The Linear No-Threshold (LNT) Model and Its Impact on Public Health

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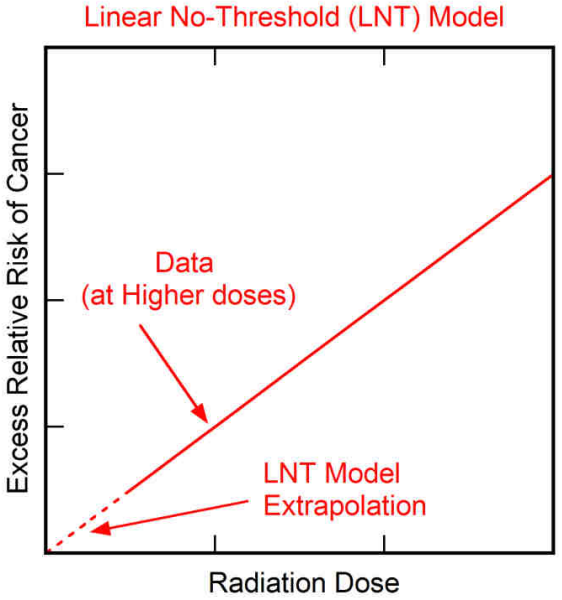
The Linear no-threshold (LNT) Model For Radiation-induced Cancer

$$\text{Excess Relative Risk (ERR)} = \frac{R - B}{B}$$

R = *Cancer Rate after Irradiation*

B = *Background Cancer Rate*



Traditional argument on why the LNT model is needed:

- In low dose regions, no significant increase in radiation-induced cancer can actually be detected
- Hence the extrapolation of risk from cancers produced by high doses to low doses is needed

Such an argument ignores significantly reduced cancers that have been observed following exposure to low radiation doses.

The LNT Model has caused Radiophobia

- LNT model has been used for radiation safety since the 1950s. Endorsed by National Academy of Sciences repeatedly, most recently in the BEIR VII Report (2006)
- Has led to fear of even the smallest amount of exposure to radiation (since there is no threshold)
- Textbooks reinforce the fear of low levels of radiation, e.g:

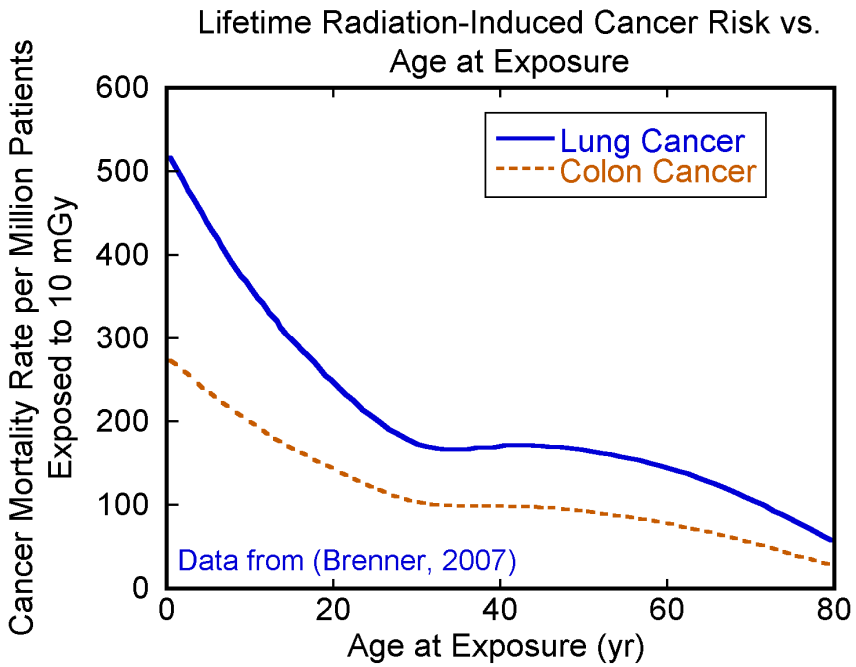
Radiobiology for the Radiologist, 6th Edition,
By Eric J. Hall, Amato J. Giaccia, 2006, Page 136:

involved. There is no reason to believe that even a single x-ray photon could not result in a base change leading to a mutation that could cause cancer or a hereditary defect. For this reason, it is considered

Computed tomography - an increasing source of radiation exposure (Brenner and Hall, NEJM, 2007)

(Over 6000 citations in Google Scholar to date)

- X-rays →Free radicals → DNA damage and mutations → Cancer
- In atomic bomb survivor data, cohort with mean dose of 40 mSv → increased cancer risk
- 15-Country Radiation Worker study (Cardis, 2005) → mean dose 20 mSv → increased cancer risk.



Conclusion:

- ❑ 1.5-2% of cancers attributable to CT scans
- ❑ Children are more sensitive to radiation-induced cancers

BEIR VII Report used the above arguments and data to support the LNT model.

Efforts by Professional Organizations to Reduce and Monitor Radiation Dose from Diagnostic Imaging

Image Wisely – Radiation Safety in Adult Medical Imaging

Image Gently – Alliance for Radiation Safety in Pediatric Imaging

AAPM is part of both the efforts.

Joint Commission issued a Sentinel Event Alert –

Radiation Risks of diagnostic imaging

IAEA – Radiation Protection of Patients advices: "Inform and discuss with patients benefits and risks of the examination"

IAEA Smart Card Project – To track radiation exposure of patients

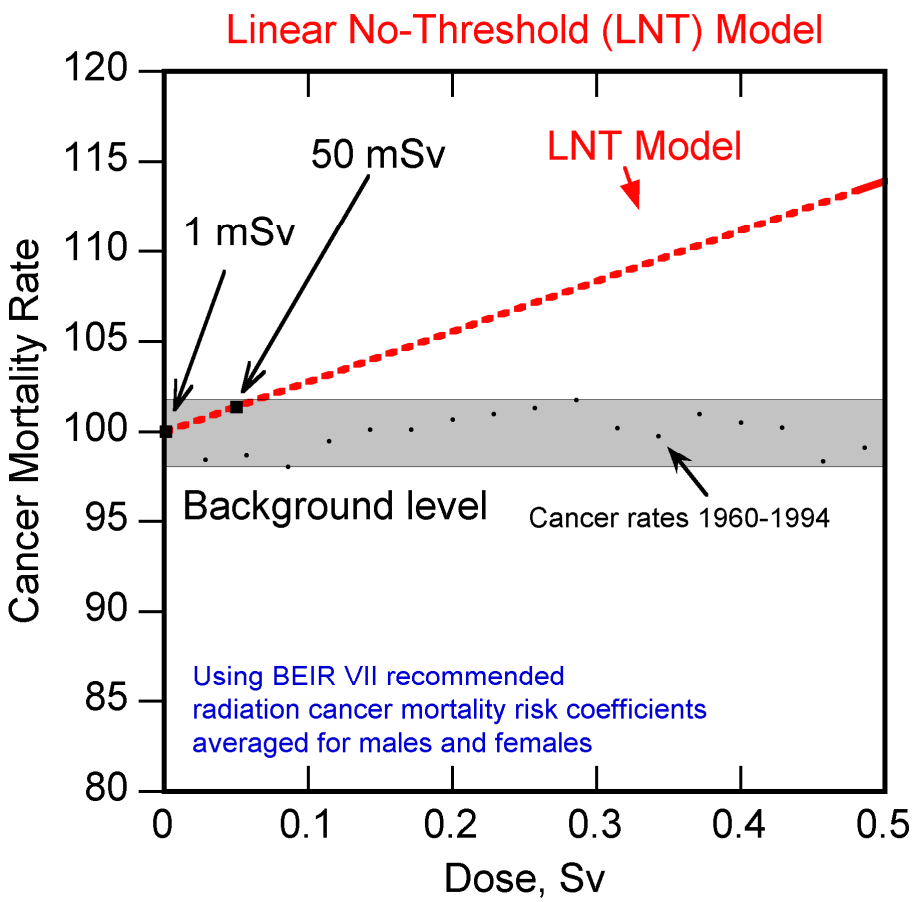
AAPM – CT Dose Summit (3 of them so far)

American College of Radiology (ACR) – CT Dose Index Registry

American Board of Radiology – Practice Quality Improvement using ACR Registry to reduce dose for specific imaging studies

NCRP – Reference Levels and achievable doses in medical imaging

Effect of low-dose radiation on cancer mortality rate (using the LNT Model)



Dose reduction efforts

e.g. 50 mSv down to 1 mSv

- cancer rate within grey area (range of normal variation)
- no health benefit.
- a total waste of resources

Would you buy an expensive drug that promised reduction of cancer rates by 2%? Obviously not.

Professional organizations are recommending expensive CT dose reduction efforts for similar reduction of cancer risk.

