%) of the tumors expressed ?? 3 antigens. MAGE-A3, -A4, Prame, NA17 and Herv-K-Mel were the most frequently expressed antigens. MAGE-A4 and/or MAGE-A3 were expressed in (34/46) 74% of the tumors regardless of the primary site. The PCR expression of MAGE-A antigens correlated with strong tissue immunostaining. Level of expression of CTAs did not appear to be influenced by primary site, tumor grade or clinical staging of the primary. In conclusion CTAs are frequently expressed in HNSCC. MAGE-A4 and/or MAGE-A3 are present at the protein level in over 70% of tumors regardless of the primary site. Clinical and histopathological characteristics of the tumor do not influence CTAs expression. Ongoing studies will determine whether CTA positive tumors can induce antigen specific immune responses both among circulating and tumor infiltrating T lymphocytes. All together this report suggests that MAGE-A4 and MAGE-A3 may be promising candidates for specific immune therapy in HNSCC.

## **P205: Alteration of Methylation Profiles for Multiple Tumor Suppressor Gene Promoters in Salivary Gland Tumors**

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**Objective:** Salivary gland tumors (SGTs) are relatively rare and diverse tumor population, comprising 5% of all head and neck tumors. Promoter methylation of CpG islands is a common epigenetic mechanism of tumor suppressor gene (TSG) transcriptional silencing in head and neck cancers, though few studies address this phenomenon in SGTs. Methylation profiling of TSGs is quickly becoming a powerful diagnostic tool for the early detection, prognosis, and even prediction of clinical response to treatment of various cancers. Promoter methylation profile of various TSGs in primary SGT tissue was therefore assessed to determine if tumor-specific alterations could be detected.

**Methods:** DNA from twenty-five tumor and five normal (parotid gland) specimens were obtained. Tumor samples included 11 adenoid cystic carcinomas, 4 mucoepidermoid carcinomas, 3 acinic cell carcinomas, 2 adenocarcinomas, and 5 pleomorphic adenomas. Promoter methylation profiles of 20 TSGs in tumor tissue were determined by fluorescence-based quantitative methylation-specific PCR (qMSP) and compared to normal salivary tissue.

**Results:** Methylation of the RASSF1A, RAR-3B2, THBS1, 3B2-catenin, MINT1, MINT31, and DAPK TSGs were found exclusively in the tumor tissue, with an incidence of 68%, 24%, 20%, 12%, 12%, 8% and 4%, respectively. Promoter methylation profiles for TSGs PGP9.5, DAPK, p16, DCC, APC, TGF-3B2, CyclinD2, CyclinA1, TIMP3, HIC1, MLH1, GSTP1, Stratifin/14-3-3 did not show significant differences between tumor and normal tissues. Of note, 9/11 (82%) of adenoid cystic carcinomas demonstrated methylation of RASSF1A.

**Conclusions:** Screening promoter methylation profiles of twenty TSGs in SGTs showed considerable heterogeneity. RASSF1A, RAR-3B2, THBS1, 3B2-catenin, MINT1, MINT31, and DAPK methylation appear to be particularly important in identifying SGTs and could potentially contribute to salivary gland carcinogenesis. Further study is needed to evaluate their possible use in detection, prognosis, and therapeutic outcome of these relatively rare tumors.

## **P206: Selection of Irrigation Fluid to Eradicate Free Cancer Cells During Head and Neck Cancer Surgery**

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**Objective:** To assess the growth inhibitory activity of various intraoperative irrigation fluids on free squamous cell cancer (SCC) cells in an animal wound model simulating head and neck cancer surgery.

**Design:** Animal study with a cancer cell-contaminated wound model and in vitro tumor growth assay.

**Subjects:** C3H/HeJ mice and syngeneic SCC VII cells.

**Interventions:** After seeding 1 million SCC VII cells at each wound, we incubated the cells in situ for 30 minutes. The wounds were irrigated for 5 minutes with 5 different fluids: distilled water, 5% betadine (povidone-iodine) solution, 3.2% hydrogen peroxide, isotonic sodium chloride (normal saline), and cisplatin. Tumor growth and wound healing were observed. Assays using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were performed to examine tumor growth inhibition in vitro with different concentrations and exposure times of betadine solution and distilled water.

**Results:** In the animal study, betadine solution significantly inhibited tumor growth at the cancer cell-contaminated wound. Hydrogen peroxide caused 3 mortalities out of 5 mice, but other solutions did not cause any mortality or wound problem. In the MTT assay, betadine solution showed significant growth-inhibitory effect at the concentration of 0.05%. Even 30 seconds of exposure to 1% betadine solution showed significant growth inhibition. These results are comparable to the effect of distilled water at the concentration of 50% (ie, half strength isotonic culture solution), and 5 minutes of exposure to 100% distilled water.

**Conclusion:** Betadine solution should be selected preferentially for irrigation fluid during head and neck cancer surgery.

## **P207: The Efficacy of Perioperative Aspirin in the Survival of Rat Microvascular Free Flap Following Preatomotic Injury**

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**Objective:** Antiplatelet and antithrombotic therapy have been widely used in microvascular free tissue transfer to reduce the risk of anastomotic failure and improve patency rates, especially in cases of perioperative trauma or vascular malpositioning. Our objective was to investigate the effect of preoperative aspirin administration on improving patency of microvascular anastomosis after a crush injury to the vascular pedicle.

**Design:** A randomized, placebo-controlled animal study.

**Subjects:** Twenty-eight male Sprague-Dawley rats were randomized into 1 of 2 groups: control group (n = 15) or aspirin group (n = 13).

**Interventions:** All rats received either placebo or aspirin by mouth 1 hour prior to surgery. A groin/abdominal free flap based on the femoral artery was elevated, with division of the artery, followed by a microvascular anastomosis. A crush injury to the vascular pedicle was simulated by clamping the femoral artery proximal to anastomosis. Flaps were monitored visually, and on the seventh postoperative day, the viability of the skin flap was evaluated, the flap elevated, and the patency of the microvascular anastomosis assessed by an investigator who was blinded regarding the treatment arm.

**Results:** Six (40%) of 15 microvascular anastomoses were thrombosed in the placebo group vs 3 (23%) of 13 in the aspirin group ( $P = .42$ ). There were 3 and 2 skin-flap necroses, respectively, in the placebo and aspirin groups.

**Conclusions:** In the animal model, preoperative aspirin administration did not significantly improve arterial anastomotic patency after an intraoperative vascular injury. There was a trend toward greater thrombosis in the placebo group.

## **P208: A Molecular Study of Recurrent Respiratory Papillomatosis Undergoing Malignant Transformation**

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**Objective:** Malignant transformation of recurrent respiratory papillomatosis (RRP) is a very rare event. The disease in these patients shows a spectrum of morphologically discrete areas from papilloma to carcinoma. The aim of this study was to assess alterations in expression of human papillomavirus (HPV) types and molecular genetic markers in each distinct focus of papilloma and carcinoma.

**Design:** Morphologically distinct areas in pathology specimens were diagnosed as papilloma, dysplasia, and carcinoma. Using the laser capture microdissection technique, we separately obtained lesions within each specimen, and these were amplified by polymerase chain reaction to check for the presence of HPV. A DNA chip was used to determine the type of HPV in each area. Immunohistochemical analysis for p53, Ki-67, and pRb was performed.

**Patients:** Three patients who underwent malignant transformation from RRP to carcinoma.

**Results:** The clinical courses of the patients were very different from one another. In all HPV-positive specimens, HPV-6 was present, and areas of coinfection with HPV-11 and HPV-16, respectively, were also found. Expression of p53 and Ki-67 increased with increasing severity of dysplastic change, whereas that of pRb showed no definite pattern of immunoreactivity.

**Conclusions:** Unlike in other reports, we found that HPV-6 may potentially promote malignant transformation in RRP. Superinfection with HPV-11 may be associated with aggressive behavior. Alteration in molecular genetic markers such as p53 may be a subsequent event in progression from benign papillomatosis to cancer.

## P209: Genetic Profiling of Oral Carcinomas and Surgical Resection Margins

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**Objective:** To determine the global gene expression signatures of oral squamous cell carcinomas (OSCCs) and histologically normal surgical resection margins.

**Design:** We used the Human U133A GeneChip arrays (Affymetrix, Santa Clara, Calif), containing over 22 000 oligonucleotide sequences. Fluorescent intensities were normalized and subjected to the Binary Structured Vector

Quantization method. Pathway analysis was performed using the Online Prediction Human Interaction Database to identify biologically relevant genetic networks. Deregulated gene expression was validated using quantitative real-time reverse- transcriptase polymerase chain reaction (QRT-PCR).

**Subjects:** Thirty-seven patients with OSCC who had surgery as primary treatment and with histologically negative margins were included in this study. Twenty-four samples (OSCCs, histologically normal resection margins, and distant normal oral mucosa) from 5 patients were analyzed by microarrays; 235 samples from 37 patients were used for validation.

**Results:** Microarray analysis revealed that some histologically normal resection margins clustered together with their corresponding tumors, indicating similar genetic profiles. A subset of 83 genes was commonly altered in tumors and margins. Pathway analysis revealed genes involved in important genetic mechanisms such as cell growth, adhesion, DNA damage, and cell death. Deregulated expression of 12 genes was validated using QRT-PCR. We showed that histologically normal resection margins and OSCCs share common genetic changes.

**Conclusions:** Our data indicate that histologically normal resection margins contain genetic alterations common to their corresponding tumors and may thus be involved in tumorigenesis, leading to recurrence. Such genes can be used, together with histopathologic analysis, to improve assessment of margin status, ultimately improving treatment and outcome.

## P210: Cancer-Supporting Factors Consistently Induced by Lipopolysaccharide-Squamous Cell Carcinoma- Monocyte Interactions

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**Objective:** Head and neck squamous cell carcinomas (HNSCCs) often inadequately differentiate and ulcerate, suggesting that surface microbial products may affect HNSCC pathogenesis. Monocyte-lineage cells (MCs) infiltrate HNSCC. Lipopolysaccharide (LPS) induces MCs to secrete interleukin (IL) 6, a STAT3-activating, vascular endothelial growth factor (VEGF) inducing cancer-supporting factor, and both MCs and IL-6 are associated with HNSCC progression. Our objective was to characterize carcinoma cell-supporting outcomes of LPS-HNSCC- monocyte interactions.

**Design:** Early-stage HNSCCs were evaluated by immunohistochemical analysis for MC (CD68/CD1a). Normal monocytes, enriched using RosetteSep (StemCell Technologies, London, England) and plastic adherence, were cultured with 5 HNSCC lines, normal or telomerase-immortalized keratinocytes, and with and without LPS. Secreted IL-6, tumor necrosis factor  $\alpha$ , VEGF, and chemokines CXCL8, CCL2, and CCL20 were measured by enzyme-linked immunosorbent assay or multiplex. Monocyte phenotype and HNSCC expression of LPS receptors CD14 and toll-like receptor 4 were determined by flow cytometry. Y705-STAT3 phosphorylation in HNSCC in response to LPS and LPS-induced factors was measured by Western blotting.

**Results:** Specimens of HNSCC contained significantly more MC than mucositis without HNSCC. Head and neck squamous cell carcinoma lines varied in constitutive cytokine and/or chemokine production and were TLR4 positive and CD14 positive and negative. In some lines, LPS enhanced CXCL8, CCL2 and/or CCL20, IL-6, and/or VEGF secretion. Similarly, HNSCC-monocyte interactions without LPS stim-

ulated IL-6 and VEGF occasionally, while LPS-HNSCC-monocyte interactions were always stimulatory. Constitutive phosphorylated Y705-STAT3 in HNSCC lines was uncommon and/or weak. Head and neck squamous cell carcinoma lines producing little to no IL-6 phosphorylated Y705-STAT3 in response to IL-6. While few unstimulated HNSCC lines constitutively secreted STAT3-activating factors, supernatants from LPS-monocyte-HNSCC cocultures consistently and strongly activated STAT3 in all cell lines, in part due to IL-6.

**Conclusion:** In monocyte-associated HNSCC, LPS consistently and strongly induces cancer-supporting factors, which in turn activate HNSCC-cell STAT3.

