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EDITORIAL

A Bloody Future for Clinical PET?

During the past few years, PET imaging has emerged as a clinical tool because of its great potential for high quality imaging.

The uniqueness of PET lies in the fact that it is capable of quantitative regional measurement of physiological parameters. A number of general factors contribute to its quantitative nature. These include the unique physical properties of coincidence imaging, which allow for the absolute measurement of activity concentrations, the availability of short-lived positron-emitting isotopes which can easily be incorporated into biologically molecules, and the ability, by using ancillary information such as radioactivity concentrations of labeled substances in the arterial blood, to estimate regional physiological parameters. The first of these factors is intrinsic to modern PET instrumentation and the second is widely exploited in PET radiochemistry as it is practiced today.

It is the third area, however, that is often ignored in emerging clinical PET studies. It is widely believed, with some justification perhaps, that the insertion of arterial lines and the subsequent collection and processing of arterial blood is not compatible with the practice of clinical PET. Practitioners argue that arterial blood sampling limits patient throughput, requires extra personnel and processing time, exposes the patient to the unnecessary risks associated with the insertion of an arterial line and exposes personnel to the risks associated with the handling of patient blood.

With the increase in clinical PET studies during the past few years, imaging alone without the use of arterial blood concentration data is beginning to be used almost exclusively in many centers. This may be a trend which limits the long-term applicability of PET. It is not entirely clear that this trend should be encouraged. There is no question that, if arterial sampling could be eliminated with only minor constraints on the applicability of the technique, we would all readily throw away our catheters. But is this a realistic goal?

Because of the desire to eliminate the burdens of arterial sampling, a number of schemes to obtain input function data have been evaluated. In the past, these have included attempts to measure signals from the cardiac

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blood pool with a coincidence detector pair operated in time-of-flight mode (*1*) and to assess blood arterial radioactivity concentration by measuring signals from the radial artery using various detector configurations (*2*). Neither of these approaches has been particularly successful because of difficulties in positioning detectors and the failure to eliminate signal from surrounding tissues. Of course, these methods could at best only give information about radioactivity concentration in whole blood in any case and would yield no information about its distribution among the blood's components or its chemical form.

In order to estimate the concentrations of different chemical species or fractions within the blood, attempts have been made to use venous blood as a model for arterial blood, particularly with the tracer fluorodeoxyglucose (*3*). Although these attempts have been unsuccessful for the most part, the use of arterialized venous blood, produced by heat-induced arteriovenous shunts in the hand, has become an accepted practice with the fluorodeoxyglucose model (*4*). However, this method is only effective for tracers that have low extraction in tissue and thus is only applicable to a limited range of studies. While this may eliminate the discomfort and risk to the patient due to the insertion of an arterial line, the problems associated with the processing of blood still remain.

The advent of tomographs with resolutions in the range on 0.5 cm^2 has made it possible to obtain input function information directly from PET image data in some situations. For imaging of the heart and some regions of the lungs, such data have been successfully obtained from the left ventricle after making appropriate corrections for signal spillover from the myocardial wall (*5–7*). The work reported by Germano et al. in this issue of the *Journal* extends this concept to the use of the abdominal aorta for renal and hepatic imaging. Although state-of-the-art resolution might limit this method, the authors have made convincing use of the size- and shape-dependent recovery coefficient to account for such limitations. This technique has the potential for achieving the best compromise between no sampling and full sampling for a limited class of situations in which only the concentration of label in whole blood is required for quantitation of physiology. Many flow tracers fall within the bounds of this constraint because they do not form labeled metabolic products in the blood. The method, however, is also limited to those situations in which a blood pool that is larger than the tomograph's resolution is located within the field of view during imaging.

Another approach to the elimination of arterial blood sampling involves the careful selection of experimental paradigms so that differences in PET signals between two controlled physiological states yield useful information. One example of this is the execution of paired stimulation blood flow studies in the brain using ^{15}O. Several dynamic protocols using inhaled $C^{15}O^2$ or injected H_2O give rise to a linear relationship between blood flow and tissue concentration (*8–10*). If one is willing to sacrifice knowledge of the overall organ flow, differences between the two stimulation states can be computed directly from tissue concentration data without an input function. Similarly, one might argue that paired stress and rest studies of myocardial blood flow fall into this category, although the cardiac output changes dramatically between studies, with the likely result that the arterial input function shape also changes.

In the same spirit, the design of advanced radiopharmaceuticals that are highly specific but do not produce labeled metabolites in the blood could considerably reduce the requirements for arterial blood sampling. This is a noble long-term goal, but it is probably not a realistic one at present.

