

CT Scans May Reduce Rather Than Increase the Risk of Cancer

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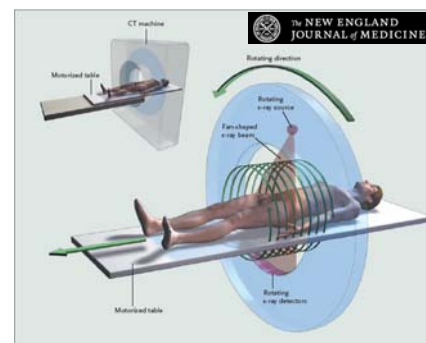
Contents

- Background information on CT
- Hypothetical nature of Brenner & Hall's claim of significant future cancers from current CT scan usage
- Background information for understanding radiation **risks** and **benefits**
- Biological bases for low-dose-radiation **activated natural protection** against cancer and other diseases
- Reasons for concluding CT scans may reduce rather than increase the risk of cancer
- Conclusions

CT Scans

- Computed tomography (CT) scan / computerized axial tomography (CAT) scan, is a procedure in which cross-sectional images (x-rays taken from many different angles) of structures of the body are created.
- Information is processed through a computer forming a three dimensional image called a **tomogram**.
- The 3-D imaging makes CT scans more informative than chest x rays.

CT Scan



D. Brenner & E. Hall, NEJM 357:2277-84, 2007.

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

Study Type	Relevant Organ	Dose (mGy or mSv)
Dental radiography	Brain	0.005
Posterior-anterior chest radiography	Lung	0.01
Lateral chest radiography	Lung	0.15
Screening mammography	Breast	3
Adult abdominal CT	Stomach	10
Neonatal abdominal CT	Stomach	20

Contrast Agent Usage

- A contrast agent (e.g., iodine-based dye, barium solution) may be administered prior to CT scan for better imaging.
- Contrast agents can be administered by injection or orally.
- A severe anaphylactic reaction (e.g., difficulty breathing) to the contrast dye may occur.
- The indicated reaction although rare can be **life threatening**, thus is a real risk not related to radiation exposure.
- Brenner & Hall did not address this real risk but rather addressed **hypothetical risks** associated with low-dose X rays from CT.

CT Used to Detect Abnormalities

- Blood clots
- Cysts
- Fractures
- Infections
- Tumors
- COPD

Brenner and Hall Indicated:

- 62 million CT scans per year are currently obtained in the United States.
- More than 4 million of these are for children.
- CT scans are used for both **symptomatic patients** and for screening of **asymptomatic patients**.

Note: CT also now being used in COPD research

Expected Increases in Asymptomatic Screening Programs

- CT colonography (virtual colonoscopy)
- CT lung screening for current and former smokers
- CT cardiac screening
- CT whole body screening

Brenner & Hall (2007)

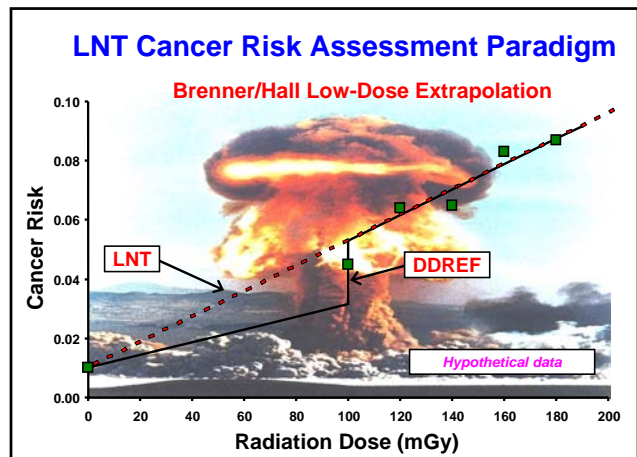
Brenner & Hall Claims of Significant Harm from CT Scans

- Harm from low-level radiation is generally evaluated based on the **linear-no-threshold (LNT) model** (hypothesis) for cancer induction.
- Brenner & Hall assigned hypothetical cancer risks for CT-related X-ray exposures based on slopes of the LNT dose-response functions derived from application of the LNT model to cancer mortality data for atomic bomb survivors in Japan.

