TEACHING EDITORIAL

Single-Photon Emission Computed Tomography to Study Cerebral Function in Man

Recent enthusiasm for single-photon emission computed tomography (SPECT) of the brain has been stimulated by pioneering work in positron ECT but has been limited by slow advances in the development of practical, single-photon radiopharmaceuticals. The annihilation reaction with coincidence counting of positron isotopes of carbon, oxygen, nitrogen, and fluorine is intrinsically ideal for studying metabolic pathways in the brain, but their widespread clinical utility is limited to a few centers because of the costly on-site cyclotrons and the need for technical support of radiochemical and radiopharmaceutical production. If the dramatic results obtained from work at these centers is to be realized by the general clinical population, single-photon radiopharmaceuticals that are free of high-technology cost and that can mimic the biodistribution of positron pharmaceuticals are required. Widespread clinical utility would then be limited only by the cost of instrumentation.

Emission computed tomography with single-photon gamma emitters can be accomplished by either adding accessories to existing gamma cameras or by purchasing dedicated transverse section systems. The two major advantages of tomography over two-dimensional imaging in nuclear medicine are: (a) the tomographic effect of separating contours with improved contrast resolution, and (b) the quantification of radiopharmaceutical distributions within the organ systems. Coded apertures, slant-hole collimators, and pinhole collimators will have limited utility in tomography of the brain due to their limited sampling angle and at best will only accomplish the first objective of single-photon tomography—separating the superficial activity from deep intracranial information (*1*). Transaxial systems avoid the limited angle problem and allow more accurate compensation for attenuation that is needed for potential quantification (*2*).

In the past, single-photon pharmaceuticals for imaging the brain have been limited to agents that cross the damaged blood-brain barrier. Many tomographic systems were shown to improve the diagnostic accuracy for imaging the brain by approximately 10% when compared with scintigraphy and were found to have similar sensitivities when compared with x-ray transmission computed tomography (CT) (*3–6*). Since x-ray computed tomography provides more specific anatomic information and, in many instances, better lesion detection, tomographic blood-brain barrier imaging has been limited to particular circumstances and problematic cases (*7*). More recently, quantification with single-photon tomography has demonstrated changes in blood volume studies of the brain that could not be detected on CT (*8*). Quantification was also found useful in the differential diagnosis of brain lesions with Tc-99m glucoheptonate (*9*).

The procedure reported in this issue by Fazio et al. (*10*) marks another step toward the realization of the goal of quantitative tomography for regional cerebral function with single-photon emitters (*10*). Regional brain perfusion can be demonstrated with dynamic imaging and equilibrium flow imaging with diffusible or extractable tracers (*11*). Dr. Niels Lassen and coworkers have shown that dynamic flow imaging is clinically feasible with single-photon tomography (*12*). Now, Dr. Fazio et al. have demonstrated that equilibrium imaging with short-lived pharmaceuticals can produce images that reflect regional brain perfusion and demonstrate physiologic changes in brain perfusion. At present this technique is limited by its invasiveness and most likely will not become the single-photon technique of choice for brain imaging. Perhaps the extractable-tracer approach ultimately will be the method for widespread clinical use.

Pharmaceuticals that are lipid soluble and have a high extraction fraction on the first pass to the brain are under development at various centers (*13,14*). The tertiary diamines and n-isopropyl-p-iodoamphetamine labeled with iodine-123 have recently been evaluated with regard to their brain

TABLE 1. SPECT TRANSAXIAL SYSTEMS

Mark IV	(UCLA)
Donner Lab.	(University of California)
Humangotron	(University of Michigan)
Tomogscanner	(J & P Engineering)
Roto-camera	(Siemens Gammasonics)*
Cleon 710 and 711	(Union Carbide)
Gamma-CAT	(Selo)
Tomomatic 64	(Medimatic A/S)
G E 400 T	(General Electric)
Gammatome T 9000	(CGR)
Headtome	(Akita + Shimadzer Seisakasho)

* Formerly Searle.

uptake and could conceivably be used for regional brain perfusion imaging by the extractable-tracer technique (*15,16*). To retain lipophilicity and at the same time to minimize protein binding has been defined as the impediment to the development of a technetium-labeled pharmaceutical that will cross the blood-brain barrier (*17*).

Each year over 400,000 Americans are hospitalized because of stroke (*18*). In many instances these patients present with the signs and symptoms of transient ischemic attacks. Unfortunately, current and near-future positron imaging facilities are accessible to only a fraction of these patients with cerebral vascular disease. Increased accessibility to emission tomography will be accomplished by development of SPECT systems as evidenced by the wide variety of instruments now available (Table 1). As single-photon pharmaceuticals and techniques are developed for assessment of regional brain perfusion, transaxial systems to perform single-photon tomography will be available to exploit the advantages of these newer radiopharmaceuticals. In the evaluation of cerebral ischemia, compensatory collateral perfusion and prognostic information would be forthcoming with the development of single-photon pharmaceuticals that reflect regional brain perfusion. A technique for the objective evaluation of medical or surgical therapies in stroke disease would have widespread clinical utility. Brain scanning, which had a peak utilization of 3,500,000 scans per year before CT scanning was developed, has now diminished to less than half that figure and will continue to decline as x-ray CT becomes more available (*19*). However, as radiotracers are developed that reflect regional brain perfusion and not merely blood-brain barrier abnormalities, nuclear medicine departments will again have a significant impact on the management of neurologic diseases. Today we are somewhat closer to the objectives expressed by Dr. Oldendorf regarding compounds that would display regional brain perfusion (*20*). With continued contribution by enthusiastic investigators, such as Dr. Fazio and his colleagues and the anticipated development of the instrumentation and radiopharmaceuticals, routine techniques for SPECT to study cerebral function in man will be achieved.

THOMAS C. HILL
Harvard Medical School
New England Deaconess Hospital
Boston, Massachusetts

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