CT scan studies – present results and the future

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CT scanning

- **A very useful, sometimes lifesaving, tool**

- 7 years from theory to first clinical use (1971)

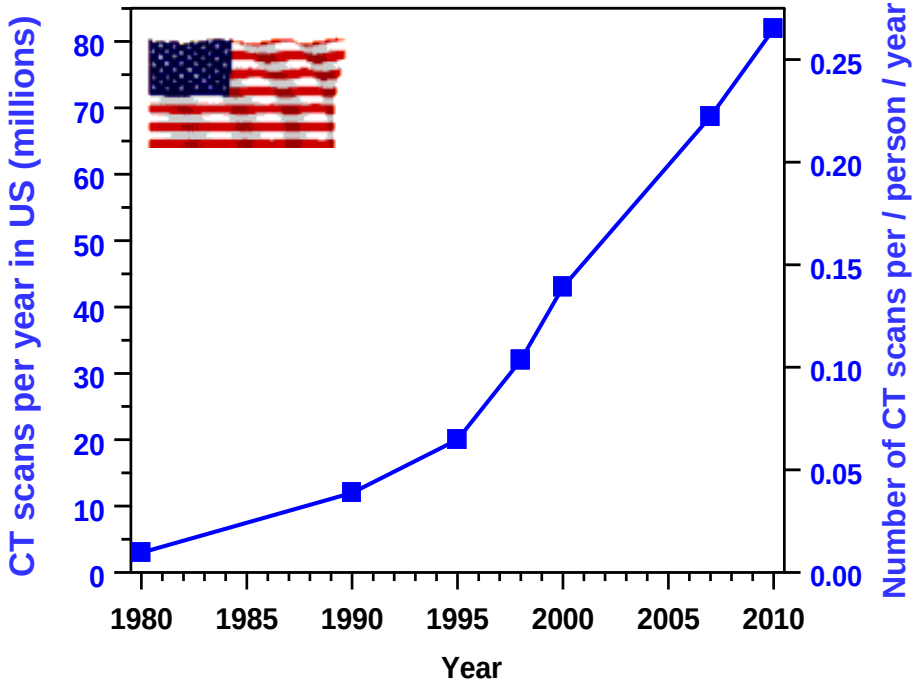
- 8 further years to a Nobel prize (1979 to Allan Cormack and Godfrey Hounsfield)

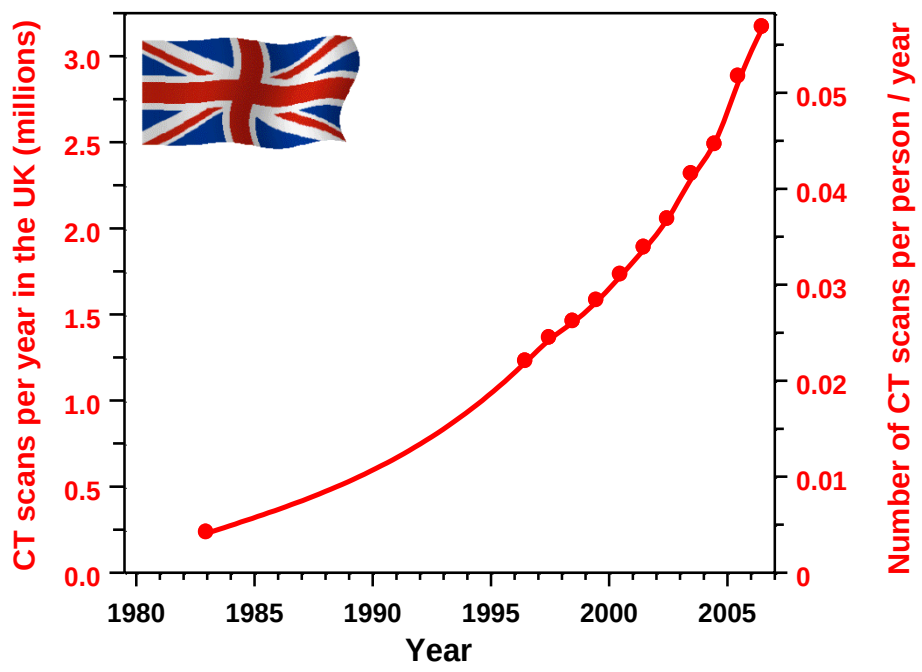
CT scan usage

- Available worldwide at over 30,000 centres (and continuing to increase)
- 11% of all medical imaging examinations in the UK
- 68% of total collective dose to UK population from medical x-ray examinations

Trends in CT usage

Frequency of CT scans per year





Early Fears

- Two risk projection studies lead to much media interest
- Brenner *et al* estimated that of the 1.6 million children in the US who get CT scans to the head and abdomen each year, about 1,500 will eventually die from a cancer induced by the radiation of those scans.
- Donnelly *et al* showed that too many CT scanners were giving children adult-sized doses, often several times higher than necessary.

