# ASSESSMENT OF MYOCADIAL VIABILITY BY RE-INJECTION $^{201}$TI MYOCARD PERFUSION SPECT AND CORRELATION OF RESULTS BY CORONARY ANGIOGRAPHY

Nahide GÖKÇORA, M.D., Neşe İLGİN, M.D., Gülin VURAL,
Halis DÖRTLEMEZ*, M.D., Övsev DÖRTLEMEZ*, M.D., Aydın AKSOY*, M.D.,
Mehmet ALKAN*, M.D., Hikmet BAYHAN**, M.D.

**Gazi University, Faculty of Medicine, Departments of Nuclear Medicine and Cardiology*, GATA Military Medical School, Department of Nuclear Medicine**, Ankara, Turkey**
**Gazi Medical Journal 3 : 151-155, 1992**

***SUMMARY :*** *Stress Thallium-201 ($^{201}$TI) myocardial perfusion imaging studies are useful in differentiating viable, reversibly ischemic areas from infarcted myocardium. This study involves the intravenous administration of an additional 1 mCi of $^{201}$TI and the search for the reversibility in 26 of the 66 patients with coronary artery disease who had perfusion abnormalities on their post-exercise images. New fill in after re-injection was observed in 17 of the 47 segments (36 %) showing persistent defect on the stress and delay images. When the angiographic results were compared with $^{201}$TI re-injection myocardial perfusions there were no statistically significant differences ($p>0.05$). The angiographic narrowing was 92+/-9.53 % for the segmental fixed defects showing fill in after re-injection. It is believed that the severity of the coronary artery lesion highly affects the early or late reversibility of the stress and delay defects observed by $^{201}$TI SPECT. Since the single injection method for the detection of ischemic myocarium is not as sensitive as double injection method it should be in use for the accurate assessment of the viable but jeopardized myocardium.*

***Key Words :*** *$^{201}$TI Stress Imaging, $^{201}$TI Delay Imaging, Re-Injection, Coronary Angiography.*

## INTRODUCTION

At present, $^{201}$TI myocardial scintigraphy is performed according to the stress/redistribution approach introduced by (Pohost et al. 1977) where imaging is performed after a single injection of $^{201}$TI at peak exercise and then 3-4 hrs later. A reversible abnormality between the initial and delayed images is considered ischemia, while a persistent defect is considered as scar. With the stress/redistribution approach two different phenomena are studied; perfusion with the initial images and the potassium-pool within the myocardium as an indication of viability with delayed images.

This approach has simplified the original method for $^{201}$TI scintigraphy which was done with two separate injections: the first at the peak exercise and the second at rest after and interval of several days.

In recent studies, the extent of presence of prior myocardial infarction is often over-estimated by the standard redistribution technique and especially if $^{201}$TI scintigraphy is performed to assess myocardial viability, a second rest injection is suggested. Recently, (Gibson et al. 1983) reported that after by-pass surgery normal thallium uptake was demonstrated in 45 % of persistent defects

detected on the standard 4 hrs delayed images.

Furthermore, (Gutman et al. 1983) reported that the time to complete redistribution after stress injection appeared related to the severity of the stenosis in the coronary artery supplying the defect. In this study, 21 % of the $^{201}$TI defects, persistent after 4 hrs showed redistribution after 18-24 hrs. Based on this observation, they introduced the 24 hrs $^{201}$TI delayed imaging as a more accurate method to detect viable myocardium. Further confirmation of 24 hrs delayed $^{201}$TI imaging as a better method for the asessment of viable myocardium has been provided by the studies performed with positron emission tomography (PTE) (Brunken et al. 1987). Reported that, 47 % of fixed defects hinted by $^{201}$TI SPECT showed significant uptake of $^{12}$F fluorodeoxyglucose as evidence of viable myocardium. On the basis of these observations suggesting that dual injection approach could be more sensitive to detect ischemia. (Rocco et al. 1988), recently described a method of $^{201}$TI re-injection imaging, using a second smaller dose of 37 MBO (1mCi) of $^{201}$TI injected at rest (re-injection) immediately after the redistribution image, instead of several days later.

## MATERIALS AND METHODS

66 consecutive patiets with documented coronary artery disease showing perfusion abnormality on the post-exercise $^{201}$TI SPECT, were selected for this study.

Coronary artery disease was determined based on significant narrowing (> 70 %) on coronary angiogram or perfusion abnormality on stress $^{201}$TI imaging. There were 46 men and 20 women, ranging in age from 35 to 70 years (mean 56.22). Sixteen patients had documented myocardial infarction, based on ECG criteria or clinical history. Six patients showed anterior wall myocardial infarction, 4 had lateral wall infarction and 6 had inferior wall infarction based on the location of Q waves on ECG.