Consequences of Reducing CT Dose

- Degradation of image quality
- Increases misdiagnoses (Increases false positives and false negatives)
- Can make CT scans non-diagnostic

➢ Can impact patients' health adversely

(Goske, 2013) CT scan of infant 19 cm body width
Size Specific Dose Estimate (SSDE) = 4.7 mGy (CT is Diagnostic)
35% dose reduction SSDE = 3.1 mGy (CT is Non-diagnostic)

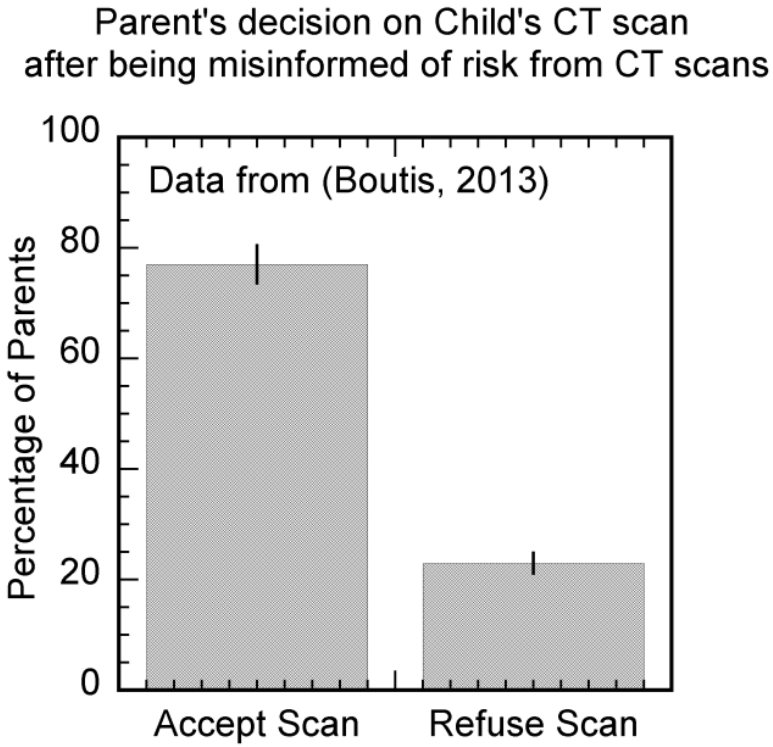
Reducing CT Radiation Dose Can Harm Patients

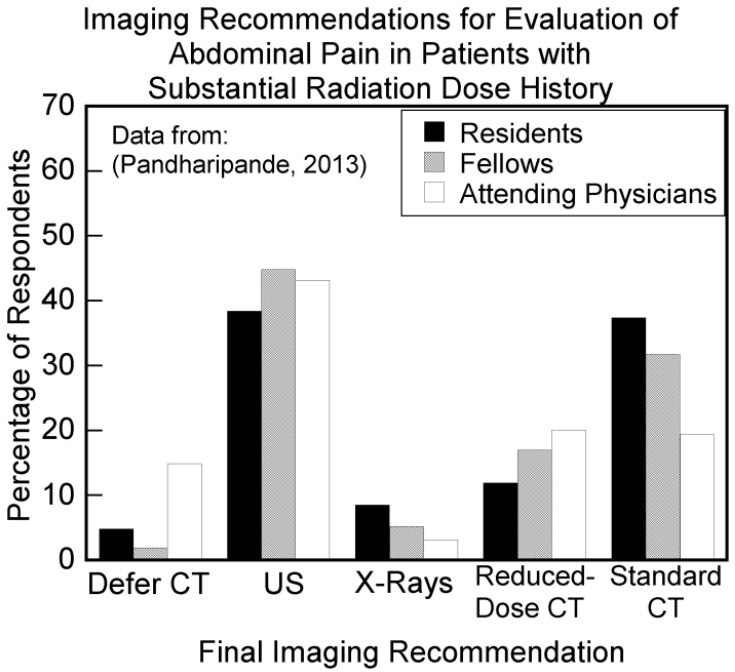
(Brody, 2014) states: “1 in 20 paediatric abdominal CT scans ….. were inadequate for diagnostic purposes due to excessive radiation dose reduction efforts.” (Image Gently is responsible for this)

Patients are being harmed by

- Poor quality or non-diagnostic CT scans being performed due to LNT model based low-dose radiation concerns

Use of the LNT Model Can Harm Patients in Radiology





Patients are being harmed by

- Patients/Parents refusing indicated diagnostic CT scans
- Physicians not prescribing the required CT scans

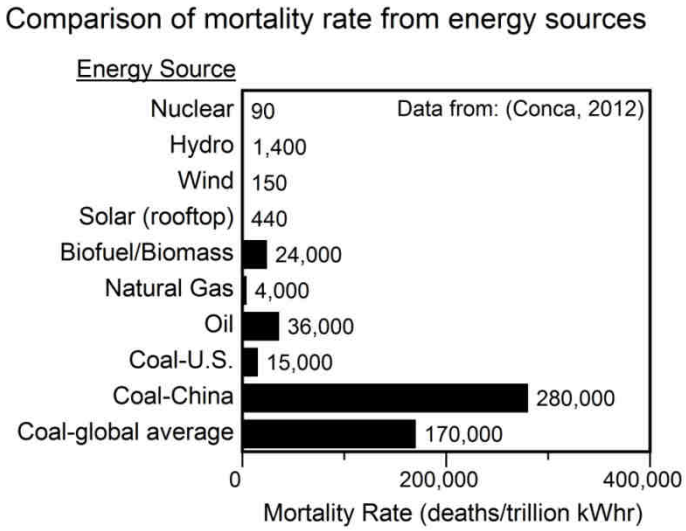
LNT Model is Responsible for Casualties and Economic Harm following Nuclear Reactor Accidents in Fukushima

In Fukushima, evacuations based on the LNT model caused:

- More than 1000 deaths, Disruption of over 100,000 lives
- Maximum dose averted due to evacuation ~70 mSv (UNSCEAR, 2013).

After the Fukushima Accidents:

Germany and Japan decided to shut down all their nuclear power plants, because of LNT model based concerns, even though nuclear power has proven to be the safest mode of power generation.



LNT model based fears are resulting in countries making more hazardous choices for energy production.

LNT Model is Responsible for Excessive Shielding and Other Costs for Radiation-related Enterprises

- Radiation Therapy Devices
- X-ray, Fluoroscopy systems
- CT, PET/CT Suites
- Irradiators
- Nuclear Reactors

If the costs are too high, the technologies can become unaffordable to some segments of the society.

Dollar Spent per Life Saved

LNT model based actions:

- Nuclear Power Plants
  (ratcheting up of regulations) - $ 2.5 Billion / life saved
- Radioactive waste management - $ 220 Million / life saved

From: Reducing the hazards of nuclear power- insanity in action
(Cohen, 1987)

Health care	$19,000 / life saved
Residential	$36,000 / life saved
Transportation	$56,000 / life saved
Occupational	$68,000 / life saved

From: Five hundred life-saving interventions and their cost effectiveness
(Tengs, 1995)

Money spent on the LNT model based efforts could have been spent much better to save many more lives.

Having seen the harm caused by the LNT model in many different areas, let us examine if the use of the LNT model has led to any benefit in terms of reduction of cancers, by examining the validity of the LNT model.

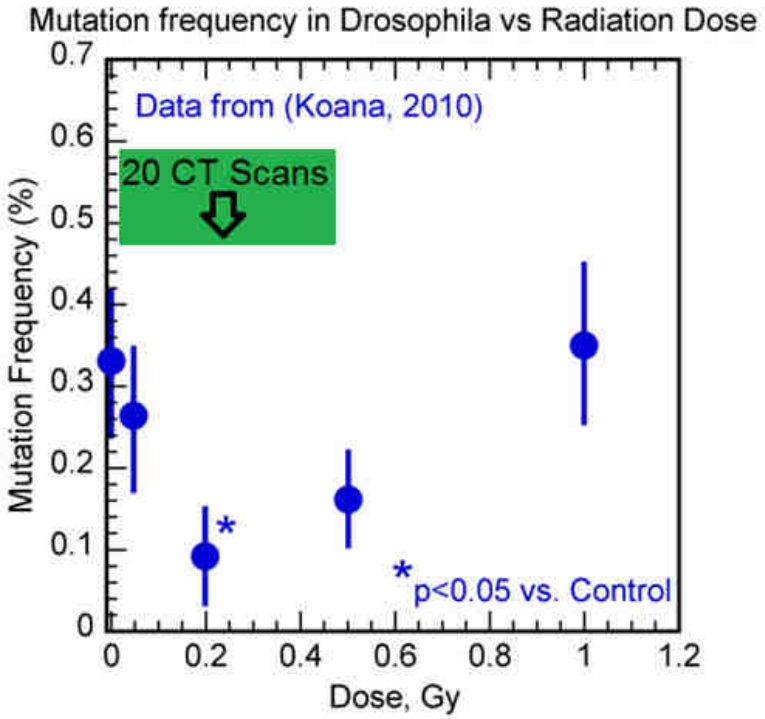
Justification for the LNT model

The Linear no-threshold (LNT) Model is justified based on the following two concepts:

- Even a small amount of radiation increases DNA damage and mutations
- Mutations increase cancers

Are these concepts valid?

