

# Technetium-99m-Tetrofosmin Regional Myocardial Uptake at Rest: Relation to Severity of Coronary Artery Stenosis in Previous Myocardial Infarction

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The aim of this study was to assess the potential role of  $^{99m}\text{Tc}$ -tetrofosmin cardiac tomography in detecting totally occluded or severely stenosed coronary arteries. **Methods:** Thirty-three patients (32 men, 1 woman; mean age,  $52 \pm 9$  yr) with chronic coronary artery disease (CAD) and left ventricular dysfunction (ejection fraction  $40\% \pm 12\%$ ) underwent resting  $^{99m}\text{Tc}$ -tetrofosmin SPECT and coronary arteriography within 2 wk. Regional distribution of  $^{99m}\text{Tc}$ -tetrofosmin activity was compared with the coronary anatomy. Tracer uptake was quantitatively analyzed in 22 segments for each patient. The activity in each segment was expressed as a percent of the peak activity. **Results:** A significant relationship between the degree of coronary artery stenosis and  $^{99m}\text{Tc}$ -tetrofosmin uptake was observed ( $\rho = -0.64$ ,  $p < 0.001$ ). Technetium-99m-tetrofosmin uptake was lower ( $p < 0.001$ ) in segments with 100% coronary occlusion with poor collateral flow ( $53\% \pm 17\%$ ) compared to segments supplied by a vessel with 50%–99% coronary stenosis ( $75\% \pm 20\%$ ) or a normal noncritically stenosed artery ( $85\% \pm 10\%$ ). Furthermore,  $^{99m}\text{Tc}$ -tetrofosmin uptake was lower ( $p < 0.01$ ) in segments with 100% coronary occlusion with poor ( $53\% \pm 17\%$ ) compared to those with good collateral flow ( $70\% \pm 20\%$ ). **Conclusion:** These results demonstrate that quantitative analysis of resting  $^{99m}\text{Tc}$ -tetrofosmin regional uptake detects the majority of segments supplied by occluded coronary arteries with poor collateral flow and suggest that this tracer may be helpful in the diagnosis of acute myocardial infarction.

**Key Words:** technetium-99m-tetrofosmin; myocardial perfusion; coronary artery disease

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**T**hallium-201 cardiac imaging has been widely used to evaluate myocardial perfusion and tissue viability in pa-

tients with coronary artery disease (CAD) (1–3). Although its value as a diagnostic and prognostic test has been well established,  $^{201}\text{Tl}$  is not ideal for imaging purposes due to its low-energy photons and its long half-life (4). To circumvent these limitations and to obtain better image quality and radiation dosimetry than those with thallium scintigraphy, several  $^{99m}\text{Tc}$ -labeled myocardial agents have been recently proposed for myocardial studies (4,5). In particular,  $^{99m}\text{Tc}$ -methoxy isobutyl isonitrile (MIBI) shows clear advantages over  $^{201}\text{Tl}$  such as onsite availability, shorter acquisition times and higher quality images (4), and has been proposed as an alternative to thallium in many of its clinical applications (6). Dilsizian et al. (7) demonstrated that  $^{99m}\text{Tc}$ -MIBI cardiac imaging detects coronary occlusion with poor collateral flow and suggested that this method may be useful in assessing patients with acute myocardial infarction. This agent must be heated, however, for  $^{99m}\text{Tc}$  labeling, and high initial hepatic activity with relatively slow clearance necessitates a delay of approximately 1 hr after administration before imaging.

Technetium-99m-tetrofosmin, on the other hand, has been proposed for myocardial imaging (8,9). Preparation of this agent does not require heating but only a 15-min incubation at room temperature (10). Previous studies demonstrated that  $^{99m}\text{Tc}$ -tetrofosmin is rapidly cleared from the blood and accumulates in the myocardium, skeletal muscle, liver, spleen and kidneys in proportion to regional perfusion (10–12) after intravenous administration. In addition, myocardial clearance of this compound is relatively slow, while background clearance is rapid (12). Clinically insignificant redistribution associated with possible early imaging (13,14) make this agent particularly attractive for detecting regional perfusion abnormalities in patients with acute ischemic syndromes.

To evaluate the potential role of  $^{99m}\text{Tc}$ -tetrofosmin cardiac tomography in detecting totally occluded or severely stenosed coronary arteries, we compared the regional dis-

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**TABLE 1**  
Clinical Data and Angiographic Results

