Understanding radiation-induced cancer risks at radiological doses

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Let's distinguish between lower-dose and higher-dose radiological examinations

<table>
<thead>
<tr>
<th>Examination</th>
<th>Relevant organ</th>
<th>Relevant organ dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental x ray</td>
<td>Brain</td>
<td>0.005</td>
</tr>
<tr>
<td>PA Chest x ray</td>
<td>Lung</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral chest x ray</td>
<td>Lung</td>
<td>0.15</td>
</tr>
<tr>
<td>Screening mammogram</td>
<td>Breast</td>
<td>3</td>
</tr>
<tr>
<td>Adult abdominal CT</td>
<td>Stomach</td>
<td>11</td>
</tr>
<tr>
<td>Adult head CT</td>
<td>Brain</td>
<td>13</td>
</tr>
<tr>
<td>Child abdominal CT</td>
<td>Stomach</td>
<td>10-25</td>
</tr>
<tr>
<td>Child head CT</td>
<td>Brain</td>
<td>20-25</td>
</tr>
<tr>
<td>Adult $^{18}$F-FDG PET</td>
<td>Bladder</td>
<td>18</td>
</tr>
</tbody>
</table>
Lifetime doses from CT

Of the ~25 million people who have CT scans this year in the US....

- 13 million will have received more than 25 mSv (effective dose) from CT over the past 20 years
- 3.8 million will have received more than 100 mSv (effective dose) from CT over the past 20 years
- 1 million will have received more than 250 mSv (effective dose) from CT over the past 20 years

Sodickson et al 2009
Taking into account

* Machine variability,
* Usage variability,
* Age variability,
* Scans done with and without contrast
* Multiple scans

Relevant organ dose ranges for CT are

5 - 100 mSv for a single series of scans
5 - 250 mSv lifetime
Atomic bomb survivor locations by dose

Green dots: Individuals exposed to between 100 and 200 mGy
Brown dots: Individuals exposed to between 5 and 100 mGy

Douple et al 2011
RERF LSS solid cancer low-dose trend tests

Cancer Mortality
• 0 – 0.1 Gy  P=0.04
• 0 – 0.15 Gy  P=0.006

Cancer Incidence
• 0 – 0.1 Gy  P=0.08
• 0 – 0.15 Gy  P=0.01

Courtesy D.L. Preston (2011), based on RERF public dataset DS02can.csv (www.rerf.or.jp)
Other low-dose epidemiological studies show similar results...

17,000 Techa River inhabitants (Krestinina et al 2007, cancer incidence)

400,000 nuclear workers (Cardis et al 2007)

Other low-dose epidemiological studies show similar results...

The Oxford Survey of Childhood Cancers

- Significant increase in childhood cancer after in-utero x-ray exposure
- Mean dose ~ 6 mGy
- 15,000 case control pairs

Doll and Wakeford 1997
Extrapolating from whole-body irradiation to partial-body radiation risks

Organ-specific dose-dependent risks are roughly independent of whether the exposure is whole-body or partial-body.

Organ cancer risks / Sv derived from A-bomb data

Organ cancer risks / Sv derived from RT data

Little 2001
For organ doses corresponding to those from higher dose exams (CT / PET / fluoroscopy), we don't need to worry about using risk extrapolation models like LNT
Estimating the radiation-induced cancer risks from CT exams

- Direct epidemiology on people who received CT scans
- Risk estimation based on organ doses
Epidemiological studies of cohorts of patients who had pediatric CT

- UK ~200,000 children
- Ontario: ~275,000 children
- Israel: ~80,000 children
- Australia ~150,000 children
- France ~25,000 children
- Sweden ~35,000 individuals
Will these studies have enough power?

• The studies are large, but the expected numbers of cases is still small
• Power may be sufficient to identify an increased risk of leukemia / thyroid / brain tumors
• But probably need larger and longer studies to assess most of the possible risk
Will the studies be long enough?

