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Segmental Analysis of Tl-201 Stress Myocardial Scintigraphy

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Thallium-201 scintigraphy of the exercised myocardium was performed in 70 male patients admitted for coronary arteriography and left-ventricular angiography. Left ventricular scintigrams were collected in left lateral, left anterior oblique (65°, 45°, and 25°), and anterior views, and the images were divided into eight segments: apical, anteroseptal, anterior, anterolateral, posterolateral, posterior, inferior, and posteroseptal. A correlative study between segmental hypoperfusion on scintigram and coronary-artery stenosis visualized by contrast arteriography allowed selection of specific segments for each main coronary artery. Hypoactivity in the apical and posterior segments did not appear reliable. Using selected segments, we were able to identify LAD disease in 84%, LCx disease in 49%, and RCA disease in 79% of documented significant stenosis, with specificity of 95%, 89%, and 88%, respectively. Coronary-artery disease could be detected in 95% of patients having more than 50% coronary-artery stenosis, with 93% specificity. In most cases, patients with two-vessel disease and three-vessel disease could not be distinguished from each other. Multiple-vessel disease suggested by segmental analysis of myocardial scintigrams after exercise was confirmed arteriographically in 88% of the patients, but 52% with scintigrams suggesting single-vessel disease had, in fact, multiple-vessel disease.

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Myocardial imaging after exercise has been developed in the last few years for noninvasive assessment of coronary-artery disease. The first tracers used, K-43 and Rb-81, are emitters of high-energy photons and require cumbersome equipment such as scanners or scintillation cameras with specially shielded collimators (*1–7*). Thallium-201, proposed in 1973 for myocardial perfusion scintigraphy (*8,9*), offers much better physical and biologic properties (*10–15*); its principal photopeaks are at 135 and 167 keV and there are x-rays from the mercury daughter at 69–83 keV (*16*). It appears to be a good tracer for visualization of myocardial infarction (*17–22*) and transient stress-induced ischemia (*23,24*).

In our previous studies (*25–27*), myocardial scintigraphy after exercise, using Tl-201, was found superior to exercise electrocardiography in sensitivity and specificity for detecting patients with coronary-artery disease. In the present work we have studied in 70 patients the relation between regional myocardial perfusion, as assessed by segmental analysis of exercise scintigraphy, and significant stenosis of the main coronary arteries documented by arteriography.

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MATERIALS AND METHODS

Patients. Exercise myocardial scintigraphy was performed in 70 male subjects aged from 28 to 66, admitted for selective coronary arteriography and left-ventricular angiography. They were given physical examination, 12-lead ECG, chest x-ray, and routine laboratory investigations. Plasma levels of CPK, SGOT, and LDH were normal in all cases.

Among the 70 patients, 21 had a typical history of previous myocardial infarction: 19 with persistent ECG pattern of necrosis and 2 without abnormal Q waves. Four more patients had Q waves of at least 0.04 sec duration, suggesting myocardial scars. Among the 45 patients with no evidence of previous myocardial infarction, 29 had a completely normal ECG and 3 had a left bundle-branch block. The remaining 13 ECGs showed nonspecific alterations of the T waves.

Exercise scintigraphy. The patients performed a graded, symptom-limited exercise test on a bicycle ergometer, beginning with a 300 kg-m/min load during 5 min and continuing with a further increase of 150 kg-m/min every 5 min until onset of chest pain, fatigue, preselected maximal heart rate, elevation or depression of ST segment, or elevation of the systolic blood pressure above 250 mm Hg. Two millicuries of [^{201}Tl] thallous chloride in saline solution, with a specific activity of more than 500 mCi/mg, were then injected into a cubital vein and the patient was asked to continue his exercise at the same load or at a lower load for another minute.