Brenner & Hall (2007).

Brenner & Hall's Approach to Calculating CT-Scan-Induced Cancers

- With the **hypothetical LNT low-dose extrapolation**, one gets a very small average hypothetical individual risk of cancer for the irradiated population (e.g., average risk = 0.0001, which is essentially zero).
- The average hypothetical risk is then multiplied by the total population size (e.g., 60 million).
- This gives a hypothetical number of cancer cases (e.g., 60 million persons x 0.0001 = 6000 cancers cases).
- Alternatively, one can sum the individual hypothetical risks to get the same answer.
- Different LNT model risk coefficients are used for different ages and different types of cancer.



Hiroshima Atomic Bomb Dome Near Epicenter

Left: Blast-wave-associated destruction.
Right: dome appearance today, a historic monument.



Contemporary pictures by Mike Coles (BBC News):

http://news.bbc.co.uk/2/shared/spl/hi/pop_ups/05/asia_pac_hiroshima_then_and_now/html/1.stm

Thermal Wave Melted Saki Bottles

In addition to blast and radiation injuries, **intensive heat** from the nuclear detonation also cause burns to victims. The population response was therefore one for combined injuries in a highly stressful environment. This is however ignored by researchers such as Brenner & Hall when using the A-bomb survivor data for cancer risk assessment.



http://www.english.uiuc.edu/maps/poets/g_/levine/bombing.htm

Hiroshima Peace Memorial Park Monument and Flame of Peace



Flame to burn until no more nuclear weapons.

http://news.bbc.co.uk/1/shared/spl/hi/pop_ups/05/asia_pac_hiroshima_then_and_now/html/10.stm

Brenner & Hall's Hypothetical Cancer Cases

- "Although the individual risk estimates ... are small, the concern about the risks from CT is related to the rapid increase in its use – small individual risk applied to an increasingly large population may create a public health issue some years in the future."
- Based on current CT usage, they estimate that within a few decades, 1.5 to 2.0 % of all cancers in the United States may be attributable to current CT usage.
- All risk is attributed to X rays from CT. No risk is considered related to use of contrast media.

Background Information Related to Understanding Radiation Risks and Benefits to Humans

Radiation-Free Myth

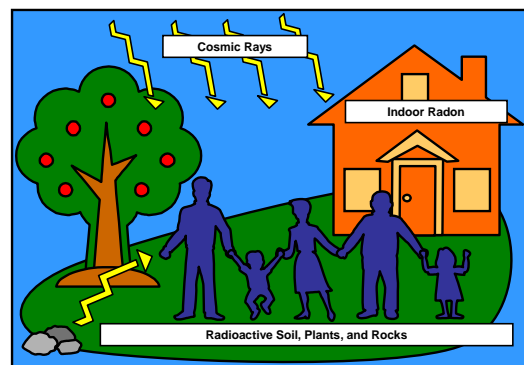
- Most members of the news media, government agencies, and general public appear to think that we humans are normally **ionizing-radiation-free** entities.
- Regulatory agencies limit human exposures to radiation based on the perception that any amount of radiation could be harmful (*BEIR VII Report*).

Report available at: www.nap.edu

Radiation Truth

- **Ionizing radiation is everywhere** throughout the universe.
- We all are exposed to natural radiation sources.
- We all contain in our bodies sources of ionizing radiation (C-14, K-40, Po-210, etc.).
- This has always been so.
- This is not likely to change for any future generation.
- **Sparsely-ionizing forms (e.g., beta and gamma)** of natural radiation in our bodies are likely promoting our health, as discussed later.

Natural Background Radiation



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.
- Also (11.2%) decays to stable Argone-40 via electron capture or positron emission.

