Dosimetry of Internal Emitters.

Lawrence E. Williams PhD

An Liu PhD, Andrew Raubitschek MD and Jeffrey YC Wong MD,
City of Hope, Duarte CA USA.

Strictly speaking, organ dosimetry is not possible. One can only estimate absorbed doses using mathematical expressions. Thus, a better title for this lecture would be **Estimation of Internal Emitter Doses**. This logical restriction follows from the invasive nature of TLD or other dose measurement device being inserted into normal tissues. Additional problems would occur with dosimeter insertion into tumor sites.

A similar argument holds in the cases of brachytherapy and external beam therapy. Their "dosimetries" are also estimations for the same reason.

E-mail contact: lwillliams@coh.org

There are two types of estimates of internal emitter absorbed dose.

Type I

This type refers to a phantom-based estimate. A typical phantom is produced by or for the MIRD Committee and is available via Mike Stabin's MIRDOSE3 Program. There are two general reasons for a type I estimate:

a. Legal considerations such as a FDA IND application or use by radiation safety committee at local institution. A very common Type I result.

b. Scientific dose comparison of two or more pharmaceuticals that target the same structure, tissue or molecule. A rare Type I result.

Type II

This estimate refers to a patient-specific computation. Such calculations are usually done as treatment plans for an individual about to undergo Radioimmunotherapy (RIT) or some other form of internal emitter therapy. Anatomic data are required and are provided by CT, MRI or other studies. This is a relatively new kind of estimate and is of direct clinical significance. It is analogous to treatment planning in external beam therapy. Type II computations are rare, but becoming more common. As RIT and other internal emitter therapies come into clinical practice, the medical physicist may be involved in Type II estimates on a recurring basis.

Standard Method of Radionuclide Dose Estimation.

This method can be applied directly to Type I computations and indirectly to Type II estimates. It is extensively covered in the MIRD Primer and other MIRD Committee literature. It may be obtained from Professor Mike Stabin at Vanderbilt University as program MIRDOSE3.

There are three steps in the method.

1. Measure organ uptake (A).

2. Model the organ biodistributions to integrate the A values. The result is a set or vector of time integrals (Ã) that must go to long times such that all decays are counted.

3. Calculate the Absorbed Doses

$$D = \mathbf{S} * \tilde{A} \qquad (1)$$

Our eq.(1) calculation provides only an ***average*** organ dose D. It is a matrix (**S**) operation whereby the Dose and Ã vectors usually have very different dimensions with those of D being larger than Ã. There is an inherent difficulty in obtaining patient time-activity data for a large number (e.g. > 5) of organs.

The rectangular matrix **S** has been previously generated using Monte Carlo (MC) methods and a standard mathematical formula for the surfaces of the body and its internal organs. Approximately 10 such phantoms are available in MIRDOSE3. This software is available free-of-charge.

Thus, for a Type I estimation, the physicist only needs to obtain and integrate the activity vector for a set of imaged organs. We will discuss Type I computations initially.

Determination of Activity (A) in a Patient's Normal Tissue and Tumor.

Methods Available.

1. Geometric Mean of Two Opposed Views (GM).

2. CAMI (CT – Assisted Matrix Inversion) Method.

3. Quantitative SPECT.

4. PET Imaging with SUV outputs.

We note that determination of A is the "the problem" in Nuclear Medicine. No standard method exists after 50 years of investigation.

PET offers an ideal way to obtain percent injected dose of activity per gram of tissue (%ID/g) in normal organs and tumor sites. Attenuation corrections are built into the PET algorithms from the beginning.

Integration of Time-Activity Curves to Determine $\tilde{A}$.

Three methods of integration are generally used.

1. Multiple exponential fits to organ or tumor data. Open model.

2. Closed compartmental models whereby one organ is connected to another via linear rate constants. Radioactive decay is one of the clearance constants for a given organ. Note that imaging and tumor therapy labels may not be the same. For example modeling may occur with In-111-Mab so as to predict the eventual patient therapy with an identical Y-90-Mab.