## P211: Salvage Neck Dissection in the Era of Combined Treatment Techniques for Head and Neck Cancer

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**Objective:** Nonsurgical therapy has become a mainstay in the treatment of head and neck squamous cell carcinoma (HNSCC). Despite excellent response rates of the primary tumor to chemoradiotherapy, there is a subgroup of patients with persistent cervical lymphadenopathy requiring salvage neck dissection (SND). Currently, there is no consensus regarding the need for further therapy for patients whose SND specimens reveal active disease. Our objective was to investigate the outcomes of patients undergoing SND following definitive chemoradiation for HNSCC.

**Design:** Retrospective review.

**Setting:** Tertiary care academic center.

**Patients:** Patients with a diagnosis of HNSCC who received nonsurgical therapy were included. Hospital records were reviewed to identify patients with persistent cervical lymphadenopathy requiring SND.

**Main Outcome Measures:** Primary tumor site, pretreatment stage, treatment technique, histopathologic characteristics of the neck specimen, and overall outcomes were recorded.

**Results:** of the 147 patients who received nonsurgical therapy for HNSCC, 21 required posttreatment SND for incomplete response in the neck. A significantly greater proportion of patients with pretreatment N3 disease required SND. Histopathologic review revealed viable SCC in 4 of 21 specimens from patients with posttreatment clinically pathologic nodes. Seventeen of 21 patients were free of disease at the last follow-up. There was no statistically significant difference between the patients with viable carcinoma in the SND specimen and those without.

**Conclusions:** Eighteen percent of pretreatment N-positive patients receiving nonsurgical therapy for HNSCC required SND in our patient population, but 44% of patients with pretreatment N3 neck disease required SND. Although 19% of specimens contained active disease at the time of SND, this finding had no significant effect on disease outcome.

## P212: Impact of Preoperative Radiation Therapy on Wound Complications Following Total Laryngectomy: The Dartmouth Experience

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**Objective:** To determine the impact of preoperative radiotherapy on the incidence and severity of wound complications following total laryngectomy.

**Design:** Retrospective cohort.

**Setting:** Tertiary academic center.

**Patients:** Consecutive sample of patients undergoing radiotherapy prior to total laryngectomy for squamous cell carcinoma from 1990 to 2005 at Dartmouth-Hitchcock Medical Center.

**Intervention:** Radiotherapy prior to total laryngectomy for squamous cell carcinoma.

**Main Outcome Measures:** Incidence of wound complications, days to onset and resolution, and need for operative management.

**Results:** Ninety patients were identified, and 34 had preoperative radiotherapy. Thirty-one patients experienced 1 or more wound complications, including pharyngocutaneous fistula ( $n = 19$ ), wound dehiscence ( $n = 12$ ), wound infection ( $n = 12$ ), tissue necrosis ( $n = 4$ ), flap necrosis ( $n = 2$ ), and flap failure (2). Preoperative radiotherapy was associated with an increased odds ratio (OR) for development of any wound complication (OR, 2.5; 95% confidence interval [CI], 1.0-6.1) ( $P = .05$ ), wound dehiscence (OR, 4.0; 95% CI, 1.1-14.5) ( $P = .04$ ), and fistula (OR, 2.2; 95%

CI, 0.8-6.2). Preoperative radiotherapy was not associated with a difference in onset, duration, or management of complications. There was no difference in the mean number of days to fistula formation (21 days with preoperative radiotherapy vs 17 days without;  $P = .50$ ), resolution (82 vs 278 days;  $P = .20$ ), or need for operative management (OR, 3.4; 95% CI, 0.3-40.1).

**Conclusions:** This study supports the finding that patients with a history of radiotherapy to the head and neck are at greater risk of developing perioperative wound complications, but it does not demonstrate a difference in the severity of complications.

## **P213: A Retrospective Study of Voice Prosthesis Use Among Patients Undergoing Tracheoesophageal Puncture for Voice Restoration**

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**Objective:** The development of voice prostheses (v.p.) and tracheoesophageal speech has improved immensely over time. Yet, many potential complications remain. These complications can be broken down into patient-related issues (Leder, 1995) such as recurrent disease or patient care of the v.p., and prosthesis-related issues (Makitie, 2003), such as rapid valve deterioration or sizing of the v.p. One means for limiting patient-related issues was the development of clinician-inserted v.p.s, thereby reducing patient responsibility for v.p. care. This approach placed a heavy emphasis on prosthesis-related issues. The purpose of this study was to investigate prosthesis usage in the first two years of recovery by patients using either patient-inserted or clinician-inserted devices to identify trends in such factors as useful v.p. life, or the need for resizing the tract for correct v.p. length.

**Methods:** The study is a records review of patients undergoing tracheoesophageal puncture (TEP) for voice restoration for the years 2003-2005 at The Ohio State University James Cancer Hospital and Solove Research Institute. Initial TEPs were completed during the laryngectomy. In 2004 use of a clinician-inserted v.p. became more common at the institution, permitting a comparison between patient and clinician-inserted devices. Data was accrued for each patient for a period of two years.

**Results:** Of the 38 patients initially accrued, only 11 (6 males, 5 females) could be tracked for the entire first two years of their recovery. The most evident trend was the change in v.p. length in the first year vs. the almost absent change in length in the second year. For the 38 patients in the first year, the initial v.p. length averaged 14.6 mm, declining to 11.01 mm. by the end of the year. For the 11 patients followed for the second year, v.p. length averaged 9.64 mm. at the start of the second year and declined to 9.09 mm.

A second trend was for short v.p. useful life. For the 11 patients, in the first 12 months, the patient-inserted devices (most often InHealth Low Pressure) averaged 47 days, as opposed to 113 days for clinician-inserted devices (most often Provox 2). In the second year, v.p. useful life increased for the patient-inserted v.p. to 75 days on average, while the useful life of the clinician-inserted devices declined to an average of 91 days.

**Conclusions:** 1. Given the cost difference between the patient-inserted (Low Pressure \$47) and the clinician-inserted (Provox 2 \$190) devices, and the relatively small difference in useful life, there was no cost benefit based on extended v.p. life in the use of the more expensive clinician-inserted devices. This conclusion is especially true in the second year of recovery. 2. Appropriate v.p. length is highly likely to change (get shorter) in the first year of recovery; therefore careful monitoring of the patient for this change is necessary. This need for careful monitoring for v.p. fit, is less in the second year.

## **P214: Olfactory Neuroblastoma: A Long-Term Clinical Outcome in a Single Institute Between 1979 and 2003**

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Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

**Objective:** Olfactory neuroblastoma is a relatively rare malignant neoplasm which arises from nasal and paranasal cavity. Anterior skull base surgery followed by postoperative radiotherapy has been considered to be the standard treatment for olfactory neuroblastoma. Meanwhile, in recent years, some have suggested less invasive techniques like craniobasal resection as alternative surgical procedures. However, a criterion for these surgical indications is not established yet. Moreover, mainly due to its slowly progressive tendency and its rarity, the long-term prognosis of olfactory neuroblastoma is not well documented and remains still unclear.

**Methods:** Out of 17 patients who were seen at our institute between 1979 and 2003 with a diagnosis of olfactory neuroblastoma, 12 patients (7 men and 5 women) received primary curative treatment. Age of these patients ranged from 25 to 73 years old (average 52.6 years old). Follow-up period was 6 to 306 months (average 98.7 months). 11 out of 12 patients underwent surgery, usually combined with radiotherapy and/or chemotherapy. Anterior skull base surgery was given to 6 patients as an initial treatment and to 8 patients through overall follow-up period. Concomitant chemo-radiotherapy was given to a patient whose disease was confined to his sphenoid sinus.

**Results:** Cause-specific 5-year and 10-year survival rates were both 64.8%, recurrence free 5-year and 10-year survival rates were 47.6% and 28.6% respectively. Of 12 patients in this series, 8 (66.7%) had recurred diseases (local recurrence 6 cases, regional recurrence 1 case, distant metastasis 1 case). Duration from initial treatment to first sign of recurrence was 6 to 78 months (average 39.1 months). All the recurrent cases were given surgical treatments as salvage therapy, including 2 patients who underwent multiple skull base surgeries.

**Conclusions:** It is noted that the progression of this disease had a biphasic pattern. Four patients who had developed recurrences within 15 months after initial treatment died of disease within 30 months after initial treatment, while, in the rest of this series, recurrences happened 40 months or later and all these patients have long survived with or without the evidence of disease at present. We have not found any factors which distinguish this rapid growth group from the long survivors, including histopathological findings. The fact that the local recurrences were seen in half of our patients supports that less invasive surgery should be deliberately considered only for those with Kadish A type whose tumors are well localized in nasal cavity.

## **P215: Systematic Review of Primary Treatment Techniques in Oropharyngeal Cancer**

J.R. Harris; **C. Diamond;** R. Hart; P. Dziegielewski; H. Seikaly

University of Alberta, Edmonton

**Objectives:** To assess and summarize the best available evidence for primary treatment techniques used for curative intent in oropharyngeal cancer.

**Data Sources:** Comprehensive electronic searches were conducted on the databases of MEDLINE, EMBASE, PASCAL, and the Cochrane Central Register of Controlled Trials.

**Study Selection:** All generated titles were reviewed independently by 2 authors, followed by independent abstract review. Each potentially relevant complete article was then independently assessed for inclusion by 2 authors. Only randomized trials and systematic reviews were included. Patients with oropharyngeal cancer of any stage being treated with curative intent were considered. Primary treatment modalities including surgery or organ preservation protocols were considered.

**Data Extraction:** Data from included studies were extracted independently by 2 authors. Discrepancies were adjudicated by committee. Quality assessment including sensitivity analysis was performed. Studies were assessed for heterogeneity and publication bias.

**Data Synthesis:** A total of 4450 titles were generated. Outcomes from studies assessing primary surgical resection or organ preservation therapy are summarized. Results on overall survival, disease-free survival, and locoregional control are presented. There are currently

no published randomized trials designed to directly compare primary surgical therapy with organ preservation therapy.

**Conclusions:** The optimal primary treatment technique for advanced oropharyngeal cancer remains controversial. Both primary surgical resection and organ preservation therapy with various protocols have been used successfully in treating this disease with curative intent. Although several studies have compared neoadjuvant, adjuvant, and concomitant treatments, no trials currently exist directly comparing primary surgery to organ preservation treatments.

## **P216: A Comparison of Drain vs No Drain Thyroidectomy: A Randomized Prospective Clinical Trial**

J.R. Harris<sup>1</sup>; **A.T. Morrissey**<sup>1</sup>; J. Chau<sup>1</sup>; W. Yunker<sup>2</sup>; B. Mechor<sup>1</sup>; H. Seikaly<sup>1</sup>

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**Objective:** To evaluate the use of surgical drains in thyroid surgery.

**Design:** Randomized, prospective, clinical trial; with cost analysis.

**Setting:** Tertiary-care referral center.

**Patients:** Fifty-five patients were enrolled in the study. They were randomized by a blinded observer into drain and no-drain groups. Inclusion criteria included all patients presenting for total thyroidectomy, hemithyroidectomy, or completion thyroidectomy. Those with massive goiters, or nodules larger than 6 cm were excluded.

**Intervention:** The use of a closed suction drain vs no drain.

**Main Outcome Measure:** Length of hospital stay.

**Results:** In the no-drain group, there was a 1.12-day reduction in hospital stay ( $P < .01$ ), with no increase in postoperative complications. This translated into a cost savings of \$2177 per patient.

**Conclusions:** Thyroid surgery without the use of a drain decreases length of hospital stay with no increase in patient morbidity. Overall cost is significantly reduced.

## **P217: Retrospective Analysis of the Utility of a Low-Profile Locking Plate System in Major Head and Neck Reconstruction**

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Medical University of South Carolina, Charleston

**Objective:** To assess outcomes of patients undergoing reconstructive procedures following major cancer-related ablative surgical procedures using a low-profile titanium locking-plate system.

