

Thallium-201: An Agent for Myocardial Perfusion and Viability Imaging

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Myocardial perfusion imaging (MPI) was first viewed as an alternative to coronary angiography for detecting coronary artery disease (CAD). A more appropriate and probably more important use is for the demonstration of myocardial ischaemia and detection of viable myocardium. In these latter applications, MPI is complimentary to coronary angiography and provides information relevant to patient management. Thallium-201 was first proposed and introduced for MPI in early seventies^{1,2}. Since then thallium has evolved as an important diagnostic modality aiding significantly in the diagnosis and management of patients with CAD. Physical Properties and Biokinetics of ²⁰¹Tl: It is a cyclotron produced radionuclide having a half life of about 73 hrs which allows convenient preparation and shipment of the material. A relative disadvantage of ²⁰¹Tl-201 is the low photon energy (68-80 keV) which results in significant tissue attenuation and scatter, degrading the images. Less than 40 sec after an i.v. injection approximately 50% of ²⁰¹Tl-201 is extracted by various tissues of the body. Myocardial extraction efficiency is extremely high -about 88% of thallium that reaches the myocardial cells will be taken up and concentrated intracellularly. The cellular uptake is mediated by active transport through Na-K ATPase pumps. Typically 4-5% of the injected dose concentrates in the myocardium while the remainder is distributed throughout other tissues³. The largest radiation dose is absorbed by the kidneys. The renal dose varies from 0.84-1.34 rad/mCi and whole body radiation is 0.21 rad/mCi⁴. Localization of ²⁰¹Tl-201 in the myocardial cells involves two phases:

a) Initial distribution:

The initial myocardial concentration of thallium is equal to the product of myocardial blood flow and extraction fraction.

b) Redistribution:

This concept was put forward by Pohost et al,⁵ in 1977 and during this phase thallium initially taken up by the well perfused myocardial and skeletal muscles slowly begins to migrate out of the cells into the blood stream (wash out). Therefore, the difference between intracellular concentration of thallium in well perfused and ischaemic cells decreases over time, as the large amount of the thallium concentrated within the well perfused cells tend to be reabsorbed by the blood stream and transported to adjacent ischaemic tissue. It has been demonstrated that significant redistribution may occur as early as 20 min after injection and it is normally completed by 4 hours. Based on these facts, ²⁰¹Tl defects may be classified as completely reversible, partially reversible and irreversible defects (i.e. infarction). However, in a recent study it has been found that 30% of irreversible defects at 4 hrs redistribution images did show viability (redistribution) after 24 hr or 30-60 min after a second dose of thallium given after 4 hr redistribution image (re-injection)⁶.

c) Reverse Redistribution:

In 5-7% of cases, the phenomenon of reverse redistribution may be seen which is defined as the appearance of new perfusion defects or worsening of stress induced defects on redistribution images. Previously it was considered as having correlation with significant CAD but recent studies do not show any such relationship⁷.

Patient Preparation

1) The patient should be kept fasting for at least 4 hours prior to the study to minimize the splanchnic uptake.

- 2) To avoid interference with physiological stress induced heart rate response, all beta-blocker and calcium channel antagonist should be discontinued about 24-48 hrs before the test.
- 3) An i.v. cannula of about 20G is inserted in a large vein (median cubital vein) for effective bolus administration of ^{201}TI .
- 4) FCC electrodes are placed for recording of 12 leads FCC at rest, during exercise and recovery phase.

Stress Test

Patient is stressed according to Bruce protocol consisting of seven-3min stages of progressively increasing speed and angle (treadmill) or load (ergometer bicycle). During the whole exercise BP, pulse and ECG is recorded for every stage of the test. For optimal results, the patient should attain 90% of his predicted maximal HR (100% 220-age in years). Accepted end points of exercise before the desired FIR is achieved are i) angina, ii) severe fatigue and dyspnea, iii) hypotension, iv) severe arrhythmia and v) significant ST depression. At peak exercise (or symptom limited end point of exercise) about 74 MBq (2 mCi) of ^{201}TI is injected i.v. as bolus and the patient is encouraged to maintain the reactant level of stress for another 1-2 min to ensure proper thallium delivery to the myocardium and minimum splanchnic pooling.