Do mutations increase with radiation dose at low doses?



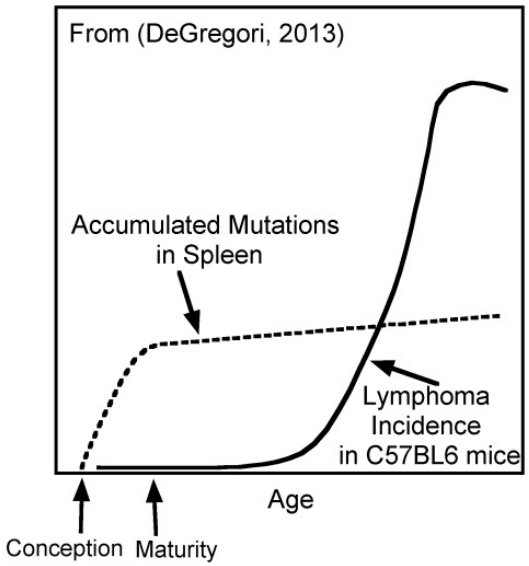
•Even in the absence of radiation, endogenous DNA damage does occur, which is much more than the damage caused by low-dose radiation **(Vilenchuk & Knudson, 2003)**.

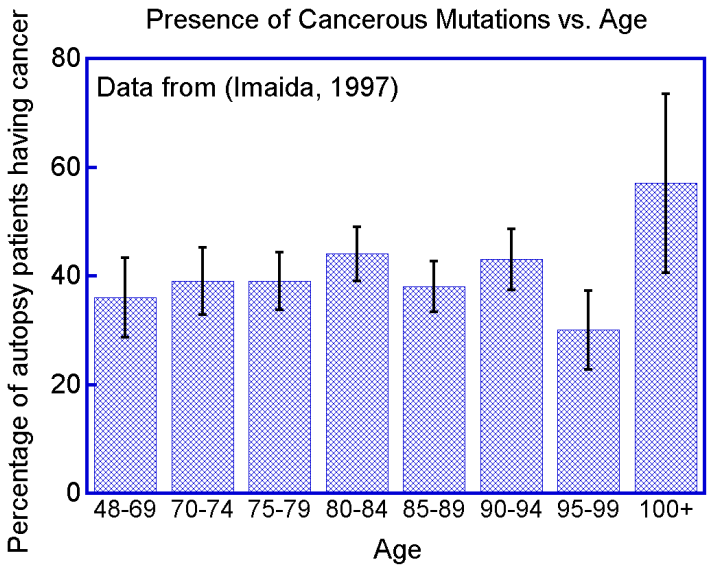
•Low-dose radiation enhances defenses (antioxidants, DNA repair enzymes, etc. collectively known as adaptive protection) **(Feinendegen, 2013)** reducing the endogenous damage in the subsequent period.

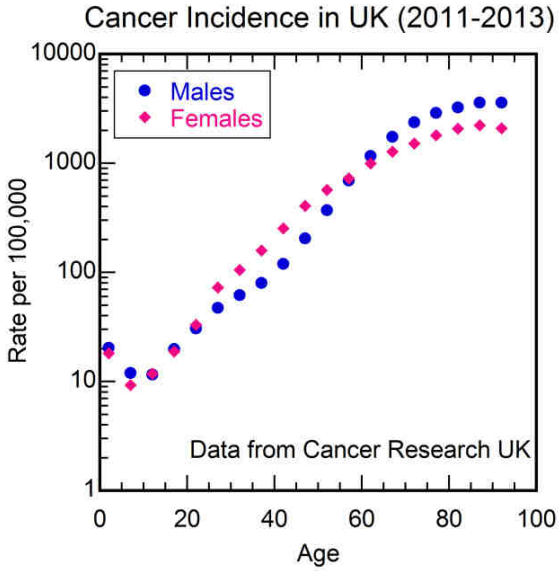
•Net Result: Less DNA damage and mutations.

Brenner assumed that CT radiation dose would increase mutations. But when the effects of defensive responses of the body are factored in, mutations would decrease following CT scans, in a manner similar to the drosophila data above.

Do Cancers Increase with Mutations?







Mutations accumulate at the highest rates during the period of growth at young age, when most cell divisions are taking place. Cancers however occur at the lowest rates during young age, for mice and humans. Percentage of patients with cancerous mutations is unchanged from middle age to old age, whereas cancer rates increase drastically at old age.

Cancers do not increase with mutations

There are many more reasons to conclude:

Mutation model of cancer is not valid.

Evidence against the mutation model of cancer

Accumulated mutations in spleen of mice increase at the highest rates from conception to maturity but lymphomas are at the lowest levels during this period (DeGregori, 2013). For humans, children have lowest cancer rates (UK Cancer Research) though they would be accumulating mutations at the highest rates.

Almost everyone has covert cancers, but lifetime risk of being diagnosed with cancer is ~30% (Greaves, 2014)

There are mutagens that are not carcinogens, e.g. Sodium Azide (National Toxicology Program, 1991)

There are carcinogens that are not mutagens, e.g. alcohol (Bagnardi, 2015)

Peto's paradox - cancer incidence does not scale with body size (and lifespan) across species. (Maciak, 2015)

Patients with xeroderma pigmentosa, who have defects in DNA repair that greatly increase sensitivity to the sun and various mutagens, have elevated rates of skin cancer but normal rates of other cancers, despite the presence of the DNA repair defect in all cells (Cairns, 1981)

Normal cells transplanted into heterologous tissues resulted in tumors (Furth, 1947) and tumor cells transplanted into normal tissue reverted to normal tissue (Illmensee, 1976)

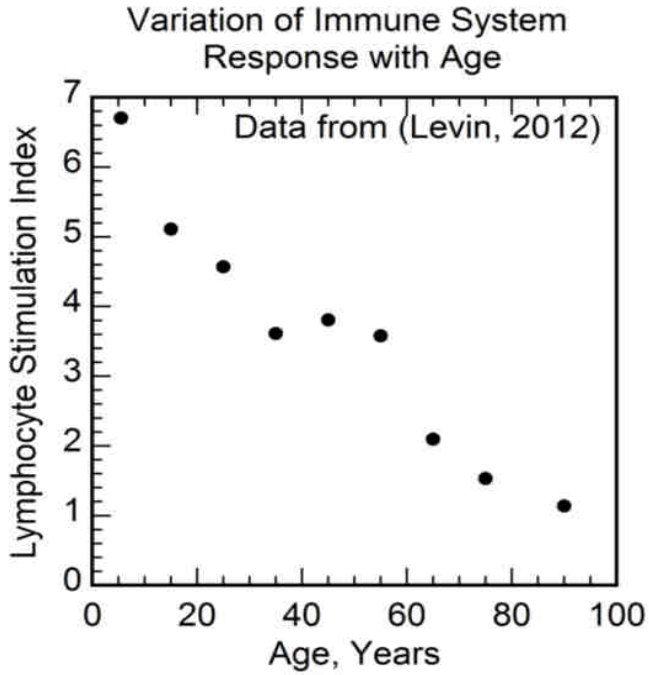
Spontaneous regression of tumor observed for several cancers (Haas, 1988)

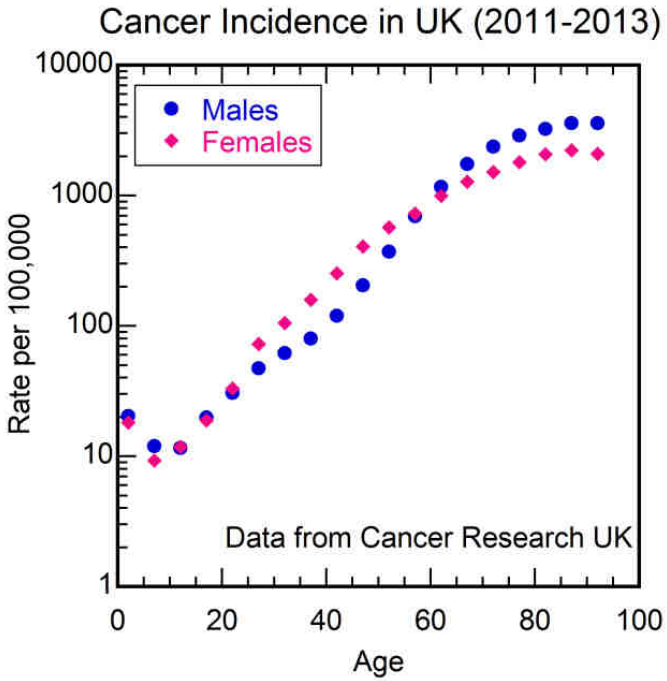
Brenner utilized mutation model of cancer, to infer that DNA damage from CT scans causes cancer. BEIR VII report used mutation model of cancer to infer low-dose radiation increases cancer risk.

