versely proportional to the number of measurements. This implies that CBF at a 120-sec scan time in gray matter is equivalent to $(13.6/10.2)^2$ equaling 1.8-fold trials of those by a 40-sec scan time, that is, the 120-sec scan time corresponds to an 80% gain in the number of trials as compared to the 40-sec scan time.

In conclusion, the optimal scan time of PET using the $H_2{}^{15}O$ method is between 90 and 120 sec. The gain of the 120-sec scan time over the 40-sec scan time corresponded to an 80% increase in the number of stimulation trials needed to provide the same statistical significance.

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EDITORIAL

Optimization of Regional Cerebral Blood Flow Measurements with PET

Several methods for measuring regional cerebral blood flow (rCBF) with PET and ^{15}O-water have been developed, evaluated and applied. These include the ^{15}O equilibrium method (*1*), the autoradiographic method (*2*), and other techniques which will be referred to, generically, as dynamic methods (*3–7*). The common theoretical basis for these techniques is the Kety model, which assumes a homogenous tissue volume with respect to blood flow and tissue type, complete first-pass extraction of a diffusible, inert tracer, and uniform distribution of tracer within the tissue volume. More detailed models of the tissue volume have been proposed, but have not been widely applied. The Kety model has two adjustable parameters, blood flow and the tissue-to-blood partition coefficient. Optimization of blood flow measurements, per se, can be accomplished by varying: (1) the total observation period, (2) the scan and blood sampling protocol, and (3) the type and magnitude of tracer administration. For example, sharp bolus injection and continuous administration of tracer are the two extremes for the shape of input function. Choosing the continuous inhalation of $C^{15}O_2$ gas and the equilibrium method permits a longer observation period and higher precision at the expense of increased radiation dose. Making a specific choice of observation period and the method of tracer administration inevitably involves a trade-off among accuracy, precision, temporal resolution, and radiation dose to the subject.

An example of a CBF optimization scheme is provided in the report by Kanno et al. in this issue of the *Journal*, which shows that increasing the scan time in the autoradiographic method from 40 to about 100 sec improved the signal-to-noise (S/N) ratio of flow measurements while holding the radiation dose to the subject constant. The value of improved S/N ratio must be balanced against the loss of temporal resolution. In some activation studies, where it is necessary to maintain physiologic steady-state in the face of habituation, better temporal resolution may outweigh improved S/N ratio. It is also important

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to note that this optimization of scan time applies only to the autoradiographic method. One cannot claim that it holds for all $H_2{}^{15}O$ bolus injection methods.

In the classic autoradiographic method, a simple ratio is formed to determine CBF from the Kety model. This experimentally measured ratio is the cumulative scan from time t = 0 to time t = 40 sec, divided by the integral of the arterial concentration curve. Since there is only one scan measurement, only one unknown parameter can be estimated and it is therefore necessary to assume a value of the partition coefficient. The autoradiographic method is however rather insensitive to the details of the kinetic model when the observation period is kept short enough so that little activity leaves the tissue volume during the measurement. A weakness of the classic autoradiographic method is its sensitivity to errors arising from unmeasured delay and dispersion of the bolus (*8,9*).

In order to achieve a more general optimization, dynamic methods must also be considered. These methods require rapid sequential tomographic measurements (3–10 sec/scan) and measurement of arterial blood concentration with high temporal sampling (≈1 sec/sample). Oxygen-15-water may be injected as a sharp bolus; or ^{15}O-CO_2 gas may be inhaled for a short period (*7,10*). Corrections are usually applied to the arterial curves in order to account for bolus dispersion and delay in the vascular system. Because many PET measurements and a complete arterial blood concentration curve are acquired, enough data exist so that it is possible to determine both the local blood flow and the effective partition coefficient for labeled water. As the total scan time is increased, statistical precision improves because more of the available photons are detected and used in the computations. However, there are at least two major limitations to dynamic methods: (1) the 123-sec half-life of ^{15}O limits useful measurement time to not much more than a tracer half-life and (2) as the measurement time is increased, the calculation of CBF becomes more dependent on the details of the kinetic model.

Practically, one might ask several questions concerning the CBF methods discussed here: How does one choose among these methods? Is there a best method? What is optimal? Only in a theoretical sense can we contrive a set of assumptions which will lead, by an irrefutable logical progression, to an answer. A practical real-world answer is simpler and at the same time much more complex: it depends.

