Threshold model of radiogenic cancer

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The linear no-threshold model of radiogenic cancer is false. Because it fails empirically against superior empiricism, it becomes misinformation and opinion, not knowledge, but it is still advocated because it lends contentment to believers. We can no longer tolerate the universal application of LNT misinformation when, as people of science, we are about helping, not harming, humanity. By Charles W. Pennington and Jeffry A. Siegel

A debate within radiation protection science has been building over many years regarding whether low-dose ionising radiation (LDIR) in the range of 0-200mGy is known to be a carcinogen [1]. The time is ripe to assess what is known and how it is known, to determine where truth lies.

The philosophy of knowledge (or the philosophy of science as a subset) was developed over many centuries, and its elements are important in adding rigor to this debate. Within this philosophy, an ontology (and, specifically, a science ontology) may be simply defined as what we know in some particular niche or entity of science-space.

'Knowing' in science requires strong foundations, and has been refined over the centuries to mean a 'justified, true belief.' Such a belief may be knowledge only under three conditions: it is certain; we believe it is true; and we have empirical justification to believe it. Stated differently, scientific knowledge arises when: we accept an objective reality; postulated rules govern that reality; and those rules may be demonstrated by empirical evidence. The empirical evidence supporting that belief or rule is called the epistemology, which makes use of reason constrained by verification through experimentation and observation. Putative facts deriving from misinformation and/or opinion can never be scientific knowledge.

Science history is a battlefield littered with rotted models, skewered evidence, and illogic once thought to be knowledge; all discarded as a result of better evidence and improved logic. These ontological failures can be traced to flawed and failed epistemologies. Accepted ontologies fail and decay in all scientific entities, but there is always a next one up, thanks to the philosophy of science. When the evidence indicates a belief is knowledge, it retains that imprimatur until it is overturned by empirical evidence supporting a new ontology.

So it is with the linear no-threshold model (LNT), confidently claimed by advocates to predict accurately the generation of radiogenic cancer from LDIR exposure. The LNT extrapolates from observed high-dose harm to assumed low-dose harm, purportedly showing that all ionising radiation is harmful. It denies any biological response to damage, asserting cumulative lifetime harm regardless of dose or dose rate.

If the basis of all ionising radiation exposure rules, regulations, guidance and effects analyses [2] were shown to be a failed ontology without valid epistemological support after more than 70 years, one would expect a significant level of concern leading to an all-out effort to extirpate such a malignancy. It has not happened.

Here, we will review the LNT ontology and examine some of the flawed and failed epistemology underpinning it, then examine the nature of the knowledge that LNT advocates are left with if its epistemology is shown to be lacking.

Principal elements of the LNT ontology

The LNT's principal assertion is that the type of harm received from high-dose radiation using a simple, cancer-induction model is exactly mirrored by that from low doses.

Specifically, the LNT asserts that putative LDIR effects based on linear proportionality from high-dose effects, where evidence shows it has legitimacy, manifest in two ways: that all acute exposures to LDIR produce radiogenic cancer and are proportional to that dose down to zero dose, regardless of dose rate; and that this effect is cumulative over a lifetime, regardless of dose rate. That is, the body responds in exactly the same way to high-dose and LDIR exposure.

The proportionality and accumulated harm can be extrapolated to another concept called "collective dose," which asserts that a given radiation dose divided among any number of people will cause the same number of cancers or deaths from cancer. If a certain dose will produce an individual cancer death with high certainty, the same dose spread over two or more people will produce a cancer death with high certainty.

In summary, the LNT's ontology says: a radiogenic cancer-dose-response can be legitimately extrapolated linearly from high doses down to zero dose; a no-harm threshold dose does not exist; the body experiences only harm from radiation; such harm is cumulative; and any radiogenic cancer mortality dose, spread among any number of people, produces a cancer mortality.

How the LNT ontology fails

To show the failure of the 'how we know' underpinnings of the LNT, a few epistemological features of the LNT are evaluated against accepted science of today.

Linear extrapolation:
The LNT is based on a model in which interaction with cells, tissue, organs and systems is the same at low doses as it is at high doses of ionising radiation, making a high-to- low-dose, linear extrapolation appear 'logical.'

But the rules of radiation effects change at low doses and dose-rates regarding radiation interaction with cells, tissues and systems, and so does the resulting dose-response relationship. In fact, dose data on the order of 0-200mGy belong in one 'box,' while the higher-dose data fall into a box where different rules apply (see Figure).

This putative linearity of dose-response is the broadest, most overarching fallacy of the LNT, since it presumes constancy of the cancer response of cells, tissues and systems over the full dose range.