What causes cancer?

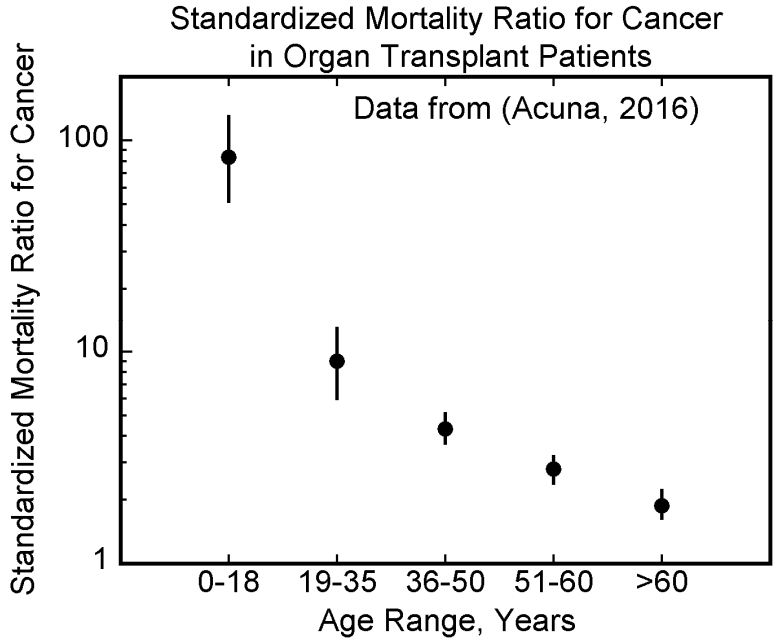
Mutations result in cancer cells. This is not cancer, since, the immune system eliminates the cancer cells or keeps them under control resulting in covert cancer (Koebel, 2007)

When the immune system is suppressed (due to aging, e.g.) covert cancers grow uncontrollably, causing cancer.





Cancer Risk when Immune System is Suppressed



The tremendous increase in cancers when the immune system is suppressed indicates immune suppression may be the primary cause of most cancers. Hence, an alternative model of cancer is the Immune Suppression Model of Cancer.

See: "Changing the Paradigm of Cancer Screening, Prevention, and Treatment", Dose-Response, (Doss, 2016)

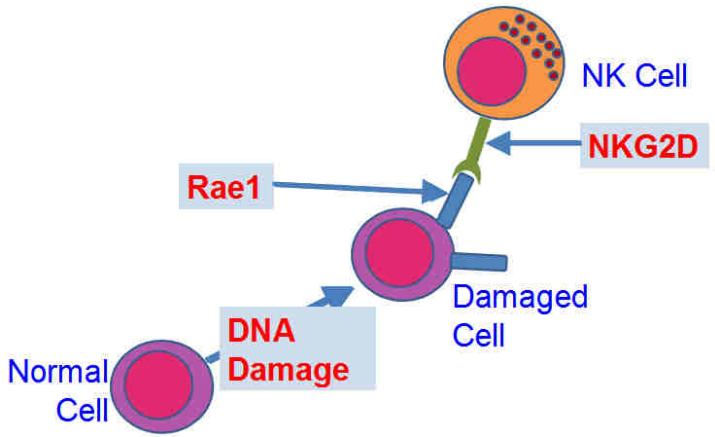
Brenner/Hall and BEIR VII report did not recognize the importance of the immune system in preventing cancers but used mutation model of cancer.

Evidence supporting immune suppression model of cancer

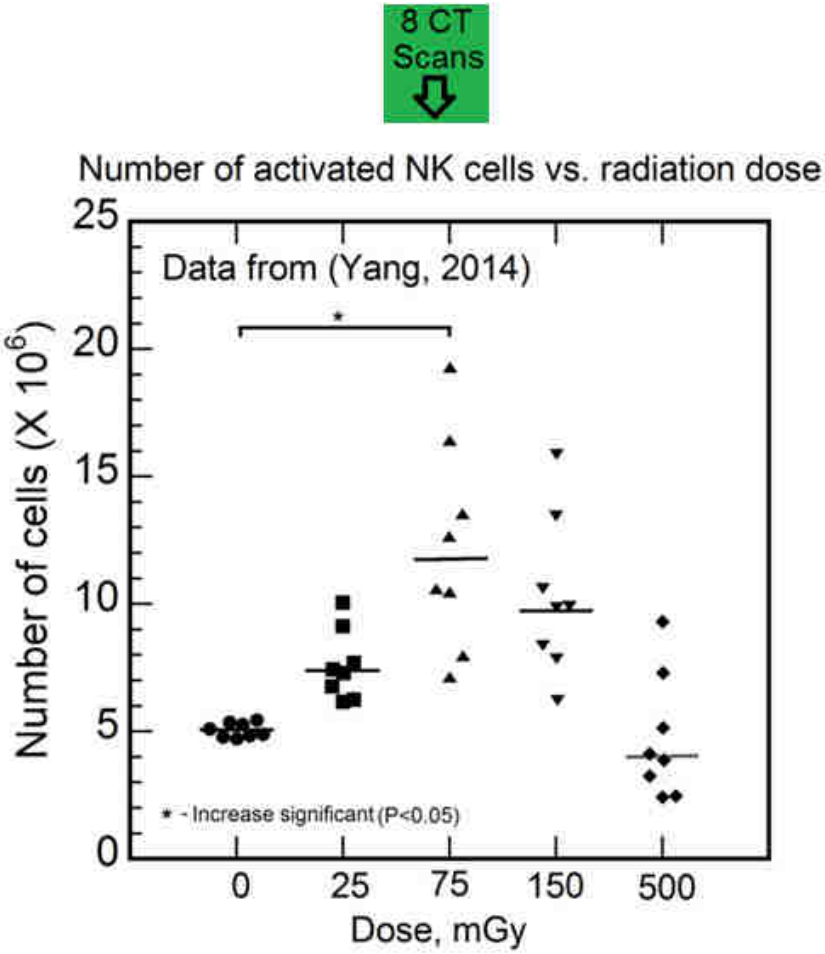
Organ transplant, HIV/AIDS patients have their immune systems suppressed and they have a much higher risk of cancers (Oliveira Cobucci, 2012)
Children have the strongest immune system , and aging reduces immune system response (Levin, 2012). Children have the lowest cancer risk and aging increases cancer risk drastically (UK Cancer Research)
Females have stronger immune system than males (Furman, 2014) and have lower risk of cancer compared to males (Siegel, 2015)
Allergy sufferers have overactive immune system and have lower risk of cancer (Wang, 2005)
Breastfeeding (Turfkruyer, 2015) and daycare attendance (Urayama, 2010) enhance immune system in infants and it reduces childhood leukemias (Amitay, 2015),
Exercise (Woods, 2009), infections (Karbach, 2012), and low-dose radiation (Yang, 2014) stimulate the immune system & reduce cancers (Orsini, 2008), (Richardson,1999), (Doss,2015)
High-dose radiation (Liu, 2003), cigarettes (Stämpfli, 2009), and alcohol (Molina, 2010) suppress the immune system and they all increase cancer risk (Ozasa, 2012), (Stämpfli, 2009), (Nelson, 2013)
Immune system is a major determinant in regulating the abscopal effect, the occasional spontaneous regression of untreated tumor following radiation therapy (Grass, 2016), (Ng,2016)

What is the effect of low-dose radiation on the immune system?

The DNA Damage Response Arouses the Immune System (Gasser and Raulet, 2006)

