Ionizing Radiation: Medical Risks – New Aspects

HUMAN RIGHTS, FUTURE GENERATIONS & CRIMES IN THE NUCLEAR AGE

15.9.2017 - Block 2:
Ionizing Radiation / Biological Effects / Hibakusha Worldwide

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Contents

• Ionising radiation – a few basics

• Studies in Japanese A-bomb survivors

• New scientific studies on medical risks of low dose ionising radiation (LDIR) in different situations

• Call for revision of recommendations of the International Commission for Radiological Protection (ICRP)
Health risks induced by ionising radiation

**Mechanism: Energy of ionising radiation**

- mutations in the genome (nuclear and mitochondrial DNA), «bystander effect»
- pathological cell phenotype / tissue
- disease / pathology e.g. skin erythema; cancer, cardiovascular, neurological, ocular and endocrine diseases, malformations, genetic effects e.g. shifts in sex odds ratio at birth (Ref.1)

Lung cancer from uranium mining in Germany known since >> 100 years

Known occupational risk for radiologists since earliest days of diagnostic radiology
Ionising radiation – the sources

- **Natural sources** (background radiation, radon)
  and

- **Artificial sources**
  - Uranium mining – processing – nuclear fuel production
  - Nuclear power plant immissions („regular“, disasters)
  - Military radioimmissions (A-bomb, included testing, Depleted Uranium DU)
  - Nuclear waste
  - Medical diagnostics: x-rays, CT-Scan, Szintigraphy, PET (Positron Emission Tomography) = main source of human exposure to artificial ionising radiation in modern life
  - Radiotherapy

→ Exposure of huge populations to different types and levels of IR
Dr. Alice Stewart (1906 – 2002, epidemiologist):

”Overall, children who were exposed to radiation in utero had about a 40% greater risk of cancer than children who were not exposed” Lancet 1956 (Ref. 2;3)
Cancer =
malignant disease based on dysregulated cell proliferation leading to locally infiltrating or distant (metastatic) destructive pathological tissue growth

Solid cancer: eg esophageal cancer
Blood cancer: Leukemia
Leukemia induced by irradiation from A-bomb

Sasaki Sadako

* 7. January 1943 in Hiroshima;
† 25. October 1955 in Hiroshima
Paper cranes – symbols of peace

千羽鶴, Sembazuru

1600 Origami - cranes were folded by Sasako hoping to overcome her leukemia
How dangerous is ionising radiation really?

- **Life Span Study (LSS):** Important study on health effects in 120 000 Japanese A-bomb survivors (Ref. 4; 5) - long follow up (still 48% of exposed population surviving on 1 January 2004)

- Actual ionising radiation **riks calculations** mainly based on LSS

- **EAR** (excess absolute risk) for cancer mortality: 5.5% / Sievert (Sv)

- **ERR** (excess relative risk) for leukemia mortality: 3.1 / Gray (Gy)

- Significant noncancer death risk demonstrated

- Risk calculations based on the «collective effective irradiation dose»: individual dose \* number of individuals
→ No threshold – every dose of ionising radiation is harmful

No threshold – every dose of ionising radiation is harmful

«low dose»
< 100 mSv
Low dose ionising radiation (LDIR): **stochastic** effects

- „low dose“: < 100 mSv as opposed to „high dose“: > 100 mSv
  … questionable, arbitrary classification „low dose“
suggesting „low risk“. But: **Both low and high doses can kill**!

- Effects of LDIR in human tissues are **stochastic** =
  - by chance
  - no immediate health effects

- **LNT: Linear-no-threshold model**…
  - high level of exposure $\rightarrow$ high probability of pathology, *and*
    low level of exposure $\rightarrow$ low probability of pathology,
  - no dose of ionising radiation without risk («no threshold»)
The **LSS risk factor calculations must be considered outdated, because**...

- Japanese 1945 A-bomb survivors:
  - short exposure to high energy gamma-radiation – not comparable to chronic alpha-, beta-, gamma-irradiation or x-rays
  - *low dose radiation range not covered* (extrapolations are subject to never ending controversies)

- No dosimetry (only dose estimates)

- Studies of RERF began in 1950 only (teratogenic, genetic effects and cancers with short latency periods missed)

- Selection bias: many early, traumatic casualties → „survival of the fittest“

- Social aspects: japanese A-bomb-survivors were ostracised… → medical family history unreliable
Difficulties of studies on ionising radiation health effects I: Lack of straightforward proof (principle of cause and effect), no smoking colts, no IR tags on cancer
Difficulties of studies on ionising radiation induced health effects II.

