Myocardial Perfusion Imaging with Technetium-99m-Sestamibi: Comparative Analysis of Available Imaging Protocols

Daniel S. Berman, Hosen S. Kiat, Kenneth F. Van Train, Guido Germano, Jamshid Maddahi and John D. Friedman

Departments of Imaging, Medical Imaging Physics and Medicine; Division of Cardiology, Cedars-Sinai Medical Center, Los Angeles; and Departments of Medicine and Pharmacology, UCLA School of Medicine, Los Angeles, California

Several protocols for rest and stress myocardial perfusion imaging with ^{99m}Tc-sestamibi have been developed, each with distinct advantages and disadvantages. The various approaches have similar sensitivities and specificities for detection of coronary artery disease (CAD), but differ mainly in their ability to identify defect reversibility. The dual-isotope approach, with a rest ^{201}Tl study and a stress ^{99m}Tc-sestamibi study, permits optimal evaluation of both stress perfusion and defect reversibility. Gated SPECT may be added to any of the protocols and aids in identifying artifacts, defining regional wall thickening and assessing ventricular function. First-pass ^{99m}Tc-sestamibi radionuclide angiography can add exercise ventricular function data to the study. Clinical trials have shown that the various protocols for ^{99m}Tc-sestamibi provide diagnostic and prognostic information comparable to that derived from traditional ^{201}Tl imaging, with the added advantage of higher quality images and increased certainty in interpretation.

Key Words: myocardial perfusion imaging; technetium-99m-sestamibi; ventricular function

J Nucl Med 1994; 35:681–688

Technetium-99m-sestamibi is a myocardial perfusion radiotracer that has been commercially available in the United States since 1990 (*1–3*). Compared to ^{201}Tl, ^{99m}Tc has a shorter physical half-life (6 hr versus 73 hr), which allows for a higher injected dose of ^{99m}Tc-sestamibi (25 to 30 mCi compared with 2 to 3 mCi of ^{201}Tl). The higher injected dose, in conjunction with adequate myocardial extraction and prolonged myocardial retention of ^{99m}Tc-sestamibi, results in a higher imaging count density on single-photon emission computed tomography (SPECT) than can be obtained with ^{201}Tl. Higher counts result in improved SPECT image quality, a principal advantage of ^{99m}Tc-sestamibi. In general, ^{99m}Tc-sestamibi produces higher-quality images than ^{201}Tl, thus increasing observer certainty and the probability that other laboratories can reproduce the results of reported clinical trials (*1–3*).

Another important characteristic of ^{99m}Tc-sestamibi is its slow myocardial washout (*4*), which ameliorates concern regarding the prolonged imaging times associated with SPECT. If, for example, the patient moves during the initial ^{99m}Tc-sestamibi SPECT study, the acquisition can be repeated without major compromise to the amount of clinical information obtained. Conversely, with ^{201}Tl, the possibility of early redistribution decreases the reliability of a repeat acquisition.

Because of its minimal redistribution and long myocardial residence time, ^{99m}Tc-sestamibi also allows for gated SPECT imaging (*5–7*), which is not generally performed with ^{201}Tl and cannot be performed with the other clinically available ^{99m}Tc-labeled myocardial perfusion agent, ^{99m}Tc-teboroxime. Another advantage of ^{99m}Tc-sestamibi is its ability to be used for combined myocardial perfusion SPECT and exercise first-pass radionuclide ventriculography studies from a single radiotracer injection (*8,9*).

Since the recent introduction of technetium-99m-labeled radiotracers for myocardial perfusion imaging, a variety of protocols for the performance of this procedure have been developed. The purpose of this paper is to assess the advantages and disadvantages of each approach. Since SPECT is the preferred (*1–3,10,11*) and most commonly used approach to myocardial perfusion imaging with ^{99m}Tc-sestamibi, this discussion will be limited to SPECT protocols.

Received Dec. 21, 1993; revision accepted Jan. 13, 1994.
This paper was presented in part at the Annual Meeting of the Society of Nuclear Medicine on June 11, 1993, as part of a Continuing Medical Education Seminar organized by the Cardiovascular Council.
For correspondence or reprints contact: Daniel S. Berman, MD, Department of Imaging, Room 5431, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, CA 90048.

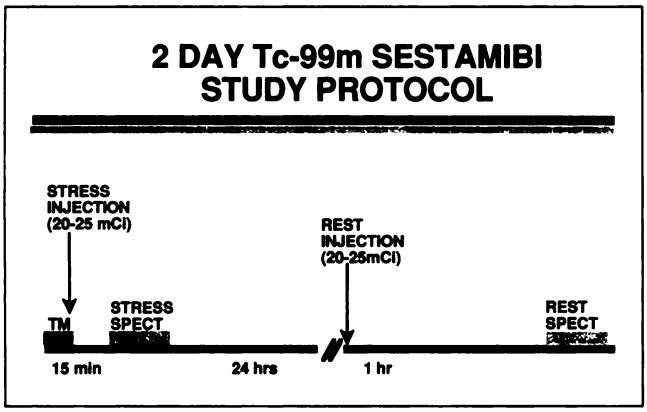

FIGURE 1. Two-day stress/rest ^{99m}Tc-sestamibi SPECT protocol.

TWO-DAY PROTOCOL

Sestamibi does not redistribute to the same extent as ^{201}Tl (*4*). Therefore, to assess stress defect reversibility with ^{99m}Tc-sestamibi, a two-injection protocol is required. A two-day protocol (Fig. 1) is optimal from the standpoint of defect contrast because it avoids contamination from one image acquisition to the next. Most commonly, the exercise study is done on the first day and the rest study on the second day, because if the exercise SPECT is totally normal, the rest SPECT is not necessary. In some patients, such as those with acute myocardial infarction (MI) or those recovering from unstable angina, it may be preferable to perform the rest SPECT first and then to evaluate whether the exercise study is appropriate.