Myocardial scintigraphy was begun as soon as possible after completion of the exercise test, but never before the tenth minute after injection. An Anger-type scintillation camera* connected to a computer† was equipped with a 140-keV converging collimator, closely applied to the chest, and located in front of the left ventricle under oscilloscopic control. The spectrometer was adjusted for the 69–83-keV x-ray of the thallium's mercury daughter, with a 25% window. Analog images were obtained in left lateral, left anterior oblique (65°, 45°, and 25°), and anterior positions. For each view, 300,000 counts were collected in approximately 5 min, so that the whole procedure was completed within 1 hr after injection. Data were stored in a 256 × 256 matrix, and contrast enhancement was obtained by a 50% cutoff of the maximal left ventricular activity determined after nine-point smoothing. The 75% isocount level was outlined for easier evaluation of regional myocardial perfusion. Analog images and images with contrast enhancement were examined by two independent observers without knowledge of the arteriographic findings. The left ventricular scintigrams were divided into eight segments: apical, anteroseptal, anterior, anterolateral, posterolateral, posterior, inferior, and posteroseptal (Fig. 1). Each segment was considered hypoperfused if the activity was below the 75% isocount level. Only segments considered hypoperfused by both observers were classified so in the final conclusion.

Coronary arteriography and left ventricular angiography. Selective coronary arteriography was performed 24 hr later according to the Judkins' technique, with the catheters proposed by Bourassa. Exposures were made on 35-mm film taken at 60 frames/sec using the Philips 9- and 5-in. image-intensifier system. Arteriograms were obtained in left and right anterior oblique positions by injection of 6–8 ml of Urografin 76%. Left ventricular angiography was performed in right anterior oblique position after injection of 60 ml of Teletrix. As recommended by the AHA Grading Committee, coro-

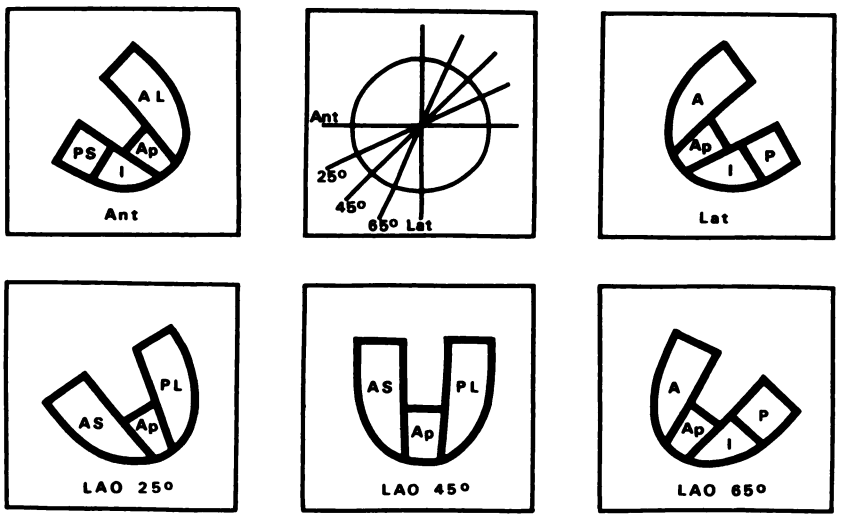

FIG. 1. Segments of left ventricular scintigram obtained in anterior (Ant), 25°, 45°, and 65° left anterior oblique (LAO), and left lateral (LAT) views: apical (Ap), anteroseptal (AS), anterior (A), anterolateral (AL), posterolateral (PL), posterior (P), inferior (I), and posteroseptal (PS).

TABLE 1. RELATION BETWEEN SEGMENTAL HYPOPERFUSION OF LEFT VENTRICULAR WALL AND CORONARY MAIN-ARTERY DISEASE

Coronary main-artery disease	Segmental hypoperfusion of left ventricular wall							
	Apical	Antero-septal	Anterior	Antero-lateral	Postero-lateral	Posterior	Inferior	Postero-septal
LAD								
$p <$	0.005	0.01	0.0005	0.005	0.025	0.25	0.10	0.25
correlation	†	†	‡	†	*	none	none	none
LCx								
$p <$	0.01	0.90	0.10	0.025	0.001	0.05	0.05	0.50
correlation	†	none	none	*	‡	*	*	none
RCA								
$p <$	0.01	0.25	0.25	0.25	0.50	0.75	0.0005	0.0005
correlation	†	none	none	none	none	none	‡	‡

Correlation: * less significant; † significant; ‡ highly significant.

