Variability in radiation dose estimates from nuclear and computed tomography diagnostic imaging

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INTRODUCTION

Radiation risk to both the patient and the imaging personnel from medical imaging procedures involving the use of ionizing radiation is a point of concern and controversy in the diagnostic imaging community. With the increased utilization of computed tomography (CT) imaging both standalone and in conjunction with nuclear tomographic imaging (positron emission tomography [PET] and single-photon emission computed tomography [SPECT]), radiation risk has received significant attention both scientifically and in the public media. Several studies are reporting significant increased risk to the patient receiving low ionizing radiation from CT and nuclear studies.1-3 These presentations lead to many questions by the imaging community on what is best for their patients, and some imaging centers are using tabulated dosimetry values to help determine the imaging protocol without a clear understanding of relative certainty in the tabulated values.

The presentation of risk data in “cancer units” has generated concern and questions from patients, referring physicians, and diagnostic imaging professionals. The expression of radiation dose in units of cancer risk is misleading for a number of reasons. First, radiation dosimetry values for radiopharmaceuticals are in general subject to considerable uncertainty,4,5 as they are based on limited biokinetic data (taken from a handful of patients or from animal data) and are derived for ‘reference’ (median) individuals (adult males, females, etc.). Doses to individual patients have significant variability due to the stochastic nature of radiation dosimetry. Second, while average dosimetry or cancer risk values can be expressed for a population, the absolute, incremental cancer risk value for any given individual from a given radiation exposure (e.g., due to a myocardial perfusion SPECT study) may not be derived from these population models. Furthermore, the confidence limits for the dose and risk estimates are not defined, and thus individual risk values should not be reported as a deterministic value with known confidence limits.

Also of importance is the uncertainty in converting radiation dosimetry to cancer risk. The extrapolation of radiation dosimetry to cancer risk is based on the linear, no-threshold (LNT) hypothesis. This hypothesis is the subject of considerable controversy as there are no data available at the dose levels experienced in diagnostic medical imaging. The data for diagnostic imaging dose level are extrapolated from observations of cancer incidence from survivors of the atomic bomb detonations and other populations exposed to high doses and dose rates. The LNT works well in defining conservative guidelines for the safe use of radiation and other forms of policy setting. However, its use to predict cancer incidence or deaths at low doses and dose rates remains a matter of considerable scientific discussion and controversy. Reporting of numerical estimates of risk associated with individual dose levels associated with particular nuclear medicine and/or CT exams represents a use of the LNT model that is inappropriate given our current understanding of the risks associated with low
doses and dose rates, such as are received in such examinations.

This statement, the first of the series, will briefly outline the contributing factors used in tabulating radiation dosimetry values for various cardiac nuclear and CT diagnostic studies. Emphasis will be provided to address the relative uncertainty in tabulated dosimetry values and the relevant importance in using these values when choosing an imaging protocol for a diagnostic study. Expanding on the uncertainty in the LNT hypothesis and its use in deriving cancer risk from dosimetry will not be addressed in this statement.

INTERNAL RADIONUCLIDE DOSIMETRY

Dose Estimation

Internal radionuclide radiation dosimetry deals with the determination of the amount and the spatial and temporal distribution of radiation energy deposited in tissue by radionuclides within the body. The energy deposited per unit mass of material is the absorbed dose where the conventional and the System Internationale (SI) units are the rad (equal to 100 erg/g) and the Gray (Gy) (equal to 1 J/kg), respectively. The calculation of internal absorbed dose requires knowledge of a number of factors and, in practice, rests on a number of assumptions. The pertinent quantities include:

1. The amount of radioactivity administered—the administered activity;
2. The rate of radioactive decay of the administered radionuclide—the physical half-life (or decay constant);
3. Each type of radiation emitted by the decaying radionuclide and its frequency and average energy of emission—the equilibrium dose constant;
4. The fraction of the administered activity which localizes in each tissue or organ—the uptake or, more completely, the time–activity function;
5. The length of time the radioactive material resides in each tissue or organ—the effective half-time (or residence time)—as derived from the time–activity function;
6. The total number of decays (nuclear transitions) which occur in each tissue or organ—the cumulated activity (equivalent to the integral of the time–activity function);
7. The size (mass) and shape of each organ and the distances between organ pairs;
8. The fraction of radiation energy which is absorbed in the tissue or organ itself as well as in other tissues and organs—the absorbed fractions or “‘S’ factors” (which depends on the size and shape of organs and the distances between organ pairs).