- **Indirect proof** with *epidemiological studies* → even in big studies: some uncertainty: statistical association or causality?

- However *epidemiological studies* (*not laboratory research*) based mainly on temporal and geographical criteria *give strongest information*

- **Long disease induction time periods** (...several decades) seen between radiation and following diseases → challenging logistical aspects of scientific work

... and many other difficulties as confounders like smoking, drinking, social problems, migration; insufficient radiation dose information; selection bias and statistical fallacies (lack of statistical power in small populations)
• Results of LSS-Study
  - still important \textit{and}
  - must be continuously updated,

• but for medical risk-factor calculations
  $\Rightarrow$ \textit{we need new, modern studies}

\ldots \textit{and there are many of them}
Modern studies on health effects of low dose ionising radiation: References 5. – 18.

20. The Nihonmatsu Declaration on the Risks of Exposure to Low Doses of Ionising Radiation, 10th October 2017; https://www.iwanami.co.jp/kagaku/eKagaku_201703_CSRP.pdf
### Studies with statistically significant health effects associated to ionising radiation

Criteria: solid cancer / leukemia / non-cancer disease / cardiovascular disease (Ref. 4. – 18.)

<table>
<thead>
<tr>
<th>Setting / Criteria</th>
<th>A-Bomb victims</th>
<th>Nuclear workers</th>
<th>Nuclear workers</th>
<th>Children living near NPP</th>
<th>Children living near NPP</th>
<th>Chernobyl victims</th>
<th>Indoor radon exposure</th>
<th>Diagnostic CT-exposure in childhood</th>
<th>Diagnostic CT-exposure in childhood</th>
<th>Children, natural background</th>
<th>Children natural background</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Author; Study</td>
<td>Pierce; Kotaro; Life Span LSS</td>
<td>Cardis; Vrijheid; 15 countries</td>
<td>Richardson; Leraud; Gillies; INWORKS</td>
<td>Kaatsch; KïKK</td>
<td>Körblein</td>
<td>Metanalysis</td>
<td>Several authors cited by IPPNW.de</td>
<td>Darby; collabor. 13 case ctrl studies</td>
<td>Pearce</td>
<td>Mathews</td>
<td>Kendall</td>
</tr>
<tr>
<td>Journal(s); Ref. No</td>
<td>Rad Res 4; 5</td>
<td>BMJ; Rad Res 6; 7</td>
<td>BMJ; Lancet hem; Rad Res; 8; 9; 10</td>
<td>Intl J Cancer; 11</td>
<td>Intl J Cancer; 12</td>
<td>IPPNW.de 13</td>
<td>BMJ 14</td>
<td>Lancet 15</td>
<td>BMJ 16</td>
<td>Leukemia</td>
<td>Environ Health Perspectives 18</td>
</tr>
<tr>
<td>Persons (N)</td>
<td>120 000</td>
<td>407 391</td>
<td>308 927</td>
<td>593 / 1766</td>
<td>7 148 / 14 208</td>
<td>&gt; 176 000</td>
<td>74 B / 135 L</td>
<td>10.9 Mio</td>
<td>680 000</td>
<td>27 447 / 36 793</td>
<td>2 093 660</td>
</tr>
<tr>
<td>Country/ Continent</td>
<td>Japan</td>
<td>US, EU, Can, Aus, s Korea, Jpn</td>
<td>GB, F, D, CH</td>
<td>EU, UDSSR</td>
<td>9 European countries</td>
<td>England Wales Scotland</td>
<td>Australia</td>
<td>Great Britain</td>
<td>Switzerland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid Cancer I Incidence / D Death</td>
<td>+ (D) 0.43 / Gy (EAR)</td>
<td>+ (D) 0.97 / Sv (ERR)</td>
<td>+ (D) 0.48 / Gy (EAR)</td>
<td>+ (D) 2.96 / Gy (ERR)</td>
<td>+ (I)</td>
<td>+ (D, lung) 0.084 / 100Bq / m3</td>
<td>+ (I, brain) 0.023 / mGy</td>
<td>+ (I) brain 0.021 / mGy + non-brain 0.027 / mSv</td>
<td>+ (I) 0.12 / mSv (ERR)</td>
<td>+ (I) 1.04 / mSv (HR)</td>
<td></td>
</tr>
<tr>
<td>Leukemia I Incidence / D Death</td>
<td>+ (D) 3.1 / Gy (ERR)</td>
<td>+ (D) 0.19 / Sv (ERR)</td>
<td>+ (I)</td>
<td>+ (I)</td>
<td>+ (I) 0.036 / mGy (ERR)</td>
<td>+ (I) 0.039 / mGy (ERR)</td>
<td>+ (I) 0.12 / mSv (ERR)</td>
<td>+ (I) 1.04 / mSv (HR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non Cancer disease I / D</td>
<td>+ (D)</td>
<td>+ (D) 0.22 / Sv (ERR)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardio-vasc. Disease I / D</td>
<td>+ (D)</td>
<td>+ (D) 0.22 / Sv (ERR)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose response</td>
<td>YES ( x 2 )</td>
<td>YES</td>
<td>Yes ( x 4 )</td>
<td>[Yes]</td>
<td>[YES]</td>
<td>YES</td>
<td>YES ( x 2 )</td>
<td>YES ( x 3 )</td>
<td>YES</td>
<td>YES ( x 2 )</td>
<td></td>
</tr>
<tr>
<td>Low dose ionising radiation</td>
<td>(+) (extrapol.)</td>
<td>19.4 mSv (mean)</td>
<td>20.9mGy</td>
<td>25.2mSv</td>
<td>[surrogate marker: dist. from NPP]</td>
<td>[surrogate marker: dist. from NPP]</td>
<td>Yes</td>
<td>+/- 100 Bq / m3</td>
<td>50-60 mGy</td>
<td>4.5 mSv</td>
<td>0.8mGy / y (controls)</td>
</tr>
</tbody>
</table>

