Radiation related cancer risk & benefit/risk assessment for screening procedures

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Considerable controversy regarding the risk of low levels of radiation – typical for diagnostic radiation exposures – since

- radiation induced cancers cannot be recognized as such
  → it is only by means of epidemiological studies that increases in the spontaneous cancer incidence rates of irradiated groups can be detected

- a significant excess of cancers has not been detected in humans for doses below around 50 to 100 mSv
  - Radiation risks evaluated at low dose levels are not based on epidemiological evidence
  - “Excess” cancer cases calculated by means of risk models are hypothetical for low dose levels
Various scientific bodies applied the

**Linear Non-Threshold (LNT) hypothesis**

[International Commission on Radiological Protection (ICRP), United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), Biological Effects on Ionizing Radiation (BEIR) committee]

**No threshold**  → **Any radiation dose** – no matter how small – **may cause detrimental health effects** (in particular the induction of cancer)

**Linearity**  → **The probability of these “stochastic effects” is proportional to the dose absorbed in the tissue**
Radiation risk – Background

LNT hypothesis

Significant observations for doses above 100 mSv

→ Extrapolation from risks determined at high dose exposures to low-dose exposures

- Linear non threshold LNT
- Supra-linear function
- Linear with threshold LT
- Radiation hormesis
- …

ICRP 103: “LNT hypothesis is considered to be the best approach to managing risk from radiation exposure”

→ “precautionary principle”
Radiation risk – Assessment

BEIR VII

Radiation risk models from BEIR VII 2006
(BEIR: Biological Effects of Ionizing Radiation)

Full review of the available biological, biophysical, and radio-epidemiological literature

• current *Life Span Study* data of the Japanese *A-bomb survivors*
  - for cancer *incidence* (1958-1998) &
  - for cancer *mortality* (1950-2000);

• current *meta analyses* based on data of medically exposed persons who were radiation exposed either
  - for diagnostic reasons or
  - for radiotherapy
Radiation risk

BEIR VII radiation risk models

• Relative Risk models
• Absolute Risk models
  - for different cancer sites
  - depending on organ dose, age, age at exposure …

→ Assessment of Lifetime Attributable Risk $LAR$ for the U.S. population:

$LAR = \text{excess lifetime risk}$, to be clinically diseased by (or to die from) a specific cancer (after radiation exposure until end of life)

$Dose \text{ and Dose Rate Effectiveness Factor } DDREF = 1.5$
Radiation risk

BEIR VII

BfS approach:

**BEIR VII models** were applied to estimate age, gender and organ specific excess lifetime risks \( LAR \) for a German population using:

- German baseline rates for cancer incidence / mortality,
- German life table data

Deviant from BEIR VII:

Modified BEIR VII model for breast cancer (conservative approach)

\[ DDREF = 1 \] (conservative approach)

These \( LAR \) values were applied to estimate \( LARs \) for specific X-ray procedures using

- organ doses from typical X-ray procedures
Lifetime attributable risk \( LAR \) for an organ dose of 100 mSv in dependence on age at exposure according to \textbf{BEIR-VII} models applied to a \textbf{German population} (German life tables and German cancer incidence rates).
Estimates of total LAR for representative CT examinations of the abdomen, pelvis, thorax, and head in dependence on the age the CT is performed.
“Baseline“ lifetime risk of developing or dying from cancer (Germany, 2010):

<table>
<thead>
<tr>
<th>All cancer excl. non-melanoma skin cancer</th>
<th>Risk of developing</th>
<th>Risk of dying from</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>51%</td>
<td>26%</td>
</tr>
<tr>
<td>Females</td>
<td>43%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Krebs in Deutschland (= German cancer report) 2009/2010, Robert-Koch-Institut 2014
www.krebsdaten.de
CT procedures predominantly discussed:

- **Lung CT** for early detection of lung cancer, in particular in smokers and asbestos workers
- **Virtual CT colonoscopy** – also denoted as CT colonography – for early detection of intestinal polyps and colorectal cancer
- **Calcium scoring**, i.e. CT quantification of coronary artery calcification (which is considered as sensitive marker of arteriosclerosis)
Example „lung CT smoker“

