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# Myocardial Perfusion Imaging Protocols: Is There an Ideal Protocol?\*

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Is there an ideal myocardial perfusion imaging protocol? In order to answer this question and choose a protocol for clinical use, one must understand the characteristics of the available radiopharmaceuticals, the protocol variables, and the advantages and disadvantages of each. After reading this article, the technologist should be able to list the ideal characteristics of a myocardial perfusion imaging agent, describe and compare the characteristics of myocardial perfusion imaging agents, discuss the relationship between coronary blood flow and myocardial uptake of various tracers, describe imaging protocols, and discuss the advantages and disadvantages of each protocol.

**Key Words:** myocardial perfusion imaging; tracer kinetics; coronary blood flow; myocardial uptake;  $^{201}\text{Tl}$ ;  $^{99\text{m}}\text{Tc}$

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**S**cintigraphic evaluation of myocardial perfusion for the diagnosis of coronary artery disease is a valuable noninvasive diagnostic imaging modality.  $^{201}\text{Tl}$  was introduced as a myocardial perfusion imaging agent in the early 1970s and remained in common use until the mid-1980s, when  $^{99\text{m}}\text{Tc}$ -labeled radiopharmaceuticals were developed and, for the most part, replaced thallium for evaluating myocardial perfusion abnormalities. The numbers of procedures performed have grown exponentially since the advent of  $^{99\text{m}}\text{Tc}$ -labeled radiopharmaceuticals for myocardial perfusion imaging.

The development of new radiopharmaceuticals, a newer generation of advanced  $\gamma$ -cameras with SPECT capabilities, and PET has dramatically revolutionized myocardial perfusion imaging. It is only natural to expect that this evolutionary process would lead to the development of various imaging protocols dealing with many variables, such as those pertaining to  $\gamma$ -cameras, radiopharmaceuticals, reimburse-

ment issues, hospital discharge policies, scheduling logistics for outpatient clinics, and patients' demographics and convenience.

The purpose of this review was to compare the salient features of the available protocols, the advantages and disadvantages of each protocol, and the kinetics of various radiotracers to gain a better understanding of the many and often competing imaging protocols. There is a plethora of literature dealing with numerous issues pertaining to every available protocol. Novices are often confused when deciding which protocol to use.

Following is a basic review of the physical properties, biodistribution, and kinetics of each radiotracer.

## RADIOPHARMACEUTICALS

Ideally, a radiopharmaceutical for myocardial perfusion imaging should have the following characteristics: myocardial uptake directly proportional to blood flow, high extraction fraction, high target-to-background ratio, and good myocardial retention and photon flux for optimal imaging.

### $^{201}\text{Tl}$

$^{201}\text{Tl}$  is a cyclotron-produced potassium analog radioisotope with a half-life of 73 h. It produces  $\gamma$ -energy rays of 170 keV (~10%) and 135 keV (~3%). The photons resulting from electron capture have energies of 69–80 keV (abundance) and are the photons used for imaging. The first-pass myocardial extraction of  $^{201}\text{Tl}$  is ~85%; however, only about 3%–5% of the total injected dose localizes in the myocardium when injected at peak exercise. The initial  $^{201}\text{Tl}$  uptake within the myocardium occurs through the active Na-K adenosine triphosphatase transport system. After the initial extraction,  $^{201}\text{Tl}$  redistributes within the myocardium.  $^{201}\text{Tl}$  has a relatively short myocardial retention. The injected dose is low (74–148 MBq [3–4 mCi]). The counting statistics are fair. The radiation dosimetry is not favorable because of the high total body absorbed dose, 0.68 rad (*I*).

### $^{99\text{m}}\text{Tc}$ -Sestamibi

Sestamibi is an isonitrile compound that, when labeled with  $^{99\text{m}}\text{Tc}$ , has a half-life of 6 h. It produces  $\gamma$ -energy rays of 140 keV (abundance), which are ideal for imaging.  $^{99\text{m}}\text{Tc}$ -Sestamibi is extracted from the coronary circulation in proportion to the coronary blood flow. The first-pass myocardial extraction fraction of  $^{99\text{m}}\text{Tc}$ -sestamibi is 55%–68%.

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The myocardial extraction is lower than that of  $^{201}\text{Tl}$  but adequate.  $^{99\text{m}}\text{Tc}$ -Sestamibi myocardial cellular retention occurs specifically within the mitochondria as a result of an electrostatic interaction. Myocardial retention is prolonged. The myocardial uptake of  $^{99\text{m}}\text{Tc}$ -sestamibi is ~1.2%–1.5% of the injected dose. Unlike  $^{201}\text{Tl}$ ,  $^{99\text{m}}\text{Tc}$ -sestamibi shows minimal redistribution. The injected dose of  $^{99\text{m}}\text{Tc}$ -sestamibi is higher than that of  $^{201}\text{Tl}$ , resulting in better counting statistics for imaging. The radiation dosimetry is favorable, with a total body absorbed dose of 0.50 rad (1).

