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Stress Thallium-201/Rest Technetium-99m Sequential Dual Isotope High-Speed Myocardial Perfusion Imaging

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OBJECTIVES Our purpose was to describe a novel, rapid stress thallium-201 (Tl-201)/rest technetium-99m (Tc-99m) agent myocardial perfusion imaging (MPI) protocol (Tl/Tc) with a high-speed MPI scanner and to compare this protocol with a standard rest/stress Tc-99m agent protocol (Tc/Tc) with respect to image quality and radiation dosimetry.

BACKGROUND Recent advances in gamma camera technology have provided opportunity for improved SPECT MPI protocols. A rapid Tl/Tc protocol that could improve image information while maintaining a low radiation burden for the patient would be desirable.

METHODS We compared high-speed SPECT MPI studies in 374 consecutive patients undergoing exercise or pharmacologic Tl/Tc protocol to those of 262 patients undergoing rest/stress Tc/Tc protocol.

RESULTS Tl/Tc imaging was accomplished in $<$20 min. Overall image quality was good to excellent in 96% and 98% of patients with the Tl/Tc and the Tc/Tc protocols, respectively ($p =$ ns). Beginning rest imaging within 2 min after rest injection with the Tl/Tc protocol did not result in reduced confidence in image interpretation. Early rest Tc images of the Tl/Tc protocol showed less extracardiac activity than was observed on standard rest imaging used in the Tc/Tc protocol (84% vs. 61%), respectively ($p < 0.01$). The normalcy rate was high in both groups (100% vs. 92%). Radiation burden was similar between the Tl/Tc and Tc/Tc protocols.

CONCLUSIONS A rapid stress Tl-201/rest Tc-99m protocol for use with high-speed SPECT MPI has image quality and radiation dosimetry similar to those observed with a conventional rest/stress Tc-99m protocol. The Tl/Tc protocol offers promise as an efficient and relatively low radiation dose method, in which the superior qualities of Tl-201 for stress imaging and of the Tc-99m agents for rest imaging can be preserved. The findings also suggest that with rapid imaging rest MPI immediately after Tc-99m agent injection may be superior to standard delayed image initiation. (J Am Coll Cardiol Img 2009;2:273–82)

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Recently, a camera system for high-speed single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has been described (1,2) and reported to provide high image quality with 2-min images, providing results that correlate well with conventional SPECT obtained for approximately 16 min. The increased photon counting sensitivity of the camera can be used to explore novel protocols that may offer advantages over standard protocols used for MPI. The purpose of this study is to describe one such protocol, which uses stress thallium-201 (Tl-201) and rest technetium-99m (Tc-99m) sestamibi or tetrofosmin and to report its comparison to a standard rest/stress Tc-99m sestamibi or tetrofosmin protocol for high-speed MPI with respect to image quality, imaging times, and doses of administered radioactivity.

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CZT = cadmium-zinc-telluride

ICRP = International Commission on Radiological Protection

LVEF = left ventricular ejection fraction

MPI = myocardial perfusion imaging

SPECT = single-photon emission computed tomography

Tc-99m = technetium-99m

TID = transient ischemic dilation

Tl-201 = thallium-201

METHODS

Study population. Two groups of patients had high-speed MPI performed at Cedars-Sinai Medical Center based on referral for clinically indicated SPECT MPI. The principal study group consisted of 374 consecutive patients who were studied with a stress Tl-201/rest Tc-99m sestamibi or tetrofosmin protocol (Tl/Tc group) between September 2007 and April 2008, and the comparison group consisted of 262 consecutive patients who were studied with a rest/stress Tc-99m sestamibi or tetrofosmin (Tc/Tc group) between November 2007 and July 2008. All patients gave written informed consent for their test data to be used for research purposes.

Imaging and stress protocols. Patients were instructed to abstain from any products containing caffeine for 24 h before the test. Whenever possible, beta-blockers and calcium-channel antagonists were terminated 48 h before testing and nitrates at least 6 h before testing. Patients performed a symptom-limited exercise treadmill test or adenosine stress using standard protocols (3,4).

The protocol for the Tl/Tc acquisition sequence is shown in Figure 1. At peak stress, patients were injected with Tl-201. The specific weight-based dose regimen employed was to inject 2 mCi in patients ≤225 lbs and 2.5 mCi in patients >225 lbs. Approximately 10 min after exercise stress or 1 min after adenosine stress a 6-min supine acquisition was performed followed by a 6-min semi-upright acquisition. Subsequently, without moving the patient from the imaging chair, Tc-99m sestamibi or tetrofosmin was injected (8 mCi in patients ≤225 lbs and 10 mCi in patients >225 lbs), and beginning 2 min after injection, a single 4-min rest acquisition was performed.

