Low-Dose-Radiation-Activated Natural Protection against Cancer and Other Diseases

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Contents

• Nuclear physics, radiation, and life
• Current vs. past natural background radiation exposures
• Current low-dose-radiation risk assessment paradigm: Linear-no-threshold
• Systems biology perspective on low-dose-radiation risks
• Radiation activated-natural-protection (ANP) a biological basis for radiation hormesis
• Implications of radiation ANP for managing radiological and chemical terrorism incidents
• Conclusions
Nuclear Physics, Radiation, and Life

• The laws of nuclear physics (known and unknown) gave us radiation (ionizing and non-ionizing) (*Gerald Looney 2003*).

• Radiation-related nucleosynthesis within stars, supernova, and during the big bang gave us H, C, O, N and the other elements.

• All life therefore appears to be due, at least in part, to radiation reactions!

http://www.sepp.org/Archive/NewSEPP/Hormesis-Looney.htm
Big Radiation Secret (Looney, 2003)

• “And … the biggest surprise and best-kept secret of all: a man isolated in … a chamber and secure from extrinsic background radiation would still experience significant intrinsic irradiation from himself.

• The human body, rather than being a chaste and inviolate vessel of biologic purity devoid of and unpenetrated by ionizing radiation, is actually its own radioactive repository and beehive of ionizing rays…”

http://www.sepp.org/Archive/NewSEPP/Hormesis-Looney.htm
Natural Radiation is Everywhere

- Plants
- Radioactive Soil and Rocks
- Indoor Radon
- Our Bodies
Natural Radioactivity from Potassium-40

- Largest source of natural radioactivity for humans, followed by carbon-14.
- Physical half-life of 1.25 billion years.
- Mainly (88.8%) undergoes beta decay (0.51 MeV average energy) to stable calcium-40.
# Natural Radioactivity from Potassium-40 in 1 Pound of Food

<table>
<thead>
<tr>
<th>Food</th>
<th>Disintegrations per second (Becquerel)</th>
<th>Beta particle emissions per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red meat</td>
<td>50</td>
<td>2682</td>
</tr>
<tr>
<td>Carrot</td>
<td>57</td>
<td>3040</td>
</tr>
<tr>
<td>White potato</td>
<td>57</td>
<td>3040</td>
</tr>
<tr>
<td>Banana</td>
<td>59</td>
<td>3147</td>
</tr>
<tr>
<td>Lima bean</td>
<td>78</td>
<td>4148</td>
</tr>
<tr>
<td>Brazil nut</td>
<td>94</td>
<td>5007</td>
</tr>
</tbody>
</table>

Based on information from [http://physics.isu.edu/radinf/natural.htm](http://physics.isu.edu/radinf/natural.htm)
### Natural Radioactivity in the Body of a Typical 70kg Adult Human

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Approx. Total Mass</th>
<th>Disintegrations per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uranium isotopes</td>
<td>90 micrograms</td>
<td>95 thousand</td>
</tr>
<tr>
<td>Thorium isotopes</td>
<td>30 micrograms</td>
<td>9.5 thousand</td>
</tr>
<tr>
<td>Potassium-40</td>
<td>17 miligrams</td>
<td>380 million</td>
</tr>
<tr>
<td>Radium isotopes</td>
<td>31 picograms</td>
<td>95 thousand</td>
</tr>
<tr>
<td>Carbon-14</td>
<td>22 nanograms</td>
<td>320 million</td>
</tr>
<tr>
<td>Tritium isotopes</td>
<td>0.06 picograms</td>
<td>2 million</td>
</tr>
<tr>
<td>Polonium isotopes</td>
<td>0.2 picograms</td>
<td>3.2 million</td>
</tr>
</tbody>
</table>

Based on information from [http://physics.isu.edu/radinf/natural.htm](http://physics.isu.edu/radinf/natural.htm)
Natural Background Radiation was Much Higher When Mammalian Life Forms Arose on Earth

“While generations of students and scientists have learned about radioactive decay and the half-lives of various radioactive elements and isotopes, virtually no one has turned the telescope around and discussed the reverse view: The same number of half-life years taken back into the past produces a double-life, a doubling of radioactivity for these elements, and an incremental terrestrial background level many times higher than today's levels.” (Looney 2003)
Protective Processes that Arose During Higher Natural Radiation Environments on Earth

Evolution in high natural radiation environments have provided mammals with:

- DNA repair
- Apoptosis
- Cell repopulation
- Immune system defenses

Do these processes therefore operate more efficiently in higher than current natural radiation environments?
Current LNT Risk Assessment Paradigm which Ignores Natural Protection Against Radiation Harm
LNT Dogma: DNA double-strand breaks are an LNT function of radiation dose; thus, cancer induction is also an LNT function of dose.