Natural Radioactivity from Potassium-40 in 1 Pound of Food

Food	Disintegrations per second (Becquerel)	Beta particle emissions per minute
Red meat	50	2682
Carrot	57	3040
White potato	57	3040
Banana	59	3147
Lima bean	78	4148
Brazil nut	94	5007

Based on information from <http://physics.isu.edu/radinf/natural.htm>

Natural Radioactivity in the Body of A Typical 70kg Adult Human

Nuclide	Approx. Total Mass	Disintegrations/day
Uranium isotopes	90 micrograms	95 thousand
Thorium isotopes	30 micrograms	9.5 thousand
Potassium-40	17 milligrams	380 million
Radium isotopes	31 picograms	95 thousand
Carbon-14	22 nanograms	320 million
Tritium isotopes	0.06 picograms	2 million
Polonium isotopes	0.2 picograms	3.2 million

Based on information from <http://physics.isu.edu/radinf/natural.htm>

Ionizing Photon Radiation Bursts from Thunder Storms

- 10-20 MeV photon radiation bursts are associated with thunder storms.
- The bremsstrahlung-associated photon radiation appears to arise just before a lightning strike and can travel kilometer distances.

Hamish Johnson, Physics World

<http://physicsworld.com/cws/article/news/31092>



Photo from: <http://www.pbs.org/wqbn/nova/sciencenow/3214/02-works.html>

Weighted Radiation Doses Often Used

- Supposedly accounts for different radiation qualities (e.g., highly ionizing vs. sparsely ionizing).
- Supposedly accounts for different sensitivities of different tissue of the body to radiation induced harm.
- Supposedly adjusts for non-uniform exposure.
- Typical units of weighted dose: sievert (Sv), millisievert (mSv).
- Corresponding un-weighted doses have units such as gray (Gy) and milligray (mGy).

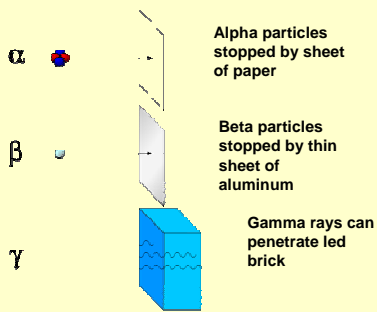
Average Annual Natural Background Radiation Doses (Weighted) to U.S. Citizens

- Inhaled radon: about 2 mSv
- Other internal radionuclides: about 0.4 mSv
- Terrestrial radiation: about 0.3 mSv
- Cosmic radiation: about 0.3 mSv

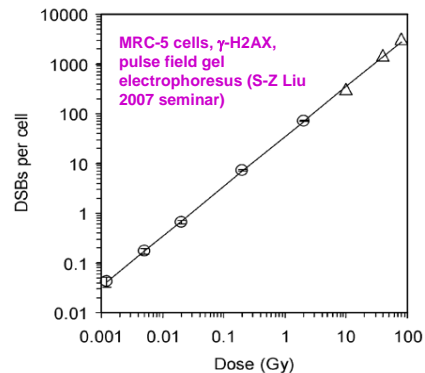
Health Physics Society

<http://www.umich.edu/~radinfo/introduction/natural.htm>

Radiation Penetration by Type



Linear-No-Threshold Paradigm



LNT Dogma: DNA double-strand breaks (DSB) are an LNT function of radiation dose; thus, cancer induction is also an LNT function of dose.

Brenner's Contradictory Views

- *In vitro* DSB are a LNT function of dose, thus cancer incidence is an LNT function of dose (early view of Brenner and others).
- Low-dose ecological studies data showing reduced risk not credible since doses are uncertain, even though known to be low.
- Can only reliably show reduced risk with *in vitro* studies but can't directly link *in vitro* results to cancer (view being expressed today by Brenner in the NCRP LNT debate in Washington, DC).

Excerpt from Brenner's Abstract for April 2008 NCRP LNT Debate

"The arguments for a linear nonthreshold model at very low doses are plausible... at this time we don't know if deviations from the predictions of this linear approach will be large or small... We are only just beginning to scratch the surface of our understanding of the impact of intercellular interactions on very low dose cancer risks, so it is more than premature to be advocating changes [from LNT] in policy or practice."

Ref: Program for 44th Annual Meeting NCRP, April 14-15, 2008.

Beyond Scratching the Surface

- Researcher around the world have gone far beyond scratching the surface with their low-dose radiation research.
- Researchers like Brenner however, will not acknowledge this for whatever reason.
- Slides that follow relate to extensive knowledge recently gained about low dose-radiation induced protective effects that invalidate the LNT model.
- These finding and other research (modeling/theoretical) motivated Scott *et al.* (2008) to publish a paper debunking the Brenner & Hall CT (2007) paper.