Techniques such as that presented by Germano et al. and those developed for blood flow imaging with water, while quite useful in their own right, do not represent a direction that will prove to be a panacea for the problem of arterial blood sampling. Attempts to moderate or eliminate the need for arterial sampling serve a very important purpose in making some PET studies such as flow measurements simpler and more efficient. But the desire to run clinical PET centers without spilling a drop of arterial blood may be a disservice to the PET technique. We must decide what we want clinical PET to be!

Will it be just Super-SPECT with better image quality and a somewhat broader range of radiopharmaceuticals, or will it be a true quantitative physiological technique uniquely measuring physiological parameters, such as neuroreceptor densities and binding rates, tumor-specific metabolism or cell division rates? If we choose the latter, and I believe we should, we must still consider arterial blood sampling and processing for many procedures despite the fact that it makes PET more complex than other nuclear medicine procedures. Rather than attempting to "get the price down" by limiting the technique in order to impress regulators, institutions establishing new centers should incorporate the cost of the apparatus, space and personnel who handle blood in their financial and physical plans in order to fully exploit the potential of PET. The pursuit of methods that obviate the need for arterial sampling is an important aspect of current PET research, but we should not rely on such methods alone at the cost of sacrificing the general power of PET.

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FIRST IMPRESSIONS

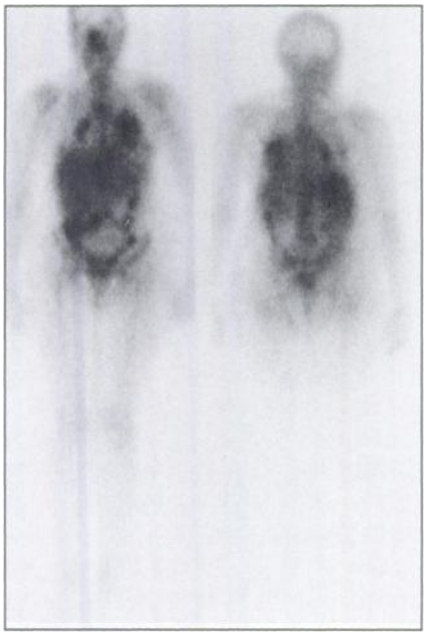

Figure 1

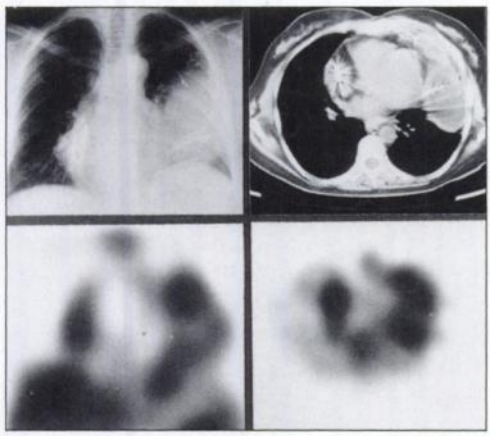

Figure 2

PURPOSE

A 51-yr-old woman underwent a dynamic cardiomyoplasty procedure 5 yr ago. The left latissimus dorsi muscle with its neurovascular supply still attached was brought into the left chest and wrapped around the left ventricle to enhance cardiac output which had been compromised by a left ventricular aneurysm. Pacemaker leads were attached to the right atrium and the left latissimus dorsi muscle in the chest to synchronize cardiac and skeletal muscle contractions. For the past 3 mo, she experienced spiking temperatures, chills and leukocytosis. Planar total-body ^{67}Ga-citrate scans in the anterior and posterior projections and 48-hr SPECT images of the chest demonstrated activity over the left lung and in the right mediastinum adjacent to the heart. A chest roentgenogram and CT scan (Fig. 2) showed a large intrathoracic mass with pacemaker electrodes in the left chest and in the right atrium of the heart. The planar and SPECT gallium images of the chest were interpreted as demonstrating an infected left latissimus dorsi muscle, infected right atrium, and abscess formation. Subsequent surgery to remove the infected electrodes showed an edematous left latissimus dorsi muscle with several abscesses at the sites of attachment of the electrodes to both the latissimus dorsi and the wall of the right atrium. The patient was treated with antibiotics and is awaiting a new pacemaker.

TRACER

5 mCi of ^{67} Ga-citrate

ROUTE OF ADMINISTRATION

Intravenous injection

TIME AFTER INJECTION

48 hr

INSTRUMENTATION

GE 3000 XRT camera

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