#### $^{99\text{m}}\text{Tc}$ -Tetrofosmin

Tetrofosmin is a diphosphine compound that, when labeled with  $^{99\text{m}}\text{Tc}$ , has a half-life of 6 h and produces  $\gamma$ -energy rays of 140 keV.  $^{99\text{m}}\text{Tc}$ -Tetrofosmin is taken up by the myocardium in proportion to the coronary blood flow. The first-pass myocardial extraction fraction is ~54%. Approximately 1.2% of the injected dose localizes in the myocardium. The myocardial uptake, retention, and blood clearance of  $^{99\text{m}}\text{Tc}$ -tetrofosmin are similar to those of  $^{99\text{m}}\text{Tc}$ -sestamibi. There is little redistribution. The hepatic clearance of  $^{99\text{m}}\text{Tc}$ -tetrofosmin is faster than that of  $^{99\text{m}}\text{Tc}$ -sestamibi (1). As with  $^{99\text{m}}\text{Tc}$ -sestamibi, the injected dose is higher than that of  $^{201}\text{Tl}$ , resulting in better counting statistics.

#### $^{99\text{m}}\text{Tc}$ -Teboroxime

Teboroxime is a boronic acid-derived, neutral lipophilic compound that, when labeled with  $^{99\text{m}}\text{Tc}$ , has a half-life of 6 h and produces  $\gamma$ -energy rays of 140 keV. Myocardial cell uptake is proportional to coronary blood flow. Being a neutral lipophilic compound, it passively diffuses across the myocardial cell membrane. The first-pass myocardial extraction fraction is high (>90%), and the washout is rapid. There is no redistribution. The injected dose is higher than that of other agents, resulting in good counting statistics for imaging. The radiation dosimetry is not favorable, with a total body absorbed dose of 0.83 rad (1). This imaging agent is not commercially available in the United States at this time. It is, however, approved by the U.S. Food and Drug Administration as a myocardial perfusion imaging agent.

#### $^{99\text{m}}\text{Tc}$ -N-NOET

$^{99\text{m}}\text{Tc}$ -N-NOET is a new myocardial perfusion imaging agent that is comparable to  $^{201}\text{Tl}$ . It is a neutral lipophilic agent. Biodistribution studies have demonstrated selective myocardial localization. Myocardial uptake is directly proportional to coronary blood flow. The first-pass myocardial extraction fraction is high.  $^{99\text{m}}\text{Tc}$ -N-NOET redistributes like  $^{201}\text{Tl}$ , thus allowing initial stress and delayed rest imaging. Clearance of pulmonary activity is rapid. The image quality is good because of low background interference. The stress and rest images provide comparable information for the diagnosis of ischemia (2,3). This agent is not yet approved for routine use in the United States.

## COMPARISON OF $^{201}\text{Tl}$ AND $^{99\text{m}}\text{Tc}$ -LABELED MYOCARDIAL PERFUSION IMAGING TRACER KINETICS

Following is a brief discussion of various tracer kinetic parameters for  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -sestamibi showing how the 2 radiotracers differ. A detailed discussion of these parameters is beyond the scope of this article.

The myocellular uptake of  $^{201}\text{Tl}$  is dependent on Na-K adenosine triphosphatase. The myocardial uptake of  $^{201}\text{Tl}$  declines with Na-K pump inhibition from adenosine triphosphate depletion. The myocellular uptake of  $^{99\text{m}}\text{Tc}$ -sestamibi reflects the mean plasma membrane potential.  $^{99\text{m}}\text{Tc}$ -Sestamibi is retained within the mitochondria as a result of an electrostatic interaction. It declines to low levels with severe cell injury (4).

Myocardial transmicrovascular transport of  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -sestamibi is variable at different blood flow levels. The capillary permeability for  $^{201}\text{Tl}$  is greater than that for  $^{99\text{m}}\text{Tc}$ -sestamibi. The parenchymal cell permeability surface area for  $^{99\text{m}}\text{Tc}$ -sestamibi is much higher than that for  $^{201}\text{Tl}$  (5).

The tracer kinetics of  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -sestamibi across myocytes are affected by low-flow ischemia. During low-flow ischemia, the information provided by  $^{201}\text{Tl}$  or  $^{99\text{m}}\text{Tc}$ -sestamibi SPECT imaging is dependent on myocardial perfusion and not on a cellular metabolic disorder (6).