Further risk projection studies

- Mostly extrapolated ‘expected’ doses and ‘expected’ cancer risks
  - i.e. no empirical data

- Projections were often limited to certain scans, mortality outcomes only and made assumptions regarding modern protocol adjustments that may not have been possible historically

Miglioretti et al (2013)

- Modelled the risks with childhood CT in seven US healthcare systems

- Estimated both effective and organ doses

- Projected that with 4million CTs done in children in the US per year, this would lead to 4870 excess cancers.

- Reducing the doses to the highest 25% exposed patients would prevent 43% of these cancers

Moving forward from predictions

Models using existing risk estimates are very useful for publicising the need for radiation protection and empirical research, but….

It is much better if we complement these studies by direct observations of the relevant health effects in populations that we want to protect.

The UK CT Scan Study

- Long-term sequelae of radiation exposure due to computed tomography in childhood and early adulthood

- Funders:
  - US National Cancer Institute
  - UK Department of Health

Cohort Study

- Patients having one or more CT scans between 1985-2002
  - First scanned aged <22 years
  - Free from cancer at first CT
- Radiology departments with available electronic RIS data of sufficient quality
  - Film / paper records from small number of Trusts

Cohort study dosimetry

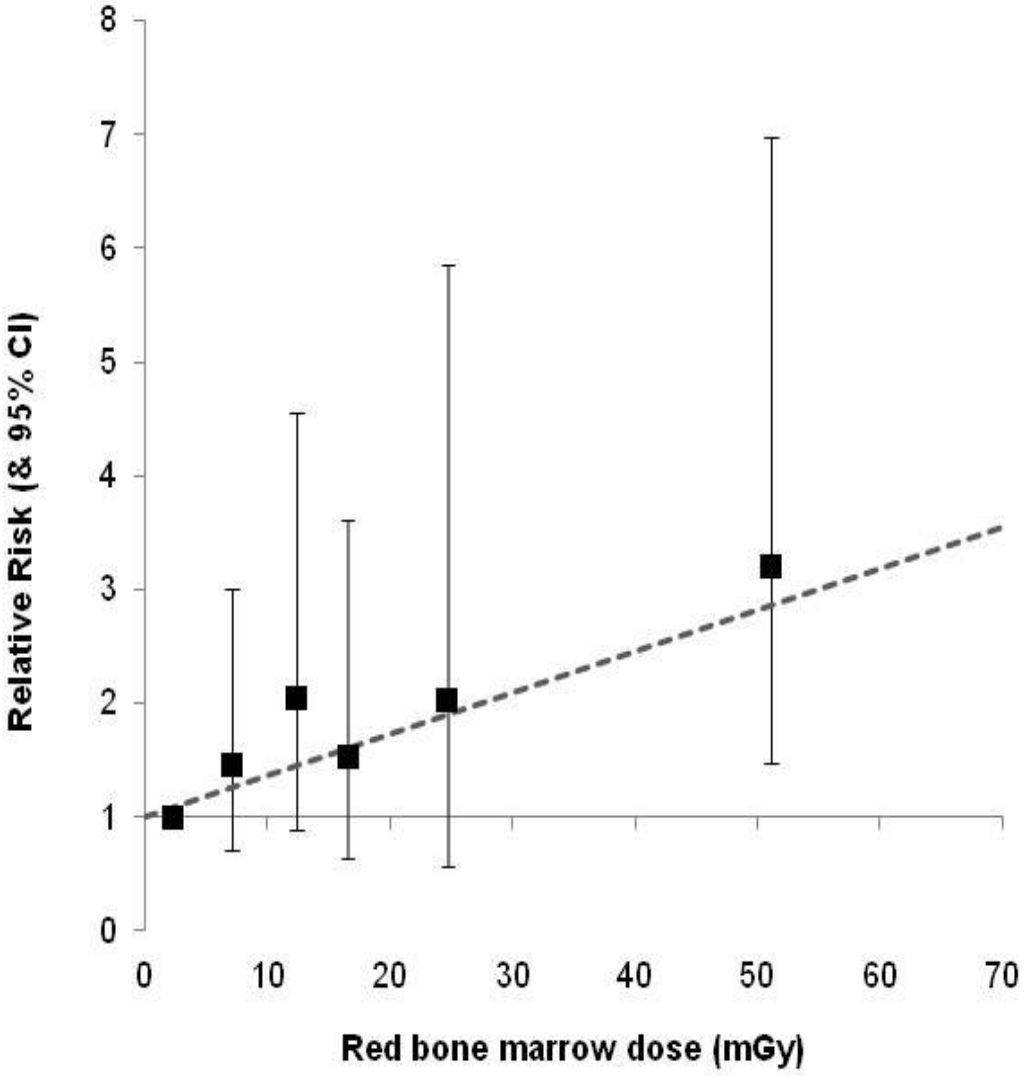
- Date and type of scan, age and sex available from electronic RIS records
- Typical CT machine settings for young people taken from 2 UK-wide surveys (1989 and 2001)
- These data combined with those from hybrid computational phantoms and Monte Carlo radiation transport techniques to give estimated absorbed organ doses (e.g. red bone marrow)
- Cumulative doses where more than one CT scan

