

Utilization Strategies for Cumulative Dose Estimates: A Review and Rational Assessment

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Over the past several years, the cancer risks associated with radiation from diagnostic imaging have received increased attention in both the medical literature and the lay press. In the midst of this heightened scrutiny, there has been growing support for the idea of tracking cumulative dose estimates that longitudinally document the accumulated medical radiation exposure of each individual patient. The authors review the current consensus model of radiation-induced carcinogenesis and use this framework to provide a rational assessment of several potential cumulative dose estimate utilization strategies.

Key Words: Cumulative radiation dose, cumulative dose estimates, cumulative dose tracking, radiation dose, radiation dose tracking, ACR Dose Index Registry, CTDI

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As the cancer risks associated with radiation in diagnostic imaging come under increased public scrutiny [1], there is growing support for the idea of tracking cumulative dose estimates (CDEs) [2] that longitudinally document the accumulated medical radiation exposure of each individual patient. However, before we embark on the task of incorporating CDEs into the practice of medicine, we should first come to a more formal and scientifically accurate understanding of what this information truly represents and how it can best be used. For the purposes of this paper, we assume that the considerable logistic and financial barriers to CDE tracking can be overcome. We focus instead on a rational consideration of several proposed CDE utilization strategies to assess which represent genuine opportunities and which are merely pitfalls. Much of the discussion focused on the issue of CDEs has been based on faulty assumptions concerning the nature of the risk associated with diagnostic x-ray exposure, which we will first seek to clarify.

A BRIEF REVIEW OF STOCHASTIC RISKS AND LINEAR NO-THRESHOLD MODELS

It is important to keep in mind that cancer induction represents just one of many potentially deleterious side effects from ionizing radiation. Deterministic effects are virtually certain to occur with doses exceeding established thresholds and exhibit dose-dependent severity. For example, at a skin dose of 5 Gy, there is near certainty of developing skin erythema, which will be worse at 10 Gy at which point it will be accompanied by additional complications not seen at 5 Gy. Deterministic effects are relatively easier to understand in that they mirror other kinds of “real world” medical complications and do not require elaborate probabilistic equations to detect or predict. However, deterministic effects are the exception rather than the rule in diagnostic radiology and are usually the result of an accident or operator oversight.

The risk for cancer due to radiation exposure in the diagnostic range is stochastic rather than deterministic (Table 1), meaning that only a likelihood of developing or dying from cancer can be estimated using mathematical models developed for this purpose. If a group of patients are irradiated with a dose in the stochastic range, a small fraction will go on to develop cancer due to chance (ie, bad luck), while the vast majority of those irradiated will experience no effects at all. In other words, it is the probability that an effect will occur, not the size of the effect, that is proportional to the insult when modeling a stochastic process. However, such complications are not easily detected on an individual basis because most radiation-induced cancers (apart from leukemia) lie latent for at least two decades, and when they do manifest, they are clinically, radiologically, and patho-

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Table 1. Summary of the characteristics of stochastic risks and deterministic effects of ionizing radiation

	Stochastic Risks	Deterministic Effects
Examples	Leukemia, other cancers	Burns, sterility, neutropenia, cataracts
Relevant dose level	Any	>0.3 Gy
Dose magnitude determines	Probability of cancer	Type and magnitude of injury
Thresholds	None (current consensus)	Each effect has a threshold
Time scale of effect	Generally 20-40 y*	Hours to weeks
Effect of each incremental dose	Independent	Often cumulative
Clinical relevance of dose history	None	Often useful

*Some radiation-induced malignancies (eg, leukemia) can manifest earlier than 20 years.

logically identical to all other cancers and thus cannot be reliably attributed to their cause.