Systems Radiation Biology Perspective for Cancer Risk Assessment

- 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 biological signaling.
- Low-dose radiation can activate protective responses at different organizational levels. Many publications show this.
- Low-dose-radiation-induced protective signaling provides a biological basis for radiation hormesis.

Radiation-Induced Protective Signaling

- Form of activated natural protection (ANP).
- Induced by low-dose, low-LET radiation and other stressors (e.g., vitamins, some chemopreventative agents, exercise).
- Enhances DNA repair/apoptosis (p53-related).
- Reactive oxygen (ROS) and nitrogen (RNS) species and specific cytokines (e.g., TGF- β 1) participate in p53-independent apoptosis.
- Immune system functions stimulated (coordinated cellular and humoral functions).
- Suppresses inflammation.

Low-Level Radiation ANP

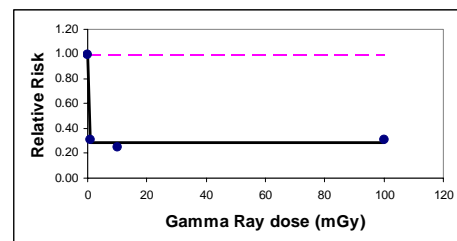
- Protects against chromosomal damage (Ed Azzam's group).
- Protects against mutation induction (Pam Sykes' group), even when the low dose follows a large dose (Tanya Day's work).
- Protects against neoplastic transformation (Les Redpath's group).
- Protects against high dose chemical- and radiation-induced cancer (Kazuo Sakai's group).
- Enhances immune system defense (Shu-Zheng Liu's group).

Low-LET Radiation ANP (continued)

- Suppresses cancer induction by alpha radiation (Chuck Sanders group).
- Suppresses metastasis of existing cancer (Shu-Zhen Liu's group).
- Extends tumor latent period (Ron Mitchel's group).
- Protects against diseases other than cancer (Kazuo Sakai's group).

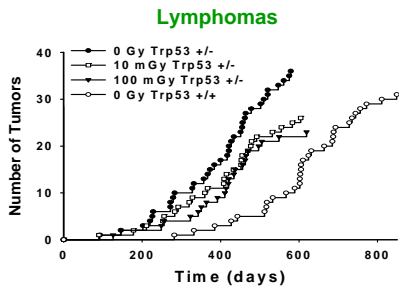
We have gone well beyond scratching the surface!

Gamma-Ray ANP Against Neoplastic Transformation in C3H 10T1/2 Cells



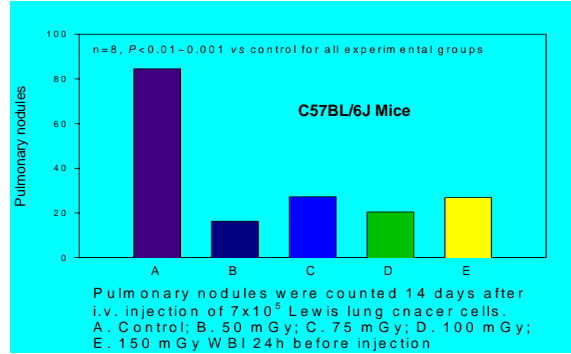
Data from Azzam et al. 1996

Gamma-Ray ANP Against Lymphomas in Cancer-Prone Mice

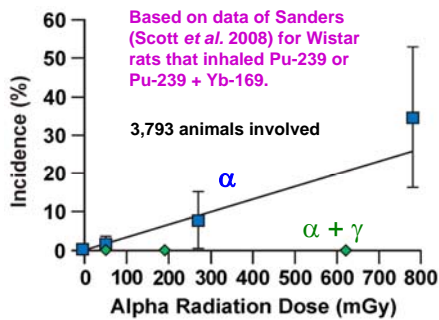


Mitchel et al. (2003); low-dose gamma rays increased latency

Prevention of Lewis Lung Cancer Metastasis via Low-Dose X-Ray ANP (S-Z Liu, 2007)

