

# Improved Diagnostic Performance of Thallium-201 Myocardial Perfusion Scintigraphy in Coronary Artery Disease: from Planar to Single Photon Emission Computed Tomography Imaging

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**Background:** This study was performed to compare Tl-201 myocardial perfusion single photon emission computed tomography (SPECT) with planar scintigraphy in the diagnosis of coronary artery disease (CAD).

**Methods:** Retrospectively, 240 of 3262 patients, with exercise-redistribution Tl-201 myocardial perfusion scintigraphy performed between January 1990 and October 1997, were analyzed to compare Tl-201 scintigraphy and coronary arteriography. Within 30 days, all 240 patients underwent both coronary arteriography and exercise-redistribution Tl-201 myocardial perfusion scintigraphy with 86 SPECT and 154 planar images acquired.

**Results:** The sensitivities of Tl-201 myocardial perfusion scintigraphy in individual coronary arteries including left anterior descending (LAD) artery, left circumflex (LCX) artery, and right coronary artery (RCA), were 77%/72%, 31%/30%, and 77%/50% in the SPECT/planar study groups, respectively. The sensitivities of CAD detection in patients with single-vessel, double-vessel, and triple-vessel diseases were 96%/82%, 91%/85%, and 96%/90% in the SPECT/planar study groups, respectively.

**Conclusion:** SPECT images provide greater advantages over planar images for better detection of the number, location, and extent of CAD. Cardiac SPECT does improve the accurate interpretation in abnormal Tl-201 distributions due to the higher contrast resolution and better separation of overlapping myocardial regions.

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**Key words:** coronary artery disease (CAD), single photon emission computed tomography (SPECT).

Tl-201 myocardial perfusion scintigraphy is widely used as a noninvasive modality to evaluate coronary artery disease.<sup>(1-4)</sup> The planar imaging method is conceivably suboptimal for assessing

myocardial perfusion because frequent overlap of both normally and abnormally perfused myocardial regions limits its ability to detect myocardial defects.<sup>(5-7)</sup> Single photon emission computed tomog-

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raphy (SPECT), which has higher contrast resolution and allows separation of overlapping myocardial regions, has the potential for overcoming this limitation of planar imaging.<sup>(8-11)</sup>

The present study was undertaken to retrospectively evaluate exercise-redistribution Tl-201 myocardial perfusion scintigraphy at our hospital. Specifically, the first goal of this study was to evaluate differences and relative sensitivities and specificities between SPECT and planar images.

## METHODS

### Patients

We retrospectively reviewed 3262 cases of exercise Tl-201 myocardial perfusion scintigraphy in our hospital from January 1990 to October 1997. Two hundred forty of the 3262 patients in whom coronary arteriography was performed within 30 days were included in this study. These 240 patients consisted of 199 men and 41 women whose mean ages were 55.6 ± 9.2 and 55.4 ± 8.4 years old, respectively (Table 1). All 240 studied patients were consecutively enrolled and had no previous coronary bypass surgery or coronary angioplasty.

### Exercise and imaging protocols

All 240 patients underwent maximally tolerated exercise on a treadmill according to the Bruce protocol with cessation of exercise for 1 of the following indications: 1) intolerable angina, 2) serial ≥ 2 mV of horizontal or downsloping ST segment depression 0.08 s after the J point over 2 or more of the limb or precordial leads, 3) marked dyspnea or fatigue, and 4) ≥ 85% of their age-predicted maximal heart rate or bi-product (systolic blood pressure in mmHg multiplied by the peak heart rate per minute) ≥ 2400 achieved during exercise in the absence of ischemic changes in electrocardiography (ECG). Patients were told to withhold beta adrenergic antagonists and nitrate medication for at least 24 hours before stress examination. Three millicuries of Tl-201 chloride was injected intravenously 1 min before termination of exercise.