The protocol for the Tc/Tc acquisition sequence was as follows: a weight-adjusted dose of Tc-99m sestamibi or tetrofosmin (8 to 10 mCi) was injected at rest, followed by a 4-min rest image acquisition in the semi-upright position beginning 30 to 60 min after injection. Patients then underwent symptom-limited standard exercise treadmill testing or adenosine stress as described in the preceding text with injection at peak stress of a weight-adjusted dose of Tc-99m sestamibi (25 to 40 mCi). Beginning 15 to 30 min after stress injection, 2-min image acquisitions were performed first in the semi-upright and then in the supine positions.

High-speed SPECT scanner and imaging method. The high-speed SPECT system uses 9 collimated, pixilated cadmium-zinc-telluride (CZT) detector columns, mounted vertically in 90° geometry (1,2) (D-SPECT, Spectrum Dynamics, Caesarea, Israel). Each of the columns consists of 1,024 (16 × 64), 5-mm thick CZT elements (2.46 × 2.46 mm). Square-hole tungsten collimators are fitted to each of the detectors, with the size of the collimator holes matching the dimensions of the detector elements. Scintigraphic data is acquired by the detector columns rotating in synchrony, focusing on the region of interest (the heart), and are saved in list mode along with R-wave markers. Before imaging in either the semi-upright or supine positions, the detector was positioned parallel to the patient's chest, and care was taken to align the heart in the center of the field of view. A 10-s pre-scan acquisition was performed at the beginning of each imaging acquisition to identify the location of the heart within the chest and to set the angle limits of scanning for each detector (region-of-interest-centric scanning). Each image set was acquired with 120 projections per detector. Transaxial images are then generated by the use of proprietary Broadview reconstruction algorithm (Spectrum Dynamics), based on the maximum likelihood expectation maximization method (1). Images were then reoriented into short-axis and vertical and horizontal long-axis slices using standard software (QPS, Cedars-Sinai Medical Center, Los Angeles, California).

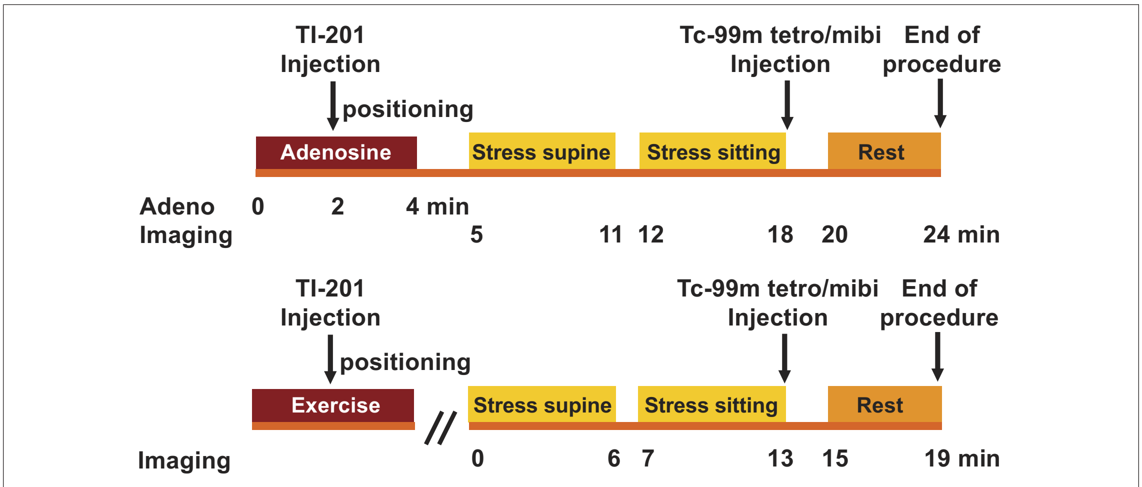

Figure 1. **Tl-201 Stress/Tc-99m Rest Protocol**

Schematic depiction of the adenosine **(top)** and exercise **(bottom)** thallium-201 (Tl-201) stress/technetium-99m (Tc-99m) rest high-speed SPECT myocardial perfusion imaging studies. At peak stress, patients were injected with Tl-201. After a 5-min post-stress monitoring period, supine and semi-upright (sitting) acquisitions were performed sequentially. Subsequently, Tc-99m sestamibi (mibi) or tetrofosmin (tetro) was injected and a single 4-min sitting rest acquisition was performed. Adeno = adenosine.

Image quality and image analyses. Image quality was assessed prospectively by an experienced imaging cardiologist for the rest/stress study combined during the clinical scan reading, and a visual 5-point grading scale of overall quality was employed (1 = uninterpretable, 2 = poor, 3 = fair, 4 = good, and 5 = excellent). For purposes of this study, scan quality was also assessed retrospectively by 2 independent experienced imaging cardiologists with no relationship to the scanner manufacturer. Only images in the upright position—the standard position for this camera—were used for this retrospective reading. Image quality was assessed separately for rest and stress scans using the same scoring system, and the degree of interfering extracardiac radioactivity was assessed with a 3-point scale: 1 = no extracardiac activity in the field of view or minor extracardiac activity not adjacent to the myocardium; 2 = extracardiac activity adjacent to the myocardium but minor and not reducing confidence in interpretation; and 3 = moderate-to-marked extracardiac activity reducing confidence in interpretation. The scores for image quality and extracardiac activity between the 2 readers were compared, and when there was a difference in scoring between the 2 readers the "worse" score was used (lower score for quality, higher score for extracardiac activity) so as to be conservative.