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>m</th>
<th>f</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>7</td>
<td>7.9</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>5.8</td>
<td>5.8</td>
</tr>
<tr>
<td>Lung</td>
<td>5.7</td>
<td>5</td>
</tr>
<tr>
<td>Liver</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>R. bone marrow</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Based on BEIR VII: Lifetime Attributable Risk $LAR$ (incidence)

- 0.2 % / 0.6 % (m / f)

- 35 mAs, 120 kV, collimation 4 mm, pitch 1.8, scan length 34 cm, $CTD_{vol}$: 3.8 mGy

- Effective dose per examination
  - 1.7 / 1.9 mSv (m / f)

20 exams between 50 and 69 years of age
Example „lung CT – female / male smoker“

$LAR$ for 20 exams between 50 and 69 years of age

$LAR$

0,0% 0,1% 0,2% 0,3% 0,4% 0,5% 0,6% 0,7% 0,8% 0,9% 1,0%

0,5 1 1,5 2 2,5 3

effective dose per examination
## Opp. / Indiv. Health Assessment – Radiation risk

<table>
<thead>
<tr>
<th>Screening scenario</th>
<th>cumulative effective dose (mSv)</th>
<th>Lifetime Attributable Risk LAR (%) (Incidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m / f</td>
<td>m</td>
</tr>
<tr>
<td>Lung CT 50 - 69 annually: 20 x</td>
<td>34 / 38</td>
<td>0.2</td>
</tr>
<tr>
<td>Colon (virtual coloscopy) 50 - 70 every 5 yrs.: 5 x</td>
<td>30 / 36</td>
<td>0.2</td>
</tr>
<tr>
<td>Heart (Calcium Scoring) 50 - 66 every 4 yrs.: 5 x</td>
<td>10 / 13</td>
<td>0.1</td>
</tr>
<tr>
<td>Mammography Screening Program 50 - 68 every 2 yrs.: 10 x</td>
<td>- / 4</td>
<td>-</td>
</tr>
</tbody>
</table>

Based on BEIR VII
Benefit?

At present, scientific evidence for the benefit from CT screening is unclear:

- Several clinical / feasibility studies
- Randomised controlled trials (RCT) for lung cancer (published results of NLST: Mort. Red. 20% / other trials: results not before 2015)

→ Except for lung cancer, no valid data from RCTs available yet – in contrast to X-ray mammography
Unknown mortality reduction

method:

\[
\frac{\text{benefit}}{\text{risk}} \geq 10
\]

required reduction in disease mortality to achieve a benefit risk ratio of at least 10
Example „lung CT – female / male smoker“

$LAR$ for 20 exams between 50 and 69 years of age

Required mortality reduction

for benefit risk ratio $\geq 10$
### Opp. / Indiv. HA – Benefit vs. radiation risk

<table>
<thead>
<tr>
<th>Screening scenario</th>
<th>required reduction in mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m</td>
</tr>
<tr>
<td><strong>Lung CT</strong></td>
<td></td>
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<tr>
<td>50 - 69 annually: 20 x</td>
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<td><strong>Colon (virtual coloscopy)</strong></td>
<td></td>
</tr>
<tr>
<td>50 - 70 every 5 yrs.: 5 x</td>
<td>41</td>
</tr>
<tr>
<td><strong>Heart (Calcium Scoring)</strong></td>
<td></td>
</tr>
<tr>
<td>50 - 66 every 4 yrs.: 5 x</td>
<td>6</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>50 - 68 every 2 yrs.: 10 x</td>
<td>-</td>
</tr>
</tbody>
</table>

- Benefit ≥ 10
- Risk ≤ 5
- Opp. / Indiv. HA – Benefit vs. radiation risk

**Note:** The table above compares the benefits and risks of different screening scenarios for lung CT, colon (virtual coloscopy), heart (Calcium Scoring), and mammography screening programs. The required reduction in mortality is calculated for both men (m) and women (f) and compared to the risk of radiation exposure.
Conclusion

- For specific CT screening scenarios, **organ doses can be estimated** through representative scanning protocols, and **radiation risks can be assessed** through established risk models.

- These radiation risks should not be completely neglected.

- This is esp. true when **data from RCTs** – demonstrating a significant benefit due to CT screening – are missing.

- However, **other adverse effects** related to CT screening may be considered as **more important**, and should be the focus of further scientific discussion.

- In this context – and as far as **radiation protection** is concerned – **radiologic follow-up procedures** (typically high dose procedures) also have to be considered.