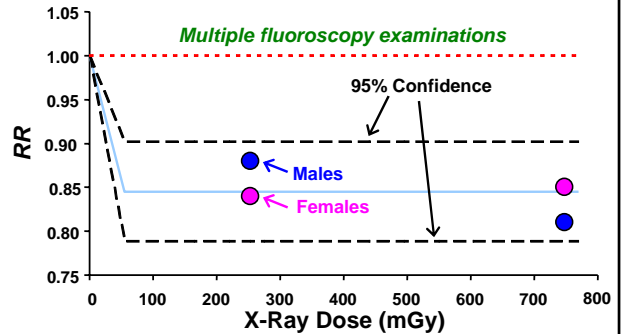


Gamma-Ray ANP Against Alpha Radiation Induced Lung Cancer



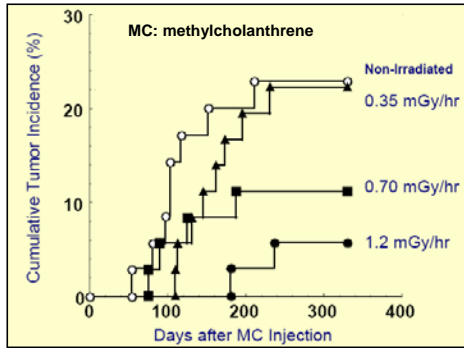
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Gamma-Ray ANP Against Spontaneous Lung Cancer in Humans



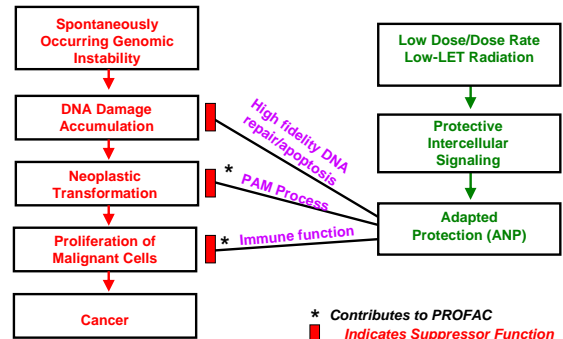
Data from GR Howe. Radiat. Res. 142:295-304,1995. Similar findings have been reported for breast cancer (Miller. N. Engl. J. Med. 321:1285-1289, 1989)

Gamma-Ray ANP Against Chemical-Induced Skin Tumors in Mice



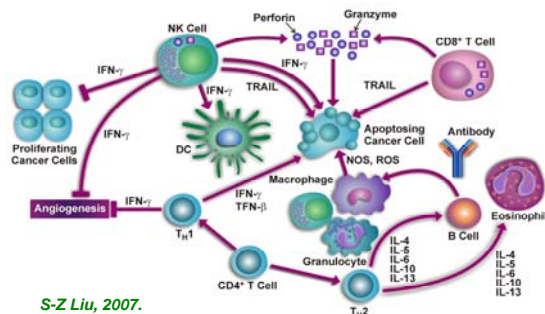
K. Sakai, International Hormesis Conference 2005

Biological Basis for Radiation ANP



ROS scavenging contributes to protection from high doses

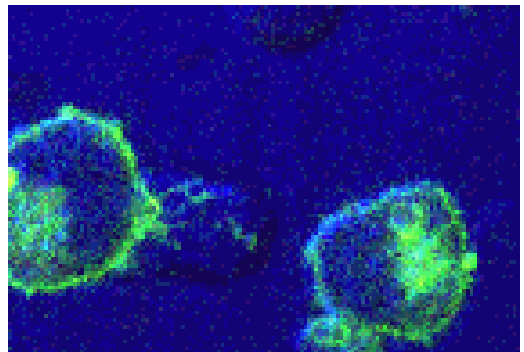
Systems-Biology-Related Tumor Control Stimulated by Low-Dose Radiation



S-Z Liu, 2007.