On Day 1, a 20- to 30-mCi ^{99m}Tc-sestamibi dose is injected at peak exercise, which is continued for 1 min at maximal workload, followed by an additional 2 min at a one stage lower workload (*1*). Acquisition begins 15 min to 2 hr postinjection. We recommend the earlier time (15–30 min) for SPECT with all of the exercise ^{99m}Tc-sestamibi protocols so as to maximize stress myocardial defect contrast.

The 15-min postexercise acquisition time also minimizes hepatobiliary or gastrointestinal interference. With this earlier imaging time, it is not necessary to give milk or a fatty meal prior to imaging to clear gallbladder activity (*12*). For exercise acquisition with any of the ^{99m}Tc-sestamibi protocols discussed here, we recommend a symmetric energy window over the 140-keV ^{99m}Tc photopeak, a high-resolution collimator and a circular 180° orbit using 64 projections from the 45° right-anterior oblique (RAO) to the 45° left-posterior oblique (LPO) position (*1*). An extensive discussion of why these acquisition parameters were selected and of the recommendations for reconstruction, display, quantitation and interpretations is presented elsewhere (*1,12–14*).

On Day 2, a 20- to 30-mCi ^{99m}Tc-sestamibi dose is injected at rest, with a 1-hr delay before SPECT imaging and administration of milk 15 min before imaging. The 1-hr delay for rest imaging is necessary to allow for adequate hepatobiliary clearance.

Summarizing the Two-Day Protocol

The two-day protocol provides optimal defect contrast with minimal background activity. Clinical trials have shown that this approach has a high accuracy for detecting CAD (*10,15*). An unequivocally normal stress ^{99m}Tc-sestamibi study on Day 1 can eliminate the need to perform the rest study on Day 2, potentially saving diagnostic costs for the patient or third-party payers.

The disadvantages of the two-day protocol are the uncertainty as to when the diagnostic procedure will be completed, and the inconvenience (for both the patient and the referring physician) of the image acquisition on the second day. Also, although this protocol is excellent for evaluating myocardial perfusion, it is suboptimal for evaluating myocardial viability because a rest SPECT study with ^{99m}Tc-sestamibi, with its minimal redistribution, is not as effective as a redistribution ^{201}Tl study for detection of defect reversibility in hibernating myocardium (*11,16*).

ONE-DAY PROTOCOL

Rest/Stress Sequence

One-day protocols for ^{99m}Tc-sestamibi have also been developed. A same-day protocol can be stress/rest or rest/stress, the latter being more widely used (Fig. 2) (*1,13,14,17*). With the rest/stress method, a lower-dose injection (8–10 mCi) is given at rest, with SPECT acquisition 1-hr later. For the rest SPECT study, we recommend a longer imaging time per stop than is used with the stress acquisition (25 sec versus 20 sec) (*1,13,14*) due to the lower injected dose employed. A 3-hr delay is recommended to maximally reduce background counts before the stress study (*13*). A 25–30-mCi ^{99m}Tc-sestamibi dose is then injected at peak exercise, with SPECT imaging performed 15 min to 2 hr postinjection. The entire rest/stress procedure takes about 5-hr. Clinical trials with this protocol have shown high sensitivity and specificity for detection of CAD (*1,18*), and the rest/stress procedure generally results in images of excellent quality (Fig. 3).

Quantitative Analysis

Through a combined effort of Cedars-Sinai Medical Center and Emory University, a sophisticated quantitative image-analysis technique for interpreting ^{99m}Tc-sestamibi myocardial perfusion SPECT images has been developed (Fig. 4) (*13,14,18*). In its first application, the program was used in same-day rest/stress ^{99m}Tc-sestamibi studies with specialized normal limits developed for this approach. The

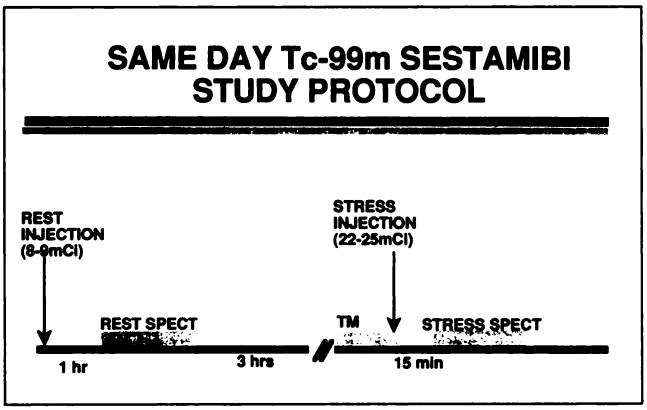

FIGURE 2. Same-day rest/stress ^{99m}Tc-sestamibi SPECT protocol.

program has demonstrated high sensitivity and normalcy rates for detecting the presence of CAD in a large multicenter trial (*18*). Normal limits to be applied to two-day and dual-isotope protocols (see below) are currently being developed (*19*).

Summarizing Same-Day Rest/Stress

The strengths of the same-day rest/stress approach is that results are available in one day and that the quantitation analysis has been thoroughly developed and validated. One limitation is that it provides suboptimal contrast between the stress perfusion defect and normal myocardium because of the background activity from the rest study. Theoretically, this limitation could reduce the sensitivity for CAD detection, particularly for mild disease; such effect, however, has not been reported to date. In addition, the two-day approach is suboptimal for the detection of hibernating myocardium since the resting phase is performed with ^{99m}Tc-sestamibi, an agent that does not redistribute as much as ^{201}Tl. Furthermore, the time required for the study is still suboptimal because of the 1-hr delay between radiotracer injection and the rest image acquisition, and because of the recommended 3-hr delay between the rest and stress studies.

