# Usefulness of reinjection image for evaluating viable myocardium in the infarcted zone on exercise thallium-201 SPECT

Seiji Tomiguchi,* Mutsumasa Takahashi,* Osamu Shimomura,* Akihiro Kojima,*
Masafumi Hara,* Yukinori Koga,* Kotaro Minoda,** Hirofumi Yasue**
and Kazuya Hayasaki***

*Department of Radiology, Kumamoto University School of Medicine
**Department of Cardiology, Kumamoto University School of Medicine
***Department of Cardiology, Kumamoto Saiseikai Hospital

Reinjection images were obtained in 23 patients with myocardial infarction by the additional injection of 37 MBq of thallium-201 after obtaining 4 hour delayed images on exercise thallium-201 SPECT (TSPECT). A redistribution index (RI) was derived of the changes in perfusion defects between immediate and 4 hour delayed images as well as immediate and reinjection images on polar bull's eye maps. The RI of reinjection images (46±27%) was significantly greater than that of 4 hour delayed images (26±26%) in patients with myocardial infarction (p<0.01). Significant redistribution after reinjection occurred in 4 of 9 patients (44%) without significant redistribution on 4 hour delayed images. Improvement in redistribution on reinjection images correlated significantly to the small extent of coronary artery disease and collateral development. The appearance of redistribution from 4 hour delayed imaging to reinjection imaging also might reflect the function of collateral development in the resting state in patients without significant redistribution on 4 hour delayed images. It has been demonstrated that underestimated viable myocardium on 4 hour delayed images in the infarcted zone can be better assessed on reinjection images. This reinjection technique is recommended in patients with no or partial redistribution on 4 hour delayed images.

Key words: reinjection, myocardial infarction, myocardial viability, exercise thallium-201 SPECT

## INTRODUCTION

RECENTLY, IT HAS BEEN SHOWN that 4 hour delayed images on exercise thallium-201 planar imaging and exercise thallium-201 single photon emission computed tomography (TSPECT) underestimate the viable myocardium in coronary artery diseases.[1-6] This underestimation has been attributed to the delayed redistribution occurring in the regions sup-

plied by the severe stenosed coronary artery.[4,5] To overcome this underestimation, several investigators recommended qualitative evaluation of additional delayed images up to 24 hours after thallium-201 injection at peak exercise[5-8] as well as a repeated rest study by means of an additional injection of thallium-201.[9-13] But, there has not been sufficient discussion of the mechanism by which the perfusion defect seen in 4 hour delayed images is improved by reinjection of thallium-201.[10-13]

The purpose of the present study was to assess redistribution in the infarcted zone quantitatively with an additional injection of thallium-201 shortly after 4 hour delayed imaging and to evaluate whether reinjection images are superior to 4 hour delayed

images for differentiating the viable from nonviable myocardium in the infarcted zone. Evaluation is also made of the relationship of redistribution to relevant coronary artery stenosis, the extent of coronary artery disease, wall motion and collateral development and the mechanism by which redistribution improves on reinjection images in patients without significant redistribution on 4 hour delayed images.
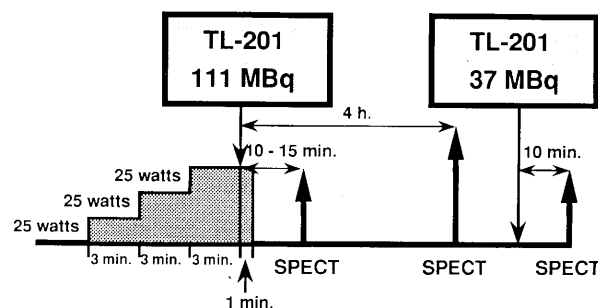
## METHODS