**Design:** Retrospective review, January 1, 2001 to December 31, 2005.

**Setting:** Academic tertiary referral center.

**Patients:** Sixty patients: 37 male, 23 female (age range, 2.5 to 85 years), who underwent major reconstruction of the maxilla and/or mandible to treat malignant disease ( $n = 54$ ), osteoradionecrosis ( $n = 3$ ), or benign neoplasms ( $n = 3$ ).

Preoperative chemotherapy or radiotherapy was used in 17% and 32% of patients, respectively, while 15% received adjuvant chemotherapy and 45% received adjuvant irradiation.

**Interventions:** Major ablative surgery of the maxilla or mandible followed by reconstruction with 2.0-mm titanium locking plate and either osteocutaneous free flap (77%), free soft tissue flap (18%), locoregional flap (8%) or alloplastic implant (5%).

**Main Outcome Measures:** Determine incidence and types of complications relative to adjuvant therapies, type of flap, comorbidities, and earlier reports of larger plating systems.

**Results:** Plate exposure was observed in 12 patients (20%); 5 plates (8%) required removal. Plate removal secondary to plate fracture occurred in 1 case, and persistent plate exposure with associated infection in the remaining 4 cases. Two patients died, and 4 patients developed recurrent disease during the follow-up period. Forty-six patients (77%) had intact plates without any complications at the time of their last follow-up.

**Conclusions:** Reconstruction of bony defects of the maxilla and mandible following major ablative cancer surgery can be successfully

done using a combination of 2.0-mm titanium locking plate and vascularized soft tissue coverage.

## **P218: Immunohistochemical Expression of Fatty Acid Synthase and ERBB2 in Oral Squamous Cell Carcinoma**

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**Background:** Several human epithelial cancers, particularly those with poor prognosis, express high levels of fatty acid synthase (FAS), a key metabolic enzyme linked to the synthesis of membrane phospholipids in cancer cells. This study investigates whether FAS immunohistochemical expression is correlated with the clinicopathological characteristics and evaluated the relationship between FAS, Ki-67 and ErbB2 immunohistochemistry staining in oral squamous cell carcinoma (OSCC).

**Methods:** Were included in this study 40 patients with OSCC from the Hospital do Cancer A.C. Camargo, São Paulo, Brazil. Clinical informations were obtained from the medical records and all histopathologic diagnosis were reviewed. Paraffin-embedded tissues were immunohistochemically analyzed for FAS, ErbB2 and Ki-67 positivity. FAS and ErbB2 (cytoplasmic and cell surface) positivity was defined as none (0), low (1), and high (2).

**Results:** Our study showed a strong positive correlation between FAS and ErbB2 expression in OSCC samples. ErbB2 was observed in the cytoplasm or at the cell membrane and both were associated with high FAS expression ( $p = 0.024$  and  $p < 0.0001$ , respectively). Microscopic characteristics as lymphatic permeation ( $p = 0.035$ ), nodal metastasis ( $p = 0.039$ ) and thickness of invasion ( $p = 0.006$ ) were associated with FAS status. Additionally, FAS, ErbB2 and Ki-67 were significantly associated with a higher risk of recurrence because it predicted both disease free survival (log-rank test,  $p = 0.0011$ ,  $p = 0.0056$  and  $p < 0.00001$ , respectively) and overall survival (log-rank test,  $p = 0.0062$ ,  $p = 0.0005$  and  $p = 0.0004$ , respectively).

**Conclusion:** These data suggest that the expression of FAS, ErbB2 and Ki-67 are associated in OSCC and may have a role in tumor progression and prognosis.

## **P219: Health-Related Quality of Life in Head and Neck Cancer: A Review of Patient-Reported Outcome Measures**

A.L. Pusic<sup>1</sup>; **J. Liu**<sup>1</sup>; C.M. Chen<sup>1</sup>; S. Cano<sup>2</sup>; K. Davridge<sup>3</sup>; A. Klassen<sup>3</sup>; R. Branski<sup>1</sup>; S. Patel<sup>1</sup>; D. Kraus<sup>1</sup>; P.G. Cordeiro<sup>1</sup>

<sup>1</sup>Memorial Sloan-Kettering Cancer Center, New York, NY; <sup>2</sup>University College London, London, England; <sup>3</sup>University of British Columbia, Vancouver

**Objective:** The primary objective of this review is to evaluate disease-specific patient-reported outcome questionnaires for use in head and neck oncology surgery. It identifies available instruments, examines their development and validation process, summarizes content, and identifies directions for future research.

**Data Sources:** A systematic review of the English-language literature was performed using the following keywords: Science Citation Index/Social Sciences Citation Index, and PsychINFO.

**Study Selection:** Articles describing instrument development and validation were identified. Measures not developed and/or validated in patients undergoing head and neck cancer surgery were excluded. After applying inclusion and exclusion criteria, we identified 14 questionnaires.

**Data Extraction:** With regard to development, 4 questionnaires were created from expert opinion alone or did not have a published development process. Seven questionnaires lacked formal item reduction.

**Data Synthesis:** Three questionnaires (European Organization for Research and Treatment of Cancer, Head and Neck Module [EORTC H&N 35], Head and Neck Quality of Life Questionnaire—University of Michigan [HNQOLQ], and Head and Neck Cancer Inventory [HNCI]) fulfilled guidelines for instrument development and validation as outlined by the Scientific Advisory Committee of the Medical Outcomes Trust.

**Conclusions:** Rigorous instrument development is important for creating valid, reliable, and responsive disease-specific questionnaires. Three instruments were noted to be particularly robust with respect

to their development and validation. As a direction for future research, alternative methods of psychometric data analysis, such as Rasch, have the potential to improve the value of health measurement in clinical practice.

## **P220: Transfusion as a Predictor of Recurrence and Survival in Head and Neck Cancer Surgery**

H. Seikaly; **J. Chau**; J. R. Harris  
University of Alberta, Edmonton

**Objective:** To determine whether perioperative transfusion of leukocyte-depleted blood is a predictor of recurrence and survival in patients with head and neck cancer.

**Design:** Retrospective case series.

**Setting:** Tertiary referral teaching center.

**Patients:** Patients undergoing head and neck surgery for malignant disease between October 1996 and October 2002.

**Intervention:** Demographic and clinical information was obtained from hospital, blood bank, and cancer registry databases and recorded onto a standardized computer spreadsheet.

**Main Outcome Measures:** The primary outcome variable was the number of units of allogeneic leukocyte-depleted blood transfused perioperatively. Multivariate analysis and logistic regression methods were used to determine whether significant associations existed between perioperative transfusion and second primary cancers, recurrence, and survival.

**Results:** Six hundred forty-seven patients met the criteria for inclusion in the study. Analysis showed significant associations between perioperative transfusion, recurrence, and survival.

**Conclusion:** Perioperative transfusion of leukocyte-depleted blood is associated with higher recurrence rates and decreased survival in patients with head and neck cancer.

## **P221: Knowledge of Head and Neck Cancer Among Medical Students at 2 Chicago, IL, Universities**

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**Objectives:** To assessing the knowledge of medical students regarding head and neck cancer (HNC) risk factors, signs, symptoms, and frequency; to evaluate oral screening recommendations, physical examination techniques, and medical school curriculum.

**Design:** Cohort study using a survey questionnaire.

**Setting:** Two metropolitan-area medical schools.

**Participants:** Of the 601 total students in the 2 M1 and M4 classes, 304 responded to the online questionnaire.

**Results:** The response rate was 51% (160 M1s and 144 M4s). Of the M4s, 96% identified voice changes, difficulty chewing and/or swallowing, lump in the neck, smoking, and chewing tobacco to be associated with HNC, compared with 66% of M1s. Furthermore, 88% and 83% of the M4s knew the risk factors of nonhealing oral sores and alcohol, respectively, compared with 24% and 41% of the M1s. Findings were significant between classes but not universities. Squamous cell carcinoma was chosen as the most common subtype by 126 M4s but only 44 M1s. Fewer than 50% of the students knew the oral screening recommendations. Most M4s believed that they examined the head and neck routinely, but most did not palpate the oral cavity. Seventy percent of the M4s reported having a lecture about HNC, while 66% had taken care of a patient with HNC.

**Conclusions:** The M4s compared with the M1s had a statistically significant greater knowledge level about HNC. Nonetheless, a deficiency remains regarding certain risk factors, oral screening guidelines, head and neck examination techniques, and medical school curriculum. Further efforts should be aimed at expanding HNC education for medical students.

## **P222: Functional Outcomes of Primary Reconstruction of Maxillary Defects**

**H. Seikaly**; J. Rieger; R. Hart; J. Wolfaardt; J.R. Harris  
University of Alberta, Edmonton

**Objective:** To evaluate the functional and cosmetic outcomes of patients who have undergone primary reconstruction of maxillary defects with a combination of fibular and forearm free flaps.

**Design:** Prospective case series.

**Setting:** Tertiary referral teaching center.

**Patients:** Fourteen patients who had undergone maxillectomy and primary reconstruction.

**Intervention:** Patients had their maxillectomy defects reconstructed with a combination of free fibular and forearm flaps.

**Main Outcome Measures:** Acoustical, aeromechanical, and perceptual speech data and modified barium swallow data were gathered at 3 evaluation times (preoperatively and before and after radiation therapy). Studio portraits were obtained preoperatively and 1 year postoperatively. All portraits were reviewed by naïve observers and rated.

**Results:** All reconstructions used a combination of fibular and forearm free flaps. There was no significant difference in the: 3jm[VPO], nasalance, or word intelligibility measurements at any of the 3 evaluation times. Swallowing evaluation showed aspiration events at any time interval. None of the patients had gastrostomy tubes. Eleven patients maintained their preoperative diet, while 1 patient tolerated a soft diet. Cosmetic assessment revealed that all patients had an excellent outcome.

**Conclusions:** Primary free-flap reconstruction of maxillary defects is an excellent option in selected patients.

## **P223: Distribution of Flow Cytometric Content in Non-Diploid Cell Populations Differ Between Glottic and Supraglottic Cancer**

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The exposure for carcinogens differ between glottic and supraglottic regions of the larynx. The supraglottic region is exposed to food, drink and saliva while the glottic is exposed to air and smoke. Is this difference reflected in the distribution of the DNA content, i.e. the DNA index (DI) in the tumour cell populations?

**Material and Methods:** Tissue samples from 36 glottic and 32 supraglottic squamous cell carcinomas (SCC) were analyzed with flow cytometry (FCM). We used a multi-step preparation technique including RNase and pepsin. The nuclei were dyed with propidium iodide. Tumours consisting of a single cell population in regard of DNA content were classified as diploid (DI=1,0), tumours with two or more populations as non-diploid (DI >1,0).

**Results:** 29 per cent of the tumours were diploid and 71% non-diploid. There was no difference in the distribution of diploid and non-diploid tumours between glottic and supraglottic SCC. When the distribution of non-diploid DNA indices between glottic and supraglottic SCC were compared, the DI values for glottic SCC: s aggregated in the tetraploid region (median DI=1,90) while the values for the supraglottic were lower (median DI=1,57). This difference was significant (p=0,034).

**Conclusion:** The origin of non-diploid DI is a multi-step process that occur either through initial loss of chromosomal material followed by polyploidisation or tetraploidisation followed by chromosomal loss. The observed difference in the distribution of non-diploid DI is either caused by differences in the multi-step carcinogenesis or due to that glottic SCC generally are diagnosed earlier in their carcinogenesis.

