Problems with the Linear No-Threshold Model and Reasons Why It Should Not be Used for Radiation Protection

Conference Paper · October 2016

CITATIONS
0

READS
242

1 author:

Mohan Doss
Fox Chase Cancer Center

SEE PROFILE
Problems with the Linear No-Threshold Model and Reasons Why It Should Not be Used for Radiation Protection

Mohan Doss, PhD, MCCPM
Medical Physicist, Diagnostic Imaging,
Fox Chase Cancer Center, Philadelphia, PA
E-mail: mohan.doss@fccc.edu

Revised Version of Presentation at the
62nd Annual Meeting of the Radiation Research Society
at Waikoloa, HI on October 17, 2016 in the Symposium:
The Linear No Threshold Model for Radiation Protection:
A Flawed Concept or Practical Reality?

Copyright © 2016 by Mohan Doss

Version 1.1 Rev

Disclaimer: Opinions expressed in this presentation are my own professional opinion, and do not necessarily represent those of my employer.
The Linear No Threshold Model for Radiation Protection: A Flawed Concept or Practical Reality?

• The above question raised by this symposium is an important one. If the wrong answer is used, it can have devastating consequences for the public.

• If it turns out we have been using the wrong answer during the past several decades, it is important to correct the error promptly, though it would be difficult.

I have no conflicts of interest to declare
How to resolve controversy regarding the cancer risk of low-dose radiation: LNT model vs. Hormesis?

• Both cannot be correct, but there are publications supporting both sides
• Publications on the wrong side would have major flaws in their reasoning and evidence, resulting in their wrong conclusion. Also, they would not consider publications supporting the other (correct) side
• When publications on one side predominantly get discredited because of faulty data, analysis, and/or interpretation, the other side gains more credibility and the controversy is resolved.
• Who should resolve the controversy? Ideally, advisory bodies such as National Academy of Sciences.
National Academy of Sciences did examine the evidence and produce the BEIR VII Report in 2006, and discussed new evidence in the BEIR VIII Scoping meeting in November 2014.

The BEIR VII Report dismissed radiation hormesis thus:

“Evidence for hormetic effects was reviewed ..................

“the preponderance of available experimental information does not support the contention that low levels of ionizing radiation have a beneficial effect. The mechanism of any such possible effect remains obscure.”

On the other hand, BIR VII Report concluded that the evidence is consistent with the LNT model.

CONCLUSION

The committee concludes that the current scientific evidence is consistent with the hypothesis that there is a linear, no-threshold dose-response relationship between exposure to ionizing radiation and the development of cancer in humans.
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?

**DNA Double-strand breaks in blood measured a short time after CT scans**

**Explanation for the data:**

Low-dose radiation (LDR) generates free radicals and causes DNA damage, which increase linearly without any threshold.

Appears to support the LNT model.

However, this is not the complete picture, as it does not include the effects of the defensive responses to the radiation dose. For this, one needs to examine mutations after an extended period, not immediately after the irradiation.
Do mutations increase with radiation dose at low doses?

Why does the mutation frequency go down with 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.

Immature sperm were irradiated at a dose rate of 0.05 Gy/min, and the frequency of sex-linked recessive lethal mutation was measured in the F2 generation.

LNT model supporting publications dismiss the importance of the biological defenses. How important are the biological defenses?
Increased DNA Damage Observed Shortly After Five Minutes of Vigorous Exercise or Low-dose Radiation Exposure

**DNA Damage from Five Minutes of Exercise**

*Significant increase compared to Rest (P < 0.05)*

Even five minutes of vigorous exercise resulted in increased DNA damage.

Vigorous exercise reduces cancer mortality significantly. The benefit from exercise is due to the enhanced defenses.

Since vigorous exercise reduces cancers, it would be extremely unwise to not exercise based on the observed DNA damage from vigorous exercise. **BEIR VII Report has used similar logic to raise concerns about the DNA damage from low-dose radiation and has dismissed the beneficial effects of enhanced defenses.**
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 do not increase with mutations but occur at the lowest rates during young age and do not increase when the accumulated mutations increase.