TABLE 2. RELIABILITY OF STRESS-INDUCED HYPOPERFUSION IN SEGMENTS BEST CORRELATED WITH LAD DISEASE

LAD disease on coronary arteriogram		Hypoperfusion on exercise scintigram			
		Apical	Anteroseptal	Anterior	Anterolateral
	49 +	40 + 9 −	17 + 32 −	23 + 26 −	16 + 33 −
	21 −	10 + 11 −	1 + 20 −	0 + 21 −	0 + 21 −
Total	70	50 + 20 −	18 + 52 −	23 + 47 −	16 + 54 −
Sensitivity		40/49 (82%)	17/49 (35%)	23/49 (47%)	16/49 (33%)
Specificity		11/21 (52%)	20/21 (95%)	21/21 (100%)	21/21 (100%)
False negative		9/20 (45%)	32/52 (62%)	26/47 (55%)	33/54 (61%)
False positive		10/50 (20%)	1/18 (6%)	0/23 (0%)	0/16 (0%)

nary-artery stenosis was graded as 25%, 50%, 75%, 90%, 99%, and 100%. Only stenoses of more than 50% were considered significant for each of the three main coronary arteries: left anterior descending (LAD), left circumflex (LCx), and right coronary artery (RCA). In each left ventricular wall region, motion was classified in normal, reduced, absent, dyskinetic, or aneurysmal.

Correlative study. The correlation between (A) segmental hypoperfusion as shown by exercise scintigrams and (B) significant stenosis of the main coronary arteries as documented by arteriograms was studied by a chi-square test between each of the 8 segments and each of the 3 main arteries. Using the coronary arteriography as a reference, the sensitivity and specificity of exercise scintigraphy were then calculated for each segment, along with the incidence of false positives and false negatives. Sensitivity was defined as the number of patients with true positive scintigrams divided by the total number of patients with positive arteriograms; specificity as the number of patients with true negative scintigrams divided by the total number of patients with negative arteriograms; false negative incidence as the number of patients with false negative scintigrams divided by the total number of patients with negative scintigrams; and false positive incidence as the number of patients with false positive scintigrams divided by the total number of patients with positive scintigrams.

RESULTS

Disagreement between the two observers concerning the presence or absence of hypoperfusion occurs in 42 of the 560 segments analyzed in the 70 patients (7.5%).

The results of the chi-square test between hypoperfusion in each of the eight segments of the left ventricular wall and significant stenosis on each of the three main coronary trunks are summarized in Table 1. A highly significant correlation is found between hypoperfusion in the anterior, posterolateral, inferior, and posteroseptal segments and stenosis of the LAD, LCx, and RCA, respectively. A significant correlation is found between hypoper-

fusion in the anteroseptal and anterolateral segments and LAD stenosis, and between apical hypoperfusion and LAD, LCx, or RCA disease. A less firm correlation is found between the posterolateral segment and LAD, and between anterolateral, posterior, and inferior segments and LCx.

The sensitivity, specificity, false-negative and false-positive incidence of hypoperfusion in the segments that correlated best with artery disease are shown in Table 2 (LAD), Table 3 (LCx), and Table 4 (RCA). The specificity of all these segments is very high (at least 88%) except for the apical region (only 25–52%). If this segment is discarded, anteroseptal, anterior, and anterolateral segments appear specific for assessment of LAD disease, posterolateral segment for LCx disease, and posteroseptal and inferior segments for RCA disease. The reliability of these associations for selected segments is shown in Tables 5–7.

We conclude that noninvasive assessment of LAD disease can be achieved with high sensitivity (84%) and high specificity (95%). Satisfactory results are obtained for detection of RCA disease, with good sensitivity (79%) and good specificity (88%), but LCx disease is recognized in only 49% of documented significant stenosis, although the specificity is good (89%).

TABLE 3. RELIABILITY OF STRESS-INDUCED HYPOPERFUSION IN SEGMENTS BEST CORRELATED WITH LCx DISEASE

LCx disease on coronary arteriogram		Hypoperfusion on exercise scintigram: Apical	Posterolateral
	35 +	30 + 5 −	17 + 18 −
	35 −	20 + 15 −	4 + 31 −
Total	70	50 + 20 −	21 + 49 −
Sensitivity		30/35 (86%)	17/35 (49%)
Specificity		15/35 (25%)	31/35 (89%)
False negative		5/20 (25%)	18/49 (37%)
False positive		20/50 (40%)	4/21 (19%)