**P224: Induction of c-Myc Dependent Cell Proliferation by TLR3 in Head and Neck Cancer**R. Pries<sup>1</sup>; L. Hogrefe<sup>1</sup>; C. Ditz<sup>1</sup>; L. Xie<sup>2</sup>; **B.J.H. Wollenberg**<sup>1</sup><sup>1</sup>University of Schleswig Holstein, Luebeck, Germany; <sup>2</sup>Zhejiang University, Hangzhou, China

Toll-like receptors (TLRs) are pattern-recognition receptors which are essential for intercellular communications of the innate immunity. So far, TLRs have been identified on various cells of the immune system and several kinds of stromal cells. In this study we investigated the expression of TLRs in human head and neck squamous cell cancer (HNSCC). Protein expression of human Toll-like receptors (TLR) 1-10 was measured in cell lines and solid tumors of head and neck squamous cell carcinoma (HNSCC). All HNSCC cell lines and 80% of solid tumors were found to express TLR3 as a predominantly cytoplasmic protein, while no other TLR proteins were expressed. TLR3 has previously been shown to contribute to the activation of NF- $\kappa$ B, a transcription factor which promotes several kinds of human cancers. Significantly, NF- $\kappa$ B expression was strongest in protein extracts from carcinoma tissue in which TLR3 was overexpressed. Inhibition of TLR3 expression in permanent HNSCC cell lines resulted in decreased expression of the oncoprotein c-Myc resulting in decreased cell proliferation. Correspondingly, overexpression of human TLR3 in mouse fibroblasts resulted in an upregulation of c-Myc and increased sensitivity for PolyI:C induced cell proliferation. Our data suggest that TLR3 contributes to the malignant phenotype leading to invasive carcinoma in HNSCC.

**P225: Genetic Analysis of Genes Involved in Signal Transduction Pathways in Oral Squamous Cell Carcinomas****D. Thurnher**<sup>1</sup>; P. Pintor dos Reis<sup>2</sup>; N. Naranjo Galloni<sup>2</sup>; J. Freeman<sup>3</sup>; D. Brown<sup>4</sup>; R. Gilbert<sup>4</sup>; P. Gullane<sup>4</sup>; J. Irish<sup>4</sup>; S. Kamel-Reid<sup>5</sup><sup>1</sup>Princess Margaret Hospital, Toronto, Ontario; <sup>2</sup>Ontario Cancer Institute and University Health Network, Toronto, Ontario; <sup>3</sup>Mount Sinai Hospital, Toronto, Ontario; <sup>4</sup>Princess Margaret Hospital and University Health Network, Toronto, Ontario; <sup>5</sup>Ontario Cancer Institute and University Health Network, University of Toronto, Toronto, Ontario

**Objective:** Oral squamous cell carcinomas (OSCCs) are malignant oral cavity tumors that account for 24% of all head and neck cancers. They are the sixth leading cause of cancer death worldwide. In a previous study, we determined the global gene expression profiles of primary OSCCs and identified a subset of deregulated genes that correlated with more advanced-stage tumors. A subset of these genes are involved in signal transduction genetic networks. Our objectives are thus to examine the expression of these genes in OSCCs.

**Design:** Tissue samples were obtained at the time of surgery from the Toronto General Hospital and snap frozen in liquid nitrogen for RNA extraction. Quantitative real-time reverse-transcriptase polymerase chain reaction using the ABI PRISM 7700 Sequence Detection System and the Sequence Detection System software (PE Applied Biosystems, Foster City, Calif) was used for relative quantification of gene expression. Data analysis was performed using the Delta Delta Ct method.

**Patients:** Sixty-eight patients with OSCC who had surgery as primary treatment were included in this study.

**Results:** Deregulated expression of  $\beta$ -catenin, a gene involved in maintaining cell-to-cell adhesion in normal cells mediating the Wnt signal transduction pathway was detected. *WISP1*, *WISP2*, *TCF4*, and *LEF1* genes are also associated with the Wnt pathway and were thus included in this study to further investigate whether the Wnt/ $\beta$ -catenin pathway is deregulated in head and neck cancer.

**Conclusion:** Deregulated expression of genes involved the Wnt/ $\beta$ -catenin pathway in OSCC.

**P226: Lack of Exon 19 and 21 EGFR Mutations in Squamous Cell Head and Neck Cancer Specimens and Cell Lines****M.L. Carlson**; B. R. Wuertz; J. Lin; G. L. Adams; R.S. Taylor; F.G. Ondrey

University of Minnesota, Minneapolis

**Objective:** It has recently been reported that epidermal growth factor receptor tyrosine kinase inhibition might be a more effective treatment strategy in patients harboring specific *EGFR* mutations. These mutations are prevalent in 3% to 7% of non-small-cell lung carcinomas. Our objective was to examine whether these mutations might be more common at other upper aerodigestive cancer sites.

**Design:** We extracted DNA from 20 head and neck squamous cell tumors and 4 squamous cell carcinoma cell lines and sequenced the receptors using previously published primer pairs. We then compared the results against reported mutations.

**Results:** We found exon 19 or 21 mutations in 0 of 20 tumors and 0 of 4 cell lines. Based on the tumor data, 97.5% confidence interval calculations would predict that no greater than 8.8% of head and neck tumors would be likely to harbor either of these mutations.

**Conclusions:** These data, derived from a small population of US patients, are comparable to results recently published of Korean and Austrian patient populations. Therefore, from this deductive analysis, we conclude that exon 19 and 21 *EGFR* mutations are not more common in head and neck cancer than in non-small-cell lung carcinoma.

**P227: Tumor Origin and Molecular Profile of Microvesicles in Serum Samples of Patients with Head and Neck Squamous Cell Carcinoma****E.U. Wieckowski**; J.T. Johnson; T.L. Whiteside

University of Pittsburgh Cancer Institute, Pittsburgh, PA

**Objective:** Serum samples from patients with head and neck squamous cell carcinoma (HNSCC) contain 50- to 100-nm membranous microvesicles (MV), which induce apoptosis of activated T cells. Our objective was to study the molecular profile and tumor origin of these MVs.

**Design:** We isolated MVs by exclusion chromatography and ultracentrifugation from serum samples of 20 patients with HNSCC, 20 healthy donors, and supernatants of tumor cell lines. Western blot analyses were performed with antibodies to MAGE 3/6, FasL, MHC classes I and II molecules, and other antigens. The MVs were tested in JAM (DNA fragmentation); caspase activation and CFSE proliferation assays were performed with activated T cells. The MVs released by tumor cells were visualized by electron microscopy and imaging. The MVs in MAGE 3/6-positive tumor supernatants and paired serum samples were compared as were MVs derived from tumor or dendritic cells.

**Patients:** 20 patients with HNSCC and 20 healthy donors.

**Results:** Both tumor and dendritic cells produced and released MVs. MAGE 3/6 was expressed on tumor-derived MVs but not on those derived from dendritic cells. Tumor-derived MVs were enriched in 42-kDa FasL, MHC class I and class II molecules, LAMP1, and LAMP3 but were negative for CD80, CD83, CD86, ICOSL, PDL-1, and TRAIL. These MVs delivered FasL- or MHC class I-mediated apoptotic signals to activated CD8+ cells. Dendritic cell-derived MVs expressed B7 costimulatory and MHC molecules and enhanced expansion of resting or activated T lymphocytes.

**Conclusion:** The molecular profile and ability to induce death in CD8+ T cells distinguished tumor-derived from dendritic-cell-derived MVs, which were stimulatory. The MV apoptotic activity in serum samples reflected T stage and nodal involvement and might be a biomarker of HNSCC progression.

## **P228: Gene-Expression-Analysis of Radiation-Induced Non-Healing Dermal Wounds of the Head and Neck**

**U.R. Goessler**<sup>1</sup>; P. Bugert<sup>2</sup>; K. Hormann<sup>1</sup>; F. Riedel<sup>1</sup>

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**Objective:** Radiotherapy as a valuable tool in the treatment of head and neck cancer is increasingly implemented in treatment regimens. As a consequence, clinicians are confronted with a rising amount of radiogenic complications such as persistent, poorly healing dermal wounds. Difficult to manage, these lesions pose a challenge in managing the treatment regimen to attain most capacious success. Interestingly, the pathophysiology of radiation-induced wounds of the head and neck is poorly understood at a molecular level.

**Methods:** Keratinocytes and fibroblasts from chronic non-healing ulcers in radiated areas as well as from healthy skin areas in the same patient were harvested from 3 patients during surgical procedures and isolated in cell culture. A proliferation assay was performed. Gene-expression was analysed by RT-PCR and Microarray, protein-expression as a control by Immunohistochemistry.

**Results:** Keratinocytes from radiogenic wounds did not show any proliferation compared to the keratinocytes from healthy, non-radiated skin areas. Fibroblasts from radiated areas showed decreased proliferation.

Keratinocytes from radiogenic wounds showed a shift from the high molecular keratins 1 and 10 to the low molecular keratins 5 and 14 compared to normal control skin. The irradiated keratinocytes showed increased expression of collagen 5 and 18, there was no significant difference in the expression of collagen 1, 2, 3 and 4.

Keratinocytes and fibroblasts from nonhealing wounds showed a decreased expression of mediators of cellular proliferation such as Transforming Growth Factor alpha and beta 1 (TGF $\alpha$ , TGF $\beta$ 1), Fibroblast Growth Factor 1 + 2 (FGF1, FGF2) and Keratinocyte Growth Factor (KGF). Mediators of angiogenesis such as Vascular Endothelial Growth Factor (VEGF) and Hepatocyte Growth Factor (HGF) also showed decreased expression in radiated tissue. The matrix-metalloproteinases MMP 2, 12 and 13 showed increased expression in radiated keratinocytes and fibroblasts. Epidermal growth factor (EGF) was not expressed by radiated as well as non-radiated keratinocytes or fibroblasts.

**Conclusion:** Our data showed a change of keratinocytes to a less differentiated state due to radiation. In addition, it seems that radiation-induced dermal injuries often fail to heal because of decreased proliferation, impaired angiogenesis and persistently high concentrations of MMPs. Better understanding of the basic pathophysiology of wound healing in radiation-induced wounds at the molecular level might feed into the development of innovative treatment strategies.

## **P229: The Role of Inhibitor of Differentiation in the Angiogenesis of Head and Neck Cancers**

**J. Lin**; Y. Hamajima; M. Komori; L. Feng; E. Caicedo; G. Adams; B. Wuertz; F. Ondrey

University of Minnesota, Minneapolis

**Objective:** Inhibitor of differentiation (Id1) is highly expressed in head and neck squamous cell carcinoma (HNSCC). However, the role of Id1 in HNSCC is poorly understood. The purpose of this study is to determine whether Id1 regulates angiogenesis in HNSCC.

**Design:** Human HNSCC tissue specimens were procured for examination of the coexpression of Id1 and CD31 (an endothelial cell marker). An HNSCC cell line (CA9-22) and a nontumorigenous keratinocyte cell line (Rhek-1A) were transfected with Id1 and harvested for evaluation of vascular endothelial growth factor (VEGF) and interleukin-8 (IL-8) promoter activities. In addition, human umbilical vein endothelial cells (HUVEC) were transfected with Id1 for evaluation of cell proliferation by 5-bromo-2'-deoxy-uridine incorporation and cell counts.

**Results:** In vivo, Id1 was coexpressed with CD31 in the human HNSCC tissue specimens as shown by double labeling immunohistochemical analysis. In vitro, Id1 transfection in CA9-22 and Rhek-1A cells significantly increased the promoter activities of both VEGF and IL-8. Id1 transfection in HUVEC increased the cell proliferation.

**Conclusions:** Id1 plays a role in the angiogenesis of HNSCC via regulation of VEGF and IL-8.

## **P230: Curcumin Suppresses IL-6 and IL-8 Production in Head and Neck Cancer Cell Lines via Inhibition of I $\kappa$ B Kinase (IKK)**

**A.N. Cohen**; M.S. Veena; E.S. Srivatsan; M.B. Wang

David Geffen School of Medicine at UCLA, Los Angeles, CA

**Background:** Late stage head and neck squamous cell carcinoma (HNSCC) remains a cancer with poor prognosis, and survival rates have not significantly changed over the past 30 years. Recently, investigations have focused on development of potential alternative and adjuvant therapies, due to the significant morbidity associated with the standard treatments of surgery, radiation, and chemotherapy. Curcumin, commonly known as the spice turmeric, has been shown to suppress the proliferation of a variety of tumor cells, including HNSCC. This suppression is believed to be partly due to inhibition of the transcription factor nuclear factor- $\kappa$ B (NF- $\kappa$ B). IL-6 and IL-8 are pro-inflammatory cytokines induced by NF- $\kappa$ B activation that have been shown to be elevated in various squamous cell carcinomas. The purpose of this study was to evaluate the effect of curcumin on IL-6 and IL-8 production in HNSCC cell lines and determine the mechanism by which these effects are modulated.