## RELATIONSHIP BETWEEN CORONARY BLOOD FLOW AND MYOCARDIAL UPTAKE OF VARIOUS RADIOTRACERS

The various kinetics and biodistributions of different radiotracers determine myocardial uptake, retention, redistribution, and washout. The relationship between coronary blood flow and the myocardial uptake of radiotracers is not linear. All commonly used radiopharmaceuticals show a plateau “roll-off” at higher blood flow levels. The radiotracers show a significant roll-off at coronary blood flow levels exceeding 2.5 mL/min/g. The roll-off is the smallest for  $^{201}\text{Tl}$  and is larger for  $^{99\text{m}}\text{Tc}$ -sestamibi and  $^{99\text{m}}\text{Tc}$ -tetrofosmin (7). A comparison of the first-pass myocardial extraction fractions of various technetium-labeled agents and thallium is shown in Table 1.

## PHYSICAL AND BIOLOGIC COMPARISONS OF MYOCARDIAL PERFUSION IMAGING AGENTS

There are significant differences in the physical and biologic properties of  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -labeled radiopharmaceuticals.

**TABLE 1**  
Comparison of First-Pass Myocardial Extraction Fractions of Various  $^{99\text{m}}\text{Tc}$ -Labeled Agents and  $^{201}\text{Tl}$

Agent	% Extraction fraction
$^{201}\text{Tl}$	82–88
$^{99\text{m}}\text{Tc}$ -Sestamibi	55–68
$^{99\text{m}}\text{Tc}$ -Tetrofosmin	54
$^{99\text{m}}\text{Tc}$ -Teboroxime	>90
$^{99\text{m}}\text{Tc}$ -NOET	75–85

Table 2 shows a comparison of various factors affecting the myocardial uptake of the radiotracers.

## VARIOUS IMAGING PROTOCOLS

### <sup>201</sup>Tl Imaging

Myocardial perfusion imaging with <sup>201</sup>Tl was commonly used until <sup>99m</sup>Tc-labeled radiotracers became available. The most commonly used procedure involves administering ~148 MBq (~4 mCi) of <sup>201</sup>Tl at peak exercise. Stress imaging is performed immediately after the <sup>201</sup>Tl injection (beginning within 5–7 min of the injection). Delayed rest (redistribution) images are obtained at 3–4 h after injection. There are several variations of delayed imaging, which can be done at up to 24 h to assess viability. In addition, a <sup>201</sup>Tl reinjection technique with an additional booster dose of 37–55.5 MBq (1.0–1.5 mCi) is used to assess myocardial viability.

### Myocardial Perfusion Imaging with <sup>99m</sup>Tc-Labeled Radiopharmaceuticals (Sestamibi or Tetrofosmin)

*Two-Day Protocol.* Two-day protocols are best in terms of taking advantage of the physical properties, pharmacokinetics, and acquisition, processing, and display parameters of <sup>99m</sup>Tc-labeled agents. Typical doses for 1- and 2-d protocols are shown in Table 3.

The advantages of 2-d protocols are as follows: flexibility of scheduling stress–rest imaging; better patient flow; ability to image obese patients; higher dose; better gated rest–stress imaging; no cross talk or cross contamination; optimal defect contrast with minimal background activity; elimination of day 2 study if stress study is normal; and high accuracy for detecting coronary artery disease in patients with a low likelihood of coronary artery disease.

The disadvantages of 2-d protocols are as follows: the need for 2 d; inconvenience for patients; delay in diagnosis; and camera time relative to that used for dual-isotope simultaneous acquisition, which is not recommended because of energy window cross talk.

*Imaging Protocol for <sup>99m</sup>Tc-Labeled Agents.* For stress imaging, 555 MBq–1.11 GBq (15–30 mCi) is injected at peak exercise. Gated SPECT is performed from 15 min to

**TABLE 3**  
Doses of <sup>99m</sup>Tc-Labeled Agents for Myocardial Perfusion Scintigraphy\*

Protocol	Sestamibi	Tetrofosmin
One-day protocol		
First dose	8–10 mCi	5–8 mCi
Second dose	22–30 mCi	15–24 mCi
Two-day protocol		
First dose	15–30 mCi	15–24 mCi
Second dose	15–30 mCi	15–24 mCi

\*Reprinted from Crawford ES, Husain SS. *Nuclear Cardiac Imaging: Terminology and Technical Aspects*. Reston, VA: Society of Nuclear Medicine; 2003:29.

2 h after injection, preferably within 15–30 min, to maximize stress myocardial defect contrast and minimize hepatobiliary and gastrointestinal interference.