Adaptive response:
LNT does not account for proven biological adaptive responses that change the shape of the LNT's dose-response line in the LDIR range. Science now shows the body responds differently to radiation at high and at low doses, as demonstrated by a variety of studies. High-dose responses are associated with extensive damage, while at low doses the body repairs or eliminates the damage through a variety of protective mechanisms, termed biological adaptive responses. A cell's low-dose damage response may be linear, but the body's overall LDIR response is to mitigate this damage, as it does for much of the

body's similar, naturally- occurring, endogenous damage due to oxygen metabolism [3,4]. As a result, the total response to radiation is non-linear.

The body's biological adaptive responses use proven mechanisms [5,6], which provide cancer protection through antioxidant production, apoptosis, immune system-mediated effects and repair of DNA double- strand breaks (DSBs). DSB repair from LDIR occurs within hours of exposure, even after CT scans [7], with DSB levels decreasing to less than baseline values within 24 hours.

Nuclear medicine imaging studies [8] show that such doses do not produce radiogenic cancer increases. Thousands of children younger than 20 who received I-131 for diagnoses (< 0.37 MBq) delivering mean thyroid doses of about 1Gy were tracked over many years, and show no evidence of increased risk of thyroid cancer due to childhood intake of I-131.

More than 150 genes are involved in DNA repair. At least six mechanisms act to decrease cancer rates and enhance longevity from the stimulation of LDIR damage to an organism's constituent parts, and these biological responses are reported to produce a benefit (ie hormesis) [9].

LNT advocates say that predicted cancer risks do not manifest because at low doses, the ratio of the radiogenic cancer risk 'signal' to the background spontaneous cancer risk 'noise' is so small, the signal becomes statistically indistinguishable from the noise. Such a claim for radiogenic signal invisibility is inaccurate in the range of LDIR, however, since many studies demonstrate reduced cancer risk and increased longevity. If harm is invisible, benefit should be, as well.

Further, science cannot distinguish the pure radiogenic signal. It cannot be differentiated from spontaneous cancer arising from the body's own metabolic damage by reactive oxygen species, which produces far more mutation events per cell per day than LDIR.

Epidemiology's true 'signal' is total cancer (spontaneous plus radiogenic), and the 'gold standard' for epidemiological data of LDIR-induced cancer is the Life Span Study (LSS) cohort of A-bomb survivors by the Radiation Effects Research Foundation, which, contrary to LNT advocates, has always purported to show that radiogenic cancer is discernible at low doses.

However, according to the latest update of LSS study results in 2017 [10], apparent threshold doses, below which there were no observable cancers, were 80mGy for females and 750mGy for males, a decidedly non-LNT outcome. Of course, the LSS data do not account for the well-known cancer mortality and morbidity increases from high stress levels and significant deprivation experienced by those survivors, especially women.

Radiation-related risk of disease at low- doses from atomic bomb radiation must be calculated on top of an uncertain background dose, and these two values can overlap, becoming indistinguishable [11].

Lastly, the LNT tenet that radiation damage is cumulative, no matter the dose or dose rate, is directly contradicted by the proven practice of fractionation of high-dose radiation therapy, demonstrating that damage recovery occurs between treatments [12].

The LNT ontology says radiogenic cancer results from LDIR all the way down to zero dose and that all such LDIR damage is cumulative. That is not supported by the present epistemology addressing biological adaptive response.

Mutations:
The LNT relies on the disproven somatic mutation model for radiogenic cancer, where cancer is the unalterable end-product of one or more driver mutations.

While mutations are necessary for cancer induction, they are now known to be insufficient to produce clinically-overt cancer. The body's adaptive response and its immune system are now recognised as being responsible for arresting the development of mutation-induced cancer and preventing cumulative damage.

Cancer is not simply the end-product of one or more enabling mutations. The immune system plays a much more significant role in the development of cancers, enough to make the 'one mutation = one cancer' model obsolete.

Cancers are known to develop from immune system suppression. Low-dose radiation stimulates the immune system, causing a reduction in cancer rates. One study reported that residents of high background radiation areas (3.3mSv/year) had increased frequencies of chromosome aberrations compared to the control population in lower background areas (1.1mSv/year), but had reduced all-cancer mortality [13]. The LNT ontology arising from an outdated model of radiogenic cancer induction is clearly not supported by the present epistemology of a more complex cancer induction process.

Spontaneous normal, oxidative processes:

The LNT dose-response ontology cannot account for cancer induction that addresses the now-proven spontaneous rate of DNA alterations from a cell's normal oxidative metabolic processes, which dwarfs the DNA alteration rate due to LDIR.

Research shows the spontaneous rate of DNA alterations resulting from cellular metabolic processes is much greater than the DNA alteration rate due to LDIR (eg, a million times greater than exposure to natural background radiation). Thus, oxygen produces far more DNA damage than LDIR. The body processes both radiogenic and endogenous DNA damage through adaptive responses (above) that are overwhelmed at high doses, but uniquely stimulated by LDIR. Therefore, the LNT is false, since high- dose effects (responses are associated with extensive damage) cannot accurately predict effects of LDIR (responses are protective).

