CONTROVERSIAL ISSUES: The linear no-threshold (LNT) debate

There are a number of controversial issues of importance in medical and radiation physics, not the least of which is the validity of the linear no-threshold hypothesis. This was the topic of a debate between Dr. Kenneth Mossman, Dr. Rudi Nussbaum, and Dr. Warren Sinclair at the 1997 Annual Meeting of the AAPM in Milwaukee. The Session was Chaired by Dr. Edward Webster who proposed that each of the presenters be invited to prepare a written version of their talks for publication in *Medical Physics*. At the same time, the Editor was arranging for Dr. John Cameron, Dr. Donald Strom, and Dr. Bernard Cohen to debate this issue, and the closely related issue of the hazards associated with radon in homes, for our Point/Counterpoint series. The following compendium of articles under the general category ''Controversial Issues'' is the result. It is expected that this will be the first of several such issues to be addressed under this title. We hope that readers will find these ''debates'' both informative and enjoyable to read.

POINT/COUNTERPOINT

The LNT model is appropriate for the estimation of risk from low-level (less than 100 mSv/year) radiation, and Low levels of radon in homes should be considered harmful to health

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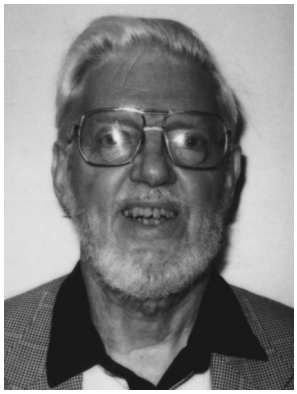
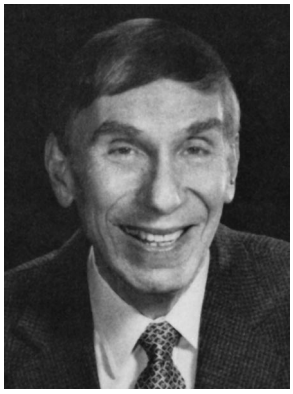
Key words: linear no-threshold hypothesis, LNT, radiation risks, risk estimation, radiation regulations, radon

The linear no-threshold hypothesis is at the heart of radiation risk calculations, standards setting, and regulatory philosophy. If the LNT ''theory'' is correct, then any small amount of radiation constitutes a risk to those exposed. On the other hand, if the ''theory'' is wrong, and risks are much lower than our present regulations are designed to protect against, then we could save considerable time, effort and expense trying to comply with overly restrictive exposure limits. Application of the LNT hypothesis has literally devastated at least one industry in the United States (the nuclear industry) while, at the same time, it has been responsible for spawning others, such as the home radon-proofing industry. It is also responsible for the employment of large numbers of regulators, inspectors and, yes, medical and health physicists. This is clearly an important issue for medical physicists and we are fortunate to have three of the world's foremost experts to debate it in our Point/Counterpoint series.

Arguing FOR both the Motions is Dr. Daniel Strom, Staff Physicist in the Risk Analysis and Health Protection Group at the Pacific Northwest National Laboratory, Richland, Washington. Dr. Strom earned his Ph.D. in Environmental Sciences and Engineering at the University of North Carolina, Chapel Hill in 1983. Among his current research interests are risk analysis, and protection against radon and its progeny. He claims to be in the middle of the spectrum of views on dose-response models.



Arguing AGAINST the motion that the LNT model is appropriate for the estimation of risk from low-level (less than 100 mSv/year) radiation is Professor John Cameron. Dr. Cameron earned his Ph.D. in Nuclear Physics in 1952 at the University of Wisconsin, Madison, where he has spent almost his entire working life and is now Professor Emeritus in the Department of Medical Physics. Also throughout his career, Prof. Cameron has been concerned with protecting people from unnecessary radiation exposure—he ''invented'' the roentgen-area-product concept in order to protect patients, for example. At the same time, however, he has continually expressed concern about over stressing the risks of radiation, which he not only considers stifling to progress (and expensive), but also frightens the general public. He is especially interested in allaying the fears of the public by educating them about radiation and its effects.