PSR / IPPNW Switzerland 2017
Studies with statistically significant health effects associated to ionising radiation

How to read this table? I.

|---------------------|-----------------|-----------------------------|--------------------|-----------------------------------|--------------------------------|------------------------|--------------------------|------------------------|---------------------------|

Horizontal lines - «criteria» referring to:

- publication(s), reference(s)
- study population
- Pathology (incidence / mortality)
  - cancer
  - leukemia
  - non-cancer disease
  - cardiovascular disease
- exposure
  - is there a dose response?
  - is there an exposure to *low* doses of ionising radiation?
Studies with statistically significant health effects associated to ionising radiation

How to read this table? II.

Colour-code for «setting»

Yellow:
Japanese A-bomb victims (LSS-study)

Blue / Green:
NPP-exposure «regular operation»

Orangebrown:
NPP-exposure «catastrophy»
(Chernobyl / Fukushima)

Pink / Purple:
Radon / medical diagnostics / natural background exposure
Summary: Studies with statistically significant health effects associated to ionising radiation

1. +/- 10 studies since 2005 showing a statistically significant association of exposure to low dose and a dose-response of ionising radiation and mortality / incidence due to severe health effects (solid cancer and leukemia or non-malignant diseases such as cardiovascular diseases)

2. N.B.: Dose-response is a strong argument for causality

3. Health effects observed already with doses of a few mSv

4. Studies published in peer reviewed journals (see references)
INWORKS - Study: Richardson B. et al., BMJ 2015 (Ref.8) 
Solid cancer deaths in nuclear workers (USA, GB, F)

- 308’297 workers, 22% (66’632) known deaths by the end of follow up of 8.2 million person years.
- among them 17’957 deaths due to solid cancers.
- Average colon dose 20.9 mGray (mGy; median 4.1 mGy).

- Results:
  - estimated rate of mortality from all cancers (non-leukaemia) 48% per Gy (90% confidence interval 20% to 79%), lagged by 10 years
  - results suggesting a linear increase in the rate of cancer with increasing radiation exposure
Relative rate of mortality due to all cancers (other than leukaemia) by categories of cumulative colon dose, lagged 10 years, in INWORKS vertical lines = 90% confidence interval (Richardson B., BMJ 2015; Ref. 8)
INWORKS Study: Gillies M., Rad Research 2017 (Ref.9)
Mortality from Circulatory Diseases and other Non-Cancer Outcomes among Nuclear Workers (USA,GB,F)

- 308'297 nuclear workers
- average cumulative equivalent dose 25.2 mSv.
- Statistically significant excess of circulatory deaths due to:
  - cerebrovascular disease,  ERR/Sv = 0.50; 90% CI: 0.12, 0.94) and
  - ischemic heart disease,  ERR/Sv = 0.18; 90% CI: 0.004, 0.36).
  (ERR = excess relative risk per Sievert)

