
Comparative Feasibility of Separate or Simultaneous Rest Thallium-201/Stress Technetium-99m-Sestamibi Dual-Isotope Myocardial Perfusion SPECT

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Separate or simultaneous rest ^{201}Tl /stress $^{99\text{m}}\text{Tc}$ -sestamibi dual-isotope SPECT are potentially efficient myocardial perfusion imaging protocols which combine the use of a high-resolution $^{99\text{m}}\text{Tc}$ tracer for stress perfusion assessment and ^{201}Tl , the current single-photon agent of choice, for viability assessment. **Methods:** To investigate the feasibility of dual-isotope myocardial perfusion SPECT protocols using rest ^{201}Tl and stress sestamibi, ^{201}Tl crosstalk into the $^{99\text{m}}\text{Tc}$ acquisition window (Group 1, $n = 26$ patients) and $^{99\text{m}}\text{Tc}$ crosstalk into ^{201}Tl windows (Group 2, $n = 25$) were studied. For Group 1, treadmill exercise with sestamibi injection and poststress SPECT ("virgin" sestamibi images) were performed, followed by rest ^{201}Tl injection and SPECT acquisition using dual-isotope windows (contaminated or "dual" images). For Group 2, the order was reversed: rest ^{201}Tl SPECT (virgin ^{201}Tl images) was performed first, followed by exercise sestamibi injection and dual-isotope SPECT. **Results:** The contribution of ^{201}Tl scatter to the dual sestamibi images (Group 1) was measured to be $2.9\% \pm 2.1\%$, while $^{99\text{m}}\text{Tc}$ crosstalk contributed $26.7\% \pm 13.0\%$ to the dual ^{201}Tl images (Group 2). Image quality was considered good to excellent in 92% of the sestamibi (virgin and dual) images and 88% of the virgin ^{201}Tl SPECT, but only in 23% of the dual ^{201}Tl studies. **Conclusions:** Technetium-99m crosstalk into ^{201}Tl windows is substantial; therefore, simultaneous dual-isotope protocols, which involve assessment of ^{201}Tl images contaminated by $^{99\text{m}}\text{Tc}$, are not recommended. On the other hand, because of the small amount of ^{201}Tl crosstalk into the $^{99\text{m}}\text{Tc}$ window, a separate acquisition dual-isotope approach employing the rest ^{201}Tl (virgin)/stress sestamibi sequence is acceptable.

Key Words: SPECT; technetium-99m-sestamibi; dual-isotope imaging; thallium-201

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Mycocardial perfusion SPECT using stress and rest $^{99\text{m}}\text{Tc}$ -sestamibi has been shown to have similar efficacy to ^{201}Tl for detection of patients with coronary artery disease and localization of diseased vessels (1-5), while providing images considered to be of higher quality than that achieved with ^{201}Tl . Standard validated protocols using either sestamibi or ^{201}Tl SPECT protocols, however, are lengthy. Stress-redistribution ^{201}Tl SPECT requires two separate data collections, 3 to 4 hr apart. Sestamibi SPECT requires several hours for same day rest/stress and 2 days for the separate day stress/rest imaging protocols (6). Furthermore, standard rest/stress sestamibi SPECT could potentially underestimate myocardial viability in hibernating myocardium (7) due to the minimal redistribution of sestamibi (8). Since standard gamma cameras have the ability to distinguish radioisotopes of differing energy, they can be used for dual-isotope SPECT acquisition, and thus offer the potential of maximizing efficiency without compromising perfusion or viability assessments. Recently, our group introduced a rest ^{201}Tl /stress sestamibi dual-isotope myocardial perfusion imaging approach using either separate acquisition rest ^{201}Tl SPECT/stress sestamibi sequence (9,10) or simultaneous acquisition (11,12). The separate acquisition rest ^{201}Tl /stress sestamibi approach would eliminate the delay between rest and stress studies, and provides rest ^{201}Tl images which are uncontaminated by the higher energy photons of $^{99\text{m}}\text{Tc}$. If proven feasible, the simultaneous dual-isotope approach would require only one data acquisition and therefore would halve camera time, significantly abbreviate the length of the overall study and reduce the frequency of unrecognized artifacts associated with separate stress and rest image acquisitions.