Finally, arguing AGAINST the Motion that low levels of radon in homes should be considered harmful to health is Professor Bernard Cohen. Dr. Cohen earned his D.Sc. in Physics in 1950 at the Carnegie Institute of Technology. Since 1958 he has served on the faculty of the University of Pittsburg, where he is Professor of Physics. He is the author of several books, including *A Homeowners Guide to Radon*, as well as numerous publications about radon and radiation. Professor Cohen is considered one of the world's leading experts on the risks associated with radon in homes.

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Argument for both motions

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OPENING STATEMENT

The linear, non-threshold (LNT) dose-response model forms the basis for all USA and international recommendations and regulations for protection of workers and the public from harmful effects of radiation at low doses. It is not used for high-dose (''deterministic'') effects, for which nonlinear, threshold models are well established.

The LNT model states that radiation detriment increases as a linear function of dose, without threshold, when averaged over all ages and both sexes. Detriment is the expectation of harm, which includes loss of life expectancy or quality of life due to fatal and nonfatal cancers and heritable ill-health. These are stochastic effects, that is, their frequency in a population, rather than their severity, is a function of dose.

Radiation protection is a risk management activity. Science is one of many inputs to risk management. There is no practical way to incorporate everything we know as scientists about radiation-induced cancer into risk management. We know that radiation biology is at least a 16-dimensional problem that includes health endpoint, response and projection model, amount of life lost, portion of organism irradiated, background incidence, who's exposed and who's affected, dose, dose rate, dose fractionation, LET (microdosimetry), sex, age at exposure, age at diagnosis, species, subspecies or genetic predisposition, and other effect modifiers (smoking, oxygen, diet, etc.), so using only two of these (dose and response) cannot possibly be correct.

While there are clearly human data that show a response threshold for some cancers (bone cancer from ingested radium, liver cancer from injected thorium, and perhaps lung cancer in nonsmoking miners exposed to radon progeny), there are many others that show no threshold at doses of concern in radiation protection (solid tumors in the Japanese bomb survivors, lung cancer in smoking miners), and one neoplasm, leukemia, for which the dose-response relationship is significantly nonlinear in the Japanese bomb survivors. There is significant reason to believe that the mechanisms of carcinogenesis differ for these diseases.

Valid scientific arguments supporting the LNT model include the following: Tumors are of monoclonal origin; low-dose radiation is a small perturbation in the effect of other carcinogens that have already exceeded most thresholds; miner, bomb survivor, and other human studies for most cancer endpoints are consistent with LNT; heritable ill-health probably follows LNT, bomb survivor data are compatible with LNT projections of heritable ill-health from animal studies. Valid scientific arguments against LNT include the following: some cogent radiation data do not show LNT behavior for some cancer endpoints; no statistically significant heritable ill-health is seen in bomb survivors (although this is consistent with the 2 Sv doubling dose from animal studies). Specious scientific arguments against LNT include the following: ''if you cannot detect a health effect, it does not exist''; ''if you cannot detect a health effect, it is of no concern''; bomb survivor and miner studies are ''high dose'' studies that are inappropriately extrapolated to low doses; oxidative damage is the same for radiation and chemicals; adaptive response occurs; threshold analogies make sense (e.g., {high, medium, low} applied to {fall, wind, impact}); hormesis is important; some chemical carcinogens have thresholds; energy imparted, not dose, is the independent variable.

Valid policy arguments for LNT include the following: it errs on the side of safety (it is ''conservative''); it is a politically acceptable status quo; at present, there is no prospect of direct measurements of effects at doses of interest; a practical system based on LNT has protected workers. Valid policy arguments against LNT include the following: it has led to expensive risk-management decisions; optimization has not worked (the ''R'' in ALARA has been ignored); small lifetime fatal cancer risks may result in insignificant life-shortening. A specious policy argument for LNT is that a threshold system is impractical.