Thallium-201 Dipyridamole Test

In a significant number of patients requiring evaluation of CAD, stress ^{201}TI is not feasible due to either limited exercise tolerance, musculoskeletal problem like arthritis or paralysis or amputation of a limb, LBBB, previous non-diagnostic ECG and if the patient is really dependent on beta-blockers or calcium channel blockers. In such cases pharmacological intervention with dipyridamole (persantin) is recommended. Dipyridamole, a pyrimidine derivative, induces myocardial hyperaemia by elevating the endogenous adenosine level which is a potent vasodilator. Myocardium supplied by a coronary artery with significant stenosis will demonstrate reduced perfusion and consequently diminished thallium-201 uptake if injected within minute after the coronary vasodilatation by dipyridamole. The presumed mechanism includes increase in coronary blood flow, 3-5 times over baseline; and coronary steal phenomenon to areas with normal coronary artery supply. A typical protocol for dipyridamole ^{201}TI imaging includes 0.568 mg/kg of dipyridamole infused over a period of 4 min followed by a bolus of 74 MBq (2mCi) of ^{201}TI 3-4 min later. Systemic and cardiac side effects can occur of which headache, dizziness, angina and ST depression are most common. Aminophylline, a xanthine derivative, in a dose of 50-200 mg i.v. can effectively counteract the systemic and local side effects⁸. In a large multicentric study no significant difference was found regarding the sensitivity and specificity of thallium stress and dipyridamole testing. However, angina occurred more frequently in conjunction with thallium stress test (63%) than with dipyridamole (31%)⁹.

Imaging

Imaging of ^{201}TI uptake should start within 3-10 min after the injection of tracer. A standardised protocol with strict quality control is necessary to ensure high diagnostic quality. Planar images are acquired in anterior, left anterior oblique 45 and 70 degree (LAO 45° & 70°) position followed by 3-4 hr delayed (redistribution) images. Alternatively, single photon emission computerized tomography (SPECT) imaging can be obtained started with an acquisition protocol shortly after the thallium injection and a repeat acquisition 3-4 hr later with identical parameters. In patients where the viability of myocardium in an affected territory is questioned, delayed images after 24 hr are acquired.

Alternatively, after 4 hr redistribution images another dose of 37 MBq (1 mCi) of ^{201}TI is injected at rest followed by acquisition of another set of images with identical parameters.

Thallium Images

The normal myocardial perfusion images at stress and rest show uniform distribution of the tracer (^{201}TI) over left ventricle with a central photon deficient area concomitant with ventricular cavity (Figures 1 and 2).