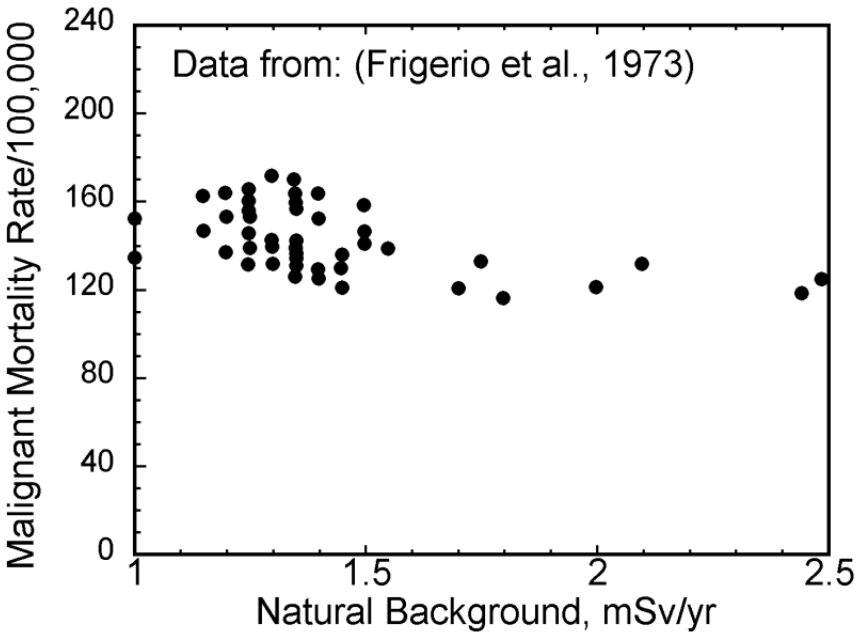


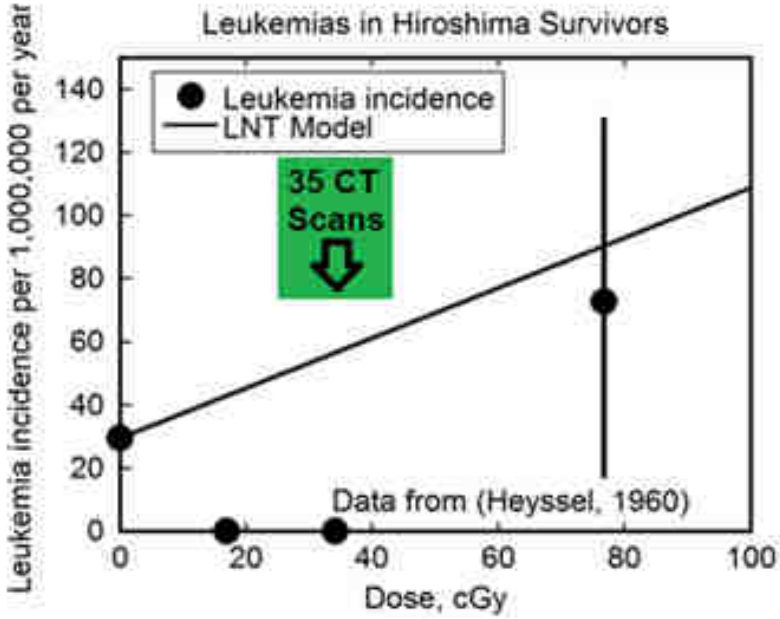
Up-regulation of Rae1 and other ligands of the NKG2D receptor. Activates NK cells.



Low-dose radiation enhances the immune system. Based on the immune suppression model of cancer, low-dose radiation would reduce cancer risk (radiation hormesis).

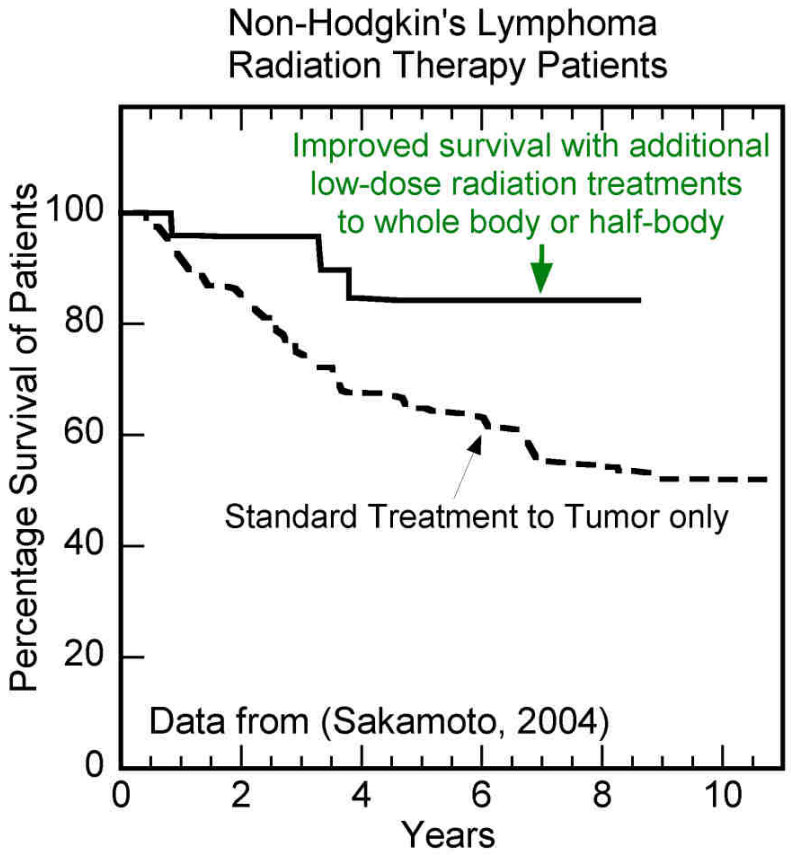
Early Hints of Evidence Against the LNT Model and/or for Radiation Hormesis





Such data were ignored by Brenner and BEIR VII Report

Effect of Repeated Low-dose Radiation Treatments in Radiation Therapy Patients



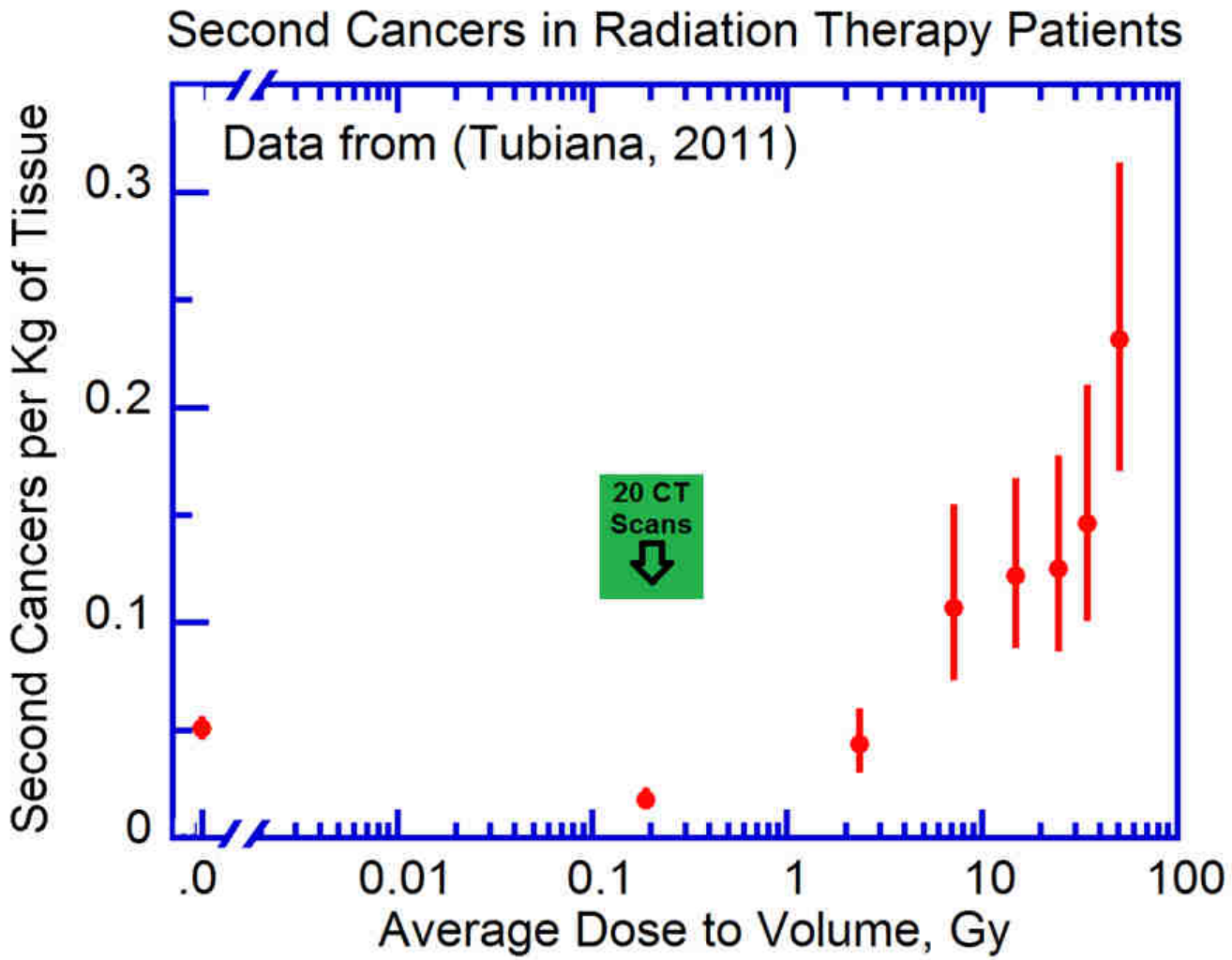
Low-dose radiation treatments:

10 cGy X 15 over 5 weeks

10 CT Scans

Brenner, BEIR VII, etc.
ignored these data

Low-dose radiation treatments had a cancer therapeutic effect contradicting the LNT model.



Brenner, BEIR VIII Scoping Meeting, etc. ignored these data

Second cancers per kg of tissue were lower for body regions having 0.2 Gy dose in comparison to body regions having no radiation dose, contradicting the LNT model.