Further, a study [14] comparing interventional cardiologists (median dose-rate of 4mSv/year) to controls exposed only to background radiation showed chronic LDIR was associated with improved antioxidant defense and increased apoptotic response.

The LNT ontology regarding cancer induction is clearly unsupported by present epistemology, because the LNT epistemology flagrantly fails to account for the generation and disappearance of DNA alterations from naturally-occurring metabolic processes.

Flaws in LNT epidemiological methods:

Today's LNT advocates and purveyors rely upon sophisticated epidemiological methods that are incorrectly applied, attributing significance to purported LNT compliance where none actually exists.

As we have seen above, there is no validated and accepted empirical research to support a reasonable epistemology for the LNT ontology. Yet LNT advocates and purveyors still cling to epidemiological studies that purportedly support it.

Analysis of published epidemiological studies supportive of LNT show huge flaws in the science. These studies generally confine their investigations to mathematical and statistical methods, without reference to the supporting science and their well-established empirical findings. This separation of the epidemiological from the empirical science, examining damage and ignoring the biological response to that damage, are central components of the major errors discussed above.

Further, such studies implicitly invoke the LNT as an a priori assumption and, based on circular reasoning, arrive at a self-fulfilling conclusion that the LNT is valid, while presenting the measured slope of a presumed linear dose-response relationship as an uncritically reviewed certainty.

Assuming the LNT a priori permits study authors to avoid any biological considerations when calculating cancer risk from LDIR. It further forces the LNT as the null hypothesis, a failure of the burden-of-proof test, which invalidates any claim of cancer causation by radiation.

Typical additional errors in such studies include:

- Defining the cumulative dose origin as zero dose, neglecting all other sources of LDIR;
- Failing to consider reverse causation or confounding by indication. This is a key consideration in medical imaging, particularly repeated imaging;
- Failing to obtain accurate dose measurements for investigation, instead assuming doses from geographic models or average doses for a given imaging technology and patient body size;
- Failing to adequately consider confounders such as smoking, socioeconomic effects, environment, etc.

Studies showing illegitimate epidemiological support for the LNT's ontology are the LNT's last bastion of defense. Such studies apply false empiricism, yielding purported LNT compliance where none actually exists.

LNT's position within science

The LNT's ontology is without empirical basis, is unsupported by currently accepted epistemology, and is, therefore, no longer science, if ever it was.

This leaves LNT advocates and purveyors simply outside of science. Nevertheless, they still cling to it as if it were holy writ, asserting that even if the LNT is wrong, it produces conservative (that is, 'safe') projections of outcomes. This is demonstrably false.

As the basis for all medical and nuclear energy radiation-regulations and policies, it is well-documented that the LNT has generated intense radiophobia that is responsible for millions suffering from radiophobia-induced mental disability over the last four decades. And many thousands have died from LNT-based policies tied to evacuations rather than using safer, shelter-in-place policies. Still the LNT debate rages on, especially within the medical imaging community.

Another possible explanation is ignorance. Van Nostrand, writing on a different topic [15], says that physicians must more critically read the literature and not just accept the "findings" of studies as fact. Medical imaging and nuclear energy experts must personally review and understand the primary literature (not relying on their beliefs or less-informed, second-hand versions) that controls the advancement of their technologies and the welfare of humanity. If putative experts do not self-educate, LNT advocates, purveyors and the media will continue to misinform the public about the effects of LDIR exposure, causing much harm; the problem is radiophobia not LDIR exposure.

The LNT has degenerated within the philosophy of science to a lower level of 'knowing' than empirical knowledge. Many disciplines unable to use empiricism rely on a path to knowledge called coherentism, where individual concepts, lacking empirical support, form a logically connected structure whose ascent to knowledge occurs if many agree it's true. Coherentism represents a decayed state of more disorder when compared to empiricism. One might also recognise

it as ‘consensus science,’ another way of saying non-science. The LNT has been cast out of empirical science, and coherentism is now its home.

Conclusion

The LNT is false. The imperial imprimatur ordained by its purveyors and advocates is not clothed in science. And because the LNT fails empirically against superior empiricism, it becomes misinformation and opinion, not knowledge. Blaise Pascal once observed, “Opinion is the mistress of error; she cannot make us wise, only content.” The LNT is still advocated and purveyed because it lends contentment to believers, whether to maintain bureaucracies, control, or a sense of conservatism.

The purpose of science is knowledge, hopefully applied with wisdom, to help accelerate human advancement. We can
no longer tolerate universal application of LNT misinformation and opinion when, as people of science, we are about helping, not harming, humanity.

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References are available on http://tinyurl.com/y7q585mm