For rest imaging, 555 MBq–1.11 GBq (15–30 mCi) is injected at rest. Gated SPECT is performed within 45–60 min after injection. A 60-min delay is optimal for adequate hepatobiliary clearance of the radiotracer.

Imaging too soon after injection will result in increased residual liver activity and increased counts in the adjacent inferior wall because of scatter and scaling. Waiting too long will decrease total myocardial count density and increase gastrointestinal interference. The optimal imaging window is when radiotracer activity has cleared from the liver and not concentrated in the gastrointestinal tract, that is, loops of bowel and the stomach (retrograde flow).

In the event that there is a significant splanchic or bowel overlap with the inferior wall, various maneuvers, such as drinking water or milk or eating fatty food, can be tried to alleviate the problem before repeating delayed imaging.

*One-Day Rest–Stress or Stress–Rest Protocol Performed with Sestamibi or Tetrofosmin.* The rest–stress sequence is significantly better than the stress–rest sequence in terms of detecting the reversibility of stress-induced perfusion deficits. With the stress–rest sequence, the rest activity obscures some of the stress defect, resulting in the degradation

**TABLE 2**  
Physical and Biologic Comparisons of Myocardial Perfusion Imaging Agents

Factor	<sup>99m</sup> Tc-Sestamibi or <sup>99m</sup> Tc-tetrofosmin	<sup>201</sup> Tl
Extraction fraction	Lower	Higher
Myocardial retention	Prolonged	Comparatively shorter
Myocardial washout	Slower	Rapid
Redistribution	Minimal	Significant
Myocardial perfusion at high blood flow	Same	Same
Injected dose	Higher	Lower
Counting statistics	Better	Fair
Physical half-life	6 h	73.1 h
Photon energy	140 kEv	68–80 kEv (abundance), 170 kEv (~10%), and 135 kEv (~3%)
Radiation dosimetry	More favorable	Less favorable

of image contrast and a reduction in the detection of true reversibility.

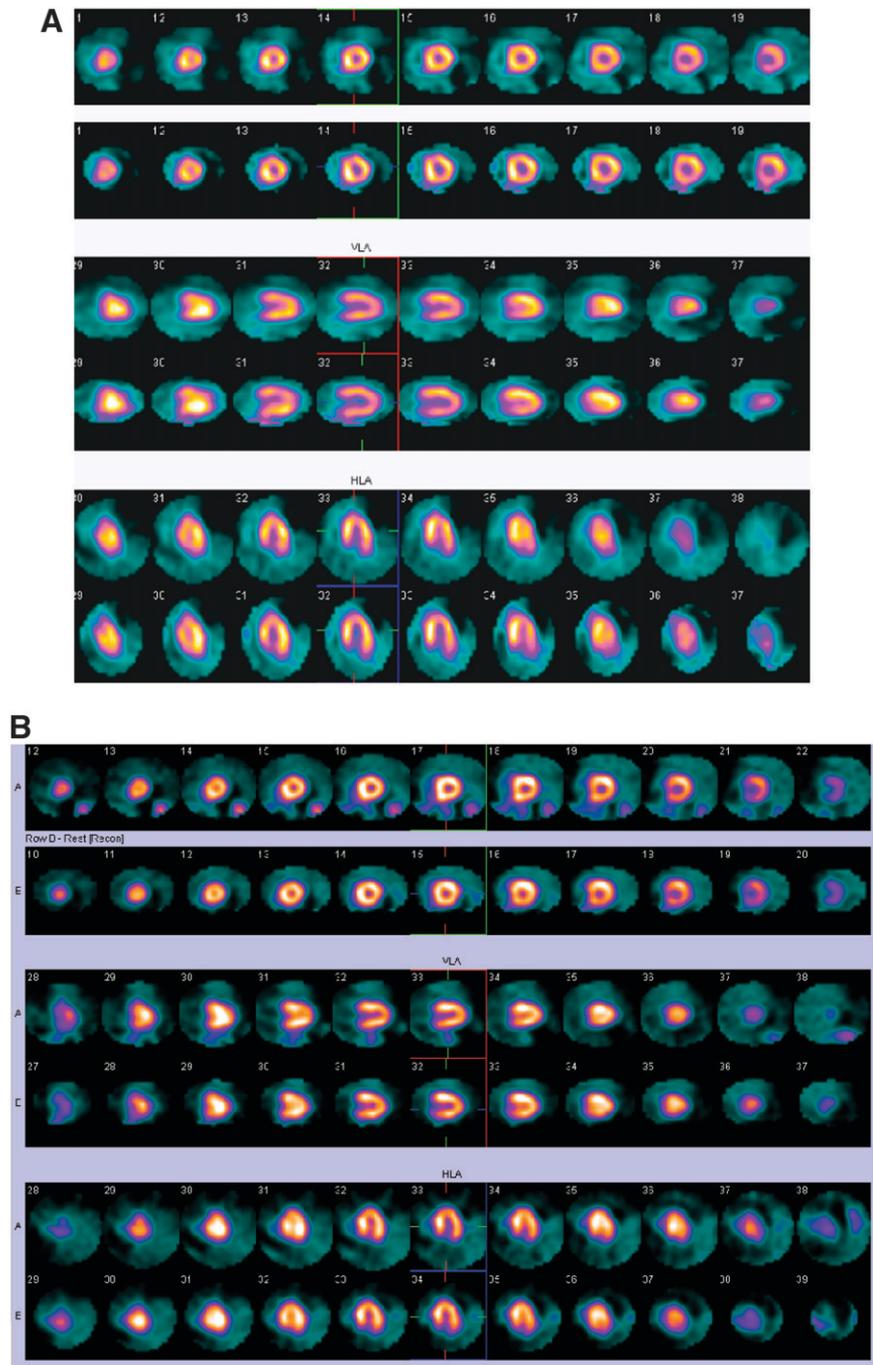
With the rest–stress sequence, there is a greater difference in counts between normal and abnormal areas of the myocardium on stress images. This difference results in better normalization of the abnormality on rest images. A 3- to 4-h delay between rest imaging and stress imaging allows radioactivity to decay by 29%–37%, thereby providing better image contrast (8,9). However, the American Society of Nuclear Cardiology guidelines (10) offer the option to proceed immediately from rest imaging to stress