**Cancers do not increase with mutations**

Somatic mutation model of cancer is not valid.
Additional evidence against the mutation model of cancer

<table>
<thead>
<tr>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almost everyone has covert cancers, but lifetime risk of being diagnosed with cancer is ~30% (Greaves, 2014).</td>
</tr>
<tr>
<td>There is a heavy burden of mutations in normal skin cells at a level similar to that seen in many cancers, but the subjects do not have skin cancer (Martincorena, 2015)</td>
</tr>
<tr>
<td>Peto’s paradox - cancer incidence does not scale with body size (and lifespan) across species. (Maciak, 2015)</td>
</tr>
<tr>
<td>Normal cells transplanted into heterologous tissues resulted in tumors (Furth, 1947) and tumor cells transplanted into normal tissue reverted to normal tissue (Illmensee, 1976)</td>
</tr>
<tr>
<td>Spontaneous regression of tumor observed for several cancers (Haas, 1988)</td>
</tr>
</tbody>
</table>
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.
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.
Additional Evidence supporting the immune suppression model of cancer

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 enhances immune system in infants (Turfkruyer, 2015) and it reduces childhood leukemias (Amitay, 2015)

Exercise (Woods, 2009) and infections (Karbach, 2012) stimulate the immune system and reduce cancers (Orsini, 2008), (Richardson, 1999)

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)
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.

LNT model supporting publications (e.g. BEIR VII Report) ignore or dismiss the importance of the immune system in preventing cancers and the enhancement of the immune system from low-dose radiation.

The enhanced immune system response would reduce cancers.
Early Hints of Evidence Against the LNT Model and/or for Radiation Hormesis

All the data show decrease in cancers or no increase in cancers at low radiation doses contradicting the LNT model and consistent with radiation hormesis.
Repeated whole-body low-dose radiation treatments (10 cGy X 15 over 5 weeks) had a cancer therapeutic effect, performing as well as chemotherapy, contradicting the LNT model.

BEIR Reports ignored such evidence. But it did discuss the 15-country study of radiation workers in an addendum to the report after the report was completed. Therefore, it must be an important study. Let us examine how good the study is.
Canadian data are clearly inconsistent with most other data. Even a graduate student would recognize this.

Instead of asking for 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.

BEIR VII Report lacked good judgment in utilizing the 15-Country Study

BEIR VII Report dismissed the observed reduction of overall cancers in such studies in comparison to general population as being due to Healthy Worker Effect.
Effect of prolonged low-dose radiation exposures on cancer

Taiwan - Residents of radio-contaminated apartments in Taiwan (Hwang, 2006)
NSWS - Radiation workers in Nuclear Shipyard Worker Study (Sponsler, 2005) This study excluded the possibility of Healthy Worker Effect since the comparison is to non-radiation workers.
British Radiologists - British Radiologists who entered service during the period 1955-1979 (Berrington, 2001) (Healthy Worker Effect cannot be used to explain the result as the comparison was between radiation and non-radiation workers.)
Mayak - Evacuated residents of villages near Mayak Nuclear Weapons Facility (Kostyuchenko, 1994)

Note: This cohort is different from the Techa River cohort.

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

BEIR VII Report ignored British Radiologists and Mayak studies which were available at the time of the report. BEIR VIII Scoping meeting in 2014 ignored results from Taiwan and NSWS studies.
What are the most important data for evaluating the health effects of low-dose radiation?

BEIR VII Report says on p.141:

Because of its many advantages, the LSS cohort of A-bomb survivors serves as the single most important source of data for evaluating risks of low-linear energy transfer radiation at low and moderate doses. This chapter describes (Hall & Brenner, 2008) Cancer risks from diagnostic radiology.

Data from atomic bomb survivors represent the "gold standard" in the quantitative assessment of radiation carcinogenesis risks at low doses. There are several
Shape of Dose-Response in the Atomic Bomb Survivor Cancer Mortality Data

In (Ozasa, 2012), ERR rises with dose from 0 to 0.25 Gy, decreases with dose from 0.25 to 0.5 Gy, and then rises with dose, resulting in a significant curvature. LNT model cannot explain the reduction of cancer risk for doses near 0.5 Gy.

