Significance of Fill-In After Thallium-201 Reinjection Following Delayed Imaging: Comparison with Regional Wall Motion and Angiographic Findings

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To identify reversible defects, reinjection of a small amount of thallium-201 (^{201}Tl) following 3-hr delayed imaging was performed in 60 patients with coronary artery disease who had perfusion abnormalities on their post-exercise ^{201}Tl images. Thallium-201 uptake was visually scored and judged as normal (Group I), reversible defect (Group II), new fill-in after reinjection (Group IIIa) and no fill-in even after reinjection (Group IIIb). New fill-in after reinjection was observed in 27 segments of the 85 segments (32%), showing persistent defect on the stress and delayed images. The wall motion in Group IIIa was worse than Group II but better than Group IIIb. Group IIIa showed Q-wave on ECG more often (69%) than Group II (27%) ($p < 0.01$), but less often than Group IIIb (85%) ($p < 0.05$). These data indicate that the reinjection ^{201}Tl imaging often identifies new fill-in in the areas of no redistribution on the delayed images and it may hold promise for assessing tissue viability which the conventional imaging may underestimate.

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Thallium-201 (^{201}Tl) myocardial imaging has been widely used to detect coronary artery disease and to characterize the coronary lesions. The unique property of the tracer to redistribute in the myocardium has been applied to differentiate reversible myocardial ischemia from scar (*1,2*). For this purpose, immediate post-exercise ^{201}Tl images are compared with 3- to 4-hr delayed images taken at rest. The post-exercise perfusion abnormalities, which improve with its uptake (redistribution), represent ischemia, whereas the initial perfusion abnormalities which persist on the delayed images are considered as myocardial scar (*1–5*).

However, several studies using stress and 3- to 4-hr delayed ^{201}Tl imaging have demonstrated that nonreversible perfusion abnormalities frequently exhibited normal perfusion after coronary revascularization (*6, 7*). In addition, these nonreversible perfusion defects occasionally have persistent metabolic activity by positron emission tomography using ^{18}F-deoxyglucose (*8–11*).

Since the extent of a persistent defect on 3–4-hr delayed images occasionally decreases on 24-hr delayed images (*12*), late ^{201}Tl imaging has recently been utilized to identify reversible ischemic myocardium (*13,14*). However, the late imaging may not necessarily provide satisfactory images due to inadequate counts with low target-to-background ratios (*15*). In addition, it is often difficult to ask out-patients to return to the hospital on the following day for the late imaging.

To solve these potential problems, reinjection of a small amount of ^{201}Tl at rest following 3–4-hr delayed imaging has been proposed to identify ischemic myocardium (*16*). Preliminary studies showed occasional fill-in of the tracer after reinjection in the areas of persistent perfusion abnormality on stress-delayed ^{201}Tl imaging (*15–17*). Thus, the purpose of this study was to clarify, with use of single-photon emission computed tomography (SPECT), the clinical significance of fill-in on the reinjection images following 3-hr delayed ^{201}Tl imaging by comparing regional wall motion, electrocardiographic (ECG), and angiographic results.

MATERIALS AND METHODS

Study Patients

Sixty consecutive patients with documented coronary artery disease who showed perfusion abnormality on the post-exercise ^{201}Tl SPECT were selected for this study. Coronary artery disease was determined based on significant narrowing

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(≥75% in diameter) on coronary angiogram (n = 53) or perfusion abnormality on stress ^{201}Tl imaging (n = 7). There were 50 men and 10 women ranging in age from 40 to 75 yr (mean = 60.9). Forty patients had documented myocardial infarction, based on ECG criteria or clinical history. Twenty patients showed anterior wall myocardial infarction, 4 lateral infarction, 14 inferior infarction, and 2 patients had both anterior and inferior infarction, based on the location of Q-waves on ECG.

Exercise ^{201}Tl Study Protocol

All patients underwent graded bicycle exercise testing starting at 25 watts with 25-watt increments every 3 min; a 12-lead ECG and blood pressure were monitored during each minute of exercise. The exercise continued until the patient had severe fatigue, chest pain, dyspnea, more than 0.2 mV of ST-segment depression or 85% of age-predicted maximal heart rate. Approximately 100 MBq (2.7 mCi) of ^{201}Tl was intravenously injected at peak exercise and the exercise continued for one additional minute. Five to 8 min later, post-exercise SPECT imaging was started. At the conclusion of imaging, patients were asked not to perform strenuous activities and to refrain from eating any carbohydrates. Three hours later, delayed SPECT imaging was started. Immediately after delayed imaging, 40 MBq (1.1 mCi) of ^{201}Tl was injected at rest. Ten minutes later, reinjection SPECT imaging was started.