## EXERCISE $^{201}$TI STUDY PROTOCOL

All patients underwent graded treadmill exercise according to the Bruce Protocol and termination criteria were achieving maximal heart rate, fatigue dyspnea, chest pain or ST segment changes of more than 2 mm. All patients were instructed to withhold beta-adrenergic blockers or calcium antagonist medications for 48 hrs and long-acting nitrates for 6 hrs before stress testing at near maximal exercise. 3 mCi of $^{201}$TI was injected and the exercise was continued for an additional minute. The patients were imaged with use of GE Starcam 2000 CRT at 5-10 minutes and 4 hours after $^{201}$TI injection. 32 projections were obtained over a semi-circular 180 degree extending form the 45 degree LPO. All images were stored on a magnetic disk using a 64-64 matrix; and quality control measures, filtering and tomographic reconstruction protocol was carried out.

The present study involved a previously described sagittal and oblique tomograms, parallel to the long and short axis of the left ventricle, extracted from the filtered transaxial tomograms. No attenuations or scatter correction were used. The thallium -$^{201}$ myocardial tomograms were divided into 5 segments for each patient (1=apex, 2=anterior, 3=lateral, 4=inferior, 5=septum) and all tomographic images were scored by and experienced observer using a 4 point scoring system (0=normal, 1=equivocal, 2=moderate, 3=severe reduction of $^{201}$TI uptake) without knowledge of the clinical history, ECG results or the coronary angiography. The criteria or reversibility were, as previously described (Pohost et al. 1977). In brief, a perfusion defect was considered present when a myocardial segment had an initial post-stress score >/=2. Stress defects with a visual score = < 2 at 4 hrs imaging was called reversible and more than or equal to 2 were called irreversible.

A second injection dose of 1 mCi $^{201}$TI was applied and after 15 minutes a second imaging was performed for these irreversible defects. Again the defects with >/= score 2 were evaluated. Coronary arteriography was performed within 50 days of the $^{201}$TI study using the standard Judkins approach. The arteriograms were interpreted by an experienced cardiologist without knowing the $^{201}$TI results. Each coronary lesion was graded as severe (>99-90 %), moderate (75-90 %) or mild (>75 %) in accordance to its luminal diameter narrowing. The angiographic data was statistically analyses using student's t test and ECG results were compared by using McNemar's test.

## RESULTS

Among the 66 patients showing coronary perfu-

sion abnormalities, on the post- exercise $^{201}$TI SPECT, 40 patients had redistribution at least in one myocardial segment, and the remaining 26 patients had no redistribution in any portion of the myocardium during the rest imaging. The re-injection and $^{201}$TI SPECT identified new "fill in" in 9 among these 26 patients (36 %). 17 out of 47 defective segments in these 26 patients showed reversibility after re-injection, whereas 30 segments (66 %) had persistent defects after re-injection (Table, Fig 1, 2). When angiographic results of these $^{201}$TI SPECT re-injection positive and negative cases were compared, there were no statistical significance between angiographic narrowing of the segments which showed new fill in after the re-injection ($p>0.05$). The mean luminal narrowing was 92 +/-9.53 % for the segments showing fill in and 97 +/-4.33 % for the segments showing no fill in after re-injection (Table 2).

The ECG results and $^{201}$TI SPECT results were confirming each other at a level of 78 % ($x2=0.03>0.05$) when the frequency of observing the OS pattern was compared with the frequency of the persistent defect seen in $^{201}$TI exercise myocardial perfusion SPECT (Table 3).

| Stress | Delay | Re-injection | n | % |
|---|---|---|---|---|
| Normal | Normal | Normal | 223 | 67.6 |
| Defect | Redistribution | Fill-in | 60 | 18.2 |
| Defect | No-redistribution | New fill-in | 17 | 5.1 |
| Defect | No-redistribution | No fill-in | 30 | 9.1 |
| **Total** | | | **330** | **100** |

Table - 1 : Number of segments in each step based on $^{201}$TI findings.

| Group | n | < 90 % | =or> 90 % |
|---|---|---|---|
| Re-injection fill-in | 17 | 4 | 13 |
| Re-injection no fill-in | 30 | 7 | 23 |

Table - 2 : Severity of narrowing on coronary arteriograms in relation to $^{201}$TI defects.

| Group | non-Q wave | Q wave |
|---|---|---|
| Re-injection fill-in | 20 | 3 |
| Re-injection no fill-in | 3 | 21 |

Table - 3 : Distribution of the segmental defects showing Q wave on ECG.