Stress/Rest Sequence

An alternative same-day approach uses the stress/rest sequence in which a low-dose stress study is followed by a high-dose rest study (*20–22*). An advantage of this approach is its convenience; cardiologists who perform the stress tests generally prefer the morning stress procedure that this protocol allows. However, this approach has been shown to be less effective than the rest/stress sequence in assessing defect reversibility (*21*). In addition, because it uses a low-dose stress study, the most important image from the standpoint of disease detection and prognosis, the stress image, does not ideally utilize the potential of extra counts provided by a ^{99m}Tc-sestamibi study. It also involves the simplest conversion from ^{201}Tl to ^{99m}Tc-sestamibi because its timing and sequence are the same as a stress ^{201}Tl reinjection protocol: a stess study followed by a rest study 4-hr later. Furthermore, this protocol offers ideal stress-defect contrast because there is no resting background activity.

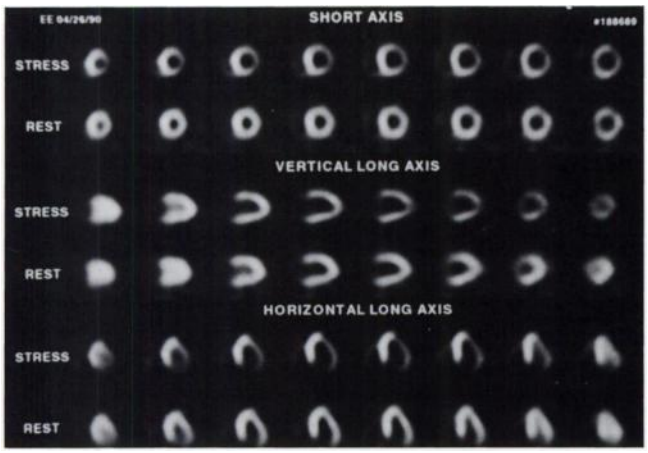

FIGURE 3. Case example of an abnormal same-day rest/stress ^{99m}Tc-sestamibi SPECT demonstrating reversible defects in the anterolateral and lateral walls. The patient had an 80% stenosis of the diagonal artery and a subtotal occlusion of the left circumflex coronary artery.

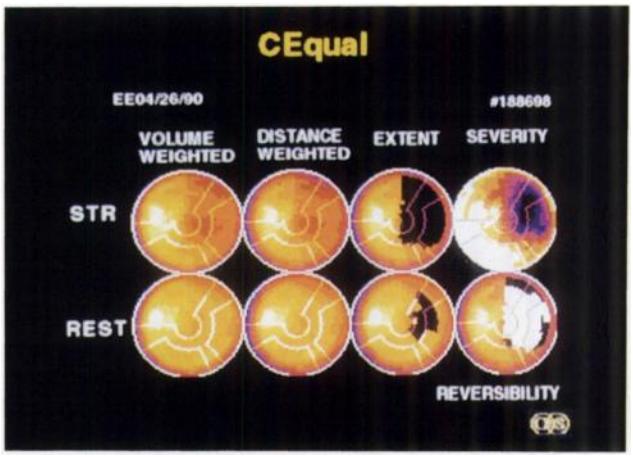

FIGURE 4. Quantitative polar maps using the CEqual program in the patient whose images are shown in Figure 3. Note that the quantitative stress defect extent polar map correctly identifies the visually observed stress defects, and that the reversibility map correctly identifies the defect as reversible.

DUAL-ISOTOPE PROTOCOL

A dual-isotope protocol—a rest ^{201}Tl study followed by a stress ^{99m}Tc-sestamibi study—combines optimal techniques for evaluating myocardial perfusion and viability (*12,23*). Conceptually, both rest and stress images can be obtained simultaneously in one SPECT acquisition, or with separate acquisitions. The costs for the radiopharmaceutical supplies of this dual-isotope procedure are comparable to those of a two-dose ^{99m}Tc-sestamibi protocol (*12*).

Simultaneous SPECT Acquisition

For completeness, we include this protocol, although its limitations, noted below, indicate that it should not yet be used routinely (*24*). With this approach (Fig. 5), 3 mCi of ^{201}Tl is injected at rest. Before any imaging is performed, the patient is exercised on a treadmill and 25 mCi of ^{99m}Tc-sestamibi is injected at peak exercise . At 15 min postinjection, the patient is imaged on the SPECT camera set up to collect images on both ^{201}Tl and ^{99m}Tc windows. This protocol could dramatically improve patient throughput and scheduling since only one SPECT acquisition is employed.

There is a technical problem, however, that must be corrected before this simultaneous SPECT acquisition protocol is used in the clinical setting. Approximately 27% of the counts detected in the ^{201}Tl window originate from cross-talk of ^{99m}Tc; i.e., simple energy-window discrimination on the ^{201}Tl peak does not completely separate the ^{201}Tl counts from the ^{99m}Tc counts (*24*). Nuclear medicine scientists are working to develop a correction for this prob-

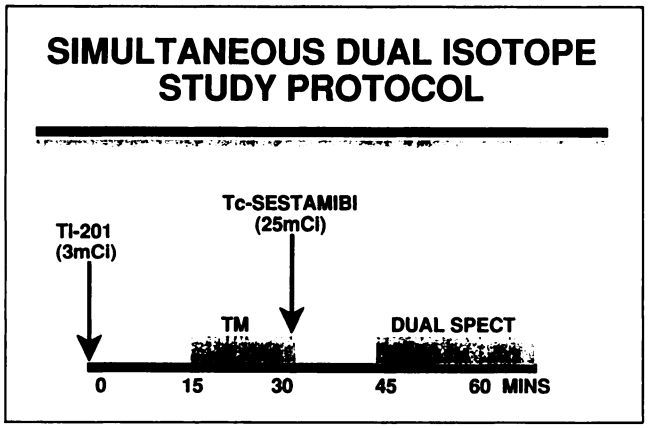

FIGURE 5. Simultaneous rest ^{201}Tl/stress ^{99m}Tc-sestamibi dual-isotope myocardial SPECT protocol. Until background subtraction techniques are developed, this protocol is not recommended.