For each SPECT study, a General Electric 400 AC/T model camera equipped with a general-purpose parallel-hole collimator interfaced to a MaxiStar computer was used. Thirty-two views were collected for 30 sec each over 180-degree arc starting from 45° left posterior oblique (LPO) to 45° right anterior oblique (RAO) projections (*18–21*). A series of transaxial slices were reconstructed with filtered backprojection using a Ramp-Hanning filter with a cutoff frequency of 0.5 cycle/pixel. No attenuation correction was used. Oblique tomograms parallel to the long- and short-axes of the left ventricle were reconstructed from the transverse slices (*18–21*).

Image Interpretations

The post-exercise, delayed, and reinjection SPECT images were displayed side-by-side to review and score the distributions. The left ventricular myocardium was divided into five segments (anterior, septal, inferior, lateral, and apical segments) (Fig. 1) (*19–21*). Thallium-201 uptake in each segment was scored by consensus of two experienced nuclear physicians using a five-point grading system, (0 = normal, 1 = equivocal, 2 = mild, 3 = moderate, and 4 = severe reduction) without knowledge of clinical, ECG, or angiographic data.

The initial perfusion image was considered normal when the post-exercise score was 0 or 1 (Group I); for a myocardial segment with a score of 2 or greater, the initial perfusion abnormality was considered abnormal. When the score decreased one or more on the delayed images, the segment was considered to show redistribution (Group II). When the score was unchanged (no redistribution) (Group III), the segments were further divided into two subgroups based on the reinjection images. When the score decreased one or more on the reinjection images, the segment was considered fill-in after reinjection (Group IIIa); when the score did not decrease with reinjection the segment was considered no fill-in after reinjection (Group IIIb).

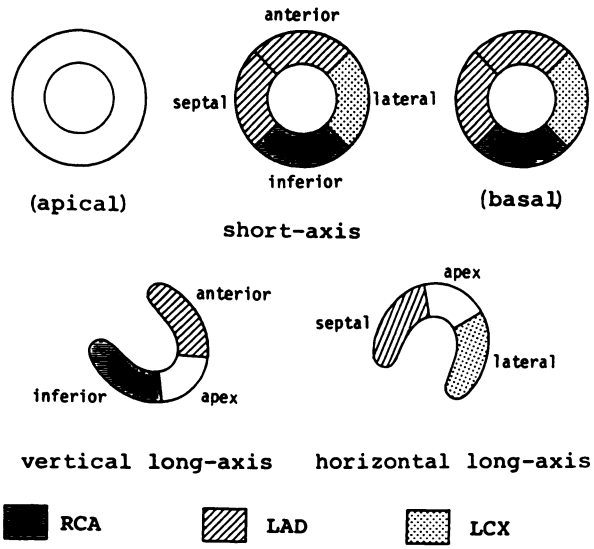

FIGURE 1
Schematic presentation of three short-axis slices, and mid vertical and horizontal long-axis slices displaying five myocardial segments. The distributions of the three major coronary arteries are also described.

Regional Wall Motion Analysis

Resting left ventricular wall motion was assessed by multigated radionuclide ventriculography in the anterior and LAO projections in 53 patients. The left ventricle was similarly divided into five segments. Two experienced nuclear physicians reviewed regional wall motion in each segment using cine-mode display without knowledge of ^{201}Tl or clinical results, and scored it using a five-point grading system (normal = 0, hypokinesis = 1, severe hypokinesis = 2, akinesis = 3, dyskinesis = 4).

Coronary Arteriography

Coronary arteriography was performed within 60 days of the ^{201}Tl study using a standard Sones or Judkins approach. The coronary arteriograms were interpreted by three experienced observers without knowing the ^{201}Tl results. Each coronary lesion was graded as complete occlusion (100%), 99%, 75%–98% or <75% luminal diameter narrowing.

Statistical Analysis

Values reported were shown as mean ± s.d. Difference in wall motion score was compared with Student's t-test or analysis of variance (ANOVA). Chi-square analysis (with Yates' correction) was used to determine difference between proportions. Probability values <0.05 were considered significant.