Ozasa et al. state:
“The curvature over the 0-2 Gy range has become stronger over time, ···························, and has become significant with longer observation”

The significant curvature in the dose-response of the atomic bomb survivor cancer mortality data is inconsistent with the LNT model.
Correcting for the negative bias in the baseline cancer rate results in a J-shaped dose-response curve consistent with radiation hormesis. (Doss, 2012), (Doss, 2013)

Since the publication of the (Ozasa, 2012) update, many LNT model supporters, have stopped referring to the atomic bomb survivor data when discussing low-dose radiation cancer risk. BEIR VIII Scoping meeting in Nov 2014 did not acknowledge this major change in the nature of the Atomic Bomb Survivor Data.
(Ozasa, 2012) stated: Zero dose is the best estimate of dose threshold, following a dose-threshold analysis.

The conclusion was challenged in a Comments to the Editor by (Doss, Egleston, Litwin, 2012) pointing out major flaws in their analysis.

– No response to the Comments by Ozasa, et al.

The Atomic Bomb Survivor data do not imply zero threshold dose.
Effect of Low-dose Radiation Treatments on Survival of Radiation Therapy Patients

Interspersed low-dose radiation treatments to the whole body or half body between the standard radiation therapy treatments to the tumor had a cancer therapeutic effect, contradicting the LNT model.

BEIR VIII Scoping Meeting (2014) ignored these and other data showing cancer therapeutic effect of repeated low-dose radiation treatments to the whole body.
Tissues having ~0.2 Gy radiation dose had reduced second cancers per kg of tissue in comparison to tissues having no radiation dose from the radiation therapy, contradicting the LNT model prediction.

Speakers at the BEIR VIII Scoping Meeting (2014) of National Academy of Sciences ignored these data.
Residential Radon and Lung Cancer

Smoking data at County level were not available. State level data were used to estimate County level data based on demographics to correct for smoking. Led to uncertainties.

Cohen study was criticized for incorrect accounting of Smoking (Heath, 2004)

Strong negative correlations found for cancers strongly linked to smoking – indicates likely confounding by smoking (Puskin, 2003)

County level smoking prevalence data are now available, e.g.:
Lung cancer mortality rates are lower in high radon counties in comparison to low radon counties for the same level of smoking.

Therefore, confounding by smoking cannot explain the reduction of lung cancers observed in high radon counties.
Results from Multiple Linear Regression
(using SigmaPlot Version 12.0)

Lung Cancer Rate (males) =
\[-11.448 - 0.0399 \times \text{Radon Level} + 3.711 \times \text{Smoking Prevalence}\]

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Std. Err.</th>
<th>(t)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-11.448</td>
<td>-5.535</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>Radon Level</td>
<td>-0.0399</td>
<td>-12.016</td>
<td>(&lt;0.001)</td>
</tr>
<tr>
<td>Smoking Prevalence</td>
<td>3.711</td>
<td>47.270</td>
<td>(&lt;0.001)</td>
</tr>
</tbody>
</table>

The dependent variable Lung Cancer Rate (males) can be predicted from a linear combination of the independent variables:

\[
P = \text{Constant} + \text{Radon Level} \times -0.0399 + \text{Smoking Prevalence} \times 3.711
\]

All independent variables appear to contribute to predicting Lung Cancer Rate (males) (\(P < 0.05\)).