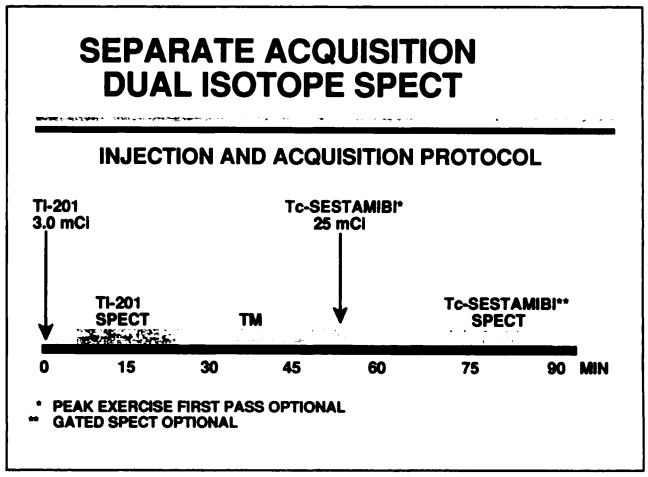

FIGURE 6. Separate acquisition rest ^{201}Tl stress ^{99m}Tc-sestamibi dual isotope myocardial perfusion SPECT protocol.

lem. Although a recent phantom study has suggested that simultaneous dual-isotope SPECT without correction for ^{99m}Tc contamination of the ^{201}Tl windows is valid (*25*) we have demonstrated clinically that this approach overestimates defect reversibility, particularly in moderate defects (*24*). Until appropriate cross-talk corrections are available, simultaneous SPECT acquisition for dual-isotope myocardial perfusion studies is not recommended (*24,26*) because myocardial viability could be overestimated by inflated counts in the ^{201}Tl images.

Separate SPECT Acquisitions

In contrast to the contribution of ^{99m}Tc to ^{201}Tl counts, the spill-over of ^{201}Tl counts into the ^{99m}Tc window is negligible (<2.9%) (*24*). Thus, a dual-isotope protocol in which rest ^{201}Tl SPECT is acquired first, followed immediately by ^{99m}Tc SPECT can be performed without the need for cross-talk correction.

In this protocol, 3 mCi of ^{201}Tl is injected at rest and the patient then undergoes ^{201}Tl SPECT acquisition (Fig. 6) (*12*). For the rest study, acquisition and reconstruction parameters identical to those used for the rest phase of the low-dose rest/high-dose stress same-day ^{99m}Tc-sestamibi SPECT protocols are used (i.e., an imaging time of 25 sec rather than 20 sec per stop is used, with the same filter as employed for the rest ^{99m}Tc-sestamibi SPECT study). High-resolution collimation is used for both the rest and exercise studies. The patient is then placed on a treadmill and at peak exercise 25 to 30 mCi of ^{99m}Tc-sestamibi is injected. The ^{99m}Tc-sestamibi SPECT image is acquired beginning 15 min postinjection. The entire procedure can be completed in 1.5 to 2.0 hr, which makes this dual-isotope, separate acquisition protocol a rapid, highly efficient procedure.

Dosimetry

Because the patient is being injected with two different radiopharmaceuticals each with different organ distributions, the dual-isotope approach does not double the radiation dosimetry of either agent alone, but gives a dose comparable to that of a typical ^{201}Tl reinjection protocol with approximate dosimetry of 1 rad whole-body and 5 rads to the critical organ (*12*).

Image Comparability

The rest ^{201}Tl and stress ^{99m}Tc-sestamibi SPECT images are similar enough that they can be easily and accurately compared (Fig. 7). The ^{201}Tl image shows slightly thicker myocardial walls than the ^{99m}Tc image because of increased scatter, a difference which generally poses no problem in interpretation. It should be recognized that throughout the history of nuclear medicine, dual-isotope techniques to assess different organ functions have been common. Lung scanning is done with ^{133}–Xe for ventilation and ^{99m}Tc for perfusion; kidney scanning is done with ^{131}I for function and ^{99m}Tc for perfusion; and cardiac PET scanning uses ^{13}N, ^{82}Rb, or ^{15}O water for myocardial perfusion and ^{18}F for viability.

Validation

The dual-isotope, separate-acquisition technique provides high sensitivity (91%–95%) and high normalcy rates (75%–82%) for detection of CAD (*12*). Furthermore, this approach has been shown to have a very high normalcy rate of 95% (Fig. 8) (*12*). An example of a patient with a reversible defect on a separate acquisition dual-isotope SPECT study is shown in Figure 9.

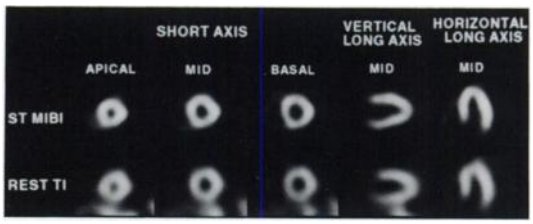

FIGURE 7. A normal case example of a separate acquisition rest ^{201}Tl (bottom row) stress ^{99m}Tc-sestamibi (top row) dual-isotope myocardial perfusion SPECT.

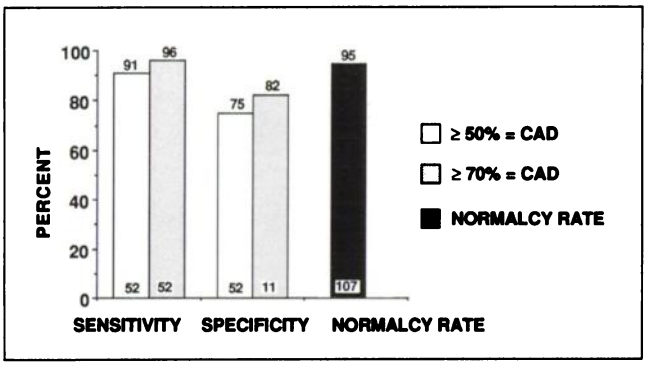

FIGURE 8. Sensitivity, specificity, and normalcy rate (solid bars) of separate-acquisition dual-isotope SPECT using two different criteria (≥50%, open bars; ≥70%, stippled bars) for coronary artery disease. Reprinted with permission from the American College of Cardiology (*Journal of the American College of Cardiology* 1993;22: 1455–1464).

