PhD thesis:

"Image Derived Input Functions for Cerebral PET Studies"

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Positron emission tomography (PET) is a medical imaging technique that can be used to measure tissue function *in vivo* quantitatively. PET makes use of radiopharmaceuticals that are labeled with a positron emitter. Apart from evaluating pathophysiological processes underlying disease, it can also be used for objective assessment of therapeutic efficacy and plays an increasing role in drug development.

Apart from a dynamic PET scan, quantification also requires a pharmacokinetic model that describes the kinetic behaviour of the tracer in tissue. Using this model it is possible to convert radioactivity concentrations, measured with a PET scanner, into quantitative pharmacokinetic parameters. For each new tracer, an appropriate tracer kinetic model needs to be developed and evaluated. Kinetic analysis requires an arterial input function, which describes the delivery of the tracer to the tissue as function of time. Traditionally, the input function is obtained by measuring activity concentrations in arterial blood (arterial sampling) during the entire PET study. Arterial sampling, however, is invasive, laborious, and sensitive to failure (clogged lines in ~ 5 to 10% of cases) and it has a small risk of adverse effects. In addition, the input function is not measured at the location of interest (e.g. the brain) and therefore a correction for delay (and dispersion) is needed.

The overall aim of the research described in this thesis was to develop and evaluate a non-invasive method for obtaining the arterial input function. Different strategies for extracting an input function from the dynamic PET images themselves (image derived input function) were evaluated. Image derived input functions were extracted from standard PET scans and from PET scans that were corrected for the limited resolution of current PET scanners using a newly developed image reconstruction algorithm. In addition, as patient motion may affect the accuracy of image derived input functions, effects of motion were evaluated together with different motion correction methods. An important criterion in this assessment was the impact on the final results of tracer kinetic analyses.

Using the method developed in this thesis, comparable results of tracer kinetic analyses were obtained with imaged derived input functions as with blood derived input functions. This method was evaluated for different tracers and two types of PET scanners. An important finding was that accurate results were obtained only when PET images were corrected for the limited resolution of the PET scanner. Furthermore, this thesis showed that patient motion has a large impact on the accuracy of the method and that correction for patient motion is necessary to obtain accurate image derived input functions.

The use of motion corrected PET images together with a reconstruction based method to correct for the limited resolution of a PET scanner enables the extraction of image derived input functions as an alternative for arterial sampling. This, in turn, will facilitate the use of quantitative PET studies in routine clinical practice.