Outcome data

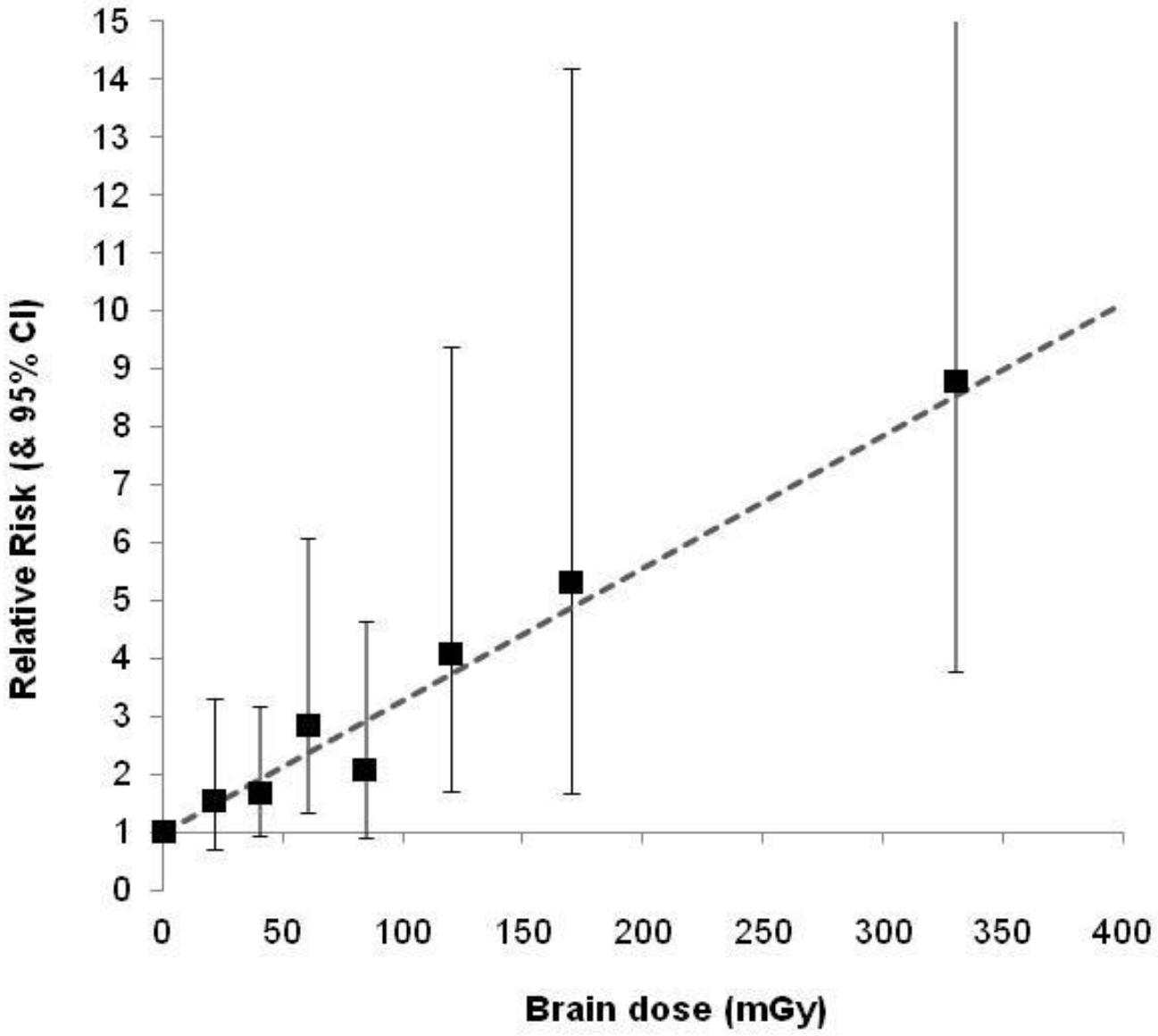
- RIS data linked with the NHSCR (1985-2008)
  - Cancer incidence
  - Mortality
  - Loss-to-follow-up (e.g. notified emigrations)

