Postprocessing and Cross Validation

Modeling and Quantification

Basic (Physics) Principles of Tracer Kinetic Modeling
Adriaan Lammertsma
Amsterdam, Netherlands

Learning Objectives:

- Understanding of first principles of tracer kinetic modeling
- Basic understanding of the use of compartment models
- Understanding the need for dynamic scanning to extract physiological parameters from images
- Understanding how to measure perfusion, volume of distribution and binding potential

A typical tracer (imaging) experiment involves injection of that tracer followed by measurement of its concentration in the organ or tissue of interest. The tracer itself is selected because of its properties, i.e. its association with a physiological, biochemical or pharmacokinetic process, such as blood flow, metabolism, and receptor density, etc.

From a clinical point of view, it is interesting to inject the tracer in a quiet (dedicated) room, wait until there is sufficient uptake of the tracer, and then position the patient in the scanner and perform a single (static) scan to measure the distribution of the tracer. However, as the tracer is injected in the bloodstream, its uptake in tissue will be determined by a number of different physiological processes, i.e. delivery to the tissue, (molecular) interactions within the tissue and clearance from the tissue. Delivery to the tissue, in turn, depends on the time course of the arterial tracer concentration, tissue perfusion and extraction fraction. It will be clear that, in general, the relationship between total signal (uptake) and specific signal (i.e. the signal related to the actual process under study) in an image will not be linear and that this relationship will vary over time.

Qualitative imaging may be sufficient for diagnostic purposes (e.g. areas of increased or decreased uptake, left/right differences, etc.). Quantification, however, is needed for pathophysiological studies that are carried out to obtain a better understanding of disease (mechanisms), and it is essential for studies aimed at following progression of disease and its subsequent modification by an intervention (e.g. medication). For true quantification of a physiological or molecular process a tracer kinetic model is essential, together with dynamic scanning in which uptake and clearance (i.e. kinetics) of the tracer are followed over time. Only in this way it is possible to extract the tissue specific signal from the total measured signal that is affected by the various processes mentioned above.

A tracer kinetic model is a mathematical description of the fate of a tracer in the body, with emphasis on the organ of interest. Using such a model, observed tissue uptake and clearance

can be related to various model parameters, provided the input function is also known. As most tracers are injected intravenously, they reach tissues through the bloodstream. Consequently, in most cases, measurement of the arterial plasma concentration over time is also needed. Although other types of models have been proposed, in practice compartmental models are used. In these models, the distribution of activity is allocated to a number of (not necessarily physical) discrete compartments. The resulting operational equation primarily contains (unknown) rate constants, describing the rate of exchange of tracer between the various compartments, which are estimated by fitting the measured data to a suitable model using non-linear regression.

In this contribution the basic principles of tracer kinetic modeling will be presented, together with the most commonly used compartment models. In addition, it will be shown how these models can be used to measure perfusion, volume of distribution and binding potential.