Radiotherapy and Radiology in the 21st Century: Risks and Benefits

Radiology

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Radiologic procedures are on the rise...

- Between 1970 and 2005 in US, annual # of
  Nuclear Medicine procedures from 3.5M to 17M
  ↑ 5X
  CT procedures from 3M to 60M
  ↑ 20X

Mettler et al. Radiology 253: 520-531

1980

Total

Medical 0.53 mSv

~15% Medical

Natural Bkd 2.4 mSv

TOTAL ~ 3.0 mSv

2006

Total

Consumer products 0.13

Medical 3.0 mSv

>50% Medical

TOTAL ~ 5.6 mSv

Background Radiation

~25% Nucl Med

~50% CT

~15%

~10%

Man-made

Mettler et al. Radiology 253: 520-531
Radiation Injury in Diagnostic Nuclear Medicine and Radiology

- **Stochastic**
  - Carcinogenesis
  - Germ-cell mutagenesis
    - A-Bomb survivor data (n ≈ 12,000): **No effect @ mean gonadal Ds = 36 rad**
    - Teratogenesis
      - A-Bomb survivor data (n ≈ 1,600): Threshold Ds ≈ 10s of rads → **No** radiogenic abortions or congenital defects @ Dx doses
      - Oxford Survey of Childhood Cancers: ~50% increase in incidence of childhood cancer per rad *in utero*, but total incidence (300 vs 200 per 10^6 births) very low
Radiation Injury in Diagnostic Nuclear Medicine and Radiology

➢ **Deterministic**

- **Skin injury**
  - 200 rad: Threshold $\rightarrow$ >1,500 rad: Ulceration
  - Sx repair

- **Fluoroscopically-guided interventions**
  - $\sim0.1\%$ significant skin injuries (1992-95)

- **CT overdose**
  - Brain perfusion studies in $>200$ stroke pts @ Cedars-Sinai (over 18 months, 2008-09)
  - 300-400 rad (vs 50 rad) to head $\rightarrow$ Hair loss, Erythema
  - Human error - Incorrect CT parameters
    - No check of displayed CTDI, DLP

*Carcinogenesis remains the concern in diagnostic imaging.*
CT and Cancer Induction?

2% of all cancers in US attributable to CT!

CT Doses
Children: 2-8 rad
Adults: 1-2 rad

Dose-Response Models

The Linear No-Threshold Model appropriate as a radiation protection standard but not for risk-benefit analysis? Newcastle upon Tyne UK study (n ≈ 100,000 children)

Excess Cancer Incidence vs. Radiation Dose

- **Current prevailing model**: BEIR V
  - Linear
  - Linear-No-threshold Model

- **Previous prevailing model**: Pre-BEIR V
  - Supra-Linear Model
  - Sub-Linear (Linear-Quadratic) Model

**Data**
- Radiation Dose: Dose-response A-Bomb data consistent with Linear-No-threshold Model down to ~10 rad
- Excess Cancer Incidence: Historical lower limit of A-bomb survivor data: ~100 rad
- Practical Threshold: <10 rad?

Historical lower limit of A-bomb survivor data: ~10 rad

Current lower limit of A-bomb survivor data: ~10 rad
Types of Radiation Exposures

**Internal**

- Low D
- D calculated
- Whole-body Systemic effects?

**External**

- High D
- D measured
- Partial-body Local effects only?

### Incidence of Ovarian Tumors

% rat pups (n = 281) with congenital abnormalities following 150 rad in utero

<table>
<thead>
<tr>
<th>Absorbed Dose (rad)</th>
<th>100</th>
<th>30</th>
<th>1</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcephaly</td>
<td>9.1</td>
<td>41</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Anencephaly</td>
<td>30</td>
<td>14</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Absent kidney</td>
<td>21</td>
<td>6</td>
<td>2.6</td>
<td>0</td>
</tr>
<tr>
<td>Cleft palate</td>
<td>52</td>
<td>38</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>Limb malformation</td>
<td>44</td>
<td>16</td>
<td>3.1</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Ullrich and Storer. IAEA/STI/PUB/489,1978

Brent et al. Rad Res 1971
15-Country Collaborative Study of Cancer Risk among Radiation Workers in Nuclear Industry