**Methods:** HNSCC cell lines CCL23, CAL27, UM-SCC1 and UM-SCC14a were treated with curcumin in increasing doses to determine the effect on IL-6 and IL-8 levels. Enzyme-linked immunosorbent assay (ELISA) was used to measure concentrations of IL-6 and IL-8 in the supernatants from the treated HNSCC cells. NF- $\kappa$ B, I $\kappa$ B kinase (IKK) and phosphorylated I $\kappa$ B levels were also evaluated using Western blot analysis, to determine the possible mechanisms involved in the cell lines' response to curcumin.

**Results:** Curcumin treatment resulted in a dose-dependent inhibition of IL-6 and IL-8 levels and suppression of proliferation in all HNSCC cell lines. All cell lines had similar NF- $\kappa$ B levels; however, two cell lines (UM-SCC1 and UM-SCC14a) had significantly higher IKK levels and as such required considerably higher doses of curcumin before inhibition of IL-6 and IL-8 occurred.

**Conclusions:** Curcumin significantly reduces IL-6 and IL-8 levels in HNSCC cell lines. This mechanism appears to be mediated via inhibition of IKK activity in the NF- $\kappa$ B pathway. Cell lines with higher concentrations of IKK required significantly higher doses of curcumin in order to reduce IL-6 and IL-8 levels. Future studies are needed to evaluate the utility of curcumin as an antineoplastic agent in HNSCC. IL-6 and IL-8 have potential use as biomarkers to measure efficacy of treatment with curcumin.

## **P231: The Identification of Epidermal Fatty Acid Binding Protein in Advanced Head and Neck Cancer Using a Proteomic Approach**

**M. Gillespie**; J. Downie; T.A. Day; J.D. Hornig; B. Oswald; J. Arthur  
Medical University of South Carolina, Charleston

**Objective:** To identify proteins overexpressed in metastatic head and neck cancers using a proteomic approach.

**Design:** We identified differential protein expression in 10 head and neck tumors with lymph node metastasis and 3 head and neck tumors without metastasis using 2-dimensional gel separation techniques and Western blot analysis.

**Results:** A protein of interest, which was present in 12 (92%) of the 13 tumors, demonstrated significantly greater expression in metastatic primary tumors. The protein spot was identified as epidermal fatty acid binding protein (e-FABP) using matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) and sequenced with an ion trap mass spectrometer. Subsequent Western blot analysis of head and neck tumors using an anti-e-FABP antibody demonstrated heavy expression in 3 of 3 patients with N2 or greater neck disease and lower levels of expression in tumors with N1 (n = 1) or N0 disease (n = 2). Normal control oral mucosa demonstrated light (n = 2) or no staining (n = 3). Due to its low molecular weight, e-FABP is filtered by the kidney. Western blot analysis of patient urine detected e-FABP in the urine of 5 (83%) of 6 patients with head and neck cancer.

**Conclusions:** Preliminary evidence suggests that overexpression of e-FABP may be a marker of advanced neck disease. In addition, the

observation that E-FABP is readily detectable in urine raises the possibility that E-FABP levels could be easily observed in patients over time. Due to its association with VEGF expression, E-FABP levels may serve as a potential marker for tumors likely to respond to Zantiangiogenic therapy.

## **P232: Up-Regulation of NK Cell Cytotoxicity Against Head and Neck Cancer in Response to ss-isRNA Requires TLR7**

R. Pries<sup>1</sup>; S. Wulff<sup>2</sup>; R. Kesselring<sup>2</sup>; L. Xie<sup>3</sup>; B.J.H. Wollenberg<sup>1</sup>

<sup>1</sup>University of Schleswig Holstein, Luebeck, Germany; <sup>2</sup>University of Schleswig-Holstein, Luebeck, Germany; <sup>3</sup>Zhejiang University, Hangzhou, China

Natural killer (NK) cells play a crucial role in the innate immunity as effectors against tumor cells and pathogen-infected cells. NK mediated host defence against tumor cells is strongly impaired in patients with head and neck squamous cell carcinoma (HNSCC). Tumor secretion of various immune suppressive mediators contributes to massively affected immune functions. In this work we demonstrate that NK cell cytotoxicity against tumor cells of HNSCC can be efficiently stimulated by single stranded immunostimulatory RNA (ss-isRNA). Analysis of cytokine secretion revealed that ss-isRNA as well triggers an increased production of interferon-gamma (IFN- $\gamma$ ). Our investigations demonstrate that supernatants of permanent HNSCC cell lines negatively affect the ss-isRNA triggered stimulation of NK cell cytotoxicity and IFN- $\gamma$  secretion. Stimulation of cytotoxicity requires Toll like receptor 7 (TLR7) and an increased expression of NK cell TLR7 was shown in response to ss-isRNA. These results suggest ss-isRNA as a potential immunostimulatory tool of human NK cells against HNSCC.

## **P233: Photodynamic Therapy for Local Persistent and/or Recurrent NPC's Development of a Light Application Device**

H. Nyst<sup>1</sup>; R. van Veen<sup>2</sup>; R. Peters<sup>2</sup>; S. Sapnol<sup>3</sup>; F. Stewart<sup>1</sup>; P. Levendag<sup>2</sup>; H. Sterenberg<sup>2</sup>; I. Tan<sup>1</sup>

<sup>1</sup>Netherlands Cancer Institute, Amsterdam, The Netherlands; <sup>2</sup>ErasmusMC, Rotterdam, The Netherlands; <sup>3</sup>Biolitec AG, Bonn, Germany

The objective of this study was to develop and evaluate the performance of a dedicated light delivery and measurement device for PDT in the nasopharyngeal cavity that achieves an optimal homogeneous and reproducible fluence rate distribution to a target area and provides proper shielding of a predefined risk areas.

**Material and Methods:** A flexible silicone applicator with incorporated light delivery and dosimetry was developed. The applicator can be inserted through the mouth and fixed in the nasopharyngeal cavity. Tissue optical phantoms were prepared on the basis of optical properties measured in vivo using diffuse reflectance spectroscopy. The fluence rate over the length of the applicator surface was measured in air, in phantoms and in five healthy volunteers.

**Results:** The fluence rate distribution over the applicator surface in air and tissue optical phantom was found to be homogeneous (SD/mean 3.8% and 18.3% respectively). However, the fluence rate distribution in five volunteers varied over the length of the applicator and was found to be significantly less homogeneous than in the optical phantoms (SD/mean ranging from 19% up to 52%). The maximum observed fluence rate build-up varied between subjects and ranged from a factor of 4.1 to 6.9. Shielding of the risk area such as the soft palate and tongue was effective.

**Conclusions:** In air and in tissue optical phantoms the fluence rate distribution is highly homogeneous. The observed large inter-subject variations originated from average differences in optical properties and nasopharyngeal geometry, whereas significant intra-patient variations in fluence rate mainly reflect local differences in geometry and optical properties. Light delivery based on a single tissue surface measurement will not be adequate. For PDT in general, these observations should be taken in consideration when developing light applicators for PDT.

## **P234: Safety of PPAR Gamma Activation Strategies for Precancerous Leukoplakia**

N. Rhodus<sup>1</sup>; L. Hohberger<sup>1</sup>; K. Cole<sup>1</sup>; E. Szabo<sup>2</sup>; F.G. Ondrey<sup>3</sup>

<sup>1</sup>University of Minnesota, Minneapolis; <sup>2</sup>NCI/NIH, Bethesda, MD;

<sup>3</sup>University of Minnesota, Minneapolis, MN

PPAR gamma is a molecular target currently under study for oral cancer prevention. FDA approved thiazolidinedione drugs used for type II diabetes bind to PPAR gamma nuclear receptors and are hypothesized to drive dysplastic cells towards decreased proliferation and increased maturation. In our ongoing Phase IIa clinical trial (NCI N01-CN-15000), we examined the safety of pioglitazone 45 mg daily given for 90 days to non-diabetic patients with high-risk oropharyngeal leukoplakia. We report here the clinical side effects and laboratory test abnormalities occurring in the first 18 patients completing the clinical trial from January 2004 until March 2006. Laboratory parameters included CBC/differential, liver function studies, electrolytes and serum glucose from blood drawn before and 12 weeks after treatment. Paired Student t-test was used to score laboratory studies. Other side effects were scored by NCI CTC version 3 criteria for the duration of the study. 1 of 18 (5.5%) participants underwent dose reduction to 30mg/daily for CTC grade 2 lower extremity edema. No other agent related symptoms occurred. The percent of patients with idiopathic peripheral edema (5.5%) compares to the published rate of 7% for diabetics. Liver function studies (AST,ALT), electrolytes, and serum glucose were not altered during 90 days of treatment with pioglitazone. Although total white blood cell counts, RBC, hemoglobin, and RBC indices were unaltered, there was a statistically significant 10% decrease in lymphocytes on the blood count differential (31.1% pre-treatment, 27.9% post-treatment (p=0.025)). Absolute lymphocyte counts were similarly decreased (2.42 pre-treatment, 1.96 post-treatment (p=0.02)). This small decrease in lymphocyte counts did not fall out of normal range for the reference laboratory, but may be related to published anti-inflammatory effects of this agent class. We conclude that 45 mg daily of pioglitazone can be delivered safely for 90 days to non-diabetic people with oral leukoplakia in a phase II clinical trial setting.

## **P235: WITHDRAWN**

## **P236: Tonsil Carcinoma Treated by Transoral Laser Microsurgery, I: Previously Untreated Tumors**

M.L. Hinni<sup>1</sup>; D.G. Grant<sup>2</sup>; J.R. Salassa<sup>2</sup>; B.W. Pearson<sup>2</sup>; W.C. Perry<sup>1</sup>

<sup>1</sup>Mayo Clinic, Scottsdale, Ariz; <sup>2</sup>Mayo Clinic, Jacksonville, FL

**Objective:** To report the oncologic and functional outcomes of transoral laser microsurgery (TLM) in the management of previously untreated squamous cell carcinoma of the tonsil.

**Design:** A 2-center prospective case series analysis of TLM in the treatment of tonsillar carcinoma.

**Setting:** Academic tertiary referral centers.

**Patients:** Fifty-four untreated patients were treated with TLM between 1996 and 2005. Pathologic T-stage distribution was T1, 26%; T2, 44%; T3, 20%; and T4, 9%. Thirty-two patients (59%) presented with stage IV disease, 14 (26%) with stage III. Neck dissections were performed in 47 patients (87%). Thirty-two patients (59%) underwent adjuvant radiotherapy. Median follow-up was 30 months; mean, 34 months; range, 1 to 91months.

**Interventions:** Transoral laser microsurgery with or without neck dissection, adjuvant radiotherapy, or chemotherapy.

**Main Outcome Measures:** Local control, locoregional control, recurrence-free survival, and overall survival. Preoperative and postoperative swallow function was assessed with the Functional Outcome Swallowing Scale.

**Results:** Overall the 5-year Kaplan-Meier local control estimate was 98%. Five-year overall and recurrence-free survival estimates were 78% and 81% respectively. For patients with follow up of 12 months or more (n = 47) 5-year local control, overall survival and recurrence-free survival estimates were 98%, 77% and 80% respectively. Five patients (9%) suffered minor post-operative complications. There was no significant clinical deterioration in swallowing function after TLM.

**Conclusions:** Transoral laser surgery is a safe and effective treatment for select early and advanced carcinoma of the tonsil.

## **P237: Tonsil Carcinoma Treated By Transoral Laser Microsurgery, II: Persistent, Recurrent, and Second Primary Tumors**

**D.G. Grant**<sup>1</sup>; J.R. Salassa<sup>1</sup>; M.L. Hinni<sup>2</sup>; B.W. Pearson<sup>1</sup>; W.C. Perry<sup>2</sup>  
<sup>1</sup>Mayo Clinic, Jacksonville, FL; <sup>2</sup>Mayo Clinic, Scottsdale, AR

**Objective:** To report the oncologic outcomes of transoral laser microsurgery (TLM) in the treatment of persistent, recurrent, and second primary squamous cell carcinoma of the tonsil.