TABLE 4. RELIABILITY OF STRESS-INDUCED HYPOPERFUSION IN SEGMENTS BEST CORRELATED WITH RCA DISEASE

RCA disease on coronary arteriogram		Hypoperfusion on exercise scintigram: Apical	Inferior	Posteroseptal
	38 +	32 + 6 −	27 + 11 −	20 + 18 −
	32 −	18 + 14 −	4 + 28 −	1 + 31 −
Total	70	50 + 20 −	31 + 39 −	21 + 49 −
Sensitivity		32/38 (84%)	27/38 (71%)	20/38 (53%)
Specificity		14/32 (44%)	28/32 (88%)	31/32 (97%)
False negative		6/20 (30%)	11/39 (28%)	18/49 (37%)
False positive		18/50 (36%)	4/31 (13%)	1/21 (5%)

TABLE 5. ASSESSMENT OF LAD DISEASE BY ANALYSIS OF ANTEROSEPTAL,* ANTERIOR,† AND ANTEROLATERAL‡ SEGMENTS OF MYOCARDIAL SCINTIGRAMS AFTER EXERCISE

Coronary arteriograms with LCx disease		Exercise myocardial scintigrams with AS, A, or AL hypoperfusion	
	49 +	41 +	8 −
	21 −	1 +	20 −
Total	70	42 +	28 −
Sensitivity	41/49 (84%)	False negative	8/28 (29%)
Specificity	20/21 (95%)	False positive	1/42 (2%)

* AS; † A; ‡ AL.

TABLE 6. ASSESSMENT OF LCx DISEASE BY ANALYSIS OF POSTEROLATERAL* SEGMENT OF MYOCARDIAL SCINTIGRAMS AFTER EXERCISE

Coronary arteriograms with LAD disease		Exercise myocardial scintigrams with PL hypoperfusion	
	35 +	17 +	18 −
	35 −	4 +	31 −
Total	70	21 +	49 −
Sensitivity	17/35 (49%)	False negative	18/49 (37%)
Specificity	31/35 (89%)	False positive	4/21 (19%)

* PL.

TABLE 7. ASSESSMENT OF RCA DISEASE BY ANALYSIS OF INFERIOR* AND POSTEROSEPTAL† SEGMENTS OF MYOCARDIAL SCINTIGRAMS AFTER EXERCISE

Coronary arteriograms with RCA disease		Exercise myocardial scintigrams with I or PS hypoperfusion	
	38 +	30 +	8 −
	32 −	4 +	28 −
Total	70	34 +	36 −
Sensitivity	30/38 (79%)	False negative	8/36 (22%)
Specificity	28/32 (88%)	False positive	4/34 (12%)

* I; † PS.

Association of all the reliable segments—i.e., anteroseptal, anterior, anterolateral, posterolateral, inferior, and posteroseptal—allows noninvasive detection of significant coronary-artery disease by exercise myocardial scintigraphy. Table 8 shows the sensitivity and specificity of this method in our series, and the incidence of false negatives and false positives. Both sensitivity and specificity are high, with only one false positive and three false negative results among the 70 patients. The false-positive result occurred in a patient with only a 50% stenosis on his dominant LCx, and an inferior myocardial scar documented by electrocardiography and left-ventricular angiography.

Potentially, identification of coronary main-artery disease by segmental analysis of exercise scintigrams might provide information on the number of diseased vessels. Comparison between the number of diseased main coronary arteries assessed by scintigraphy and by coronary arteriography is depicted in Table 9. Among 13 cases with one-vessel disease, nine (69%) were correctly identified by scintigraphy, one was classified as normal, and three as two-vessel disease. Among 17 cases with two-vessel disease, seven (41%) were correctly identified, seven were classified as one-vessel disease, one as normal, and two as three-vessel disease. Among 25 cases with three-vessel disease, eight (32%) were correctly identified, 13 classified as two-vessel disease, three as one-vessel disease, and one as normal. When the results of Table 9 are considered for each column, prediction of three-vessel disease by scintigraphy was correct in eight out of ten cases (80%), two-vessel disease in seven out of 24 cases (29%), and one-vessel disease in 9 out of 19 cases (47%). In fact, 52% of the patients with three-vessel disease were considered as two-vessel disease by scintigraphic criteria. Since this method does not appear suitable to distinguish between two-vessel and three-vessel disease, these two groups of patients were combined into one group of multiple-vessel disease. Table 10 shows the reliability of exercise myocardial scintigraphy for assessment of single- and multiple-vessel disease, as compared with arteriographic findings. Nine patients among 13 (69%) with single-vessel disease and 30 patients among 42 (71%) with multiple-vessel disease were correctly identified. Prediction of single-vessel disease was correct in only 9 scintigrams out of 19 (47%) and prediction of multiple-vessel disease in 30 scintigrams out of 34 (88%).