- 15-Country collaborative cohort study of cancer risk among 407,391 nuclear industry workers monitored individually for external radiation and with average follow-up > 10 year

- Dose-related increase in all cancer mortality
  - n: 5,233 deaths
  - ERR/Sv: 0.97
  - 90% CI: 0.28 - 1.77

- ED ≈ 2 mSv (2 rad)
  Significantly increased cancer risk @ < 150 mSv (15 rad)

- Caveats (Dauer et al.)
  - Exclusion of workers from previous 3-country study risk showing no increased cancer risk*
  - No smoking data - More smokers among higher-D/higher-risk workers?
  - Notably high Canadian risk estimates - Dosimetry?
  - Large error bars

Consistent with Linear No-threshold Model
Projected Excess Cancer Risk in Pediatric Osteosarcoma Patients Undergoing TI201 Scanning

Kaste et al. AJR 194: 245-249, 2009

- 73 patients - 32 males, 15 yo
  - 41 females, 14 yo
- 3 studies - 4.4 mCi /study
  - BSA-adjusted
- ED - males: 19 rem
  - females: 22 rem
- BEIR VII risk ERRs

<table>
<thead>
<tr>
<th>Age at Exposure (y)</th>
<th>Effective Dose, ED (rem/mCi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
</tr>
</tbody>
</table>

Excess Cancer Risk (per 100)

**Males**

- Incidence: 6.0 /100 up to 5 yo
- Mortality: 3.0 /100 up to 5 yo
- Incidence: 2.0 /100 at 15 yo
- Mortality: 1.0 /100 at 15 yo

**Females**

- Incidence: 13 /100 up to 5 yo
- Mortality: 5.2 /100 up to 5 yo
- Incidence: 3.1 /100 at 15 yo
- Mortality: 1.4 /100 at 15 yo

Neoadjuvant Tx
- Tumor-bearing leg
- Normal leg

Baseline

9 wk

Pre-Sx: 35 wk
## Measured Excess Thyroid Cancer Risk in Thyroid Patients Undergoing I131 Dx


- **Sweden**
- **1952-1969**
- **≥ 20-yr FU**
- Individual thyroid dosimetry

<table>
<thead>
<tr>
<th>Reason for I131 Dx</th>
<th>No prior neck XRT</th>
<th>Prior neck XRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid cancer?</td>
<td>Other</td>
<td>Thyroid cancer?</td>
</tr>
<tr>
<td>n</td>
<td>11,015</td>
<td>24,010</td>
</tr>
<tr>
<td># Thyroid Cancers</td>
<td>69</td>
<td>36</td>
</tr>
<tr>
<td>Male, Female (%)</td>
<td>14, 86</td>
<td>23, 77</td>
</tr>
<tr>
<td>Age - 1st Exposure (yr)</td>
<td>44</td>
<td>43</td>
</tr>
<tr>
<td>- % &lt; 20 yo</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Total AA (mCi)</td>
<td>0.068</td>
<td>0.043</td>
</tr>
<tr>
<td>Thyroid Uptake (%)</td>
<td>39</td>
<td>38</td>
</tr>
<tr>
<td>Total Thyroid Dose (rad)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25 - SIR *</td>
<td>3.7</td>
<td>0.45</td>
</tr>
<tr>
<td>- 95% CI</td>
<td>1.6-7.3</td>
<td><strong>0.15-1.1</strong></td>
</tr>
<tr>
<td>25-50 - SIR *</td>
<td>3.8</td>
<td>1.1</td>
</tr>
<tr>
<td>- 95% CI</td>
<td>2.0-6.6</td>
<td><strong>0.43-2.2</strong></td>
</tr>
<tr>
<td>50-100 - SIR *</td>
<td>2.6</td>
<td>0.86</td>
</tr>
<tr>
<td>- 95% CI</td>
<td>1.3-4.8</td>
<td><strong>0.37-1.7</strong></td>
</tr>
<tr>
<td>&gt;100 - SIR *</td>
<td>3.7</td>
<td>1.3</td>
</tr>
<tr>
<td>- 95% CI</td>
<td>2.6-5.0</td>
<td><strong>0.73-2.1</strong></td>
</tr>
</tbody>
</table>

