EDITORIAL

Is Redistribution Important in Sestamibi Myocardial Imaging?

The FDA has recently approved two technetium-labeled myocardial imaging agents for clinical use. The expanded armamentarium of nuclear cardiac imaging poses challenges and opportunities to select the most appropriate procedure in any given patient. Although ^{99m}Tc-sestamibi and ^{99m}Tc-teboroxime are perfusion imaging agents, their characteristics differ considerably from each other and from ^{201}Tl (*1–8*). One of these differences is related to the washout, or more appropriately, net clearance. The net clearance of ^{201}Tl from the myocardium depends on the gradient between the intracellular concentration and blood concentration. The clearance is higher at maximal exercise than submaximal exercise; it is higher at exercise than rest, and it is higher with exercise than with pharmacologic testing. The blood-thallium concentration, and hence, clearance may be changed with food intake or with ribose infusion. Thallium clearance is the basis for classifying perfusion defects into fixed or reversible and in assessing myocardial viability. The rate of clearance also has been used in the detection of coronary stenosis and predicting the number of diseased coronary arteries. It is for these reasons that thallium images are acquired as soon as possible after injection and the patient is advised against having a heavy meal between the initial and redistribution images.

Myocardial uptake of sestamibi and its clearance are quite different from that of ^{201}Tl. Piwnica-Worms et al. (*4*) suggest that myocardial uptake of sestamibi involves passive distribution across plasma and mitochondrial membranes and that at equilibrium sestamibi is sequestered within the mitochondria by a large negative transmembrane potential. Beanlands et al. (*2*) suggest the presence of special binding sites for sestamibi; reversible injury could result in the loss of membrane integrity or the loss of binding sites, resulting in a decrease in sestamibi concentration. In their experiments, cell injury was induced by a cytochrome C oxidase inhibitor (sodium cyanide) and sarcolemmal membrane detergent (triton X-100). Meerdink and Leppo (*6*) concluded from experiments done in isolated perfused rabbit hearts that the net myocardial retention for sestamibi tends to increase despite a constant coronary perfusion pressure during acute tissue hypoxia and membrane ATPase inhibition. On the other hand, in these experiments, hypoxia and ouabain appeared to have an opposite effect on thallium kinetics. Glover and Okada (*3*) and Okada et al. (*9*) showed that clearance of sestamibi is small and is similar in normal and ischemic myocardium (15% over 4 hr). The negligible redistribution has been suggested to be on the basis of low blood levels of sestamibi and long myocardial retention. The above data suggest that imaging after injection of sestamibi can be postponed for several hours since the redistribution is not a clinically important phenomena. In fact, in our initial experience, imaging was started 2 hr after injection, although at the present time, imaging is often started 30–60 min after injection because minimal clearance in the range of 10%–15% may occur (*10*).

In this issue of the *Journal*, Taillefer et al. (*11*) present data suggesting that sestamibi redistribution may be more important than hitherto appreciated. They obtained planar sestamibi images in 25 patients with coronary artery disease 1 and 3 hr after exercise and measured the count ratio and clearance in the normal and ischemic myocardium. Segmental analysis showed 48 ischemic segments at 1 hr and 46 at 3 hr. The ischemic-to-normal wall ratios were 0.73 ± 0.10 at 1 hr and 0.83 ± 0.12 at 3 hr. The clearance (15% ± 8%) in ischemic segments was significantly lower than the clearance in normal segments (26% ± 12%, $p < 0.001$). These results indicate that the higher ratio at 3 hr is due to faster clearance from the normal myocardium. The clearance rates in the study were similar to those reported by Franceschi et al. (*8*); 27% ± 8% at 6 hr in normal myocardium and 16% in ischemic myocardium.

Although the number of ischemic segments were not statistically different at 1 and 3 hr, the diagnostic certainty especially in the presence of mild abnormality may be affected. These results are also clinically relevant because the delay may result in underestimation of the severity and the extent of the perfusion abnormality. It is not entirely clear whether this process of redistribution may account for the variability between the size of the perfusion abnormality measured by thallium and by sestamibi reported by Narahara et al. (*12*) or for the variability between the extent of the perfusion abnormality and exercise left ventricular function reported by Jones et al. (*13*). For example, Narahara et al. observed that exercise-induced sestamibi perfusion defects were smaller than the thallium defects and Jones et al. found variability between exercise left ventricular ejection fraction and the size of the sestamibi perfusion defect. Of note, Narahara et al. obtained thallium and Jones et al. obtained left ventricular ejection fraction images earlier than the corresponding sestamibi images. The results of Taillefer et al. (*11*) were obtained with planar images, which because of "shine through" and overlapping activity, may be more obvious

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than those obtained with SPECT. Observations by Taillefer et al. are also important in relation to timing of imaging in patients with acute myocardial infarction undergoing thrombolytic therapy (*14*). Until further data are available, it seems prudent to begin imaging within 1 hr after sestamibi injection.

Further studies using SPECT imaging are needed to address clearance rate and its impact on assessment of the area at risk.

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