imaging during a 1-d protocol as long as the higher dose is 3.5–4.0 times the lower dose.

Images from a 2-d protocol and images from a 1-d (rest–stress) protocol are shown in Figure 1. Both studies are normal. The studies were obtained with the same camera. The images from the studies are very comparable in features and quality.

#### One-Day Dual-Isotope Acquisition Protocol

A 1-d dual-isotope protocol with  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$ -sestamibi can be performed with separate acquisition or



**FIGURE 1.** (a) Images obtained with 2-d  $^{99\text{m}}\text{Tc}$ -sestamibi protocol. Findings are normal. (b) Images obtained with 1-d  $^{99\text{m}}\text{Tc}$ -sestamibi protocol. Findings are normal.

simultaneous acquisition. In a separate acquisition of  $^{201}\text{Tl}$  rest images, the contribution of  $^{201}\text{Tl}$  to the  $^{99\text{m}}\text{Tc}$  energy window is negligible ( $\sim 2.9\%$ ). Correction for cross contamination between the 2 energy windows is not required. The overall sensitivity and specificity for the detection of coronary artery disease are  $\sim 90\%$  (11,12).

**Dual-Isotope Separate-Acquisition Protocol.** For the rest  $^{201}\text{Tl}$ -stress  $^{99\text{m}}\text{Tc}$  protocol, 111–148 MBq (3–4 mCi) of  $^{201}\text{Tl}$  is injected in the upright position to decrease lung uptake. Rest  $^{201}\text{Tl}$  SPECT is performed after 10–15 min. When rest imaging is complete, the patient is sent for treadmill or pharmacologic stress testing. Next, 555 MBq–1.11 GBq (15–30 mCi) of the  $^{99\text{m}}\text{Tc}$ -labeled agent is injected, and SPECT acquisition is begun at 15 min after injection.

For viability assessment, the patient can be given a second injection of thallium and reimaged on the following morning; alternatively, thallium can be given the night before imaging begins. Figure 2 is a diagram of dual-isotope imaging protocol options. The images from a normal dual-isotope study are shown in Figure 3.

The advantages of the dual-isotope separate-acquisition protocol are as follows: a short duration of the entire study ( $< 2$  h); no need for cross talk correction; insignificant contribution of counts from  $^{201}\text{Tl}$  to the  $^{99\text{m}}\text{Tc}$  window; minimization of the problem of cross contamination; optimal defect contrast; comparable rest and stress images; true rest study, which allows a better evaluation of reversible defects; viability assessment; favorable dosimetry; patient convenience; and sensitivity and specificity of  $\sim 90\%$ .

The disadvantages of the dual-isotope separate-acquisition protocol are as follows: comparison of stress–rest images obtained with 2 isotopes with different characteristics; variability in attenuation factors; differences in image resolution; greater Compton scatter of  $^{201}\text{Tl}$  than of  $^{99\text{m}}\text{Tc}$ ; greater myocardial wall thickness with  $^{201}\text{Tl}$  than with  $^{99\text{m}}\text{Tc}$  be-

cause of increased scatter; less-than-optimal transient ischemic dilatation evaluation because of left ventricular cavity being larger with  $^{99\text{m}}\text{Tc}$ ; difficulty in evaluating minimal reversible defects; and low photon energy of  $^{201}\text{Tl}$ , a feature that is not ideal for obese patients.