* SIR, Standardized Incidence Ratio = Observed / Expected # of thyroid cancers

### Threshold > 100 rad?
Image Quality

Diagnostic Information Content

Optimum Dose
Dose-Reduction Strategies in CT

• Reduce tube voltage (kVp)
  
x-ray flux & dose $\propto kVp^2$

• Reduce tube current (mA)
  
x-ray flux & dose $\propto mA$

• EKG-controlled tube current modulation (ECTCM)
  
Cardiac motion least during diastole, greatest during systole → 
Image quality best during systole, worst during systole → 
EKG-triggered mA reduction during systole

Application- and Patient-adapted CT protocols becoming the standard

Reduces ED for MSCT coronary angiography >50% without loss of diagnostic information content
## Radiation Dosimetry in PET (and SPECT)

<table>
<thead>
<tr>
<th>FDG PET-CT</th>
<th>(^{18}\text{FDG} 10 \text{ mCi})</th>
<th>PET w/ (^{68}\text{Ge}) Transmission Scan*</th>
<th>PET-CT w/ &quot;Low-Dose&quot; CT *</th>
<th>PET-CT w/ &quot;Diagnostic&quot; CT *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>4.4</td>
<td>4.4</td>
<td>4.4</td>
<td>6.8</td>
</tr>
<tr>
<td>Bone Marrow</td>
<td>0.48</td>
<td>0.49</td>
<td>0.53</td>
<td>2.3</td>
</tr>
<tr>
<td>Breasts</td>
<td>0.34</td>
<td>0.35</td>
<td>0.38</td>
<td>1.8</td>
</tr>
<tr>
<td>Liver</td>
<td>0.58</td>
<td>0.60</td>
<td>0.66</td>
<td>3.2</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.64</td>
<td>0.66</td>
<td>0.70</td>
<td>2.5</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.48</td>
<td>0.51</td>
<td>0.54</td>
<td>2.4</td>
</tr>
<tr>
<td>Effective Dose</td>
<td>1.1</td>
<td>1.1</td>
<td>2.0</td>
<td>3.3</td>
</tr>
</tbody>
</table>

*Transmission Scan Contribution*  
- ED (rem): 3%  
- Critical Organ (rad): 49%  

- Cylinder filled with aqueous solution of F18 (71%)

<table>
<thead>
<tr>
<th>Radiotracer</th>
<th>kVp</th>
<th>mAs</th>
<th>Pitch</th>
<th>Attenuation Correction + Anatomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Low-dose&quot; CT</td>
<td>120</td>
<td>64</td>
<td>1.5</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>Total</td>
<td>140</td>
<td>190</td>
<td>1.25</td>
<td></td>
</tr>
</tbody>
</table>

*No difference in SUVs*

Adapted from  
NUREG/CRL-6345 1996.  
Risk-Benefit Analyses: Example

^{18}FDG PET in pre-operative assessment of suspected NSCLC

**Data**

- Conventional pre-op work-up → Thoracotomy: 81% (78 / 97)
  Thoracotomy futile: 41% (39 / 78)
- Conventional pre-op work-up with PET → Thoracotomy: 65% (60 / 92)
  Thoracotomy futile: 21% (19 / 60)
- Surgery (Sx)-related mortality: 6.5%
- With PET → Avoided futile Sx: 20%

**Extrapolation**

- Conventional pre-op work-up → Futile-Sx deaths: 3,766 /yr
- Conventional pre-op work-up + PET → Futile-Sx deaths: 1,547 /yr
- **Gross** benefit of pre-op PET - Lives saved w/ PET: 2,219 /yr
- ^{18}FDG ED / 10 mCi: 0.7 rem
- Excess cancer deaths (@ 0.05%/rem): 77 /yr
- **Net** benefit of pre-op PET - Lives saved w/ PET: 2,142 /yr

Summary and Conclusions

- Other than for I131 (thyroid), there are no data on excess risk in Dx
  - University of Newcastle on Tyne study pending
  - Caveats: Measured vs Projected excess risks
  - Uncertainty in dose estimates ±25-50%

- Implications (eg for Dose-rate effect) of “Radiation Worker” study (Cardia et al. 2007)?

- For Dx & Tx I131 (thyroid):
  - No excess thyroid cancer risk @ thyroid doses up to 100 rem
  - No excess leukemia risk @ marrow doses up to 20 rem

- *Practical* threshold for cancer induction: 10s of rem?

Thank You!