

Optimization of PET Study Design and Analysis by an Impulse Response Function Approach

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As a functional imaging modality, positron emission tomography (PET) allows the 4-dimensional observation and measurement of physiological and biochemical properties of biological systems *in vivo*. In order to extract useful information from the raw dynamic data, kinetic analysis methods must be employed. Graphical analysis methods are currently the most commonly used to create estimates of relevant system parameters. While easily implemented and computationally fast, these methods do have limitations, including a tendency to appear to provide valid parameter estimates when the data under investigation do not meet the criteria of the methods. Similar limitations in existing kinetic analysis methods have been the driving forces behind the development of new methods over the years and are the impetuses behind the work presented here.

This thesis presents three novel dynamic PET analysis methods, one an adaptation of a previously described method, and two original methods. Chapter 1 provides background information as well as an introduction to the specific limitations inherent in some currently used analysis methods. Chapter 2 presents a restricted-model-order (RMO), basis function-based impulse response function (IRF) modeling method that is an adaptation of DEPICT, a method developed by Gunn *et al.* The RMO method sacrifices a bit of the data-driven nature of DEPICT but excludes results that are physiologically improbable. Chapter 3 presents the use of expectation-maximization in the calculation of

direct estimates of IRFs. This method is extremely data-driven and does not assume any initial model for the IRF. Finally, Chapter 4 presents a universal graphical analysis method. This method makes no *a priori* assumptions as to the reversibility or irreversibility of the tracer under investigation and can be applied universally across tracers of both kinetic types. At the same time, the method maintains the computational speed and ease of use common to all graphical analysis methods.

The three methods developed and implemented in this work are able to accurately estimate important system parameters and provide additional useful kinetic information. They improve on or avoid some of the limitations of several previously described techniques. The three methods represent additional tools for use in dynamic PET data analysis.