QUANTITATIVE FUNCTIONAL IMAGING USING DYNAMIC POSITRON COMPUTED TOMOGRAPHY AND RAPID PARAMETER ESTIMATION TECHNIQUES (LOCAL CEREBRAL BLOOD FLOW, GLUCOSE TRANSPORT, PHYSIOLOGICAL MODELING)

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Positron computed tomography (PCT) is a diagnostic imaging technique that provides both three dimensional imaging capability and quantitative measurements of local tissue radioactivity concentrations in vivo. This allows the development of non-invasive methods that employ the principles of tracer kinetics for determining physiological properties such as mass specific blood flow, tissue pH, and rates of substrate transport or utilization. A physiologically based, two-compartment tracer kinetic model was derived to mathematically describe the exchange of a radioindicator between blood and tissue. The model was adapted for use with dynamic sequences of data acquired with a positron tomograph. Rapid estimation techniques were implemented to produce functional images of the model parameters by analyzing each individual pixel sequence of the image data. A detailed analysis of the performance characteristics of three different parameter estimation schemes was performed. The analysis included examination of errors caused by statistical uncertainties in the measured data, errors in the timing of the data, and errors caused by violation of various assumptions of the tracer kinetic model.

Two specific radioindicators were investigated. ('18)F-fluoromethane, an inert freely diffusible gas, was used for local quantitative determinations of both cerebral blood flow and tissue:blood partition coefficient. A method was developed that did not require direct sampling of arterial blood for the absolute scaling of flow values. The arterial input concentration time course was obtained by assuming that the alveolar or end-tidal expired breath radioactivity concentration is proportional to the arterial blood concentration. The scale of the input function was obtained from a series of venous blood concentration measurements. The method of absolute scaling using venous samples was validated in four studies, performed on normal volunteers, in which directly measured arterial concentrations were compared to those predicted from the expired air and venous blood samples. The glucose analog ('18)F-3-deoxy-3-fluoro-D-glucose (3-FDG) was used for quantitating the membrane transport rate of glucose. The measured data indicated that the phosphorylation rate of 3-FDG was low enough to allow accurate estimation of the transport rate using a two compartment model.