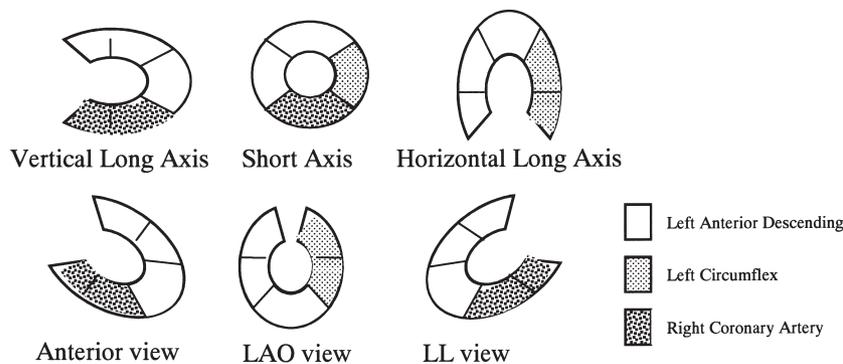
The stress images of Tl-201 myocardial perfusion scintigraphy were performed 5-10 min after stress exercise, while delayed images were taken after 4 hours of rest. Of the 240 studies included,

there were 86 SPECT and 154 planar studies. For imaging, 2 energy windows were set over the 80- (20%) and 167-keV (20%) photopeaks of Tl-201 by ADAC pegasys, equipped with a low-energy, high-resolution, para-hole collimator. For SPECT acquisition, 180° rotational tomography was used, extending from 45° of the right anterior oblique to the left posterior oblique position.<sup>(12)</sup> Thirty-two projections were obtained during the 180° rotation with each imaged for 40 s. All projections were stored in a 64 × 64, 16-bit matrix. For planar acquisition, myocardial imaging was started in a 45° left anterior oblique (LAO) view because of good separation of the territories between the left anterior descending (LAD) artery and the left circumflex (LCX) artery/right coronary artery (RCA). Anterior and left lateral views were subsequently obtained with each imaged for 500 s, in a 128 × 128, 16-bit matrix.<sup>(13)</sup> All planar studies were imaged with the heart positioned in the center of the field of view.

### Computer analysis and interpretation

The raw data for the rotational tomography were smoothed using a 9-point weighted algorithm. Filtered back-projection was then performed using a Butterworth filter with a cutoff of 35% of the Nyquist frequency and an order of 5. Transaxial tomograms were reconstructed and encompassed the entire heart. Short-axis, and vertical and horizontal long-axis tomograms were extracted from the filtered transaxial tomograms by performing a coordinate transformation with interpolation.<sup>(14)</sup> All tomograms were reconstructed at 1-pixel thickness (6.2 mm) per slice without attenuation or scatter correction. The slice views were displayed by the rainbow color-scale after serial normalization with linear algorithm.

Interpretations were performed by experienced readers who were unaware of the results of the exercise and coronary arteriography. The reader independently scored each vascular territory of the exercise-redistribution scintigrams according to a 5-point scale: 1=definitely normal, 2=probably normal, 3=equivocal, 4=probably abnormal, and 5=definitely abnormal. A defect had to be present in a segment at 2 or more image orientations to be scored as 3, 4, or 5. The segment model with exclusion of the basal septal segment was used for interpretation on both SPECT and planar images. Figure 1 (top) shows the



**Fig. 1** Representation of segments in a variety of vascular territories on SPECT (top) and planar (bottom) images.

representation of the segments in various vascular territories on each SPECT image orientation; while Fig. 1 (bottom) shows each planar image orientation.<sup>(15)</sup> Either fixed, reversible, or reversed-reversible defects, scoring no less than 3, were interpreted as abnormal perfusion defects in this study.

**Coronary arteriography**

The coronary arteriograms were interpreted by the consensus opinion of 2 or more cardiologists who were unaware of the scintigraphic results. Coronary stenosis was estimated by visual analysis of the maximal percent luminal diameter narrowing revealed in any projection, and was categorized as normal, mild (> 50% to 75% narrowing), moderate (> 75% to 90%

narrowing), and severe (> 90% to 100% narrowing).