**Design:** A 2-center prospective case series analysis of TLM in the treatment of tonsil carcinoma.

**Setting:** Academic tertiary referral centers.

**Patients:** Twenty-three patients were treated with TLM between 1996 and 2005. Sixteen of these were TX NX with persistent or locally recurrent disease at a previously treated primary site. The estimated T stage of these patients was T1, 5; T2, 6; T3, 4; and T4, 1. Seven of the 23 patients had second primary tumors within previously treated fields staged as follows: T1, 3; T2, 3; and T3 1. Previous treatment included radiotherapy, chemotherapy, surgery, or a combination of some or all of these. Neck dissections were performed in 9 of 23 patients. Three of 23 patients received postoperative radiotherapy. Median follow-up was 14 months; mean, 23 months; range, 1 to 71 months.

**Interventions:** Transoral laser microsurgery with or without neck dissection, adjuvant radiotherapy, or adjuvant chemotherapy.

**Main Outcome Measures:** Local and locoregional control and recurrence-free and overall survival.

**Results:** The 5-year Kaplan-Meier estimates were as follows: local control, 98%; recurrence-free survival, 81%; and overall survival, 78%. The average duration of hospital stay was 2 days. Three patients (13%) experienced postoperative hemorrhage.

**Conclusions:** Transoral laser microsurgery is a safe and effective treatment for select persistent, recurrent, and second primary squamous cell carcinoma of the tonsil.

## **P238: Quality Control Monitoring of a Cancer Database Using Visualization Software**

**M.A. Nance**; C.H. Snyderman; D.E. Eibling; K. Sochats  
University of Pittsburgh, Pittsburgh, PA

**Objective:** An important aspect of quality control is identification of changes in outcome. Detection of change can then be used to identify contributing factors and institute corrective actions if necessary. Our objective was to evaluate treatment outcome patterns for patients with squamous cell carcinoma of the head and neck treated at our institution in the last 30 years.

**Design:** We adapted a database visualization software suite for our Head and Neck Oncology Registry containing over 150 000 data points on 5000 deidentified patients.

**Results:** Tumor recurrence rates compared on a yearly basis are displayed and illustrate a significant decrease in rates of recurrence during the 1990s with a plateau in the current decade. Reasons for the declining recurrence rate were then explored.

**Conclusions:** This data visualization tool facilitates real-time interactive database exploration with the intent of detecting large trends and subtle relationships to generate new hypotheses for further investigation. The interactive characteristics of the system allow dynamic access to individual records and concurrently selected cohorts, for in-depth study of patient characteristics, treatment strategies, and outcomes.

## **P239: Immunotherapy of Established Murine Squamous Cell Carcinoma Using Dendritic Cell-Tumor Fusion Hybrids**

**W.T. Lee**; H. Tamai; P. Cohen; S. Shu  
Cleveland Clinic, Cleveland, Ohio

**Objective:** To investigate the therapeutic efficacy of dendritic cell-tumor fusion hybrids against a murine squamous cell carcinoma (SCC).

**Design:** Squamous cell carcinoma VII is a poorly immunogenic murine SCC in C3H (H-2K) mice. Subdermal tumors were established by inoculation in the midabdomen of mice. Tumor diameter were measured with a Veneer caliper and used as an indication of treat-

ment efficacy. Dendritic cells were generated from bone marrow cells, cultured with cytokines for 8 days, harvested, and mixed with cultured tumor cells in a 1:1 ratio. Cell fusion was achieved by exposing the cell mixture to an alternate electrical current to bring cells into alignment and close together, followed by a short direct electrical current pulse.

**Subjects:** C3H mice.

**Interventions:** Mice with 3-day established subdermal SCC VII tumors were vaccinated by inguinal intranodal injection of fusion cells (0.3 ? 106/side). To support the development of antitumor immunity, mice were given adjuvant injections intraperitoneally. Anti-OX40R monoclonal antibody or interleukin 12 was used. Treatment groups included no treatment, anti-OX40R monoclonal antibody or interleukin 12 adjuvant alone, fusion cells alone, and fusion cells with adjuvant.

**Results:** Mice treated with adjuvant or fusion cells alone did not show a statistical difference in tumor growth compared with controls. In contrast, mice treated with fusion cells and adjuvant showed a significant decrease in tumor size compared with untreated mice ( $P = .002$ ).

**Conclusions:** Dendritic cell-tumor fusion hybrid immunotherapy can significantly impact SCC VII growth, which supports the concept of using dendritic cell-tumor fusion cells as an immunotherapy approach against human SCC.

## **P240: Expression of Cell Cycle Regulators as Markers of Field Cancerization and Second Primary Tumors in Larynx Squamous Cell Carcinoma**

**R.D. Farhadieh**<sup>1</sup>; R. Smee<sup>1</sup>; C.G. Rees<sup>2</sup>; L. Yang<sup>2</sup>; P.J. Russell<sup>3</sup>  
<sup>1</sup>Prince of Wales Hospital, Sydney, Australia; <sup>2</sup>University of New South Wales, Sydney Australia; <sup>3</sup>Oncology Research Center, University of New South Wales, Sydney Australia

**Objective:** To establish the correlation of cyclin A1 and mutant p53 in head and neck squamous cell carcinoma (HNSCC), in primary laryngeal SCC, and incidence of second primary tumors (SPTs).

**Design:** A retrospective cohort of 106 patients with a mean follow-up time of 57.8 months. Using immunohistochemical analysis, we evaluated patients for protein expression of cyclin A1 and mut-p53.

**Results:** Positive protein expression of cyclin A1 and mut-p53 expression were noted in 83 of 106 and 25 of 106 patients, respectively. There were no statistically significant correlations between cyclin A1, mut-p53, and standard clinicopathologic parameters. Twenty-five patients were diagnosed as having new primary tumors during the follow-up period. A statistically significant correlation was noted between cyclin A1 expression and diagnosis of SPTs ( $P = .002$ ).

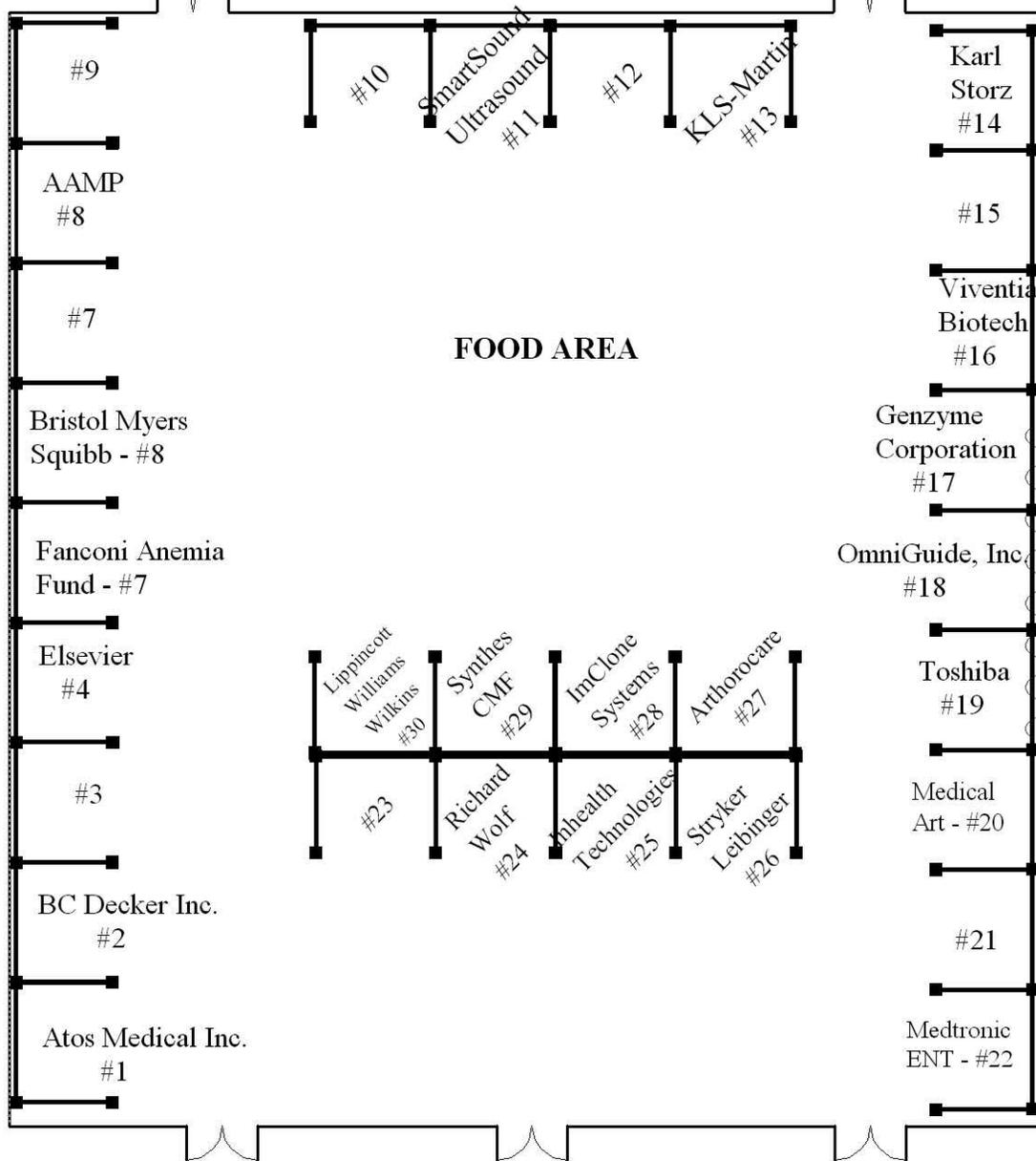
**Conclusion:** Field cancerization as a consequence of widespread genomic assault secondary to alcohol and tobacco abuse is a well-known feature of HNSCCs. In patients with HNSCC, there is a 2% to 10% per annum risk of developing SPTs. There are conflicting theories on the origins of SPTs. To date no biological marker has been discovered that would reliably herald this development. This would have a significant bearing on clinical approach to patient management beyond the isolated treatment of the diagnosed tumor. Cyclin A1 is a cell-cycle regulator involved in G1/S cell transition. There is growing evidence that overexpression of cyclin A1 favors entry of cells into the S phase and thus favors cell proliferation. Cyclin A1 expression may represent an irreversible widespread genomic change that favors further cell proliferation and future malignancies. A closer surveillance of these patients may be warranted.



# Exhibit Hall Floorplan

American Head and Neck Society  
2006 Annual Meeting & Research Workshop  
Chicago Marriott Downtown  
**Grand Ballroom**

August 17-20, 2006



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### THE AMERICAN HEAD AND NECK SOCIETY, INC.

