appropriate background activity and attenuating media to mimic clinical situations, defects representing infarct and ischemia can also be identified.

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EDITORIAL

Simultaneous Thallium-201/Technetium-99m Dual-Isotope Cardiac SPECT: Ready for Prime Time?

Simultaneous dual-isotope SPECT myocardial perfusion imaging with ^{201}Tl and ^{99m}Tc-sestamibi may potentially provide a very attractive means to evaluate patients with known or suspected coronary artery disease. A ^{201}Tl dose is administered with the patient at rest, and a ^{99m}Tc-sestamibi dose is then given during peak exercise. Subsequent dual-isotope imaging could simultaneously provide images of both rest and stress perfusion distribution. Potential clinical advantages of this approach are substantial and multifold. Since only one single SPECT acquisition is required, patient throughput could be doubled, substantially increasing the cost-effectiveness of instrumentation and personnel and increasing the satis-

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doubled, substantially increasing the cost-effectiveness of instrumentation and personnel and increasing the satisfaction of patients and referring physicians. In an environment of decreasing reimbursement and managed care, this approach could serve to increase productivity while at the same time decrease cost.

Another advantage inherent to simultaneous dual-isotope imaging is the elimination of image artifacts associated with a lack of reproducibility of acquisition parameters between the stress and rest images. Such factors include differences in patient positioning, distance between the camera and chest wall, angle of the SPECT rotational arc and the configuration of elliptical orbits. There are also patient-related parameters that may vary between the stress and rest acquisitions, such as the position of the breasts (especially in women with large, pendulous breasts), degree of elevation of the left hemidiaphragm (more elevated after ingesting fluid or swallowing air), depth of respiration, and patient motion.

The cardiovascular nuclear medicine community has been extremely circumspect about this approach, with even the most vocal advocates of dual-isotope studies who now use separate image acquisitions for ^{201}Tl and ^{99m}Tc-sestamibi, cautioning that the simultaneous dual-isotope approach is not yet "ready for prime time." Concern has stemmed primarily from the fact that there is substantial downscatter of the high-dose sestamibi distribution into the low-dose ^{201}Tl window, creating the potential for overestimation of ischemia since the ^{99m}Tc-sestamibi stress activity would substantially contribute to the ^{201}Tl image. Also, since spatial and contrast resolution are poorer for the low-dose resting ^{201}Tl image, actual fixed defects due to myocardial scarring may be less well defined with ^{201}Tl than ^{99m}Tc. Thus, defect reversibility, i.e., ischemia, might be overestimated.

Unfortunately, with an eye to performing studies more rapidly or more economically, many laboratories are too quick to embrace attractive new imaging methods without a thorough, systematic basic science and clinical validation. For example, for ^{201}Tl a variety of "two-step" reinjection methods arose to evaluate myocardial viability, circumventing the validated "three-step" (stress image → rest image → rest reinjection → rest image) technique. The methods that have been adopted vary from reinjection 20 min after exercise to 15 min before the 3-hr delayed image. For ^{99m}Tc-sestamibi, rest/stress dose ratios and the interval between the two one-day protocol acquisitions vary widely. Quantitative CEqual analysis is incorrectly applied to studies acquired with parameters quite different than those that were used to validate the CEqual software.

Technologists performing studies and physicians interpreting scans must be cognizant of the serious clinical implications of indiscriminantly varying SPECT acquisition and processing parameters without prior validation. For instance, for ^{99m}Tc-sestamibi SPECT, laboratories without a high-resolution collimator have substituted a low-energy, all-purpose collimator. What is the impact of the associated increase in image count density and decrease in spatial resolution? For both ^{201}Tl and sestamibi, filters are freely substituted to make images appear "crisper," "smoother," or "less noisy." Moreover, filters vary considerably among vendors. What is the impact on test sensitivity and specificity? On a busy day a technologist might decide to shorten the acquisition time (and increase the dose??) to increase patient throughput. What are the consequences with regard to count density, resolution, sensitivity and specificity? What differences are introduced by changing from a circular orbit to an elliptical orbit or from a patient-centered acquisition to a heart-centered acquisition? Variations in any of these factors may significantly impact on test accuracy and should be investigated with well controlled phantom experiments and clinical trials. Nuclear medicine technologists and physicians nonchalantly vary these parameters without prior validation and without full knowledge of the associated clinical impact. Of greater concern, physicians with only a passing familiarity with basic science and instrumentation may be totally unaware of the impact of varying parameters. (Alas, credentialing should be the subject of another editorial).