RESULTS

Thallium-201 Reinjection Findings

Of 60 patients showing perfusion abnormality on the post-exercise ^{201}Tl-SPECT, 43 patients (72%) had redistribution in at least one myocardial segment and the remaining 17 patients had no redistribution in any myocardial segment. The reinjection ^{201}Tl-SPECT identified new fill-in in 5 of the 17 patients (29%) (Fig. 2),

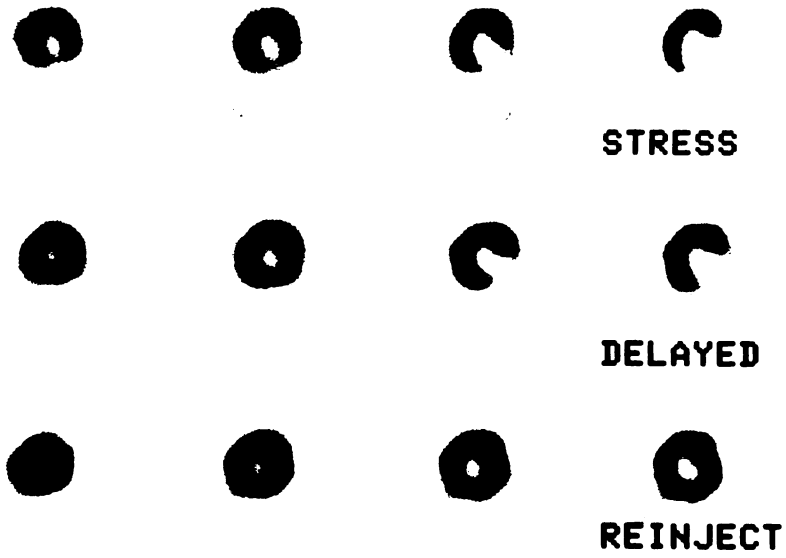

FIGURE 2
Four representative short-axis slices of post-exercise (top), 3-hr delayed (middle) and reinjection (bottom) imaging of a patient with lateral wall myocardial infarction. The post-exercise ^{201}Tl imaging shows perfusion defect in inferoposterior and posterolateral regions without definite redistribution on the delayed images. The reinjection imaging clearly shows new fill-in of the tracer in inferoposterior and posterolateral regions.

whereas 12 patients (71%) had persistent defect even after reinjection (Fig. 3).

Of 300 myocardial segments, 130 segments (43%) showed normal perfusion on the post-exercise ^{201}Tl images (Group I). Of 170 segments with post-exercise perfusion abnormality, 85 segments (50%) showed redistribution (Group II), and the remaining 85 segments showed no redistribution (Group III) on the delayed images. The reinjection ^{201}Tl-SPECT identified new fill-in in 27 segments (32%) (Group IIIa), while the remaining 58 segments (68%) did not show any improvement after reinjection (Group IIIb) (Table 1).

Relation to Regional Wall Motion

Radionuclide ventriculography was obtained in 51 patients to assess regional wall motion. Regional asynergy was observed in 143 of the total 255 segments (56%). The mean wall motion score was 0.54 ± 0.90 in Group I. The score in Group II (0.97 ± 1.18) was significantly higher than that in Group I ($p < 0.01$), but it was lower than that in Group III (2.36 ± 1.28) ($p < 0.01$), indicating less severe wall motion abnormality in Group II than that in Group III. When Group III was further divided into two subgroups, based on the findings of the reinjection imaging, the wall motion score in Group IIIa (1.64 ± 1.29) was lower than that in Group II ($p < 0.05$) but higher than that in Group IIIb (2.71 ± 1.12) ($p < 0.01$) (Table 2), suggesting that wall motion abnormality in Group IIIa was more severe than in Group II but less severe than in Group IIIb.

When anterior and apical segments were selected for analysis, the wall motion score in Group IIIa ($1.55 \pm$