Since dual-isotope approaches cause images derived from the energy window(s) of one radioisotope to be contaminated by spillover from the other tracer, it is important to establish the degree of this contamination in separate and simultaneous acquisition dual-isotope imaging, as well as its effect on defect severity. The goal of this study was

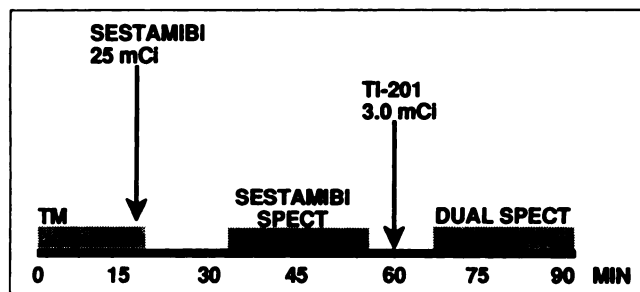


FIGURE 1. Schematic outline of the exercise and imaging protocols used for Group 1 (TM = treadmill exercise).

to explore the feasibility of these two dual-isotope myocardial perfusion SPECT approaches by: (1) determining the degree of isotope crosstalk in dual-isotope SPECT by both visual and quantitative analysis, and (2) visually assessing the image quality of the contaminated ^{201}Tl and sestamibi dual-isotope studies.

METHODS

Patient Population

The study population consisted of two groups. The degree of ^{201}Tl crosstalk into the dual-isotope SPECT sestamibi images was studied in 26 patients (Group 1, mean age: 65 ± 9 yr, 23 males, 3 females). To assess the degree of sestamibi crosstalk on dual-isotope SPECT ^{201}Tl images, a separate population of 25 patients (Group 2, mean age: 67 ± 4 yr, 22 males, 3 females) was studied.

Exercise and Imaging Protocols

Patients in Group 1 first received sestamibi injection (20–30 mCi) at peak treadmill exercise followed by sestamibi SPECT 15–30 min later. Thallium-201 (2.5–3.5 mCi) was then injected at rest and SPECT acquisition was performed 10–15 min later using dual-isotope ($^{99\text{m}}\text{Tc}$ plus ^{201}Tl) energy windows (Fig. 1). All patients in Group 1 had sestamibi perfusion defects by visual analysis. There were a total of 27 myocardial perfusion defects, 9 of which were anterior/apical, 10 were inferior, and 8 were lateral wall defects (one patient had both an anterior and a lateral wall perfusion defect).

For patients in Group 2, rest ^{201}Tl injection and rest SPECT were performed first. Treadmill exercise was then performed and sestamibi was injected at peak stress followed by SPECT using dual-isotope windows (Fig. 2). All patients in Group 2 had rest ^{201}Tl defects by visual analysis. There were a total of 27 myocardial perfusion defects, 11 of which were anterior/apical, 11 were inferior, and 5 were lateral wall defects (two patients had both an anterior/apical and an inferior wall perfusion defect).

Special Terminology for This Study

For clarity of nomenclature, the stress sestamibi studies acquired prior to rest ^{201}Tl injection and therefore uncontaminated by ^{201}Tl crosstalk (Group 1 patients) will be referred to as virgin stress sestamibi. The rest ^{201}Tl studies acquired prior to exercise and therefore uncontaminated by sestamibi crosstalk (Group 2 patients) will be referred to as the virgin rest ^{201}Tl . The simultaneously acquired rest ^{201}Tl and stress sestamibi SPECT will be called dual rest ^{201}Tl and dual stress sestamibi, respectively.

SPECT Acquisition and Processing Protocols

SPECT acquisition was performed using a Siemens gamma camera equipped with 75 photomultiplier tubes, a 0.25-in. thick (0.64 cm) NaI crystal and a low-energy, high-resolution, parallel-hole collimator. Sixty-four projections (20 sec/projection) were obtained over a semicircular 180° arc, extending from the 45° right anterior oblique to the left posterior oblique position. Virgin stress sestamibi SPECT acquisition (Group 1) used a symmetric 15% window centered on the 140-keV photopeak. For virgin rest ^{201}Tl SPECT (Group 2), a 20% symmetric energy window centered on the 68–80-keV peak and a 10% window centered on the 167-keV peak were used. Dual SPECT acquisition used a 15% symmetric window over the 140-keV $^{99\text{m}}\text{Tc}$, a 15% symmetric window over the 68–80-keV ^{201}Tl and a 10% symmetric window over the 167-keV ^{201}Tl photopeaks. Each projection image was corrected for uniformity with a 30-million count image of a uniform cobalt-57 flood source. Center of rotation correction was also performed. All image sets were reviewed in cinematic display format for assessment of patient motion (13). Projection images were filtered with a Butterworth filter before reconstruction. In particular, stress sestamibi images were filtered using a Butterworth filter of order 2.5 and a cut-off frequency of 66% of Nyquist, while a Butterworth filter of order 5 with a cut-off frequency of 50% of Nyquist was used for the rest ^{201}Tl SPECT images. Image reconstruction was based on filtered backprojection with a ramp filter and produced transverse tomograms (slices) of 6.2 mm axial thickness, encompassing the entire heart. Sagittal and oblique tomograms parallel to the long and short axes of the left ventricle were extracted from the transaxial tomograms by performing a coordinate transformation with appropriate interpolation (14). Attenuation or scatter correction was not applied.