The linear no-threshold (LNT) theory refers to the graph relating the incidence of excess cases of lethal cancer (y) due to a radiation dose (x), which is assumed to be a straight line that passes through the origin. According to a conservative interpretation of the available evidence, there is no threshold: all radiation exposure is assumed to carry some risk for cancer, and thus there are no safe doses, only tolerable levels of risk that must be weighed against the possible benefits of the scan. It is the manifold implications of linearity that are more easily overlooked. A straight line has a constant slope, so a given dose increment produces the same incremental increase in risk for cancer regardless of where it falls along the x axis. The clinical correlate of this is that the 1st CT scan is just as “dangerous” in terms of absolute cancer risk as the 10th or even the “ n th” scan [3], assuming the same body part is scanned, using a similar technique, and so on. There is no buildup of sensitivity with increasing dose from repeated CT scans. If there were, the response would not be linear, and all our current LNT-based risk estimates would be worthless.

Figure 1 is derived from the report of the National Academy of Sciences’ Seventh Committee on the Biological Effects of Ionizing Radiation (BEIR VII) [4] and shows solid tumor cancer risk as a function of radiation exposure on the basis of epidemiologic data from the Japanese Life Span Study (LSS) fitted to the constraints of the LNT model (ie, a best-fit line passing through the origin). One striking feature of these data is their relatively large error range, easily understood when one considers that the LSS is a retrospective attempt to salvage data from an uncontrolled “experiment” in which the subjects received an instantaneous dose consisting of a mixture of x -rays, γ -rays, neutrons, α particles, and β particles. A great deal of uncertainty arises when applying the BEIR VII risk model to contemporary imaging patients who accrue cumulative dose gradually through many small exposures, the vast majority of which are due to x -rays. Furthermore, the total exposure levels for the most convincing LSS data points lie above 100 mSv, whereas most diagnostic imaging examinations result in acute exposures well below 50 mSv. As a result, risk

estimates in this region are derived by extrapolation, introducing more uncertainty.

Although this issue lies beyond the scope of this paper, we concede that cogent scientific arguments can be made both against linearity and for a threshold [5]. However, the LNT theory is not unique in this regard, as most standards of care in medicine derive from consensus opinions or meta-analyses assembled from numerous studies, each of which is flawed and none of which is perfect. For the purposes of this review, we consider that the continued strong support of the last 3 consecutive BEIR committees [4] and the most recent recommendations of the International Commission on Radiological Protection [6] provide sufficient evidence that LNT models are an ethical and transparent interpretation of

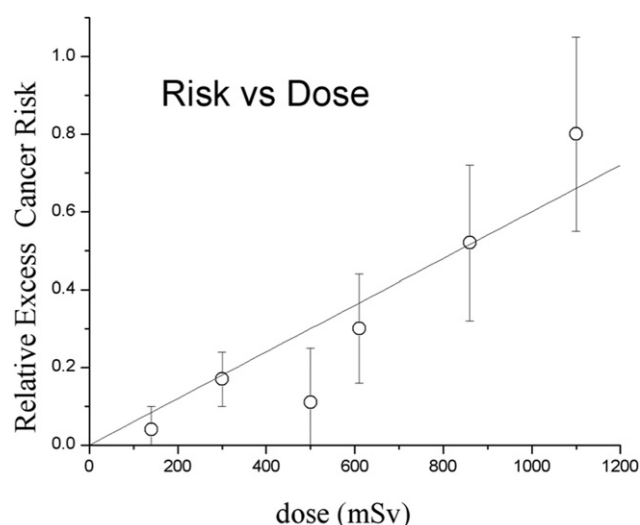


Fig 1. Excess relative risks of solid cancer for Japanese atomic bomb survivors. Plotted points are estimated excess relative risks of solid cancer incidence (averaged over both genders for exposure at age 30 years and surviving to age 60 years). The linear no-threshold model is illustrated using regression analysis to construct a line passing through the origin that best fits these data. The operating region for CT scans and medical x -ray examinations is below 100 mSv, and the risks of radiation exposure in this range are based on extrapolation rather than primary data. Adapted from National Research Council [4].

the best available data. An equally important argument is that of consistency. Because the LNT has long been the consensus model, all widely used quantitative models of radiation-induced cancer risk are based on it. In particular, the widely quoted papers reporting population cancer risks due to diagnostic imaging that are often used to justify CDE tracking were all derived using LNT models [1,7]. We therefore have little choice but to adhere to the LNT model if we wish to use CDE information to quantify risk, which is presumably what we are attempting to measure and reduce, at least from a population perspective.