Lowe et al. are to be commended for their article appearing in this issue of the *Journal* (*1*). Varying individual parameters systematically in well controlled phantom experiments, these authors investigate the feasibility and potential limitations of simultaneous ^{201}Tl/^{99m}Tc dual-isotope SPECT. This type of phantom evaluation is mandatory when evaluating a new technique with such clinically far-reaching applications as well as such potentially serious errors. In the SPECT phantom experiments they performed, Lowe et al. demonstrated that myocardial-to-defect count ratios for both ^{201}Tl and ^{99m}Tc were very similar for studies acquired using separate single-isotope and dual-isotope acquisitions. Computerized quantitation of defect size yielded similar results for separate and dual-isotope acquisitions. Finally, subjective interpretation of the phantom images by experienced observers was nearly the same for the two methods. These results are quite promising and certainly support further investigation and clinical validation of the dual-isotope method.

However, it is not yet time to convert your lab to dual-isotope SPECT! Readers must also consider study limitations and difficulties in extrapolating these phantom data to actual patient studies, which the authors elaborate fairly and appropriately in their Discussion section. The phantom myocardial defects were large and easily recognized (Figs. 2–5), probably more so than those encountered in most routine clinical studies. The phantoms, of course, were stationary and free of cardiac and respiratory motion, therefore making the defects appear even more clearcut.

Perhaps the greatest difficulty in extrapolating these data to clinical studies is the limited experiments performed to investigate the effect of

attenuation configurations encountered in actual patients. The "thorax" of phantom A was a uniform, water-filled, elliptical cylinder. Phantom B, constructed to simulate a patient's body more closely, contained only a spine and lungs. Unfortunately, somewhat like models from a fashion magazine, these phantoms contained no chest wall fat, no sternum, no breasts, no left hemidiaphragm and no abdominal protuberance, all of which are more likely to create differential attenuation and scatter effects for ^{201}Tl versus ^{99m}Tc. In phantom A, downscatter from ^{99m}Tc into the ^{201}Tl window created only a 10% reduction in myocardium-to-defect count ratio in the infarct model. Even in phantom B, limited "anatomic" scatter and attenuation introduced a considerable degradation of image quality and defect recognition, with the myocardium-to-defect ratio decreasing from 2.96 to 1.77 (Table 1).

The amount of Compton scatter is directly proportional to density and thickness of the scattering medium because the probability of multiple low-angle scattering events increases as gamma-ray energy decreases. In patients with increased thoracic attenuation, this effect would tend to make fixed defects appear reversible since ^{99m}Tc downscatter would "fill in" the ^{201}Tl defect. The opposite effect could occur due to differential attenuation of ^{201}Tl versus ^{99m}Tc. Attenuation is directly proportional to the thickness of the attenuator and inversely proportional to the energy of the isotope. Therefore, ^{201}Tl attenuation is greater than that for ^{99m}Tc, potentially resulting in the appearance of "reverse redistribution" of defects that are truly fixed, and a "fixed" appearance of defects that are mildly reversible. Therefore, in obese patients, patients with diaphragmatic elevation and in women with large breasts—all commonly encountered in clinical practice, and all of whom depart considerably from the "Twiggy" shape of phantoms A and B—the favorable results of this phantom study may not be applicable.

Another consideration for dual-isotope imaging is the considerable variation of tracer distribution concentration extrinsic to the heart between ^{201}Tl and ^{99m}Tc-sestamibi. For ^{201}Tl, liver activity is minimal in stress images but greater in resting studies. For exercise or pharmacologic stress ^{99m}Tc-sestamibi studies, the amount of liver activity varies depending on the injection-to-imaging interval. Bowel tracer concentration may be considerable and may be two or three times greater than that in the myocardium. If ^{99m}Tc bowel activity scatters into the ^{201}Tl photopeak, an inferior sestamibi stress defect might appear reversible in the ^{201}Tl rest study. The potential of ^{99m}Tc downscatter into the ^{201}Tl window was not addressed by Lowe et al.

Cardiac SPECT studies are plagued by patient motion artifacts. In stress/rest studies, patient motion in one but not at all acquisitions can result in significant test inaccuracy. Motion at a different time or in a different direction between acquisitions can also affect accuracy. Simultaneous dual isotope acquisition will not totally circumvent this source of artifact. Instead, motion artifacts will most often result in fixed defects. Resolution of small defects is better with ^{99m}Tc than ^{201}Tl as demonstrated by Lowe, et al. in a phantom B experiment (attenuation present) (Table 1). Motion artifacts, which are usually relatively small, may result in defects which appear to be reversible rather than fixed.

In summary, the excellent phantom study by Lowe et al. takes us a large step forward on our way to simultaneous ^{201}Tl/^{99m}Tc dual-isotope myocardial perfusion imaging. Although the potential advantages of this method with regard to convenience and cost-effectiveness are enormous, we should not yet jump to embrace it clinically. Considerably more phantom work needs to be done, particularly addressing the issues of attenuation and scatter, and subsequent well controlled clinical trials are mandatory.

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