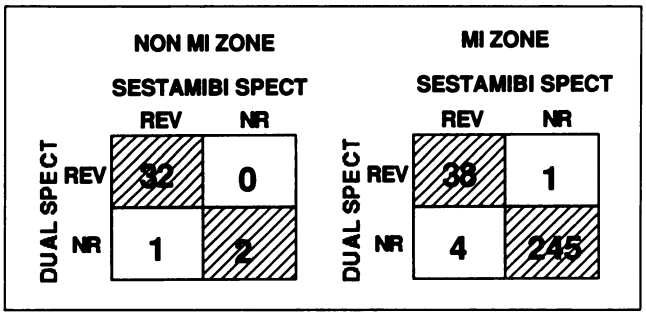

FIGURE 10. Comparison of defect reversibility type and dual-isotope SPECT and rest/stress ^{99m}Tc-sestamibi SPECT. Hatched regions indicate agreement: non-MI zone, 97% (kappa = 0.79, $p < 0.001$); MI zone, 98% (kappa = 0.93, $p < 0.001$). NR = nonreversible, rev = reversible. Reprinted with permission from the American College of Cardiology (*Journal of the American College of Cardiology* 1993;22:1455–1464).

In the prognostic evaluation of patients at risk for subsequent cardiac events, a study of 579 patients followed over 1 yr showed that the dual-isotope technique for myocardial perfusion studies provides incremental information over that provided by medical history and exercise variables (*27*). When the stress ^{99m}Tc-sestamibi study is normal, the probability of MI or cardiac death is <1% (*27*) throughout all ranges of CAD likelihood. When the ^{99m}Tc-sestamibi study is moderately or severely abnormal, the likelihood of future cardiac events increases throughout the spectrum of pretest CAD likelihoods. The incremental prognostic information of sestamibi appears comparable to that provided by ^{201}Tl (*28,29*).

To determine whether the dual-isotope approach provides an accurate assessment of defect reversibility, the perfusion defects were first compared with those from rest/stress ^{99m}Tc-sestamibi studies (*12*). Thirty-one patients who had undergone dual-isotope imaging returned for rest ^{99m}Tc-sestamibi studies. Concordance in defect type as reversible or nonreversible was 97% in non-MI zones and 98% in MI zones (Fig. 10). The dual-isotope study, therefore, provided virtually identical information to the rest/stress ^{99m}Tc-sestamibi study (Fig. 9).

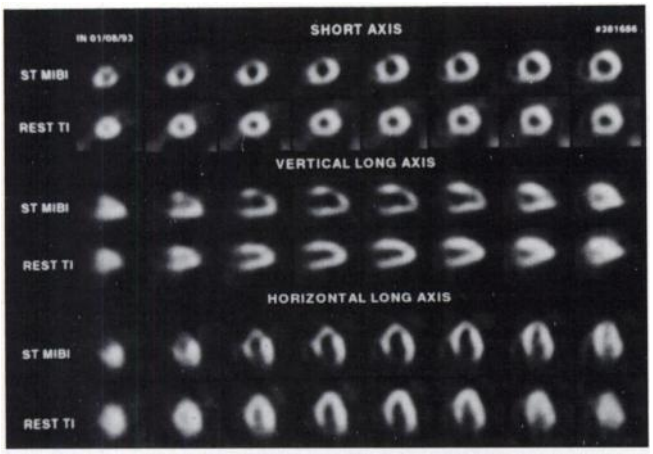

FIGURE 9. Case example of a reversible defect from separate-acquisition dual-isotope SPECT. Rows 1, 3, and 5 demonstrate the stress ^{99m}Tc-sestamibi images; rows 2, 4, and 6 show the rest ^{201}Tl images. A clear, large, severe, reversible defect is noted in the left anterior descending coronary artery territory.

Delayed ^{201}Tl Imaging

The principal benefit of this dual-isotope approach over two-dose ^{99m}Tc-sestamibi protocols lies in the assessment of defect reversibility. With rest/stress ^{99m}Tc-sestamibi studies, hibernating myocardium may appear to demonstrate the pattern of nonreversibility due to the minimal redistribution of sestamibi (*16*). With ^{201}Tl, however, redistribution imaging has a higher chance of identifying hibernating myocardium. With the dual-isotope protocol, this benefit is realized by performing a redistribution ^{201}Tl study after the rest injection when resting ^{201}Tl is present; i.e., patients with resting defects may be asked to return the next day for a delayed ^{201}Tl study (Fig. 11) to assess reversibility. The 24-hr delayed ^{201}Tl study in patients who have perfusion defects on the initial dual-isotope study increases reversible territory by 10%–15% compared with a rest/stress ^{201}Tl study alone (*30*).

To avoid turning the dual-isotope technique into a two-day imaging protocol, inpatients can be injected with ^{201}Tl the night before (Fig. 12). The next morning, they can undergo a 12-hr redistribution ^{201}Tl study, followed by a stress ^{99m}Tc-sestamibi study. There is no need for further imaging after the stress SPECT study, potentially saving a day of hospitalization in comparison to stress-redistribution ^{201}Tl studies. It is important to note that, for quantitation with this dual-isotope SPECT approach, standard ^{99m}Tc-sestamibi limits developed for the rest/stress ^{99m}Tc-sestamibi SPECT (*13,14*) can be used for the stress interpretation (*31*) due to the minimal contribution of ^{201}Tl to the ^{99m}Tc window (Fig. 13). However, to assess defect reversibility, special rest ^{201}Tl normal limits should be employed (*19,31*), not the standard rest/stress ^{99m}Tc-sestamibi normal limits.

