C00-2011-7

A METHOD FOR THE DETERMINATION OF REGIONAL BLOOD FLOW IN TISSUES BY MEANS OF STIMULATED X-RAY FLUORESCENCE

FINAL REPORT

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January 1, 1969 - August 31, 1973

Prepared for the U.S. Atomic Energy Commission under Contract No. AT(11-1)-2011.

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ABSTRACT

Instrumentation and methodology were developed to measure the regional cerebral blood flow (rCBF) and regional cerebral blood volume (rCBV) in vivo by stimulated x-ray fluorescence. This method consisted of injecting an iodinated radiographic contrast material into the bloodstream of the subject to be studied and then passing a narrow collimated beam of x-rays through a selected region of the brain. This beam excited or fluoresced the iodinated contrast material and the resulting fluorescent x-rays were detected by an externally placed x-ray detector. The intensity of the fluorescent x-rays was used to regionally determine the amount of blood per volume of brain tissue (rCBV) and the change of this parameter with time (rCBF). This method was validated with phantom and animal studies by comparisons to more conventional in vitro techniques and was found to have an accuracy of about $\pm$4% in the measure of rCBV and rCBF in rhesus monkeys, and $\pm$10% in human subjects. This method was used to make the first absolute measurements of rCBV in living subjects. The method was also used to evaluate the role of cerebral blood volume in the regulation and control of cerebral blood flow in normal subjects, selected patients with cerebral pathology, and animal studies in which cerebral hemodynamic and metabolic changes were induced.

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The purpose of the work supported under AEC Contract No. AT(11-1)-2011 was to design, build, and evaluate a stimulated x-ray fluorescence system for the non-invasive, in vivo, and regional measure of blood flow in tissues.

The initial phase of this work involved the design and construction of a high resolution x-ray fluorescence spectrometer and a high intensity x-ray source. A high resolution (300 mm^2 x 5 mm) Si(Li) x-ray detector was purchased and evaluated in terms of its energy resolution, count rate stability, and x-ray detection efficiency. The single phase x-ray generator that was used in the initial work as a source of stimulating radiation was replaced by a high output 3 phase, 12 pulse rectified unit. Collimators were then designed for the x-ray detector and x-ray tube, and the spatial resolution and sensitivity were evaluated with phantom studies.[1,2] The results from this work[1,2] indicated that using an intravenous injection of iodinated radiographic contrast material as a blood tracer would permit the quantitative measure of the amount of radiographic material per volume of tissue , and this could be converted to the amount of blood per volume of tissue. The amount of blood per volume of tissue is the fractional blood volume. Since the blood volume in the brain (CBV) was considered to be an important factor in the control and regulation of blood flow in the brain, the method was evaluated for the measure of regional cerebral blood volume (rCBV). The accuracy of the stimulated x-ray fluorescence in the measure of

rCBV was evaluated with animal experiments in dogs and rhesus monkeys by controlled comparison between the in vivo fluorescence technique and conventional in vitro techniques as described in References 1 and 3. It was found that rCBV could be measured in a 1 cc volume of the dog and monkey brain with an accuracy of $\pm$4% by the non-invasive in vivo stimulated x-ray fluorescence technique.

The x-ray fluorescence technique was also applied to the regional measure of cerebral vascular mean transit time in dogs and monkeys.[1,4] From the vascular mean transit time ($\bar{t}$) and the cerebral blood volume (CBV) one can then calculate the cerebral blood flow from the central volume principle ($CBF = CBV/\bar{t}$). However, the vascular mean transit time measurement required a direct arterial injection and since the intended purpose of this work was to develop a non-invasive measure of blood flow, the emphasis of the x-ray fluorescence work was shifted to the non-invasive measure of cerebral blood volume.

The x-ray fluorescence technique was next applied to the measure of rCBV in 13 normal human volunteers.[5] At this point the x-ray fluorescence method had provided the first measurements of rCBV in the living dog, monkey, and human, and a program was started to use this technique to accurately determine the role of CBV in the control and regulation of cerebral hemodynamics in a living subject and evaluate the technique in terms of its clinical facility as a diagnostic indicator of cerebral pathology.

The following studies were carried out with the above purpose in mind: (1) The correlation between CBF, arterial blood carbon dioxide tension and CBV was measured[4,6] to determine the role of CBV in normal changes in CBF; (2) the changes in CBV as a function of arterial blood pressure were measured[7] to investigate the involvement of CBV in the autoregulation of CBF; (3) the changes in CBV which occur during cerebral seizures[8] were measured to evaluate hemodynamic changes that occur during metabolically active states of seizure; and (4) the changes in CBV and CBF were evaluated[9] following cerebral angiographic studies to evaluate the perturbation of cerebral angiographic circulation time measurements due to the transient vasodilation effects of radiographic contrast materials. All of the above experiments were carried out in rhesus monkeys and established the first fundamental correlations between the cerebral blood volume and cerebral blood flow, arterial blood carbon dioxide tension, and seizure in the living subject.

In addition to the animal studies and normal human subject studies, the x-ray fluorescence method was used to study patients with pseudotumors[10] to evaluate the clinical status of cerebral hemodynamics in these patients. Results indicated that the patients had normal hemodynamic status and that the cerebral blood vessels were dilated in an autoregulated response to the increased intracranial pressure present in the patient with pseudotumor.

After some improvements in the facilitation of data handling by automating the data analysis by on-line computation, the project was transferred to the support of the National Institutes of Health under Grant No. 5 ROl HL15423-02.

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