Effect of low-dose radiation exposures on cancer

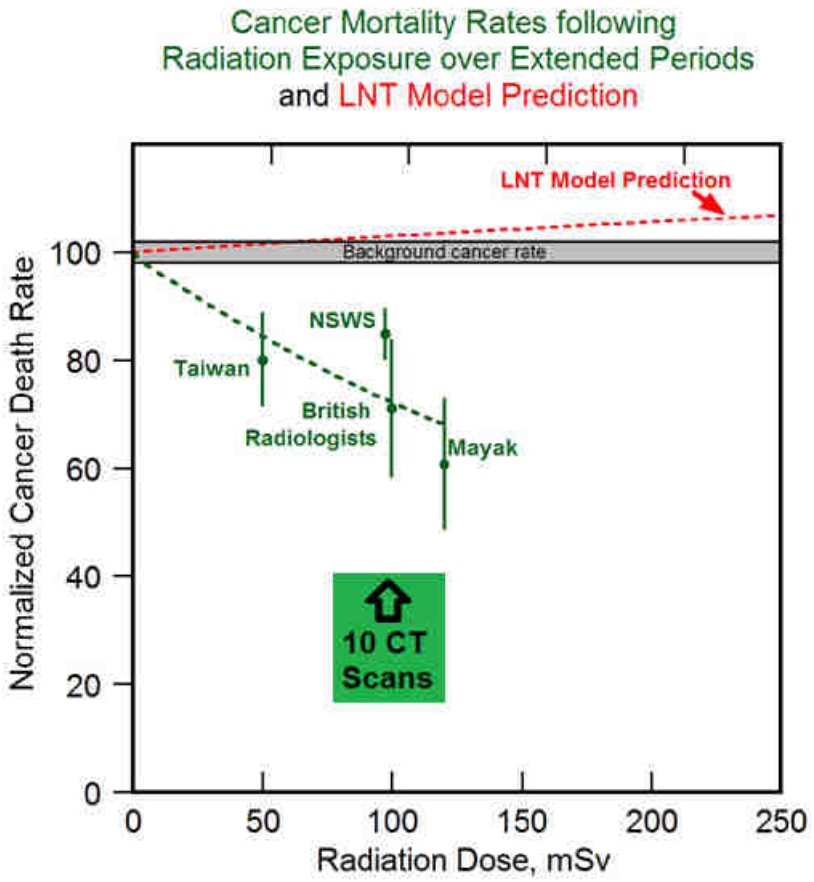


Figure legend:

LNT model Prediction – Using BEIR VII Report (NRC, 2006)

Taiwan - Residents of radio-contaminated apartments in Taiwan (Hwang, 2006)

NSWS - Radiation workers in Nuclear Shipyard Worker Study (Sponsler, 2005)

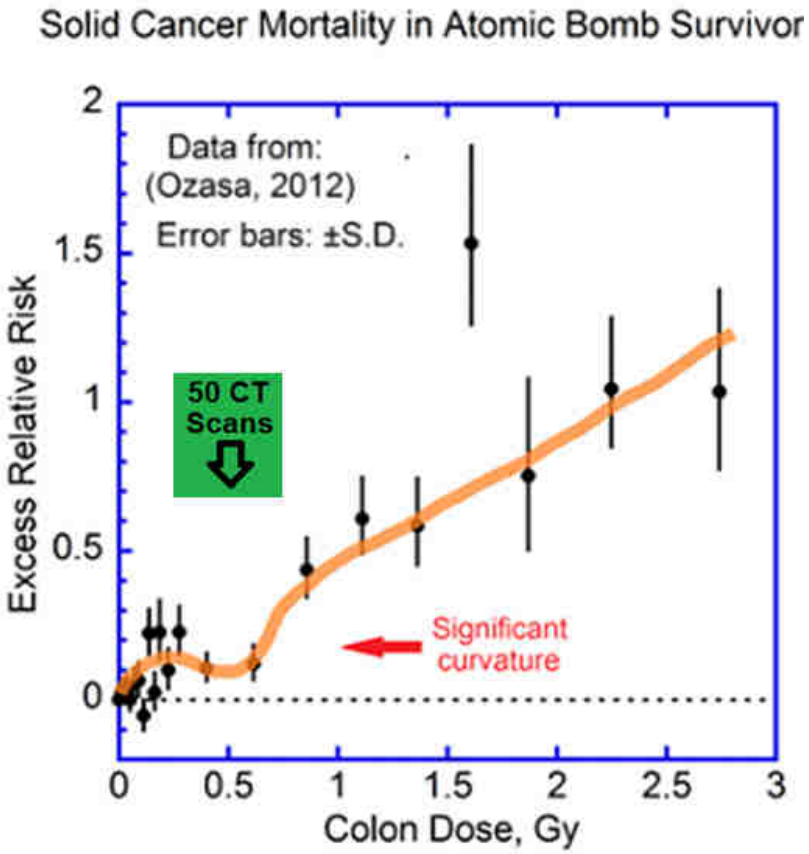
British Radiologists - British Radiologists who entered service during the period 1955-1979 (Berrington, 2001)

Mayak - Evacuated residents of villages near Mayak Nulcear Weapons Facility (Kostyuchenko, 1994)

Brenner, BEIR VII/BEIR VIII Scoping Meeting, etc. ignored these data

Low-dose radiation exposures have resulted in reducing cancers contradicting the LNT model prediction

Atomic Bomb Survivor Data are Inconsistent with the LNT Model

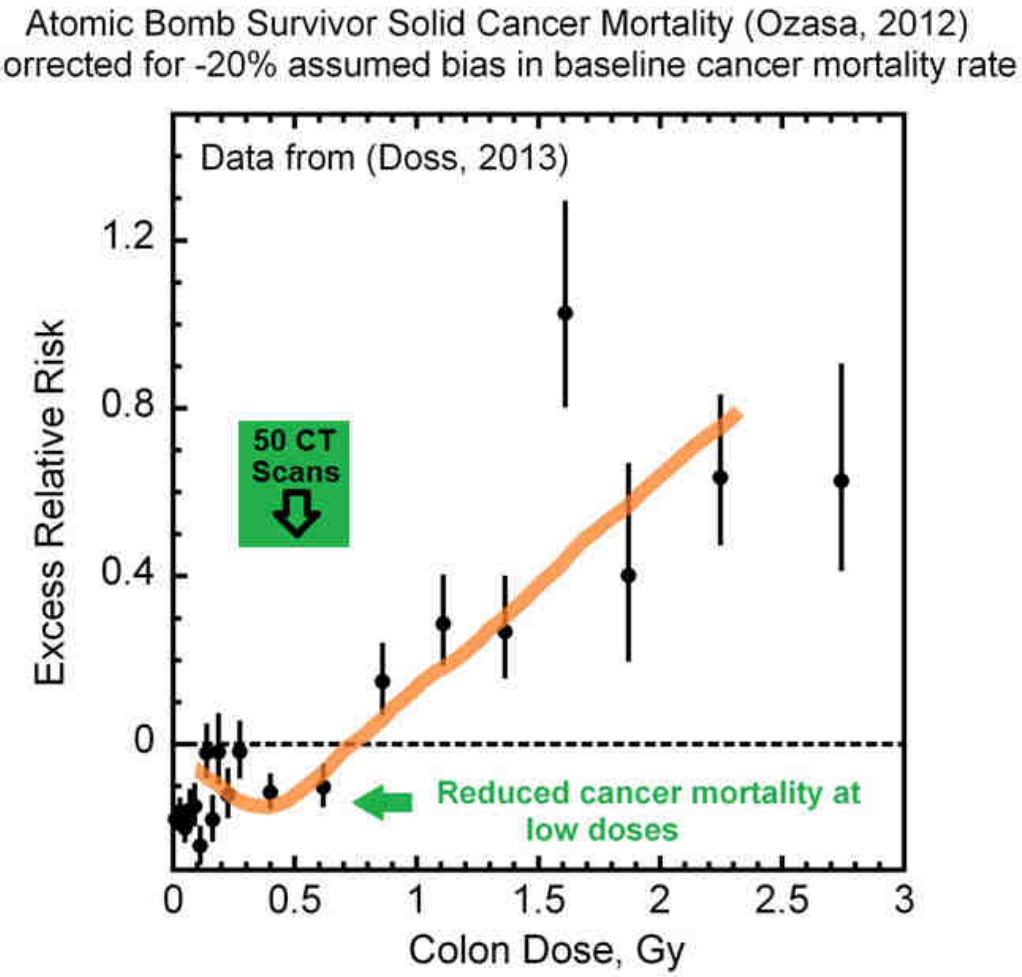


LNT model was assumed in the analysis of the data to extract the Excess Relative Risks.

As radiation dose increases from 0.25 Gy to 0.5 Gy, cancers decrease, results in significant curvature in dose-response relationship, contradicting the LNT model.

Atomic bomb survivor data, universally acknowledged to be the most important data to assess the health effects of radiation, no longer support the LNT model.

