Epidemiological Support of the Linear Nonthreshold Model in Radiological Protection: Implications of the National Council on Radiation Protection and Measurements Commentary 27 for the Radiologist

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All models are wrong but some are useful.

—George Box, 1976 [1]

INTRODUCTION

For over 40 years, the linear nonthreshold (LNT) model has been used to manage human radiation exposures, and it has been adopted by radiology communities to include the ACR and other national and international radiology societies, medical physics, and health physics societies and regulatory bodies [2]. Recently, the National Council on Radiation Protection and Measurements (NCRP) reviewed the epidemiological science behind the model and provided a report [3]. This report primarily focuses on cancer effects, and it is one of several national and international periodic reviews of recent scientific evidence on the health effects of ionizing radiation at low doses and low-dose rates, which are pertinent to the radiologist; it is important for the radiologist to understand the strength and weaknesses of these results, issues of ongoing uncertainty, and identified areas for potential further research.

This report states:

> While the ongoing development of science requires a constant reassessment of prior and emerging evidence . . . NCRP concludes that, based on current epidemiologic data, the LNT model (with the steepness of the dose-response slope perhaps reduced by a DDREF [dose and dose-rate effectiveness] factor) should continue to be used for radiation protection purposes. This update is in accord with the judgment by other national and international scientific committees, based on somewhat older data than in this Commentary (e.g., ICRP [International Commission on Radiological Protection], 2007 [4]), that no alternative dose-response relationship appears more pragmatic or prudent for radiation protection purposes than the LNT model.

"Low dose" is defined by the International Commission on Radiological Protection as a qualitative term to mean relatively low level of dose and typically refers to doses lower than 100 mSv (or 100 mGy for low linear energy transfer radiation) based on knowledge of radiation effects. In medical imaging procedures, low dose usually refers to 10 to 100 mSv for adult patients or even lower for children. For the protection of the public from environmental exposure, "low dose" usually refers to a level around natural exposure (ie, a few millisieverts per year). A low-dose rate is defined as <5 mGy per hour.

EPIDEMIOLOGY SUMMARY

Evidence of health effects, principally cancer, from ionizing radiation at high (>1 Sv) and moderate (>100 mSv to 1 Sv) doses in a linear dose effect is well known. There is ongoing controversy about the use of the LNT model to extrapolate the potential risk to low dose because of (1) the limited evidence of health effects at these low doses and dose rates, (2) the variation in radiation biology data (from animal and cellular studies), and (3) the costs of applying said radiation protection policy.

An important challenge of studying health effects at low dose comes from a low signal-to-noise ratio: the likely cancer risk is small against the large background rate of cancer at about 40% lifetime risk in developed countries. The LNT model is an overall protection model based on a summary of available evidence.

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Therefore, the NCRP Commentary reviewed the most recent 10 years of epidemiological studies on solid cancer risk from low-dose radiation as well as leukemia risk from low-dose rates.

There were 29 major epidemiologic studies reviewed and rated by quality criteria. Uncertainties in each study's dosimetry, epidemiologic methods, and statistical approach were evaluated; ratings were provided as strong, moderate, weak to moderate, no support, and inconclusive for support of the LNT model for radiation protection [3]. These studies include the Life Span Study of Japanese atomic bomb survivors, large radiation worker studies, including INWORKS and Chernobyl cleanup workers, cancer risk from radiation accidents, and cancer risk from childhood CT scanning. One complex factor that was reviewed was the dose and dose-rate effectiveness factor, used to convert the relative risk of harm from high- and moderate-exposure dose studies to those at low dose. Most scientific bodies recognize that radiation delivered at low exposures or lower dose rates is likely less effective at producing biological outcomes by about a factor of 1.5 to 2; this commentary agreed that a dose and dose-rate effectiveness factor is probably appropriate but also suggested a need for further research.

After this rating, the expert panel categorized the 29 studies' degree of support for the LNT model as: 5 providing strong support, 6 moderate support, 9 weak to moderate support, 5 no support, and 4 inconclusive. Thus, 20 of 29 studies provided at least some support for the LNT model. Of interest, the experts noted inadequacies in research design, epidemiologic data, and dosimetry, which may have overestimated the effects in the pediatric CT studies.

The commentary concludes that although there was moderate support for the LNT model, it is not proved or disproved, but it is a pragmatic and prudent basis for radiation protection. Furthermore, the NCRP, like other international bodies, conclude that the risk of cancer below 100 mGy is uncertain but small [4].

In a secondary outcome analysis, the report did not find significant noncancer effects at low doses, including cardiovascular disease, cataracts, or thyroid dysfunction (rated either inconsistent or null). However, ongoing research will provide more results.

CONTEXT MATTERS

Current radiology practice allows us to use advanced imaging for lifesaving procedures daily. We must understand when to advise our patients, their families, and our colleagues about which imaging procedures are appropriate, when procedures may not be appropriate, and when imaging protocols may not be optimized for the clinical indication. Continual review of the referral indications and dose management of the protocols is required to provide excellent patient care. With continued growth in CT use (there were a record 91.4 million CTs performed in the United States in 2019), understanding how we use imaging and potential radiation health effects do matter. Recently, Rehani et al described over 2.5 million patients in five large hospitals with 1.3% receiving >100 mSv cumulative effective doses from repeat CT scans in less than 5 years [5]. Some of these patients received this >100 mSv cumulative effective dose within 1 day and 20% were under age 50 years. These moderate doses reach a level at which some may have consequent adverse health effects. Does this matter if we are saving lives? If the imaging is justified and optimized, then no. But we should be aware of the benefit and risk and continue to look at dose management (ie, of repeat imaging studies on the same CT body part).

Newer radiation biology research in animals and epidemiological research in radiation exposed groups include astronauts, radiation therapy patients, environmental exposures and accidents, the Life Span Study, and radiation workers. Emerging research suggests potential radiation effects that include cardiovascular disease, benign thyroid diseases, cognitive effects, immune dysfunction, and changes to the gut microbiome. Each of these areas of research requires a commitment to better understanding of the cellular and molecular mechanisms responsible.

FUTURE RESEARCH NEEDS

The commentary does not deal with integration of radiation biology and radiation epidemiology for which a focus of ongoing research is needed; however, the NCRP does have other scientific committees dedicated to that important goal [6]. Needs include more biobanking of tissue samples and the development of biomarkers of radiation risk linked with epidemiological studies. The commentary also identifies the potential for research on stray radiation in patient dosimetry records from radiation therapy. More than 80% of children and 70% of adults now survive their initial cancer treatment, with the majority receiving radiation therapy. Until such patient dose registries, including stray radiation doses, are created, we will continue to rely heavily on the Japanese Life Span Study studies and other high-quality, low-dose epidemiology studies.

CONCLUSIONS

This most recent comprehensive review of the strengths and weaknesses

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of the major epidemiology studies concludes that the LNT model remains pragmatic and prudent for radiological protection purposes. It does not support a threshold model for solid cancers at this time.

How we interpret and set policies based on evidence behind the LNT model is as important as, if not more important than, the decision to support this model. These policies are adopted and adapted at the regional, national, and local levels based on the resources, socioeconomic needs, and ethical values of our communities [6].

Radiologists should understand the strengths and weaknesses of the LNT model and why we use it for setting policy in radiation exposure for our patients, radiation workers, and the public. As George Box notes [1], there is no perfect model but some that are more useful than others.

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