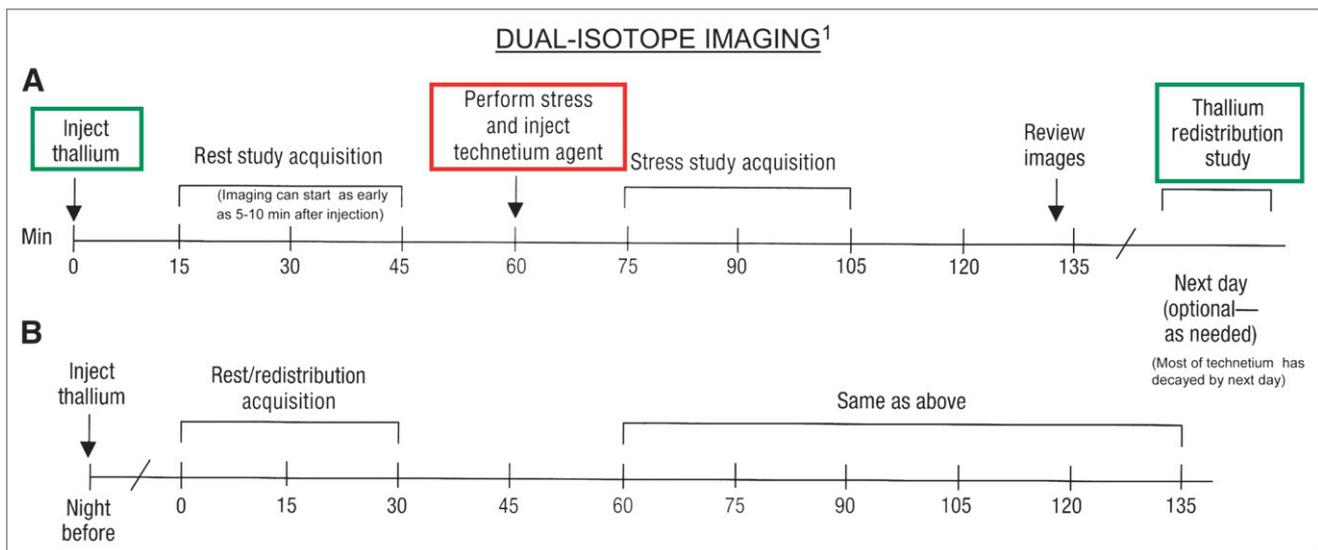
Figure 4 shows the normal cavity size difference between a  $^{201}\text{Tl}$  scan and a  $^{99\text{m}}\text{Tc}$ -labeled agent scan. Myocardial wall thickness is greater with  $^{201}\text{Tl}$  than with  $^{99\text{m}}\text{Tc}$ -labeled agents. This normal difference in cavity size is attributable to  $^{201}\text{Tl}$  scatter.

**Dual-Isotope Simultaneous-Acquisition Protocol.** The dual-isotope simultaneous-acquisition protocol is based on the unproven assumption that the effect of cross talk between the energy windows of  $^{201}\text{Tl}$  and  $^{99\text{m}}\text{Tc}$  is insignificant. Downscatter of high-energy  $^{99\text{m}}\text{Tc}$ -sestamibi into the lower-energy  $^{201}\text{Tl}$  window results in an  $\sim 20\%$  reduction in defect contrast with  $^{201}\text{Tl}$  and in the overestimation of defect reversibility (12). Downscatter correction methods are not conclusive and have not been clinically validated.