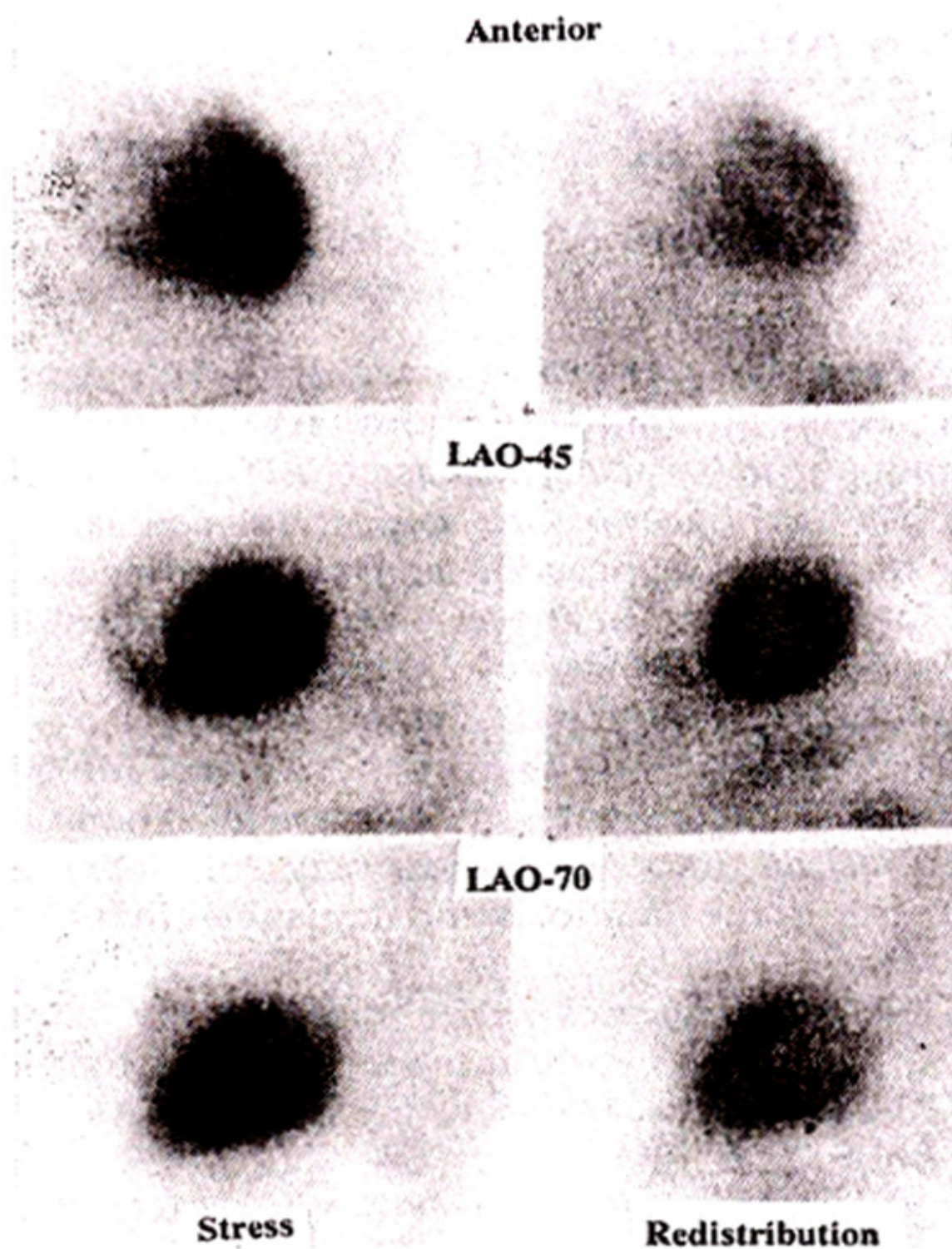


Figure 1: Stress and 3 hr redistribution (rest) Tl-201 images in a normal volunteer.