CUMULATIVE DOSE ESTIMATES ARE NOT RELEVANT TO RATIONAL PRESCAN RISK VS BENEFIT ANALYSIS

If we concede that our understanding of the relationship between dose and cancer risk is both linear and stochastic, one can draw the analogy that in terms of cancer risk, performing a CT scan is akin to a game of chance. According to the International Commission on Radiological Protection model [6], the hypothetical risk for a fatal cancer resulting from a typical abdominal scan (8-mSv effective dose) is approximately 0.04%, and the implied odds (1:2,499) are similar to those of drawing the ace of spades twice in a row from a 52-card deck (1:2,703). In the latter case, assuming the card is replaced and the deck well shuffled between draws, the odds are the same for each draw. Similarly, the odds of generating the seed of a fatal cancer are the same for each CT scan, whether it is the 1st or the 10th scan. To complicate matters, consider that the results of each draw from the deck will remain secret for 20 to 40 years. That is, if our gambler draws the two sequential aces of spades, a "secret cancer chit" is issued in her name, payable in 20 to 40 years by death. However, she will never know it, because by the time she is diagnosed, this brief game of chance played at the ER scanner will be a remote memory and one of thousands of possible causes for her malady.

The tendency of some care providers to believe that CDEs are relevant to bedside decision making amounts to a medical manifestation of the "the gambler's fallacy," the notion that past results of independent random events influence future probabilities. This is a well-known form of cognitive bias that arises when subjects confuse the difference between dependent and independent events or misinterpret the implications of the "law of averages." The most famous example supposedly occurred in Monte Carlo in the summer of 1913, when the roulette wheel landed on black 26 consecutive times. As the streak grew longer, more and more gamblers wagered increasingly larger sums on red because it was "due" to win, while fewer wagered on black. Predictably, the only party known to have profited was the casino. Of course, each spin of the wheel was a truly independent event and the outcomes of prior trials were irrelevant to the next

spin. According to the LNT, spins of the CT gantry are similarly independent in terms of cancer risk, so that a priori knowledge of CDE is not helpful in assessing future scan risk. A provider who believes otherwise, who insists that because of a patient's high CDE, the next scan is somehow more likely to cause cancer, is falling for the same powerful cognitive bias that has helped keep casinos in the black for centuries.

The odds that a given radiation exposure will cause cancer depend on the dose, the body part irradiated, the patient's gender and age, and a host of genetic and physiologic factors. But as long as we adhere to the LNT model, they have nothing to do with prior exposure. Furthermore, because the odds are remote and secret, they lie in stark contrast to the very real and obvious risks facing patients who seek medical care. The risk for dying from cancer in one's lifetime from all causes is about 20% [8], while the scan in this scenario increases this risk by only 0.04% to 20.04%. Even for patients with several scans in their history, the risk is still on the order of 100 times less than their natural cancer risk, whereas the scan itself may be lifesaving.

Estimating the possible benefits of a scan and attempting to weigh them against such small risks is more an art than a science. It is the question of whether "to scan or not to scan." Is it nobler to embrace the present, or to eschew its possible benefit because of a small future risk? No person on earth can avoid the 1:5 odds of developing fatal cancer from the thousand natural shocks that flesh is heir to. Indeed, those who have already been scanned many times are more likely to have been dealt the "secret fatal cancer chit" at some point in their past [3], in which case they have nothing to lose and perhaps much to gain from a potentially life-prolonging CT scan. The delayed nature of radiation-induced cancer reduces its effect on mortality compared to more immediate risks of the same absolute probability; that is, one may die in an accident before the fatal cancer manifests.