- Excluded patients with existing cancer and those diagnosed with leukaemia within 2 years of first CT scan (5 years for brain tumours)
  - Sensitivity analyses with greater years of exclusion

Leukaemia dose-response



Brain dose-response



Sensitivity analyses

- Excluding all scans in the 10 years prior to a brain tumour diagnosis gave a higher dose-response than in the original analysis
  - i.e. the opposite to that expected if bias from CT related to diagnosis was driving the findings
- Little evidence of non-linearity of the dose-response for either leukaemia or brain tumours

Main findings of the UK study

- Significant associations between the estimated radiation doses and subsequent incidence of leukaemia and brain tumours

- Assuming typical doses:
  - 5-10 head CTs (≈50mGy to RBM) give an estimated tripling of risk of leukaemia
  - 2-3 head CTs (≈60mGy to the brain) give an estimated tripling of risk of brain tumour

Strengths and weaknesses

- We used empirical data
- Cohort approach avoided recall bias (exposure data from medical records)
- Nationwide cancer registration (97% ascertainment)
- Used a careful approach to avoid those with existing cancers

Strengths and weaknesses

- Dosimetry was improved on previous estimates
  - Provided organ doses
- Uncertainties still exist
  - Not expected to bias the findings
- Unable to obtain individual-level parameter data for such a large and historical cohort

The Australian CT Study

- Cohort study of 10.9 million people identified through Medicare
- Patients aged under 20 years
- Scans between 1985 and 2005
- Exposed cohort: 680,211
- Less detailed dosimetry than in the UK study (and primarily based on effective doses)

The Australian CT Study

- IRRs for all cancers fell with increasing lag times
- 1 year: IRR 1.24 (95% CI 1.20, 1.29)
- 5 years: IRR 1.21 (95% CI 1.16, 1.26)
- 10 years: IRR 1.18 (95% CI 1.11, 1.24)

The Australian CT Study

- IRRs for specific cancers
  - Raised IRRs for nearly all cancer types
    - Including Hodgkin's Lymphoma and melanoma
    - Not including breast or lymphoid leukaemia

The Australian CT Study

- Additional considerations
  - Missing exposures from tertiary hospitals
  - Leukaemia risks increased with age at exposure
  - Brain and other solid tumours had high excess rates within 5 years of first CT
    - But, brain tumour incidence was still increased at 15 years from the first exposure

International collaboration

- Similar studies were underway in:
  - Canada, Sweden, Israel and France
- EU-funded collaborative study (EPI-CT) began in 2011
- New study underway in Brazil
- Most studies are using a similar study design and collaborations are underway re dosimetry

EPI-CT Objectives

- Establish a large multinational European cohort of paediatric and young adult patients who received CT scans
- Describe patterns of use of CTs over time and between countries
- Develop individual estimates of organ-specific doses from paediatric CT scans using a unified improved method for dose estimation for paediatric and young adult patients
- Evaluate the radiation-related risk of cancer in this cohort
- Test biological markers of CT-irradiation effects (pilot study)
- Develop methods to characterize quality of CT images in relation to the corresponding examination dose
- Provide recommendations for a “harmonised” approach to CT dose optimisation for paediatric patients in Europe

EPI-CT: Estimated cohort size per country

CT scan epidemiology – the future

- Further risk-based analyses of all cohorts, including pooling of cohorts
- Uncertainties analyses
- Long-term follow-up of all the cohorts, and more cohorts to be added
- More national cancer registries throughout Europe – covering all ages

CT scan epidemiology – the future

- Need to establish registries of non-cancer conditions, e.g. cataracts
- Continued improvements in dosimetry and better availability of indication data
- More harmonised ethical approval systems

CT scan epidemiology – the future

- Better and easier data linkage throughout Europe
  - Including links with other disease registries, e.g. congenital anomalies
- Do we need better guidelines?
  - Certainly need to make sure that justification guidelines are followed

Interpretation of the evidence so far

- The immediate benefits outweigh the (small) risks in most settings when CT is used appropriately

- Of utmost importance is that, where CT is used, it should only be used where fully justified from a clinical perspective