**Statistical analysis**

For overall detection of CAD, the sensitivity was defined as the proportion of patients with arteriographic results of coronary stenosis out of those who had a Tl-201 scintigraphic defect in at least 1 of the coronary territories. Specificity was defined as the proportion of patients with normal coronary arteriograms among those who had normal Tl-201 scintigrams. Sensitivity for detection of disease in the given coronary arteries was defined as the percent of patients with diseased (> 50% stenosis) coronary arteries among those who had definite Tl-201 scintigraphic defects in their corresponding territories.

**Table 1.** Clinical History of the 240 Patients

Risk parameter	Total (N=240)	Planar (N=154)	SPECT (N=86)	<i>p</i> $\pi$
Age*	55.6; 9.1	53.9; 8.9	58.6; 8.6	0.7111
Gender				0.9122
Men	199 (83%)	128 (83%)	71 (82.5%)	
Women	41 (17%)	26 (17%)	15 (17.5%)	
MI <sup>†</sup> history	99 (41%)	68 (44%)	31 (36%)	0.2211
Hypertension history	113 (47%)	71 (46%)	42 (49%)	0.6842
Obesity, high TG or cholesterol <sup>‡</sup>	126 (53%)	80 (52%)	46 (54%)	0.8188
Habitual smoker over 10 years	135 (56%)	84 (55%)	51 (59%)	0.4763
Diabetes mellitus	39 (16%)	23 (15%)	16 (19%)	0.6067
Family history of CAD	13 ( 5.4%)	5 ( 3.2%)	8 ( 9.3%)	0.0469

Age\*: age is presented as the mean; standard deviation in years.

MI<sup>†</sup>: either acute, recent, or old myocardial infarction.

Obesity, high TG or cholesterol<sup>‡</sup>: body weight  $\geq$ 80 kg, serum triglyceride  $\geq$ 180 mg%, or cholesterol  $\geq$ 240 mg%.

*p* $\pi$ : unpaired *t*-test was used for age, and chi-square test was used for the others between planar and SPECT studies.

**Table 2.** Treadmill Exercise Data of the 240 Patients

Exercise termination	Total (N=240)	Planar (N=154)	SPECT (N=86)	<i>p</i> *
Intolerable angina	40 (17%)	33 (21%)	7 ( 8%)	0.0081
Marked dyspnea or fatigue	88 (37%)	69 (45%)	19 (22%)	0.0005
Serial ST depression ≥2 mV	45 (19%)	24 (16%)	21 (24%)	0.0927
≥85% max. HR or bi-product ≥2400	67 (28%)	28 (18%)	39 (45%)	< 0.0001

*p*\*: Chi-square test was used between planar and SPECT studies.

**Table 3.** Results of Arteriograms and Planar and SPECT Scintigrams of the 240 Patients

CAD	Arteriograms (N=240)	Planar scintigrams (N=154)	SPECT scintigrams (N=86)	<i>p</i> *
1VD	75 (31%)	80 (52%)	38 (44%)	0.2488
2VD	51 (21%)	31 (20%)	21 (24%)	0.4393
3VD	67 (28%)	3 ( 2%)	4 ( 5%)	0.2327
Any VD	193 (80%)	114 (74%)	63 (73%)	0.8965
Normal	47 (20%)	40 (26%)	23 (27%)	0.8965

**Abbreviations:** CAD: coronary artery disease; SPECT: single photon emission computed tomography.

*p*\*: Chi-square test was used between planar and SPECT studies.

