

Dose Optimization to Minimize Radiation Risk for Children Undergoing CT and Nuclear Medicine Imaging is Misguided and Detrimental

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ABSTRACT

A debate exists within the medical community on whether the linear no-threshold (LNT) model of ionizing radiation exposure accurately predicts subsequent radiogenic cancer incidence. We evaluate the evidence that refutes LNT, and its corollary efforts to reduce radiation exposures for CT and nuclear medicine imaging in accord with ALARA (as low as reasonable achievable), particularly for children. Further, we review studies demonstrating that children are *not*, in fact, more radiosensitive than adults in the radiological imaging dose range, rendering dose reduction for children unjustifiable and counterproductive. Efforts to minimize nonexistent risks are futile and a major source of persistent radiophobia. Radiophobia is detrimental to patients and parents, induces stress, and leads to avoidance of imaging or suboptimal image quality, both increasing misdiagnoses and consequent harm, with no compensating benefits.

Key words: Radiological imaging; linear no-threshold; ALARA; dose optimization; radiophobia; children

Introduction

Ionizing radiation is thought by many to cause cancer, based on uncritical acceptance of the linear-no-threshold model (LNT), despite absence of valid evidence for doses below 100-200 mGy (1). Moreover, the LNT extrapolation from high- to low-dose radiation has been shown to be empirically false and *decidedly harmful to millions of people*, both in medicine and with respect to government policies regarding nuclear power plants (1-4). So there is a great divide over low-dose radiation exposure. Herein, we argue that low-dose/dose-rate radiation does not *cause*, but in most people *helps prevent*, cancer, as shown by sound, empirical, experimental and observational studies. The research on how we know LNT is false and on its detrimental consequences is briefly summarized herein.

This article was prompted by an upcoming all-day Categorical Seminar, titled *Radiation Dose Optimization in Pediatric Nuclear Medicine*, at the SNMMI Annual Meeting in June 2017 in Denver. The program advertises thirteen presentations on assessing and communicating radiation risk in children, on absorbed dose estimation, on dose reduction, and on radiopharmaceutical guidelines. The seminar focuses on communicating what is, in fact, fictitious risk, while emphasizing dose reduction that is consequently needless, on resulting superfluous enhanced accuracy of dose estimation, and on improvement in activity-administration guidelines. The underlying intent to lower future cancer risk, while desirable, goes astray, as the premise is based on the erroneous LNT and the resulting ALARA (as low as reasonably achievable) principle. It further aims at procedure standardization in pediatric nuclear medicine, with which we have no quarrel. More accurate dosimetry can improve guidelines for radiopharmaceutical activity administration and is a reasonable pathway to optimization of *image quality*. However, it is wholly misguided for *radiation protection* purposes.

LNT and its corollary, ALARA, – based on linking radiation absorbed dose to probability of future cancers, no matter how low the dose or dose rate – are defended despite their proponents' disarming dual admissions that, because of the low-dose radiation signal-to-noise problem, there is no evidence favoring LNT for low-doses, nor can there be. Proponents often defend their reliance on LNT on the grounds that even if there *is* a dose threshold, below which there is no harm, LNT's consequent overestimation of harm *errs on the side of caution*. Seemingly sound, this application of the precautionary principle ignores empirical low-dose radiation research, while offering no refutation, and denies responsibility for the radiophobia generated by LNT, with its attendant harms, and the concomitant deprivation of the probable cancer-*inhibiting* effects of low-dose radiation (1,4).

The precautionary principle is useful only if action to control the feared agent has no, or less harmful, side effects. However, for radiological imaging, collateral negative consequences of radiophobia-based dose reduction exceed the putative harms of radiation. These consequences include misdiagnoses due to both imaging avoidance and nondiagnostic image quality, as well as use of alternative imaging procedures, such as longer-duration MRI studies having higher sedation risks for children, as we have

reported (1). The harmful consequences of misdiagnoses resorting to exploratory surgical alternatives are greater than LNT-based fictitious predictions of harm. And they are more immediate than any future cancer risks that are putatively avoided by ALARA dose-reduction strategies (5).

A worldwide movement has arisen in response to the scientifically unsupportable call to decrease dose. We concentrate here on the *pediatric* CT and nuclear medicine dose “optimization” efforts generated by the Image Gently Alliance for children who are a more socially and medically vulnerable population. The efforts aim not only to improve diagnostic quality, a laudable objective, but also to lower the fictitious risk of future cancer. Recognizing the antagonism between these contradictory objectives, Dr. Donald Frush, chair of the Image Gently Alliance, states that the Alliance seeks to provide “balance” between them, while disclaiming any responsibility for the media-driven radiophobia (6). Reasonable as this might be if, in fact, there were a risk of cancer from CT or nuclear medicine imaging, “balance” between diagnostic benefit and cancer risk can no longer claim innocence in the absence of such risk. “Balance” between truth and falsehood is no balance at all.