Quantitative Assessment of Isotope Crosstalk

Isotope crosstalk was evaluated by quantitatively measuring one of its predicted effects, the decrease in defect severity in dual studies relative to the corresponding virgin study. First, raw maximal count circumferential profile myocardial polar maps were created for each virgin/dual pair using our previously published methods developed for sestamibi SPECT (5,15) and normalized to a common maximum. Then, a reasonably small (<50% of the apparent defect diameter) region of interest (ROI) was manually drawn and centered on the defect in the virgin polar map (an area of uptake reduced by more than 10%–20% relative to surrounding areas) using the Explorer® software package (16), and then copied to the exact same location in the dual polar map. Another ROI was drawn on a contralateral, normally perfused area in the virgin map and was copied to the dual map. Average counts/pixel were calculated for all ROIs, and the ratio of counts in the defect-to-

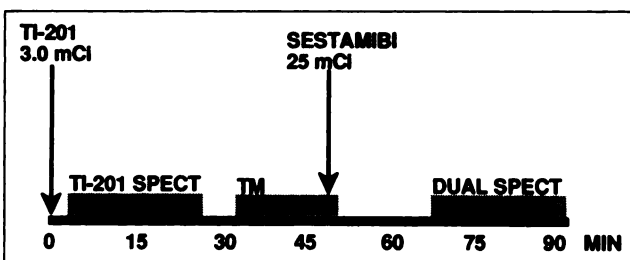


FIGURE 2. Schematic outline of the exercise and imaging protocols used for Group 2 (TM = treadmill exercise).

counts in the normal myocardium (within each normalized polar map) was chosen as a comparative measure of defect severity.

Visual Scintigraphic Interpretation

For purposes of visual interpretation, all short-axis and vertical long-axis tomograms were displayed on transparency film in 12.4-mm groupings using a staggered (overlapping) summation of adjacent 6.2-mm slices (6,17) with the intensity of each image normalized to the maximal pixel value in that image. Separate films were obtained displaying aligned slices of the dual or virgin stress sestamibi with the corresponding virgin or dual rest ^{201}Tl SPECT. The myocardial tomograms were divided into 20 segments for each patient. These segments were defined as six evenly spaced regions within representative apical, mid and basal ventricular cuts of the short-axis views (18 segments), plus the anteroapical and inferoapical segments of the mid-vertical long-axis cut (6,18). Two blinded experts interpreted all the tomographic images and each segment was scored by consensus using a five-point system (0 = normal radioisotope uptake, 1 = mildly (equivocally) reduced, 2 = definitely but only moderately reduced, 3 = severely reduced and 4 = absent uptake). SPECT images from all of the patients within each group were pooled and were presented to the readers in a random fashion. A stress defect was defined by a segment on the stress sestamibi SPECT with a score of ≥ 2 . Segmental defect reversibility was defined as nonreversible (stress/rest segmental score: 2/2, 3/3, 4/4), minimally reversible (stress/rest segmental score: 3/2, 4/3), partially reversible (stress/rest segmental score: 2/1, 3/1, 4/2) or reversible (stress/rest segmental score: 2/0, 3/0, 4/1, 4/0).

Visual Scintigraphic Evaluation of Image Quality

The quality of each SPECT image was also subjectively scored using a five-point system (0 = unacceptable, 1 = poor, 2 = fair, 3 = good and 4 = excellent) (9,19). Scoring criteria were based on evaluation of image uniformity, defect clarity, endocardial and epicardial border definition, and apparent target-to-background ratio.

Statistical Analysis

The mean differences for continuous variables were compared using the Student's t-test. All continuous measures were summarized as the mean value \pm s.d. The alpha level of significance was set at 0.05. For analysis of segmental agreement, the kappa (κ) statistic and its standard error were used as a measure of agreement. A value of 1 denotes perfect agreement, while 0 indicates no agreement beyond chance. In general, κ values of ≥ 0.6 are considered indicative of good agreement (20).