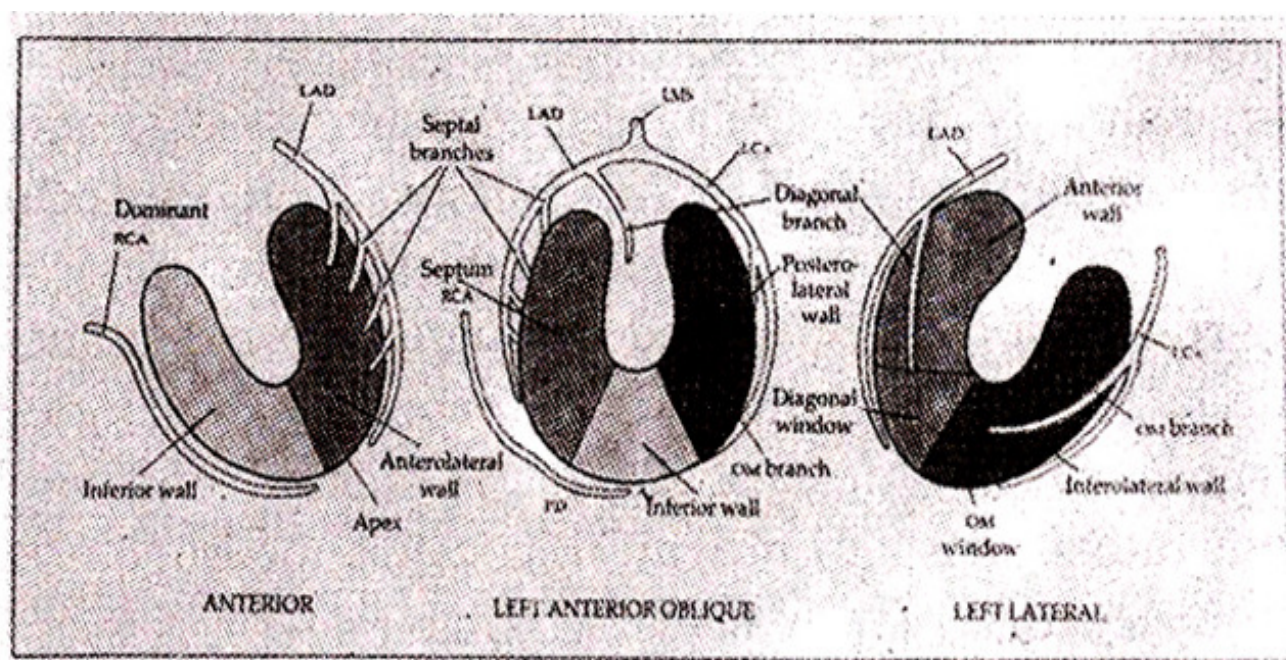


Figure 2: Diagrammatic representation showing different myocardial segments and their blood supply.

Areas of reduced perfusion (perfusion defect) on stress images is suggestive of myocardial ischaemia and it is the disappearance or persistence of this perfusion defect on redistribution image which decides about the reversible or irreversible (infarct) nature of the ischaemia respectively (Figures 3 and 4).