Under Section 803 of the Not-for-Profit Corporation Law

1. The name of the Corporation is THE AMERICAN HEAD AND NECK SOCIETY, INC.
2. This Corporation has not been formed for pecuniary profit or financial gain, and shall not be conducted or operated for profit, and no part of the assets, income or net earnings of the Corporation is distributable or shall inure to the benefit of the directors, officers, or other private persons, except to the extent permitted under the Not-for-Profit Corporation Law. Upon the dissolution of this Corporation, no director, officer, or other private person shall be entitled to any distribution or division of its remaining property or its proceeds, and the balance of all money and property of the Corporation shall pass to, or shall inure to the benefit of, those organizations described in Section 201 of the Not-for-Profit Corporation Law and Section 501(c)(3) of the Internal Revenue Code of 1986, which are not private foundations described in Section 509(a) of such Code. Any such assets not so disposed of shall be disposed of by the Supreme Court of the State of New York for the County in which the principal office of the Corporation is then located, as provided by law, exclusively for such purposes or to such organization or organizations as said Court shall determine, which are organized and operated for the purposes set forth in Paragraph "3" below.
3. The purposes for which the Corporation is formed and the powers which may be exercised by the Corporation, in addition to the general powers set forth in Section 202 of the Not-for-Profit Corporation Law of the State of New York, are:
  - (a) to advance knowledge relevant to medical and surgical control of neoplasms of the head and neck;
  - (b) to solicit, obtain, apply for, and spend funds in furtherance of any activities or purposes of the Corporation;
  - (c) in general, to do any and all acts or things and to exercise any and all powers which may now or hereafter be lawful for the Corporation to do or exercise under and pursuant to the laws of the State of New York for the purpose of accomplishing any other purpose of the Corporation as set forth herein;
  - (d) to engage in any and all lawful activities incidental to any of the foregoing purposes of the Corporation.
4. The Corporation is organized exclusively to achieve public objectives, including for such purposes, the making of distributions to organizations that qualify as exempt organizations described in Section 115 or Section 501(c)(3) of the Internal Revenue Code of 1986, provided that such organizations are not private foundations described in Section 509(a) of such Code. The Corporation shall not carry on any other activities not permitted to be carried out by a corporation exempt from federal income tax under Section 501(c)(3) of such Code or by a corporation contributions to which are deductible under Section 170(c)(2) of such Code (or the corresponding provisions of any future United States Internal Revenue Law.)
5. Nothing contained herein shall authorize this corporation to undertake or to carry out any of the activities specified in paragraphs (b) through (u) of Section 404 of the Not-for-Profit Corporation Law, or to establish, maintain or operate a hospital or to provide hospital service or health-related service, a certified home health agency, a hospice, a health maintenance organization, or a comprehensive health services plan, as provided for by Article 28, 36, 40 and 44, respectively, of the Public Health Law or to solicit, collect or otherwise raise or obtain any funds, contributions or grants from any source, for the establishment, maintenance or operation of any hospital or to engage in the practice of medicine or any other profession required to be licensed by Title VIII of the Education Law.
6. No substantial part of the activities of this Corporation shall consist of carrying on propaganda or otherwise attempting to influence legislation, and the Corporation shall not participate in, or intervene in (including the publication or distribution of statements), any political campaign on behalf of any candidate for public office.
7. The Corporation is a corporation as defined in subparagraph (a)(5) of Section 102 of the Not-for-Profit Corporation Law, and it is a Type B Corporation.
8. The principal office of the Corporation is to be located in the City of Syracuse, County of Onondaga and State of New York.
9. The territory in which the Corporation's activities are principally to be located is the territorial limits of the United States of America, the Domain of Canada and the Pan-American countries.
10. The number and manner of election or appointment of the directors constituting the Board of Directors shall be as provided in the Bylaws, except that the number of said Board members shall not be less than three (3). Members of the Board of Directors need not be residents of the State of New York. The names and addresses of the Directors of the Corporation who shall act until the first meeting of the Board of Directors, all of whom are over the age of eighteen (18) and are citizens of the United States, are:

<u>Names</u>	<u>Addresses</u>
[Names and Addresses omitted.]	
11. Management of the business and affairs of the Corporation is vested in the Board of Directors which shall use its best efforts to carry out in good faith the purposes of the Corporation.
12. To further the Corporation's objectives and purposes, the Corporation shall have and may exercise all of the powers conferred by the New York Not-for-Profit Corporation Law in pursuit of the purposes expressed in Paragraph THREE hereof. Without limiting the generality of the foregoing, the Corporation shall have power to sue and be sued, to own, take title to, receive and hold, lease, sell and resell, in fee simple or otherwise, property real, personal or mixed wherever situated and however acquired, without limitation as to amount or value. The Corporation shall have authority to encumber property by deed of trust, pledge or otherwise; to borrow money and secure payment of same by lien or liens of the realty or personal property of the Corporation; to lease, build, erect, remodel, repair, construct and/or reconstruct any and all buildings, houses or other structures necessary, proper or incident to its needs and proposes; and to do any and all things incident to the carrying out of the objectives and purposes as stated and as limited herein. The Corporation shall have full powers or management, investment and reinvestment and the collection of all rents, revenues, issues and profits arising therefrom.
13. The Corporation is to have members.
14. The Corporation is to be divided into such classes of members as the By-Laws provide. The designation of each class of members, the manner of election or appointment, and the qualification and rights of the members of each class (including conferring, limiting, or denying the right to vote) shall be set forth in the By-Laws.
15. The Secretary of State of the State of New York is hereby designated as the agent of the Corporation upon whom process may be served, and the post office address to which the Secretary of State shall mail a copy of any such process served upon him is as follows: c/o Richard R. Gacek, MD, Professor and Chairman, Department of Otolaryngology, State University of New York Health Science Center, 750 East Adams Street, Syracuse, New York 13210.

## ARTICLE I

**Section 1.** The name of the Corporation shall be The American Head and Neck Society, Inc.

## ARTICLE II

**Section 1.** The purpose of this Society is to promote and advance the knowledge of prevention, diagnosis, treatment and rehabilitation of neoplasms and other diseases of the head and neck.

**Section 2.** It is the objective of this Society to promote and advance research in neoplasms and other diseases of the head and neck.

**Section 3.** It is the objective of this Society to promote the highest professional and ethical standards.

## ARTICLE III

**Section 1.** Members of this Society shall be designated as Fellows, and shall consist of six classes

- (a) Active
- (b) Honorary
- (c) Corresponding
- (d) Senior
- (e) Associate
- (f) Candidate

**Section 2.** Active Fellows of this Society shall be those who maintain a license to practice medicine and who are actively engaged in prevention, diagnosis, treatment and rehabilitation of neoplasms and other diseases of the head and neck.

**Section 3. Qualifications for Active Fellowship.** An applicant for Active Fellowship shall be a Diplomate of a particular specialty board, or have credentials that are equivalent to those issued by member boards of the American Board of Medical Specialties. Surgeons must be a member of the American College of Surgeons, a Fellow of the Royal College of Surgeons (Canada), or have similar credentials. A significant portion of practice shall be concerned with neoplasms and other diseases of the head and neck. Further qualifications and requirements for Active Fellowship are contained in the By-Laws, Article VI, Sections 1 and 2.

**Section 4. Qualifications for Honorary Fellowship.** Honorary Fellowship shall be a distinction bestowed by the Society on an individual who has made outstanding contributions to the field of head and neck oncology.

**Section 5. Qualifications for Corresponding Fellowship.** Corresponding Fellowship shall be granted to those who, in the judgment of the Council, are actively engaged in the prevention, diagnosis, treatment and rehabilitation of neoplasms and other diseases of the head and neck and who reside in a country other than the United States or Canada.

**Section 6. Qualifications for Senior Fellowship.** Any Active Fellow, upon cessation of active practice, may request by writing to the Secretary a change in status to Senior Fellowship.

**Section 7. Qualifications for Associate Fellowship.** A candidate for election to Associate Fellowship shall be a physician, dentist or allied scientist who has demonstrated a special interest in the field of head and neck oncology.

**Section 8. Qualifications for Candidate Member.** The trainee currently enrolled in, or a graduate of, an approved residency program in Otolaryngology, Plastic Surgery, or General Surgery or in a Fellowship Program approved by the

Joint Training Council may become a Candidate Member. This nonvoting membership is subject to fees established by the Council. The membership shall expire if the candidate member has not made application for Active Fellowship in The American Head and Neck Society, Inc. five years after the completion of training.

**Section 9. Privileges of Members.** All members shall have the same rights and privileges except that only Active Fellows in good standing shall have the privileges of voting in the conduct of the affairs and business of the Society or of holding office or of chairing Standing Committees.

## ARTICLE IV

### Meetings

**Section 1.** The annual meeting of this Society shall be held at such time and place as may be fixed by the Council at its annual meeting.

**Section 2.** The annual meeting shall consist of at least one scientific session and one business session.

**Section 3.** The scientific session shall be open to all Fellows of the Society and members of the medical profession. Attendance at any business session is limited to Fellows of the Society.

**Section 4.** Only Active Fellows in good standing shall have the privilege of a vote in conduct of the affairs and business of the Society.

## ARTICLE V

### Officers

**Section 1.** The officers of this Society shall be President, President-Elect, Vice-President, Secretary, and Treasurer.

## ARTICLE VI

### Board of Directors

**Section 1.** The governing body of this Society shall be the Council, consisting of the President, President-Elect, Vice-President, Secretary, Treasurer, and Past Presidents (for a period of three years following the termination of term of office). In addition, there shall be nine Fellows-at-Large, three of whom shall be elected each year to serve terms of three years each. At no time shall the Council exceed eighteen in number. The manner of election of officers and members of the Council is stated in the By-Laws, Article VII, Sections 1 and 2.

## ARTICLE VII

### Amendments to the Constitution or Bylaws

**Section 1.** A proposed amendment to the Constitution or By-Laws must be submitted to the Secretary in writing not less than two months before a meeting of the Council, and must be signed by at least two Active Fellows. The Secretary shall forward the proposed amendment to the Constitution and Bylaws Committee for review and comment. The Constitution and Bylaws Committee will make a periodic review of the Constitution and Bylaws and recommend modification which may be submitted as amendments. Any proposed amendment must first be acted upon by the council. The Secretary shall mail a copy of any proposed amendment to each Active Fellow not less than one month prior to the annual meeting of the Society. Two-thirds vote of the Active membership present at the meeting shall be required for acceptance.

## ARTICLE I

### Rights and Duties of Members

**Section 1.** Any Active Fellow shall have all the rights of Fellowship, shall be subject to all the duties, roles and responsibilities incumbent upon the members of any scientific parliamentary body.

## ARTICLE II

### Delinquents

**Section 1.** Unless excused by the Council, a Fellow delinquent in dues for two consecutive years, or attendance for four consecutive years, shall be dropped from Fellowship. Delinquency in dues is defined as failure to pay by the end of the calendar year.

## ARTICLE III

### Dues

**Section 1.** The amount of the Society's dues shall be determined by the Council. The Council shall have the authority to establish an initiation fee or special assessment.

## ARTICLE IV

### Order of Business

**Section 1.** The regular order of business at annual meetings shall be carried out in a manner prescribed by the Council.

## ARTICLE V

### Special Provisions

**Section 1.** All conditions, circumstances, emergencies or contingencies not covered by this Constitution and its Bylaws shall be dealt with and administered by the directive of the Society's Council, subject to approval by the membership at the next annual meeting.

## ARTICLE VI

### Qualifications for Fellowship

**Section 1.** Candidates desiring election to Fellowship in any class other than Associate Fellow must hold a valid, unrestricted license to practice medicine in the state or country in which they reside and shall be proposed by two Active Fellows with at least one from the applicant's local geographical area. A special form will be provided by the Secretary for this purpose. Both of the sponsors must submit letters of recommendation pertaining to the qualifications of the candidate.

**Section 2.** Special Qualifications for Active Membership.

A. In addition to fulfilling the requirements under the Constitution, Article III, Section 3, surgeon candidates must submit evidence that they have the skill and capacity to diagnose and treat neoplasms and other diseases of the head and neck.

B. An applicant for Active Fellowship shall provide documentation that he has received adequate training in the management of patients with head and neck tumors and that a significant portion of current professional activity is devoted to the care of such patients. Such documentation will include a description of experience during residency and/or fellowship training, a summary of subsequent post training experience, and a listing of at least 35 patients with head and neck tumors managed during preceding year.

Additional evidence of academic activity such as one paper published on cancer of the head and neck is required.

C. Active Fellows must be members of the American College of Surgeons or its equivalent.

**Section 3.** Special Qualifications for Corresponding Fellowship.

A. Corresponding Fellows shall be physicians who, by their professional associations and publications, would appear in the judgment of the Council to be qualified to treat neoplasia and diseases of the head and neck. All proposals for candidates for Corresponding Fellowship shall be accompanied by a curriculum vitae of the candidate, a letter of recommendation from at least two Active Fellows. The delinquent clause relative to failure to attend meetings will not pertain to this class of membership.

**Section 4.** Election to Fellowship

A. All proposals for candidates for any class of Fellowship shall be sent to the Council through the Secretary. Subsequent to approval by the Council, nominees' names must be circulated to the membership at least 120 days before the annual meeting. Fellows shall be given an opportunity to make written objections at least 90 days in advance of the annual meeting. Objections will be investigated by the Credentials Committee and presented to the Council for a vote. The Council will use the AMA Code of Ethics as a guide in this matter.

