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EDITORIAL

Toward Absolute Quantitation of Cerebral Blood Flow Using Technetium-99m-HMPAO and a Single Scan

A simple method for estimating absolute regional cerebral blood flow (rCBF) using a ^{99m}Tc radiopharmaceutical would be useful for research and clinical applications. In our own clinical studies using ^{99m}Tc-HMPAO, we often ponder whether the activity in the right hemisphere is down or the left hemisphere up and whether blood flow is globally changed. It would be helpful to have ready answers to such questions, and the work of Pupi et al. is a welcome step in that direction.

Techniques to quantitate rCBF using kinetic analysis of ^{99m}Tc-HMPAO uptake require fixed-ring cameras that are sufficiently sensitive to sample regional brain activity on a minute by minute basis. Kinetic approaches also require a lengthy and sophisticated analysis, and in general, the estimation of rate constants can be biased significantly by relatively small systematic errors in data acquisition. Thus, a kinetic analysis of HMPAO uptake, while theoretically sound and very much appropriate for research, is not at all suited to routine clinical use.

In contrast, the technique described by Pupi et al. requires only one SPECT measurement of regional brain activity, performed at a time after injection when the amount of radiopharmaceutical in the brain is essentially stable. This single-scan approach makes it possible, in theory, to quantitate rCBF using any SPECT system. Since the amount of brain activity depends not only on flow but also on the amount of radiopharmaceutical delivered to the brain, the single-scan technique still requires substantial laboratory work: after rapid arterial blood sampling, the portion of ^{99m}Tc-HMPAO that is freely diffusable across the blood brain barrier must be distinguished from total blood activity through a rapid octonol extraction technique. The resulting arterial input function is summarized by its integral, which, along with the single SPECT measurement of brain activity, is used to compute a regional brain clearance of HMPAO.

The authors compare the regional clearance of HMPAO with rCBF measured through the injection of microspheres into the left ventricle during angiography. The microsphere technique is theoretically sound and serves as an excellent standard against which quantitation using HMPAO can be validated. One drawback of the experimental design is that the HMPAO and microsphere studies were performed on different days, apparently without controlling factors which may affect rCBF, such as changes in sensory stimulation and ventilation.

While the single scan approach would significantly simplify and therefore extend the ability to measure cerebral blood flow, the technique in its present form may not yet be ready for routine use. One concern is that, after placement of an arterial line, the performance of rapid blood sampling and octonol extraction is at least moderately labor-intensive. Before switch-

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ing to an automated pump and agitator, blood sampling and octanol extraction in our laboratory required the participation of six investigators for lengths of time ranging from 25 min to 2 hr. Even with a more automated system, we found it necessary to involve at least three investigators in each study. Furthermore, for absolute quantitation, we agree with the need for careful phantom work to convert units of activity from the camera into concentrations of activity in the brain. Results from phantom studies are very much machine-dependent, and the performance of phantom studies requires sophistication as well as additional equipment and time.

A second and more important concern, which Pupi et al. describe, is that the results of this study can be applied only to neurologically normal patients. In fact, since a rigorous compartmental model would predict a more complicated relationship between HMPAO clearance and rCBF, it would be best to confirm the simple linear relationship on a new set of normal subjects. Because the linear relationship is empirical, application of the technique to a patient with a neurologic disorder will require a set of experiments on patients with that specific disorder.

A third concern is that, even if the same linear relationship were to hold for pathologic, as well as normal brain regions, the large residuals from the linear fit of Figure 4 suggest that the accuracy of the single scan technique is limited. For example, based on Figure 4 and the linear regression equation, a regional blood flow by microspheres of 0.5 ml/min/g could be assigned an HMPAO blood flow estimate ranging from 0.3 to 0.7 ml/min/g, an error of ± 40%. The large F-statistic associated with the linear fit only implies a strong correlation between the microsphere and HMPAO clearances; the F-statistic does not imply that HMPAO clearance is a consistently accurate technique to estimate blood flow.

Thus, while Pupi et al. have made significant progress toward the goal of a simple way to estimate absolute rCBF using a ^{99m}Tc radiopharmaceutical, much work remains. It may be possible to replace arterial sampling with some form of venous sampling, and the labor associated with the octonol extraction portion of the exam can be reduced through automation. More critical, however, is that the single-scan technique must be validated for abnormal, as well as normal patients, and estimates of blood flow based on HMPAO clearances must be demonstrated to be reasonably precise. A technique that meets these goals will be a very useful addition to the practice of nuclear medicine.

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