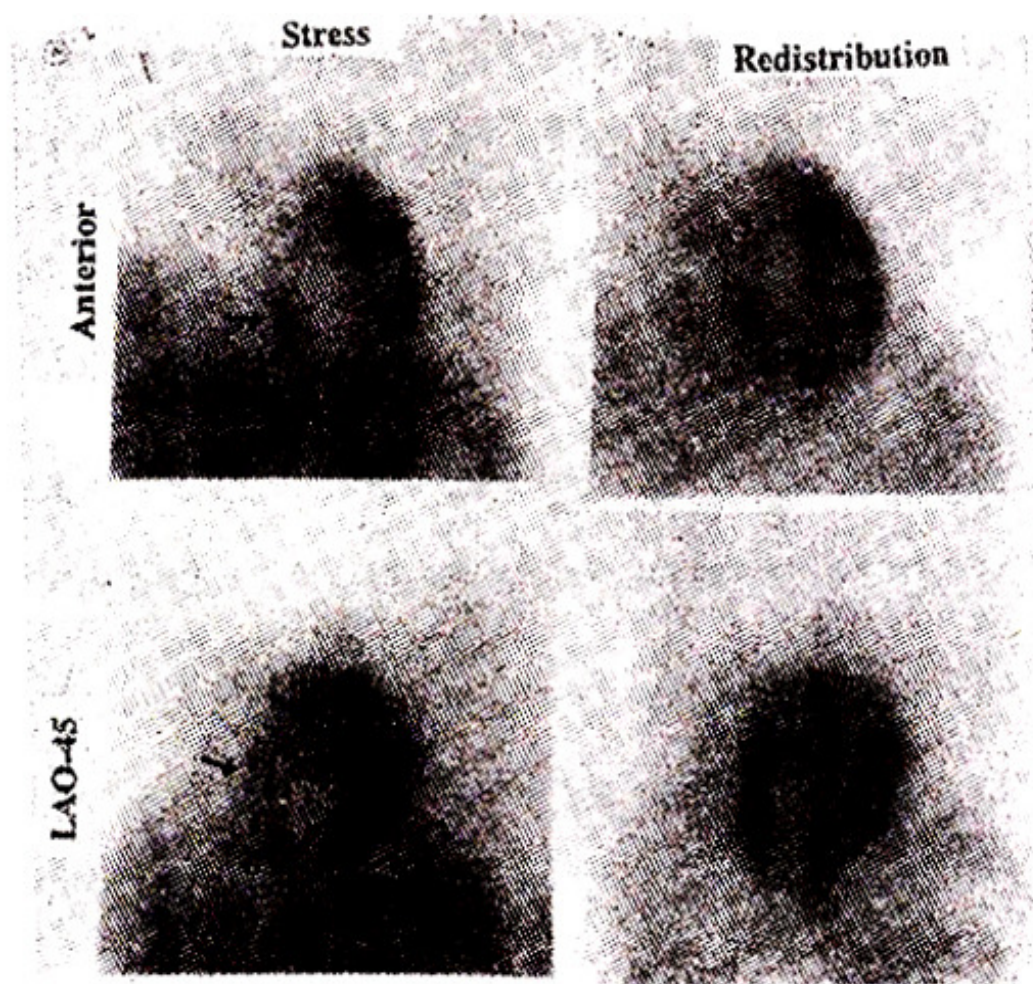


Figure 3: Stress Tl-201 images showing significant "reversible" ischemia of the inferior wall and septum in the anterior and LAO 45° views respectively (arrow head).