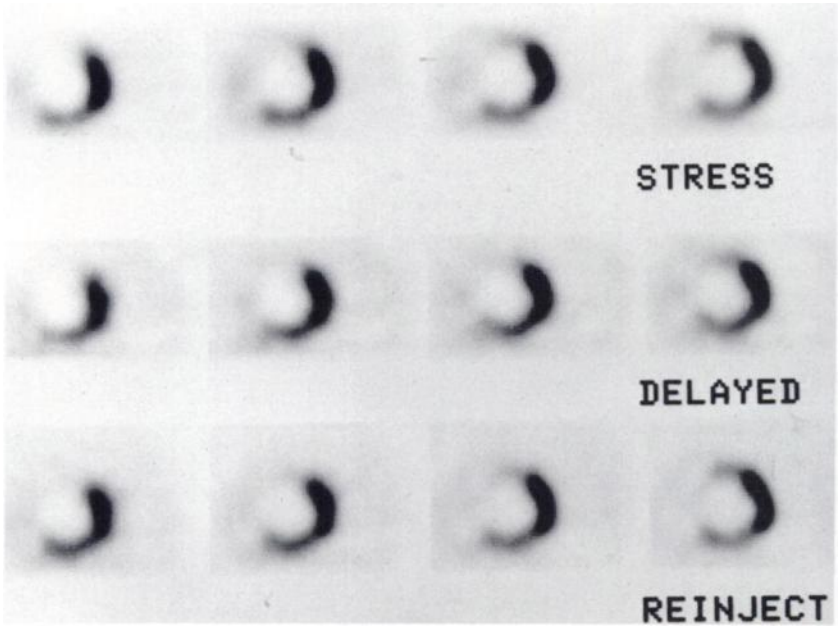

FIGURE 3
Four representative short-axis slices of post-exercise (top), 3-hr delayed (middle) and reinjection (bottom) imaging of a patient with anterior wall myocardial infarction. A large perfusion defect is seen in anterior and septal regions without redistribution on the delayed images. Similar distribution is observed in the reinjection imaging without definite fill-in of the tracer in the same areas.

TABLE 1
Number of Segments in Each Group Based on ^{201}Tl Findings

Group	^{201}Tl findings			n (%)
	Stress	Delayed	Reinjection	
I	Normal	Normal	Normal	130 (43%)
II	Reduced	RD	Fill-in	85 (28%)
IIIa	Reduced	no RD	New fill-in	27 (9%)
IIIb	Reduced	no RD	no fill-in	58 (19%)
Total				300 (100%)

RD = redistribution.

1.23) was higher than that in Group II ($p < 0.05$) but lower than that in Group IIIb (2.89 ± 0.92) ($p < 0.01$). The similar results were obtained when inferior and lateral segments were selected for analysis. Again, the score in Group IIIa (1.40 ± 1.02) was higher than that in Group II (0.62 ± 0.88) but lower than that in Group IIIb (2.32 ± 1.38) ($p < 0.05$ each).

Relation to Q-wave on ECG

Forty patients showed Q-wave myocardial infarction on ECG. When the ^{201}Tl findings were compared to the presence of Q-wave on ECG, there were 82 Q-wave segments, all of which corresponded to the areas of abnormal perfusion on post-exercise ^{201}Tl images. Twenty segments (27%) of those in Group II showed Q-wave on ECG. The segments in Group IIIa showed Q-wave on ECG more often (69%) than in Group II (27%) ($p < 0.01$) but less often than in Group IIIb (85%) ($p < 0.05$) (Table 3). On the other hand, of 69 segments showing no Q-wave on ECG, 14 segments (21%) did not reveal redistribution on the routine ^{201}Tl study and were considered as myocardial fibrosis. The reinjection imaging identified new fill-in in eight of them (57%) (Table 3).

Relation to Coronary Narrowing

Coronary narrowing on arteriogram was divided into moderate narrowing with <99% and severe narrowing with 99% or 100%. In the segments in Group IIIa, severe narrowing was observed more often (73%) than in Group II (49%) ($p < 0.05$), although similar frequency was observed in Group IIIa with that in Group IIIb (76%) (Table 4).

TABLE 3
Number of Segments Showing Q-wave on ECG in Each Group

Group	n	non-Q-wave	Q-wave
II	75	55 (73%)	20 (27%)
IIIa	26	8 (31%)	18 (60%)
IIIb	50	6 (15%)	44 (85%)

*$p < 0.01$.
†$p < 0.05$.

DISCUSSION

This study highlights the ability of reinjection ^{201}Tl-SPECT to detect viable myocardium in patients exhibiting no redistribution on their routine stress and delayed ^{201}Tl imaging. Reinjection SPECT identified new fill-in after reinjection in approximately one-third of the segments with persistent defect on the routine imaging. This subgroup had more severe wall motion abnormalities than those showing redistribution on the delayed images, but the wall motion in these segments was better than those where no fill-in was observed even after reinjection, suggesting that these segments may represent severely ischemic but potentially viable myocardium.