Patient no.	Sex	Age (yr)	Site of previous myocardial infarction	Degree of stenosis (%)		
				LAD	LCx	PDA
1	M	42	Anteroseptal	80	800	800
2	M	44	Inferior, Anterior	75	100*	30
3	M	51	Anteroseptal	80	100*	0
4	M	54	Anterior	80	0	0
5	M	53	Septal	95	50	0
6	M	55	Inferior	0	100*	100
7	M	49	Anteroseptal	100*	80	80
8	M	51	Inferolateral	50	100	0
9	F	64	Septal	100*	0	100*
10	M	56	Anterior	100*	0	0
11	M	43	Inferolateral	70	100*	0
12	M	64	Anterior	100*	0	100*
13	M	41	Anterior	100*	0	0
14	M	55	Inferior	50	0	100
15	M	68	Inferior	60	0	100
16	M	57	Anteroseptal	99	0	0
17	M	43	Inferior	0	0	99
18	M	25	Inferolateral	0	0	70
19	M	59	Lateral	100	0	0
20	M	46	Anterior	60	0	0
21	M	52	Anteroseptal	100	60	0
22	M	60	Anteroseptal	80	0	0
23	M	48	Anterior	60	0	0
24	M	65	Anterior	100	50	70
25	M	57	Septal	100*	99	90
26	M	60	Anteroseptal	75	0	0
27	M	55	Inferior	0	40	100*
28	M	53	Inferolateral	60	100*	100*
29	M	53	Inferolateral	60	70	0
30	M	49	Inferolateral	50	70	75
31	M	45	Inferior	0	0	100
32	M	61	Inferolateral	0	90	100*
33	M	50	Anterior	85	0	0

\*Good collateral flow.

LAD = left anterior descending artery; LCx = left circumflex artery; PDA = posterior descending artery.

tribution of resting <sup>99m</sup>Tc-tetrofosmin with coronary anatomy in patients with stable chronic CAD and previous myocardial infarction who underwent coronary arteriography.

## MATERIALS AND METHODS

### Patients

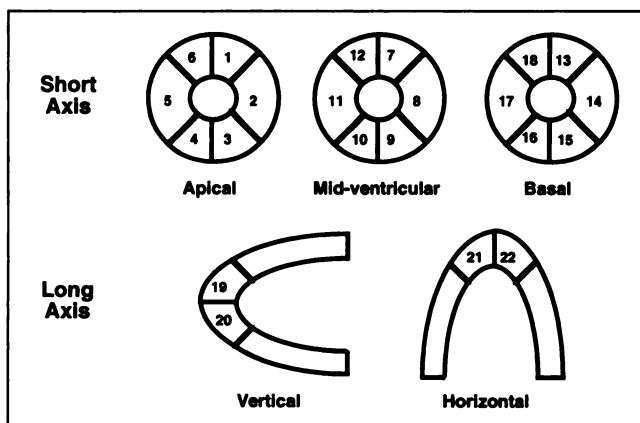
Thirty-three consecutive patients (32 men and 1 woman; mean age, 52 ± 9 yr) with previous myocardial infarction and angiographically proven CAD were studied (Table 1). The mean left ventricular ejection fraction by resting equilibrium radionuclide angiography was 40% ± 12%. All patients had previous clinically and electrocardiographically documented myocardial infarction. No patient, however, had acute myocardial infarction or unstable angina within 2 mo of the study. Four of the patients were revascularized in the acute stage of myocardial infarction. Radionuclide studies were performed after withdrawal of all medications. All patients gave informed consent as part of the protocol approved by the Institutional Clinical Research Subpanel on Human Studies of our institution.

### Coronary Angiography

A percutaneous transfemoral approach was employed using Seldinger's technique within 2 wk of the radionuclide studies. Each artery was filmed in 4–6 projections, including angulated views in the sagittal plane. All images were recorded on 35-mm film at 50 frames/sec, reviewed on a Tagarno projector and interpreted by a consensus of three independent observers unaware of the clinical condition of the patients. Stenoses of coronary vessels were coded according to American Heart Association criteria (15). Significant stenoses were defined as a reduction ≥50% in the luminal diameter of at least one of the three major epicardial coronary vessels. The cineruns were continued in order to record images of collaterals which filled late, after the visualization of the major coronary vessel. Arteries with partial or complete filling of the epicardial segment via collaterals were defined as having an efficient collateral circulation.

### Technetium-99m-Tetrofosmin Preparation and Imaging

Technetium-99m-tetrofosmin was prepared from a freeze-dried kit (Myoview, Amersham International, Buckinghamshire, UK) (12) by reconstitution with approximately 6 ml of a sterile sodium



**FIGURE 1.** Diagram of the standard segmentation scheme used for regional quantitative analysis of resting <sup>99m</sup>Tc-tetrofosmin cardiac tomography.

perchnetate solution containing 740–925 MBq. All patients received an intravenous injection of <sup>99m</sup>Tc-tetrofosmin (740 MBq) under control conditions. After an overnight fast, all patients were instructed to consume a light fatty meal or a glass of milk after tracer injection and before imaging. About 30 min after <sup>99m</sup>Tc-tetrofosmin administration, resting cardiac SPECT was performed.

