nm/PRELIMINARY NOTE

FLUORESCENCE DETECTION: APPLICATION TO THE STUDY OF CEREBRAL BLOOD FLOW

Paul B. Hoffer,* Robert E. Polcyn, Robert Moody, Henry J. Lowe and Alexander Gottschalk

The Pritzker School of Medicine of The University of Chicago and the Argonne Cancer Research Hospital, Chicago, Illinois†

The feasibility of imaging thyroidal iodine in patients who have received no radionuclides has been established (*1,2*). In this procedure K-shell fluorescence of the stable iodine within the thyroid gland is induced by exposure to an external source of ^{241}Am (gamma energy approximately 60 keV). The resulting K_α characteristic radiation (x-ray energy, 28.5 keV) is detected with a high-resolution lithium-drifted silicon detector which permits good scatter discrimination even at this low photon energy. Thyroid scans produced by this method now supplement standard ^{125}I and ^{131}I scans at our institution.

It has been suggested by Tinney (*3*), Ter-Pogossian (*4*) and one of us (*5*) that a similar system could be used for dynamic transit time and blood-flow determinations within the brain and other organs. The principal advantage of such a system over current isotopic methods is that where the irradiation from the collimated exciting source (^{241}Am) and the detector field of view overlap a tomographic effect is created defining a discrete tissue volume from which data are collected. When the region of interest is adjusted to below the scalp and calvarium, blood flow within the brain can be measured without interference from activity in superficial structures. A nonradioactive "tracer" must be introduced into the blood if regional flow is to be measured. This "tracer" should ideally be of medium-to-high atomic number and just sufficient in quantity to give statistically reliable results. Iodine and xenon are the only elements currently available for such vascular studies.

The applicability of such a system to cerebral transit time and blood-flow determinations was demonstrated in the following experiments.

Experiment 1. A rhesus monkey weighing approximately 7 kg was anesthetized, and a cut-down was performed on the left common carotid artery. The external carotid artery was occluded and a No. 20 Cournand needle was inserted into the left internal carotid artery. The animal was then placed beneath our fluorescent detector (3.3 Ci ^{241}Am, annular source, 200-mm² lithium-drifted silicon detector). The region of interest (a volume of approximately 3 cm³) was adjusted so that it was below the

Received April 17, 1969; revision accepted June 20, 1969.

For reprints contact Paul B. Hoffer, Argonne Cancer Research Hospital, 950 E. 59th St., Chicago, Ill. 60637.

* Scholar in Radiological Research of the James Picker Foundation.

† Operated by The University of Chicago for the United States Atomic Energy Commission.

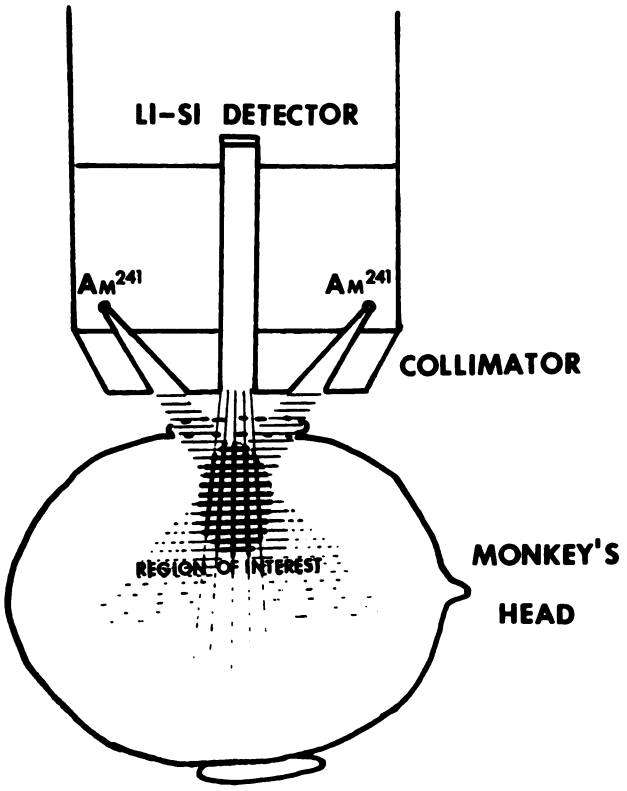

FIG. 1. Diagrammatic representation of experimental setup. "Region of interest" in monkey's brain represents region in which radiation from ^{241}Am source and detector collimation overlap. Actual configuration of this region is more complicated than indicated in diagram. Region does, however, approximate an ovoid 3 cm in height and 1.5 maximum diameter. Radiation dose to irradiated brain was estimated at 50 mrads per study.

