Relationship between Paediatric CT Exposure and Cancer Risk

Meeting Report

IARC, Lyon, 1-2 June 2006 – Princess Takamatsu

Thursday, 1 June 2006

Elisabeth Cardis opened the meeting and welcomed the participants.

Background and objective of the meeting

Elaine Ron briefly summarized main reasons for increased interest in computed tomography (CT) scans:

- The use of CT scans has grown rapidly over the past two decades.
- Radiation doses from these scans are substantially greater than from conventional X-rays.
- Paediatric CT scans are of particular concern because in comparison with adults, children are exposed to higher doses (the relevant dose range for paediatric CT is 6 - 100 mSv).
- Children are generally more sensitive to the carcinogenic effects of radiation.
- Children have a longer life-span to express radiation-related cancer.

She also introduced the meeting goals:

- To discuss potential for collaborative study (availability of data and feasibility of conducting studies in the participating countries)
- To discuss study methods (preferred cohort study designs)
- To set up eligibility criteria for participation
- To evaluate the feasibility of biological repository collection
- To discuss potential funding sources
- To discuss issues of data protection and study ethics

Presentation of the UK-NCI pilot study

Mark Pearce presented the findings of a pilot study, funded by the National Cancer Institute, which aimed to assess the information available from CT records held by the four Radiology Departments within the three National Health Service (NHS) hospitals in the city of Newcastle upon Tyne in Northern England. The objectives of the pilot study were to test planned methodologies by identifying exposed individuals, collecting adequate dosimetric and confounding information and developing a data abstraction form. These findings are particularly relevant to the planning of a much larger national study of the potential long-term sequelae of radiation exposure from CT usage in the paediatric and young adult populations, which it is hoped will in turn be part of a multi-country study.

In the UK, majority of CT scans, particularly for paediatric patients, are performed in NHS centres. All individuals living (legally in the UK) have an NHS number and are entitled to free treatment. A third advantage of the NHS is that using the British system of flagging people for follow-up at the National Health Service Central Registry (NHS-CR), information on and cancers and deaths occurring in the cohort can be provided by the NHS-CR. The Newcastle Hospitals NHS Trust in the United Kingdom includes three hospitals, including the main children's centre for the North of England and serves a population of around 3,000,000 people.

The work in the pilot study consisted of the 3 phases. During Phase I, 4 part-time radiology assistants already working for the NHS were recruited. Methods to identify exposed populations in the radiology department of the Royal Victoria Infirmary from on-site storage of film records and from a central

electronic database covering all 4 units were developed and evaluated. An initial data abstraction form was developed, tested on 20 radiology records in the Royal Victoria Infirmary and then appropriately modified. Newcastle's electronic database includes the following information that can be used for identification of exposed persons:

a. Patient name
b. Date of birth
c. NHS number
d. Radiology unit
e. Hospital identification number
f. Date of scan
g. Type of scan (including part of body and whether contrast used)
h. Referring clinician (and their speciality) and hospital department
i. Postcode (zip code)

During Phase II, 100 radiology records from the RVI (from different time periods) were used to assess the availability from CT film records of:

j. Type of CT
k. Number of repeats
l. Machine settings (KVP, mAs, pitch)
m. Type of machine
n. Protocols in use at time of scan
o. Patient age at examination
p. Patient body weight
q. Reason for scan

The consistency of referrals and recording of information across time and between hospitals in the Newcastle NHS Trust (Royal Victoria Infirmary, Freeman Hospital, and Newcastle General Hospital) was evaluated during Phase III.

Overall, 333 film records were abstracted. The availability of information from records was found as follows:

- Date of birth/ age recorded on all records
- Referring clinician or ward reported on all but 4 records (which were found on electronic data)
- Reason for scan missing on 15
- Slice thickness missing on 3
- Total number of slices only on 60 records mA or mAs missing on only 2 records
- Tilt or pitch missing on 16 records
- Type of scanner missing on 2 records, but can be ascertained from other records
- Patient height and weight not available

Concerning record storage, the 4 units have different storage policies. As a rule, adult films are destroyed after 8 years, while paediatric films are kept for 25 years. Some paediatric films are stored off-site, with difficulties in accessing them. The problem is similar, if anything worse, across the UK.

It is not feasible therefore to have large scale CT film record abstraction for the UK CT cohort and electronic data are to be used for a cohort study. CT film data can be used in nested case-control study for a smaller group of subjects.