RESULTS

Quantitative Analysis of Isotope Crosstalk

The contribution of ^{201}Tl scatter was measured to be $2.9\% \pm 2.1\%$ in the dual sestamibi images (Group 1) while $^{99\text{m}}\text{Tc}$ crosstalk contributed $26.7\% \pm 13.0\%$ to the dual ^{201}Tl images (Group 2). Comparisons of defect severity between virgin and dual images were 0.58 ± 0.14 versus 0.59 ± 0.14 (mean Δ : 0.007 or 1.2%, $p = 0.01$) for sestamibi, and 0.49 ± 0.13 versus 0.59 ± 0.15 (mean Δ : 0.11 or 22%, $p = 0.0001$) for ^{201}Tl studies, respectively (Fig. 3).

Visual Assessment of Isotope Crosstalk

Comparison of Dual and Virgin Stress Sestamibi SPECT (Group 1). The segmental score agreement be-

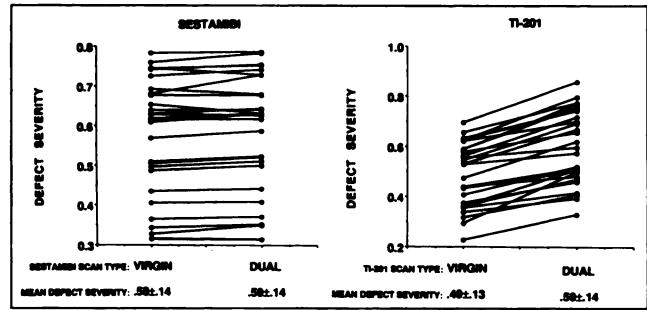


FIGURE 3. Comparison of defect severity between stress and dual SPECT. Mean $\Delta = 0.007$ or 1.2% between dual and virgin sestamibi, $p = 0.01$. Mean $\Delta = 0.11$ or 22% between dual and virgin ^{201}Tl , $p = 0.0001$.

tween virgin stress sestamibi and dual stress sestamibi SPECT in 520 SPECT segments was 98% (Table 1). When the 361 segments with a visual score of 0 by dual stress sestamibi and virgin stress sestamibi were eliminated, the exact agreement remained high at 93% (148/159), with a kappa statistic of 0.88. Further analysis was made of the definite but not severe virgin stress sestamibi defect (segmental score of 2). Of 98 such segments, dual stress sestamibi scores were concordant in 94 (96%), with no systematic overestimation or underestimation of the virgin scores. Therefore, a high degree of concordance was maintained between virgin and dual stress sestamibi, even in segments with a definite but only moderate defect on the virgin study.

Comparison of Dual and Virgin Rest ^{201}Tl SPECT (Group 2). Agreements for segmental score are shown in Table 2. The agreement between dual and virgin rest ^{201}Tl from 500 SPECT segments was 88%. When the 334 segments with a visual score of 0 by dual rest ^{201}Tl and virgin rest ^{201}Tl were eliminated, the exact agreement between dual virgin and rest ^{201}Tl was reduced to 63% (104/166), with a kappa statistic of 0.51. Further analysis was made of the virgin rest ^{201}Tl segments with moderate (visual defect score of 2) defects. Of the 72 such segments with a score of 2 on virgin rest ^{201}Tl SPECT, 35 (49%) were given the same score of 2, 3 segments (4%) were given a more severe score of 3, while the remainder ($n = 34$ segments) were given a

TABLE 1
Segmental Score Agreement: Virgin Versus Dual Stress Sestamibi SPECT

Score	Virgin stress sestamibi				
	0	1	2	3	4
Dual	361	1	0	0	0
Stress	3	18	1	0	0
Sestamibi	0	1	94	2	0
	0	0	3	31	0
	0	0	0	0	5

Exact agreement: 98% (509/520) κ : 0.96 \pm 0.01

TABLE 2
Segmental Score Agreement: Virgin Versus Dual Rest Thallium-201 SPECT

Score	Virgin rest ²⁰¹ Tl				
	0	1	2	3	4
0	334	6	6	0	0
Dual	1	22	28	1	0
Rest	2	0	35	12	1
²⁰¹ Tl	3	0	3	30	2
	4	0	0	0	17

Exact agreement: 88% (438/500) κ : 0.76 \pm 0.03

score of 1 (n = 28 or 39%) or 0 (n = 6 or 8%) by dual rest ²⁰¹Tl. Thus, although overall segmental score agreement was high (88%), there appeared to be a systematic underestimation (lower visual score) of the rest ²⁰¹Tl defect severity by dual rest ²⁰¹Tl SPECT, which was particularly evident in moderate defects.