Conclusion:
- Estimates of associations between radiation dose and non-cancer mortality comparable with those observed in atomic bomb survivor studies
- “The findings of this study could be interpreted as providing further evidence that non-cancer disease risks may be increased by external radiation exposure, particularly for ischemic heart disease and cerebrovascular disease.”
Radon: A recognized severe health risk by low dose ionising radiation

• Radon – a naturally occurring noble gas – and its decay products emit Alpha-radiation

• Mean effective dose / person / year: 1.1 mSv (Germany)

• A statistically significant dose response effect of low dose ionizing radiation from indoor radon exposure and lung cancer has been demonstrated (Darby et al. 2005; Ref. 14)

• The risk factor is 8.4 % / 100 Bq / m3.

• In Europe, 9 % of lung cancer deaths and 2% of all cancer deaths are attributed to ionizing radiation due to indoor radon.

• In Switzerland, every year +/- 240 persons die of radon induced cancer

• The international community started in 2005 to understand low dose ionising irradiation by indoor radon as being a severe health risk

• Building legislation has implemented standards which aim at lowering radon exposure for inhabitants
The Swiss BAG warns (2006):

«Radon causes lung cancer»

BAG Switzerland:
Bundesamt für Gesundheit =
Swiss Federal Office of
Public Health

«Legal informations for
estate agents and
construction experts»
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• «Collective effective dose is not intended as a tool for epidemiological risk assessment, and it is inadequate to use it in risk projections. The aggregation of very low individual doses over extended time periods is inappropriate, and in particular, the calculation of the number of cancer deaths based on collective effective doses from trivial individual doses should be avoided» (Ref. 19)

This wording is scientifically inappropriate in 2017
Conclusions:

- Modern scientific studies confirm the linear no threshold model (LNT) and support the validity of epidemiological risk calculations for severe health effects due to ionising radiation doses far below 100mSv (i.e. «low dose ionising radiation» ; Ref. 20).

- The LNT forms the basis for radiation protection of the public exposed to low dose ionising radiation, e.g. after nuclear accidents.

- The risk factor (EAR = Excess Absolute Risk) for cancer death due to ionising radiation has to be adapted from 5.5% / Sv to → 20% / Sv. (Ref.1).

- Significant increase of mortality related to non-cancer deaths (e.g. cardiovascular) due to low dose ionising radiation in the order of cancer-related mortality has been observed. This must be officially acknowledged.

→ ICRP 103 (2007) must be revised
Command of the hour: **IIRP = «integrative ionising radiation protection»**

Apart from already established radiation protection standards *(as for nuclear industry workers, medical exposure, building law in view of radon exposure)* for all situations, where populations are exposed to low doses of ionising radiation, e.g.

- uranium mining,
- exposure to fallout from A-bomb tests and in A-bomb survivors
- exposure to depleted uranium
- regular and accidental exposure by nuclear power plants,
- exposure with NPP decommissioning and nuclear waste management
- etc.

**the medical principle of prevention** in view of the unalienable Human Right of Health should be respected.
Abstract

C. Knüsli "Ionizing Radiation: Medical Risks – New Aspects“

• Since its detection ionising radiation [IR] has been recognised as a major human health risk inducing a broad variety of biological cellular changes. Characteristically, high IR doses are associated with deterministic whereas lower IR doses are related to stochastic effects respectively. Biological research establishing reliable biomarkers in low dose IR is still limited in contrast to higher dose and dose-rate IR. Radioprotection concepts have been developed and respective measures were widely implemented in the medical fields and in occupational exposure in the nuclear industry. According to the current recommendations of the International Commission on Radiological Protection (ICRP publication 103; 2007) the risk for lethal cancer disease in adults amounts to 5.5%/Sievert. Carcinogenicity is the hallmark of IR, however lethal IR impact of noncancer – e.g. cardiovascular – diseases has been shown to be in the same order as death to radioinduced malignancy. Modern epidemiological studies on nuclear workers, on populations exposed to fallout from nuclear power plant accidents, on natural background irradiation as well as radiodiagnostic studies confirm the dose response relationship of low dose IR and its detrimental health impacts. These studies corroborate the Linear No Threshold [LNT] concept and underline the usefulness of collective dose calculations. The latter allow extrapolations of health risks in large populations exposed to low doses of ionising radiation. Current scientifically based understanding calls for acceptance of risk estimations at doses as low as 1 mSv and below and therefore asks for a revision of the ICRP-recommendations which are outdated one decade after their effective date.