''All models are wrong, and some are useful'' (Box, 1979). Use of the LNT model as a basis for setting standards for radiation protection against stochastic effects at low doses still makes good policy sense. The LNT model should not be used for individual risk predictions (either prospectively or retrospectively) or for priority-setting; for these applications, the detailed, unbiased risk assessments that account for all known variables should be used.

REBUTTAL TO PROFESSOR CAMERON

Cameron invokes the dose-rate dependency of health effects of radiation, a well-established phenomenon. It has long been known that if pairs of microscopic DNA lesions are sufficiently separated either in time or in space, they do not interact; if they occur close enough in time and space, they may interact.[1] This is accounted for in current versions of the LNT model by using a dose and dose rate effectiveness factor (DDREF).

Three recent reviews[2–4] have confirmed that there are thresholds for some kinds of radiation-induced cancer, and one kind of leukemia has never been seen in excess in irradiated populations. This in no way implies that there are thresholds for all kinds of cancer, especially with evidence to the contrary.

REBUTTAL TO PROFESSOR COHEN

Contrary to Cohen's claim, there are good data supporting LNT in the dose regions low enough to be directly applicable

to many important radiation protection problems, including indoor radon. These data are from underground miners,[5,6] indoor case-control studies,[7] and Japanese bomb survivors.[8]

Cohen's free radical argument is irrelevant because oxidative damage by free radicals at single sites is almost completely repaired, whether the free radicals are caused by chemicals or radiation. The damage of concern from radiation is caused by moderate to large clusters of ionization[9] formed at the end of charged particle tracks (the Bragg peak), for which there is no chemical analog. Understanding such damage does not require postulating an impairment of BDM. One-time inductions of adaptive response (''enhancement of BDM'') take significant doses (e.g., 150 mGy), and like a suntan (also an adaptive response) it fades with a half time of days to weeks. I know of no evidence that adaptive response can be maintained indefinitely, or induced by dose rates on the order of 1 mSv per year. It requires no extrapolation from human data (early radiologists) to conclude that repeated doses of 150 mGy to maintain adaptive response would cause deterministic effects and excess cancer.

Finally, the county-radon-lung cancer ecologic study is not a logically compelling design. Conclusions of an ecologic study are good for hypothesis generation, not hypothesis testing. For ''Principles for Evaluating Epidemiologic Data in Regulatory Risk Assessment,''[10] see www.sph.umich.edu/group/eih/UMSCHPS/epidprin.htm.

CONCLUDING REMARKS

In the face of conflicting science, the LNT model continues to be a useful basis for radiation protection. It should not be used for individual risk estimates, but it is useful for setting standards.

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[3]National Council on Radiation Protection and Measurements (NCRP), ''Principles and Application of Collective Dose in Radiation Protection,'' Report No. 121 (NCRP Publications, Bethesda, MD, 1995).

[4]Advisory Committee on Radiological Protection, ''Biological Effects of Low Doses of Radiation at Low Dose Rate,'' ACRP-18 (Atomic Energy Control Board of Canada, Ottawa, Canada, 1996).

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[8]D. A. Pierce, Y. Shimazu, D. L. Preston, M. Vaeth, and K. Mabuchi, ''Studies of the Mortality of Atomic Bomb Survivors. Report 12, Part I. Cancer: 1950–1990,'' Radiat. Res. **146**, 1–27 (1996).

[9]D. T. Goodhead, ''Radiation Tracks in Biological Materials: Initial Damage in Cells, DNA and Associated Structures,'' in *Proceedings of the NCRP No. 13*, edited by M. L. Mendelsohn (NCRP Publications, Bethesda, MD, 1992), pp. 25–37.

[10]Federal Focus, Inc., *Principles for Evaluating Epidemiologic Data in Regulatory Risk Assessment. Developed by an Expert Panel at a Conference in London, England, October 1995* (Federal Focus, Inc., Washington, DC, 1996).

