Positive trends in radiation risk assessment and consequent opportunities for LINAC applications

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• Introduction
• Radiation risk in perspective
• Linear no-threshold hypothesis – controversy
• Positive trends (since LINAC12)
• LINAC applications
• Conclusions
Nice to meet: ionizing radiation (1895)
Nice to meet: radioactivity (1896)
Radon therapy

radiation before its discovery

• Radon spas –
  Herodotus and Hippocrates:
  • arthritis & other inflammatory conditions

• Mainstream medicine – Europe
• “Alternative treatment” – USA
First 50+ years: no fear

X-ray shoe fitter
Radiation Safety Norms

- 1895 – 1920  No control, high exposures
  - frequent accidents
- 1921 – 1936  700 mSv/year (0.2 R/day)
  - natural background $\times 300$
  - no damage reported till now
  - 1927: X-ray mutagenesis discovered
- 1936 – 1949  350 mSv/year (0.1 R/day)
- 1949 – 1958  150 mSv/year (0.3 R/week)
- 1958 – 1991  50 mSv/year – professional limit
- 1991 – 20 mSv/year – professional limit
  - natural background $\times 8$
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Perception of nuclear hazards
Perception of nuclear hazards
Darwin, Australia 1942

Sendai, Japan 2011

Kfar Yehezkel
Israel, 1976
How many A-bomb survivors died of radiation-induced cancers?
How many A-bomb survivors died of radiation-induced cancers?

<table>
<thead>
<tr>
<th>Colon dose (Gy)</th>
<th>Number of subjects</th>
<th>Person-years</th>
<th>Number of deaths</th>
<th>Number of excess cases²</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.005</td>
<td>38,509</td>
<td>1,465,240</td>
<td>4,621</td>
<td>2</td>
</tr>
<tr>
<td>0.005–</td>
<td>29,961</td>
<td>1,143,900</td>
<td>3,653</td>
<td>49</td>
</tr>
<tr>
<td>0.1–</td>
<td>5,974</td>
<td>226,914</td>
<td>789</td>
<td>46</td>
</tr>
<tr>
<td>0.2–</td>
<td>6,356</td>
<td>239,273</td>
<td>870</td>
<td>109</td>
</tr>
<tr>
<td>0.5–</td>
<td>3,424</td>
<td>129,333</td>
<td>519</td>
<td>128</td>
</tr>
<tr>
<td>1–</td>
<td>1,763</td>
<td>66,602</td>
<td>353</td>
<td>123</td>
</tr>
<tr>
<td>2+</td>
<td>624</td>
<td>22,947</td>
<td>124</td>
<td>70</td>
</tr>
<tr>
<td>Total</td>
<td>86,611</td>
<td>3,294,210</td>
<td>10,929</td>
<td>527</td>
</tr>
</tbody>
</table>

Solid cancer 1950-2003: 527 + 94 ≈ 600

Leukemia

600 / 11,000:

Radiation is a rather weak (!) carcinogen
How many radiation-induced mutations?
How many radiation-induced mutations?

0 (none)

Radiation mutagenesis

- 1927 – discovered in flies (Herman Müller)
- 1946 – Nobel prize
- 2014 – “not yet” observed in the offspring of the A-bomb survivors
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LNT – too mechanistic; Physiology is not linear!

LNT for Paracetamol:

Lethal Dose LD50 = 2 g/kg (50% die)
LD50 ≤ 200 g (few of us weigh above 100 kg)
1 caplet: 0.5 g
Lethal probability: 50% × 0.5 / 200 = 0.125%

1 out of 800 patients should die of single caplet – obviously wrong

Radiation:
less toxic => non-linearity less clear
A-bomb survivors’ life-span study
A-bomb survivors’ life-span study

Data

LNT: Var = 1.60 ± 2σ
A-bomb survivors’ life-span study

![Graph showing excess mortality ratio vs colon dose (Sv). The graph includes data points and fitted lines for LNT and Sigmoid models with variances.]
A-bomb survivors’ life-span study

Socol & Dobrzynski, *Dose-Response* (in print)
CT-induced childhood cancer?

Pearce et al. (Lancet 2012; 380: 499–505) \( p=2\% \ (0.12\times0.18) \)

Too good to be honest
To summarize:

LNTH

• Has never been proven
• Cannot be refuted – even A-bomb survivors do not provide enough statistics

“A theory which is not refutable by any conceivable event is non-scientific. Irrefutability is not a virtue of a theory (as people often think) but a vice.”

