

Thallium 201 Myocardial Imaging

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In recent years technological advancements in nuclear medicine have resulted in increasing interest in the use of radioisotope techniques in the evaluation of cardiac disease, and cardiovascular nuclear medicine has developed into a useful noninvasive tool in clinical cardiology. Myocardial infarct imaging with technetium-99m pyrophosphate has been demonstrated to be a reliable method in the diagnosis of suspected myocardial infarction.^{1,2} Radioisotope cardiac flow studies are useful in the diagnosis and follow-up of congenital heart disease,³ and gated cardiac blood pool imaging is emerging as an important technique in the evaluation of left ventricular function and ejection fraction.^{4,5} One of the more promising recent applications of nuclear medicine in cardiology has been the development of myocardial perfusion imaging in the evaluation of coronary artery disease. Thallium 201 is the major radioisotope employed in myocardial perfusion imaging and this report will review its basic properties and its use in the diagnosis of ischemic heart disease.

Myocardial Perfusion Imaging

Myocardial perfusion imaging (MPI) refers to the use of certain radioisotope tracers which are rapidly and selectively concentrated in the heart. It is based on the principle that myocardial uptake of these isotopes occurs primarily as a function of myocardial blood flow and function. The resultant pattern of activity provides an assessment of regional myocardial blood flow by comparing the amount and distri-

bution of activity in different areas of the heart. Regions of normal and abnormal myocardium are thereby distinguished by the presence and location of differences in myocardial radioactivity. Of the various radioisotopes which have been used for MPI, thallium 201 possesses the best radiation characteristics (Table 1) and has been the most widely investigated. Thallium 201 is an analogue of potassium and exhibits similar biologic and physical properties⁶; it is a monovalent cation with a half-life of 73 hours and is readily concentrated in the myocardium by an active transport process involving membrane sodium-potassium adenosinetriphosphatase (ATPase). Thallium 201 emits low-energy photons which permit imaging with a scintillation camera and provide for high spatial resolution; it has a high myocardial extraction ratio, with 80% to 90% of an injected dose concentrated in the heart within the first few minutes, and exhibits a high myocardial-to-background ratio which contributes to improved image resolution. These features allow for prompt imaging following injection and a low patient radiation dose.

Myocardial activity with MPI is dependent on both the initial distribution of the radioisotope and its subsequent redistribution with time. The distribution phase is most important with early imaging and is determined both by isotope delivery to different regions of the heart and by myocardial extraction. Radioisotope delivery is a flow-dependent process and has been shown experimentally to be proportional to regional myocardial blood flow.⁷ Myocardial extraction of thallium 201 is a cell-dependent process requiring functioning myocardial cells. Distribution of thallium 201 occurs rapidly into normal areas

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of myocardium but may be significantly delayed to zones of diminished coronary blood flow and may be absent in regions of abnormal function which are unable to concentrate the isotope. Redistribution is homogeneous in normal hearts but is heterogeneous in zones of significantly diminished flow or function. Washout of thallium 201 begins early from normal areas and is detectable at one hour; while this is in process from normal areas, continuing uptake is often occurring into flow-limited areas which exhibit initially delayed myocardial uptake. These regions will eventually show normalization of activity if viable myocardium is present, and redistribution is usually complete within one to four hours.⁸ Areas of persistently diminished activity generally indicate impaired myocardial function and represent myocardial infarction.

Technique

Thallium 201 in a dose of 1 to 2 mCi is administered intravenously either at rest or at the peak of exercise when MPI is used in conjunction with treadmill exercise testing. Myocardial images are recorded using a stationary or portable scintillation camera. Early images are obtained 10 to 15 minutes after injection and reflect the status of myocardial perfusion at the time of injection. If the early image is abnormal, delayed imaging three to four hours later is performed to look for redistribution into ischemic areas. Multiple views are obtained to assess the different areas of myocardium with minimal superimposition and overlap. Interpretation is done by comparison of regional myocardial activity; a normal image will demonstrate a relatively homogeneous distribution of radioisotope within the left ventricle (Figs 1 and 2), and an abnormality is represented by diminished activity, appearing as a "cold" area (Fig 3). A defect which is persistent on late images indicates damaged myocardium or scar (Fig 4), and a transient defect which is present on early images but has resolved with delayed imaging represents an area of reversible ischemia (Fig 5). Difficulty with interpretation may occur when only small differences in regional activity are present, but this may be improved by use of computer processing techniques.