The standard methodology used for internal dose calculations in medicine was developed by the Medical Internal Radiation Dose Committee (MIRD) of the Society of Nuclear Medicine (SNM) and is generally referred to as the “MIRD schema” or “MIRD formalism.” Similar reference data have been developed by the International Commission on Radiological Protection (ICRP). Dosimetry for diagnostic radiopharmaceuticals is generally based on (a) average organ time–activity data in animal models and/or in a small cohort of human subjects and (b) age- and gender-specific “average” models of human anatomy. To the extent that specific patients deviate kinetically and anatomically from the respective kinetic and anatomic averages, tissue dose estimates will be erroneous and individual patient variations in anatomy and in radiopharmaceutical kinetics may result in substantial deviations from population-average dose estimates. However, nuclear cardiology and, to a large extent, nuclear medicine are diagnostic specialties, and the associated risk–benefit analyses implicitly performed by the clinician are straightforward: relatively low administered activities yield important diagnostic information whose benefit far outweighs any potential stochastic risk associated with the attendant normal-tissue radiation doses. Such small risk–benefit ratios are very forgiving of possible inaccuracies in dose estimates.

Uncertainties in Dose Estimates

It is difficult, and perhaps impossible, to actually derive the errors in absorbed dose estimates to the organs of an individual patient calculated on the basis of reference dose coefficients (such as the rad-per-mCi administered values tabulated in a radiopharmaceutical’s Package Insert). With respect to the foregoing enumeration of pertinent quantities, the administered activity (quantity 1) can be accurately measured in a dose calibrator and the contribution of the error in this measurement to the overall error in the organ–dose estimates can be considered negligible. The physical half-life and equilibrium dose constants (quantities 2 and 3, respectively) are well-defined parameters of a radionuclide and the errors in authoritative reference values of these parameters can likewise be considered negligible, except in some cases involving particularly low energy or low abundance emissions, like Auger electrons. The differences in the organ-specific time–activity functions and cumulated activities (quantities 4, 5, and 6) between those measured in animal models or a human-subject cohort and in an individual patient can be substantial and are the largest source of error. Aydogan et al.'s systematically evaluated uncertainties in dose estimates for an 123I-labeled brain agent, propagating error across all terms, using first-order error propagation.
and Latin Hypercube Sampling methods. They found that variability in reported dose estimates may be as much as a factor of two, and were most heavily influenced by interpatient differences in radiopharmaceutical biokinetic parameters and target organ mass. It is of course essential to propagate ALL sources of error, even minor variations in decay data, through the dose equation described above.

Intuitively, such errors are likely larger when the reference dose coefficients are based on animal rather than human time-activity data. Further, even if determined in a human cohort, such errors may be exacerbated if the time–activity data were measured in healthy human subjects free of the various pathologies encountered among patients undergoing nuclear cardiology and nuclear medicine tests. The anatomic differences in total-body and organ sizes and shapes and in the distances between organ pairs (quantity 7) and therefore differences in organ-to-organ absorbed fractions between the pertinent anthropomorphic model and an individual patient may likewise be considerable. The quantitative effects of such differences are “compensatory” to some extent and minimize their impact. For example, if a patient is larger than the “matching” anthropomorphic model, each larger organ of the patient will absorb a larger fraction of radiation energy than the corresponding anthropomorphic organ, resulting in an over-estimate of the organ dose. However, because absorbed dose is the ratio of energy absorbed to mass, the larger organ masses compensate at least in part for the larger energies absorbed and thereby maintain the organ-dose estimates in the phantom matched relatively closely to those in the patient. Nonetheless, anatomic differences between the respective anthropomorphic phantoms and individual patients introduce an additional dosimetric error, and a value of 10% to 20% is probably not unreasonable.