G. Dranoff. Nat Rev Cancer 4: 11-22, 2004.

Cytotoxic T Lymphocyte Destroying Cancer Cell



S-Z Liu, 2007 presentation at Canadian hospital

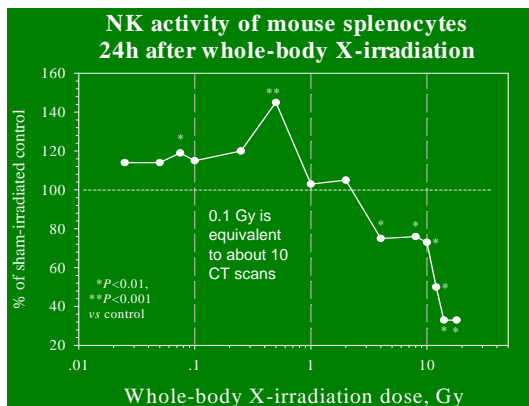
Immune Functions Stimulated by Low Doses of Low-LET Radiation

- Enhanced tumor antigen presentation (*INF γ* ; decreased *IL-10*).
- Enhanced NK cell and CD8⁺ T-cell function (*IL-2*).
- Enhanced T_H1 helper cell immunity and cytotoxicity (*IL-12*, *IL-18*).
- Inhibition of angiogenesis (*IL-12*, *IL-18*).
- Induce tumor cell apoptosis (*TNF- α*)
- Increased macrophage antitumor activity (*local ROS releases*).

Increases in green: S-Z Liu, Dose-Response 5:39-47, 2007

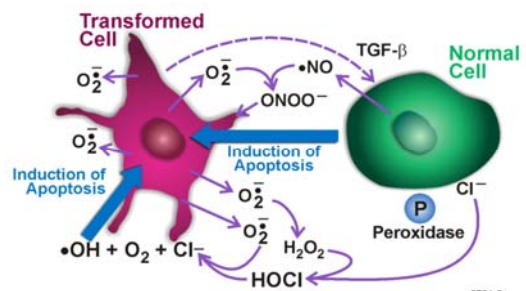
Low-Dose X-Ray Stimulated Cellular Immunity in Mice (S-Z Liu, 2007)

Parameter	Dose (mGy)	Change (%)	P value
NK activity	75	+19	< 0.05
Mac. activity	75	+52	< 0.05
Cytotoxic T Lymphocytes	75	+40	< 0.01
Antibody depen. cell mediated cytotoxicity	75	+30	< 0.05
T cell proliferat.	77	+101	< 0.01

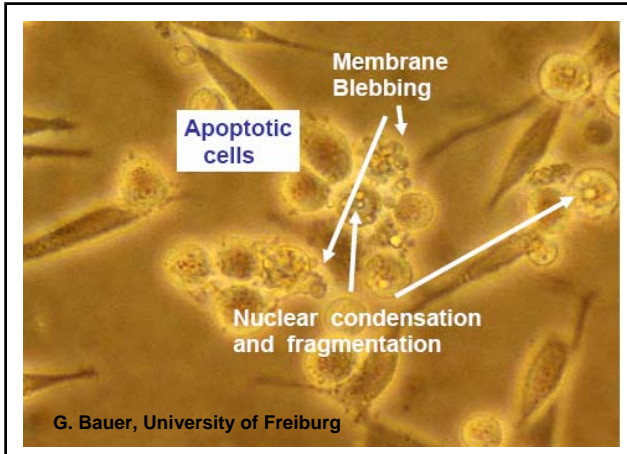


Fan XH and Liu S-Z. JNBUMS 1989, 15:551

Protective Apoptosis Mediated (PAM) Process in Fibroblast



G. Bauer 2000: Autocrine self-destruction



PROFAC, A Measure of ANP Efficiency

- **PROFAC** stands for protection factor and is a population average.
- Introduced in Scott's stochastic model for cancer induction by radiation.
- **Cancer suppression PROFAC**: Expected fraction of cancer cases that do not occur that would have occurred in the absence of radiation ANP.

Scott and Di Palma Dose-Response 5: 230-235, 2006.

Protection Factors Against Cancer in Humans¹

Region or Group	Effect	PROFAC
High radon levels, USA	all cancers	0.35
Canada, nuclear industry workers	Leukemia	0.68
US DOE labs workers	Leukemia	0.78
Mayak Plutonium facility workers	lung cancer	0.86 ²

Proportion of spontaneous and other cancers prevented!