### Study patients

The case materials consisted of 23 patients (16 males and 7 females) with myocardial infarction who had perfusion defects on the immediate postexercise images and demonstrated no or only partial redistribution on 4 hour delayed images on TSPECT. Their ages ranged from 35 to 81 years (mean age 65). Sites of myocardial infarction were determined by ECG and left ventriculogram. There were 11 anteroseptal, 3 anterior, 4 inferoposterior, 2 inferior, 2 posterolateral, and 1 posterior myocardial infarctions. The mean interval from the most recent infarction to the study was 9.7 months (range 1 to 72). To determine the threshold value of the perfusion defect, 10 patients without significant coronary artery stenosis were also studied. Coronary angiography was performed in these patients for suspected angina pectoris. No patient had hypertensive, valvular or cardiomyopathic disease. They consisted of 7 females and 3 males, their ages ranging from 48 to 78 years (mean age 62). All patients were free of drugs for 24 hours before TSPECT.

### Reinjection protocol (Fig. 1)

Exercise testing was performed on an upright bicycle ergometer with a work load starting at 25 watts and increased by 25 watts every 3 minutes. Exercise was carried out to the onset of angina pectoris, an increase in their age-predicted maximal heart rate ($>85\%$), a fall in blood pressure ($>10$ mmHg), dyspnea, ST segment depression ($>0.2$ mV), frequent multifocal ventricular extrasystole ($>10$/min) or fatigue. At the end of the test, a dose of 111 MBq of thallium-201 was injected intravenously and the patient continued to exercise for another minute. SPECT images were obtained at 10 to 15 minutes (immediate postexercise image) and after 4 hours (4 hour delayed image) following the injection of thallium-201. In addition, after 4 hour delayed imaging, an additional 37 MBq of thallium-201 was reinjected and a reinjection image was obtained 10 minutes after reinjection.

### Tomographic acquisition

A rotatable camera (ZLC 37-ECT, Shimadzu, Kyoto,



**Fig. 1** Reinjection method. Single photon emission computed tomography (SPECT) was performed immediately (10–15 min) and 4 hours after the injection of 111 MBq of thallium-201. After 4 hour delayed imaging, an additional 37 MBq of thallium-201 was injected and SPECT was re-performed.

Japan) equipped with a low energy high resolution collimator and interfaced to a digital computer (Scintipac 2400, Shimadzu, Kyoto, Japan) was used for all studies. Thirty planar acquisitions were obtained for 20 seconds each over a 180° arc extending from the 45° left posterior oblique projection to the 45° right anterior oblique projection. Transverse slices (6 mm thick) of the body were reconstructed by a filtered back projection method, with a Shepp & Logan filter, and the attenuation correction was not applied. Short axis slices parallel to the short axis of the left ventricle were obtained by further processing of the transverse slices.

For quantitative analysis, circumferential maximum count profiles were obtained from each of the short axis slices from the apex to the base. Each short axis slice was divided into 60 radial segments at 6° intervals. Circumferential maximum count profiles were arranged into a polar bull's eye map with the most apical profile placed in the center of the map and the most basal profile at the periphery of the map. The bull's eye map was displayed with a color code showing the percent of each pixel count to the maximum pixel count on the map. These methods were applied to immediate postexercise, 4 hour delayed and reinjection images.

### Quantitative index of redistribution

Bull's eye maps of normal controls were reconstructed for 10 patients without significant coronary artery stenosis ($<25\%$). The data were obtained for immediate postexercise images and 4 hour delayed images. Distribution of the percent of each pixel count to the maximum pixel count on the map was $80\pm10\%$ (mean$\pm$SD) in the immediate postexercise maps and $79\pm10\%$ in 4 hour delayed maps. Thus, the lower limit of normal thallium distribution was found to be $55\%$ (mean$-2.5$SD). In patient studies, the region with less than a $55\%$ threshold level was

considered to be the perfusion defect on each bull's eye map.

To assess redistribution quantitatively, the redistribution index (RI) was derived on bull's eye maps from the following formula;

$$RI=(AI-AD \text{ or } AR)/AI \times 100(\%)$$

AI: area in the perfusion defect on immediate postexercise image

AD: area in the perfusion defect on 4 hour delayed image

AR: area in the perfusion defect on reinjection image

The area of perfusion defect was defined by digital summing of pixels less than 55% of the maximum. Significant redistribution was considered present when RI increased to over 25%,[5] and study patients were divided into three groups according to their redistribution pattern.