Technical Considerations

Some persistent ^{201}Tl perfusion defects are due to myocardial ischemia, based on studies before and after revascularization (*6,7*) or comparative studies with metabolic imaging using positron emission tomography (*8–11*). Therefore, a new technique should be explored for detecting ischemia in areas of persistent defects on the routine ^{201}Tl imaging. Since some severely ischemic myocardial segments redistribute long after ^{201}Tl administration, the late redistribution imaging has been proposed for enhanced detection of myocardial ischemia (*13,14*). However, late imaging often provided

TABLE 2
Regional Wall Motion Score in Each Group

Group	n	Wall motion score
I	104	0.54 ± 0.90
II	75	0.97 ± 1.18
IIIa	25	1.64 ± 1.29
IIIb	51	2.71 ± 1.12

*$p < 0.01$.
†$p < 0.05$.

TABLE 4
Severity of Narrowing on Coronary Arteriograms in Each Group

Group	n	Coronary arteriogram	
		<99% stenosis	≥99% stenosis
II	79	40 (51%)	25 (49%)
IIIa	26	7 (27%)	19 (73%)
IIIb	50	12 (24%)	38 (76%)

*$p < 0.01$.
†$p < 0.05$.

unsatisfactory images due to relatively poor image quality (*15*). The reinjection of a small amount of ^{201}Tl following the delayed imaging is another alternative for this purpose (*15,16*). Reinjection imaging provides higher count density, which enables precise assessment of change in tracer concentration such as redistribution in the areas of initial perfusion abnormality with adequate counts and good quality images, particularly in the case of ^{201}Tl-SPECT. In addition, the entire study can be completed within 4–5 hr on the same day, although the tracer has to be administered twice in this method. The total injected dose was 140 MBq (3.8 mCi), which was acceptable in respect of radiation dose to the patient.

We used SPECT imaging for this study because it has become a widely used technique, which may enhance detection of myocardial ischemia (*19–23*) and quantify ischemia or infarcted myocardium (*24–27*). In addition, change in tracer concentration in initially hypoperfused segments may be precisely assessed with separation of the activity in the adjacent areas (*28*).

Mechanisms of Fill-in

The reinjection ^{201}Tl images represent part delayed images and part resting perfusion images. Two separate injections of the perfusion tracer, such as nitrogen-13-ammonia (*10,29*) and technetium-99m isonitrile (*30*), at rest and during exercise demonstrated reversible ischemia more often than stress and delayed imaging using single injection of ^{201}Tl. In addition, Blood et al. (*31*) on his comparative study between delayed ^{201}Tl images and resting images described that more than 20% of the patient showed larger perfusion defect on the delayed imaging than the resting imaging, and approximately half of them had occluded coronary arteries which supplied the defect areas without evidence of myocardial infarction. Ritchie et al. (*32*) also showed similar findings. Therefore, reinjection imaging may reasonably resolve some perfusion abnormality, particularly in the areas supplied by severe coronary stenosis.

In the case of severe coronary stenosis, the tracer delivery to the ischemic area may be severely prolonged due to a lack of post-stress hyperemia or resting hypoperfusion so that the equilibrium of ^{201}Tl in the potassium pool is not reached within 3–4 hr. In this respect, reinjection or late redistribution imaging will help reach this equilibrium state and, thus, identify fill-in of the tracer in the severely ischemic myocardium (*13,14*). Gutman et al. (*12*) demonstrated an inverse relation of the rate of ^{201}Tl redistribution with severity of coronary stenosis. In our results, although about half of the segments showing redistribution also had severe (≥99%) coronary stenosis, the new fill-in of the tracer after reinjection was more often observed in the segments supplied by severe coronary stenosis.

Redistribution also depends on plasma ^{201}Tl concentration within 2 hr after injection. Low plasma ^{201}Tl concentration often lack redistribution in the ischemic myocardium (*33–35*). Therefore, it is quite reasonable that reinjection of a small amount of ^{201}Tl may enhance detection of reversible perfusion defect in the areas with ischemic myocardium by an increase in plasma ^{201}Tl concentration.

In comparison with regional wall motion, the degree of redistribution correlated with the severity of wall motion abnormality, which was consistent with a previous report (*36*). Furthermore, the segments showing new fill-in after reinjection had less severe wall motion abnormality than those without fill-in even after reinjection. The preliminary reports also support our findings (*15,16*). Thus, these segments may contain severely ischemic but viable myocardium.

