

DESIGN AND EVALUATION OF RADIOTRACERS FOR DETERMINATION OF  
REGIONAL CEREBRAL BLOOD FLOW WITH PET

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## ABSTRACT

The tracer kinetics of 4-Fluoro(<sup>18</sup>F)-, 4-Bromo(<sup>82</sup>Br)- and 4-Iodo(<sup>125</sup>I)-antipyrine and <sup>15</sup>O-water were compared in a cat or baboon animal model. First-pass cerebral extraction and clearance with alterations in PaCO<sub>2</sub> were measured for whole brain. The Renkin/Crone model was used to evaluate brain capillary permeability-surface area product for 4-<sup>18</sup>FAP in cats. Positron-emission-tomographic measurements required development of an instrument and technique for control of the arterial concentration of the radiotracer as a ramp function, so that tracer concentration changes due to radioactive decay or altered physiological processes could be accurately described with PET. Pharmacokinetic and tissue-distribution studies in cats were used to determine dosimetry for 4-<sup>18</sup>FAP. 4-Bromoantipyrine labeled with <sup>78</sup>Br (t = 6.5 m) is suggested as a tracer for determination of rCBF with PET.

## KEYWORDS

Tracer kinetics; cerebral blood flow; position emission tomography; radiotracer design.

## INTRODUCTION

Recent research in neuroscience and nuclear medicine with radionuclides of short half-life and position emission tomography (PET) has focused on the measurement of local cerebral glucose uptake and metabolism (Reivich, Kuhl, Wolf and co-workers, 1979; Sokoloff and colleagues, 1977), and of the regional cerebral metabolic rate of oxygen (Depresseux, Raichle and co-workers, 1981; Lenzi and others, 1981). Cerebral blood flow can be evaluated by conventional techniques with <sup>133</sup>Xe, and the new PET technology using <sup>77</sup>Kr, <sup>15</sup>NH<sub>3</sub>, <sup>15</sup>OH<sub>2</sub> and other tracers. None of the freely diffusible radiotracers are completely satisfactory for all CBF determinations. 4-Iodoantipyrine-<sup>14</sup>C (IAP) is the standard for evaluation of rCBF by the autoradiographic diffusible tracer technique (Sakurada and co-workers, 1978). Unfortunately, the rapid *in vivo* deiodination of IAP limits the integrity of a IAP tracer to the first 30-90 s after injection. Antipyrine does not have an adequate partition coefficient through the blood brain barrier. Other missing links include: an adequate model to couple CBF and local cerebral metabolic processes; and documentation that PET can be used to quantitatively determine rCBF in normal and physiopathological states.

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