Perfusion defect assessment was performed prospectively using computer-assisted visual interpretation in the same fashion as is currently used for conventional SPECT and positron emission tomography MPI in our laboratory (3), employing the 17-segment, 5-point scoring system (4,5). Summed stress score, summed rest score, and summed difference score (SDS) were obtained by adding the scores of 17 myocardial segments. Summed stress score <4 was defined as normal scans (4). All these perfusion scores were based on both images of semi-upright and supine positions. Perfusion defects represented by the perfusion scores at stress and rest, as described in the preceding text, were used to interpret the MPI studies using the 5 levels of certainty: 1) normal; 2) probably normal; 3) equivocal; 4) probably abnormal; and 5) definitely abnormal (3).

For purposes of assessment of ventricular function, the list mode data were reconstructed into 8 frames/cardiac cycle, and left ventricular ejection fraction (LVEF) at rest and post-stress were determined using a semiautomatic algorithm (QGS, Cedars-Sinai Medical Center). Rest/post-stress LVEF ratio was further calculated.

Transient ischemic dilation (TID) ratio was assessed using the automatic quantitation algorithm and operating on the summed perfusion data (5). After calculation of endocardial volumes, the algorithm derives the TID ratio as the ratio of left ventricular cavity volumes at stress to those at rest.

Radiation dosimetry. Organ doses were estimated using the most recent International Commission on Radiological Protection (ICRP) dose coefficients for each radiopharmaceutical, as reported in ICRP Pub-

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Table 1. Characteristics of Patients

	Tl/Tc Group (n = 374)	Tc/Tc Group (n = 262)
Age (yrs)	62 ± 13	60 ± 14
Men	208 (56%)	149 (57%)
BMI (kg/m^2)	28.5 ± 7.2	28.4 ± 6.4
Prior myocardial infarction	34 (9%)	23 (9%)
Prior revascularization	57 (15%)	39 (15%)
Diabetes	76 (20%)	60 (23%)
Hypertension	243 (65%)	160 (61%)
Hypercholesterolemia	229 (61%)	143 (55%)
Smoking	27 (7%)	23 (9%)
Typical or atypical angina	128 (34%)*	126 (48%)
Shortness of breath	101 (27%)	55 (21%)
Abnormal resting ECG	174 (47%)	112 (43%)
Ischemic stress ECG	49 (13%)	28 (11%)
Pre-scan likelihood of CAD	0.47 ± 0.34	0.48 ± 0.31
Exercise	191 (51%)	125 (48%)
Adenosine stress	183 (49%)	137 (52%)

*p < 0.001 versus rest/stress Tc-99m (Tc/Tc group). Tl/Tc group = stress Tl-201/rest Tc-99m.
BMI = body mass index; CAD = coronary artery disease; ECG = electrocardiogram.

lication 80 (6) for Tc-99m tetrofosmin and Tc-99m sestamibi and in ICRP Publication 53 Addendum 5 (7) for Tl-201. Doses reported for Tc-99m were averaged between Tc-99m sestamibi and tetrofosmin. Effective doses of the protocols were determined from organ doses using tissue weighting factors specified in ICRP Publication 103 (8).

Statistical analysis. All continuous variables are expressed as mean ± standard deviation. Univariate analyses of continuous variables were performed using the Student *t* test (2-tailed). Univariate analyses of categorical variables were compared using the chi-square test. A probability value <0.05 was considered statistically significant. The pre-scan likelihood of coronary artery disease (CAD) was based on age, sex, symptoms, risk factors, and the results of the subject's stress electrocardiogram (9), and normalcy rate was assessed in patients with a <10% pre-scan likelihood of CAD.

RESULTS

Clinical characteristics. Characteristics of patients studied with the 2 high-speed MPI protocols are shown in Table 1. The overall pre-scan likelihood of CAD or ischemia in both groups was in the intermediate range. The patients in the 2 groups had similar clinical characteristics (p = NS) with the exception that atypical or typical angina was more frequent in the Tc/Tc group (p < 0.001). Of the patients who underwent the Tl/Tc protocol, 92% and 96% were not under the influence of a beta-blocker or a calcium-channel blocker, respectively, at the time of stress testing. In the Tc/Tc group, these numbers were 90% and 94% for beta-blocker and calcium-channel blocker, respectively. In the Tl/Tc group, 183 (49%) patients underwent adenosine stress, and among these patients, 92 (50%) individuals performed a low-level stress (treadmill walk) during the infusion. In the Tc/Tc group, 137 patients (52%) were infused with adenosine, and of these individuals, 66 (48%) performed a treadmill walk during the infusion. In the Tl/Tc protocol group, 123 (33%) patients received sestamibi and 251 (67%) received tetrofosmin. The corresponding numbers in the Tc/Tc protocol were 238 (91%) for sestamibi and 24 (9%) for tetrofosmin.