MRC-5 cells, γ-H2AX, pulse field gel electrophoresus (S-Z Liu, 2007)
Risk Implication of LNT Model

• Any amount of radiation will cause cancers in a very large population.
• Doubling the radiation dose doubles the number of cancer cases.
• Allows use of weighted doses, fixed risk coefficients, and back-of-the-envelope calculations of cancer risk.
• Such back-of-the-envelope calculations following the Chernobyl accident led to predictions of up to hundreds of thousands of cancer deaths.
• The predicted large number of deaths did no occur.
LNT-Based Radiation Protection System

• **Equivalent dose**: A weighted tissue-specific dose that is intended to account for the different effectiveness of different radiation types.

• **Effective dose**: A weighted dose intended to relate non-uniform exposure to uniform gamma-ray exposure over the body.

• The indicated doses are justified based on the LNT hypothesis.

• **Typical dose units**: sievert (Sv) and millisievert (mSv)

• Humans are protected by limiting effective dose.
Radiation Limits (Metting 2006)

- Public drinking water (EPA): 0.04 mSv/y
- Releases to air (EPA): 0.1 mSv/y
- Security personnel scanners (ANSI): 0.25 mSv/y
- Public exposure (DOE, NRC): 1 mSv/y
- DOE administrative control: 20 mSv/y
- Worker exposure (DOE, NRC): 50 mSv/y

Average background radiation exposure in the U.S. is approximately 3 mSv/y
Systems Radiation Biology
Perspective for Cancer Induction

• Although the risk of DSB rises linearly with dose, a second risk relates to the probability that initial DSB will lead to cancer.

• The second risk is a nonlinear function of dose and is influenced by protective signaling (L. Feinendegen).

• The protective signaling provides a biological basis for radiation activated natural protection against diseases.
Added Low-Dose, Low-LET Radiation Protects Us

- Protects against chromosomal damage (Ed Azzam’s group)!
- Protects against mutation induction (Pam Sykes’ group), even when the low dose follows a large dose (Tanya Day’s work)!
- Protects against neoplastic transformation (Les Redpath’s group)!
- Protects against high dose chemical- and radiation-induced cancer (Kazou Sakai’s group)!
- Enhances immune system defense (Shu-Zheng Liu’s group)!
Added Low-LET Radiation Protects Us (continued)

- Suppresses cancer induction by alpha radiation (Chuck Sanders group)!
- Suppresses metastasis of existing cancer (Kiyohiko Sakamoto’s group)!
- Suppresses growth of transplanted lymphoma cells (Kaushala Prasad Misra’s group)!
- Extends tumor latent period (Ron Mitchel’s group)!
- Protects against diseases other than cancer (Kazuo Sakai’s group)!
Systems Radiation Biology Related Activated Natural Protection (ANP)

- Spontaneously Occurring Genomic Instability
  - DNA Damage Accumulation
  - Neoplastic Transformation
  - Proliferation of Malignant Cells
  - Cancer

- Low Dose/Dose Rate Low-LET Radiation
  - Protective Intercellular Signaling
  - Adapted Protection

- High fidelity DNA repair/apoptosis
- * Immune function
- * PAM Process

* Contributes to PROFAC

Indicates Suppressor Function
Protective Apoptosis Mediated (PAM) Process in Fibroblast

Systems-Biology-Related Tumor Control Stimulated by Low-Dose Radiation

S-Z Liu, 2007b.

Cytotoxic T Lymphocyte Destroying Cancer Cell (S-Z Liu, 2007)
# Low-Dose X-Ray Stimulated Cellular Immunity in Mice (S-Z Liu, 2007)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dose (mGy)</th>
<th>Change (%)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NK activity</td>
<td>75</td>
<td>+19</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Mac. activity</td>
<td>75</td>
<td>+52</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Cytotoxic T Lymphocytes</td>
<td>75</td>
<td>+40</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Antibody depen. cell mediated cytotoxicity</td>
<td>75</td>
<td>+30</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>T cell proliferat.</td>
<td>77</td>
<td>+101</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
NK activity of mouse splenocytes 24h after whole-body X-irradiation

*P<0.01, **P<0.001 vs control

(Fan XH and Liu S-Z. JNBUMS 1989,
Low-Dose-Rate Gamma Ray ANP against MC-Induced Skin Tumors

K. Sakai, 2005 International Dose-Response Conference presentation
### Gamma-Ray ANP Against Diseases Among Nuclear Shipyard Workers