Overview of the full UK-NCI study (M. Pearce)

Study design

Following the pilot study, a nationwide cohort study was proposed with an objective to assess the risk of cancer in children and young adults after paediatric CT exposure.The proposed study will have two phases. First, it is planed to conduct a retrospective follow-up study of a cohort of 200,000 children under the age of 15 years who underwent CT scanning, for a non-oncological reason, between 1985 and 1995 in the UK. Cancer incidence will be evaluated in the study cohort in relation to exposure to CT scans. In phase II a nested case-control study of leukaemia will be conducted to assess dose-response more precisely by using estimates of bone marrow dose for individual CT scans. This two-phase approach will restrict collection of detailed radiation exposure information to a small subgroup of the cohort, making the entire study more feasible.

Study population

The study cohort will be identified from electronic radiology department listings of patients who had one or more CT scans between 1985 and 1995 at large radiology departments of regional paediatric centres in the UK.

Data collection

Electronic data to be collected: patient name, date of birth, sex, NHS number, radiology unit, hospital ID, date and type of scan, referring clinician/ward & specialty. Cross linkage will be performed both between and within datasets, including those for the period 1996-2006, to allow the number of scans to be estimated. Additional abstraction of film data for older records, particularly those at risk of being destroyed, will be carried out. This will increase study power, but the intention is to not do this unless absolutely necessary.

Confounders

Confounding by indication is an important aspect of this study that needs to be addressed. For all cancers diagnosed within five years of the last CT scan, medical records will be obtained to check that the CT scan was not performed for investigation of symptoms or signs related to a subsequent cancer diagnosis. All previous oncology patients will be excluded. Post code information from the electronic listings will allow the calculation of a Townsend Score, a measure of community-level SES in the UK based on census data.

Exposure assessment

Doses will be calculated using the CT-EXPO (version 1.5) computer software in collaboration with Dr David Brenner. This software permits dose calculations for all common current and past CT scanners, for adults and children (details can be found in Ref 60). The key determinants of organ dose are: 1) the type of CT scan (e.g., brain or abdominal, axial or helical, the pitch and whether contrast used), 2) the age or weight of the patient, 3) the type of CT scanner used and 4) the date of scan. Given this information, organ doses can be calculated for each individual. A case-control study will use more refined dosimetry due to more detailed information being available.

Follow-up

Follow-up for cancer incidence and mortality will span 1985-2005. Using the UK system of flagging people for follow-up at the National Health Service Central Registry (NHSCR), information on cancers and deaths occurring in the cohort will be provided by the NHSCR. Case-ascertainment will be maximized by linking the cohort with regional cancer registries..

Cases

The study will focus on leukaemia as the main individual outcome; brain, thyroid and breast neoplasms will be evaluated in later follow-ups when the cohort members will be older.

Nested case-control study of leukaemia

The case-control study of leukaemia will include all cases of leukaemia occurring in cohort members. For each case, six matched controls will be identified from the study cohort, using sex, year of birth

(+/- 1 yr), and region of residence as matching factors. Eligible controls will be alive on the date of diagnosis of the respective case and have no history of cancer. Manual data abstraction for CT scan information will be applied for all cases and controls, to augment the electronic data and calculate individual doses to the bone marrow in more precise manner.

Ethics and data access

Umbrella consent for abstracting medical records can be given by the Patient Information Advisory Group (PIAG) without obtaining individual consent from the patients under study; Research Ethics Committee approval and Caldicott approval for accessing identifiable data from hospitals, as well as Honorary NHS contracts for staff accessing NHS information are also required for a study of this nature.

Statistical power

Assuming no radiation effect, the study cohort of 200,000 children would accumulate approximately 2,330,000 person years of follow-up and an expected number of 404 newly diagnosed cancers, excluding non-melanoma skin cancer (NMSC), including 58 leukemias and 43 brain cancers. The predicted number of incident malignancies of radiosensitive tissues (leukemia, breast, thyroid & brain cancers) is 123. For total cancer, the study will have 80% power to detect an overall SIR of 1.07, whereas SIRs of 1.36 and 1.40 can be detected for leukemia and brain tumors, respectively.