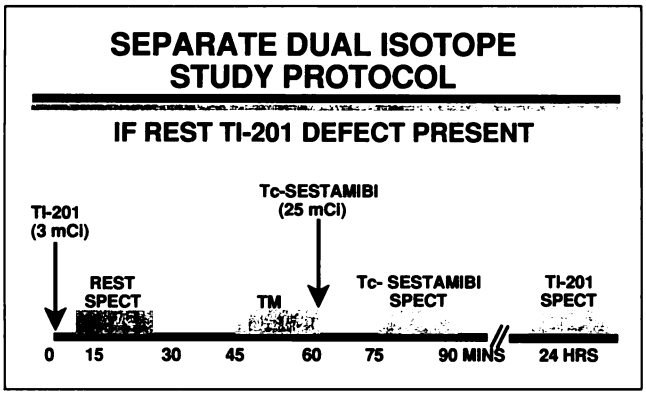

FIGURE 11. Late redistribution protocol for separate-acquisition dual-isotope myocardial perfusion SPECT, which may be employed if the rest ^{201}Tl study demonstrates a defect.

Summarizing Separate-Acquisition Dual-Isotope SPECT

The strengths of the separate acquisition dual-isotope approach include the following: It is a highly efficient protocol, completed in <2 hr, faster than either the same-day or two-day ^{99m}Tc-sestamibi approaches or ^{201}Tl protocols. This advantage is appreciated by patients, technologists and referring physicians. The method has no significant count contribution from the rest SPECT to the stress SPECT, preserving optimal defect contrast. Perhaps most importantly, the method allows for the optimal single-photon assessment of hibernating myocardium through redistribution ^{201}Tl imaging. Finally, with radiotracer injection the night before redistribution and stress testing, hospitalization time can be reduced by avoiding the need for 24-hr imaging after the stress study.

The limitations of this approach appear to be minor. If one were to perform first-pass imaging in conjunction with the protocol, it could only be performed with the exercise phase due to the low dose injected at rest. The slight difference in cavity size noted between the rest ^{201}Tl and

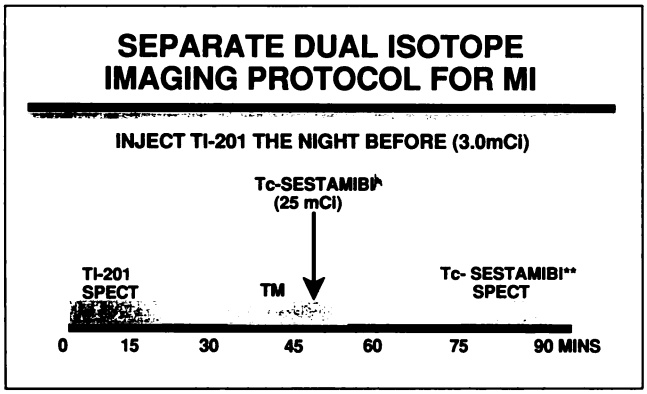

FIGURE 12. Efficient separate acquisition dual-isotope myocardial perfusion SPECT protocol for patients with prior MI or others in whom viability is questionable. Thallium-201 is injected the night before, with or without imaging. On the next day, the redistribution and stress imaging is performed. This approach obviates the need for further redistribution imaging after the stress study.

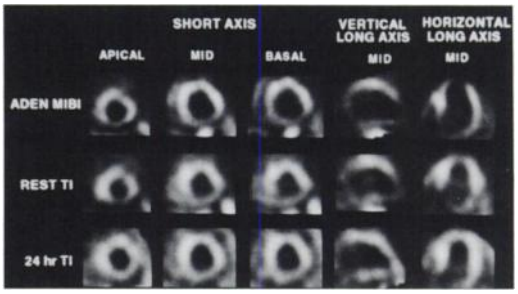

FIGURE 13. Case example of a separate acquisition dual isotope myocardial perfusion SPECT showing adenosine sestamibi stress tudies (*to row*), rest ^{201}Tl studies (*middle row*), and 24-hr redistribution studies following a rest injection (*bottom row*). The stress/rest studies alone demonstrated a large left ventricle and a severe reversible defect in the apical left ventricular wall. These first images showed a nonreversible defect in the interior left ventricular wall. By 24-hr redistriubtion imaging, however, the inferior wall defect was seen to be clearly reversible. Reprinted with permission from W. B. Saunders, Philadelphia, PA, from *Cardiology Clinics*, 1994: in press.

stress ^{99m}Tc-sestamibi SPECT images, even in normals, makes the assessment of transient ischemic dilation of the left ventricle slightly more difficult with the dual-isotope approach. Nonetheless, we have demonstrated that with appropriate compensation for this normal difference, it is still possible to assess pathologic-transient ischemic dilation with the dual-isotope study (*32*). In our experience of over 8000 separate acquisition dual-isotope studies performed to date, we have found these limitations to be minor.

PHARMACOLOGIC STRESS

All of the ^{99m}Tc-sestamibi rest/stress protocols (two-day, same-day, dual-isotope) are likely to work well with the pharmacologic stressors—dipyridamole, adenosine and dobutamine. When these agents are used, the protocols change only slightly; the stress image is acquired 1 hr instead of 15 min after pharmacologic stress injection to allow for adequate hepatobiliary clearance of the radiotracer. The accuracy of ^{99m}Tc-sestamibi studies with pharmacologic stress is comparable to that of exercise ^{99m}Tc-sestamibi imaging (*33,34*).

GATED STRESS STUDIES

Gated SPECT is an ancillary protocol that can be added to any of the ^{99m}Tc-sestamibi approaches (*5–7*). It is typically performed with the poststress SPECT acquisition starting 15–30 min after the stress ^{99m}Tc-sestamibi injection. This approach can provide information on both stress perfusion and resting ventricular function after injection of a single dose. Following ^{99m}Tc-sestamibi stress injection, assessments of regional wall motion and resting ejection fraction on gated SPECT have correlated well with findings on contrast ventriculography (*35*), gated blood-pool studies (*36*) and echocardiography (*7*). Assessment of myocardial thickening is also possible with gated SPECT (*7*) in patients without prior MI . The assessment of wall motion

and wall thickening potentially allows for the evaluation of defect reversibility from to the gated stress study alone (*7*). Of further value, rest left-ventricular ejection fraction (LVEF) can be measured accurately with gated SPECT (*36,37*). Our group has recently reported and validated a completely automatic method for assigning ventricular borders and measuring LVEF from gated SPECT (*37*).