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>SMR</th>
<th>p value</th>
<th>PROFAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic, endocrine, metabolic</td>
<td>0.69 ± 0.12</td>
<td>4.9 x 10^{-3}</td>
<td>0.31</td>
</tr>
<tr>
<td>All respiratory disease</td>
<td>0.62 ± 0.08</td>
<td>1.0 x 10^{-6}</td>
<td>0.38</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.68 ± 0.04</td>
<td>&lt; 10^{-14}</td>
<td>0.32</td>
</tr>
<tr>
<td>Emphysema</td>
<td>0.63 ± 0.26</td>
<td>7.7 x 10^{-2}</td>
<td>0.37</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.30 ± 0.43</td>
<td>5.2 x 10^{-2}</td>
<td>0.70</td>
</tr>
<tr>
<td>All infectious &amp; parasitic</td>
<td>0.86 ± 0.72</td>
<td>4.2 x 10^{-1}</td>
<td>0.14</td>
</tr>
<tr>
<td>Total mortality</td>
<td>0.78 ± 0.04</td>
<td>1.9 x 10^{-8}</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Based on combining SMR data from Sponsler and Cameron (2005).
Gamma-Ray ANP Against Alpha Radiation Induced Lung Cancer

Based on data of Sanders (2007) for Wistar rats that inhaled Pu-239 or Pu-239 + Yb-169.

3,793 animals involved

\[ \alpha + \gamma, \text{PROFAC} = 1 \]
Protection Factors (PROFAC) for Radon-Spa Areas in Japan (Misasa)

<table>
<thead>
<tr>
<th>Cancer Site or Type</th>
<th>PROFAC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>Leukemia</td>
<td>0.47 ± 0.016</td>
<td>0.56 ± 0.016</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.55 ± 0.016</td>
<td>0.60 ± 0.016</td>
</tr>
<tr>
<td>Breast</td>
<td>0.74 ± 0.014</td>
<td>(results not reported)</td>
</tr>
<tr>
<td>Lung</td>
<td>0.81 ± 0.012</td>
<td>0.53 ± 0.016</td>
</tr>
<tr>
<td>Colon/rectum</td>
<td>0.86 ± 0.011</td>
<td>0.70 ± 0.015</td>
</tr>
</tbody>
</table>

Radon exposure involves a beta/gamma component, which is considered protective. Data from Mifune et al. 1992
Central Estimate of Indoor Radon PROFAC Against Lung Cancer

Implications of Radiation ANP for Reducing Harm from Radiological and Nuclear Weapons

- Low dose, sparsely ionizing radiation could be used to enhanced hematological recovery following lethal whole body irradiation as a result of radiological or nuclear incidents (Lu Cai, 2008).
- Survivors of high radiation and chemical doses from radiological, nuclear, and chemical weapons could be at a high risk for cancer occurrence.
- Using repeated low doses or low-dose-rate exposure to sparsely ionizing radiation alone of in combination with other cancer preventative agents could reduce the number of cancer occurrences.
- Research is needed on determining optimal scheduling of doses and protective agent combinations.
- Age, genetic characteristics, and other factors may be important.
Conclusions

• Radiation ANP appears to be an evolutionary gift derived from the higher natural background levels that previously existed on Earth.
• Radiation ANP includes molecular (DNA repair), cellular (PAM process), immune system components.
• Radiation ANP provides a biological basis for radiation hormesis, since low doses and dose rates stimulate protection while high doses and dose rates are inhibitory.
• Low-dose, sparsely radiation could be used to enhance hematological recovery after lethal damage to bone marrow from radiological or nuclear terrorism incidents.
Conclusions (continued)

• Radiation ANP could be used in preventing cancer among high-risk individuals following terrorist or other incidents involving high radiation or genotoxic chemical exposures.

• Age, genetic characteristics, and other factors may be important determinants of the level of protection afforded.

• More research is needed related to using low-dose radiation to prevent disease occurrences for high-risk individuals.
International Collaborations

- Dietrich Averbeck, France
- Ed Azzam, USA
- Georg Bauer, Germany
- Doug Boreham, Canada
- Shu-Zheng Liu, China
- Jerry Cuttler, Canada
- Kaushala Prasad Misra, India
- Ron Mitchel, Canada
- Les Redpath, USA
- K. Noy Rithidech. USA
- Kazou Sakai, Japan
- Chuck Sanders, Korea
- Maurice Tubiana, France
Acknowledgements

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Other Related Presentations

http://www.radiation-scott.org
Backup Slides
Ionizing Photon Radiation Bursts from Thunder Storms

- 10-20 MeV photon radiation bursts are associated with thunder storms.
- The ionizing radiation arises just before a lightening strike and can travel kilometer distances.