Administered activities. Actual administered activities (mean ± standard deviation) and sample sizes for Tl/Tc acquisition sequence were 2.2 ± 0.3 mCi for stress Tl-201 injections, 8.9 ± 1.7 mCi for rest sestamibi injections, and 8.8 ± 2.6 mCi for rest tetrofosmin injections. The radiation dose was higher for men compared with women (2.2 ± 0.4 mCi vs. 2.1 ± 0.3 mCi for stress, p < 0.01, and 9.1 ± 3.0 mCi vs. 8.5 ± 1.3 mCi for rest, p < 0.02, respectively). For Tc/Tc acquisition sequence, administered activities were 8.2 ± 0.6 mCi for rest sestamibi (n = 238), 8.3 ± 0.7 mCi for rest tetrofosmin (n = 24), and 36.0 ± 3.6 mCi for stress sestamibi. Men had similar radiation dose compared with women for this protocol (36.5 ± 2.0 mCi vs. 36.1 ± 1.7 mCi for stress, p > 0.05, and 8.2 ± 0.6 mCi vs. 8.1 ± 0.6 mCi for rest, p > 0.05, respectively).

Image quality. Overall image quality was deemed good or excellent by the initial reader in 96.0% of patients with the Tl/Tc protocol and 97.7% of patients with the Tc/Tc protocol (p = NS) (Table 2). Combining the results of 2 retrospective readers, the image quality for the stress and rest images were similar and was scored to be good or excellent in greater than 98% of studies in both groups. There was no significant difference for overall, stress, and resting image quality between the 2 groups (p = NS). There was also no significant difference found in image quality between exercise and adenosine stress (p = NS). It is noteworthy that despite beginning rest imaging 2 min after injection in the Tl/Tc group, 99% of the rest images revealed good or excellent quality.

Table 3 shows extracardiac activity by scan protocol and stress type. On the stress images, 97% or greater were grade 1 studies (no extracardiac activ-

Table 2. High-Speed SPECT MPI Image Quality by Scan Protocol and Stress Type

	Tl/Tc Group Exercise (n = 191)	Tl/Tc Group Adenosine (n = 183)	Tc/Tc Group Exercise (n = 125)	Tc/Tc Group Adenosine (n = 137)
Overall image quality*				
Uninterpretable or poor	0 (0%)	2 (1.1%)	0 (0%)	0 (0%)
Fair	5 (2.6%)	8 (4.4%)	0 (0%)	6 (4.4%)
Good or excellent	186 (97.4%)	173 (94.5%)	125 (100%)	131 (95.6%)
Stress image quality†				
Uninterpretable or poor	0 (0%)	2 (1.1%)	0 (0%)	0 (0%)
Fair	1 (0.5%)	1 (0.5%)	0 (0%)	1 (0.7%)
Good or excellent	190 (99.5%)	180 (98.4%)	125 (100%)	136 (99.3%)
Resting image quality†				
Uninterpretable or poor	0 (0%)	2 (1.1%)	0 (0%)	1 (0.7%)
Fair	1 (0.5%)	1 (0.5%)	1 (0.8%)	1 (0.7%)
Good or excellent	190 (99.5%)	180 (98.4%)	124 (99.2%)	135 (98.5%)

$p > 0.05$ for all comparisons between groups and stress type. *Prospective; †retrospective.
MPI = myocardial perfusion imaging; other abbreviations as in Table 1.

ity) in all groups except the adenosine stress Tc/Tc group, in which 84% had grade 1 studies ($p < 0.001$ vs. the adenosine stress Tl/Tc group). Overall on the rest images, grade 1 studies were found in 84% of patients in the Tl/Tc group compared with 61% in the Tc/Tc group ($p < 0.01$). Grade 2 extracardiac activity was less frequently seen on rest images in the Tl/Tc group than in the Tc/Tc group ($p < 0.001$). Thus, comparing the 2 protocols, both resting and adenosine stress images in the Tl/Tc group had significantly less frequent extracardiac activity than observed with the Tc/Tc group ($p < 0.001$). We also observed that in the Tl/Tc protocol extracardiac activity on the rest study was independent of whether sestamibi or tetrofosmin was used for rest imaging. An extracardiac activity grade of 1 was seen in 79% of the patients who received sestamibi and in 78% of the patients who received tetrofosmin. An extracardiac activity grade of 2 was seen in 21% of patients receiving sestamibi and in 22% of the patients receiving tetrofosmin. An extracardiac activity grade of 3 was seen in only 1 patient in the entire study. Table 4 shows image quality by gender and body mass index in the Tl/Tc group. Gender and weight had no significant effects on image quality.

