# EPI-CT: Epidemiological study to quantify risks for paediatric computed tomography and to optimise doses

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## Background

The worldwide increasing use of paediatric computed tomography (CT) raises the question of possible late effects from exposure to ionizing radiation. The European collaborative EPI-CT project aims at studying the cancer risks and the underlying biological markers in a large international cohort study.

## Material and methods

From 2008 to 2010, a European feasibility study CHILD-MED-RAD was performed coordinated by the International Agency of Research on Cancer (IARC). The feasibility and optimal methods to study the late effects of medical ionizing radiation exposure in childhood were assessed in nine countries. We evaluated eligible study populations, prevalence and magnitude of exposure by source, relevant outcomes and study design. National partners independently performed literature searches, expert interviews, surveys, site visits and data explorations. National findings were discussed jointly and recommendations made for a European study on paediatric CT, EPI-CT, the design of which is described below.

## Project outline

EPI-CT is an international collaborative study of the health effects of childhood and adolescent exposure to ionizing radiation from CT scans. The study is underway or starting in 11 countries (with partners from 18 institutions). The study comprises 3 main parts:
(I) An epidemiological cohort study to evaluate the late effects (primarily cancer) of radiation exposure and describe the CT usage patterns,
(II) A dosimetry package to develop sophisticated methodology for individual CT dosimetry and contribute to further dose optimisation strategies,
(III) A biological pilot study to explore the role of genetic factors for individual radiation susceptibility and validate potential biomarkers of exposure and sensitivity.

## Objectives

1. Establish a multinational cohort of paediatric patients who received CT scans.
2. Describe patterns of use of CTs over time and between countries.
3. Develop individual estimates of organ-specific doses from paediatric CT scans using improved methods for dose estimation.
4. Evaluate the radiation-related risk of cancer in this cohort.
5. Pilot feasibility of non invasive biologic sample collection for a large-scale fully integrated epidemiology and biology study in the future.
6. Explore biological markers of individual radiation sensitivity and radiation exposure.
7. Develop methods to characterise quality of CT images in relation to the corresponding examination dose.
8. Provide recommendations for a “harmonised” approach to CT dose optimisation for paediatric patients in Europe

## Results

This project will provide direct epidemiological evidence on the potential cancer risk from exposure to low doses of ionizing radiation in the large multinational European cohort. This will be the largest, and the most statistically powerful study of paediatric CT scans undertaken to date. Based on conservative assumptions, the analyses will have sufficient statistical power to detect a SIR of 1.16 for leukaemia and of 1.1 for all cancers, respectively.

The project will provide advanced individual organ dosimetry methods for paediatric CT examinations.

The results from the explorative biological approaches will ease further comprehensive epidemiologic-biologic research and may lead to new biomarkers of radiation sensitivity.

Finally, the results will contribute to optimisation and justification of the use of CT scanning in paediatric health care settings.

The first results are expected in 2015.

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## Description of national cohorts

| | Cohort and exposure information | | | | | Outcomes | | | |
|---|---|---|---|---|---|---|---|---|---|
| Country | Age range | Start cohort accrual | Hospital selection criteria | Source of cohort information | Cohort size [2] | Childhood cancer incidence | Adult cancer incidence | Cancer and non- cancer mortality | Record linkage |
| Belgium | 0-15 | 2002 | Population size | PACS | 30 000 | Yes | Yes | Yes | Deterministic |
| Denmark | 0-18 | 2000 | Population size | PACS | 30 000 | Yes | Yes | Yes | Deterministic |
| France | 0-5[1] | 2000 | Population size | RIS/PACS | 90 000 | Yes | Possible | Yes | Deterministic |
| Germany | 0-15 | 1985 | Population size | RIS/PACS | 140 000 | Yes | No | Possible | Probabilistic |
| Netherlands | 0-18 | 1998 | Possibly all | PACS | 40 000 | Yes | Yes | Yes | Probabilistic |
| Norway | 0-20 | 2005 | Possibly all | RIS/PACS | 20 000 | Yes | Yes | Yes | Deterministic |
| Spain | 0-20 | 2005 | Population size | RIS/PACS/other | 200 000 | Yes | Since 2010 | Yes | Deterministic |
| Sweden | 0-18 | 1984 | Population size | RIS/PACS/other | 95 000 | Yes | Yes | Yes | Deterministic |
| UK | 0-21 | 1985 | Possibly all | RIS/PACS/other | 400 000 | Yes | Yes | Yes | Deterministic |
| Total | 0-21 | 1984-2002 | | | 1 045 000 | | | | |

## Power Calculations

| Cohort size | | | Leukemia | | | All cancer combined | | |
|---|---|---|---|---|---|---|---|---|
| Subjects | Average follow-up[6] | Person years | Incidence[3] | Expected[4] | SIR[5] | Incidence[3] | Expected[4] | SIR[5] |
| 1 000 000 | 10y | 10 000 000 | 4.8 | 480 | 1.13 | 13.6 | 1360 | 1.08 |
| 1 000 000 | 7.5y | 7 500 000 | 4.8 | 360 | 1.15 | 13.6 | 1020 | 1.09 |
| 750 000 | 7.5y | 5 625 000 | 4.8 | 270 | 1.18 | 13.6 | 765 | 1.10 |

[1] 0-10 years starting from 2007 on
[2] estimated size, corrected for multiple examinations per patient and oncologic indications, where possible

[3] age standardized childhood cancer incidence per 100 000 for the period 1980 to 2007 in Germany
[4] expected childhood cancer cases in the cohort
[5] smallest measurable SIR with $\alpha$=0.05 and $\beta$=0.2
[6] the calculated mean follow-up period for the entire cohort is 9.1 years

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