3. Numerical integration. Difficulty in interpolation and extrapolation of organ activities makes numerical results suspect.

Two Corrections to MIRDOSE3 Estimates of Absorbed Dose.

1. Correct Ã (patient) to allow substitution into the MIRDOSE3 program.

This is done in a Type I estimation. It is required since the patient or volunteer does not have the same organ mass sizes relative to total body mass as the nearest relevant phantom available. For example, assume a female patient having the same total body mass as the adult female MIRD phantom. Yet the woman may have a kidney set that is twice the size of that used in the adult female phantom. Her renal uptake must then be scaled downward by a factor of two before being inserted into the standard dose formula (1) cited above.

In formula: $\tilde{A}(\text{MIRD}) = \tilde{A}(\text{patient}) * \frac{m\ (\text{MIRD})/M\ (\text{MIRD})}{m\ (\text{patient})/M\ (\text{patient})}$ (2)

The multiplication in eq.(2) is essentially a perfusion correction where m is the organ mass and M the total body mass. We would retain the standard S values for the resultant dose estimates that refer to the **phantom**. Again, this is a Type I result.

2. Correction for organ **S** values in MIRDOSE3 to Compute a Patient-specific average organ absorbed dose.

This is a Type II calculation and **S** is corrected via:

$\mathbf{S}_{np} = \mathbf{S}_{np}\ (\text{MIRD}) * m\ (\text{MIRD})/m\ (\text{patient})$ (3)

Where np implies non-penetrating radiation (beta or alpha) used to effect the therapy. This correction follows from the fact that dose (and **S**) goes inversely with mass of the target organ or tissue.

We have neglected photon contributions in eq. (3). Such terms are, by definition, small relative to the particulate contributions.

Errors in Absorbed Dose Estimates.

1. The A value is uncertain to +/- 30% in GM. CAMI leads to errors of +/- 10% in anthropomorphic phantoms.
Problems occur due to confusion of two organs into one object by the radiologist or physicist. A particular difficulty for the cancer patient. Fusion of anatomic with nuclear images is recommended in the determination of which organs and tumors are visible.

2. Ã, the time integral of A, is uncertain to +/- 10% due to integration and modeling difficulties. Either open or closed models are possible. Numerical integration is not as wise since it may neglect biological clearance.

3. $\mathbf{S}_{np}$ for non-penetrating radiation is uncertain up to factors of two or three-fold due to variation in patient organ masses. This is, by far, the largest error in eq. (1). Thus, anatomic imaging is required. Since we deal with cancer patients, these data are usually available.

Conclusions on Internal Emitter Absorbed Dose Estimates.

Two types of dose estimation are required for internal emitters. Type I refers to the legal and scientific application and uses a MIRD phantom – usually the adult male or female. Type II refers to patient-specific estimation and is a treatment plan. Here, the physicist will estimate the total activity limit given an organ absorbed dose limit. Such limits are typically taken from external beam practice. Their applicability to the slowly delivered dose in RIT can be questioned, however.

Average organ doses can presently be estimated using MIRDOSE3 and appropriate corrections. These results can be uncertain to factors of two or three-fold unless organ mass and whole body mass corrections are made. Anatomic data are essential in the corrections.

Eventually, point source functions or Monte Carlo calculations will be done for the specific patient so that Type II computations will not require use of any MIRDOSE phantom **S** values. A novel feature of such future computations of dose will be the ability to separate organs; e.g., obtaining an estimated dose to the right kidney vs. an estimated dose to the left kidney. In the MIRD strategy, the two kidneys were used as a **single target** in the original MC computation. We realize that the right kidney is often within the space of the liver. If we have elevated hepatic uptake, the right kidney will receive substantially more radiation dose than the left. This will be part of the treatment planning. A similar MIRD simplification argument holds for the left and right lung, and the two cerebral hemispheres.

Another advantage of future estimates made with point source or complete MC calculations is that dose-volume histograms will be an intrinsic output of the algorithm. Such results will be directly analogous to similar developments going on in external beam treatment planning. Average dose, like any average parameter, is essentially not worth as much as the distribution it was derived from.

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