In comparison with ECG findings, ~80% of those showing new fill-in after reinjection and Q-waves on ECG. Histologic studies demonstrated that the segments having Q-wave on ECG occasionally exhibited only mild fibrosis (*37,38*). Brunken et al. (*39*) also showed persistent metabolic activity on PET in ~50% of the Q-wave regions. Thus, the segments exhibiting Q-wave on ECG may not always represent irreversible myocardium. Furthermore, the reinjection imaging identified the new fill-in in 8 of 14 segments (57%), showing no Q-wave on ECG but no redistribution on the delayed images. Reinjection imaging is a valuable means for enhanced detection of reversible ischemic myocardium.

Limitations

The study population was drawn from patients with coronary disease who had perfusion abnormalities on their post-exercise ^{201}Tl images and, therefore, had severe coronary artery disease. On the other hand, the reinjection of ^{201}Tl may not be needed in those who did not have any perfusion abnormalities on the initial images.

Although the segments with new fill-in after reinjection represent ischemic myocardium with less abnormal wall motion when compared to segments with no fill-in, whether these segments will improve after revascularization has not yet been proven. Preliminary studies, however, suggest that those segments are likely to improve in regional function after coronary angioplasty (*17*) or bypass grafting (*40*) and to have metabolic activity on positron emission tomography (*41,42*).

It may be difficult to compare stress ^{201}Tl findings on three-dimensional tomographic images with regional wall motion on planar radionuclide ventriculogram at rest. This may cause relatively large variations of wall motion score in each group. These inherent difficulties were minimized by assigning five large ventricular regions and by averaging wall motion score for comparison. The mean wall motion score in each group was

significantly different. In addition, similar differences were also observed when anterior and inferior segments were separately assessed. Furthermore, the degree of redistribution may partly represent resting myocardial perfusion and, therefore, it was reasonably correlated with regional function at rest.

CONCLUSIONS

Our results suggest that reinjection of ^{201}Tl following delayed imaging often shows new fill-in in the areas of persistent defect on routine stress and delayed imaging. Since these segments had relatively preserved wall motion and Q-wave on ECG less often than those with no fill-in, even after reinjection, these segments should be separately assessed for future treatment. Reinjection ^{201}Tl imaging should be performed when no redistribution was observed on the delayed images, and it may hold promise for identifying severely ischemic but potentially viable myocardium.