Brief presentations from individual groups

The presentations made by Suminori Akiba, Anssi Auvinen, Olivier Catelinois, Gabriel Chodick, Gael Hammer, Magnus Kaijser, Vicki Kirsh, Cecile Ronckers, Joachim Schüz, Philipp Trueb and Florent de Vathaire are summarised in the enclosed table (see Table 1)

Discussion on study design

Cohort vs. case-control study

E. Ron suggested that the best approach would be to conduct a cohort (retrospective follow-up) study and in a second phase, in the countries where it is feasible, a nested case-control study of leukaemia using more precise individual bone marrow dose estimates. All meeting participants were asked about possibilities of conducting the cohort study and their replies are summarized in Table 2.

Table 2

Country	Possible design of the study
Canada, Ontario	Cohort study planned
Denmark	Cohort possible, preference for hospital-based over nation-wide study
Finland	Case-control preferred
	Cohort possible though; preference for hospital-based over nation-wide study
France (2 groups)	Feasibility study necessary to pilot exposure assessment in hospitals; efforts underway by 2 groups who will join forces; Childhood cancer is only outcome possible to study at present
Germany	Cohort, multi-centre hospital-based using example of ongoing study on medical X-rays in Munich; Follow-up currently only feasible for childhood cancer; in some regions also for adult cancer but with less uniform coverage
Israel	Cohort, direct record-linkage with cancer registry (all ages) based on medical files of 1 or 2 large HMO's
Japan	Cohort possible, preference for prospective study
	Case-control challenging, in particular in metropolitan areas

Country	Possible design of the study
	More possibilities in Nagasaki and Hiroshima prefectures (which have tumour registries)
Netherlands	Cohort preferred but likely challenging in view of required individual consent that IRB and/or cancer registry impose unless we can qualify for the exceptions rules (Cancer registry review board = more strict than IRBs and current law);
	Case-control feasible; pilot study needed to address exposure assessment through parental report and/or GP medical files
Sweden	Cohort, direct record linkage with cancer registry and other registries
Switzerland	Currently detailed collection of dosimetric data and CT details but no protocol/collaboration for follow-up in place
	Contact with heads of regional cancer registries needed
UK	Cohort, study protocol ready; follow-up through cancer registry and National Health Service Central Register
Other countries potentially interested / able to contribute	
South Korea	Contac persons Drs Mina Ha or Daehee Kang (both former NCI)
	[Ronckers/Ron]
Greece /Italy / Spain	No nation-wide cancer registry though high utilization rate in Greece
Norway	Contact person (T.Tynes?) [Drs Cardis/Schüz]
Luxemburg	Possible, collaboration with M. Blettner ongoing

Availability of data, ethical constraints and study costs will affect the decision of the appropriate study design. From the data presented, in all countries except the Netherlands, Japan, and Finland, a retrospective cohort study appears to be feasible. However, Drs. Auvinen, Ronckers, and Akiba will examine the possibility of conducting a retrospective cohort study and other technical considerations, using national or regional data.

Study population and outcomes

The second issue of the discussion was the study population and outcomes. It was agreed that there would be four possible approaches:

a. In those countries (e.g. Sweden, Israel) where personal data can be obtained on children who did not have CT and cross linked to national cancer registries, the study population may include a cohort of exposed children and a matched unexposed cohort
b. Cohorts in other countries (e.g. the UK) will follow only exposed children; dose-response analyses will be conducted within the countries
c. In countries (e.g. France) with only paediatric cancer registries, outcome data would be limited to childhood cancers
d. In countries where a retrospective cohort design is not feasible, a prospective cohort study will be set-up; if this is not feasible, a case-control study will be performed.

It seems that there is a sufficient variability in doses received to the bone marrow even within the exposed population; the proportion of abdominal and other types of CTs with potentially important doses to the bone marrow needs to be evaluated though. More information from radiology records is needed from almost all countries to have a better idea on possible exposures.

The common exclusion criteria would be: prior cancer and Down syndrome. Premature birth and specific diseases that involve multiple radiodiagnostic procedures were also discussed as possible criteria for exclusion; information about this may not, however, be available in all countries.

The main outcomes of interest would be leukaemia and all cancers (limited to the age before 15 years at onset in the countries where only childhood registries exist). Other outcomes, such as IQ, cataract, cardiovascular diseases might be also of interest in the countries where it is feasible. Setting up a study with a prospect to follow the cohorts for cancer and non-cancer outcomes might have more chances in obtaining funding, particularly from the EU.