¹Jaworowski Z. Symposium "Entwicklungen im Strahleschutz", Munich, 29 November 2001.

²Scott BR. Dose-Response, 2007.

Gamma-Ray ANP Against Diseases Among Nuclear Shipyard Workers

Cause of Death	SMR	p value	PROFAC
Allergic, endocrine, metabolic	0.69 ± 0.12	4.9 × 10 ⁻³	0.31
All respiratory disease	0.62 ± 0.08	1.0 × 10 ⁻⁶	0.38
Pneumonia	0.68 ± 0.04	< 10 ⁻¹⁴	0.32
Emphysema	0.63 ± 0.26	7.7 × 10 ⁻²	0.37
Asthma	0.30 ± 0.43	5.2 × 10 ⁻²	0.70
All infectious & parasitic	0.86 ± 0.72	4.2 × 10 ⁻¹	0.14
Total mortality	0.78 ± 0.04	1.9 × 10 ⁻⁸	0.22

Based on combining SMR data from Sponsler and Cameron (2005).

Scott et al. (2008) Paper that Debunks Brenner & Hall Paper

- Four test of the LNT model are discussed. None were passed.
- Points out why A-bomb survivor data should not be used for assessing cancer risk from CT.
- Points out why epidemiological studies relied upon for LNT responses miss showing hormetic or threshold-type dose responses for cancer induction.

B.R. Scott et al., Journal of American Physicians and Surgeon 13(1):8-11, 2008.
<http://www.jpands.org/vol13no1/scott.pdf>

Why A-Bomb Survivor Data Should Not Be Used

- A-bomb produce blast and thermal injuries in addition to radiation injuries.
- Such combined injuries adversely impact on immune system functioning and this leads to a shift in the dose-response curve for cancer induction to the left.
- Genetic risk factors for A-bomb victims differ from those for U.S. citizens receiving CT scans.

Procedures Used in Epidemiological Studies that Favor LNT Risk Functions

- Dose lagging (ignoring some of the radiation dose) which shifts the dose-response curve to the left, as was done in Cardis and colleagues discussed by Brenner and Hall as supporting evidence for increased cancer risk at low doses.
- Averaging risk over wide dose intervals in cohort studies, as was done for A-bomb survivor cancer data cited by Brenner and Hall to infer increase risk for the entire weighted dose interval 10 – 150 mSv.
- Averaging odds of cancer over very wide dose intervals before calculating the odds ratio in case-control studies.

Procedures Used (continued)

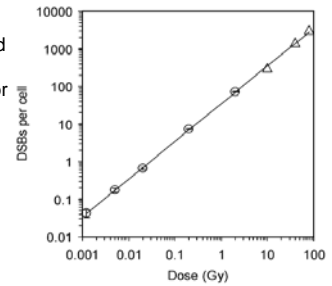
- Including individuals who receive low-dose radiation in the unexposed group in cohort and case-control studies.
- Employing linear extrapolation from high to low doses after dose lagging and risk or odds averaging over wide dose intervals.
- Not adjusting for the impact of combined injuries and differences in genetic susceptibilities when using A-bomb survivor data to assess cancer risk for another population.
- Ignoring radiation ANP for no apparent reason other than it does not fit the LNT model.

Dose Lagging Procedure as Discussed in Scott *et al.* (2008)

- Based on assumption of wasted dose.
- Contradicts LNT hypothesis which implicates each small dose increment as being equally effective.
- No wasting occurs when each increment in dose shortens tumor latent period was demonstrated by animal data.
- No wasting occurs when added dose increments contribute to cancer suppression (i.e., ANP).

Dose Lagging Procedure (continued)

- No evidence of dose wasting has been reported for inducing DNA double strand breaks, mutation, or neoplastic transformation.
- Discarding radiation dose under the presumption of dose wasting could mistakenly support and LNT-type dose response.



Conclusions

- Doses from a single CT scan are in the range for ANP against cancer.
- Multiple scans separated in time would be expected to repeatedly stimulate protective signaling.
- There is no credible evidence that radiation from current usage of CT in the United States is causing future cancers in adults.
- For children, the situation is more uncertain.
- Risk estimates for children based on a-bomb survivor data however cannot be considered credible.

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