Children Are Not More Radiosensitive Than Adults

The focus on children is founded on their *social* vulnerability and on a false *biological* assertion that children are more radiosensitive than adults. This assertion is based on both an indisputable fact and a false assumption: first, on the *fact* of more rapid cell division leading to greater mutation opportunities, and second, on the *assumption* that increased mutations entail increased cancer risk. But, like LNT itself, the latter assumption ignores evidence-supported adaptive responses that either repair mutations through enhanced repair enzymes or remove the unrepaired cells by apoptosis and/or, most importantly, the immune system (1,3,7). Absent these evolution-provided naturally-selected defenses, the far more frequent (by about a million-to-one) endogenous mutations in almost every cell – due to reactive oxygen species (ROS) from normal metabolism – would produce cancer minute by minute. Mutations or epigenetic changes are necessary, but not sufficient, to produce clinical cancer.

Most importantly, Preston et al. studied Japanese atomic bomb survivors who were younger than 6 at the time (8). Their results indicated no significant difference between adult-onset, solid-cancer incidence of the control group and that of subjects who had received acute exposures of up to 200 mSv as children. CT and nuclear medicine imaging employs doses an order of magnitude or more below that figure. Thus, there is *epidemiological* evidence that children are *not* more radiosensitive to such imaging.

In addition, relevant evidence from a study in individuals undergoing CT examination indicates that at low radiation exposures, initial radiation-induced damage is generally repaired or eliminated by the body’s adaptive responses in a matter of hours. Löbrich et al. (7), for example, showed that minutes following exposure, CT scans initially induce an increase in DNA double-strand breaks (DSBs) compared with pre-CT levels. But repair of these DSBs occurs subsequently. In fact, in all but one patient, the DSBs were

repaired to *less than* the initial (pre-CT) background levels at some time between 5 and 24 hours, suggesting that the low-dose CT exposure also induced repair of the pre-existing and ongoing endogenous DNA damage, as well as the radiogenic damage. This is evidence of a beneficial (hormetic) effect of low-dose ionizing radiation – and argues against radiogenic causation of either solid cancers or leukemias in children or adults.

Furthermore, the immune system, once established in older children, is more vigorous than that in adults, declining in efficiency with age, and low-dose radiation has been shown to stimulate immune systems to reduce cancer rates (9). Fahey et al., nevertheless, claim it is prudent to strive for “optimal” administered activity in children with a patient-size-related dose, defining “optimal” as lowering dose while providing the diagnostic information necessary for proper care (10). While insufficient dose has resulted in nondiagnostic studies, this trade-off is thought to be necessary, but only by ignoring the body’s proven defensive responses.

As with Preston’s study (8), much of the current thinking about the risks of ionizing radiation is based on certain interpretations of the Hiroshima/Nagasaki Life Span Study (LSS). As we have reported (1), these data, properly interpreted, invalidate LNT. Supportively, the French Academy of Sciences (11) reported that these data provided evidence for protective, adaptive responses and no valid evidence for harm below 100 mGy. Despite this contrary evidence, the National Academy of Sciences’ BEIR VII Report (12) still endorsed LNT for solid cancers and, further, attributed a risk two to three times higher in children. Unaware perhaps of the BEIR Committee’s distortion of its own cited data, most radiologists and nuclear physicians look to this widely regarded voice of authority. Indeed, we have found and revealed BEIR VII’s egregious misquoting of one of its chosen sources that actually came to the opposite conclusion, in line with our contention (4).

Voices of “Authority” Do More Harm than Good

Unfortunately, many imaging professionals do not read scientific literature critically. For their understanding of LNT/ALARA/dose optimization, they rely on “expert” opinion, as offered in reports by NAS’s BEIR Committee, ICRP, NCRP, etc. that mutually reinforce each other. Further, many investigators *discount* the work of those with whom they disagree, rather than even *attempting* to refute it, instead appealing to citations from these authoritative organizations as though they were established fact, rather than mere opinion that closer examination proves them to be.

There are two large epidemiological studies that have been frequently cited as evidence to support the claim of increased cancer risk in children due to CT, as we have reported (1,4). But according to UNSCEAR and even Dr. John Boice (13), president of NCRP, these results are likely untrue. Inaccurate dosimetry and implausible risk estimates were apparent; association was conflated with causation; and medical indication rather than radiation was likely the source of the apparent association (i.e., reverse causation). Further, again as we reported and as underscored by Dr. Boice, two more recent epidemiological studies in France and Germany in 2015 found no significant excess

cancer risk in children from CT scans, "...once adjustment was made for conditions that prompted the scan, family history, or other predisposing factors known to be associated with increased cancer risk" (13). Thus, confounding by indication (reverse causation) must be ruled out completely, or observed excess cancer risk may be falsely, and facily, attributed to CT exposure.