### SPECT Acquisition and Processing

SPECT imaging was performed using a rotating large field of view gamma camera (Elsint SP4HR, Haifa, Israel) equipped with a low-energy, all-purpose, parallel-hole collimator and connected with a dedicated computer system. Thirty-two projections (40 sec/projection) were obtained over a semicircular 180° arc, which extended from the 30° right anterior oblique to the left posterior oblique position. A 20% symmetric energy window centered on the 140-keV peak was used. All projection images were stored on magnetic disc by means of a 64 × 64 word matrix. Each projection image was corrected for nonuniformity, with a 120-million count image obtained weekly from a uniform <sup>57</sup>Co flood source. The mechanical center of rotation was determined from the projection data to align the detector data with respect to the reconstruction matrix (16). The raw data were initially smoothed with a nine-point weighted average algorithm. Filtered backprojection was then performed with a low-resolution Butterworth filter with a cutoff frequency of 0.5 cycles/pixel, order 5, to reconstruct transverse axial tomogram of 6.2 mm thickness per slice which encompassed the entire heart. Sagittal and oblique tomograms parallel to the long and short axis of the left ventricle were then extracted from the filtered transaxial tomogram by performing a coordinate transformation with the appropriate interpolation (17). No attenuation or scatter correction was used.

### Data Analysis

For each study, tomograms were divided into 22 segments (Fig. 1). Each segment was assigned to one of the major vascular territories. The anterior descending artery territory included the anterior wall (segments 1, 6, 7, 12, 13 and 18), septum (segments 5, 11 and 17) and apical wall (segments 19, 21 and 22). The right coronary artery was assigned the inferior wall (segments 3, 4, 9, 10, 15 and 16). The left circumflex artery was assigned the lateral wall (segments 2, 8 and 14). The inferoapical wall (segment 20) was assigned to the right coronary artery if the inferior wall in the apical portion of the short-axis view (segments 3 and 4) showed a

perfusion defect and the anteroapical wall (segment 19) was normal.

Regional <sup>99m</sup>Tc-tetrofosmin uptake was quantitatively analyzed as previously described (18). Briefly, in each tomogram, the myocardial region with the maximum counts was used as the normal reference region. Tracer uptake in all other myocardial segments were then expressed as a percentage of the activity measured in the reference region. The mean value of <sup>99m</sup>Tc-tetrofosmin uptake obtained in segments corresponding to one individual artery was assigned to each vascular territory. Segments having less than 50% of the maximal uptake were categorized as Grade 1; segments with an uptake between 50% and 70% were categorized as Grade 2; segments with an uptake over 70% were categorized as Grade 3. Thus, each segment was categorized as having (1) severely reduced uptake, (2) moderately reduced uptake or (3) normal uptake.

### Classification of Myocardial Segments

Myocardial segments were grouped on the basis of the coronary anatomy in the corresponding vascular territories into three groups: Group 1 (total coronary occlusion, 100% of stenosis); Group 2 (significant coronary stenosis, from 50% to 99%); and Group 3 (nonsignificant coronary stenosis, <50%, or normal coronary vessels). Furthermore, myocardial segments with total coronary occlusion (Group 1) were subgrouped in Group 1A and Group 1B according to the absence or the presence of good collateral vessels, respectively.

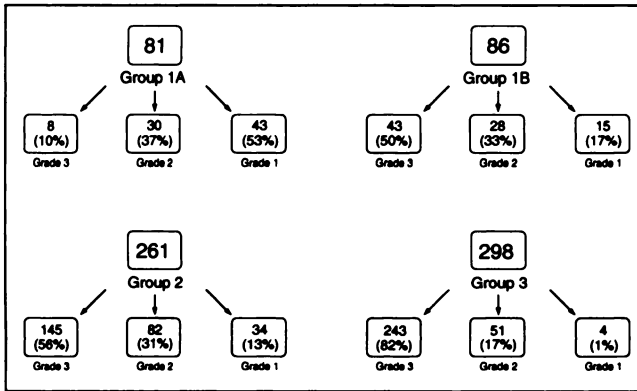
### Statistical Analysis

Data are expressed as mean ± 1 s.d. Differences in the mean values were assessed by Student's t-test for unpaired data, with Bonferroni's correction for multiple groups comparison. Each group of values was compared with all the others. Chi-square analysis was used to assess differences between proportions. Spearman correlation coefficient ( $\rho$ ) was used to assess the relationship between <sup>99m</sup>Tc-tetrofosmin uptake and the degree of coronary narrowing. Probability values <0.05 were considered significant.