High-speed SPECT MPI findings and interpretation. Overall, the average degree of perfusion abnormality observed in the 2 groups was very small at rest and stress (Table 5). No significant differences were found in rest LVEF and TID ratio between the 2 groups. However, as shown in Table 5, patients in the Tl/Tc group had slightly larger reversible defects and a small but significantly increased post-stress LVEF and rest/post-stress LVEF ratio ($p < 0.05$). However, there was no significant difference in the percent of patients who developed moderate to severe ischemia (defined as a SDS ≥5) or with a low post-stress ejection fraction (LVEF <45%) between the 2 groups. In patients who had moderate to severe ischemia (Tl/Tc group [n = 30] and Tc/Tc group [n = 14]) there were 2 in each group who exhibited TID, and there was no

Table 3. Extracardiac Activity by Scan Protocol and Stress Type

	Tl/Tc Group Exercise (n = 191)	Tl/Tc Group Adenosine (n = 183)	Tc/Tc Group Exercise (n = 125)	Tc/Tc Group Adenosine (n = 137)
Stress image quality				
Extracardiac activity grade 1	191 (100%)	178 (97.3%)*	123 (98.4%)†	115 (83.9%)
Extracardiac activity grade 2	0 (0%)	5 (2.7%)*	2 (1.6%)†	21 (15.3%)
Extracardiac activity grade 3	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)
Resting image quality				
Extracardiac activity grade 1	158 (82.7%)*	155 (84.7%)*	74 (59.2%)	86 (62.8%)
Extracardiac activity grade 2	33 (17.3%)*	28 (15.3%)*	51 (40.8%)	50 (36.5%)
Extracardiac activity grade 3	0 (0%)	0 (0%)	0 (0%)	1 (0.7%)

*$p < 0.001$ versus Tc/Tc group; †$p < 0.001$ versus adenosine stress.
Abbreviations as in Table 1.

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Table 4. High-Speed SPECT MPI Image Quality by Sex and BMI in the Tl/Tc Group

	Men (n = 208)	Women (n = 166)	BMI <30 kg/m^2 (n = 261)	BMI ≥30 kg/m^2 (n = 113)
Overall image quality*				
Uninterpretable or poor	1 (0.5%)	1 (0.6%)	0 (0%)	2 (1.8%)
Fair	7 (3.4%)	6 (3.6%)	11 (4.2%)	2 (1.8%)
Good or excellent	200 (96.2%)	159 (95.8%)	250 (95.8%)	109 (96.5%)
Stress image quality†				
Uninterpretable or poor	1 (0.5%)	1 (0.6%)	0 (0%)	2 (1.8%)
Fair	1 (0.5%)	1 (0.6%)	1 (0.5%)	1 (0.6%)
Good or excellent	206 (99.0%)	164 (98.8%)	260 (99.6%)	110 (97.3%)
Resting image quality†				
Uninterpretable or poor	1 (0.5%)	1 (0.6%)	0 (0%)	2 (1.8%)
Fair	1 (0.5%)	1 (0.6%)	1 (0.5%)	1 (0.6%)
Good or excellent	206 (99.0%)	164 (98.8%)	260 (99.6%)	110 (97.3%)

$p > 0.05$ for all comparisons between gender and BMI subgroups. *Prospective; †retrospective.
MPI = myocardial perfusion imaging; other abbreviations as in Table 1.

significant difference in the rest/post-stress LVEF between the 2 subgroups (1.03 ± 0.16 vs. 1.05 ± 0.13, $p > 0.05$).

Radiation dosimetry. Effective doses and their organ contributions (weighted equivalent doses) are illustrated in Figure 2. The effective dose was 11.9 mSv for the Tl/Tc study protocol, with 9.7 mSv coming from the Tl-201. In comparison, the effective dose was 11.2 mSv for the Tc/Tc study protocol. Regarding organ equivalent doses, the highest doses were those to the kidney (43 mSv), testes (34 mSv), and lower large intestine (31 mSv) for the Tl/Tc protocol, and those to the gallbladder (51 mSv), upper large intestine (28 mSv), and kidneys (32 mSv) for the rest-stress Tc-99m study.

Normalcy rate. In the Tl/Tc group, 36 patients with a <10% likelihood of CAD, high-speed SPECT MPI studies were all normal (normalcy rate = 100%). In the Tc/Tc group, 12 of 13 patients with low likelihood of CAD were normal (normalcy rate = 92%) (p = NS). Case examples are shown in Figures 3 and 4.