Karl Popper

*Conjectures and Refutations* 1963
Hormesis (adaptive response)

- Immunization
- Physical exercise (gym)

*May bio-active radiation be beneficiary for human health?*

Yes – UV! ☀

High dose – sunburns and skin cancers ☹

Low dose – sun tanning ☺ ☺ ☺ ☺ ☺ ☺

Underexposure – severe health problems ☹
Radiation hormesis (adaptive response) hypothesis

U.S. Shipyard workers

Sponsler R. and Cameron J.R.
Radiation hormesis (adaptive response) hypothesis

Cuttler J. and Pollycove M. Dose-Response 7 (2009) 52–89
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Positive trends (since LINAC12)

• Offensive on Linear No-Threshold hypothesis; defensive stance of LNTH proponents

• Softening of advisory bodies' position regarding LNTH

• Japan – pro-nuclear changes
Offensive on LNTH


• Publications

• Debates
  • E.Calabrese vs. R.Cicerone  *Archives of Toxicology*  87(2013):2063-81, 88(2014):171-172
Softening of advisory bodies' position

- ICRP on low-dose cancers: “Speculative, unproven, undetectable and ‘phantom’ numbers”

- IAEA: “safe for everyone” level:
  2.5 mrem/h ≈ 100 × (natural background)

- UNSCEAR: “no discernible health effects” due to Fukushima
Japan – pro-nuclear changes

- Fukushima prefecture – partial re-settlement
- Tokyo – pro-nuclear governor elected (2014)
- Nuclear phase-out plans scrapped (2014)
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LINAC Applications

- Medical
  - cancer
  - inflammations & infections

- FEL
  - for EUV lithography

- food, plastics etc.
Leukemia: supplementary low-dose irradiation (LDI)

Survival, supplementary irradiation
Survival, without irradiation

Irradiation:
15 R per exposure
150 R total
Twice per week

Patients in both groups received chemotherapy and localized tumor high-dose radiation.

Low-dose irradiation for cancer

• Increased efficiency
  • especially for leukemia & angiosarcoma
• No adverse side effects
• Potential prophylaxis

BUT

• Serious R&D needed
Low-dose irradiation for inflammations & infections

- Used for centuries
- Clinically proven
- Attractive: concerning development of antibiotic-resistance
  e.g., Group A Streptococcus (GAS):
  ~ 500,000 deaths / year
  ("flesh-eating bacteria")

Long-term benefits of radon spa therapy in rheumatic diseases: results of the randomised, multi-centre IMuRa trial

Historical use of x-rays: Treatment of inner ear infections and prevention of deafness

El Calabrese and G Dhawan
FEL for EUV source

Example of high power FEL [\(\sim >10\text{kW}\)]

\[\lambda = 13.5\text{nm}\]

Injector

LINAC

Beam dump

Undulator

An FEL has the potential of high power source, for example over 10kW to multiple scanners. But FEL for EUV source is still in the conceptual stage.
Conclusions

• “The (radiation) devil is not as dangerous as usually depicted”

• More and more people understand this

• Medical, semiconductor lithography, and other applications anticipated
Appendices
Radiation around us

**curious facts**

- I’m radioactive; You’re too.
  - \(^{40}\text{K},^{14}\text{C}\) et al. present in all living cells

- US FDA: spirits should be radioactive for human consumption!

### Radionuclides in the Body (Bq = s\(^{-1}\))

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Activity (Bq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{40}\text{K})</td>
<td>4000</td>
</tr>
<tr>
<td>(^{14}\text{C})</td>
<td>3700</td>
</tr>
<tr>
<td>(^{210}\text{Po})</td>
<td>40</td>
</tr>
<tr>
<td>(^{3}\text{H})</td>
<td>23</td>
</tr>
<tr>
<td>(^{235}\text{U})</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Radiation accidents

“Radium girls” ~ 1925

Acute radiation effects: ~5000 workers
Bone sarcomas: 85 workers
Chernobyl vs. natural

Lifetime radiation doses in various regions of Europe

Ch. High-50 Ci/km², Medium-15 Ci/km² Low-5 Ci/km²

Dose, mSv per 70 years

Source: Z. Jaworowski, 2006

World average

Chernobyl areas