Agreement for segmental defect reversibility pattern is shown in Table 3. The agreement of defect type between dual rest ²⁰¹Tl and virgin rest ²⁰¹Tl images for reversible, partially reversible, minimally reversible and nonreversible defects was 68%. A systematic overestimation of reversibility was observed using dual ²⁰¹Tl SPECT.

Image Quality Assessment. Good to excellent quality was considered to be present in 92% of all virgin and dual sestamibi and 88% of the virgin rest ²⁰¹Tl images, with the remaining images of both being considered of fair quality. On the other hand, only 23% of the dual ²⁰¹Tl studies were considered good, the remaining were assessed as having fair (67%) or poor (10%) image quality (Table 4).

Case Examples

Figure 4 shows representative short-axis, mid vertical and horizontal long-axis sestamibi tomographic slices of a patient from Group 1 with an anterior-apical perfusion defect. The perfusion defect pattern is visually identical for virgin and dual stress sestamibi SPECT. The degree of ²⁰¹Tl crosstalk into the dual sestamibi images was 4%.

TABLE 3
Agreement of Segmental Reversibility Pattern Between Virgin Rest Thallium-201/Stress Sestamibi and Dual Rest Thallium-201/Stress Sestamibi SPECT

		Virgin rest ²⁰¹ Tl			
		NonREV	MinREV	PartREV	REV
Dual	NonREV	58	2	0	0
	MinREV	13	23	2	0
Rest	PartREV	26	5	18	0
²⁰¹ Tl	REV	5	1	4	24

Exact agreement: 68% (123/181). κ : 0.56 \pm 0.05.

NonREV = nonreversible, MinREV = minimally reversible, PartREV = partially reversible and REV = reversible.

TABLE 4
Comparisons of SPECT Image Quality

	Image quality			
	Poor	Fair	Good	Excellent
Virgin stress sestamibi (n = 26, Group 1)	0	2 (8%)	19 (73%)	5 (19%)
Dual stress sestamibi (n = 51, Groups 1 and 2)	0	4 (8%)	40 (78%)	7 (14%)
Virgin rest ²⁰¹ Tl (n = 25, Group 2)	0	3 (12%)	21 (84%)	1 (4%)
Dual rest ²⁰¹ Tl (n = 51, Groups 1 and 2)	5 (10%)	34 (67%)	12 (23%)	0

Comparisons of defect severity between virgin and dual images were 0.49 versus 0.50 (Δ :0.01 or 2.0%).

Figure 5 shows representative short-axis, mid vertical and horizontal long-axis ²⁰¹Tl tomographic slices of a patient from Group 2 who had a prior inferior and apical myocardial infarct. Compared to the virgin rest ²⁰¹Tl SPECT, there is increased background activity, and the defect appears to be milder and smaller in the dual rest ²⁰¹Tl images. The degree of ^{99m}Tc crosstalk into the dual ²⁰¹Tl images was 35%. Comparisons of defect severity between virgin and dual images were 0.36 versus 0.47 (Δ :0.11 or 31%).

For purposes of illustration, a virgin stress sestamibi and a virgin rest ²⁰¹Tl SPECT (from two separate patients) were acquired using dual-isotope windows. Figure 6A shows a single tomographic short-axis slice of a virgin ²⁰¹Tl study (uncontaminated) acquired using dual-isotope (sestamibi and ²⁰¹Tl) windows. There is minimal crosstalk observed in the technetium window (myocardial count ratio between ²⁰¹Tl and technetium windows was 14.3:1).

Figure 6B shows a single tomographic short-axis slice from a sestamibi study (uncontaminated) acquired using dual-isotope windows, demonstrating a substantial amount of sestamibi crosstalk into the ²⁰¹Tl windows (myocardial count ratio between technetium and ²⁰¹Tl windows was 3.6:1).

DISCUSSION

In this study, we have examined the feasibility of rest ²⁰¹Tl/stress sestamibi dual-isotope myocardial perfusion

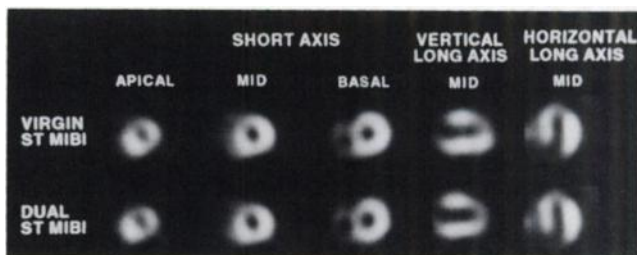


FIGURE 4. Representative virgin and dual stress sestamibi short-axis (left to right = apical to basal, vertical and horizontal long-axis) tomographic slices from a Group 1 patient with an anterior defect.