Dr. David Brenner et al. (14) published an article in 2001 that was widely promoted by the media, accelerating the prevalence and intensity of radiophobia. It has been cited in the scientific literature over a thousand times since. On the basis of an LNT calculation involving unsupported parameters with significant uncertainties, they projected that approximately 500 children under the age of 15 years would eventually die of CT-caused cancer. Some years later, in the *New England Journal of Medicine*, the same Brenner, with Hall, predicted that up to 2% of all cancers in the United States "could" be due to CT scans (15). Importantly, these erroneous and irresponsibly fear-amplifying predictions were based on CT doses completely unknown for individual patients using risk estimates from the LSS cohort. These risk estimates are not applicable to children undergoing CT examinations in the U.S., for one thing because it is most unlikely that the radiation will have played a causal role in children who do develop cancer after a CT scan. Further, whatever the cancer rates in bomb survivors, they were also subjected to the confounding factors of severe trauma and deprivation, which are known to interfere with immune system function and hence enhance susceptibility to all sorts of ailments.

Brenner subsequently reported wholly unjustified conclusions, again promoting widespread radiophobia, this time with respect to DSBs in only 3 pediatric patients after undergoing CT exams (16). Even acknowledging the work of Löbrich et al. (7) that repair or removal of initial damage was expected within several hours, this group obtained data only at 1 hour after the CT scans, which, as expected, demonstrated increased DSBs compared to pre-CT levels. Yet they concluded that their findings supported LNT at very low doses in young children and that "even very low ionizing radiation exposure relevant to diagnostic CT exposure can leave a mark in the somatic DNA," significantly and irresponsibly omitting the qualifier, "for perhaps a few hours." Astonishingly, they recommended that, based on this admittedly incomplete evidence, "When possible, CT exams should be limited or avoided by possibly applying non-ionizing radiation exposure techniques such as US or MRI." Such alternatives are sometimes medically warranted, but should be based only on use of the most appropriate imaging modality, not on radiation exposure.

The Search for Accuracy in the Absence of Validity

The "dose-optimization" movement in nuclear medicine has prompted intense *de novo* efforts to develop numerous complex anatomical phantoms and better pharmacokinetic data and models to more accurately estimate absorbed doses for diagnostic procedures (as opposed to therapeutic treatments) (17). Furthermore, the current consensus guidelines for radiopharmaceutical administered activity are considered inadequate and in need of updating. This more precise and labor-intensive endeavor is deemed necessary to improve the practice of pediatric nuclear medicine imaging by providing excellent image

quality at the lowest radiation dose possible; but the obsession over lowering radiation dose is a futile and laborious attempt to minimize what is, in fact, a nonexistent risk.

Much effort has already been expended in assessing use of ^{99m}Tc -DMSA in children. For example, to illustrate the relative superfluity of such precision, the highest effective dose in one such imaging exam is only about one-third the average annual natural background radiation dose received per person in the U.S. – 3.1 mSv and ranging up to 80 times greater elsewhere in the world. This dose, therefore, is well within the hormetic zone, i.e., below the threshold for harm.

The original aim of the radiopharmaceutical guidelines was to reduce the *variability* of administered activities. This is praiseworthy for better standardization of *image quality*, but irrelevant for *radiation protection* purposes. The need for better accuracy in dose estimation to further minimize a nonexistent risk, based solely on the erroneous LNT, is entirely misdirected, and, as a serious unintended consequence, serves only to amplify long-standing public and professional radiophobia.

Conclusion

Many critics argue for termination of the fictitious LNT, along with its epiphenomenal ALARA and the Image Gently Alliance, but must contend with a well-ensconced paradigm – one backed by world-wide advisory organizations and regulatory agencies, whose overlapping members have invested reputations and labor. Critics must fight not only for predominance of empirical evidence, but also against such things as the widely accepted yet misapplied “justification” and “optimization” principles of the ICRP (1). Eliminating *any and all* diagnostic medical procedures that are not clinically warranted is important. But attempting to lessen fictitious risk by lowering dose in studies that *are* clinically warranted is a misapplication of the principles. It is protection from radiophobia, rather than from low-dose radiation, that will benefit both children and adults.

The Image Gently Alliance and myriad international affiliated groups harm patients and parents by promoting radiophobia while offering fictitious protection against nonexistent risks. We do not suggest a cavalier approach by discounting dose optimization, but only in service of diagnostic quality. Public misperceptions, while not being disregarded or ignored, must not be endorsed; rather they must be *corrected* through accurate information. The public’s trust in medical practitioners can only be attained if we convince the public and physicians alike that there is no harm in radiological imaging.

Accurate information about low-dose radiation is the only way to undo fear, as decades of failed alternative approaches and concessions have shown. While it may *seem* reasonable to attempt to assuage public fears by accommodating their misperceptions through lowering dose despite the absence of harm, this only reinforces their misperceptions. Radiophobia is detrimental to patients and parents, induces stress, and leads to avoidance of imaging or suboptimal image quality, both producing misdiagnoses.

This can only be overcome by rejection of the LNT fiction and its corollary principle, ALARA, and by termination of the Image Gently Alliance.

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