It depends on the properties of the instrumentation at hand and on other constraints. Obviously, the precision of CBF measurements can be improved by increasing the amount of radioactivity injected; but the precision of the measurements will not improve, and may decrease, at high count rates due to instrument dead-time and/or random coincidence rates. Other practical limits also exist, for example radiation dose to the subject. Also, in studies with repeated bolus injections, radiation protection for personnel becomes an important consideration because of the necessity to handle 100–200 mCi of activity for each injection. In such cases, one might consider elaborate radioactivity handling schemes. But, the results of optimization do not indicate a vast superiority of one method over all others; so inhalation of the radioactivity, which eliminates direct handling of the radioactivity, rather than intravenous injection may be appealing, even though it is not mathematically optimal.

It depends on the relative cost of the studies. The simpler study procedures such as the equilibrium method and autoradiographic techniques are not as technically demanding as the dynamic measurements, occupying fewer personnel and requiring less data processing. Such trade-offs may be acceptable in some circumstances.

It depends on the way the data are to be used. In research studies comparing different groups, subject-to-subject variability may overwhelm modest increases in the S/N ratio obtained by optimizing individual CBF measurements. On the other hand, in studies emphasizing repeated measurements within subjects, optimization may significantly reduce the number of subjects needed to test a given hypothesis.

The current state-of-the-art is rather encouraging: there are several PET methods for measuring CBF which have been widely accepted. Each has its advantages and weaknesses, none is perfect. There is no doubt that a theoretically sound examination of the measurement strategy is necessary and desireable. But, examining the CBF method in isolation is insufficient. Practical considerations should be seen as necessary constraints to the optimization.

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(continued from page 1914)

SELF-STUDY TEST
Skeletal Nuclear Medicine
ANSWERS

bones, including the auditory ossicles, however, can be involved by Paget's disease.

Although the humerus is not one of the more common sites of Paget's disease, it is a relatively common site for sarcomas. In one series the femur was the most common site of sarcoma (33%), followed closely by the humerus (27%). Neoplastic changes within Pagetic bone probably occur in fewer than 1% of the cases. The most common type of sarcoma encountered is osteosarcoma (50%–60%). Less often, the lesion is a fibrosarcoma, chondrosarcoma, or malignant fibrous histiocytomas. Giant cell tumors also arise in Pagetic bone.

Although trigeminal neuralgia and blindness can occur as secondary changes in Paget's disease of the skull, they are much less common than deafness.

One of the roentgenographic hallmarks of Pagetic bone is enlargement of the affected bone. This enlargement of vertebral bodies helps distinguish Paget's disease from the changes caused by metastases. The bone enlargement is probably responsible for deafness and the other neurologic complications of Paget's disease involving the skull.

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ITEMS 22–26: Solitary Scintigraphic Abnormalities in Patients with Cancer

ANSWERS: 22, F; 23, T; 24, F; 25, F; 26, F

A number of studies have been reported on solitary bone scan abnormalities in patients with known extraosseous malignancies or primary bone tumors. Although there is variability between the series, it is clear that the likelihood that a solitary bone scan abnormality is a metastasis will vary with its location in the skeleton. Vertebral lesions are likely metastatic, whereas, rib and periarticular lesions are likely benign in nature.

A solitary metastasis appears quite often as a focus of increased uptake on the bone scan in association with normal radiographic findings. Photon-deficient lesions may be due to metastases that interrupt the vascular supply to the affected bone or to very aggressive metastatic disease with large lytic lesions but relatively little reparative response. The lesions of multiple myeloma typically have little or no reparative response. Most photon-deficient lesions, however, are due to benign causes, such as benign tumors, avascular necrosis, artifacts, or surgical defects.

Solitary abnormalities of the ribs most often are benign. In one series they were due to malignancy in only 10% of the cases. The overall likelihood that a single focus of increased uptake in a rib is due to metastasis is only 31%. Very commonly, a solitary focus of increased uptake on the bone scan is secondary to trauma; this is particularly true of a rib lesion.

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Note: For further in-depth information, please refer to the syllabus pages included at the beginning of *Nuclear Medicine Self-Study Program I: Part I.*