## RESULTS

### Coronary Angiography

Table 1 illustrates the results of coronary angiography in all patients. In five patients, significant stenosis of all three major coronary vessels was present. Thirteen patients had significant stenosis of two major coronary arteries and only one coronary vessel was significantly stenosed in 15 patients. Sixteen patients had at least one totally occluded epicardial coronary artery and four patients showed two totally occluded coronary arteries. In nine patients with one totally occluded coronary vessel, there was an efficient collateral circulation. In the four patients with two totally occluded coronary vessels, there was an efficient collateral circulation at least in one of these occluded arteries. Of the 726 myocardial segments analyzed in the 33 patients, 167 (23%) were supplied by totally occluded coronary vessels (Group 1), 261 (36%) were supplied by coronary vessels with significant stenoses (Group 2) and 298 (41%) were supplied by normal or nonsignificantly stenosed coronary vessels (Group 3). Of the 167 myocardial segments with total coronary occlusion (Group 1), 81 (49%) were supplied by totally occluded coronary vessels with poor collateral



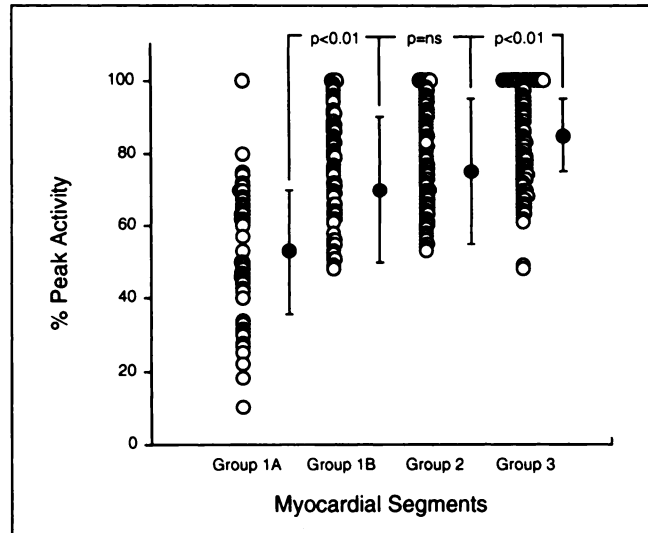
**FIGURE 2.** Nomograms of resting  $^{99m}\text{Tc}$ -tetrofosmin cardiac imaging findings in each group of myocardial segments subgrouped on the basis of percent coronary stenosis. (Grade 3 = normal uptake (uptake over 70%); Grade 2 = moderately reduced uptake (uptake between 50 and 70%); Grade 1 = severely reduced uptake (uptake less than 50%).)

flow (Group 1A) and 86 (51%) were supplied by totally occluded coronary vessels with good flow (Group 1B). In particular, myocardial segments of Group 1A were present in eight patients, while myocardial segments of Group 1B were present in 12 patients.

#### Regional Technetium-99m-Tetrofosmin Uptake

A significant relationship was observed between rest-injected  $^{99m}\text{Tc}$ -tetrofosmin uptake and the degree of coronary artery stenosis  $r = -0.64$ ;  $p < 0.001$ ). Technetium-99m-tetrofosmin cardiac imaging findings in all groups of myocardial segments are shown in Figure 2. In Group 1A (100% coronary occlusion with poor collateral flow), 43 (53%) segments showed a severe reduction (Grade 1) of  $^{99m}\text{Tc}$ -tetrofosmin uptake, 30 (37%) showed a moderate reduction (Grade 2) of  $^{99m}\text{Tc}$ -tetrofosmin uptake and 8 (10%) showed normal (Grade 3)  $^{99m}\text{Tc}$ -tetrofosmin uptake. In Group 1B (100% coronary occlusion with good collateral flow), 15 (17%) segments showed a severe reduction (Grade 1) of  $^{99m}\text{Tc}$ -tetrofosmin uptake, 28 (33%) showed a moderate reduction (Grade 2) of  $^{99m}\text{Tc}$ -tetrofosmin uptake and 43 (50%) showed normal (Grade 3)  $^{99m}\text{Tc}$ -tetrofosmin uptake ( $p < 0.01$  versus Group 1A). In Group 2 (50%-99% coronary stenosis), 34 (13%) segments showed a severe reduction (Grade 1) of  $^{99m}\text{Tc}$ -tetrofosmin uptake, 82 (31%) showed a moderate reduction (Grade 2) of  $^{99m}\text{Tc}$ -tetrofosmin uptake and 145 (56%) showed normal (Grade 3)  $^{99m}\text{Tc}$ -tetrofosmin uptake ( $p < 0.001$  versus Group 1A and  $p = \text{ns}$  versus Group 1B). Finally, in Group 3 (normal coronary artery or nonsignificant stenosis), 4 (1%) segments had severe reduction (Grade 1) of  $^{99m}\text{Tc}$ -tetrofosmin uptake, 51 (17%) had moderate reduction (Grade 2) of  $^{99m}\text{Tc}$ -tetrofosmin uptake and 243 (82%) had normal (Grade 3)  $^{99m}\text{Tc}$ -tetrofosmin uptake ( $p < 0.001$  versus Groups 1A, 1B and 2).