Group A: this group had significant redistribution on a 4 hour delayed image.

Group B: this group had no significant redistribution on a 4 hour delayed image, but had it on a reinjection image.

Group C: this group had no significant redistribution on either a 4 hour delayed or a reinjection image.

## Coronary arteriography

Selective coronary arteriography and left ventriculography were performed in all patients. Each coronary artery lesion was graded according to the luminal diameter: 100%, 91 to 99%=99%, 76 to 90%= 90%, 51 to 75%=75%, 26 to 50%=50%, 25% or less=25%. The extent of coronary artery disease was assessed with a three classification scoring system: 1=single vessel disease, 2=double vessel disease, 3=triple vessel disease (extent score). Significant stenosis was considered to be present in

patients with more than 50% stenosis. Wall motion abnormalities were also assessed with a four classification scoring system: 0=normal, 1=hypokinetic, 2=akinetic, 3=dyskinetic (wall motion score) on a left ventriculogram. Three experienced observers reviewed coronary artery stenosis, wall motion and collateral development. Their consensus was used in the data analysis. All studies were performed within 30 days before and after TSPECT.

## Statistical analysis

All the obtained data were expressed as the mean± SD. Paired t-test was used to compare the RI between difference two groups. The chi square test was applied to compare the frequency differences in significant redistribution in two groups. A P value<0.05 was considered significant.

## RESULTS

*(1) Comparison of redistribution index in 4 hour delayed and reinjection images*

RI was obtained for 4 hour delayed and reinjection images in 23 patients with myocardial infarction. The RI of reinjection images (46±27%) was significantly greater than that of 4 hour delayed images (26±26%) in patients with myocardial infarction (p<0.01). Nine of 23 patients (39%) had no significant redistribution on 4 hour delayed images. Of these 9 patients, significant redistribution occurred in 4 patients (44%) on reinjection images (Fig. 2).

A summary of relevant coronary artery stenosis, extent of coronary artery disease, wall motion and collateral development in 4 patients with significant redistribution on reinjection images (Group B) is shown in Table 1. Severe stenosis of the relevant coronary artery was present in all of 4 patients. Of these 4 patients, three patients had single vessel disease and the other patients had double vessel disease, but no patient had triple vessel disease.
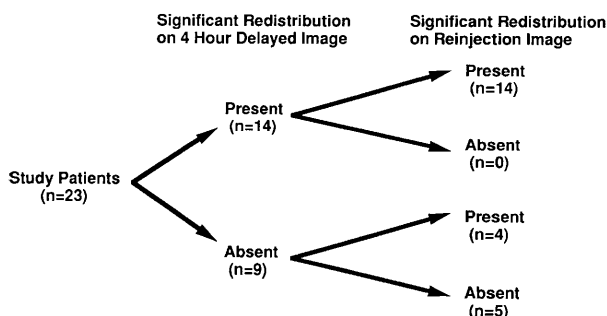


**Fig. 2** Correlation of significant redistribution on 4 hour delayed image and reinjection image. Significant redistribution on 4 hour delayed image was not present in nine of 23 patients with myocardial infarction (Group B and Group C). Of these 9 patients, four patients had a significant redistribution on the reinjection image (Group B).