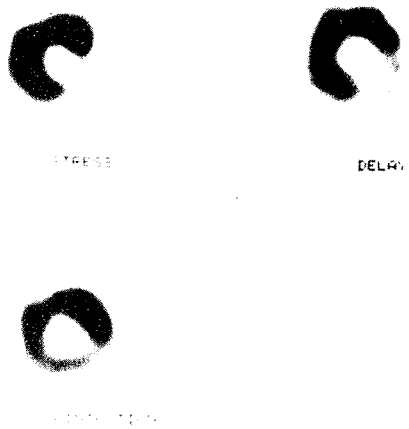


Fig. 1 : Three representative short axis slices of post-exercise, 3 hr delayed and re-injection imaging of a patient with lateral wall infarction. The re-injection imaging shows new fill-in of the tracer in infero-lateral regions.

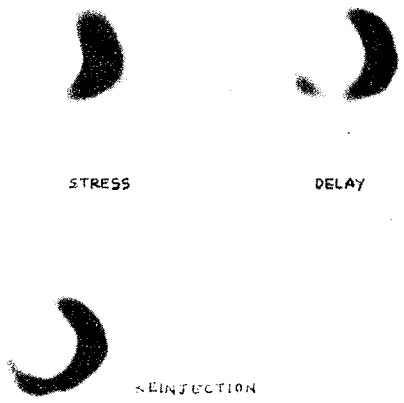


Fig. 2 : Three representative short axis slices of post-exercise, 3 hr delayed and re-injection imaging from a patient with antero-septal myocardial infarction.

## DISCUSSION

The assessment of myocardial viability by using standard imaging techniques is often imprecise. No criteria have been found to accurately distinguish hibernating myocardium from myocardial fibrosis on the basis of regional ventricular function measurements obtained by contrast ventriculography or radionuclide angiography. Moreover, several studies have demonstrated that between 25 % and 50 % of the patients with apparently irreversible perfusion defects on exercise/rest $^{201}$TI imaging may have a manifestation of normal $^{201}$TI uptake at rest after re-vascularization (Brundage et al. 1984; Rozanski et al. 1981). Thus $^{201}$TI scintigraphy when routinely performed as an exercise study followed by 3-4 hrs redistribution imaging,

may be inadequate in identifying viable myocardium. It has now been shown that late $^{201}$TI redistribution imaging at 8-72 hrs will detect thallium uptake in a large number of myocardial regions that appears to have irreversible defects at 3-4 hrs (Cloninger et al. 1988). However, late imaging after 24 hrs provides unsatisfactory images due to relatively low counting efficiency and poor image quality (Kiat et al. 1988). As an alternative approach to this issue (Dilsizian et al. 1990), applied a new method and demonstrated that the re-injection of a small amount of $^{201}$TI at rest immediately after 3-4 hrs of redistribution imaging resulted in enhanced thallium uptake in 30-50 % regions with apparently irreversible defects on the redistribution images.

This increased regional thallium activity after re-injection represented viable myocardium, which was confirmed by the results of coronary angioplasty. In a subset of patients improvement in regional thallium uptake and wall motion at rest after coronary angioplasty occured in 87 % of the irreversible defects manifesting enhanced thallium activity after re-injection on the preangioplasty studies, whereas such improvement in regional perfusion and function after angioplasty occured in none of the segments that remained irreversible after thallium re-injection images taken before angioplasty (Dilsizian et al. 1990; Ohtani et al. 1990).

Furthermore (Bonow et al. 1991), suggested that exercise $^{201}$TI scintigraphy with rest re-injection provided information comparable to that obtained by PET in identifying viable myocardium in patients with chronic coronary artery disease.

Using SPECT imaging Hansen et al. compared iodine-123 pentadecanoic acid (IPPA) to thallium-201 in patients with chronic ischemic heart disease. They demonstrated that, regions of myocardial ischemia were identified as areas of increased uptake and/or delayed clearence of IPPA. These regions corresponded to the areas of reduced thallium uptake (Heo et al. 1988).

This study highlights the effects of re-injection $^{201}$TI SPECT to detect viable myocardium in patients exhibiting no redistribution on their routine stress and delayed scan. Comparison of the angiographic findings observed in segments showing new fill-in after re-injection with that of the segments showing no fill-in after re-injection.

New fill-in by re-injection $^{201}$TI SPECT imaging in approximately one-third of the segments with persistent defect on the routine imaging was observed. In comparison with ECG findings, 30 % of those showing new fill-in in after re-injection had Q waves on ECG (Brunken et al. 1986) also showed persistent metabolic activity on PET in approximately 50 % of the Q wave regions. Thus, the segments exhibiting Q waves on ECG may not always represent irreversible myocardium. Furthermore, the re-injection imaging identified new fill-in in 12 segments of the 16 segments showing no Q wave on ECG but no redistribution on the delayed images.