B. Election to any class of membership shall require three-fourths favorable vote of the Council.

C. A candidate for Active Fellowship must be present at the annual meeting to be inducted.

## ARTICLE VII

### Officers of the Society

**Section 1. Election of Officers.** The officers of the Society shall be a President, President-Elect, Vice-President, Secretary, and Treasurer, who shall be elected at regular annual business meetings of the Society.

**Section 2. Accession to Office.** The newly elected officers shall assume their duties before the adjournment of the meeting at which they have been elected.

**Section 3. Tenure of Office.**

A. The President and President-Elect, and Vice-President shall serve for a term of one year. The Secretary and the Treasurer shall serve for a term of three years and may be elected to one additional term.

B. An outgoing President (Past President) automatically becomes a member of the Council to serve for a period of three years. A past-president's membership on the Council which shall be terminated by death or other incapacity to serve shall remain vacant until filled by regular succession.

**Section 4. Vacancies in Office.** Vacancies in office occurring between elections shall be filled by appointment by the President. These appointments shall be subject to written approval of a majority of the Council. Should the office of the President become vacant between elections, it shall automatically be filled by the President-Elect. Should the offices of both President and President-Elect become vacant, these offices will be served by the Secretary.

**ARTICLE VIII****Duties of the Officers****Section 1. Duties of the President.**

- A. The President shall preside at meetings of the Society and shall have the power to preserve order and to regulate the proceedings according to recognized rules.
- B. He shall serve as Chairman of the Council.
- C. He shall appoint standing and special committees, except the Nominating Committee. See Article X, Section 2.
- D. He shall fill vacancies in offices that occur in the interim between regular meetings subject to approval by a Council majority.
- E. He shall be an ex-officio member of all standing committees.

**Section 2. Duties of the Vice President.**

- A. The Vice-President shall serve and assist the President and President-Elect.
- B. Oversees the work of the committees. Shall direct, plan and implement the long range and strategic planning retreat of the Council listed in Article IX section 2E.

**Section 3. Duties of the President-Elect.**

- A. He shall perform all duties that may be delegated to him by the President.
- B. In the absence of the President, the President-Elect shall perform all duties of the President and shall preside at all meetings.

**Section 4. Duties of the Secretary.**

- A. He shall keep or cause to be kept in permanent form an accurate record of all transactions of the Society.
- B. He shall send due notice of all meetings to members; notice of at least 15 days shall be provided prior to Council meetings.
- C. He shall notify all committee members of their appointments and the duties assigned to them.
- D. He shall notify all applicants for membership of the action taken by the Society.
- E. He shall keep a correct alphabetical list of members, together with their current addresses and shall supply application forms to members who apply for same.
- F. He shall act as custodian of all papers of the Society and its committees.

**Section 5. Duties of the Treasurer.**

- A. He shall collect, receive and be accountable for funds accrued by the Society from dues or other sources.
- B. He shall deposit all moneys in a special bank account under the official name of the Society, in a city of his choice.
- C. He shall disburse from the treasury such funds as may be necessary to meet appropriations and expenses of the Society.

His financial records shall be audited at each regular annual meeting by a specially appointed auditing committee, who will report at the business session.

Shall prepare and submit an annual budget for the following year to the Finance committee for subsequent approval of the Council at the fall meeting.

**ARTICLE IX****The Council**

**Section 1. Composition of the Council.** The Council shall consist of the officers, the three immediate Past Presidents, and nine Fellows at Large, three of whom shall be elected annually to serve staggered three-year terms. A Fellow at Large elected to the Council may not succeed himself.

**Section 2. Duties of the Council.**

- A. The Council shall conduct the affairs of the Society during the interim between sessions.
- B. The Council shall pass on all applicants for Fellowship and present its recommendations to the Society at one of its business sessions so that necessary action may be taken.
- C. The Council shall report to the members at regular business sessions all decisions and recommendations made so as to obtain approval of the whole membership of its actions.
- D. Should the membership disapprove of any action of the Council the questions shall be referred back for further consideration and reported at the next business meeting.
- E. The Council shall have a long range and strategic planning retreat at least every three years.

**Section 3. Quorum and Manner of Acting.**

- A. A majority of officers and Council members shall constitute a quorum. A majority of the quorum at any meeting of the Council shall constitute action by the Council unless otherwise provided by law or by these By-Laws.
- B. Any action required or permitted to be taken at a meeting of the Council may be taken without a meeting if a consent in writing setting forth the action to be taken shall be signed by all Council members entitled to vote.
- C. Meetings may be conducted by telephone provided that all officers and Council members participating in such a meeting may communicate with each other. A majority of officers and Council members shall constitute a quorum for telephone meetings and the act of a majority of the quorum shall constitute action by the Council.
- D. Officers and Council members shall not receive compensation for their services, but, by action of the Council, expenses may be allowed for attendance at meetings of the Council or for official representation of the Society and the Council may underwrite any activities that it deems essential to the functioning of the Society.

**ARTICLE X****Committees**

**Section 1.** Other than as specifically stated below, The President shall appoint committee members to serve for three years. Initial appointments shall be staggered such that approximately one-third of committee members shall change each year (other than the Scientific Program Committee and Nominating Committee).

**Section 2. Scientific Program Committee.** This committee shall be appointed by the President to serve for one year and shall consist of at least three Active Fellows. It shall be the duty of this committee to establish a scientific program at the Annual Meeting.

**Section 3. Nominating Committee.** The Nominating Committee shall consist of the three immediate past presi-

dents and two Active Fellows elected at the business meeting. The Nominating Committee shall be chaired by the immediate past President. This committee shall prepare a slate of officers and members-at-large of the Council for vote at the next annual meeting. (See Article VII, section 2).

**Section 4. Credentials Committee.** This committee shall be chaired by the President and shall additionally consist of the two immediate Past Presidents plus two Active Fellows appointed by the President. In addition, the Secretary shall be a member, ex officio. The Credentials Committee shall advise the Council on the credentials of candidates for membership.

**Section 5. Education Committee.** This committee shall consist of at least three Active Fellows. It shall be the duty of this committee to develop appropriate educational activities for the Society.

**Section 6. Research Committee.** This committee shall consist of at least six Active Fellows. It shall be the duty of this committee to: increase the quality and quantity of research conducted in head and neck oncology; encourage the design and implementation of new research protocols; review applications for research funds; and suggest possible new methods of research funding.

**Section 7. Council for Advanced Training in Oncologic Head and Neck Surgery.** This committee shall consist of ten Active Fellows, each to serve a five-year term, with appointments staggered so that two Active Fellows are appointed to membership on this committee each year. The President's appointments to this committee shall be submitted for approval by the Council. It shall be the duty of this committee to evaluate training programs as to whether they qualify for Phase III training and to make recommendations to this Society concerning what constitutes adequate training in head and neck oncologic surgery.

**Section 8. Constitution and By-Laws Committee.** This committee shall consist of at least five Active Fellows, with the Secretary serving ex-officio. It shall be the duty of this committee to completely evaluate the Constitution and By-Laws every three years to maintain their relevance.

**Section 9. Finance Committee.** This committee shall consist of three Active Fellows elected at the business meeting to serve three year terms so that one member is elected each year. The Treasurer shall be an ex officio member. It shall be the duty of this committee to audit the financial records of the Society and review investments and to report at the annual business meeting. It shall review the financial reports of the Treasurer prior to the presentation to the Council.

**Section 10. Standing Committees.** Other standing Committees shall be constituted as described in the Policies and Procedures.

**Section 11. Ad hoc Committee(s).** As necessary, the President may appoint one or more Ad Hoc committees to serve for one year.

## ARTICLE XI

### Quorum

**Section 1.** A quorum for any meeting of the Council shall be a majority of those persons then serving as members of the Council.

**Section 2.** A quorum for the regular business session of the society shall be 18 Active Fellows.

## ARTICLE XII

### Society Assets

**Section 1.** The interest in the funds property and other assets of the Society of any member whose membership shall terminate for any reason except the dissolution of the Society shall, ipso facto, immediately cease and such members and the representatives of such member shall have no claim against the Society or against the other members of their representatives or any of them.

**Section 2.** In the case of dissolution of the Society, the funds, property, and other assets shall be used for the purpose of furthering the expressed purposes for which this Society was formed and no member shall be entitled to receive any of the assets upon liquidation.

**Section 3.** If the Society's annual receipts exceed the annual expenses in any given year, the Council may, by a majority vote, elect to distribute the surplus for such scientific or educational uses as the Council shall deem to be most consistent with the Society's purposes; or it may, should it reasonably anticipate a need for operating surplus to meet future expenses, accumulate such surplus in an interest bearing account or otherwise.

## ARTICLE XIII

### Indemnification

**Section 1.** The Society shall indemnify any and all of the directors or officers former directors or officers, employees, agents, or any person who may have served at its request or by its election as a director or officer of another society or association, or his heirs, executors and administrators, against expenses (including attorney fees, judgments, fines and amounts paid in settlement) actually and necessarily incurred by them in connection with the defense or settlement of any action, suit or proceeding in which they, or any of them, are made parties or a party, by reason of being or having been directors or a director, officer, employee or agent of the Society or of such other Society or association, except in relation to matters as to which any such action, suit or proceeding to be liable for willful misconduct in the performance of duty and to such matters as shall be settled by agreement predicated on the existence of such liability. The termination of any action, suit, or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent shall not, of itself, create a presumption that the person is engaged in willful misconduct or in conduct in any way opposed to the best interests of the Society. The provisions of this section are severable, and therefore, if any of its provisions shall contravene or be invalidated under the laws of a particular state, country or jurisdiction, such contravention or invalidity shall not invalidate the entire section, but it shall be construed as if not containing the particular provision or provisions held to be invalid in the particular state, country, or jurisdiction and the remaining provisions shall be construed and enforced accordingly. The foregoing right of indemnification shall be in addition to and not exclusive of other rights to which such director, officer, employee or agent may be entitled.

**ARTICLE XIV****Merger Provisions**

To facilitate the merger of the Society with The Society of Head and Neck Surgeons, an Illinois nonprofit corporation ("SHNS"), pursuant to an agreement calling for the SHNS to be dissolved and its assets transferred to the Society and the Society recast as The American Head and Neck Society, Inc. ("AHNS") to serve as a successor of both entities, notwithstanding any other provision of the Constitution or these By-Laws to the contrary:

1. The Council shall be expanded as necessary to include the officers and directors of the SHNS, who shall serve on the Council with their voting status as provided by the SHNS bylaws until their term of office within the SHNS shall expire. The Council shall return to its size and with its composition provided in Article IX hereof through the passage of time.
2. The President-Elect of the SHNS shall become as President-Elect of the AHNS following the completion of his term as President-Elect of the SHNS. The President-Elect of the Society shall become President of the AHNS to serve a term of six months (i.e., from May 15, 1998 through November 14, 1998), whereupon the said President-Elect of the SHNS shall serve as President of the AHNS to serve a term of six months (i.e., from November 15, 1998 through the membership meeting in May of 1999 or until his successor shall assume office). During the combined one-year

term of office, the two said individuals shall regularly consult and cooperate with each other on all meaningful and significant decisions to be made during the year so that it may appear that they are serving as co-presidents for the full year, provided, however, that the AHNS shall have only one President in office at one time. At the conclusion of this one-year term, the President-Elect next in line shall succeed to the Presidency.

3. The members of the SHNS shall be admitted to the Society recast as the AHNS in the membership category that correspond to that which they hold in the SHNS. More specifically, Active Members of the SHNS shall become Active Fellows of the AHNS; Senior Member of the SHNS shall become Senior Fellows of the AHNS. Consulting Members of the SHNS shall become Associate Fellows of the AHNS. International Corresponding Members of the SHNS shall become Corresponding Members of the AHNS. Honorary Members of the SHNS shall become Honorary Fellows of the AHNS. Candidate Members of the SHNS shall become Candidate Members of the AHNS.
4. The Council shall act to preserve the unique heritage and history of the SHNS and the ASHNS.