Myocardial Infarction

One area of clinical application of thallium 201 MPI is in the diagnosis of myocardial in-

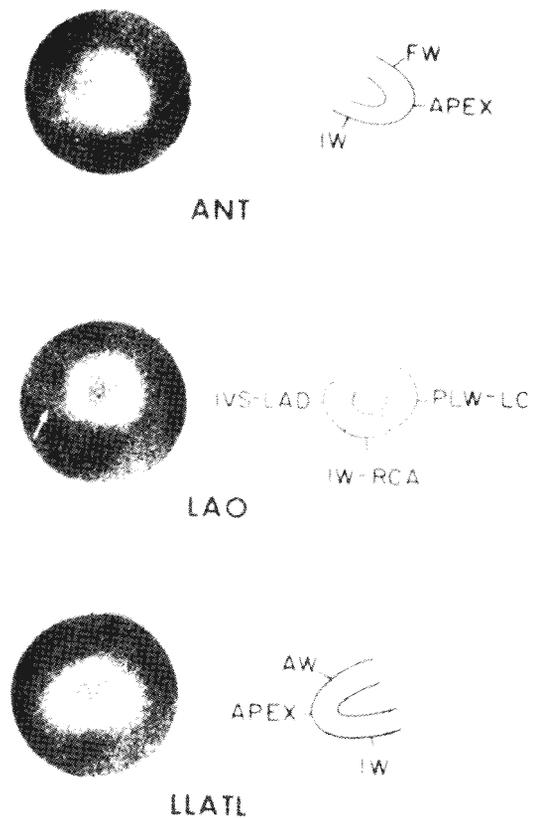


Fig 1—Normal thallium 201 MPI in the anterior (ANT), left anterior oblique (LAO), and left lateral (LLATL) projections. Myocardial uptake in the left ventricle is intense and homogeneous. The diagram to the right of each image indicates the ventricular and coronary anatomy in each projection. AW = anterior wall; FW = free wall; IVS = interventricular septum; IW = left ventricular inferior wall; LAD = left anterior descending artery distribution; LC = region of left circumflex artery; PLW = posterior lateral wall; RCA = right coronary artery distribution.

farction. Several investigators have demonstrated a high sensitivity for thallium 201 in the detection of acute myocardial infarction.⁹⁻¹¹ In these studies sensitivity was greater than 95% in patients with transmural infarction and from 80% to 85% for nontransmural infarction. Sensitivity is unaffected by location of infarction but is dependent on infarct size, with decreased

TABLE 1
Myocardial Perfusion Imaging

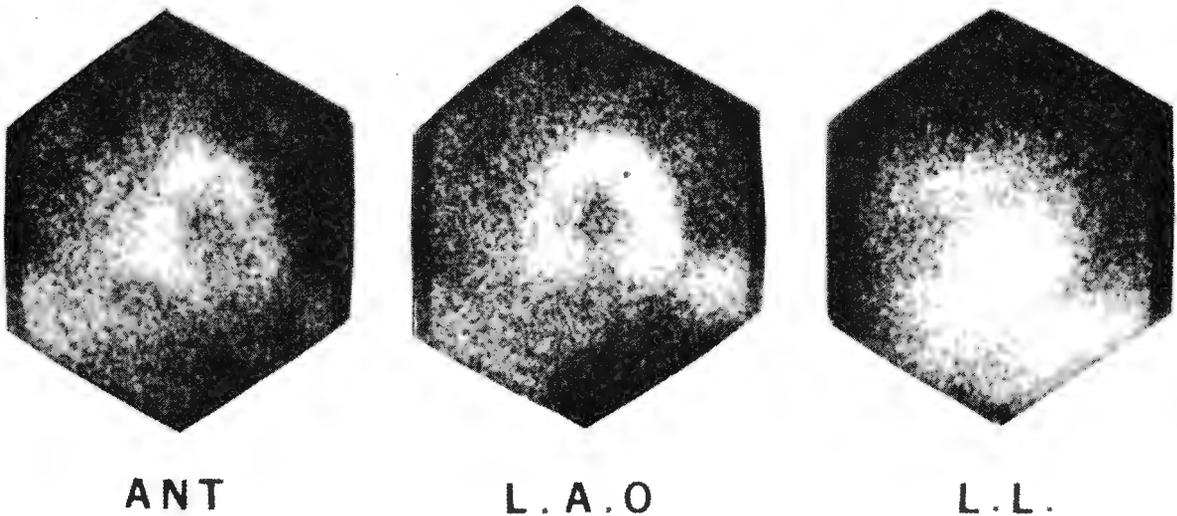
- Radionuclides: K-43, Rb-81, Cs-129, Tl-201
- Analogues of K⁺: physical and biologic
 - Tl-201 - best radiation characteristics
 - t_{1/2} - 73 hours
 - low-energy emission characteristics
 - high myocardial extraction ratio (80%)
 - high myocardial-to-background ratio
 - low patient radiation dose (.07 rad/mCi)
 - usual dose = 1 to 2 mCi