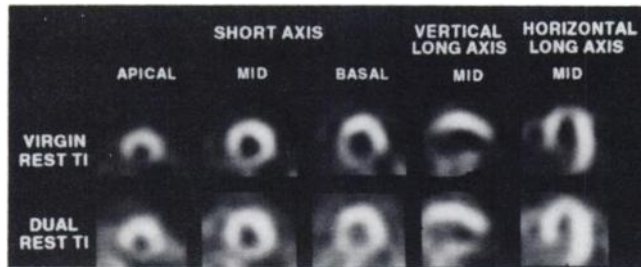


FIGURE 5. Representative virgin and dual rest ^{201}Tl SPECT images from a Group 2 patient with an inferior and apical myocardial infarct. Display format is the same as in Figure 4.

SPECT. Quantitative and visual assessments of the degree of isotope crosstalk associated with dual-isotope imaging demonstrated that sestamibi crosstalk into the dual rest ^{201}Tl images is substantial but that ^{201}Tl crosstalk into the dual stress sestamibi images is very small. Consequently, separate acquisition dual-isotope SPECT with virgin rest ^{201}Tl and dual stress sestamibi images, appears to be an acceptable approach, while simultaneous acquisition with dual ^{201}Tl and dual sestamibi images appears unacceptable without energy correction for the sestamibi spillover in the dual ^{201}Tl images.

Effect of ^{201}Tl Crosstalk Into the Dual Stress Sestamibi Energy Window

Thallium-201 crosstalk into the $^{99\text{m}}\text{Tc}$ window was shown to contribute only $2.9\% \pm 2.1\%$ of the dual sestamibi defect counts, with minimal difference (1.2%) in normalized defect severity between virgin and dual sestamibi SPECT. Although the minimal difference was shown to be statistically significant ($p = 0.01$), it is considered to be too small to be of clinical importance. These results reflect the low abundance of high-energy photons in the ^{201}Tl energy spectrum and the relatively low dose (compared to the sestamibi injection) of injected ^{201}Tl . Visually, a high segmental score agreement (98%) was observed between dual and virgin stress sestamibi SPECT, with no systematic underestimation of virgin sestamibi defect severity even when segments with moderate (visual score of 2) defects were analyzed. Image quality was good to excellent as on the virgin stress sestamibi studies (92% for both) as frequently in the dual stress sestamibi studies. The data from this study suggest that image quality and defect severity of the stress sestamibi SPECT obtained using separate acquisition dual-isotope myocardial perfusion SPECT (rest ^{201}Tl injection and SPECT followed by stress sestamibi injection and dual SPECT) (9) is minimally affected by ^{201}Tl contamination.

Effect of Sestamibi Crosstalk Into the Dual Rest ^{201}Tl Energy Windows

Because of the higher energy of the $^{99\text{m}}\text{Tc}$ photons and the higher dose of sestamibi used compared to that of ^{201}Tl , sestamibi crosstalk into dual rest ^{201}Tl images has the potential of obscuring ^{201}Tl defects. Technetium-99m crosstalk into ^{201}Tl windows was shown to contribute 27%

of the dual ^{201}Tl counts, with a 22% reduction in normalized defect severity between virgin and dual rest ^{201}Tl SPECT. Although our qualitative clinical results demonstrated high (88%) agreement of the dual rest ^{201}Tl segmental scores when compared to the corresponding virgin rest ^{201}Tl (Table 2), there was a systematic underestimation of the rest ^{201}Tl defect severity score. The underestimation was most marked when the virgin rest ^{201}Tl score was 2, occurring in 47% of such segments. Since this implies that a score of 2 would be considered a score of 1 or 0, this also was associated with a substantial systematic overestimation of defect reversibility by dual ^{201}Tl (Table 3). In our initial abstract (11) assessing the feasibility of simultaneous dual-isotope studies, we reported that 87% of segments had identical scores by dual rest ^{201}Tl compared to rest sestamibi SPECT. This correlates very strongly with the overall 88% agreement noted above between dual rest ^{201}Tl and virgin rest ^{201}Tl . In our preliminary work (11), however, we failed to recognize the importance of separately analyzing the effects of tissue crosstalk with simultaneous dual-isotope imaging on the reversibility patterns in the setting of the moderate ^{201}Tl defects (visual score of 2). Furthermore, while most (88%) of the virgin rest ^{201}Tl SPECT studies were considered as good to excellent and none as poor or unacceptable, the majority (67%) of the dual ^{201}Tl studies were assessed as having only fair image quality, and 10% were of poor quality. The data from this portion of the study show that defect severity and image quality of the rest ^{201}Tl study are significantly affected by $^{99\text{m}}\text{Tc}$ contamination when simultaneous dual-isotope myocardial perfusion SPECT is performed.