It also helps to consider that the stochastic risk for cancer from repeated CT scans is not analogous to the act of chopping down a tree, whereby the repeated blows of an axe cause the tree to weaken gradually until it topples. For a stochastic risk, there is no buildup of injury with each insult but rather only an accumulation of probability. Our CT patient has either "dodged the bullet" of radiation-induced cancer in her previous scans, or she has been hit. Only information on whether she has already been hit would be useful, although this is unfortunately unknowable. Her lifetime CDE is not helpful at all.

Because CDEs of any consequence are much larger than any single dose, adding them to the decision-making process can bias things in one direction only: that of increased perceived risk. This may cause patients or poorly informed physicians to irrationally decide against medically indicated CT scans, a phenomenon that has already been reported in the lay press [9]. The suggested

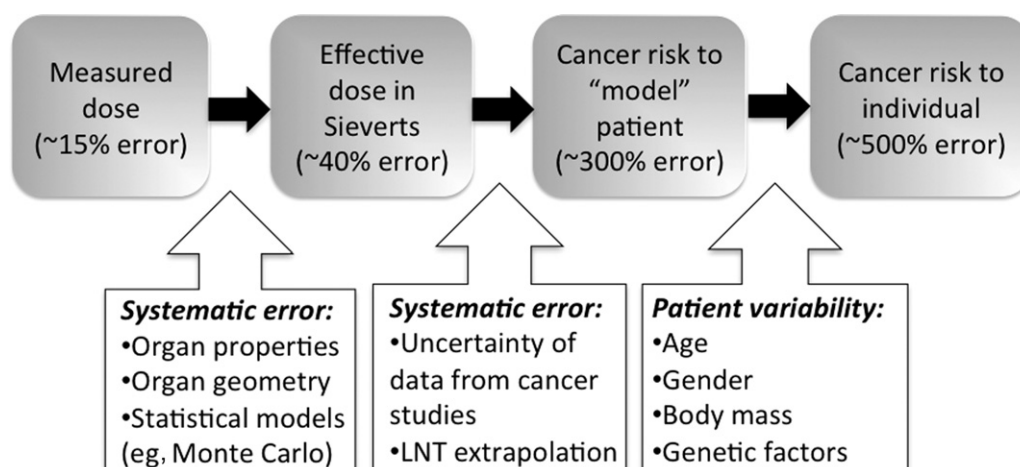


Fig 2. Increasing levels of uncertainty at each step of the dose and risk estimation process using effective dose. Adapted from Martin [11]. LNT = linear no-threshold.

patient dose card for keeping one's personal CDE data close at hand is a good example of a well-intentioned but ill-advised attempt to control medical radiation exposure. Simply being aware of the effective dose to which a patient has been exposed has no rational clinical application. It would be far better to expend time and energy keeping a thorough imaging history to avoid unnecessarily duplicative studies.

For a final analogy, there is a small and stochastic risk that you will be involved in a fatal auto accident on your commute to work. Do you need to keep a record of how many times you have made the commute in the past, and would such a log affect your decision as to whether to make the trip tomorrow? The likely answer is "no" on both counts, both because the prior commutes are irrelevant and because the benefit of work generally outweighs the risk of commuting. CDEs should likewise never dissuade a rational provider from performing a medically indicated scan because past risks cannot be undone. Patients should be imaged only when the possible benefits of the scan under consideration are likely to outweigh its hypothetical risks, regardless of CDE. If performed, the dose of the scan should always be kept as low as possible while preserving the image quality requisite for its clinical indication. To suggest that patients with high CDEs merit some special consideration undermines the universality of these principles, which apply to every patient and every scan.