Dose reconstruction

Introduction to ionizing radiation from CT scans and fundamentals of dosimetry was given by Isabelle Thierry-Chef. It appears that there is a wide exposure variation even within the same type of CT scanner and/or CT procedure, which depends on a hospital or even on a radiologist. In some of the countries (e.g. France, Germany, UK), efforts were made to issue guidelines for standardized application of CT procedures. The only computer software available for calculating paediatric organ doses from CT examinations is the CT-EXPO (version 1.5), written by Georg Stamm and Hans Dieter Nagel. This software permits dose calculations for all common current and past CT scanners. The minimum set of parameters necessary to calculate individual organ doses needs to be developed. The following parameters to be obtained from the radiology files were suggested: patient's characteristics (age, gender, height & weight), type of device (manufacturer …), tube characteristics (kVp, mAs …), slice thickness / total number, pitch, filter, etc. A dosimetry subcommittee will finalize the list.

Friday, 2 June 2006

Criteria for inclusion of study centres in collaborative study

There was a common sense that in order to have enough statistical power to explore a possible association between CT exposure in childhood and consecutive cancer risk, the planned study needs to assemble a big international cohort.

In case a country can only contribute a population-based or hospital based case-control study, such can potentially be incorporated in pooled analyses of both phases, but:

- Combined cohort / case-control analysis is challenging and may introduce noise
- Power of a population based case-control study is very low + inefficient given expected exposure prevalence of 1-2% (a nested case-control study approach is preferable)
- Case-control study only offers results for one endpoint

Size of the study population varies from country to country: in the UK study it is estimated that 58 cases of leukaemia would be diagnosed in a cohort of 200,000 which will allow 80% power to detect a risk ratio of 1.36. Leukaemia is probably the only single type of cancer with sufficient power in a study of this size.

One should keep in mind that large international studies with too many contributors pose challenging problems. On the other hand, small countries/centres with nationwide cancer registries and well established instruments for follow-up could altogether increase the study power. The minimum size of the study population required per country/centre is difficult to specify a priori and more information will be needed (including crude dose distributions) in order to define it.

Minimal personal data: for appropriate follow-up and exposure assessment, the minimal information on exposed population should include personal identifiers, age at examination, date of examination and gender.

Age range at exposure: in some countries (France, Germany) the cohort will have a limited age range at CT due to the limited range of ages for which the outcome data can be obtained (up to 15 or perhaps 18 for cancer incidence), although future follow-up based on mortality could be envisaged. In other countries, the age of 18 (or 20 in Switzerland) is preferred, since teens at the age of 15 to 18 years have relatively more scans. Any participating country should provide the estimated age distribution of paediatric CT patients.

Calendar years of CT scans: to avoid the need for manual abstraction of data from paper records and to ensure more uniform quality of data, the earliest year at exposure is likely to be around1990 (1988 in

the UK) or the first year with computerized records available. The latest year is 2000, to allow sufficient follow-up period. Some countries might, however, continue to collect data up to the present and decide on the appropriate censoring date at the time of analysis.

Exclusion criteria: to avoid confounding by indication, oncology patients who were diagnosed within 5 years from the CT scan should be excluded from study. Patients with other serious diseases which are potentially related both to CT and cancer (e.g. epilepsy) should also be noted so that they can be excluded or taken into account in the analysis. More discussions with radiologists are need to understand the major reasons for CT. Data on the use of contrast material might be indicative to referral (e.g. no use of contrast material in head CT might suggest trauma).

Ethical issues and data protection

It is likely that individual consent will not be required for this study in most of the countries (Canada, Denmark, Finland, France, Israel, Germany, Sweden, and the UK) as no contact with study subjects will be made. This is not necessarily the case in the Netherlands and Japan. In Netherlands, however, it is still possible to obtain ethical review board approval for data abstraction without individual consent. Most of the national ethical review committees would absolutely need an exact list of items to be abstracted from radiology/medical records.

Given the uncertainty in epidemiologic data collection and obtaining permissions from ethical review boards, discussion on creating a repository of biological samples is premature and probably not appropriate at this stage (particularly if no contact with study subjects is made).

Data protection in some countries (Germany) may include encoding of ID and other identifying data. In several countries sending encoded data for pooled analysis to IARC may also require special permission from the ethics boards. Note that no personal identifier which could allow identification of the study subject should be sent to IARC. In the UK, sending data outside the EU might be an obstacle. In many countries ethical boards and in particular university hospitals, are negative about using portal to access datasets on a server.

Organisation of possible collaborative study

In order to set up the collaborative study, obtaining a support form radiologists is essential. E. Ron suggested to use a brochure prepared by NCI, which explains rationale for conducting the study.