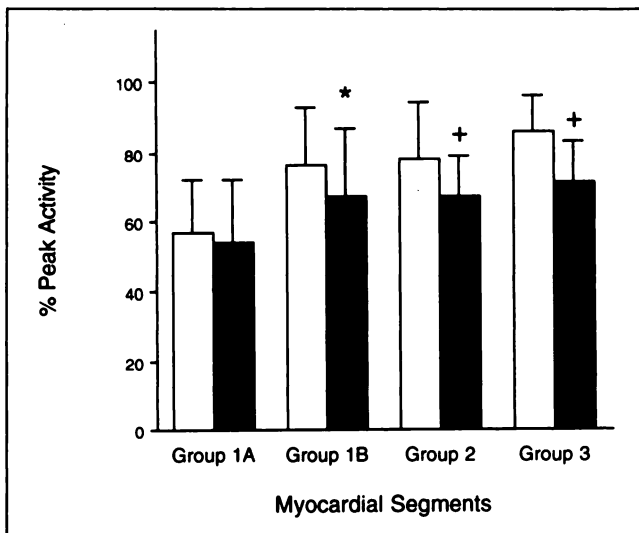
Figure 3 shows individual data points and mean value of  $^{99m}\text{Tc}$ -tetrofosmin uptake in each group of myocardial segments expressed as a percent of peak activity. The uptake



**FIGURE 3.** Individual data points (open circles) and mean values (closed circles) of resting  $^{99m}\text{Tc}$ -tetrofosmin uptake (expressed as a percent of peak activity) in each group of myocardial segments subgrouped on the basis of percentage of coronary stenosis.

was significantly lower ( $p < 0.001$ ) in segments supplied by a coronary artery with 100% occlusion and poor collateral flow (Group 1A) ( $53\% \pm 17\%$ ) compared to those supplied by a coronary vessel with 50%-99% stenosis (Group 2) ( $75\% \pm 20\%$ ) or a normal noncritically stenosed coronary artery (Group 3) ( $85\% \pm 10\%$ ). Furthermore,  $^{99m}\text{Tc}$ -tetrofosmin uptake was significantly lower ( $p < 0.01$ ) in segments with 100% coronary artery occlusion with poor collateral flow compared to those with 100% coronary artery occlusion with good collateral flow (Group 1B) ( $70\% \pm 20\%$ ). Finally, tracer uptake was not significantly different between segments supplied by a coronary vessel with 50%-99% stenosis and those with 100% stenosis and good collateral circulation.

In the 298 segments supplied by a normal or noncritically stenosed coronary artery,  $^{99m}\text{Tc}$ -tetrofosmin uptake ranged from 48%-100% of peak activity (mean  $85\% \pm 10\%$ ). The large majority (82%) of these segments, however, had  $^{99m}\text{Tc}$ -tetrofosmin uptake of more than 70%, and tracer uptake was severely reduced (i.e.,  $< 50\%$ ) in only 4 (1%) segments. In the 81 segments supplied by an occluded coronary artery with poor collateral flow,  $^{99m}\text{Tc}$ -tetrofosmin uptake ranged from 10%-100% of peak activity (mean  $53\% \pm 17\%$ ). In 90% of these segments  $^{99m}\text{Tc}$ -tetrofosmin uptake was either severely ( $n = 43$ ) or moderately ( $n = 30$ ) reduced, whereas only 8 (10%) segments showed tracer uptake of more than 70% (Fig. 3). There was considerable overlap of values in normal territories when compared with territories supplied by a 50%-99% coronary artery stenosis and territories with 100% coronary occlusion and good collateral flow (Fig. 3). By utilizing a lower limit of normal of 65% (mean 85% for normal - 2 standard deviations), however,  $^{99m}\text{Tc}$ -tetrofosmin correctly detected 64 (79%) of 81 segments with occluded vessels with poor collateral



**FIGURE 4.** Regional resting <sup>99m</sup>Tc-tetrofosmin uptake (expressed as a percent of peak activity) in myocardial segments related to noninfarcted territories (open bars) and myocardial segments related to infarcted territories (closed bars). \* $p < 0.05$  and  $p < 0.01$  versus segments related to noninfarcted territories, respectively.

flow and correctly assigned 281 (94%) of 298 segments supplied by vessels with noncritical stenosis.