It is undoubtedly true that there are instances in which CDEs could prove helpful in dissuading overscanning by providers who are not open to rational arguments or lack fundamental knowledge of radiation biology (we will refer to these as "irrational providers" for descriptive rather than pejorative purposes). Although this may constitute an effective short-term strategy, it is a double-edged sword because CDEs can then be used in the future by the same irrational providers as a reason not to

order medically indicated scans. Thus, although it is tempting to use CDEs as a weapon of last resort in dissuading irrational overutilization, it is a tenuous strategy because it ultimately relies on misconceptions about radiation-induced cancer. Even the selective and well-intentioned exploitation of these misconceptions by a radiologist or medical physicist can be perceived as reinforcing them by granting them an expert seal of approval.

CUMULATIVE DOSE ESTIMATES AND IMPLIED CANCER RISKS ARE HIGHLY INACCURATE WHEN APPLIED TO INDIVIDUALS

Even if one is not dissuaded by the arguments above, considerable problems remain when one attempts to inform the care of actual patients with the current real-world measures of CDE, which are neither designed for nor tailored to individuals. Despite popular misconception, neither the volume CT dose index nor the dose-length product reported by a scanner for each patient (and likewise recorded in the dose report for that patient) represent the actual absorbed or effective dose to the patient, despite this implied association [10]. Rather, they reflect the dose that would be delivered to a 32-cm diameter plastic cylinder (phantom) if it were scanned using the same scan technique factors. The same plastic phantom likewise serves as a dose surrogate for each and every patient, regardless of body size (diameter) or body region scanned (abdomen, chest, cervical spine). Compared with the advances in CT image reconstruction, the dose information currently provided by a CT scanner is quite primitive and has remained essentially unchanged for 3 decades. As a result, the uncertainty in metrics of effective dose (in sieverts) is approximately 40% for phantom-based reference patients and exhibits an even larger variation when individual patient characteristics are considered [11] (Figure 2).

Table 2. Summary of irrational and rational uses of CDEs

Irrational uses for CDEs

- Imaging patients with high CDEs more sparingly than other patients
- Quantifying cancer risk for individual patients

Rational uses for CDE (qualifying statements)

- Testing the LNT model in a longitudinal fashion (perhaps not possible in the United States)
- Comparing centers to identify those that overirradiate patients (although the ACR Appropriateness Criteria[®] and ACR Dose Index Registry may be more practical)
- Identifying patient populations at risk to accrue high cumulative doses (although it is unclear what impact such information will have on patients)

CDE = cumulative dose estimate; LNT = linear no-threshold.

Even if there were a method that allowed us to relate CT dose index to effective dose with perfect certainty, there is still considerable uncertainty in the cancer risk associated with effective dose (Figure 2) due to the limitations of the Japanese LSS discussed above. As a result, cancer risk estimates for reference patients have an inherent uncertainty of $\pm 300\%$, which balloons to more than $\pm 500\%$ when accounting for variability due to patient characteristics (eg, age, gender) [11]. The International Council on Radiation Protection [6] offers a specific but oft-ignored admonition that “the use of effective dose is not appropriate for estimating the risk to an individual patient resulting from a diagnostic x-ray exam”; rather, it was designed for use with a specific population in radiation protection. Cumulative dose estimates and their associated theoretical cancer risk will often represent a sum of many separate dose estimates, which will introduce additional systematic errors and further increase the level of uncertainty, such that the risks for individuals calculated on the basis of their CDEs could reasonably be expected to top 500%. Even if CDEs were useful at the bedside, which they are not, this type of information is simply not robust enough to use clinically. Imagine informing a patient that his prior CT scans have led to an excess cancer risk of somewhere between 5% and 25%. How exactly would this affect his subsequent care, other than by adding to his confusion and stress?

SOME RATIONAL USES FOR CUMULATIVE DOSE ESTIMATES MAY EXIST AT THE HEALTH SYSTEMS LEVEL

Although there are obvious limitations to the use of patient-specific CDEs, there are some potential applications that may make individual dose tracking worthwhile (Table 2).