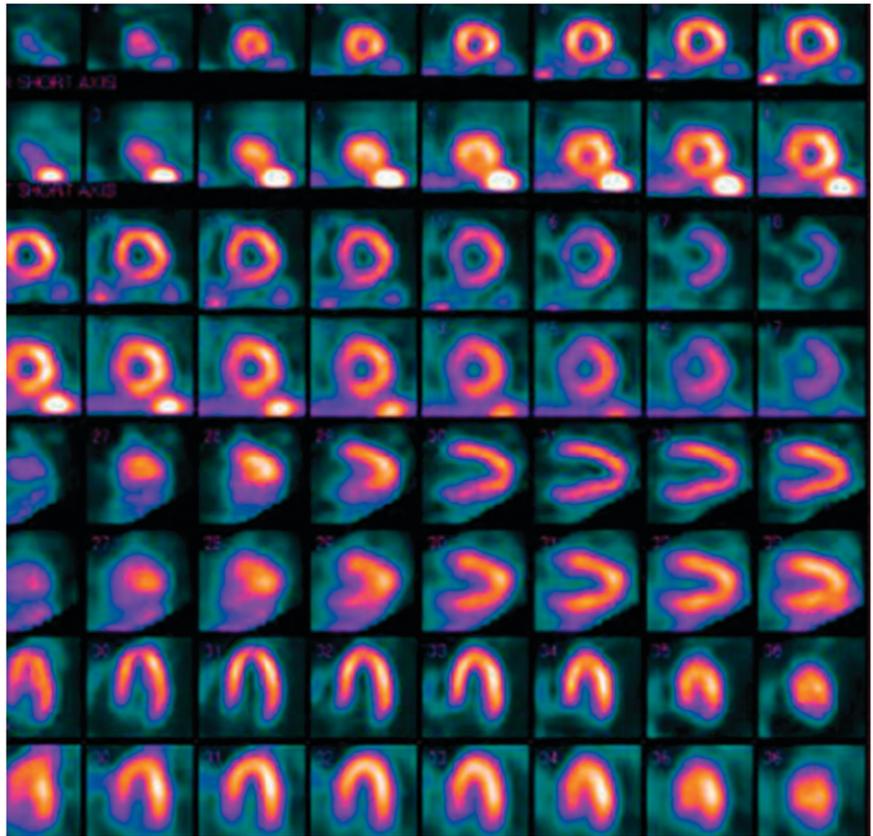
For the simultaneous rest  $^{201}\text{Tl}$ -stress  $^{99\text{m}}\text{Tc}$ -sestamibi SPECT protocol, 111 MBq (3.0 mCi) of  $^{201}\text{Tl}$  is injected at rest. The stress study is performed within 30 min. After the stress acquisition, 925 MBq (25 mCi) of  $^{99\text{m}}\text{Tc}$ -sestamibi is injected at peak exercise, and dual SPECT studies are acquired within 30 min.

The advantages of the dual-isotope simultaneous-acquisition protocol are as follows: no need for 2 separate imaging sessions; reduced camera acquisition time; shorter study duration; fewer motion artifacts than with separate rest and stress acquisitions; and exact registration between images obtained with  $^{201}\text{Tl}$  and images obtained with  $^{99\text{m}}\text{Tc}$ .

The disadvantages of the dual-isotope simultaneous-acquisition protocol involve cross talk and downscatter; the contribution of scattered and primary photons from the



**FIGURE 2.** Dual-isotope imaging. Reprinted from Crawford ES, Husain SS. *Nuclear Cardiac Imaging: Terminology and Technical Aspects*. Reston, VA: Society of Nuclear Medicine; 2003;33.



**FIGURE 3.** Images obtained with  $^{99m}\text{Tc}$ -sestamibi (top row of each pair of rows) and  $^{201}\text{Tl}$  (bottom row of each pair) in dual-isotope protocol. Findings are normal.

first radionuclide into the photopeak window of the second radionuclide results in a significant degradation of image quality, image resolution, and quantitation. This protocol is not recommended because of the problem of downscatter.

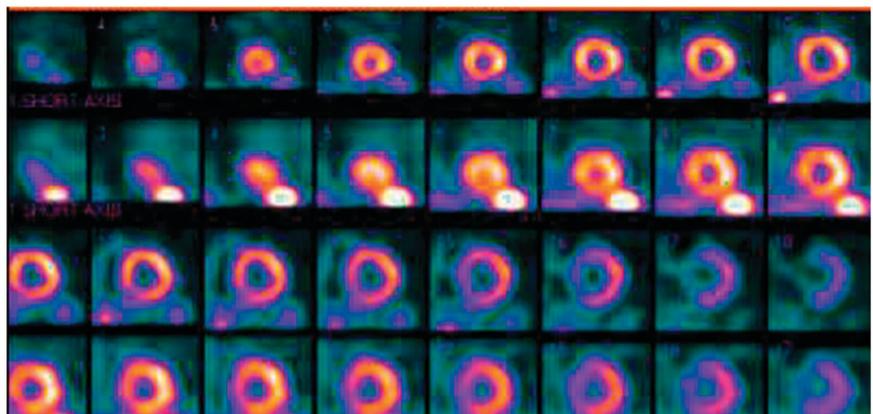
*Dual-Isotope Cross Talk Correction Methods.* Several methods are available for correcting dual-isotope cross talk. Downscatter correction methods are not conclusive and have not been clinically validated. A detailed review of various methods is available in physics books dealing with this subject.