**Table 4.** Sensitivity and Specificity for Overall Detection of Individual CAD (Luminal Diameter > 50% Stenosis) by Exercise TI-201 Scintigraphy

Arteriographic	Sensitivity			Specificity		
	Planar study	SPECT study	<i>p</i> *	Planar study	SPECT study	<i>p</i> *
CAD						
LAD	77/107 (72%)	39/51 (76%)	0.5487	40/47 (85%)	25/35 (71%)	0.1307
LCX	20/ 67 (30%)	11/36 (31%)	0.9407	83/87 (95%)	49/50 (98%)	0.4350
RCA	39/ 78 (50%)	30/39 (77%)	0.0053	68/76 (89%)	37/47 (79%)	0.1012

**Abbreviations:** CAD: coronary artery disease; LAD: left anterior descending; LCX: left circumflex; RCA: right coronary artery.

*p*\*: Chi-square test was used between planar and SPECT studies.

**Table 5.** Sensitivity and Specificity of Scintigraphic Analysis for Detection of CAD (Luminal Diameter > 50% Stenosis)

CAD	Arteriograms	Sensitivity		<i>p</i> *
		Planar study	SPECT study	
1VD	75	40/ 49 (82%)	25/26 (96%)	0.0783
2VD	51	34/ 40 (85%)	10/11 (91%)	0.6140
3VD	67	37/ 41 (90%)	25/26 (96%)	0.3697
Multi VD	118	71/ 81 (88%)	35/37 (95%)	0.2472
Any VD	193	111/130 (85%)	60/63 (95%)	0.0434
		Specificity		
Normal	47	19/ 24 (79%)	12/23 (52%)	0.0509

Abbreviations are same as Table 3.

*p*\*: Chi-square test was used between planar and SPECT studies.

Specificity for detection of the disease in the given coronary arteries was defined as the percent of patients with normal coronary arteries among those whom had normal TI-201 scintigraphic results in their corresponding territories. Comparable clinical

data were analyzed utilizing unpaired t-test for age (Table 1) and left ventricular ejection fraction (Table 7) parameters, and Chi-square test for others (Tables 1-6) between planar and SPECT studies.

**Table 6.** Sensitivities and Specificities of Planar (N=49) and SPECT (N=26) Scintigraphy in Patients with Single Vessel Disease

Arteriographic	Sensitivity			Specificity		
	Planar study	SPECT study	<i>p</i> *	Planar study	SPECT study	<i>p</i> <sup>†</sup>
CAD	29/34 (85%)	15/15 (100%)	0.1170	14/15 ( 93%)	9/11 (82%)	0.3639
LAD	2/ 3 (67%)	3/ 5 ( 60%)	0.8504	44/46 ( 96%)	20/21 (95%)	0.9394
LCX	7/12 (58%)	6/ 6 (100%)	0.0628	35/37 ( 95%)	16/20 (80%)	0.0866
RCA	11/15 (73%)	10/11( 91%)	0.2613	34/34 (100%)	12/15 (75%)	0.0071

Abbreviations are same as Table 4.

LCX/RCA\*: combined territories of LCX and RCA in 1VD with either LCX or RCA.

*p*<sup>†</sup>: Chi-square test was used between planar and SPECT studies.

**Table 7.** Left Ventricular Ejection Fraction by Contrast Ventriculography

LVEF	Planar study	SPECT study	<i>p</i> <sup>†</sup>
All patients	0.57 ; 0.16 (N=75)	0.56 ; 0.15 (N=71)	0.8299
Patients with MI history	0.46 ; 0.11 (N=31)	0.48 ; 0.16 (N=26)	0.5878
Patients without MI history	0.65 ; 0.13 (N=44)	0.61 ; 0.14 (N=45)	0.2609

*p*<sup>†</sup>: unpaired *t*-test was used between planar and SPECT studies.