Study protocol

An epidemiology sub committee (including Drs. Pearce, Auvinen, Schüz, Kaijser, and representative from IARC and NCI) was formed for further discussion. The basis for the protocol – particularly concerning study organisation, data sharing, data analysis and publication – could be the protocol used for the Interphone study. IARC wil be responsible for circulating the first draft of the study protocol.

Dose reconstruction

The nested case-control study will focus on better estimation of the dose from the CT scans. The dose reconstruction will use several personal characteristics and machine parameters. It should also include data on past angiography and exposure to diagnostic and therapeutic radiology. There is a wide variety of procedures and uniform standards in the EU were accepted only in 2002. For the study of leukaemia, doses to the bone marrow are most significant (including head CTs in very young children). Contacts should be made with experts in the field such as the dosimetry group (head, Dr. Shaum from Luxemburg) which work on standardization of protocols in Europe. A dosimetry subcommittee (including D.Brenner, H-D.Nagel, Shaum, P.Trueb, one person from STUK and Isabelle Thierry-Chef) was set-up.

Funding

For EU countries, funding may be sought from the EU Euratom Programme. The EU is currently finalising its workprogramme for the 7th framework programme (FP7), which should be published shortly, with the first call for proposal in the fall of 2006 or in early 2007. It is not known whether epidemiology will be in the first call or in a later call (calls are generally issued yearly). More details

on the specific research areas/instruments should be available in June-July. Co-funding from national sources is necessary.

The non-EU countries would need separate funding; mechanisms have already been explored for Israel and Canada.

Timetable

The timetable is dependant upon the closing date for the next call of the 7th framework Euratom program (early 2007). A common study protocol (or at least a detailed outline of such a protocol) will be absolutely essential to prepare a grant application. Development of the protocol includes the following: providing data from each participating country on size of cohort, data available for assembling a cohort, range of calendar years with available electronic data on CT scans, sample of historical records on CT scans (approximately 100 records), data on types of paediatric CTs in order to evaluate dose distribution in the exposed population.

In countries where the availability of such data is uncertain (France, Germany, Switzerland, Denmark, Finland, and Japan), feasibility studies should be conducted within the next six months.

The following timetable was agreed:

Task	
Feasibility questionnaire for obtaining data from hospitals/health care/insurance databases	July-August 2006
Providing data from each participating country: • Size of cohort • Information available for identification of cohort members • Range of calendar years with available electronic data on CTs • Analysis of a sample of historical radiology records • Data on types of CTs to evaluate dose distribution	September 2006*
Meeting of epidemiology subcommittee	November 2006
Application for funding to Euratom 7th framework programme	Early 2007

* for France, Germany, Switzerland, Denmark, Finland, the Netherlands and Japan – it could take 6 months from now

Enclosures

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Table 1-Summary of presentations form individual countries

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Table 1 General information about ongoing/possible study by country

Country/region	Age at exposure	Size of population considered	Coverage	Study design	Number of CTs performed by time period	Identification of exposed population	Information available from records	Case ascertainment follow-up	Study period
Canada:									
BC	<18	919.000	Province - all hospitals	Cohort st population based	NA	Linkage with provincial health insurance records of claims for CT procedures		Linkage with provincial cancer registry	CT exp 1986-1996, case ascert 1986-2005
Quebec	<18	1,59 million	Province	-	NA	Possibly through the health insurance files		NA (Medicare records?)	NA
Ontario	<18	2,7 million	Province – 4 major childrens' hospitals	Possibly cohort st (hospital based)	<1995 50.000 1995-99 140.000 2000+ 198.942	Through both electronic (av 7 most recent years) and paper radiol records (av. since 1980)	Referral info, reason for CT, part of body, slice thickness indication of mA setting, pitch, No of slices, type of scanner, patient age, weight, height	Unique health insurance ID to link CT exp to Ontario CR (98%completeness) and to Mortality reg; nationwide CR also can be used (migration from the province 10%/year)	Back to 1995
Denmark	<18	1,2 million	Nationwide, 31 CT scanners, 7 major hospitals	Cohort st possibly hospital based, in Zealand could be population based	NA	*through database of CTs (since 2004) CPR ID, *hospital-discharge registry *active retrieval through radiology records	needs to be checked	CPR ID number linkage with Danish CR (+childhood, path, hospital discharge registries), vital status and	CT exp back until 1980? case ascert available since 1943