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REFERENCES

1. Pohost GM, Zir LM, Moore RH, McKusick KA, Guiney TE, Beller GA. Differentiation of transiently ischemic from infarcted myocardium by serial imaging after single dose of thallium-201. *Circulation* 1977; 55:294–302
2. Verani MS, Jhingran S, Attar M, Rizk A, Quinones MA, Miller RR. Post-stress redistribution of thallium-201 in patients with coronary artery disease, with and without prior myocardial infarction. *Am J Cardiol* 1979; 43:1114–1122.
3. Beller GA, Watson DD, Ackell P, Pohost GM. Time course of thallium-201 redistribution after transient myocardial ischemia. *Circulation* 1980; 61:791–797.
4. Rozanski A, Berman DS, Gray R, et al. Use of thallium-201 redistribution scintigraphy in the preoperative differentiation of reversible and nonreversible myocardial asynergy. *Circulation* 1981; 64:936–944.
5. Berger BC, Watson DD, Burwell LR, et al. Redistribution of thallium at rest in patients with stable and unstable angina and the effect of coronary artery bypass surgery. *Circulation* 1979; 60:1114–1125.
6. Gibson RS, Watson DD, Taylor GJ, et al. Prospective assessment of regional myocardial perfusion before and after coronary revascularization surgery by quantitative thallium-201 scintigraphy. *JACC* 1983; 1:804–815.
7. Liu P, Kiess MC, Okada RD, et al. The persistent defect on exercise thallium imaging and its fate after myocardial revascularization: does it represent scar or ischemia? *Am Heart J* 1985; 110:996–1001.
8. Brunken R, Schwaiger M, Grover-McKay M, Phelps ME, Tillisch J, Schelbert HR. Positron emission tomography detects tissue metabolic activity in myocardial segments with persistent thallium perfusion defects. *JACC* 1987; 10:557–567
9. Tamaki N, Yonekura Y, Yamashita K, et al. Relation of left ventricular perfusion and wall motion with metabolic activity in persistent defects on thallium-201 tomography in healed myocardial infarction. *Am J Cardiol* 1988; 62:202–208.
10. Tamaki N, Yonekura Y, Yamashita K, et al. SPECT thallium-201 tomography and positron tomography using N-13-ammonia and F-18-fluorodeoxyglucose in coronary artery disease. *Am J Cardiac Imaging* 1989; 3:3–9.
11. Brunken RC, Kottou S, Nienaber CA, et al. PET detection of viable tissue in myocardial segments with persistent defects at Tl-201 SPECT. *Radiology* 1989; 172:65–73.
12. Gutman J, Berman DS, Freeman M, et al. Time to complete redistribution of thallium-201 in exercise myocardial scintigraphy: relationship to the degree of coronary artery stenosis. *Am Heart J* 1983; 106:989–995.
13. Cloninger KG, DePuey EG, Garcia EV, et al. Incomplete redistribution in delayed thallium-201 single photon emission computed tomographic (SPECT) images: an overestimation of myocardial scarring. *JACC* 1988; 12:9545–9963.
14. Kiat H, Berman DS, Maddahi J, et al. Late reversibility of tomographic myocardial thallium-201 defects: an accurate marker of myocardial viability. *JACC* 1988; 12:1456–1463.
15. Ohtani H, Tamaki N, Yonekura Y, et al. Assessment of resting thallium-201 reinjection after stress-delayed Tl imaging: comparison with 24-hr scan and regional wall motion. *Kaku Igaku* 1990; 27:9–15.
16. Rocco T, Dilsizian V, Maltais F, Strauss HW, Boucher CA, McKusick KA. Thallium-201 reinjection after delayed imaging demonstrates fill-in to regions with "fixed" defects [Abstract]. *J Nucl Med* 1988; 29:769.
17. Dilsizian V, Rocc TP, Freedman NMT, Leon MB, Enhanced detection of ischemic but viable myocardium by the reinjection of thallium after stress-redistribution imaging. *N Engl J* Med 1990; 323:141–146.
18. Tamaki N, Mukai T, Ishii Y, et al. Comparative study of thallium emission myocardial tomography with 180° and 360° data collection. *J Nucl Med* 1982; 23:661–666.
19. Tamaki N, Yonekura Y, Mukai T, et al. Segmental analysis of stress thallium myocardial emission tomography for localization of coronary artery disease. *Eur J Nucl Med* 1984; 9:99–105.
20. Tamaki N, Yonekura Y, Mukai T, et al. Stress thallium-201 transaxial emission computed tomography: quantitative versus qualitative analysis of coronary artery disease. *J Am Coll Cardiol* 1984; 4:1213–1221.
21. Nohara R, Kambara H, Suzuki Y, et al. Stress scintigraphy using single-photon emission computed tomography in the evaluation of coronary artery disease. *Am J Cardiol* 1984; 53:1250–1254.
22. Fintel DJ, Links JM, Brinker JA, Frank TL, Parker M, Becker LC. Improved diagnostic performance of exercise thallium-201 single photon emission computed tomography over planar imaging in the diagnosis of coronary artery disease: a receiver operating characteristic analysis. *J Am Coll Cardiol* 1989; 13:600–612.
23. DePasquale EE, Nody AC, Depuey EG, et al. Quantitative rotational thallium-201 tomography for identifying and localizing coronary artery disease. *Circulation* 1988; 77:316–327.
24. Tamaki S, Nakajima H, Murakami T, et al. Estimation of infarct size by myocardial emission computed tomography with thallium-201 and its relation to creatine kinase-MB release after myocardial infarction in man. *Circulation* 1982; 66:994–1001.
25. Caldwell JH, Williams DL, Harp GD, Stratton JR, Ritchie JL. Quantitation of size of relative myocardial perfusion defect by single-photon emission computed tomography. *Circulation* 1984; 70:1048–1056.
26. Wolfe CL, Jansen DE, Corbett JR, et al. Determination of