EPA, BEIR Reports, etc. have exercised poor judgement in attributing the observed reduction of lung cancers in high radon areas to confounding by smoking.
Low-dose radiation exposures in a wide variety of situations resulted in reduction of cancers.
How about publications that claim increased cancer risk from low-dose radiation?
Publications that claim to support the LNT model

- Have major flaws in study design, data, analysis, or interpretation
- Utilize 90% CI to demonstrate increased cancer risk when 95% CI (which they previously used) would show no increased cancer risk
- Use evidence that is of marginal significance and do not consider important confounding factors.
- Have insufficient statistics to distinguish between radiation hormesis and LNT models but calculate radiation risk coefficient using a linear model
- Generally do not discuss other publications that show reduced cancer risk from low-dose radiation.
- Discuss increased cancer risk from a single type of cancer (which could result from chance, considering the lower statistics) while ignoring the overall reduction in cancers.
- Claim low-dose radiation health effects are unknown by ignoring available evidence and utilizing faulty evidence, and/or by combining data from high, low, and very low radiation exposures.
## Publications claiming cancer risk from low-dose radiation

<table>
<thead>
<tr>
<th>Study</th>
<th>Criticism</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Leuraud, 2015), (Richardson, 2015) – INWORKS studies</td>
<td>(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.</td>
</tr>
<tr>
<td>(Kendall, 2013) Childhood Leukemias vs. Natural Background Radiation</td>
<td>(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 &amp; daycare attendance, which result in 20% and 30% cancer reduction respectively.</td>
</tr>
<tr>
<td>(Pearce, 2012) (Mathews, 2013) Cancers following childhood CT scans</td>
<td>(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.</td>
</tr>
<tr>
<td>(Hwang, 2008) Taiwan apartment residents</td>
<td>One cancer type had higher incidence (90% CI), quite likely due to chance. (Doss, 2013): Reduction of all cancers (95% CI).</td>
</tr>
<tr>
<td>(Schonfeld, 2013) Techa River solid cancer mortality</td>
<td>Statistics not sufficient to determine dose-response shape; LNT model was used for analysis. (Jargin, 2014): Possible medical examination bias in higher dose population.</td>
</tr>
<tr>
<td>(Krewski, 2006), (Darby, 2005) Radon lung cancer</td>
<td>(Fornalski, 2011): Bayesian analysis of 28 studies shows no dose-dependence can be determined.</td>
</tr>
</tbody>
</table>
Overall Conclusion

Low-dose radiation can reduce cancers.
Harms from the Use of the LNT Model
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
- Ruining of the local economy, disruption of over 100,000 lives

Maximum dose averted due to evacuation ~70 mSv (UNSCEAR, 2013). Would have reduced cancers. There was no need to evacuate.

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.
Use of the LNT Model is Harmful to Patients in Radiology

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

Patients are being harmed by

• Patients/Parents refusing indicated diagnostic CT scans
• Physicians not prescribing the required CT scans
• Poor quality or non-diagnostic CT scans being performed due to LNT model based low-dose radiation concerns
The Effect of the LNT Model on the War on Cancer

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).

(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”.

Abandoning the LNT model in the 1980s would have led to much greater progress in the war on cancer.
Efforts to Discontinue use of the LNT Model

Group Efforts to eliminate the use of the LNT model

• Scientists for Accurate Radiation Information (SARI) (2013)
  http://radiationeffects.org/
  Mission: To prevent harm due to misinformation regarding radiation.
  SARI Petition to NRC: Discontinue use of the LNT model
  - Petition is being considered by NRC

• XLNT Foundation (2015)
  http://www.x-lnt.org/
  Mission: To educate the public on low-dose radiation health effects
  & campaign to eliminate the use of the LNT model

▲ Mohan Doss is one of the founding members of SARI.
▼ Mohan Doss is the President of the XLNT Foundation.
Summary and Conclusion

- LNT model is not justifiable as it is based on the concepts: even a small amount of radiation increases mutations, and mutations cause cancer
- Somatic mutation model of cancer is not valid, and low-dose radiation does not increase but decreases overall mutations because of the adaptive response of increased defenses
- Suppression of the immune system is the primary cause of cancer
- Low-dose radiation boosts the immune system, and so would reduce cancers
- Plenty of evidence for radiation hormesis and against the LNT model, including the Atomic Bomb Survivor Data and radon-lung cancer data
- Publications supporting the LNT model have major flaws
- Many major adverse consequences from the use of the LNT model

Conclusion: LNT model should not be used for radiation protection