A separate analysis of <sup>99m</sup>Tc-tetrofosmin uptake was performed dividing the myocardial segments related to noninfarcted territories ( $n = 447$ ) from those related to infarcted territories ( $n = 239$ ) (Fig. 4). In noninfarcted territories, <sup>99m</sup>Tc-tetrofosmin uptake was significantly lower ( $p < 0.001$ ) in segments supplied by a coronary artery with 100% occlusion and poor collateral flow ( $n = 18$ ) ( $57\% \pm 15\%$ ) compared to segments supplied by a coronary vessel with 50%–99% stenosis ( $n = 112$ ) ( $78\% \pm 16\%$ ) or a normal noncritically stenosed coronary artery ( $n = 286$ ) ( $86\% \pm 10\%$ ). Furthermore, <sup>99m</sup>Tc-tetrofosmin uptake was significantly lower ( $p < 0.001$ ) in segments with 100% coronary occlusion with poor collateral flow compared to those with 100% coronary occlusion with good collateral flow ( $n = 31$ ) ( $76\% \pm 17\%$ ). Tracer uptake was not significantly different in segments supplied by a coronary vessel with 50%–99% stenosis and segments with 100% coronary stenosis and good collateral circulation (Fig. 4). In infarcted territories, <sup>99m</sup>Tc-tetrofosmin uptake was significantly lower ( $p < 0.05$ ) in segments supplied by a coronary artery with 100% occlusion and poor collateral flow ( $n = 63$ ) ( $54\% \pm 18\%$ ) compared to segments supplied by a coronary vessel with 50%–99% stenosis ( $n = 149$ ) ( $67\% \pm 12\%$ ) or a normal noncritically stenosed coronary artery ( $n = 12$ ) ( $71\% \pm 12\%$ ). In addition, <sup>99m</sup>Tc-tetrofosmin uptake was significantly lower ( $p < 0.01$ ) in segments with 100% coronary occlusion with poor collateral flow compared to those with 100% coronary occlusion with good collateral flow ( $n = 55$ ) ( $67\% \pm 20\%$ ). Finally, tracer uptake was not significantly different in segments supplied by a noncritically stenosed coronary artery, segments with

50%–99% coronary stenosis and segments with 100% stenosis and good collateral flow (Fig. 4).

## DISCUSSION

Technetium-99m-tetrofosmin is a myocardial perfusion imaging agent with potential advantages over other available myocardial tracers. A new kit formulation yields a preparation containing the lipophilic, cationic, diphosphine <sup>99m</sup>Tc-tetrofosmin on reconstitution at room temperature with <sup>99m</sup>Tc-pertechnetate, leading to faster preparation (12). The hepatic uptake is acceptably low, even at rest, and hepatic activity further declines over time (13). Early imaging can be performed (within 15–30 min), reducing the waiting time for patients as well as total study time (8,9). Although these methodological observations are less important than biological characteristics, they are important in clinical practice, especially in patients with acute ischemic syndromes. Dilsizian et al. recently demonstrated that quantitative analysis of rest <sup>99m</sup>Tc-MIBI uptake on planar cardiac imaging detects coronary occlusion with poor collateral circulation and suggested that this agent may be useful in the diagnosis of myocardial infarction (7). MIBI require heating, however, for <sup>99m</sup>Tc-labeling and high initial hepatic activity with relatively slow clearance necessitates a delay of approximately 1 hr after administration before imaging.

In this study, we compared the regional myocardial distribution of resting <sup>99m</sup>Tc-tetrofosmin with coronary anatomy in patients with stable chronic CAD and previous myocardial infarction who underwent coronary arteriography. Our data demonstrate that <sup>99m</sup>Tc-tetrofosmin uptake after rest injection is inversely related to the degree of coronary artery stenosis in such patients. Our results also suggest that quantitative analysis of resting <sup>99m</sup>Tc-tetrofosmin cardiac tomography can differentiate territories supplied by a totally occluded coronary artery with poor collateral flow from those supplied by normal or noncritically stenosed coronary vessels. Regional <sup>99m</sup>Tc-tetrofosmin uptake was significantly lower in myocardial segments supplied by a coronary artery with 100% occlusion and poor collateral flow compared to segments supplied by a coronary vessel with 50%–99% coronary stenosis or a normal noncritically stenosed coronary artery. In particular, in the majority (82%) of myocardial segments subtended by an artery with noncritical stenosis <sup>99m</sup>Tc-tetrofosmin uptake was higher than 70% of peak activity, while tracer uptake was severely reduced (<50% of peak activity) in only a few segments (1%). Conversely, in the majority (90%) of myocardial segments supplied by an occluded coronary artery with poor collateral flow, <sup>99m</sup>Tc-tetrofosmin uptake was reduced. Although there was considerable overlap of values in normal territories when compared with territories supplied by nonoccluded coronary arteries, by using a lower normal limit of 65%, <sup>99m</sup>Tc-tetrofosmin correctly detected 79% of segments with occluded vessels with poor

collateral flow and correctly assigned 94% of segments supplied by vessels with noncritical stenosis.

These results are in agreement with those of previous studies performed in patients with CAD using resting thallium and  $^{99m}\text{Tc}$ -MIBI cardiac imaging (7,19). In particular, Dilsizian et al. (7) demonstrated that rest  $^{99m}\text{Tc}$ -MIBI myocardial scintigraphy detects coronary occlusion with poor collateral flow and suggested that this method may be useful in assessing patients with acute myocardial infarction. Maurea et al. (19) showed that both rest-injected  $^{201}\text{Tl}$  and resting  $^{99m}\text{Tc}$ -MIBI uptake reflect the severity of coronary artery stenosis in patients with CAD; however, these previous studies were performed using planar cardiac imaging. In the present study, we used a tomographic approach to acquire and analyze rest  $^{99m}\text{Tc}$ -tetrafosmin images. SPECT minimized the problem of overlap of noncardiac structures and may improve the detection of abnormal myocardial segments. Furthermore, it may also enhance the detection of disease in the individual vascular territories and improve the correlation between tracer uptake and degree of stenosis in nonoccluded coronary arteries.

