CT Scans and Cancer Risk: Past, Present & Future Studies

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How Can Pediatric CT Scan Studies Contribute?

• Low dose range (1-100mGy)
• Fractionated exposures
• Children - radiosensitive population
• Exposures primarily to radiosensitive organs – red bone marrow and brain
# Pediatric CT Studies Overview

<table>
<thead>
<tr>
<th>Population</th>
<th>N exposed</th>
<th>Publications</th>
<th>Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>180,000</td>
<td>Pearce et al (Lancet, 2012)</td>
<td>Additional data collection</td>
</tr>
<tr>
<td>Australia</td>
<td>680,000</td>
<td>Mathews et al (BMJ, 2013)</td>
<td>Individual dosimetry construction</td>
</tr>
<tr>
<td>EPI-CT</td>
<td>1 million</td>
<td>2017</td>
<td>Data collection &amp; dosimetry</td>
</tr>
<tr>
<td>Canada</td>
<td>350,000</td>
<td>2016</td>
<td>Data collection complete</td>
</tr>
</tbody>
</table>
UK Pediatric CT Study: Design

PIs: Mark Pearce (Newcastle), Amy Berrington (NCI)
Collaborators: Mark Little, Choonsik Lee (NCI)

Record linkage, Retrospective Cohort, Internal Comparison

100+ Radiology departments

CTs age 0-21 yrs 1980-2003

Cancers & deaths <2009
Leukemia/MDS Risk & Red Bone Marrow Dose (n=74)

**ERR/mGy = 0.036 (95%CI: 0.005 - 0.120)**

p-trend = 0.010
Brain Tumors Risk & Brain Dose (n=135)

ERR/mGy = 0.023 (95% CI: 0.010 - 0.049)  
p-trend<0.0001

Pearce et al (Lancet 2012)
Comparison with ERR/mGy from A-bomb Data

Life Span Study

Single acute exposure ($\gamma$ rays & small neutron dose)
Restricted to 0-21yrs at exposure & follow-up <15 yrs
Potential Bias for Brain Tumors: Reverse Causation
Confounding by Indication

Underlying condition related to cancer & the condition related to CT scan frequency

Reproduced from DOWN'S SYNDROME ASSOCIATION Website (www.downs-syndrome.org.uk)
UK Assessment of Potential Biases: Results 2015

Pathology reports

Radiologist’s comments

Death certificates
UK: Dose Uncertainty Assessment 2015

Patient-specific CT technique parameters

- Abstract 1000 films from hospitals
- Reconstruct doses using NCI-CT (Dr Lee, NCI)
- Incorporate into analyses with uncertainty
Australian Pediatric CT Study

PI: Professor John Mathews (Melbourne)
Collaborators: Dr Zoe Brady, Sarah Darby (Oxford)
• 10.6 million unexposed and 680,000 exposed
• Number of CT scans, all cancers & site-specific
• RR=1.16 (1.13-1.19) per CT scan (1 year exclusion)
• Dose reconstruction – expected publications 2015
• Other exposures – publications 2015/16
• Potential biases – publications 2015
European Study: EPI-CT

Ausra Kesimiene, Elisabeth Cardis, Mark Pearce, Michael Hauptmann, Isabelle Thierry-Chef

• 2011-16 EU grant
• 1 million children
• 9 countries
• 2000+ PACs data
• Expanded UK cohort
• Results 2017
Canadian Pediatric CT Study

PI: Dr Vicki Kirsh (Cancer Care Ontario)
Collaborators: Amy Berrington, Choonsik Lee (NCI)

• 350,000 Exposed Children
• Ontario state hospitals linked to cancer registration
• Follows UK CT model for dosimetry & analysis
• Some additional clinical data to incorporate
• Data collection completed – publication 2016
## International CT Pooling Project: 2017

- **Aims:** Assess consistency, effect modification, tumor subtypes, breast & thyroid cancer

### Study Population

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Leukemias</th>
<th>Brain Tumors</th>
<th>Breast Cancers</th>
<th>Thyroid Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>544,000</td>
<td>200</td>
<td>226</td>
<td>116</td>
<td>207</td>
</tr>
<tr>
<td>Canada</td>
<td>350,000</td>
<td>249</td>
<td>454</td>
<td>111</td>
<td>94</td>
</tr>
<tr>
<td>UK</td>
<td>180,000</td>
<td>74</td>
<td>135</td>
<td>33</td>
<td>28</td>
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<tr>
<td>Israel</td>
<td>30,000</td>
<td>6</td>
<td>22</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,104,000</strong></td>
<td><strong>529</strong></td>
<td><strong>837</strong></td>
<td><strong>263</strong></td>
<td><strong>337</strong></td>
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(Australia/Canada - estimated eligible case numbers)
Timeline for Key Ongoing Studies

- 2015:
  - UK bias analyses
  - Australian doses

- 2016:
  - Canadian results

- 2017:
  - EPI-CT results
  - Int Pooling results
Comments on Value of Pediatric CT

Strengths
- Direct study of low-dose range (0-100mGy)
- Exposure based on medical records (no recall bias)
- Childhood exposure and risk of leukemia & brain tumors, possibly thyroid and breast cancer
- Dose-response relationships

Limitations
- Potential biases need further evaluation – but shouldn’t be generalized across cancer types
- Highly individualized dosimetry challenging (100k+ patients)
- Generalizability to adulthood exposure uncertain
Other Diagnostic Exposure Cohorts

- Ronckers et al (CEBP 2008) Scoliosis cohort
  - Breast cancer dose-response (p=0.06) with X-ray dose (mean 120mGy)

- Rajaraman et al (BMJ 2011) UK Childhood Cancer Study
  - Increased risk (non-significant) of all cancers and leukemia from *in utero* exposures

- Australian CT study will examine other exposures
  - Nuclear medicine publication 2015

- Congenital heart disease & fluoroscopy
  - France, UK, Canada & Denmark studies in progress