Evidence for Radiation Hormesis in Atomic Bomb Survivor Data

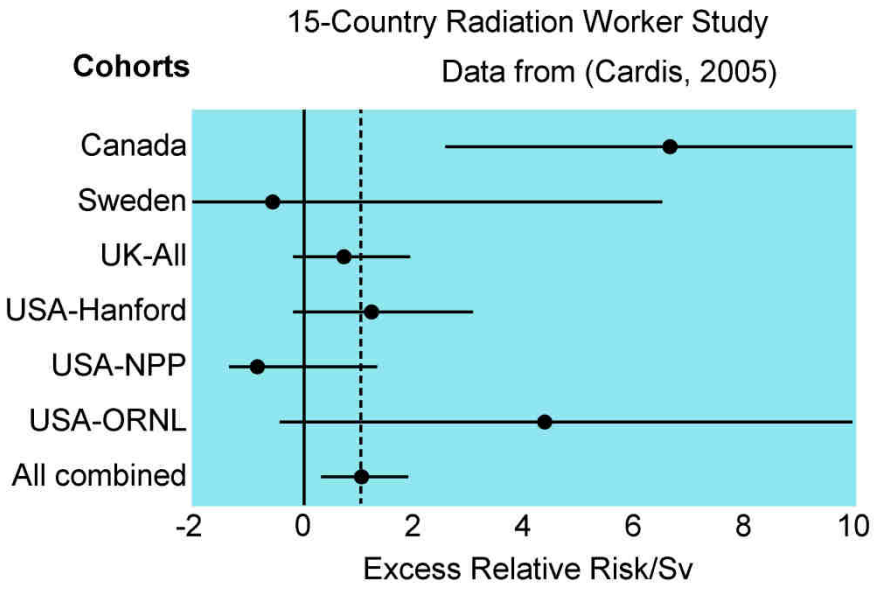


The shape of dose-response curve, with the correction for the likely bias in the baseline cancer rate, is consistent with the concept of radiation hormesis.

In atomic bomb survivor data, low radiation doses reduced cancers.

15-Country Study of Radiation Workers

(Cardis, 2005)



It is clear the Canadian data are inconsistent with most other data.

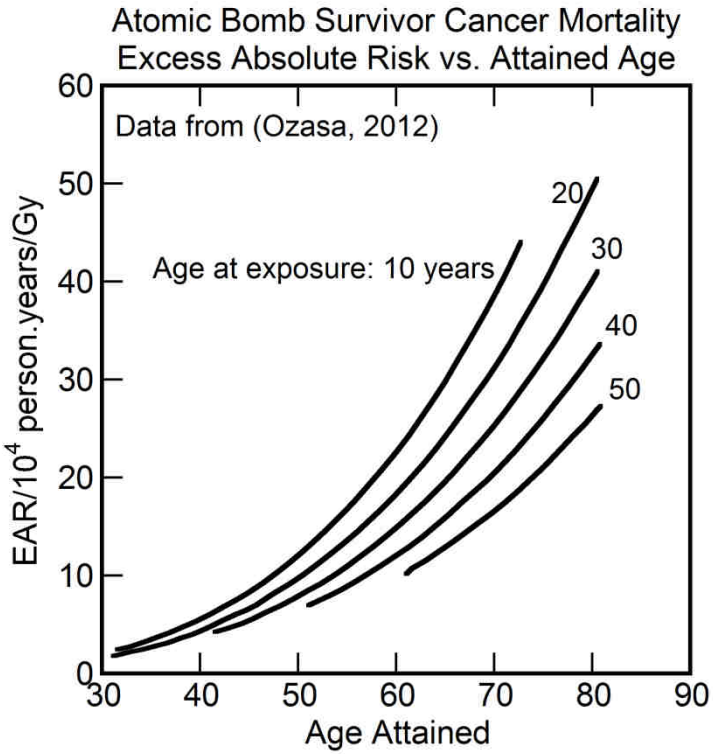
Instead of asking for a re-evaluation of Canadian data, BEIR VII Report utilized the radiation risk coefficients from the study to support claims of low-dose radiation carcinogenicity.

In 2011, CNSC withdrew Canadian data because of faults identified in them, negating the conclusion of the 15-Country Study.

Brenner quoted these data to support cancer risk from CT scans

Are children more radio-sensitive?

Data generally shown to claim higher radio-sensitivity of children



However, excess cancers are observed for high-dose radiation exposures only in atomic bomb survivors.

Only by LNT model extrapolation, these graphs are extended to low-doses.

But since, cancer rates reduced at low doses in atomic bomb survivors, extension of the graph to low doses is not valid.

Higher sensitivity of children to radiation-induced cancers is for high-dose radiation only. This cannot be extrapolated to low-doses as the LNT model is not valid.

Are children more radio-sensitive?

Other arguments used to raise concerns regarding low-dose radiation exposures in children:

Children

- have higher proportion of dividing cells,
- more susceptible to mutations due to radiation.

This argument ignores defenses triggered by low-dose radiation.

Low-dose radiation → enhances antioxidants, DNA repair enzymes,…

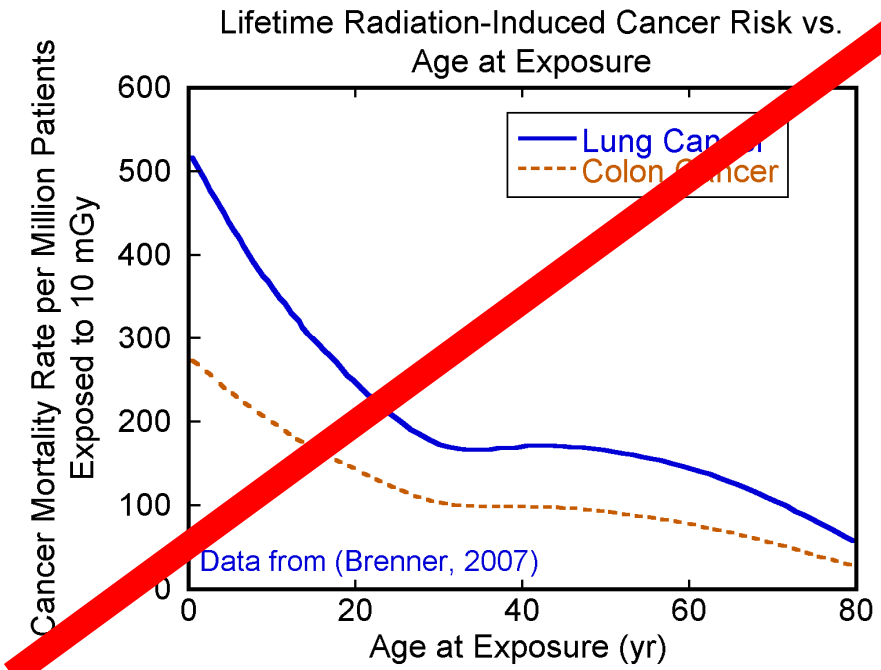
- reduces overall mutations
- enhances the immune system
    - would reduce cancers

There should be no concerns regarding low-dose radiation exposures to children, e.g. from CT scans

Computed tomography - an increasing source of radiation exposure (Brenner and Hall, NEJM, 2007)

(Over 6000 citations in Google Scholar to date)

- X-rays → Free radicals → DNA damage and mutations → Cancer
- Atomic bomb survivor data, cohort with mean dose of 40 mSv → increased cancer risk (Pierce, 2000) (Preston, 2003 and Preston, 2007)
- 15-Country Radiation Worker study (Cardis, 2005) → mean dose 20 mSv → increased cancer risk.



Conclusions:

Direct evidence from epidemiologic studies that the organ doses corresponding to a few CT scans resulted in an increased risk of cancer.

•The evidence is reasonably convincing for adults and very convincing for children.

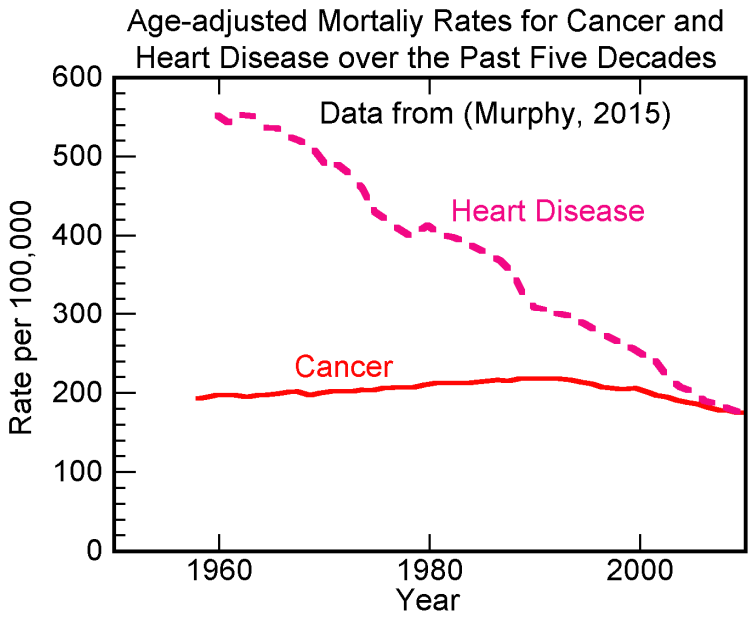
•1.5-2% of cancers attributable to CT scans

BEIR VII Report used same arguments.