Of the myocardial segments with a severe reduction of  $^{99m}\text{Tc}$ -tetrafosmin, 61% were supplied by an artery with total occlusion and 35% were supplied by a vessel with significant but subtotal stenosis. A possible explanation for the occurrence of subtotal stenosis in a segment with a severe reduction of  $^{99m}\text{Tc}$ -tetrafosmin uptake is resumption of anterograde flow as a result of recanalization after myocardial infarction (7,20). Patients who had successfully revascularized in the acute phase of myocardial infarction may still have severe perfusion abnormalities when cellular necrosis had been completed by the time of revascularization. In this situation, regional perfusion assessed by  $^{99m}\text{Tc}$ -tetrafosmin uptake may not be closely related to the severity of stenosis on major coronary arteries. Only four of our patients, however, were revascularized in the acute stage of myocardial infarction.

Another interesting finding of this study is that regional  $^{99m}\text{Tc}$ -tetrafosmin uptake was significantly lower in myocardial segments supplied by an artery with total occlusion with poor collateral flow compared to those subtended by a vessel totally occluded with good collateral flow. Previous studies demonstrated that an efficient collateral circulation was associated with the presence of viable myocardium, but not with necrotic tissue in patients with acute or chronic CAD (21-23). Sabia et al. (22) suggested that the myocardium remains viable for a prolonged period in many patients with acute myocardial infarction and an occluded infarct-related artery, and tissue viability appears to be associated with the presence of collateral blood flow within the infarcted bed. In particular, these authors demonstrated that there was an association between improvement in regional function within an infarct bed after late reperfusion and the extent of collateral blood flow to that bed before reperfusion (22). These observations and the results of the present study may have important clinical implica-

tions in the evaluation of patients with ischemic left ventricular dysfunction, particularly when myocardial viability is in question. In such patients, a severe reduction of coronary blood flow frequently occurs under resting conditions, and thus quantitative analysis of resting  $^{99m}\text{Tc}$ -tetrafosmin uptake may be particularly useful in identifying myocardial territories supplied by an occluded artery with good collateral flow which might show functional recovery after revascularization.

There are some limitations in the present study. The first limit could be the lack of computer quantitation of coronary arteriography (24,25). There might be discordance, however, between physiology and anatomy when using quantitative coronary arteriography (26). Although quantitative coronary arteriography may improve the correlation between the percent of coronary artery stenosis and flow in territories with critical but not total narrowing, this criticism does not apply to totally occluded coronary vessels. Thus, as previously suggested (7), conclusions in this particular setting are valid even in the absence of quantitative coronary arteriography. Second, the assignment of each myocardial segment to one of the three major coronary arteries was arbitrary and therefore could be incompletely accurate. Although the use of tomographic, rather than planar imaging techniques, allows the matching of regions more precisely, a certain margin of error was unavoidable and the actual anatomic relation between the radionuclide data and coronary angiography may be imprecise. This methodology, however, has already been widely used in previous studies (7,18,19,27,28). Because our patient population was small, similar studies in a larger series are required to confirm our results.

## CONCLUSION

This study demonstrated that regional distribution of resting  $^{99m}\text{Tc}$ -tetrafosmin is significantly related to the percent of coronary artery narrowing. In addition, rest-injected  $^{99m}\text{Tc}$ -tetrafosmin cardiac imaging allows identification of the majority of myocardial segments supplied by occluded coronary arteries with poor collateral flow. These findings may have important clinical implications, especially in the evaluation of patients with suspected myocardial infarction.

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## REFERENCES

1. Pohost GM, Zir LM, Moore RM, et al. Differentiation of transiently ischemic from infarcted myocardium by serial imaging after a single dose of thallium-201. *Circulation* 1979;55:294-302.
2. Gibson RS, Watson DD, Craddock GB, et al. Prediction of cardiac events after uncomplicated myocardial infarction: a prospective study comparing pre-discharge exercise thallium-201 scintigraphy and coronary angiography. *Circulation* 1983;68:321-336.
3. Kottler TS, Diamond GA. Exercise thallium-201 scintigraphy in the diag-