**Table 1** Summary of relevant coronary artery stenosis, extent of coronary artery disease, wall motion and collateral development in 4 patients with significant redistribution on reinjection image

| Case | Coronary artery stenosis | Extent of CAD | Wall motion | Collateral development |
|------|------|------|------|------|
| 1 | 100% | SV | Akinetic | Present |
| 2 | 100% | SV | Akinetic | Present |
| 3 | 99% | SV | Dyskinetic | Absent |
| 4 | 100% | DV | Akinetic | Present |

CAD: coronary artery disease, SV: single vessel disease, DV: double vessel disease, TV: triple vessel disease

**Table 2** Comparison of relevant coronary artery stenosis, extent scores and wall motion scores in three groups

| | Relevant coronary artery stenosis (%) | Extent score | Wall motion score |
|---|---|---|---|
| Group A | 95.1±4.9 | 1.8±0.7 | 1.6±0.5 |
| Group B | 99.5±0.6 | 1.3±0.5 | 2.3±0.5 |
| Group C | 91.5±12.8 | 2.3±0.5 | 2.0±0.6 |

\* between Extent score Group B and Group C; \*\* between Wall motion score Group A and Group B

$*p<0.01$, $**p<0.05$

**Table 3** Comparison of presence of collateral development between group B and group C

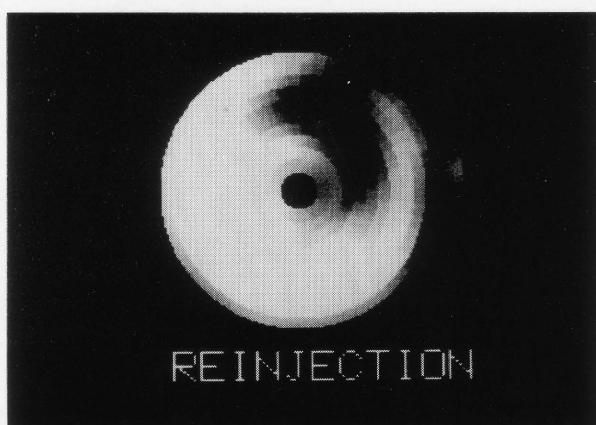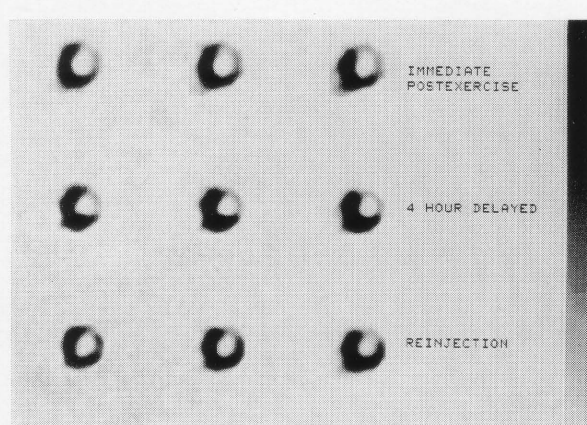| Collateral development | Present | Absent |
|---|---|---|
| Group B | 3 | 1 |
| Group C | 0 | 5 |

$p<0.05$
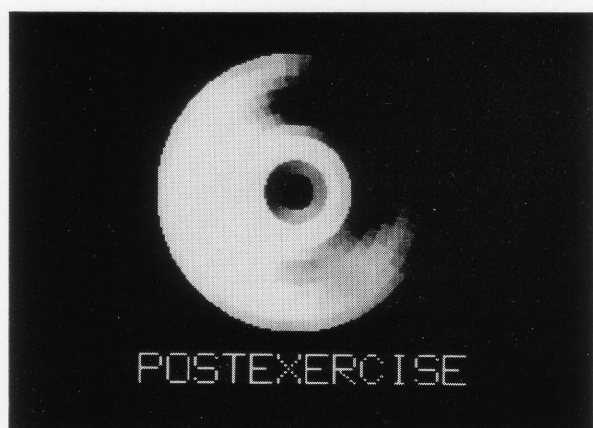


A



B



C



D

**Fig. 3** A 68-year-old male with posterolateral myocardial infarction. On coronary angiography, the infarcted zone was supplied by the left circumflex coronary artery (LCX) with total occlusion. The left anterior descending coronary artery (LAD) had a 99% stenosis but the right coronary artery had no significant stenosis with collateral development to LAD and LCX. Akinesis was present in the infarcted zone. A: demonstrates anterior, anterolateral, and posterolateral defects. B: demonstrates partial redistribution in the anterior and posterolateral walls. C: demonstrates significant redistribution in the anterior and posterolateral walls after reinjection. D: Three representative short-axis slices of immediate postexercise (top), 4 hour delayed (middle) and reinjection (bottom) images. A perfusion defect in the anterior and posterolateral walls is observed on immediate postexercise images. The 4 hour delayed images demonstrate a small amount of redistribution in the anterior wall. But, significant redistribution in the anterior and posterolateral walls is observed on reinjection images.