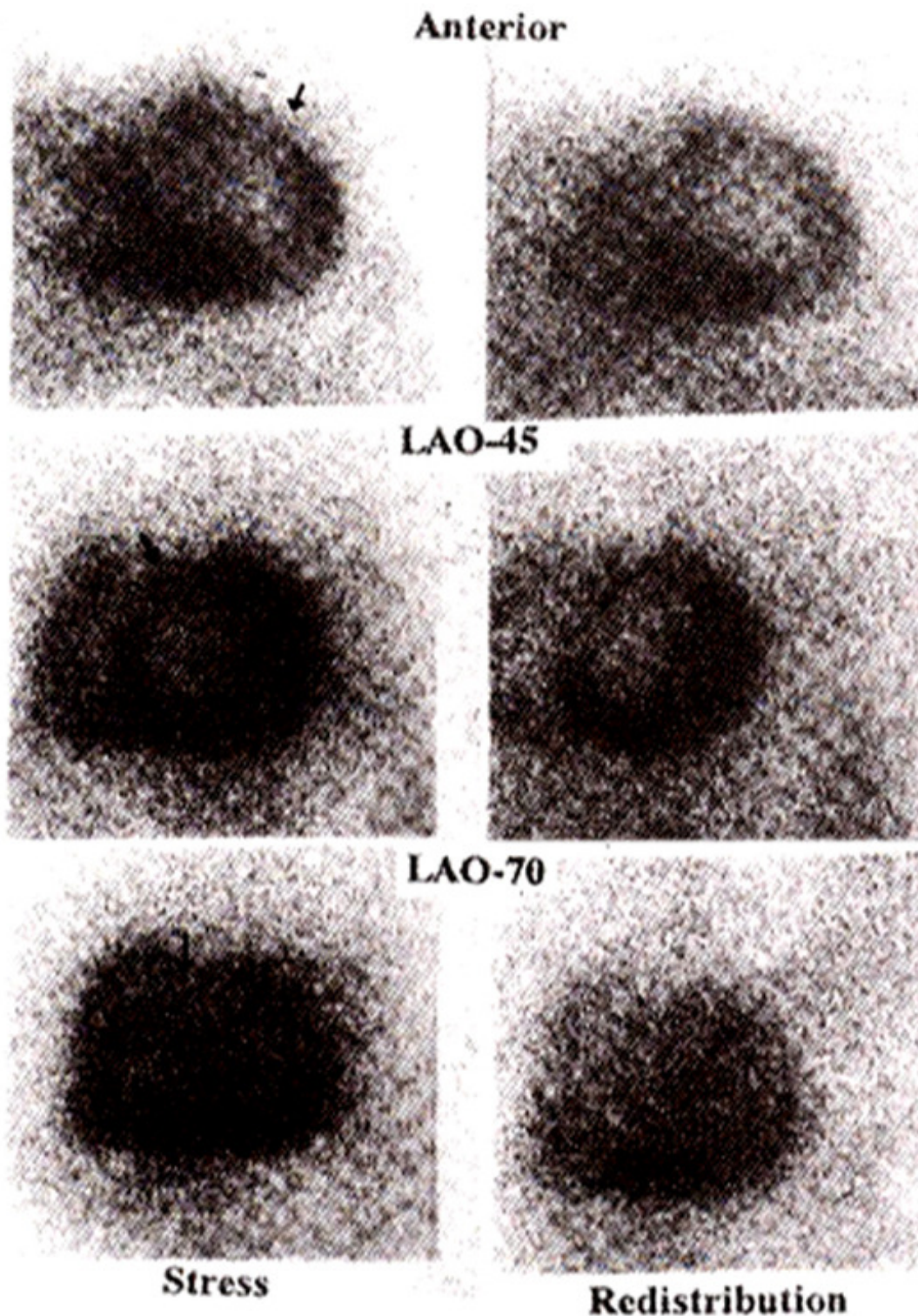


Figure 4: Stress Tl-201 study showing moderate "irreversible" anteroseptal ischemia (arrow head).

The right ventricle is not normally visualized on the rest images and only faintly on exercise images. It is due to 3 times lesser myocardial mass and 10% lesser perfusion of the RV. Pronounced visualization of the RV is seen in cases of RV hypertrophy, pulmonary hypertension or extensive LV infarction. Non-visualization or perfusion defect in RV on stress images is seen in 30% cases of inferior wall

myocardial infarction (Right Coronary Artery territory). Increased lung uptake of Thallium-201 can occur on the initial images immediately after exercise. This is an important marker of exercise induced LV dysfunction and can be correlated with an abnormally increased ED left ventricular pressure and capillary wedge pressure. This highly abnormal finding is most often seen in patients with significant CAD, frequently related to multivessel disease. In occasional patients with “balanced coronary disease” this phenomenon of increased lung uptake may be present as the only abnormality without perfusion defect¹⁰.

Sensitivity and Specificity of ²⁰¹Tl Test

Exercise ²⁰¹Tl imaging has a sensitivity and specificity in the range of 80- 90% as compared with a sensitivity of 60-70% for exercise ECG¹¹. The accuracy of detecting an individual stenosis is dependent on several factors. These include the severity of stenosis and also the number of vessel involved. Because thallium-201 imaging is based on relative distribution of tracer, the region with the most severe reduction in blood is the region with a visual thallium defect; in patients with multivessel or tripple vessel disease of same severity, no perfusion abnormality may be appreciated (false negative). The sensitivity for three major coronary vessels is usually best for left anterior descending artery, intermediate for right coronary artery and relatively less for left circumflex artery.

Clinical Applications

The clinical utility of thallium-201 imaging depends to a great extent on its predictive value. It should be remembered that a positive test result in a group with a high probability of disease pre-test adds little to the diagnostic accuracy beyond that achieved by a proper clinical evaluation. A negative test in a group with a low probability of disease pre-test only confirms that pre-test low likelihood of CAD. Therefore, the patients most suited for thallium stress scanning are those with moderate likelihood of CAD as symptomatic individual with negative ECG or vice-versa. Thallium imaging may also be used to evaluate patients who have undergone coronary artery bypass graft (CABG), patients who have had AMI and to monitor the result of percutaneous transluminal coronary angioplasty (PTCA). In this latter group of patients the suggested clinical procedure is to image the patients prior to PTCA and then again three or more days following the angioplasty. Single Photon Emission Computerized Tomography (SPECT) imaging allows the quantitation of the size and extent of the lesions, in particular infarct. It also offers a better ability to diagnose the extent of CAD as compared to planar images. However, it should be emphasized that planar imaging when combined with quantitative analysis of circumferential profiles is an adequate clinical method for diagnosing the presence or absence of CAD¹².