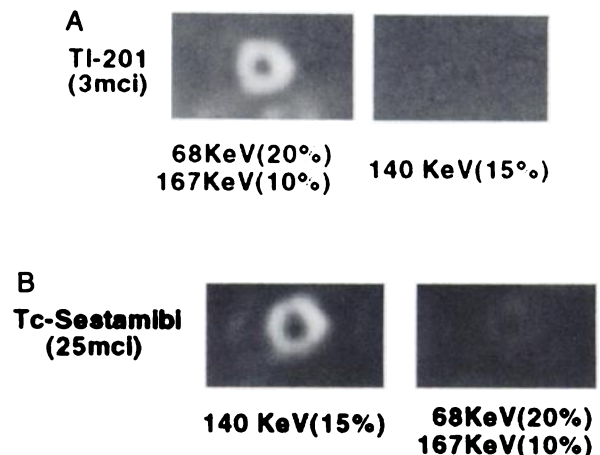


FIGURE 6. (A) Single ventricular tomographic short-axis slice from a ^{201}Tl study (uncontaminated) acquired using dual-isotope (technetium (140 keV) and thallium (68 keV, 167 keV)) windows. Note that there is only minimal crosstalk observed in the technetium windows (myocardial count ratio between thallium and technetium windows was 14.3:1). (B) Single ventricular tomographic short-axis slice from a sestamibi study (uncontaminated) acquired using dual-isotope windows demonstrates a substantial amount of sestamibi crosstalk into the ^{201}Tl windows (myocardial count ratio between technetium and ^{201}Tl windows was 3.6:1).

Potential Advantages and Disadvantages of Separate Acquisition Rest ^{201}Tl /Stress Sestamibi Dual-Isotope SPECT

As of early 1994, we have used the separate acquisition rest ^{201}Tl /stress sestamibi dual-isotope SPECT (9,10) as our routine clinical protocol in over 8,000 patients. This approach is highly efficient. In comparison to rest/stress sestamibi same-day protocols, separate acquisition dual-isotope SPECT eliminates the 1-hr waiting period between rest sestamibi injection and SPECT. It also eliminates the delay between SPECT acquisitions required by stress redistribution ^{201}Tl and suggested for same day rest/stress sestamibi studies. Therefore, an entire (rest plus stress) study can be completed within 90 min. Our work on separate acquisition dual-isotope SPECT has previously shown that this protocol provides high sensitivity, specificity and normalcy rates with exercise (9) or pharmacologic (10) stress protocols. In addition, the rest ^{201}Tl /stress sestamibi reversibility pattern has been shown to be comparable to the rest/stress sestamibi SPECT (9,21). The latter finding is in concordance with the previously published data demonstrating similar perfusion defect size by rest sestamibi and rest ^{201}Tl (22). Perhaps most importantly, the use of resting ^{201}Tl in the dual-isotope technique allows the detection of hibernating myocardium by performance of redistribution ^{201}Tl imaging. In this regard, patients can be brought back for late imaging the next day, or a rest-redistribution study can be completed before the stress sestamibi injection. We have recently demonstrated that incorporation of 24-hr rest-redistribution ^{201}Tl scintigraphy into the separate acquisition dual-isotope protocol detects an additional 17% of patients and 12% of coronary territories with reversible defects which would go undetected by rest/stress scintigraphy alone (23).

Since two radioisotopes of differing energy are employed by the dual-isotope approach, differences in defect resolution may be introduced (9). It is conceivable that small, mild nonreversible defects by rest/stress sestamibi imaging might erroneously be identified as reversible by rest ^{201}Tl /stress sestamibi dual-isotope imaging. This issue has been addressed in a previous study (9) from our institution in which an exact segmental agreement of 98% for a defect reversibility pattern was demonstrated between separate acquisition rest ^{201}Tl /stress sestamibi dual-isotope SPECT and separate day stress/rest sestamibi SPECT. Although spillover from rest ^{201}Tl somewhat reduces dual sestamibi defect severity, it does so by a very small amount, thus representing a lesser problem than the effect of the residual rest sestamibi activity on the stress sestamibi images with the standard same-day rest/stress sestamibi protocols. Also, different filters are used for rest ^{201}Tl and stress sestamibi to optimize image quality of each data set; however, the difference in filters is unlikely to be affecting the assessment of defect reversibility. In fact, the filters employed for rest ^{201}Tl and exercise sestamibi in the dual-isotope protocol (9) are identical to those used for the

same-day rest sestamibi and exercise sestamibi studies (17,24,25).