Argument against the motion that the LNT model is appropriate for the estimation of risk from low-level (less than 100 mSv/year) radiation

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OPENING STATEMENT

No! LNT is not appropriate to estimate risks to any population at any dose or dose rate. LNT is an unrealistic theoretical model contradicted by much human and animal data. Unrealistic because it is unusual for a biological response to be linear over even one decade. It would be even more unlikely that it would be linear at or near zero when the body must have natural defenses to survive the 40 million radioactive disintegrations per hour inside the average adult. The LNT assumption is alledgedly based on radiation-induced cancer among the A-bomb survivors which showed an apparent threshold of about 30 cGy, even for leukemia. The dose rate to the A-bomb victims was about a million times greater than that encountered by radiation workers. If the dose had been protracted over a few months or years, the apparent threshold would have been much higher. For example, while A-bomb victims had a high leukemia incidence eight years post exposure, Chernobyl victims with comparable doses spread over weeks or months had no significant increase in leukemia. There is good evidence that the body has a protective mechanism referred to as apoptosis. That is, injured cells are programmed to ''commit suicide'' to protect the organism. Prof. Sohei Kondo[1] calls the low dose rate where all damaged cells are eliminated the apoptosis dose rate. At the higher necrotic dose rate, apoptosis cannot keep up. Tissue repair errors lead to cancer induction. Kondo cites two examples to support his model. Rats exposed to a total of 25 working level (WL) months at rates of 2 WL and 100 WL had markedly different lung cancer incidence.[2] At a rate of 2 WL lung cancer was at the background rate of about 0.5%. At a rate of 25 WL, a necrotic dose rate, lung cancers were about three times the background rate. The skin of mice were irradiated with beta rays to a limited area three times a week for life or until the appearance of skin cancer.[3] At a dose rate of 1.5 Gy/week there was no skin cancer. At a necrotic dose rate of 3 or more Gy/week there was 100% incidence of skin cancer. In humans a similar dramatic effect was seen in radium induced osteogenic sarcomas among the radium dial painters. There was no radium induced bone cancer until the skeletal dose exceeded 10 Gy (200 Sv). From 20 Gy to 500 Gy the incidence of osteogenic sarcomas was essentially constant at $28\pm6\%$. Bond[4] points out that it is inappropriate to predict individual risks from epidemiological data. He feels radiation is a public health problem.

REBUTTAL TO DR. STROM

When scientists argue it indicates a lack of definitive data. I think all of us agree there are no definitive data to show radiation risk at the levels now set for radiation workers and the public. My greatest concern is the use of the LNT model by the news media and others to produce fear. Many science teachers are often unaware of the relatively large amount of radioactivity in their own body—almost 10 000 Bq. Our greatest need is to educate the public about radiation. I suggest that every TV weather map show real time radiation levels in nGy/h for radiation monitoring stations in their area and around the country. The public would see the actual radiation levels near nuclear power plants and far from nuclear power plants in the mountains.

In addition every commercial passenger airplane should have a clearly visible radiation monitor that shows the radiation level continously during flight including its value as the plane flies at high altitude. By this means the public would become familiar with radiation levels and their variation.

The dose from every diagnostic radiology exam should be explained by the RT in terms of the time to get approximately the same dose from background radiation. This can be done by means of a small brochure that gives typical values for common x-ray exams. Medical fluoroscopes should be required to have a dose-area product meter so that these larger doses can also be explained in terms of background radiation.

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Argument against the motion that low levels of radon in homes should be considered harmful

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OPENING STATEMENT

The answer to this question is largely dependent on the validity of the linear no-threshold theory (LNT) of radiation carcinogenesis. There are no *data* supporting LNT in the low dose region; it is based on the following reasoning: Since we believe that even a single particle of radiation hitting a single DNA molecule in a single cell nucleus can initiate a cancer, the number of cancers initiated is proportional to the number of such hits, which is proportional to the dose. It has long been known that there are biological defense mechanisms (BDM) which prevent all but a very tiny fraction of initiating events from developing into a clinical cancer, but it has been tacitly assumed that these BDM are not affected by radiation.