Table 5. High-Speed SPECT MPI Findings and Interpretation by 2 Groups

	Tl/Tc Group (n = 374)	Tc/Tc Group (n = 262)
SSS	1.9 ± 4.3	1.6 ± 4.4
SRS	0.7 ± 3.0	0.8 ± 3.4
SDS	1.2 ± 2.4*	0.8 ± 1.9
SDS ≥5	30 (8%)	14 (5%)
Normal	221 (59%)	163 (62%)
Probably normal	35 (9%)	32 (12%)
Equivocal	50 (13%)	26 (10%)
Probably abnormal	21 (6%)	11 (4%)
Abnormal	45 (12%)	30 (11%)
Nondiagnostic	2 (1%)	2 (1%)
Transient ischemic dilation	1.01 ± 0.16	1.03 ± 0.15
Rest LVEF	63 ± 13%	64 ± 12%
Post-stress LVEF	63 ± 12%*	61 ± 13%
Post-stress LVEF <45%	25 (7%)	14 (5%)
Rest/post-stress LVEF ratio	1.00 ± 0.12*	0.97 ± 0.11

*$p < 0.05$ versus Tc/Tc group.
LVEF = left ventricular ejection fraction; MPI = myocardial perfusion imaging; SDS = summed difference score; SRS = summed rest score; SSS = summed stress score; other abbreviations as in Table 1.

DISCUSSION

For decades, it has been known that Tl-201 has higher first-pass myocardial extraction fraction at high flow rates compared with Tc-99m sestamibi or Tc-99m tetrofosmin (10). Early in the validation of SPECT MPI with Tc-99m sestamibi, it was reported that perfusion defects were larger and more severe when Tl-201 was the perfusion tracer than with Tc-99m sestamibi (11,12). It has been suggested that the stronger relationship between myocardial blood flow and myocardial uptake of Tl-201 compared with sestamibi or tetrofosmin in situations such as maximal exercise or pharmacologic coronary vasodilation could potentially improve the ability to detect mild coronary stenosis (13). Nonetheless, Tc-99m sestamibi (and later Tc-99m tetrofosmin) became by far the dominant perfusion tracers for SPECT MPI, due in part to the higher count rates of the Tc-99m agents and the flexibility derived from the lack of significant redistribution of these tracers (13). Given the availability of the high-speed MPI for rapid imaging and the above noted

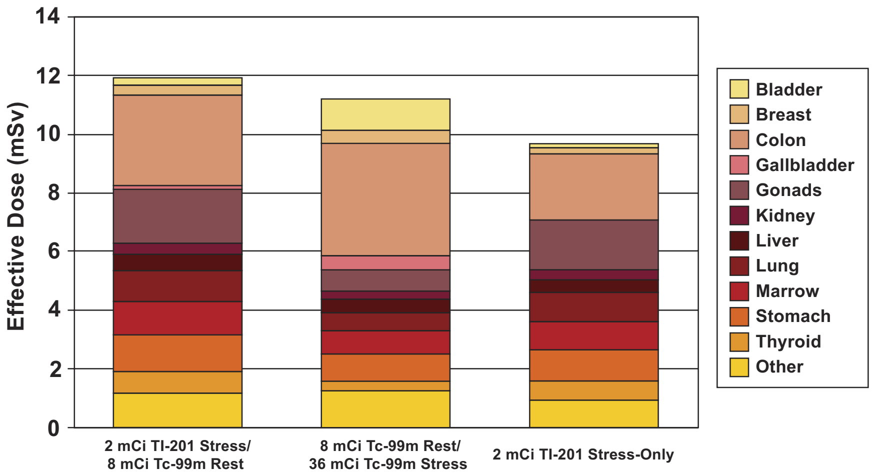

Figure 2. Effective Dose and Organ Weighted Equivalent Doses of High-Speed MPI Protocols

The effective dose was 11.9 mSv for the Tl/Tc study protocol with a similar but slightly lower effective dose of 11.2 mSv for the Tc/Tc study protocol. The effective dose of Tl-201 used in the Tl/Tc study protocol was 9.7 mSv. The individual organ equivalent doses are represented by the horizontal bars for each of the study protocols. MPI = myocardial perfusion imaging; other abbreviations as in Figure 1.

advantages of Tl-201 as a stress agent, we sought to explore the protocol described in this study.

This is the first study to describe the use of a stress Tl-201/rest Tc-99m protocol using the high-speed SPECT MPI system. The findings show that the approach is very rapid, with less than 20-min imaging time despite obtaining both semi-upright and supine post-stress images, and can be achieved with a radiation dose that is similar to that associated with rest/stress Tc-99m agent imaging and more than 50% lower than that associated with previously described rest Tl-201/stress Tc-99m protocols (14). The image quality was as good as observed with the rest/stress Tc-99m protocol. The frequency of interfering extracardiac activity was significantly lower with the Tl/Tc protocol than with the Tc/Tc protocol, after adenosine stress and, importantly, at rest. Moreover, there was no difference between sestamibi and tetrofosmin in the extracardiac activity on the rest images in the Tl/Tc protocol. The normalcy rate is also seen to be high.