TABLE 8. ASSESSMENT OF SIGNIFICANT CORONARY-ARTERY DISEASE BY ANALYSIS OF ALL THE RELIABLE SEGMENTS OF MYOCARDIAL SCINTIGRAMS AFTER EXERCISE

Coronary arteriograms with LAD or LCx or RCA disease		Exercise myocardial scintigrams with AS, A, AL, PL, I, or PS hypoperfusion	
	55 +	52 +	3 −
	15 −	1 +	14 −
Total	70	53 +	17 −
Sensitivity	52/55 (95%)	False negative	3/17 (18%)
Specificity	14/15 (93%)	False positive	1/53 (2%)

TABLE 9. ASSESSMENT OF THE NUMBER OF DISEASED CORONARY ARTERIES BY MYOCARDIAL SCINTIGRAPHY AFTER EXERCISE

Coronary arteriography		Myocardial scintigraphy after exercise			
		Predicted no. of diseased vessels			
No. of diseased vessels	No. of patients	0	1	2	3
0	15	14	0	1	0
1	13	1	9	3	0
2	17	1	7	7	2
3	25	1	3	13	8
Total	70	17	19	24	10

TABLE 10. ASSESSMENT OF SINGLE- OR MULTIPLE-VESSEL DISEASE BY MYOCARDIAL SCINTIGRAPHY AFTER EXERCISE

Coronary arteriography		Myocardial scintigraphy after exercise		
		Predicted normal (N), single-vessel (SV), or multiple-vessel (MV) disease		
Normal, single-vessel, or multiple-vessel disease	No. of patients	N	SV	MV
N	15	14	0	1
SV	13	1	9	3
MV	42	2	10	30
Total	70	17	19	34

DISCUSSION

Thallium-201 is well suited to the visualization of stress-induced ischemia since it is cleared from the blood very rapidly and the amount distributed to the left ventricular myocardium remains essentially unchanged for at least 1 hr after injection (*9–15*). The uptake of Tl-201 by the left ventricular wall is related to regional myocardial blood flow (*22*). In patients with coronary-artery disease, the increase in regional myocardial flow is limited when

the lumen of the involved artery is narrowed by approximately 50% (*28*). Thus, myocardial imaging with injection of Tl-201 at peak exercise should provide information on regional coronary-artery disease in man.

Our correlative study between segmental hypoperfusion as assessed by exercise scintigraphy, and significant coronary artery stenosis as documented by arteriography, leads to conclusions that were not all expected on an anatomic basis. The apical region is perfused through the LAD, but hypoactivity in the apical segment can be found in LAD, LCx, or RCA disease, and in normal subjects (Fig. 2). This poor specificity is reflected in Tables 2–4. In order to avoid a high incidence of false positive results, hypoactivity limited strictly to the narrow apical region (Fig. 1) must be considered unreliable and therefore discarded. Larger areas of decreased activity, extending to surrounding regions, may be significant.

The posterior and inferior regions can be perfused through the right coronary artery in the right-dominant type of coronary-artery distribution, or through the left circumflex artery in the left-dominant type. Hypoactivity in the posterior region was found in 35 of our 70 patients, with only a slightly significant correlation with LCx disease. This high incidence of hypoactivity in this region may be due to the greater distance between this portion of the myocardium and the chest wall, with greater x-ray absorption, as compared with the anterior and lateral regions in the left lateral view. Because of its lack of strong correlation with coronary-artery disease in our series, this segment was also discarded.

With other procedures, such as the recording of the left lateral view with the patient lying on his right side (*21*), the significance of posterior hypoactivity might be enhanced.