The strengths of gated SPECT lie in the acquisition of additional global and segmental function data, and in minimizing the need for a rest study in some patients. In addition, gated SPECT can help identify artifacts (*38*). Limitations of gated SPECT are the increased processing and interpretation time requirements. With faster and more sophisticated computers, however, this limitation can be minimized.

First-Pass Radionuclide Angiography Adjunct

A first-pass radionuclide angiography study can be added to any of the ^{99m}Tc-sestamibi imaging protocols (*8,9,39*). For bicycle exercise studies, these first-pass procedures can be performed with standard scintillation cameras. Because of the patient motion associated with treadmill exercise, treadmill first-pass procedures require the use of a simulation camera/computer system which can correct for patient motion (*8,9*). We have shown that a specialized gamma camera with motion correction capability, placed at the head of the treadmill, can be used for accurate assessment of peak exercise ejection fraction (*9*).

The combination of peak treadmill exercise first-pass information with exercise SPECT provides incremental information over SPECT and clinical information alone in the identification of patients with multivessel disease (*39*). In patients without known disease who are undergoing myocardial perfusion imaging for diagnostic purposes, the peak exercise first-pass function data are useful for catergorizing patients as having a low or high likelihood of CAD when the results of SPECT alone indicate an intermediate likelihood of disease. Given the above-noted incremental information in identifying patients with multivessel disease, the peak exercise first-pass studies are also likely to be effective for prognostic purposes in patients who have an intermediate prognosis following the SPECT study (*27*). First-pass studies are also effective in increasing interpreter confidence when there is uncertainty remaining after the SPECT study.

The first-pass adjunct, therefore, can provide incremental diagnostic and prognostic information to the assessment of a variety of patient subsets. Limitations are the additional technical complexity of the procedure, the additional camera time for bicycle studies and the specialized equipment required for treadmill first-pass studies.

CONCLUSION

There are multiple validated protocols for myocardial SPECT with ^{99m}Tc-sestamibi in the assessment of myocardial perfusion and defect reversibility. Instead of considering the requirement to choose from these options as a confusing problem, it can be viewed as an opportunity to tailor this myocardial imaging procedure to the needs of individual facilities and patients.

ACKNOWLEDGMENTS

The authors thank Linda E. Ketchum for editorial assistance and Susana Polykronis for preparation of the manuscript.

REFERENCES

1. Berman DS, Kiat H, Van Train K, Garcia E, Friedman J, Maddahi J. Technetium-99m sestamibi imaging in the assessment of chronic coronary artery disease. *Semin Nucl Med* 1991;21:190–212.
2. Berman DS, Kiat H, Maddahi J. The new 99m-Tc myocardial perfusion imaging agents: 99m-Tc-sestamibi and 99m-Tc-teboroxime. *Circulation* 1991;84:17–21.
3. Kiat H, Berman DS, Maddahi J. Myocardial perfusion imaging using technetium-99m radiopharmaceuticals. *Radiol Clin N Am* 1993;31:795–815.
4. Taillefer R, Primeau M, Costi P, Lambert R, Leveille J, Latour Y. Technetium-99m sestamibi myocardial perfusion imaging in detection of coronary artery disease: comparison between initial (1-hr) and delayed (3-hr) postexercise images. *J Nucl Med* 1991;32:1961–1965.
5. Faber TL, Akers MS, Peshock RM, Corbett JR. Three dimensional motion and perfusion quantification in gated single photon emission computed tomograms. *J Nucl Med* 1991;32:2311–2317.
6. Mannting F, Mannting MGM. Gated SPECT with technetium-99m-sestamibi for assessment of myocardial perfusion abnormalities. *J Nucl Med* 1993;34:601–608.
7. Chua T, Kiat H, Germano G, et al. Gated technetium-99m sestamibi for simultaneous assessment of stress myocardial perfusion, post-exercise regional ventricular function and myocardial viability: correlation with echocardiography and rest thallium-201 scintigraphy. *J Am Coll Cardiol*, 1994; 23:1104–1111.
8. Borges-Neto S, Coleman RE, Jones RH. Perfusion and function at rest and treadmill exercise using Tc-99m sestamibi: comparison of one and two day protocols in normal volunteers. *J Nucl Med* 1990;31:1128–1132.
9. Friedman J, Kiat H, Beitendorf J, et al. Validation and preliminary application of simultaneous treadmill exercise ejection fraction and myocardial perfusion scintigraphy [Abstract]. *Circulation* 1990;82:III-321.
10. Kiat H, Maddahi J, Roy L, Friedman J, Berman DS. Comparison of Tc-99m methoxy isobutyl isonitrile with thallium-201 imaging by planar and SPECT techniques for assessment of coronary disease. *Am Heart J* 1989;117:1–11.
11. Maddahi J, Rodrigues E, Berman DS. Assessment of myocardial perfusion by single-photon agents. In: Pohost G, O'Rourke R, eds. *Principles and practices of cardiovascular imaging*. Boston: Little, Brown; 1991:179–219.
12. Berman DS, Kiat H, Friedman J, et al. Separate acquisition rest thallium-201/stress Tc-99m sestamibi dual isotope myocardial perfusion SPECT: a clinical validation study. *J Am Coll Cardiol* 1993;22:1455–1464.
13. Garcia EV, Cooke D, Van Train KF, et al. Technical aspects of myocardial perfusion SPECT imaging with technetium-99m sestamibi. *Am J Cardiol* 1990;66:23E–31E.
14. Van Train K, Areeda J, Garcia E, et al. Quantitative same day rest-stress Tc-99m sestamibi SPECT definition and validation of normal limits and criteria for abnormality. *J Nucl Med* 1993;34:1494–1502.
15. Maddahi J, Kiat H, Van Train K, et al. Myocardial perfusion imaging with technetium-99m sestamibi SPECT in the evaluation of coronary artery disease. *Am J Cardiol* 1990;66:55E–62E.
16. Dondi M, Tartagni F, Fallani F, et al. A comparison of rest sestamibi and rest-redistribution thallium single photon emission tomography: possible implications for myocardial viability detection in infarcted patients. *Eur J Nucl Med* 1993;20:26–31.
17. Taillefer R, Gagnon A, Laflamme L, Gregoire J, Leveille J, Phaneuf D. Same day injections of Tc-99m 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.
18. Van Train KF, Garcia EV, Maddahi J, et al. Multicenter trial validation for quantitative analysis of same-day rest-stress Tc-99m sestamibi for myocardial tomograms. *J Nucl Med* 1994;35:609–618.
19. Kiat H, Areeda J, Van Train K, et al. Quantitative assessment of stress defect extent and reversibility on rest Tl-201/stress Tc-99m sestamibi dual isotope myocardial perfusion SPECT: a prospective validation [Abstract]. *Circulation* 1993;88:I-440.
20. Buell U, Dupont F, Uebis R, et al. Technetium-99m methoxy-isobutyl-