Dual isotope imaging. In the past, we have advocated the use of dual isotope imaging as a means by which sequential imaging can be performed without having a significant contribution of the second image to the first (15). The current study similarly exploits the

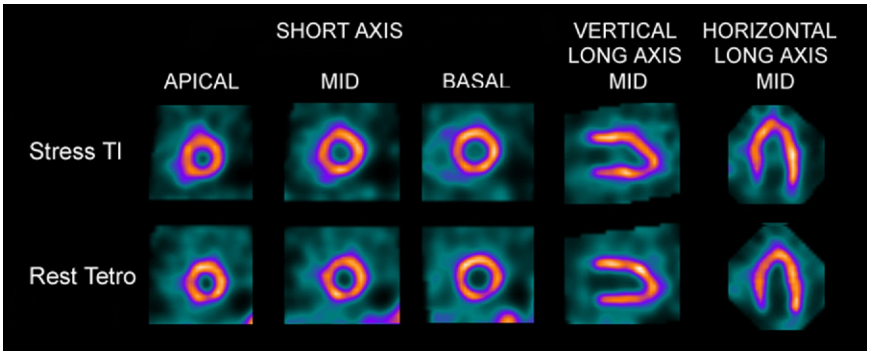

Figure 3. Adenosine Stress Tl/Tc Protocol: Normal Myocardial Perfusion

Adenosine stress Tl-201/rest Tc-99m tetrofosmin high-speed SPECT myocardial perfusion imaging of a 60-year-old man with a history of hypertension, diabetes, and liver failure being evaluated for liver transplantation. Invasive coronary angiography subsequently revealed normal coronary arteries. Note the absence of significant extracardiac activity on the rest Tc-99m tetrofosmin (Tetro) images despite initiation of imaging 2 min after rest injection. Abbreviations as in Figure 1.

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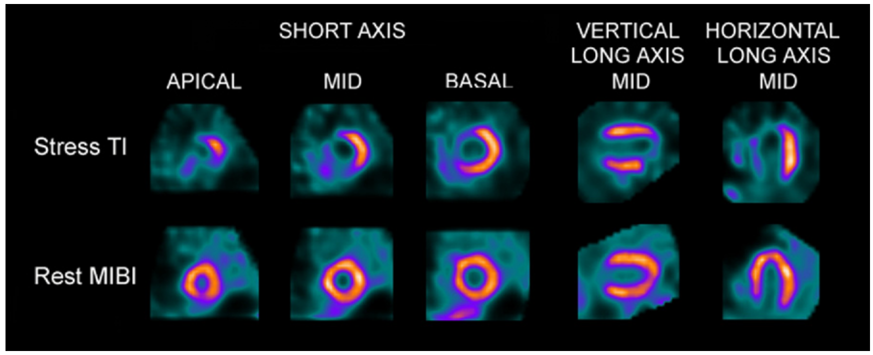

Figure 4. Exercise Tl/Tc Protocol: Abnormal Myocardial Perfusion

Tl-201/rest Tc-99m sestamibi (MIBI) high-speed myocardial perfusion imaging shows extensive defects in anterior, septal, and apical walls as well as transient ischemic dilation on exercise MPI of a 56-year-old man with atypical chest pain. Invasive coronary angiography revealed occlusion of the mid-left anterior descending artery. Note the absence of significant extracardiac activity on the rest Tc-99m MIBI images despite initiation of imaging 2 min after rest injection. Abbreviations as in Figure 1.

ability of SPECT to distinguish between the energy of emissions of different radioisotopes. The high-speed SPECT MPI camera employed in this study is particularly well suited to perform dual isotope imaging due to its use of CZT solid state detectors, which have superior energy resolution compared with sodium iodide crystals used in conventional SPECT (1). Preliminary data suggest that with this camera simultaneous dual isotope imaging may be feasible (16). If borne out by further study, the stress Tl-201/rest Tc-99m protocol described in this study could be accomplished with simultaneous dual isotope imaging, further decreasing imaging time and potentially reducing sources of error associated with separate image acquisitions. Alternatively, simultaneous imaging could be performed keeping total imaging time and image quality the same while decreasing administered activity and radiation dose to the patient.

The Tl-201 stress/Tc-99m rest approach takes advantage of the attributes of each of the tracers. As noted in the preceding text, the use of Tl-201 as the stress tracer provides the opportunity to have a more linear relationship between myocardial uptake and myocardial blood flow at the time of marked increase in flow that occurs with maximal exercise or pharmacologic stress. However, Tc-99m sestamibi (and Tc-99m tetrofosmin) has superior characteristics to Tl-201 when initial imaging after rest injection is used as a method to assess myocardial viability or perfusion defect reversibility (17).