Detection of Viable “Hibernating” Myocardium

Identifying preserved myocardium viability in the presence of severe left ventricular dysfunction is becoming increasingly more important for clinical decision making in identifying which patients with CAD will most benefit from revascularization (CABG, PTCA). In recent years there has been a greater appreciation among clinicians for recognising the phenomena of ‘stunned or hibernating’ myocardium^{13,14}. Both of these pathophysiologic states may result in profound regional LV dysfunction in the absence of necrosis. Assessing regional systolic function alone by such technique as 2D echo, radionuclide angiography or contrast ventriculography is insufficient to distinguish between irreversibly injured and viable but dysfunctional myocardium. Myocardial thallium imaging of perfusion and metabolism can provide clinically relevant information pertaining to myocardial viability in the presence of regional and global myocardial systolic dysfunction. This ability to differentiate between acute necrosis or scar from viable but asynergic myocardium can assist the clinician in identifying the patients with CAD who might benefit most from bypass surgery or angioplasty (Figure 5).

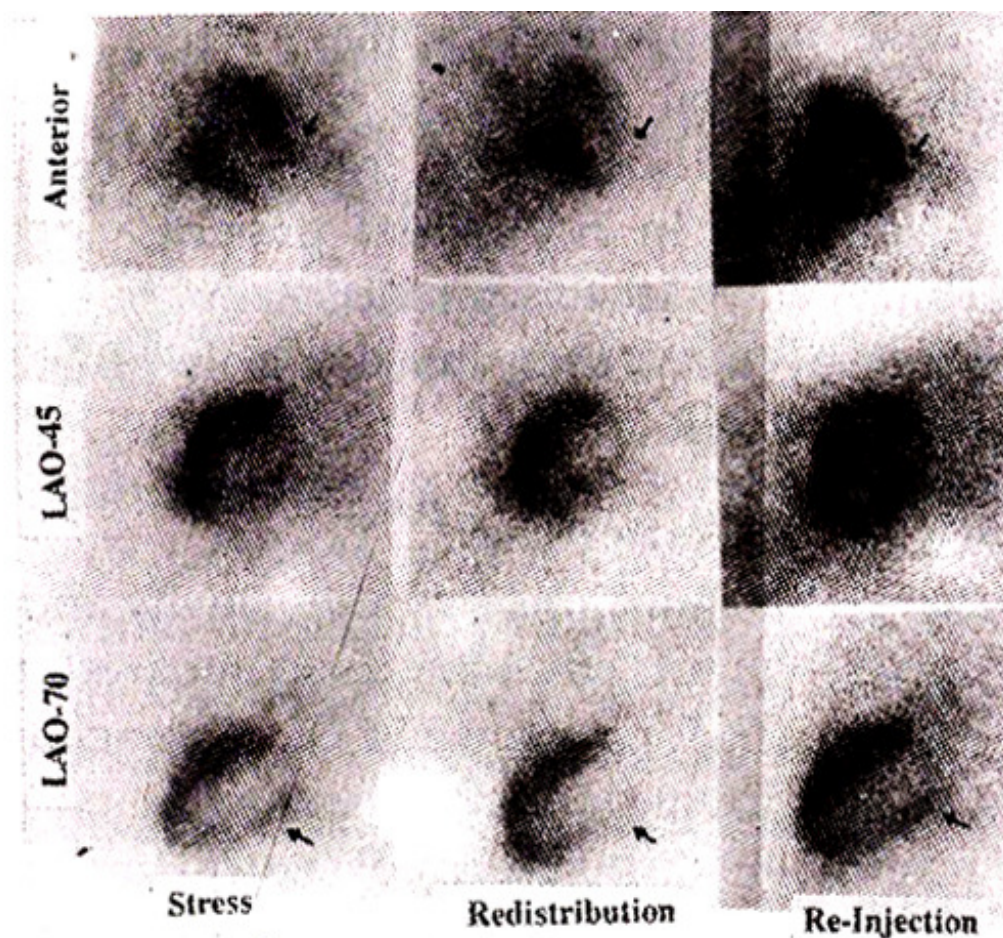


Figure 5: Stress and 3 hr redistribution Tl-201 images showing "fixed" perfusion abnormality in the lateral and posterior wall in LAO 45° and 70° views (arrow head). After reinjection of Tl-201 fair localization of tracer seen in these defects (hibernating myocardium).

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