

Image Based Radionuclide Dosimetry Techniques

Eric Visser (Nijmegen)

Quantitative imaging using PET/(CT) or SPECT/(CT)^[1,2] is essential for radionuclide dosimetry. Dosimetric models rely on the quantitative uptake (that is in Bq and not in arbitrary "count" units) of the radiopharmaceutical in whole organs, tumours, specific tissue, or in individual image voxels.

As opposed to external beam radiotherapy, where the radiation dose is administered only during a limited time, in radionuclide therapy, the radiopharmaceutical resides in the patient's body and gradually reduces in concentration due to biological clearance and physical decay. For this reason, the time-integrated activity is needed, and several scans have to be made in the course of time to adequately perform this integration. The number of scans is usually determined by a trade-off between numerical accuracy of the dose values on one side, and patient comfort, personnel and financial aspects on the other side. Typically, 3 – 5 scans are made in dosimetry studies.

The European Council Directive 2013/59/EURATOM requires amongst others the following (article 56): "... exposures of target volumes shall be *individually planned* and their delivery appropriately verified, taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure". Although there might be some discussion as to how "individually" should be exactly interpreted, this directive is a strong case for individual patient-based and predictive radionuclide dosimetry.

During the last decades, many important improvements have taken place in radionuclide dosimetry:

- (i) 2D, planar gammacamera imaging has been replaced by 3D, SPECT imaging. In this way, the problem of overlapping organs and inadequate attenuation correction has been dealt with, thus leading to better quantification of radiopharmaceutical uptake in tissues and organs and, if necessary, on the voxel basis.
- (ii) CT has been added (SPECT/CT) which allowed for better, patient-specific attenuation and scatter correction.
- (iii) Dosimetric models have evolved throughout the years. Originally, the MIRD formalism^[3] was carried out for whole organ dosimetry. In this approach, the organ dose originates from the time-integrated activity in all other organs and is assumed to be the sum of all these contributions scaled by S-factors. S factors form a matrix (S_{ij}) expressing the contribution of the activity in "source" organ j to the dose in "target" organ i. These S-factors have been pre-calculated using Monte Carlo simulations for computational phantoms representing e.g. adult male, female, children of several ages, pregnant women, etc. The S-factors as obtained by these first "stylized" mathematical phantoms have been widely used e.g. in the popular OLINDA software package^[4]. However, more realistic, voxel based phantoms have been used to obtain S-factors for many different ages and body sizes. The recently released version OLINDA 2.0 e.g. is based on these types of computational phantoms^[5].

When using the MIRD formalism, one is able to use individual patient data (that is time-integrated activity coefficients) for dose calculations assuming that each patient can be more or less realistically represented by a certain computational phantom. However, this may not always be the case, and furthermore, only mean organ doses are being calculated, leaving doses to tumours, glands or other non-organ tissues unaddressed. A further step toward individual dosimetry is obtained by voxel-wise calculations of doses based on time series of 3D quantitative images for each patient separately. In the ideal case, full Monte Carlo simulations are being done using the activity from SPECT or PET, and the electron density from CT to simulate the absorption of the emitted particles (which is another advantage of CT next to its use for attenuation and scatter correction). However, these calculations are very time consuming (they may last a day or more), and are thus not very attractive for the clinical practice. An alternative approach is obtained using the convolution of the voxel activity with radionuclide- and tissue-dependent dose kernels^[6]. This method is fast, but it should be mentioned that it is only appropriate for homogeneous tissue. Another approach consists of using full Monte Carlo simulations for the photon interactions, while assuming local absorption of the electrons, thus reducing the simulation time to typically 5 – 10 minutes^[7].

In this lecture, I will present and explain the above-mentioned issues with the emphasis on the practical approach and the techniques that have to be used. These include amongst other the way to obtain quantitative images, the alignment of CT and SPECT images, the role of the partial volume effect, the drawing of regions or volumes of interest, the working of OLINDA.

References:

1. Bailey, D.L. and K.P. Willowson, *An evidence-based review of quantitative SPECT imaging and potential clinical applications*. J Nucl Med, 2013. **54**(1): p. 83-9.
2. Bailey, D.L. and K.P. Willowson, *Quantitative SPECT/CT: SPECT joins PET as a quantitative imaging modality*. Eur J Nucl Med Mol Imaging, 2014. **41 Suppl 1**: p. S17-25.
3. Bolch, W.E., et al., *MIRD pamphlet No. 21: a generalized schema for radiopharmaceutical dosimetry--standardization of nomenclature*. J Nucl Med, 2009. **50**(3): p. 477-84.
4. Stabin, M.G., R.B. Sparks, and E. Crowe, *OLINDA/EXM: The second-generation personal computer software for internal dose assessment in nuclear medicine*. Journal of Nuclear Medicine, 2005. **46**(6): p. 1023-1027.
5. Stabin, M.G., et al., *Realistic reference adult and paediatric phantom series for internal and external dosimetry*. Radiat Prot Dosimetry, 2012. **149**(1): p. 56-9.
6. Grassi, E., et al., *Quantitative comparison between the commercial software STRATOS((R)) by Philips and a homemade software for voxel-dosimetry in radiopeptide therapy*. Phys Med, 2015. **31**(1): p. 72-9.
7. Hippeläinen, E., M. Tenhunen, and A. Sohlberg, *Fast voxel-level dosimetry for (177)Lu labelled peptide treatments*. Phys Med Biol, 2015. **60**(17): p. 6685-700.