

Quantitative assessment of cerebral blood flow using Technetium-99m-hexamethyl-propyleneamine oxime: part I, Design of a mathematical model

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To design a mathematical model for quantifying cerebral blood flow using ^{99m}Tc -hexamethyl-propyleneamine oxime (HM-PAO), basic studies were performed in animals and human volunteers. Microautoradiography revealed that HM-PAO crossed the blood-brain barrier. Thin layer chromatographic studies demonstrated the rapid disappearance of free HM-PAO in the brain tissue. Back diffusion from brain to blood was found negligible. From these observations, the familiar microsphere model was employed in the measurements of blood flow with HM-PAO. This, however, resulted in much lower flow values than simultaneously obtained values with the labeled microspheres. This underestimation was ascribed to the high affinity of HM-PAO to blood cells and serum protein. Taking the binding of HM-PAO to blood components into consideration, the following model equation was designed for quantifying cerebral blood flow: $Ce(t) = Ca(t) - kCa(t) * \exp(-kt)$, $Cb(T) = F \int_0^T Ce(t) dt$, where Ce and Ca are the free HM-PAO concentration in the intravascular space and the arterial whole-blood concentration of HM-PAO, respectively, as a function of time (t), Cb is the brain activity concentration, k is the rate constant for the binding of HM-PAO to the blood components, F is the blood flow value, T is time of measurement, and $*$ denotes the operation of convolution. In clinical studies, $Ca(t)$ and $Cb(T)$ are obtainable from a dynamic single photon emission computerized tomographic study of the brain and multiple arterial blood sampling, respectively. The values for F and k can be estimated using a non-linear least squares fitting method.

Key words: ^{99m}Tc -hexamethyl-propyleneamine oxime, Single photon emission computerized tomography, Cerebral blood flow