Multi-Centre Trials involving Radionuclide Therapy

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Multi-Centre trials involving radionuclide therapy often require the acquisition and evaluation of patient-specific dosimetric data for proving the safety or efficacy of a treatment regimen. Internal dosimetry in nuclear medicine could be based on the so called “MIRD formalism”, first standardised in the 1960’s [1], with the initial aim of estimating average doses to critical organs resulting from diagnostic procedures.

Essentially this methodology allows the calculation of absorbed dose using the simplified version of the basic equation: \( D = A \times S \).

- \( D \): the mean absorbed dose to a target region from the cumulated activity in a source region.
- \( A \): the cumulated activity (i.e. the integral of the activity-time curve from zero to infinity) in a given source region. \( A \) denotes the total number of radioactive decays occurring within an organ in which a radiopharmaceutical accumulates.
- \( S \): the radionuclide specific S factor per unit cumulated activity in a source region. This factor accounts for the energy released from each radioactive decay and the relative geometry of the source organ and the organ for which the absorbed dose is to be calculated.

The cumulated activity is dependent on biological parameters whilst the S factor deals with the physical components of the absorbed dose. There is no assumption with respect to the source or target other than that the radioactive distribution is homogeneous in the source region.

Patient-specific absorbed dose calculations for tumours and for normal organs present two main challenges:

1. The first is that of the assessment of the in-vivo biokinetics (the “time-activity curve”). This is done either by image quantification or by external counting / dose rate measurements with probes. The counts recorded in an image or by a probe will be converted to absolute or relative values of activity. The biokinetics in blood or blood-related tissues will be determined via in-vitro measurements of the activity concentration in the corresponding samples.

2. The second issue that arises is that of the absorbed dose calculation itself, and particularly the need to deal with problems caused by a non-uniform uptake of activity and by non-standard organ geometries. A comprehensive overview on methods and instrumentation is compiled by the MIRD committee and published in pamphlet 16 [2].

For dosimetry assessments in multi-center trials the appropriate methodology for the dose assessment and the equipment needed for determining the biokinetics must be identified at an early stage of the trial. A detailed manual describing all the procedures that need to be performed at each site should be compiled in order to avoid misinterpretation of the procedures involved. All sites should comply with the pre-defined requirements. In a dry-run the performance of each site is evaluated. Strict QC measures need to be implemented and followed, including the dose calibrators.

In many trials a dose coordinating center (DCC) is identified which is responsible for collecting the data and for the final calculation of the absorbed doses.

The use of a dosimetry protocol in a clinical trial is – in many cases- rather complex. Therefore, the individual steps need to be supervised closely by the corresponding site monitors and the DCC. An external audit of the complete process by an independent reviewer is advised as this might avoid conceptual problems.

References