Publications claiming cancer risk from low-dose radiation

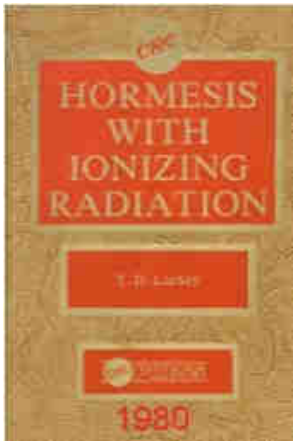
Study	Criticism
(Leuraud, 2015), (Richardson, 2015) – INWORKS studies	(Doss, 2015), (Sacks, 2016): Ignored medical radiation dose, which was small compared to occupational dose in early years but was much higher in later years. Used 90% CIs.
(Kendall, 2013) Childhood Leukemias vs. Natural Background Radiation	(Doss, 2014), (Sacks, 2016): Data are of marginal significance. All cancers RR=1.03 (1.00-1.07 95%CI). Did not consider confounding by breastfeeding & daycare attendance, which result in 20% and 30% cancer reduction respectively.
(Pearce, 2012) (Mathews, 2013) Cancers following childhood CT scans	(Cohen, 2013), (Walsh, 2014), (Boice, 2015), (Sacks, 2016): Potential for Reverse causation; data not consistent with present knowledge on radiation-induced cancers, not consistent with A-bomb survivor data.
(Hwang, 2008) Taiwan apartment residents	One cancer type had higher incidence (90% CI), quite likely due to chance. (Doss,2013): Reduction of all cancers (95% CI).
(Schonfeld, 2013) Techa River solid cancer mortality	Statistics not sufficient to determine dose-response shape; LNT model was used for analysis. (Jargin, 2014): Possible medical examination bias in higher dose population.
(Krewski, 2006), (Darby, 2005) Radon lung cancer	(Fornalski, 2011) : Bayesian analysis of 28 studies shows no dose-dependence can be determined.

The Effect of the LNT Model on the War on Cancer

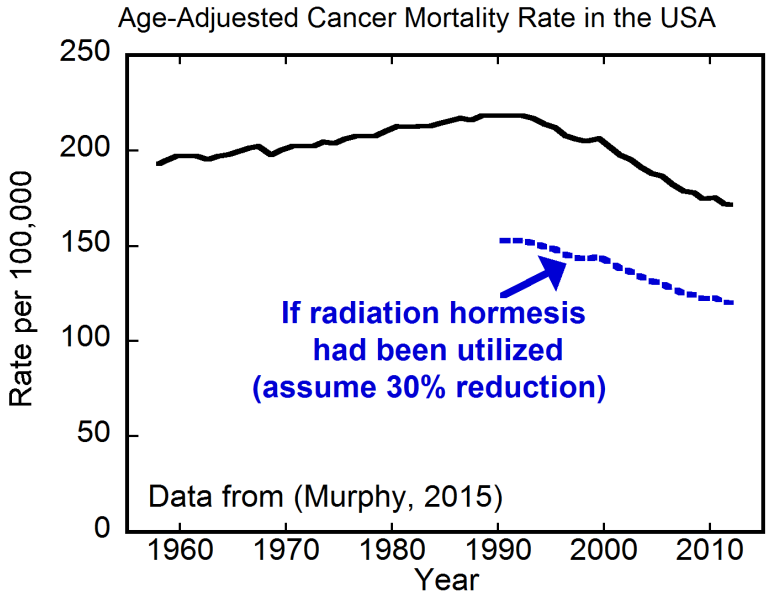


(Thun, 2006)

"without reductions in smoking, there would have been virtually no reduction in overall cancer mortality in either men or women since the early 1990s".



LNT Model blocked study of radiation hormesis in the 1980s when it was proposed as a method of reducing cancers (Hormesis with Ionizing Radiation, TD Luckey, 1980).



Abandoning the LNT model in the 1980s would have led to much greater progress in the war on cancer.

Impact of the LNT Model on Public Health (Summary)

- Dose reduction efforts in Diagnostic Imaging – no reduction in cancer risk to patients but harm due to non-diagnostic images
- CT scans not being performed due to patient/parent concerns or physician concerns – harm to patients due to missed diagnoses or misdiagnoses
- Fukushima – Over 1000 deaths caused by evacuation and no reduction of cancer risk
- Nuclear Power – More hazardous choices being made for power generation – more fatalities
- Excessive shielding and other costs – Life-saving devices become not affordable
- Dollars per life saved – Too high with LNT model related efforts. Money better spent on other, more cost effective endeavors, for more lives saved.
- War on cancer – Millions of preventable cancer deaths per yr.

Who is responsible for the immense harm caused by the LNT model?

- Advisory bodies (NAS, ICRP, NCRP, UNSCEAR, WHO, IAEA, etc.)
- Influential Scientists (Brenner, Hall, etc.)
  - Lack of due diligence, ignoring data supporting radiation hormesis, accepting poor quality data supporting the LNT model
- EPA Staff policy: "effects that appear to be adaptive, non-adverse, or beneficial may not be mentioned" from (EPA, 2004) "*An examination of EPA risk assessment principles and practices*"
  - Unhealthy attitude of regulators towards public health
- Regulatory Agencies (EPA, NRC, FDA, CNSC, etc.)
- Professional Organizations (AAPM, HPS, ACR, ABR, JC, etc.)
  - Blind acceptance of advisory body recommendations regarding the LNT model without challenging them
- Popular media with their appetite for sensational stories
  - Give plenty of free publicity to articles claiming increased cancers from low levels of radiation
  - Provide little coverage of publications showing no increased cancer risk from low levels of radiation or radiation hormesis

Dilemma: What is the Correct Course to Follow Now?

Continue with the Status Quo? (Use of the LNT model)

- Based on the arguments and evidence presented, our actions would contribute to tremendous waste of public funds for no health benefit but harm to the public.
- It is ethically wrong. Would violates AAPM Code of Ethics: "Members shall place primary importance on the welfare of patients and only participate in patient care activities that are in the best interest of the patient."
- Truth will ultimately come out. The longer we wait to correct our course, the worse we will look.

Change to a new paradigm recognizing radiation hormesis?

- Most of the scientists and the public would not be aware of the current state of knowledge and so would not support it
- Need a major education campaign, with little resources
- Advisory bodies have proven to be agents of status quo
- Most professional organizations would not change without advisory bodies' recommendations

AAPM Position Statement on Radiation Risks from Medical Imaging Procedures (March 2017)

Some excerpts from the Statement & Comments on them in ()

- should use the lowest radiation dose necessary to accomplish the clinical task. (Advocates ALARA though no benefit but only harm from reducing dose)
- there is no convincing epidemiological evidence of increased cancer incidence or mortality from low radiation doses (< 100 mSv). (Does not mention the observed reduction of cancer mortality for low radiation doses)
- anticipated benefits outweigh any small potential risks. (Ignores radiation hormesis)
- AAPM discourages describing potential risks associated with medical imaging (Ignores radiation hormesis)
- improve medical imaging by optimizing radiation doses (Advocates ALARA though no benefit but only harm from reducing dose)

Path Forward – Suggestions for AAPM actions

- Challenge advisory bodies which continue to support present approach to radiation safety based on the LNT model (through debates, etc.)
- Revise the Position Statement on radiation risks quoting the arguments and the vast evidence supporting radiation hormesis and the invalidity of the arguments and evidence supporting the LNT model.
- Discontinue all campaigns for ALARA and dose reduction in diagnostic imaging as there is no benefit but only potential harm from dose reduction at these low doses.
- Recognize the importance of radiation hormesis for preventing diseases, and encourage its study and use.

Summary and Conclusions

- LNT model is justified based on the concepts: even a small amount of radiation increases mutations, and mutations cause cancer
- Concepts justifying the LNT model are not valid. Suppression of the immune system is the primary cause of cancer. Low-dose radiation boosts the immune system, and so would reduce cancers (radiation hormesis)
- Plenty of evidence for radiation hormesis and against the LNT model, including the Atomic Bomb Survivor Data
- Publications supporting the LNT model have major flaws
- Many major adverse consequences from the use of the LNT model: in diagnostic imaging, nuclear power, cancer, etc.
- Reason for these adverse consequences – Advisory bodies, regulatory agencies, professional organizations, scientists because of their lack of due diligence, ignoring of evidence for radiation hormesis, acceptance of poor quality data
- Action needed by professional organizations like AAPM: Challenge advisory bodies on the LNT model in view of contradictory evidence, discontinue dose reduction efforts in diagnostic imaging, recognize radiation hormesis and recommend its study and use.