## RESULTS

Table 1 shows the various risk factors for ischemic heart disease in all 240 patients between the SPECT and planar groups with respect to gender, hypertension, diabetes mellitus, obesity, hypertriglyceridemia, hypercholesterolemia, and habitual smoking for over 10 years.<sup>(16,17)</sup> Relatively higher incidence of familial CAD history was found in patients of the planar group, but the case number was low in both planar and SPECT groups. Conditions for termination of the treadmill exercise are shown in Table 2. In the planar group, relatively more patients suffered from intolerable chest pain, marked dyspnea, or fatigue before serial ischemic ECG changes, sub-maximal heart rate, or a bi-product  $\geq 2400$  could be reached during exercise.

Table 3 lists the results of coronary arteriography and exercise TI-201 myocardial perfusion scintigraphy with either SPECT or planar study in all 240 patients studied. Sixty-three of 86 SPECT scintigrams showed perfusion defects; these were seen in the territories of 1, 2, and 3 vessels in 38, 21, and 4 cases, respectively. One hundred fourteen of 154 planar scintigrams showed perfusion defects; these were seen in the territories of 1, 2, and 3 vessels in 80, 31, and 3 cases, respectively. Coronary stenosis (> 50%) was present in 193 patients, where-

as 47 patients had angiographically normal coronary arteries.

By analysis of the SPECT images, 60 (95%) of 63 patients with coronary stenosis showed abnormal images: 39, 11, and 30 patients had abnormal perfusion defects at corresponding territories in those with stenosed LAD arteries, LCX arteries, and RCAs, respectively. By interpretation of planar images, 111 (85%) of 130 patients with coronary stenosis showed abnormal images: 77, 20, and 39 patients had abnormal perfusion defects at corresponding territories in those with stenosed LAD arteries, LCX arteries, and RCAs, respectively (Table 4).

In the SPECT group, 63 of 86 patients had coronary stenosis with 26, 11, 26 patients having single-vessel disease (1VD), double-vessel disease (2VD), and triple-vessel disease (3VD) each. In the planar group, 130 of 154 patients had coronary stenosis with 49, 40, and 41 patients having 1VD, 2VD, and 3VD each. Overall sensitivity and specificity were 95.2% (60/63) and 52.2% (12/23) in the SPECT group, whereas they were 85.4% (111/130) and 79.2% (19/24) in the planar study group. In patients with 1VD, 2VD, and 3VD, the sensitivities were 96% (25/26), 91% (10/11), and 96% (25/26) by SPECT images, whereas they were 82% (40/49), 85% (34/40), and 90% (37/41) by planar images, respectively (Table 5).

In 26 patients with IVD in the SPECT group, sensitivities were 100% (15/15), 60% (3/5), and 100% (6/6) for involvement of the LAD arteries, LCX arteries, and RCAs respectively. In 49 patients with IVD in the planar study group, sensitivities were 85% (29/34), 67% (2/3), and 58% (7/12) for involvement of the LAD arteries, LCX arteries, and RCAs, respectively. However, if the territories of LCX and RCA were combined together, sensitivities for involvement of either the LCX arteries or RCAs were 91% (10/11) in the SPECT group and 77% (10/13) in the planar study group (Table 6).

## DISCUSSION

Because of referral bias with respect to which patients underwent coronary arteriography, the specificity determined in patients with normal coronary arteriograms was 52% (N=23) for SPECT and 79% (N=24) for the planar study. Limitations of inadequate specificity in TI-201 myocardial perfusion scintigraphy have also been observed in many laboratories, which are mainly due to image attenuation artifacts and normal variants which are falsely interpreted as CAD defects.<sup>(18)</sup> A mild age discrepancy (58.5 ± 8.6 vs. 53.9 ± 8.9 years old) was found between the SPECT and planar groups. Different proportions of conditions before termination of the treadmill exercise, as shown in Table 2, may have been caused by different morbidities for myocardial infarction (36% vs. 44%) in the SPECT and planar groups. As compared with both groups, the ejection fraction of the left ventricle, as revealed by contrast ventriculography, was lower in patients with a history of myocardial infarction, which may have reduced the exercise tolerance (Table 7).