The most important and obvious implication of having CDE data available for a large number of patients is that this represents the best means of “testing” the LNT hypothesis at the low levels of ionizing radiation involved

in diagnostic imaging. Over decades, careful study of the correlation of CDEs with health outcomes in large patient cohorts can potentially revolutionize our understanding of radiation-induced carcinogenesis and its relevance to diagnostic imaging. It would be helpful, of course, if the CDE of the future were based on more realistic patient-specific dose values than those currently provided by the CT dose index. However, it seems reasonable to assume that both our independent variable measurements (eg, current and future CDEs) and our dependent variable measurements (eg, cancer surveillance mechanisms) will be orders of magnitude more precise, accurate, and relevant to the question of medical imaging than LSS data. At the same time, any epidemiologic study that seeks to prove or disprove the LNT would have to be exceedingly large, enrolling hundreds of thousands of patients. Furthermore, such a study would be difficult or impossible to conduct in the United States, where the lack of a national cancer registry would make long-term follow-up extremely costly and logistically difficult.

Another potential use for CDEs is to identify and reduce differences in the quality of care between imaging centers. Data recently released by CMS [12] indicate that some centers expose patients to more radiation than other centers, and similar research in the radiology literature has identified widespread overutilization of high-dose scanning protocols in a manner discordant with the ACR Appropriateness Criteria[®] [13]. Determining system wide benchmarks for average patient CDE (adjusted for diagnosis and overall complexity) would provide an interesting outcome measure that effectively integrates the net impact of local scanning protocols and utilization practices. However, one can argue that the combination of the ACR Appropriateness Criteria (which address utilization) and the ACR Dose Index Registry[®] (which addresses dose and protocol optimization) together sufficiently address these needs without requiring a separate CDE registry.

From a health disparities standpoint, CDE data may help identify patients with chronic conditions or with certain demographic parameters who are at risk for accruing high CDEs regardless of where they are treated. In certain instances, it may be advisable to raise imaging thresholds or generate indication-specific protocols for such populations to mitigate their cancer risk due to imaging in a prospective fashion. One potential example would be a chest CT protocol designed specifically for surveillance scans in children with cystic fibrosis [14].

Generally speaking, the notable feature that these potential rational uses of CDEs have in common is that they are macroscopic, aimed at patient populations rather than individuals, and do not involve real-time decision making at the point of care. At the same time, it is clear that for each of these rational strategies, there are significant hurdles as well as potentially more viable and prac-

Table 3. Summary of our reasoning as to why CDEs are not clinically useful

Reasons CDEs should not be used clinically
<ul style="list-style-type: none"> ● CDE does not influence the risk or benefit of a given CT scan and thus plays no role in deciding whether or not to image a patient ● Cancer risk estimates based on CDEs are so error prone when applied to individuals that they are not clinically helpful even for this purpose ● High CDEs and cancer risks will induce anxiety about exposures that cannot be undone, adversely affecting patients for no rational reason ● High CDEs and cancer risks will be used (irrationally) as justification to avoid medically indicated examinations

CDE = cumulative dose estimate.

tical alternatives. As such, it remains unclear in this era of fiscal restraint whether the sum total of these rational strategies delivers sufficient value to patients to justify the cost of CDE tracking as well as offset the potential misuses of CDE data alluded to above.

CONCLUSIONS

A rational consideration of potential CDE utilization strategies according to the current consensus model of radiation-induced carcinogenesis reveals that there is no role for this information in the care of individual patients (see Table 3 for a summary). On the contrary, CDEs are susceptible to irrational interpretation (by patients and physicians alike) and may actually harm patients by dissuading medically indicated scans. The issue of whether to scan or not to scan will remain a complex bedside decision and does not benefit from CDEs. Although there may be some rational CDE utilization strategies at the health systems level, the practicality and cost-effectiveness of these strategies remain unclear. We thus encourage radiologists, their clinical colleagues, and their professional societies to adopt the stance that CDEs have no role in the rational care of individual patients and are currently useful for research purposes only. Although we

concede that CDEs may occasionally be of use in deterring irrational overutilization, we fear that their widespread clinical use will just as often motivate irrational underutilization.

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