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Fig 2—Normal thallium 201 study with exercise (GXT) in the anterior (*left*), left anterior oblique (*center*), and left lateral (*right*) views. Activity in the left ventricle is homogeneous and intense, and there is activity seen in the right ventricle in the left and center panels. Right ventricular activity is often detectable with exercise. This patient had typical angina pectoris with normal coronary arteries on angiography and a false-positive exercise electrocardiogram.

THALLIUM - 201 MYOCARDIAL SCINTIGRAMS



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Fig 3—Abnormal thallium 201 rest image in the anterior (ANT), left anterior oblique (LAO), and left lateral (LL) projections in a patient with acute anterior myocardial infarction. A large area of diminished activity is evident in the anterior and apical regions of the left ventricle in each projection.

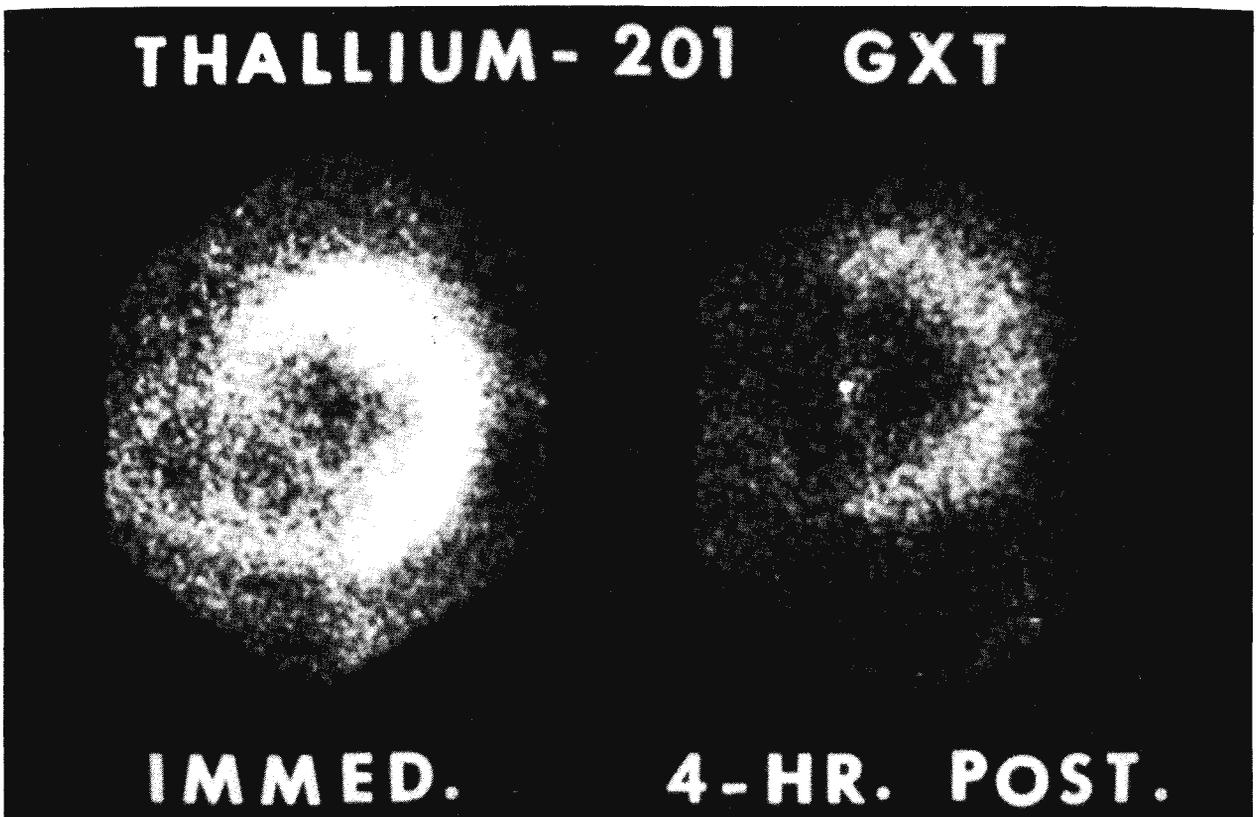


Fig 4—Thallium 201 exercise MPI with early (*left*) and delayed (*right*) images in the left anterior oblique projection in a patient with atypical chest pain and history of previous myocardial infarction. The immediate image shows an anteroseptal defect and the delayed image recorded four hours later shows no redistribution into this area, indicating a fixed or irreversible defect from previous myocardial infarction.