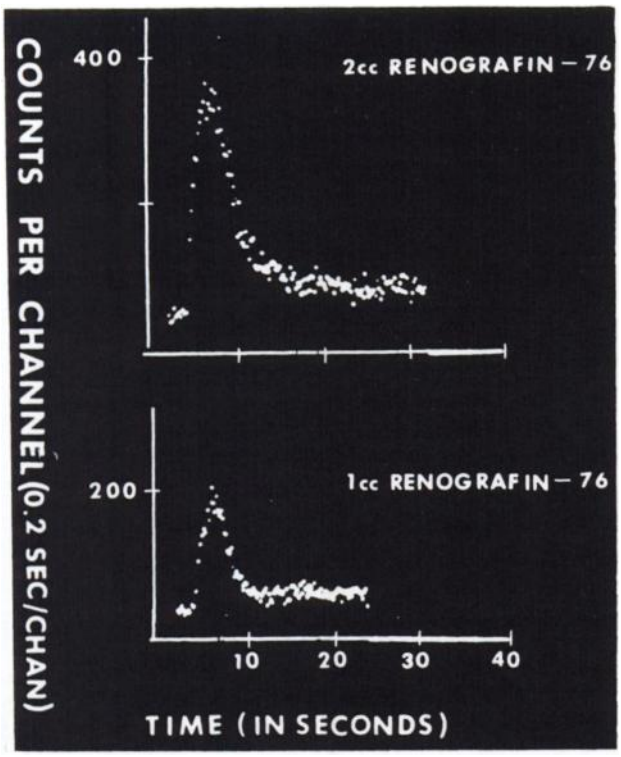

FIG. 2. Curves produced after intracarotid injection (internal carotid artery) of 1 and 2 cc of Renografin-76, respectively. Points on curve represent total fluorescent counts of iodine within region of interest at 0.2-sec intervals following injection.

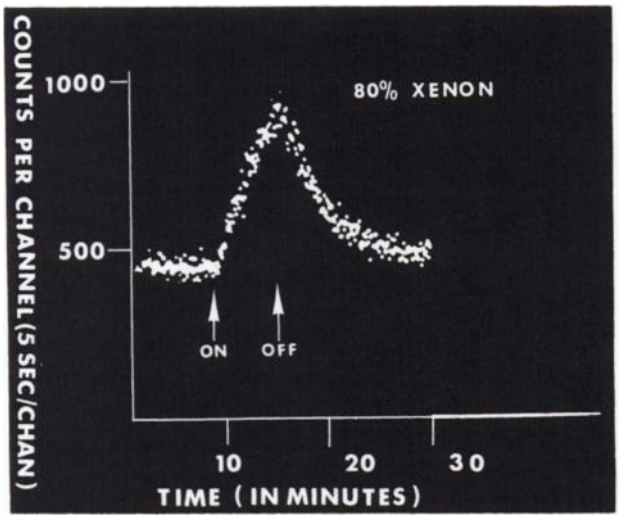

FIG. 3. Xenon clearance curve. Animal was initially equilibrated on 100% oxygen. Eighty percent xenon and 20% oxygen was then administered for 6 min (period between arrow marked "on" and arrow marked "off"). Rebreathing system was then flushed with oxygen before clearance phase. Counts were collected at 5-sec intervals per channel.

level of the calvarium on the left side (see Fig. 1). A 3% window was set on the pulse-height analyzer (Canberra Model No. 1413) bracketing the 28.5-keV K_α characteristic x-ray peak of iodine (window width 28–29 keV). The count information was then routed to a multichannel analyzer (RIDL Model No. 34-12B) operating in a time-sequence scaling mode. Test injections of Renografin-76 (meglumine diatrizoate, 37% iodine) were made into the left carotid artery and counts were collected over a 0.2-sec interval per channel for a period of about 30 sec (see Fig. 2). The maximum radiation dose to the brain per study was estimated at 50 mrads. The curves obtained correspond to those that would be anticipated with radionuclide or dye-dilution techniques.