Potential Advantages and Disadvantages of Simultaneous Acquisition Rest ^{201}Tl /Stress Sestamibi Dual-Isotope SPECT

If a reliable correction method for the crosstalk of $^{99\text{m}}\text{Tc}$ in the ^{201}Tl windows is devised, optimized and made generally available, the simultaneous dual-isotope approach would offer many advantages over currently available imaging techniques. Typically, the simultaneous acquisition rest ^{201}Tl /stress sestamibi dual-isotope SPECT protocol takes only 1 hr from the rest ^{201}Tl injection to completion. This is 4–5 times faster than standard stress-redistribution ^{201}Tl or rest/stress sestamibi protocols, resulting in greater patient convenience and more rapid reporting. Also, critical to the widespread application of SPECT, which is frequently limited by available camera time, the simultaneous dual-imaging approach would optimize resource utilization by halving camera utilization time compared to conventional SPECT protocols, thus potentially doubling throughput with the existing equipment and personnel. Furthermore, if rest and stress studies were acquired simultaneously, many sources of error associated with the standard separate rest/stress acquisition protocol would be eliminated, or artifacts more readily identified as such. These include artifactual defects occurring as a result of patient motion during the rest or the stress study alone, shifting breast or other soft tissue attenuation, change in patient positioning between the two acquisitions, and imprecise selection of appropriate slices or re-orientation angles for comparison of rest and stress images. With either dual-isotope approach, if imaging needed to be repeated (e.g., severe patient motion), the stress sestamibi myocardial perfusion information will be virtually unchanged due to the nominal sestamibi redistribution (8), while the rest ^{201}Tl myocardial viability information will, if anything, be enhanced by the later imaging time and the additional tracer redistribution.

As reported, however, our results demonstrated significant $^{99\text{m}}\text{Tc}$ crosstalk (downscatter) into the ^{201}Tl windows, resulting in a significant reduction of rest ^{201}Tl defect severity. Therefore, although simultaneous dual-isotope SPECT is an appealing protocol, for clinical purposes it will require crosstalk correction to accurately assess defect reversibility. The correction for $^{99\text{m}}\text{Tc}$ downscatter is not trivial, since its contribution to the lower energy portion of the spectrum is not simply a scaled quota of the photopeak counts, and thus cannot be addressed by simple subtraction (26,27). Several laboratories including our own are currently working on this important problem. Until this problem is solved, we *do not* recommend clinical application of simultaneous dual-isotope protocol in myocardial imaging.

Lowe et al. (28) used a phantom study to address the feasibility of simultaneous rest ^{201}Tl stress sestamibi dual-isotope SPECT. They reported a 10% reduction in defect

contrast in dual ^{201}Tl as a result of $^{99\text{m}}\text{Tc}$ crosstalk and suggest that these changes were minimal. It is difficult to make clinical extrapolations from phantom data, especially when variable organ attenuation and the resulting photon scatter are not taken into account. Furthermore, the overall 10% reduction of defect contrast covered a wide spectrum of defect size and severity rather than emphasizing the mild to moderate defect. As we have reported in the present study, when all defects were considered, the differences between dual and virgin ^{201}Tl studies were indeed small; however, in the subgroup of patients with mild to moderate defects, this difference was substantial. We agree with the editorial comments of DePuey (29), which address the paper of Lowe et al. (28), and join him in recommending that the simultaneous dual-isotope approach should not yet be embraced clinically.

CONCLUSIONS/CLINICAL IMPLICATIONS

The present study documents the major contribution of $^{99\text{m}}\text{Tc}$ crosstalk into the ^{201}Tl acquisition windows but only a very small amount of ^{201}Tl crosstalk into the $^{99\text{m}}\text{Tc}$ window. These findings support the validity of the separate acquisition rest ^{201}Tl /stress sestamibi dual-isotope SPECT protocol (9,10), and indicate that the simultaneous dual-isotope protocol should not be used until satisfactory techniques for correction of $^{99\text{m}}\text{Tc}$ crosstalk are developed.

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