Timing of the rest imaging. To our knowledge, this is the first study to explore the feasibility of immediate imaging after rest Tc-99m tracer injection for SPECT MPI. Standard guidelines state that there must be at least a 30-min to 1-h delay between rest injection and rest imaging with the Tc-99m perfusion tracers (18). The rationale behind the 30-min to 1-h delay requirement has been that there is frequently excessive hepatic uptake of radioactivity on standard early rest images such that the inferior wall of the heart is obscured. An important finding of this study relates to the minimal impact of extracardiac activity on the rest study, despite the use of a protocol in which rest imaging began 2 min after the rest injection. Importantly, extracardiac activity was significantly less frequent with the Tl/Tc protocol than with the Tc/Tc protocol in which the delay in initiation of image acquisition was the recommended 30 to 60 min. Of note, there was no difference in the extracardiac activity seen in the early post-rest injection images between sestamibi and tetrofosmin. A possible explanation for the excellent results with early post-injection rest imaging is that with the high-speed camera rest imaging may be completed rapidly before extracardiac radioactivity has reached maximum. The results of this study raise the possibility that imaging immediately after rest injection of Tc-99m agents with other scintillation camera systems capable of rapid imaging may be feasible without significant hepatic interference.

Radiation dosimetry. One of the drawbacks of Tl-201 for SPECT MPI is the associated higher radiation burden associated with this tracer compared with that seen with Tc-99m (14). Considerations of the more than double radiation exposure with the conventional rest Tl-201/stress Tc-99m dual isotope protocols resulted in the recent conversion in our laboratory to a low-dose/high-dose, Tc-99m single isotope protocol for standard gamma camera imaging. The

Tl/Tc protocol takes advantage of the higher sensitivity of the high-speed SPECT MPI camera, which results in the ability to use Tl-201 as the stress tracer, while at the same time exposing the patient to nearly as low a radiation burden as is associated with conventional Tc/Tc protocols (14). The average effective dose to the patient was 11.9 mSv with Tl/Tc group, and 11.2 with Tc/Tc, the latter employing Tc-99m doses equivalent to those used with standard Anger camera acquisition.

Upright and supine imaging. For many years, the standard post-stress acquisition protocols in our laboratories for conventional SPECT MPI have included both prone and supine post-stress imaging (3,19–22). Our interpreters have found that the combination of prone and supine imaging improves their diagnostic accuracy, due to an improved ability to distinguish true perfusion defect from artifact (e.g., attenuation, patient motion). With this approach, the reader or the computer algorithm employed in interpretation requires the stress image to be consistently abnormal in the same location on the 2 acquisitions. In view of this prior experience, we introduced a 2-position stress acquisition for use with high-speed SPECT MPI in this study. Since the camera design currently does not allow prone imaging, we used the supine position for the second image. The reader had both images to evaluate for purposes of this study. Whether the supine image was necessary with this system and whether the supine image can be acquired for a shorter time as with our conventional shorter prone image acquisition will require further study.

Study limitations. No coronary angiographic or other validation of the perfusion and function findings of this study are reported, since only a small proportion of the patients in this study underwent coronary angiography or other stress imaging study. Computer-based quantitative analysis was not used for image interpretation since normal limits were not available for the protocol employed, and interpretation was based on semiquantitative visual analysis by a single experienced nuclear cardiologist. The normalcy rate, while exceedingly high, was observed in a relatively small number of patients and needs further evaluation. The study was performed in a single laboratory, and whether similar results can be obtained in other centers will require further study. The rest injection with the Tl/Tc protocol was made approximately 20 min after exercise and 15 min after adenosine stress, potentially at a time of post-stress stunning that could affect the ability to observe stress-induced wall motion abnormalities or TID of the LV. We have not tested the ability of stress Tl-201/rest Tc-99m sestamibi protocol to evaluate myocardial viability in the current study. Whether rest Tc-99m agent injection shortly after stress in the manner used in the Tl/Tc study provides assessment of myocardial viability as effectively as with a nitroglycerin augmented rest Tc-99m or 24-h Tl-201 imaging would also require further study. In addition, the reversible defect was slightly larger and the stress defects also tended to be larger in patients with Tl/Tc protocol when compared with those with Tc/Tc protocol. To fully understand these differences, a separate study using Tl/Tc versus Tc/Tc protocol in the same patients would be needed.

CONCLUSIONS

A rapid stress Tl-201/rest Tc-99m protocol for use with high-speed SPECT MPI has image quality and radiation dosimetry similar to those observed with a rest/stress Tc-99m protocol. The protocol offers promise as an efficient, relatively low radiation dose method, in which the superior qualities of Tl-201 for stress imaging and of the Tc-99m agents for rest imaging can be preserved. In addition, the findings also suggest that with rapid imaging, rest MPI immediately after Tc-99m agent injection may be superior to standard delayed image initiation.

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