The quantity of iodinated contrast material injected into the carotid artery for this study is in excess of the amount that would be advisable in man. Preliminary human studies carried out in association with carotid arteriography, however, indicate that doses of as little as 3 cc of Renografin (meglumine diatrizoate, 29% iodine) can be used for this purpose although statistical reliability of the data obtained is marginal.

It would be helpful if the problem of intra-arterial injection of the "tracer" could be eliminated. The inherent tomographic nature of the technique avoids interference from "tracer" in tissues outside of the region of interest. Intravenous injection of the iodinated contrast material has so far proven inadequate because it has been impossible to produce a discrete bolus with the necessary volume of contrast material. A clearance technique was therefore considered (6) and is described in Experiment 2.

Experiment 2. A rhesus monkey weighing approximately 7 kg was anesthetized and intubated with a cuffed endotracheal tube. The endotracheal tube was attached to a closed rebreathing system with CO_2 absorber. The animal was then placed beneath the fluorescent detector. The apparatus was adjusted so that the region of interest (a volume of approximately 3 cm^3) was below the level of the calvarium in the midline. A 3% window bracketing the 29.8-keV K_α characteristic peak of xenon was set on the pulse-height analyzer. The count information was again routed to a multichannel analyzer operating in the time-sequence scaling mode. One hundred percent O_2 was initially administered to the animal, and baseline background readings were obtained. A mixture of 80% xenon, 20% oxygen was then administered to the animal for 6 min. At the end of this period, the xenon-oxygen mixture was abruptly flushed from the system by 100% oxygen, and the animal was maintained for the remainder of the clearance period on 100% O_2 with frequent flushing of the rebreathing system to prevent accumulation of xenon. The clearance curve obtained (see Fig. 3) is apparently monophasic. The radiation dose

to the animal was estimated to be less than 3 rads for the entire 30-min period.

Xenon is an inert gas that is mildly anesthetic in 80% concentration at atmospheric pressure. An inert xenon clearance study could be done on a reasonably cooperative patient. This would do away with the need for intracarotid or intravenous injection. The patient would simply breathe a xenon-oxygen mixture. It is unnecessary for the xenon to be in equilibrium with the compartment prior to the start of the clearance study. We have not concerned ourselves with the problem of xenon recirculation in this preliminary experiment. The fact that the clearance curve is monophasic is reasonable when it is considered that the study deals only with a selected "region of interest" which, in this case, is principally the white matter of the brain, and that the monkey was anesthetized (*7*).

CONCLUSION

Two methods of combining a nonradioactive "tracer" and fluorescent detector for the determination of cerebral transit time (Experiment 1) and blood flow are demonstrated. Since both methods detect fluorescent activity exclusively in a predetermined volume of brain, it is possible to avoid recording "tracer" activity from overlying bone and soft tissue. The need for selective arterial injection can be eliminated by using the stable xenon clearance technique. The only drawback is the expense of the xenon gas.

ACKNOWLEDGMENT

The fluorescent detector used in these experiments consists of a 200-mm² lithium-drifted silicon detector manufactured by the Nuclear Equipment Corp. and an annular 3.3-Ci ^{241}Am source manufactured by Monsanto Research Corp.

REFERENCES

1. HOFFER, P. B., JONES, W. B., CRAWFORD, R. B., BECK, R. N. AND GOTTSCHALK, A.: Fluorescent thyroid scanning. A new method of imaging the thyroid. *Radiology* **90**:342, 1968.

2. HOFFER, P. B., CHARLESTON, D. B., BECK, R. N. AND GOTTSCHALK, A.: Fluorescent scanning: A new investigative technique. In *Medical Radioisotope Scintigraphy,* Vol. I, IAEA, Vienna, 1969, p. 261.

3. TINNEY, J. F.: Personal communication, 31 May 1968.

4. TER-POGOSSIAN, M. M.: Personal communication.

5. HOFFER, P. B.: Fluorescent thyroid scanning. *Am. J. Roentgenol., Radium Therapy Nucl. Med.* **105**:721, 1969.

6. POTCHEN, E. JAMES: Personal communication.

7. SOKOLOFF, L.: Action of drugs on cerebral circulation. *Pharmacol. Rev.* **11**:1, 1959.