isonitrile SPECT to evaluate a perfusion index from regional myocardial uptake after exercise and at rest: results of a four hour protocol in patients with coronary heart disease and in controls. *Nucl Med Commun* 1990;11: 77–94.
21. Heo J, Kegel J, Iskandrian AS, Cave V, Iskandrian BB. Comparison of same-day protocols using technetium-99m-sestamibi myocardial imaging. *J Nucl Med* 1992;33:186–191.
22. Korkmaz ME, Mahmarian JJ, Koutelou MG, Verani MS. Quantitative stress followed by rest Tc-99m sestamibi single photon tomography for detection and vascular localization of coronary artery stenosis [Abstract]. *J Am Coll Cardiol* 1993;21:464A.
23. Berman DS, Kiat H, Van Train K, Friedman JD, Wang FP, Germano G. Dual isotope myocardial perfusion SPECT with rest thallium-201 and stress Tc-99m sestamibi. In: Verani MS, ed. *Cardiology clinics*. Philadelphia: W. B. Saunders; 1994:in press.
24. Kiat H, Germano G, Friedman JD, 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.
25. Lowe VJ, Greer KL, Hanson MW, Jaszczak RJ, Coleman RE. Cardiac phantom evaluation of simultaneously acquired dual-isotope rest thallium-201/stress technetium-99m SPECT imaging. *J Nucl Med* 1993;34:1998–2005.
26. DePuey EG. Simultaneous thallium-201/technetium-99m dual-isotope cardiac SPECT: ready for prime time? Editorial *J Nucl Med* 1993;34:2006–2008.
27. Berman DS, Palmas W, Kiat H, Cabico JA, Cohen I, Friedman JD. Incremental prognostic value of exercise dual isotope (rest thallium-201/stress technetium-99m sestamibi) myocardial perfusion SPECT [Abstract]. *Circulation* 1993;88:I-486.
28. Ladenheim M, Kotler T, Pollock B, Berman DS, Diamond G. Incremental prognostic power of clinical history, exercise electrocardiography and myocardial perfusion scintigraphy in suspected coronary artery disease. *Am J Cardiol* 1987;59:270–277.
29. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging. a diagnostic tool comes of age. *Circulation* 1991;83:363–381.
30. Kiat H, Biasio Y, Wong FP. Frequency of reversible resting hypoperfusion in patients undergoing rest Tl-201/stress Tc-sestamibi separate acquisition dual isotope myocardial perfusion SPECT [Abstract]. *J Am Coll Cardiol* 1993;21:222A.
31. Kiat H, Areeda J, Germano G, et al. Applicability of quantitative same-day rest/stress Tc-sestamibi limits to separate acquisition dual isotope SPECT [Abstract]. *J Nucl Med* 1994: in press.
32. Palmas W, Berman DS, Hosen K, et al. Quantitative assessment of transient ischemic dilatation in separate acquisition dual isotope myocardial perfusion SPECT [Abstract]. *Circulation* 1992;86:I-45.
33. Kettunen R, Huikuri HV, Heikkila J, Takkunen JT. Usefulness of technetium-99m-MIBI and thallium-201 in tomographic imaging combined with high-dose dipyridamole and handgrip exercise for detecting coronary artery disease. *Am J Cardiol* 1991;68:575–579.
34. Matzer L, Kiat H, Friedman J, et al. Separate acquisition dual isotope myocardial perfusion SPECT using pharmacologic stress. *J Am Coll Cardiol* 1991;19:127A.
35. Quaife RA, Faber TL, Corbett JR. Quantitative three-dimensional SPECT assessments of myocardial perfusion, function and viability using stress perfusion imaging with Tc-99m-sestamibi [Abstract]. *J Nucl Med* 1992;33: 926.
36. DePuey EG, Nichols K, Dobrinsky C, Slowikowski J. Left ventricular ejection fractions from gated Tc-99m-sestamibi SPECT [Abstract]. *J Nucl Med* 1992;33:927.
37. Moriel M, Germano G, Kiat H, et al. Automatic measurement of left ventricular ejection fraction by gated SPECT technetium-99m-sestamibi: a comparison with radionuclide ventriculography [Abstract]. *Circulation* 1993;88:I-582.
38. DePuey EG, Rozanski A. Gated Tc-99m sestamibi SPECT to characterize fixed defects as infarct or artifact [Abstract]. *J Nucl Med* 1992;33:927.
39. Palmas W, Friedman JD, Kiat H, Silber H, Berman DS. Improved identification of multiple vessel coronary artery disease by addition of exercise wall motion analysis to technetium-99m sestamibi myocardial perfusion SPECT [Abstract]. *J Nucl Med* 1993;34:130P.