Collateral development was observed in three of these 4 patients and markedly disturbed wall motion was observed in four.

### (2) Relationship of redistribution to relevant coronary artery stenosis, extent of coronary artery disease and wall motion

The degree of coronary artery stenosis, mean extent score and wall motion score were compared in three groups. The results are listed in Table 2. There was no significant difference in the degree of relevant coronary artery stenosis among the three groups. Severe stenosis of relevant coronary stenosis was observed in all groups (Group A 95.1±4.9%, Group B 99.5±0.6%, Group C 91.5±12.5%). The mean extent scores in Group B (1.25±0.5) were significantly lower than those in Group C (2.25±0.5) ($p<0.05$), but did not differ from those in Group A (1.85±0.8). The mean wall motion scores in Group B (2.3±0.5) were higher than those in Group A (1.6±0.5) ($p<0.05$), but did not differ from those in Group C (2.0±0.6). These data suggested that significant redistribution on a 4 hour delayed image (Group A) was observed more often in patients with slightly disturbed wall motion than in patients with severely disturbed wall motion. In patients without significant redistribution on a 4 hour delayed image, significant redistribution on a reinjection image was present more often in patients with coronary artery disease limited in extent.

### (3) Relationship of redistribution on reinjection image to collateral development in patients without significant redistribution on 4 hour delayed image (Group B and Group C)

Three of 4 patients in Group B had collateral development, but none of 5 patients in Group C had collateral development (Table 3). There was significant difference between Group B and Group C ($p<0.05$) in the incidence of collateral development. This suggested that significant redistribution on a reinjection image correlated to the function of collateral development in the resting state in patients without significant redistribution on 4 hour delayed images (Fig. 3).

## DISCUSSION

Additional imaging after 8 to 24 hours following the injection of thallium-201 on TSPECT was recommended to differentiate viable from nonviable myocardium.[5-7] The thallium reinjection method was also recommended to improve underestimation of myocardial viability on 4 hour delayed images.[9-13] But why the redistribution on 4 hour delayed images was improved by reinjection of thallium-201 was not sufficiently discussed.[10-13]

In this study, the thallium reinjection method has been applied to evaluate myocardial viability in the infarcted zone quantitatively with TSPECT, because the quality of reinjection images was superior to that of delayed images at 8 to 24 hours.

Cloninger et al.[5] noted that in 13 of 28 patients (46%) with myocardial infarction there was further redistribution between 4 hour and 8 to 24 hour delayed images. Brunken et al.[2] also noted that in about 40% of regions with Q waves on ECG and severe hypokinesis in a wall motion study, and considered to be myocardial infarction, metabolic activity was seen in a study with positron emission computed tomography with $^{18}$F-2-deoxy-glucose. These percentages were similar to our results showing that four of 9 patients (44%) with no significant redistribution on 4 hour delayed images had significant redistribution on reinjection images.

Kiat et al.[6] showed that in 70 of the 74 segments (95%) with late redistribution at 18 to 72 hours thallium perfusion improved after successful coronary angioplasty or bypass surgery, and considered that these segments indicated viable myocardium because redistribution represented regional distribution of the potassium pool. The frequency of redistribution which they reported was higher than that in our results because they studied patients with and without myocardial infarction. Recently, Dilsizian et al.[10] and Ohtani et al.[11] indicated that abnormal wall motion of the myocardium with significant redistribution on reinjection images improved after coronary angioplasty or bypass surgery. We also considered that the myocardium in the regions with redistribution of thallium-201 was viable. Thus, the reinjection of thallium-201 was considered to be a useful method to use in evaluating viable myocardium in the infarcted zone, as with late imaging.