Dr. Robert Loevinger, one of the originators of the MIRD schema, has cogently stated that “…there is in principle no way of attaching a numerical uncertainty to the profound mismatch between the patient and the model (the totality of all assumptions that enter into the dose calculation). The extent to which the model represents in some meaningful way a patient, or a class of patients, is always open to question, and it is the responsibility of the clinician to make that judgment.” Recent data report that organ doses for individual patients derived from reference dose coefficients are generally accurate to no better than 30% to 50% and variability may be as much as a factor of 2 or more.4,5

**Strategies to Minimize Dose**

Three variables are important in the internal dosimetry of nuclear cardiology protocols: (i) the biologic half-life or clearance of the radiopharmaceutical(s), (ii) the amount of radioactivity administered, and (iii) the choice of acquisition and processing protocols. Careful attention to optimization of each of these factors can decrease dose to patients.

1. **Optimization of clearance.** There are few practical interventions than can increase clearance of radiopharmaceuticals. Encouraging oral hydration after injection can decrease time to micturition, thereby decreasing doses, especially to the urinary bladder. This should be applied with caution in patients with congestive heart failure.

2. **Optimization of activity administered.** The administered activity should be adjusted such that a quality diagnostic study is expected in a clinically reasonable time. Standard ranges of administered activities for common SPECT protocols are defined in the ASNC Imaging Guidelines.10 These doses, based on collective experience in the field, represent the lowest activities compatible with obtaining the necessary diagnostic information from the test. In most cases, there is no margin for further reducing the activity without compromising the medical value of the procedure. Administered activities can be decreased at the expense of increased imaging time. However, acquisition times that are too long commonly present motion artifacts in the images as the patient may be unable to remain still during the entire acquisition.

3. **Selection of protocols/radiopharmaceuticals.** Current standard practices, reflected in ASNC guidelines, offer physicians performing cardiac SPECT stress testing a variety of protocols from which to select balancing patient comfort/scheduling and diagnostic benefit. These protocols have been designed to minimize patient risk (i.e., radiation dose) while maintaining the diagnostic benefit of the test. Recent advancements in camera and processing technologies may provide comparable diagnostic information with a fraction of the currently prescribed dose. These new technologies are currently being validated to assure that the current levels of diagnostic benefit are maintained for the patient.

**EXTERNAL DOSIMETRY FROM CT**

**Dose Estimation**

The effective dose ($E$) of a CT examination reflects the non-uniform radiation absorption of the partial body exposure relative to a whole-body radiation dose. It is calculated from the dose to individual organs and the relative radiation risk assigned to each organ.
Appropriate organ risk weighting factors have been published by the ICRP, and several calculation methods exist for the determination of $E$. Approaches to measure $E$ include the physical measurement of ionizing events in physical phantoms through one of several different techniques, and computer simulation from a mathematical patient phantom and model photon transport (i.e., Monte Carlo Simulation). One relatively simple method, which is frequently used clinically, estimates $E$ from the dose length product ($DLP$) as displayed by the CT scanner using the following relationship:

$$E = k \times DLP$$

Values for the conversion factor $k$ have been published for the head, neck, abdomen, and pelvis. The $DLP$ is an indication of the integrated radiation dose of the entire examination and incorporates the scan time

$$DLP = CTDI_{vol} \times scan\_length$$

where $CTDI_{vol}$ is the volume computed tomography dose index and the $scan\_length$ is a measure of the length of body irradiated in cm. This index is an indication of the magnitude of doses that is delivered to the patient which is dependent on the scanner model and acquisition protocol. The $CTDI$ patient estimates, as provided by the scanner, are extrapolated from dosimetry values based on measurements of a dosimetry phantom. This estimate of $E$, while fairly simple, generally agrees with more complex measurements, usually varying by no more than 10% to 15%.