In our previous attempt to identify regional artery disease, based on the anatomic distribution of the main coronary trunks (*27*), hypoactivity in the inferior region was attributed to RCA or LCx disease without distinction between these two arteries, since the left- or right-dominant type of coronary-artery distribution could not be assessed without knowledge of the arteriographic data. The present study allows attribution of the inferior segment of the left ventricular scintigram to the RCA with reasonably low incidence (13%) of false positive results.

The relation between the other segments and the corresponding arteries, summarized in Table 1, strikingly reflects what could be expected from anatomic considerations. The strongest correlation is found in the segment located in the center of each arterial territory, and there is a trend toward overlapping in the anterolateral segment for LCx disease, and in the posterolateral segment for LAD disease.

Assessment of LAD and RCA disease can be achieved with a good specificity, as a result of the selection of the most reliable segments, and with good sensitivity due to the association of these segments. In LCx disease, unfortunately, the posterolateral segment is the only region strongly correlated with arteriographic findings, so that sensitivity cannot be increased by association with other segments. In fact, isolated LCx disease occurs very rarely (no case in our 70 patients), so that the poor sensitivity of exercise myocardial scintigraphy for detection of LCx stenosis does not affect the overall sensitivity for detection of coronary-artery disease.

In our series, 52 out of 55 patients with significant coronary-artery stenosis were correctly identified, as were 14 out of 15 patients without significant stenosis. As already discussed in a previous work (*27*), there is a major difference between this and other studies of exercise myocardial scintigraphy: since our purpose was to detect significant coronary stenosis by revealing both myocardial infarction and stress-induced ischemia, we include all abnormalities

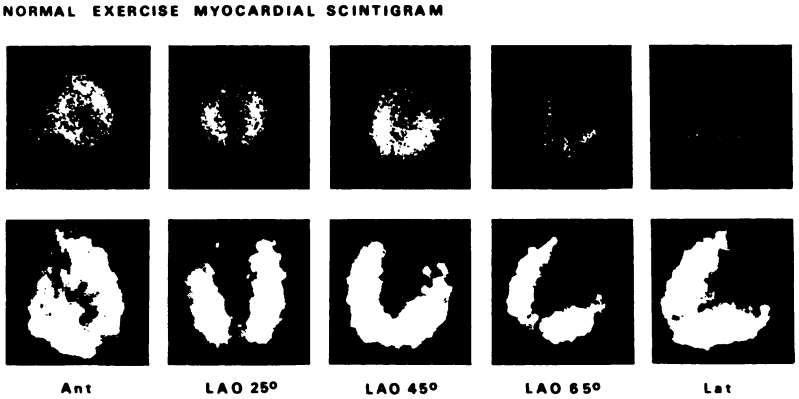

FIG. 2. Myocardial scintigrams after exercise of normal subject in anterior (Ant), 25°, 45°, and 65° left anterior oblique (LAO), and left lateral (Lat) views. Top panels: analog images. Lower panels: with contrast enhancement by 50% cut-off after nine-point smoothing. Note apical hypoactivity in several views.

in the analysis, not only new perfusion defects that were not evident on rest scintigrams. This variation in method may account in part for our very high sensitivity as compared with those of other laboratories (*23,24*). Other factors of possible significance are (A) a longer time between injection and the end of exercise, (B) collection of five images, (C) use of a 140-keV converging collimator to provide higher resolution for the 69–83-keV x-ray (*20,29*), and (D) the selection of our patients, since subjects studied for consideration of surgery in Europe have more severe disease than in the United States.

Moreover, it must be kept in mind that specificity is a function of patient population; hence a larger incidence of myocardiopathy could lead to a higher rate of false-positive results.

Prediction of multiple-vessel disease by exercise myocardial scintigraphy was correct in 88% of our cases, but half of the patients thought to have single-vessel disease by scintigraphic analysis actually had multiple-vessel disease. In fact, segmental analysis of exercise myocardial scintigrams allows identification of the most compromised myocardial territories. This functional aspect may be of practical importance for coronary bypass surgery. Discrepancies between exercise scintigraphy and coronary arteriography might yield interesting information on the availability of collateral blood flow under stress conditions. Our method appears as a promising noninvasive technique for assessment of regional myocardial perfusion in patients with suspected coronary-artery disease.

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FOOTNOTES

* Pho/Gamma III, Searle Radiographics, Des Plaines, Ill.
† Simis III, Informatek, Orsay, France.

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