Country/region	Age at exposure	Size of population considered	Coverage	Study design	Number of CTs performed by time period	Identification of exposed population	Information available from records	Case ascertainment follow-up	Study period
								migration - through population registry	
Finland	<15	1 million	Nationwide 5 major university hospitals?	Preference - population based case-control st; hospital based cohort study - possible	1995-99 9.100	Trough radiology departments because no information on CTs from discharge registry available	Needs to be checked	Through CR; hospital discharge registry, vital status – from population reg	CT exp-? case ascert 1975-2003
France									
IRSN	<5	5.000	Nationwide – 15 regional hospitals (of 27)	feasibility st - cohort st hospital based	NA	through paediatric radiological departments' files, computerized files NA	Needs to be checked	Through national paediatric cancer registry (<15y)	CT exp 1995-2000 case ascert 2000-2007, for leukaemia could be back to 90-95'
IGR	<15	10.000	Nationwide – 10 major paediatric radiol depts	Feasibility st – hospital based cohort	NA	through paediatric radiological departments' files, computerized files NA	Needs to be checked	Through national paediatric cancer registry (<15y), possibly to use health insurance database	CT exp 1993-1996
Germany	<15	12 million	70 departments	Cohort st hospital based, large clinics only	20.000/year	Through records of radiol dept, compulsory recordings on CTs since 2000	Standardized electronic recordings since 2000	Matching with German Childhood Cancer registry	2000-2005
	<15	98.000		Cohort st	<1995- 0	Through records of		Same as above	CT exp 1997-2004

Country/region	Age at exposure	Size of population considered	Coverage	Study design	Number of CTs performed by time period	Identification of exposed population	Information available from records	Case ascertainment follow-up	Study period
Munich				hospital based (includes X-rays and CTs)	1995-99 500 2000+ 2.000	radiol dept			case ascert 1997-2004
Israel *Maccabi HCS*	<18	570.000	1 or 2 big HMO's	Cohort st	<2000 NA 2000+ 4.000/year	Through MHS centralized database av. since early 1990's	gender, age at exposure, body parts scanned, sedation, medical diagnosis	using PID linkage with Israel NCR	1999-2005 1999-2003
Japan.									
Aomori pr	<15	210.000	Prefecture	Cohort st preferably-prospective	1000 / year	Through records of 3 major children hospitals	needs to be checked	Active follow-up of entire children population	?
Kagoshima	<15	0.26 million	Prefecture	Cohort st preferably-prospective	1000 / year	Through records of 2-3 major children hospitals	needs to be checked		
Nagasaki pr	<18?	286.102	Prefecture – 6 hospitals	*Prospective cohort st hospital based *Retrospective cohort st pop based	NA	Through records of radiolog depts of 6 hospitals		Linkage with Nagasaki CR and medical record	CT exp 1991-2001 case ascert 1996-2006
Netherlands	<15 <20	3mln 4mln	Nationwide, large academic and non-academic centres only	Cohort st hospital based, vs. case-control st. population based	1990 11.000 2004 26.000	*Electronic patient listings from radiology departments, radiology files *if case-cntrl design – through GP files	needs to be checked	Through nation-wide CR pathol database, vital status through municipal resident reg, registry of deaths	CT exp from 1985 onwards case ascert from 1989 onwards
Sweden	<18	700.000	Nationwide, 2-4 univers.	Cohort st hospital based	<1990 1.500 1990-94 4.000	Through computerized	Complete inf on dose av. since	Through CR, vital st through	CT exp and case ascert

Country/region	Age at exposure	Size of population considered	Coverage	Study design	Number of CTs performed by time period	Identification of exposed population	Information available from records	Case ascertainment follow-up	Study period
			hospitals considered (out of 7)	with CT of head, thorax and/or abdomen	1995-99 20.000 2000+ 30.000	records of radiology departments	early 2000	death and population registries	from 1992 onwards, allowing for latency
Switzerland	<20	1,6 mln	Nationwide ?	Cohort?	NA yet	Radiology departments?	Differs by hospital	Possibly through regional CR	?
UK	<15	Cohort of 200.000 children 3 million (total pop)	Nationwide, large radiol depts	1st phase – cohort st, hospital based 2nd phase nested case-control st of leukaemia	1991-2000 9.000	*Through radiology dept electronic listings *paper records from years with no electronic listings – if needed	type of CT, age & weight of patient, type of CT scanner, date scan.	*through NHS Central registry *linking with regional cancer registries of England	CT exp 1985 – 1995 case ascert 1985 - 2005