*Hamish Johnson, Physics World*


*Photo from:*

http://www.pbs.org/wgbh/nova/sciencenow/3214/02-works.html
## Sources of Natural Background Radiation (BEIR VII Report, 2006)

<table>
<thead>
<tr>
<th>Exposure Pathway</th>
<th>Percentage contribution to the dose to humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosmic rays, high-LET</td>
<td>4%</td>
</tr>
<tr>
<td>Ingestion, high-LET</td>
<td>5%</td>
</tr>
<tr>
<td>Inhalation, high-LET (radon)</td>
<td>52%</td>
</tr>
<tr>
<td>Cosmic rays, low-LET</td>
<td>12%</td>
</tr>
<tr>
<td>Ingestion, low-LET</td>
<td>7%</td>
</tr>
<tr>
<td>Earth surface, low-LET</td>
<td>20%</td>
</tr>
</tbody>
</table>
LET, linear energy transfer: average energy lost
NCRP 2008 Meeting in Washington, DC

Dose-Response Relationships

Probability of cancer

Background incidence

Background dose

Dose

LNT Debate:
D. Brenner
vs.
D. Averbeck
Current Radiation Risk Assessment Paradigm: Linear No-Threshold
BEIR VII Low-Dose, Low-Dose-Rate Extrapolation

Cancer Risk vs. Radiation Dose (mSv)

- LNT
- DDREF

Neutron + gamma
LNT-Associated Radiation Phobia Following a Dirty Bomb Incident

Radiation-Phobia-Associated Impacts:

- **Loss of lives** associated with frantic evacuations.
- **Severe injuries** during evacuations.
- **Increased suicides** and abortions.
- **Increased psychosomatic disorders**.
- **Increased drug/alcohol/cigarette abuse**.
- **Permanent abandonment of properties** with low-level contamination.
CT Scan

## Typical Organ Radiation Doses from Radiologic Studies (Brenner & Hall 2007)

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Relevant Organ</th>
<th>Dose (mGy or mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental radiography</td>
<td>Brain</td>
<td>0.005</td>
</tr>
<tr>
<td>Posterior-anterior chest radiography</td>
<td>Lung</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral chest radiography</td>
<td>Lung</td>
<td>0.15</td>
</tr>
<tr>
<td>Screening mammography</td>
<td>Breast</td>
<td>3</td>
</tr>
<tr>
<td>Adult abdominal CT</td>
<td>Stomach</td>
<td>10</td>
</tr>
<tr>
<td>Neonatal abdominal CT</td>
<td>Stomach</td>
<td>20</td>
</tr>
</tbody>
</table>
## Hypothetical Cancer Cases for a Population of 50 Million Based on BEIR VII Risk Coefficient

<table>
<thead>
<tr>
<th>Radiation Dose (mSv)</th>
<th>Hypothetical Average Individual Risk</th>
<th>Hypothetical Radiation-induced Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.01</td>
<td>500 thousand</td>
</tr>
<tr>
<td>10</td>
<td>0.001</td>
<td>50 thousand</td>
</tr>
<tr>
<td>1</td>
<td>0.0001</td>
<td>5 thousand</td>
</tr>
<tr>
<td>0.1</td>
<td>0.00001</td>
<td>5 hundred</td>
</tr>
</tbody>
</table>
Evolutionarily-Derived Contributors to Low-Dose, Low-LET Radiation Induced Protection

- Induced DNA DSB repair, for doses above a threshold, which may be dose-rate dependent (W. Olipitz and colleagues).
- Stimulated immunity against cancer (S-Z Liu’s group).
- Protective apoptosis medicated (PAM) (G. Bauer’s group).
Small Doses of Low-LET Radiation Protected From Inversion Mutations in pKZ1 Mice

Small X-ray dose given hours after 1000 mGy dose protected
Diagnostic X-Ray ANP Against Spontaneous Lung Cancer in Canadian TB Patients

Multiple fluoroscopy examinations

PROFAC ≈ 0.15

95% Confidence

Upper Bound X-Ray PROFAC Against Breast Cancer

Low-Dose X-Ray ANP Against Lung Cancer

75 mGy 24h before Lewis lung cancer cell implantation

C57BL/6J Mice

S-Z Liu, 2007
Thymic Lymphoma Study of S-Z Liu

- Low dose X rays (25, 75, or 100 mGy) given before large X ray dose (1.75 Gy) to mice.
- Time interval between low and high dose was 6, 12, or 24 hours.
- Four cycles of dosing were given apparently to reduce acute toxicity.

Low Dose ANP Against High Dose X-Ray Induced Thymic lymphoma in C57BL/6J Mice: Evidence for Stochastic Thresholds

HDR=1.75 Gy x 4

S-Z Liu, 2007

Time interval before HDR
- 6h
- 12h
- 24h

% of lymphoma

1.75Gy
25mGy+1.75Gy
75mGy+1.75Gy
100mGy+1.75Gy

*P<0.05, **P<0.01 vs 1.75Gy x 4
Prolongation of Life Span of db/db Mice by Low Dose Rate Irradiation

Diabetic mice, Sakai K, IDRS 2006

Gamma rays
Indoor Radon Lung Cancer PROFAC Distribution

Based on data from Thompson et al. (2008).
Related Literature

Related Literature (continued)

- Thompson RE et al. Health Phys. 94(3)228-241.