**Uncertainties in Dose Estimates**

The effective dose calculations use many assumptions and $E$ describes the relative whole-body dose for a particular examination. It should be stressed that effective dose ($E$) is not the received radiation dose for any particular patient. It is rather, a useful concept for comparing the relative radiation detriment among diagnostic procedures and protocols, when the calculated doses are for patient populations with comparable age and sex distribution. It is also important to remember that these radiation dose calculations are estimates, which are based on many assumptions. Sources of error in estimating $E$ in CT examinations include the following:

1. **Body size.** Patients who are larger than ideal size absorb more radiation, and to different organs than usually estimated. Also, the weighting factor of dosage depth does not take into consideration patient size.
2. **Gender differences.** For example, the female breasts have a higher sensitivity to the effects of radiation than those of the male. The female gonads may receive more radiation scatter than those of the male, depending on the part of the body undergoing the CT examination.
3. **Body position.** For example, a CT examination of the chest with the patient in the supine position is associated with a lower effective dose than the same examination in the prone position because of issues related to the depth of X-ray penetration.
4. **Individual variation from average models.** For example, individual organ sensitivity may vary from idealized models because of age, organ size, or location.
5. **Method uncertainty.** Errors in exposure dose measurement as each technique has limitations.

McCollough and Schueler\textsuperscript{11} in a recent review concluded that “a factor of 2 difference in estimate in effective dose is neither atypical nor of serious concern.”

**Methods to Minimize Dose**

While it is logical and in keeping with the principles of ALARA to use the minimum radiation dose necessary in cardiac CT examinations, there are little data testing the effect of specific radiation sparing approaches on diagnostic quality. Cardiac CTA imaging protocols are also not standardized and maintaining diagnostic accuracy is important. An examination which is non-diagnostic, of course, exposes the patient to radiation without benefit. However, the experience of numerous physicians is that through attention to detail of the CT acquisition, excellent image quality can be maintained at a lower radiation exposure.

Consideration of the following acquisition parameters should be made to minimize the dose to the patient.

1. **Scan length (in cm).** The region of the patient’s body in the FOV is variable in the Z direction and affects radiation absorption (via changes in the DLP). For cardiac CT examinations, proper attention to scan length should be made. For example, rather than rigidly scanning from carina to diaphragm (frequently recommended by scanner manufacturers) the operator should review the examination of the preliminary calcium scan, to set the upper limit above the apex of the left anterior descending artery (the highest artery) and the bottom of the posterior descending artery, leaving sufficient but not excessive margins, cranial and caudal, to the heart to allow for movement.\textsuperscript{12} If no calcium score is done, the levels can be set from mid-pulmonary artery to diaphragm below the heart. It is also vital to instruct the patient to breath-hold to the same depth as the arteries may otherwise be cut off. Multipurpose
examinations of the chest tend to have long Z-axis acquisitions. For example, both scan length and scan time are affected by the decision to do a full-lung “triple rule out” examination and there is a consequent marked increase in radiation exposure. Thus, there must be a rational reason to use this technique.

2. **Scan time (in seconds).** Scan duration is a variable affected by the table pitch in helical scans, which is in turn affected by the number of slices in the scanner, the size of the detector array, and the use of additional modalities such as dual source tubes. It is also obviously affected by scan length as well as slice thickness, with increase in thickness leading to faster pitch, shorter time, and lower dose. The radiation dose is approximately proportional to the duration of the scan.

3. **Tube amperage.** Tube mA is a variable setting that affects the number of photons generated and so affects image signal/noise. Radiation dose is approximately proportional to mA, and customarily, amperage can be adjusted for body mass and configuration. Patients with higher mass will experience higher photon scatter and higher noise, while thinner patient can obtain images of good quality using lower amperage. Failure to adjust mA downward for thin patients will result in unnecessary radiation.