It is now recognized[1] that cancer initiating hits on DNA molecules, indistinguishable from those caused by radiation, occur at a very high rate due to random thermal agitation and chemical attack by free radicals—about 6000 hits per cell each hour, or 50 000 000 per year. Since 1 cGy (1 rad) of radiation causes only about 20 such hits per cell, it is obvious that the latter are inconsequential. How, then, can radiation cause cancer? The only possible answer is that radiation can degrade our BDM. Several biological mechanisms have been proposed to explain this, but none of them give any reason to believe that this degradation is linearly proportional to dose, as required to justify LNT.

On the contrary, there is abundant indisputable evidence that low doses of radiation *enhance* BDM.[2] It has been shown in numerous independent experiments, both *in vitro* and *in vivo*, that low dose pre-exposure substantially reduces the number of chromosome breaks and the number of gene mutations produced by later high dose radiation exposures. It has also been shown that low dose radiation stimulates the activity of the immune system as measured by various indicators. Thus, the theoretical basis for LNT is completely negated, and there is a clear suggestion that low level radiation may actually be protective against cancer.

Experimental data predominantly support the latter viewpoint, or at least the existence of a threshold below which radiation is essentially harmless. Data on luminous watch dial painters[3] who got radium into their bodies by tipping their brushes with their tongues, shows a clear statistically significant threshold behavior. Leukemia among Japanese A-bomb survivors,[4] and breast cancer among Canadian tuberculosis patients[5] exposed by frequent fluoroscopy, both show statistically significant decreases with increasing dose in the low dose region.

But the data most directly relevant to our question are from a compilation of average radon levels in homes for 1729 U.S. counties, well over half of all U.S. counties and comprising about 90% of the total U.S. population. The results[6] show a statistically indisputable tendency for lung cancer rates, with or without correction for smoking prevalence, to *decrease* with increasing radon level; the slope is discrepant with the prediction of LNT by 20 standard deviations! It was shown that ''the ecological fallacy'' and other weaknesses of ecological studies do not apply to this work. Effects of over 60 potential confounding factors were studied, several other tests were applied, and the data and results have been available for two years, but there has been no explanation for this discrepancy other than that LNT fails in the low dose region, grossly over-estimating the cancer risk from low level radiation.

REBUTTAL TO DR. STROM

Strom states that solid tumors in Japanese A-bomb survivors and lung cancer in miners show no threshold at doses of concern in radiation protection, and later states that it is ''specious'' to argue that these ''are high dose studies that are inappropriately extended to low dose.''

The A-bomb survivor data[4] show no statistically significant evidence that there is not a threshold below 25 cSv (25 rem). In fact, using those data, it is easy to show that there is a 30% probability that the risk *decreases* with increasing dose up to 20 cSv. By contrast, EPA and NRC are now squabbling over 0.015 vs 0.025 cSv as a regulatory limit for radiation protection.

If our data showing a strong *decrease* in lung cancer rates for *increasing* radon exposures in U.S. Counties is interpreted directly as risk vs exposure to individuals, there is no statistically significant discrepancy between it and the miner data. This was shown by Ken Kase at the 1997 Milwaukee meeting of AAPM. These data cover a range of radon levels that EPA estimates to be causing over 10 000 deaths per year in the U.S.

I do not understand Strom's statements that it is specious to argue that ''adaptive response occurs'' and that ''hormesis is important.'' There is an indisputable body of evidence, accepted by ICRP and UNSCEAR, supporting adaptive response. There is certainly a great deal of evidence, albeit not conclusive, supporting hormesis; this has been the topic of several large international conferences, at least two books, etc. I see nothing specious about pointing out that adaptive response or hormesis *can* explain why linear no-threshold theory fails.

I take this opportunity to apologize for my misinterpretation of the Billen paper.[1] The ''6000 hits per hour'' are not necessarily cancer initiating events, and there are certainly differences between the damage done by radiation and by chemical attack. The situation is quite complicated, but Billen's paper concludes that ''spontaneous DNA damage

may be many orders of magnitude greater than that caused by low radiation doses.'' Billen now says that the ''*may be*'' was over-conservative and can be modified to ''*according to available evidence, should be*.''

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