Planar imaging suffers from technical limitations including poor lesion contrast, spatial overlap of myocardial regions, and variable attenuation by breasts and the diaphragm. For visual interpretation of TI-201 planar images, in addition to inspection for perfusion defects, attention should be given to correct positioning of the patient, and potential artifacts caused by unusual rotation of the heart, or soft tissue attenuation. Although these variables, to a certain extent, should be represented in the pool of normal subjects, extreme cases may exceed the lower limit of normal and appear as TI-201 perfusion defects.

SPECT did improve the accurate interpretation

for better detection of diseased coronary arteries with abnormal TI-201 distributions due to the higher contrast resolution, better separation of overlapping myocardial regions, and soft tissue attenuation from various non-cardiac structures. In our retrospective study, the overall CAD detection improved from 85% by planar images to 95% by SPECT images. Almost all CADs of patients were detected on SPECT images. It was mentioned by others that TI-201 SPECT is more useful in precisely predicting diseases of individual coronary arteries.<sup>(8,12)</sup> However, as revealed in Table 4 in our study, without considering the number, location, or extent of the diseased vessels, there was no significant difference in either the sensitivity or specificity for detecting diseased individual coronary arteries on either SPECT or planar images. SPECT imaging has potential advantages over planar imaging, including higher lesion contrast, less background activity, and quantitation of the extent and size of the lesions.<sup>(19)</sup> The ability of SPECT images to accurately predict the number and location of diseased vessels is still suboptimal but considerably better than that of planar images. Both overestimation and underestimation occurred in comparison with the coronary arteriography as the gold standard.

In considering the number of diseased coronary vessels, most false-negative results occurred in patients with single-vessel disease on planar images (Table 5). Detection of CAD in corresponding locations of a particular vessel was better for LAD arteries, and worse for LCX arteries. Diminished sensitivity for detection of CAD distributed in LCX arteries was also found on both planar and SPECT images in other studies.<sup>(7,11)</sup> It is well recognized that there are relatively thickened left ventricular lateral walls, diaphragmatic attenuation effects of the inferoposterior walls, and prominent biases in the territories around LCX arteries and RCAs. However, as shown in Tables 4 and 6, SPECT images had better sensitivity for detecting CAD in the area around RCAs than did planar images for both overall CAD and single-vessel disease in our study.

SPECT scintigraphy detected myocardium at risk with higher sensitivity and specificity than did planar scintigraphy in either single-, double-, or triple-vessel disease. Although coronary arteriography is usually considered the gold standard for establishing a diagnosis of CAD in patients with chest

pain and for demonstrating its severity by delineating focal coronary arterial obstruction, data from myocardial perfusion imaging provide unique physiological information about the extent of at-risk myocardium in the supply areas of stenotic coronary arteries. The more severe and extensive the CAD is, the greater the total area with hypoperfusion or non-perfusion on exercise TI-201 myocardial perfusion scintigraphy is. The risk area assessment by exercise TI-201 myocardial perfusion scintigraphy is superior to mere determination of the diseased coronary arteries on coronary arteriography for identifying patients with multi-vessel CAD who are at the highest risk for an adverse outcome. Although not achieved in our study, quantitation of TI-201 uptake and washout can help optimally assess the extent and severity of regional myocardial perfusion abnormalities, distinguish ischemia from infarctions, and thus promote better concordance in multi-vessel CAD.<sup>(20,21)</sup>

### Conclusions

Exercise TI-201 myocardial perfusion scintigraphy with SPECT study provides relatively greater advantages over planar study in patients with CAD for better detection of diseased coronary arteries, in both single- and multi-vessel disease. In addition, in patients with multi-vessel disease, SPECT images also offer better detection of at-risk myocardium in a different way from what coronary arteriography does. Furthermore, quantitation of TI-201 uptake and washout in the cardiac SPECT study may promote the precise detection of the number, location, severity, extent, and even the viability of CAD.

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