left ventricular mass using single-photon emission computed tomography. *Am J Cardiol* 1985; 56:761–764.
27. Pringent F, Maddahi J, Garcia EV, Satoh Y, Van Train K, Berman D. Quantification of myocardial infarct size by thallium-201 single-photon emission computed tomography: experimental validation in the dog. *Circulation* 1986; 74:852–861.
28. Tamaki N, Mukai T, Ishii Y, et al. Clinical evaluation of thallium-201 emission myocardial tomography using a rotating gamma camera: comparison with seven-pinhole tomography. *J Nucl Med* 1981; 22:849–855.
29. Tamaki N, Yonekura Y, Senda M, et al. Value and limitation of stress thallium-201 single photon emission computed tomography: comparison with nitrogen-13-ammonia positron tomography. *J Nucl Med* 1988; 29:1181–1188.
30. Kahn JK, McGhie I, Akers MS, et al. Quantitative rotational tomography with ^{201}Tl and ^{99m}Tc 2-methoxy-isobutyl-isonitrile. *Circulation* 1989; 79:1282–1293.
31. Blood DK, McCarthy DM, Sciacca RR, Cannon PJ. Comparison of single-dose and double-dose thallium-201 myocardial perfusion scintigraphy for the detection of coronary artery disease and prior myocardial infarction. *Circulation* 1981; 58:777–788.
32. Ritchie JL, Albro PC, Caldwell JH, Trobaugh GB, Hamilton GW. Thallium-201 myocardial imaging: a comparison of the redistribution and rest images. *J Nucl Med* 1979; 20:477–483.
33. Budinger TF, Knittel BL. Cardiac thallium redistribution and model [Abstract]. *J Nucl Med* 1987; 28:588.
34. Angello DA, Wilson RA, Palac RT. Effect of eating on thallium-201 myocardial redistribution after myocardial ischemia. *Am J Cardiol* 1987; 60:528–533.
35. Nelson CW, Wilson RA, Angello DA, Palac RT. Effect of thallium-201 blood levels on reversible myocardial defects. *J Nucl Med* 1989; 30:1172–1175.
36. Bodenheimer MM, Banka VS, Fooshee C, Hermann GA, Helfant RH. Relationship between myocardial perfusion and the presence of severity and reversibility of asynergy in patients with coronary heart disease. *Circulation* 1978; 58:789–795.
37. Bodenheimer MM, Banka VS, Hermann GA, Trout RG, Pasdar H, Helfant RH. Reversible asynergy: histopathologic and electrocardiographic correlations in patients with coronary artery disease. *Circulation* 1976; 53:792–800.
38. Stinson EB, Billingham ME. Correlative study of regional left ventricular histology and contractile function. *Am J Cardiol* 1977; 39:378–386.
39. Brunken R, Tillisch J, Schwaiger M, et al. Regional perfusion, glucose metabolism, and wall motion in patients with chronic electrocardiographic Q-wave infarctions: evidence for persistence of viable tissue in some infarct regions by positron emission tomography. *Circulation* 1986; 73:951–963.
40. Ohtani H, Tamaki N, Yonekura Y, et al. Value of reinjection thallium-201 SPECT imaging after delayed imaging for identifying reversible ischemia [Abstract]. *J Nucl Med* 1990; 31:743.
41. Bonow RO, Bacharach SL, Cuocolo A, Dilsizian V. Myocardial viability in coronary artery disease and left ventricular dysfunction: thallium-201 reinjection vs. fluorodeoxyglucose [Abstract]. *Circulation* 1989; 80:II–377.
42. Tamaki N, Ohtani H, Yonekura Y, et al. Can reinjection thallium-201 SPECT replace FDG-PET for assessing tissue viability? [Abstract]. *J Nucl Med* 1990; 31:742.

EDITORIAL:
Rest Reinjection of Thallium-201 After Redistribution Imaging: New Questions, Old Solution

At present, thallium-201-chloride (^{201}Tl-chloride) remains the radiopharmaceutical most widely applied for the clinical evaluation of myocardial perfusion in patients with coronary artery disease (CAD). Thallium uptake is, at least in part, an energy requiring process (*1–3*); it is therefore reasonable to speculate that the accumulation of this agent at the cellular level is indicative of persistent metabolic activity, and thus may infer tissue viability. At a more practical level, because perfusion and contractile function are typically "coupled," regional thallium uptake can also provide a clinical index of myocardial viability. However, a number of recent publications (*4–7*), including the paper by Tamaki et al. presented in this issue of the *Journal* (*8*), have indicated that conventional stress/redistribution thallium imaging may overestimate the extent of infarction in patients with CAD and thereby underestimate viable, and potentially jeopardized, myocardium.

The initial application of thallium in CAD patients involved separate injections of the agent during exercise and, days to weeks later, at rest (*9–10*). This approach provided temporally discrete assessment of myocardial perfusion under different physiologic conditions. Perfusion abnormalities present on both stress and rest studies were attributed to prior infarction, in contradistinction to perfusion defects that appeared only after stress injection: these latter abnormalities were attributed to exercise-induced ischemia. The important derivative implication of this interpretive paradigm was that perfusion defects that persist on repeat imaging after rest injection infer the absence of ischemic, jeopardized myocardium in the corresponding segments.

A major alteration in thallium imaging derived from the seminal work by Pohost et al. (*11*) at the Massachusetts General Hospital.

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