

The recent approval of ^{90}Y -labeled Zevalin™ (IDEC Pharmaceuticals Corp., San Diego, CA) for radioimmunotherapy of non-Hodgkin's lymphoma has highlighted the regulatory requirement of patient-specific internal radiation dosimetry during clinical trials, to assess the safety and efficacy of targeted therapeutic radiopharmaceuticals.

The currently accepted methodology for calculating individualized absorbed dose estimates employs the MIRDO model of absorbed dose in reference phantoms, $S \times \bar{A}$, where S is average absorbed dose per decay for a given target volume and radionuclide, and \bar{A} is the total number of decays in a given source volume. Patient-specific values of \bar{A} are computed from serial whole body gamma camera images for critical organs (kidneys, liver, lungs, spleen) and tumors, and from blood samples (for marrow dosimetry), using a pre-treatment, diagnostic administration radiolabeled with either the therapy radionuclide (e.g., ^{131}I), or an imageable surrogate (e.g., ^{111}In for ^{90}Y). A transmission scan of a radiation source through the patient may be included, for gamma ray attenuation correction, D , and reference sources of the radionuclide included for instrument calibration (counts/min/ μCi , C). The formula for \bar{A} is given by:

$$\int_0^{\infty} A(t) \times D / C dt$$

where $A(t)$ is counts/min obtained from the gamma camera image or blood sample at time t . The value of S , and thus absorbed dose, should be corrected for patient organ mass, M_p (e.g., via CT or MR volume measurements), by the factors M_r/M_p (for β 's) and $[M_r/M_p]^{1/3}$ (for γ 's), where M_r is the MIRDO reference organ mass.

Current methods provide gross estimates of average dose over whole organ or tumor volumes, and thus cannot answer local dosimetry questions. Voxel-based (3D) methods are under development, which utilize quantitative SPECT images and CT or MR images as inputs to radiation transport algorithms, to allow computation of isodose contours and DVHs, as used in radiotherapy treatment planning.

The current approved regimen for Zevalin radioimmunotherapy requires pre-treatment whole body imaging of ^{111}In -Zevalin at 2-24 hr, 48-72 hr and (optionally) 96-120 hr, to qualitatively assess whether the biodistribution is acceptable. This requirement leaves open the possibility of future pre-treatment, patient-specific dosimetry, which is enabled by the addition of an immediate (0 hr) whole body image, or a transmission image and reference source, and which the medical physicist may be asked to perform.

Siegel JA, Thomas SR, Stubbs JB, et al. MIRDO Pamphlet No. 16. *J Nucl Med* 1999; 40:37S-61S.

Wiseman, G. A., Kornmehl, E., Leigh, B., et al. Radiation Dosimetry Results and Safety Correlations from ^{90}Y -Ibritumomab Tiuxetan Radioimmunotherapy for Relapsed or Refractory Non-Hodgkin's Lymphoma: Combined Data from 4 Clinical Trials. *J Nucl Med* 2003; 44:465-474.

Bolch WE, Bouchet LG, Robertson JS, et al. MIRDO Pamphlet No. 17. *J Nucl Med* 1999; 40:11S-36S.

Educational Objectives:

1. To understand the physics and technical aspects of quantitative imaging and blood sampling for radioimmunotherapy dosimetry.
2. To obtain knowledge of the current computational framework for estimating absorbed dose in critical organs and tumors from internally administered radionuclides.
3. To become familiar with voxel-based methods of estimating absorbed dose from internally administered radionuclides.