When the angiographic data was compared; the mean luminal narrowing (97+/- 4.33 %) for the segments showing no fill-in after re-injection was more than the mean luminal narrowing for the segments showing new fill-in after re-injection (92+/- 9.53 %). This difference was not statistically significant ($p>0.05$). It was concluded that, the severity of the coronary artery lesion can cause prolongation of the tracer delivery to the ischemic area due to lack of post-stress hyperemia or resting hypoperfusion, so that equilibrium of $^{201}$TI in the potassium pool is not reached within 2-4 hrs. In this respect, the re-injection or late redistribution imaging may help to reach this equilibrium stage and may identify new fill-in of the tracer in severely ischemic myocardium (Cloninger et al. 1988; Kiat et al. 1988; Tamaki et al. 1990). The present data is consistent with previous reports, suggesting that approximately 30 % segmental perfusion defects assigned by conventional delayed imaging show fill-in after rest re-injection. Since these segments had Q wave on ECG less often than those with no fill-in even after re-injection, they should be seperately assessed for future treatment.

The authors believe that, $^{201}$TI re-injection delayed imaging protocol prevents the Nuclear Medicine physician from over-estimation of the size of infarctions with coronary artery disease and the severity of the coronary lesion highly affects the early or late reversibility of the stress and delay defects observed by $^{201}$TI SPECT.

Re-injection $^{201}$TI imaging should be performed when no re-distribution was observed on the delayed images, and it may hold promise for identifiying severely ischemic but potentially viable myocardium.

**Correspondence to :** Dr.Nahide GÖKÇORA
Gazi Üniversitesi Tıp Fakültesi
Nükleer Tıp Anabilim Dalı
Beşevler
06510 ANKARA - TÜRKİYE
Phone : 4 - 212 65 65 / 415

**REFERENCES**

1. Bonow R, Dilsizion V, Cuocola A : Identification of viable myocardium in patients with chronic coronary artery disease and left ventricular dysfunction. Comparison of thallium scintigraphy with re-injection and PET imaging with $^{1e}$ F-fluorodeoxyglucose. Circulation 83 : 26-37, 1991
2. Brundage BH, Massie BM, Botvitnick EH : Improved regional ventricular function after successfull surgical revascularization. J Am Coll Cardiol 3 : 902-908, 1984
3. Brunken R, Tillisch J, Schwaiger M : 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 73 : 951-963, 1986
4. Brunken R, Schwaiger M, Grover-McKay M : Positron emission tomography detects tissue metabolic activity in myocardial segments with pesistent thallium perfusion defects. JACC 12 : 557-567, 1987
5. Cloninger KG, DePuey EG, Garcia EV: Incomplete redistribution in delayed thallium$^{-201}$ single photon emission tomography images : An over-estimation of myocardial scarring. JACC 12 : 9945-9963, 1988
6. Dilsizian V, Rocco TP, Freedman NMT : Enhanced detection of ischemic but viable myocardium by the re-injection of thallium $^{-201}$ after stress-redistribution imaging. N Eng J Med 323 : 141-146, 1990
7. Gibson RS, Watson DD, Taylor GJ : Prospective assessment of regional myocardial perfusion before and after coronary revascularization surgery by quantitative thallium$^{-}$ $^{201}$ scintigraphy. JACC 1 : 804-815, 1983
8. Gutman J, Berman DS, Freeman M : Time to complete redistribution thallium$^{-201}$ in excercise myocardial scintigraphy; Relationship to the degree of coronary artery stenosis. Am Heart J 106 : 980-995, 1985
9. Heo J, Herman GA, Abdulmassih S : New myocardial perfusion imaging agents : Description and applications. Am Heart J 115 : 1111-1117, 1988
10. Kiat H, Berman DS, Maddahi J : Late reversibility of tomographic myocardial thallium $^{-201}$ defects : On accurate marker of myocardial viability. JACC 12 : 1456-1463, 1988
11. Ohtani H, Tomakin N, Yonekura Y : Assessment of resting thallium$^{-201}$ re-injection after stress-delayed $^{201}$ TL imaging : Comparison with 24 hour scan and regional wall motion. Kaku Igaku 27 : 9-15, 1990
12. Pohost GM, Zir LM, Moore RH : Differentiation of transiently ischemic from infarcted myocardium by serial imaging after a single dose of $^{201}$TI. Circulation 55 : 294-302, 1977
13. Rocco TP, Dilsizian V, Maltais F : Thallium-201 re-injection after delayed imaging demonstrates fill-in to regions with fixed defects. J Nucl Med 29 : 769, 1988
14. Rozanski A, Berman DS, Gray R : Use of thallium-201 redistribution scintigraphy in the preoperative differentiation of reversible and non-reversible myocardial asynergy. Circulation 64 : 936-944, 1981
15. Tamaki N, Ohtani H, Yonekura Y : Significance of fill-in after thallium -201 re-injection following delayed imaging comparision with regional wall motion and angiographic findings. J Nucl Med 31 : 1617-1623, 1990