4. **Tube voltage.** Tube kVp affects the peak photon energy and affects image contrast. In general, kVp is less frequently adjusted for body mass than mA, although new studies suggest that protocols utilizing 100 or 80 kVp may be effective in thin patients for reducing dosage in coronary calcium measurements or coronary CT angiography without degrading diagnostic accuracy. Tube voltage has a more dramatic effect on radiation dosage, which varies approximately with the square of the kVp.

5. **Electrocardiographic pulsing.** Current generation scanners are capable of varying tube current output (mA) in synchrony to the patient’s electrocardiogram. This is done to reduce radiation during phases in the cardiac cycle when the heart is moving more dynamically. The ideal “pulsing window” (when current becomes maximal) is as short as possible. This becomes a complex decision as there is a trade-off between pulse width, heart rate, and scanner type. All current-generation cardiac-capable scanners have built-in software that either varies pulsing window width with heart rate or allows the operator to customize these protocols. The use of ECG pulsing can decrease radiation dose by 50% or more and is generally recommended unless other parameters threaten the image quality (such as irregular heart rate).

6. **Patient body mass.** The decision whether to image a particular patient becomes complex when scanning patients above ideal body mass. In general, these patients will experience higher than usual radiation doses because of scatter and the requirement for high tube output. When added to an increase in failure rate due to poor image quality, consideration of risk–reward needs to be made.

7. **Scanner type.** In general, increasing the number of detector-rows and reducing detector size tends to increase the radiation dose due to the increasing surface area of lead collimators (which can only be so thin while still being effective) in comparison to detector area. This is balanced against reduced scan time so the end result is complex. In addition, complex effects are also produced by dual source scanners which have two X-ray sources and detector rings operating during the scan time, but have a reduced scan time and heart rate variable pitch. Theoretically, dual source scanners reduce the scan duration because their faster temporal resolution allows imaging faster heart rates thereby reducing diastolic time. In practice, this effect is balanced by the need for wider pulsing windows at higher heart rates due to dynamic heart motion.

8. **Sequential scanning vs retrospective gating.** Because variable reconstruction windows have typically been necessary, retrospective gating is standard, but this results in longer effective scan durations because some tube output is present throughout the cardiac cycle (although not constant if ECG pulsing is used). In patients with slow and very steady heart rates, extremely low radiation doses can be achieved by sequential scanning with tube output only during a narrow ECG window. This is not in general use, but is an active area of developmental work.

**SUMMARY**

All diagnostic imaging protocols should be constructed to minimize the radiation exposure to the patient while providing the best possible information for an accurate diagnosis. Diagnostic imaging saves thousands of lives each year by providing medical information to the physician for better medical management of the patient for the overall outcome of the patient’s health. While there may be a finite risk associated with a diagnostic study using low level ionizing radiation, the typical patient presents a higher risk by not having the imaging study performed.

There is considerable uncertainty in dosimetry point estimates for both nuclear and CT imaging protocols. Due to the large uncertainties inherent to the tabulated
values and the additional uncertainty when applied to a specific body habitus, small difference in dosimetry values should not be used solely to define the appropriate imaging protocol. When choosing a diagnostic protocol careful consideration should be given to the incremental diagnostic benefit versus the radiation risk. Also due to the high uncertainty in patient-specific doses estimates, cumulative dose monitoring on a patient basis is difficult to estimate, thus making decision to perform a diagnostic test based solely on radiation risk problematic and uncertain.

Reducing radiation dose to the patient should always be a primary consideration in the development of new or modification of existing protocols. However, the reduction should not impact the quality and accuracy of the clinical information from the study.

The risk of the study should never be considered without considering the benefit or the risk of not doing the study. While the benefit of a test is difficult to quantify, its estimate likely has comparable uncertainty as the radiation risk.

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**Acknowledgment**

Dr. Budoff is a member of the speakers bureau for GE Healthcare. Dr. Einstein receives grant support from Covidien, is a consultant for GE Healthcare, and has travel expenses covered by GE Healthcare, INVIA, Philips, and Toshiba America Medical Systems. Dr. Bateman serves as a consultant to Bracco, Covidien, and Lantheus Medical Imaging.

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