The mechanism in which late redistribution images are superior to 4 hour delayed images in evaluating myocardial viability in patients with ischemic heart diseases has been discussed.[6,14] Gutman et al.[14] showed that late redistribution, seen at 18 to 24 hours after injection of thallium-201, was present in 23 of 107 defects (21%) on the immediate postexercise images and that the time to complete redistribution correlated with the severity of relevant coronary artery stenosis. In this condition, myocardial blood flow in the regions supplied by severely stenosed coronary artery might be reduced in the resting state as well as during exercise and the equilibrium of thallium-201 in the potassium pool was not reached within 4 hours.[12,13] Reinjection imaging helped in reaching this state of equilibrium.[12,13]

A low plasma thallium-201 concentration induced a lack of redistribution in the ischemic myocar-

dium.[12,13] Reinjection of a small amount of thallium-201 might cause significant redistribution on reinjection images by increasing the plasma thallium-201 concentration.[12,13]

Gutman et al.[14] also noted that late redistribution was a consequence of stenosis of both relevant and non-relevant coronary arteries. Late redistribution was obtained when the slow washout of thallium-201 resulting from reduced coronary arterial flow was seen in both segments supplied by relevant and non-relevant coronary arteries. Thus, this phenomenon was seen in patients with multivessel disease. However, in the present study significant redistribution on reinjection images significantly increased in patients with single and double vessel disease, but not in patients with triple vessel disease. These results were considered to be incompatible with the results shown by Gutman et al.[14] The mechanism by which the perfusion defect improved on reinjection images might be different from by which the perfusion defect improved on the late redistribution image.

Reinjection images were thought to reflect the myocardial blood flow in the resting state when there was no difference between stenosed and non-stenosed coronary arterial flow. Therefore, the distribution of thallium-201 into viable myocardium in the infarcted zone might be apparent when the thallium-201 was administered in the reinjecting state. This was considered to be one of the reasons why reinjection images were superior to 4 hour delayed images in detecting viable myocardium. But in this study, severely relevant coronary artery stenosis was present in all three groups. When the relevant coronary arterial flow was severely reduced, the flow into the infarcted zone from other regions supplied by non-relevant coronary arteries was considered to be an important factor in determining whether or not viable myocardium exists in it. The degree of stenosis of the non-relevant coronary artery was also an important factor. In this study, coronary artery disease limited in extent and collateral development were observed to be more often in patients with significant redistribution on reinjection images (Group B) than in patients without it (Group C). The function of collateral development in the resting state was therefore considered to relate to the mechanism by which redistribution on a 4 hour delayed image was improved by the reinjection of thallium-201.

Thallium-201 exercise scintigraphy is the method used in evaluating myocardial viability, but it reflects only myocardial perfusion. However, in precise evaluation of myocardial viability, another method is needed. At present, positron emission computed tomography with ^{18}F-2-deoxy-glucose is the best method to use in assessing the myocardial viabil-

ity.[2-4,13,15,16] But it can not be used in every institution. We could not evaluate incomplete redistribution in the infarcted zone in this study. Further investigation may be needed with more materials for more reliable statistical analysis.

## CONCLUSION

It is important to assess the myocardial viability in the infarcted zone because it is one of the significant criteria for percutaneous transluminal coronary angioplasty and coronary bypass surgery. In the present study, reinjection images proved to be useful in evaluating of myocardial viability in the infarcted zone. Significant redistribution on reinjection images correlated to the small extent of coronary artery disease and collateral development. The appearance of redistribution from 4 hour delayed imaging to reinjection imaging might also reflect the function of collateral development in the resting state in patients without significant redistribution on 4 hour delayed images. We conclude that reinjection imaging is recommended for patients with no or partial redistribution on 4 hour delayed images.

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