Moore's correction method corrects only for the contribution of  $^{99m}\text{Tc}$  to the  $^{201}\text{Tl}$  primary 70-keV window. The 3-window transformation method involves 2 single-isotope acquisitions and 1 dual-isotope acquisition. Simultaneous

cross talk correction by this method is slightly better than that by Moore's correction method. In the convolution cross talk correction method, convolution filters are derived from point response functions for  $^{99m}\text{Tc}$  and  $^{201}\text{Tl}$  point sources. Acquisitions are done with  $^{99m}\text{Tc}$  only,  $^{201}\text{Tl}$  only, and with a mixture of  $^{99m}\text{Tc}$  and  $^{201}\text{Tl}$ . The average point response function is used in the creation of a filter.

## CONCLUSION

There is no single best protocol that addresses all of the issues. From the standpoints of tracer kinetics, physical properties, and the laws of physics, the 2-d  $^{99m}\text{Tc}$ -labeled agent myocardial perfusion imaging protocol is perhaps the



**FIGURE 4.** Normal cavity size difference between images obtained with  $^{99m}\text{Tc}$ -sestamibi (top row of each pair of rows) and those obtained with  $^{201}\text{Tl}$  (bottom row of each pair) in dual-isotope protocol.

best. The 1-d rest–stress  $^{99m}\text{Tc}$ -labeled agent myocardial perfusion imaging protocol may be a better choice for some clinics. The 1-d dual-isotope separate-acquisition protocol is a good alternative. The dual-isotope simultaneous-acquisition protocol is a suboptimal choice until an approach for downscatter correction is conclusive and validated clinically.

Again, there is no single best protocol. Each protocol has advantages and disadvantages, which must be understood and taken into consideration when one is choosing a protocol. The staff members in each clinic need to determine which protocol will work best for them and consistently maintain it for better comparison when repeat studies are performed on the same patient.

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## REFERENCES

1. Crawford ES, Husain SS. *Nuclear Cardiac Imaging: Terminology and Technical Aspects*. Reston, VA: Society of Nuclear Medicine; 2003.

2. Fagret D, Marie PY, Brunotte F, et al. Myocardial perfusion imaging with technetium-99m-Tc NOET: comparison with thallium-201 and coronary angiography. *J Nucl Med*. 1995;36:936–943.
3. Sinusas AJ. Technetium 99m-N-NOET: although not equivalent to thallium-201, it still offers new opportunities [comment]. *J Nucl Cardiol*. 2000;7:185–188.
4. Piwnica-Worms D, Chiu ML, Kronauge JF. Divergent kinetics of  $^{201}\text{Tl}$  and  $^{99m}\text{Tc}$ -sestamibi in cultured chick ventricular myocytes during ATP depletion. *Circulation*. 1992;85:1531–1541.
5. Leppo JA, Meerdink DJ. Comparison of the myocardial uptake of a technetium-labeled isonitrile analog and thallium. *Circ Res*. 1989;65:632–639.
6. Ayalew A, Marie PY, Menu P, et al.  $^{201}\text{Tl}$  and  $^{99m}\text{Tc}$ -MIBI retention in an isolated heart model of low-flow ischemia and stunning: evidence of negligible impact of myocyte metabolism on tracer kinetics. *J Nucl Med*. 2002;43:566–574.
7. Zaret B, Beller G. *Clinical Nuclear Cardiology*. 3rd ed. Philadelphia, PA: Mosby; 2005:216.
8. Van Train KF, Garcia EV, Maddahi J, et al. Multicenter trial validation for quantitative analysis of same-day rest-stress technetium-99m-sestamibi myocardial tomograms. *J Nucl Med*. 1994;35:609–618.
9. Taillefer R, Gagnon A, Laflamme L, et al. Same day injections of  $^{99m}\text{Tc}$ -methoxy isobutyl isonitrile (hexamibi) for myocardial tomographic imaging: comparison between rest-stress and stress-rest injection sequences. *Eur J Nucl Med*. 1989;15:113–117.
10. Henzlova MJ, Cerqueira MD, Mahmarian JJ, Yao SS; Quality Assurance Committee of the American Society of Nuclear Cardiology. Stress protocols and tracers. *J Nucl Cardiol*. 2006;13:e80–e90.
11. Berman DS, Kait H, Friedman JD, et al. Separate acquisition rest thallium-201/stress technetium-99m sestamibi dual-isotope myocardial perfusion single-photon emission computed tomography: a clinical validation study. *J Am Coll Cardiol*. 1993;22:1455–1464.
12. Kiat H, Germano G, Friedman J, et al. Comparative feasibility of separate or simultaneous rest thallium-201/stress technetium-99m-sestamibi dual-isotope myocardial perfusion SPECT. *J Nucl Med*. 1994;35:542–548.