- nosis and prognosis of coronary artery disease. *Ann Intern Med* 1990;113:684-702.
4. Berman DS. Technetium-99m myocardial perfusion imaging agents and their relations to thallium-201. *Am J Cardiol* 1990;66:1E-4E.
  5. Leppo J, De Puey G, Johnson LL. A review of cardiac imaging with sestamibi and teboroxime. *J Nucl Med* 1991;32:2012-2022.
  6. Maddahi J, Kiat H, Berman DS. Myocardial perfusion imaging with technetium-99m-labeled agents. *Am J Cardiol* 1991;67:27D-34D.
  7. Dilsizian V, Rocco TP, Strauss HW, Boucher CA. Technetium-99m isonitrite myocardial uptake at rest. I. Relation to severity of coronary artery stenosis. *J Am Coll Cardiol* 1989;14:1673-1677.
  8. Rigo P, Leclercq B, Itti R, Lahiri A, Braat S. Technetium-99m-tetrofosmin myocardial imaging: a comparison with thallium-201 and angiography. *J Nucl Med* 1994;35:587-593.
  9. Tamaki N, Takahashi N, Kawamoto M, et al. Myocardial tomography using technetium-99m-tetrofosmin to evaluate coronary artery disease. *J Nucl Med* 1994;35:594-600.
  10. Kelly JD, Forster AM, Higley B, et al. Technetium-99m-tetrofosmin as a new radiopharmaceutical for myocardial perfusion imaging. *J Nucl Med* 1993;34:222-227.
  11. Sinusas AJ, Shi QX, Saltzberg MT, et al. Technetium-99m-tetrofosmin to assess myocardial blood flow: experimental validation in an intact canine model of ischemia. *J Nucl Med* 1994;35:664-671.
  12. Higley B, Smith FW, Smith T, et al. Technetium-99m-1,2-bis[bis(2-ethoxyethyl)phosphine]ethane: human biodistribution, dosimetry and safety of a new myocardial perfusion imaging agent. *J Nucl Med* 1993;34:30-38.
  13. Jain D, Wackers FJTh, Mattera J, McMahon M, Sinusas AJ, Zaret BL. Biokinetics of technetium-99m-tetrofosmin: myocardial perfusion imaging agent. Implications for a one-day imaging protocol. *J Nucl Med* 1993;34:1254-1259.
  14. Sridhara BS, Braat S, Rigo P, Itti R, Cload P, Lahiri A. Comparison of myocardial perfusion imaging with <sup>99m</sup>Tc-tetrofosmin versus <sup>201</sup>Tl in coronary artery disease. *Am J Cardiol* 1993;72:1015-1019.
  15. Austen WG, Edwards JE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease: report of the ad hoc committee for grading of coronary artery disease, Council on Cardiovascular Surgery, American Heart Association. *Circulation* 1975;51:7-34.
  16. Kiat H, Maddahi J, Roy LT, Friedman J, Resser K, Berman DS. Comparison of technetium-99m-methoxy isobutyl isonitrite with thallium-201 for evaluation of coronary artery disease by planar and tomographic methods. *Am Heart J* 1989;117:1-11.
  17. Borrello JA, Clinthorne NH, Rogers WL, Thrall JH, Keyes JW. Oblique-angle tomography: a reconstructing algorithm for transaxial tomographic data. *J Nucl Med* 1981;22:471-473.
  18. Cuocolo A, Soricelli A, Pace L, et al. Adenosine technetium-99m-methoxy isobutyl isonitrite myocardial tomography in patients with coronary artery disease: comparison with exercise. *J Nucl Med* 1994;35:1110-1115.
  19. Maurea S, Cuocolo A, Pace L, et al. Rest-injected thallium-201 redistribution and resting technetium-99m methoxyisobutylisonitrite uptake in coronary artery disease: relation to the severity of coronary artery stenosis. *Eur J Nucl Med* 1993;20:502-510.
  20. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. *N Engl J Med* 1980;303:897-902.
  21. Fujita M, Ohno A, Wada O, et al. Collateral circulation as a marker of the presence of viable myocardium in patients with recent myocardial infarction. *Am Heart J* 1991;122:409-414.
  22. Sabia PJ, Powers ER, Ragosta M, Sarembock IJ, Burwell LR, Kaul S. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. *N Engl J Med* 1992;327:1825-1831.
  23. Bartenstein P, Schober O, Hasfeld M, Schafers M, Matheia P, Breithardt G. Thallium-201 single photon emission tomography of myocardium: additional information in reinjection studies is dependent on collateral circulation. *Eur J Nucl Med* 1992;19:790-795.
  24. Gould KL, Kelley KO. Experimental validation of quantitative coronary arteriography for determining pressure-flow characteristics of coronary stenosis. *Circulation* 1982;66:930-937.
  25. Marcus ML, Skorton DJ, Johnson MR, et al. Visual estimates of percent diameter coronary stenosis: "a battered gold standard." *J Am Coll Cardiol* 1988;11:882-888.
  26. Marcus ML, Harrison DG, White CH, et al. Assessing the physiological significance of coronary obstruction in patients: importance of diffuse, undetected atherosclerosis. *Prog Cardiovasc Dis* 1988;31:39-56.
  27. Rocco TP, Dilsizian V, McKusick KA, Fishman AJ, Boucher CA, Strauss HW. Comparison of thallium redistribution with rest "re-injection" imaging for the detection of viable myocardium. *Am J Cardiol* 1990;66:158-163.
  28. Schelbert HR. Myocardial ischemia and clinical applications of positron emission tomography. *Am J Cardiol* 1989;64:46E-53E.