Median latency time: The time required to accumulate 50% of the predicted total lifetime radiation-induced absolute cancer risk.
<table>
<thead>
<tr>
<th>Institution</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>International Agency for Research on Cancer</td>
<td>France</td>
</tr>
<tr>
<td>Johannes Gutenberg-Universität Mainz</td>
<td>Germany</td>
</tr>
<tr>
<td>Säteilyturvakeskus</td>
<td>Finland</td>
</tr>
<tr>
<td>Karolinska Institutet</td>
<td>Sweden</td>
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<tr>
<td>University of Newcastle upon Tyne</td>
<td>UK</td>
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<tr>
<td>Centre de Recerca en Epidemiologia Ambiental</td>
<td>Spain</td>
</tr>
<tr>
<td>Institut Gustave Roussy</td>
<td>France</td>
</tr>
<tr>
<td>Kraeftens Bekaempelse (Danish Cancer Society)</td>
<td>Denmark</td>
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<tr>
<td>Het Nederlands Kanker Institute</td>
<td>Netherlands</td>
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Dose-based approach to estimating the radiation-induced cancer risk for a CT exam,

1. Estimate the dose to each organ, as a function of age, gender, and type of CT exam

2. Apply estimates of age-, gender-, and organ-specific risks-per-unit dose
   (low-dose risks from A-bomb survivors, “transferred” to a Western population)

3. Sum the estimated risks for all organs
Estimated % lifetime attributable cancer mortality risk, as a function of age at exam, for a single CT scan

CT risk estimates based on risks per unit dose estimated in BEIR VII
What are the uncertainties associated with these risk estimates?

About a factor of 3 in either direction
Should we be primarily concerned about children and young adults?
There is an increasing realization that lifetime cancer risks due to radiation exposure in middle age may be larger than we had thought.

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From BEIR-VII (2006)

BEIR-VII

Shuryak et al JNCI 2010
... and of course most CT scans are given in middle age

Age distribution of CT scans, US, 2007

From
Berrington de Gonzalez et al 2009
CT Benefits and Risks

- The individual radiation risks from CT are small, but almost certainly non zero
- So if a CT scan is medically justified, the benefit / risk ratio for any individual will typically be very large
- Different considerations for CT screening, however
For CT screening we do have to quantitatively balance benefits vs. risks.

Low-dose CT lung screening in ever smokers

- **Individual Risk**: 5%*
- **Benefits**: 20%†

* Brenner 2004
† NLST 2011
The two main issue with CT risks

1. The individual radiation risks from CT are small, but almost certainly non zero, so if a CT scan is medically justified, the benefit / risk ratio for any individual will typically be very large
   - That being said it’s always important to keep the CT doses per scan as low as is feasible

2. But ~¼ of all CTs may be clinically unjustified (~20 million /yr in the US), and here the benefit /risk ratio will be very small
   - For these clinically unjustified CT scans, even though the individual radiation risk will still be very small, when multiplied by ~20 million/yr, the potential exists to produce a significant long-term public health concern
   - So a key issue is to minimize clinically unnecessary CT scans
A roadmap to reduce the long-term health consequences of radiation exposure from radiological exams

- Reduce dose per scan
- Reduce unneeded scans
- Training
- New technology
- Quality control
- Decision rules
A better alternative to effective dose

- replace effective dose (i.e. summed organ doses, each weighted with committee-generated numbers) ....
- with “effective risk” (i.e. summed organ doses, each weighted with actual epidemiologically-based cancer risks)

Effective risk would perform all the comparative functions that we agree are needed, but

1) would eliminate the subjectivity associated with committee-generated weighting factors,
2) Would allow age to be taken into account
3) would provide a more intuitively interpretable quantity relating to risk

Brenner, BJR 2008
Effective Dose vs. Effective Risk

\[ Effective \ Dose \quad E = \sum_{T} w_T \ H_T \]

\( H_T \) are the tissue-specific equivalent doses in tissues \( T \)

\( w_T \) are committee-defined dimensionless tissue-specific weighting factors

\[ Effective \ Risk \quad R = \sum_{T} r_T \ H_T \]

\( r_T \) are lifetime radiation-attributable organ-specific cancer risk estimates (per unit equivalent dose to tissue \( T \))

The effective risk is thus a generic lifetime radiation-attributable cancer risk