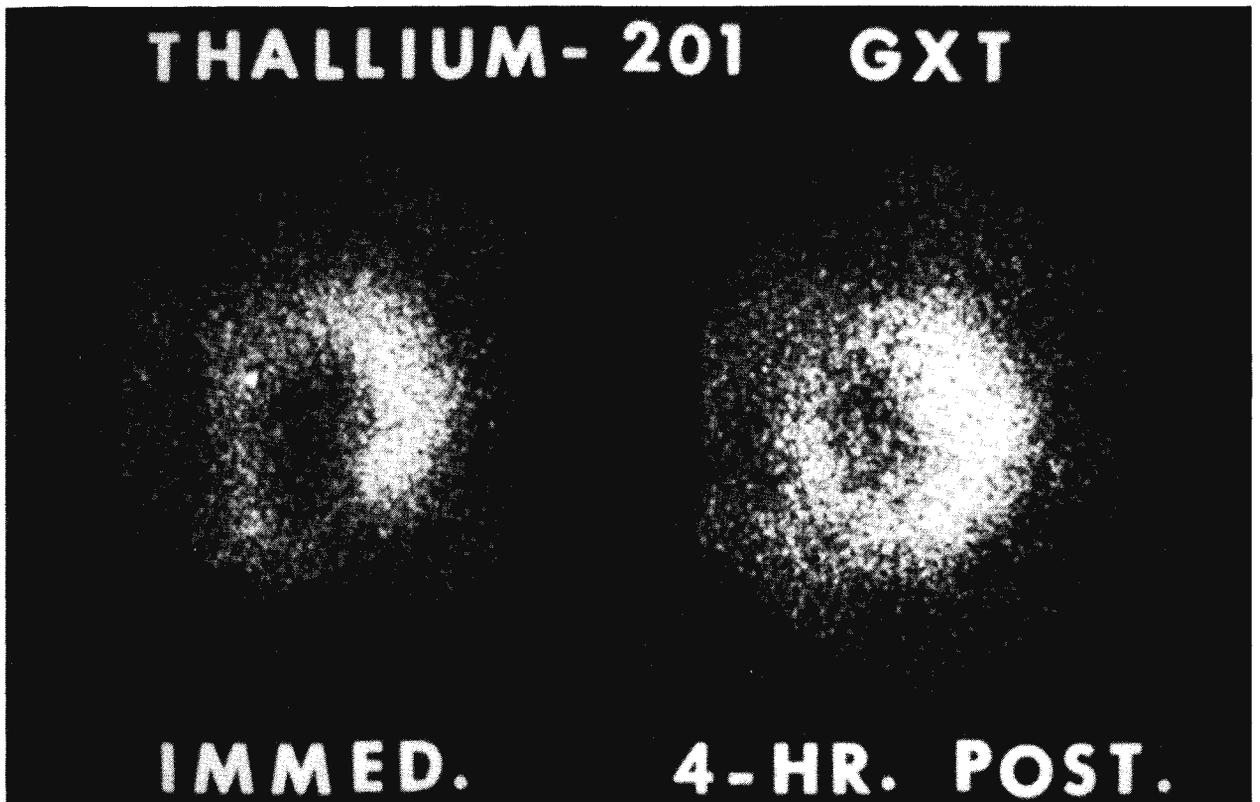


Fig 5—Thallium 201 exercise (GXT) study in a patient with angina pectoris. The image at left was recorded immediately following completion of exercise and demonstrates a large area of markedly diminished activity in the anteroseptal region of the left ventricle. The image at right was obtained four hours later and shows redistribution of activity into the anteroseptal region with normalization of activity, indicating reversible, exercised-induced ischemia.

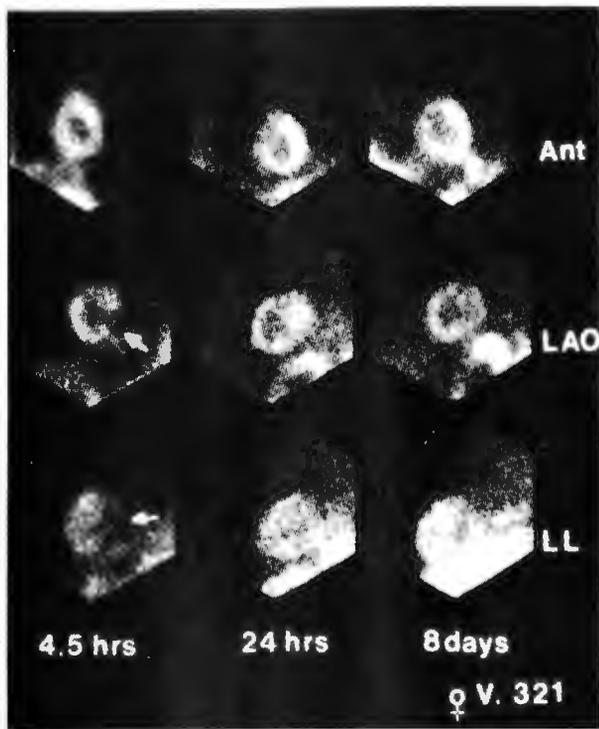


Fig 6—Serial thallium 201 MPI in anterior (ANT), left anterior oblique (LAO), and left lateral (LL) projections in a patient with posterior wall infarction. Arrows indicate a defect at 4.5 hours after onset of chest pain. This defect is diminished on the repeated studies 24 hours and 8 days later, especially in the LAO view.

sensitivity in small infarctions. Sensitivity is also dependent upon time, with rare false-negative studies being obtained in the first 6 hours after infarction and an increased incidence of false-negative results observed after 24 hours.⁹ In addition, serial thallium 201 studies in the same patient have also demonstrated that the size of the defect often changes with time, usually being largest during the first 24 hours and becoming smaller and more stable in size after 48 hours (Fig 6).⁹ This observation probably indicates detection of zones of reversible peri-infarction ischemia in addition to acute infarction in its early course which resolves with time,

TABLE 2
Exercise Thallium Imaging

CLINICAL APPLICATIONS

- Improved sensitivity over exercise testing alone
- Clarification of equivocal stress test
- Diagnosis when stress test uninterpretable
 - Conduction defect (LBBB)
 - Left ventricular hypertrophy
 - Resting ST-segment abnormality
 - Digitalis effect
- Identification of false-positive stress test
- Evaluation of coronary bypass graft function

leaving only the residual area of infarction apparent on subsequent images. The size of the defect with thallium 201 MPI also correlates well with the size of the infarct as determined by serum enzyme techniques,¹² pathological analysis,¹¹ and quantitative left ventricular angiography.¹³ However, application of thallium 201 MPI in suspected myocardial infarction is limited in patients with previous myocardial infarction because of the isotope's inability to distinguish new infarction from old infarctions or ventricular aneurysm. There is also reduced specificity with small infarctions (as with serum enzymes and electrocardiographic diagnosis) because of the limits of resolution of the technique.¹⁴ In addition, MPI at rest may be abnormal with early imaging in some patients having unstable an-

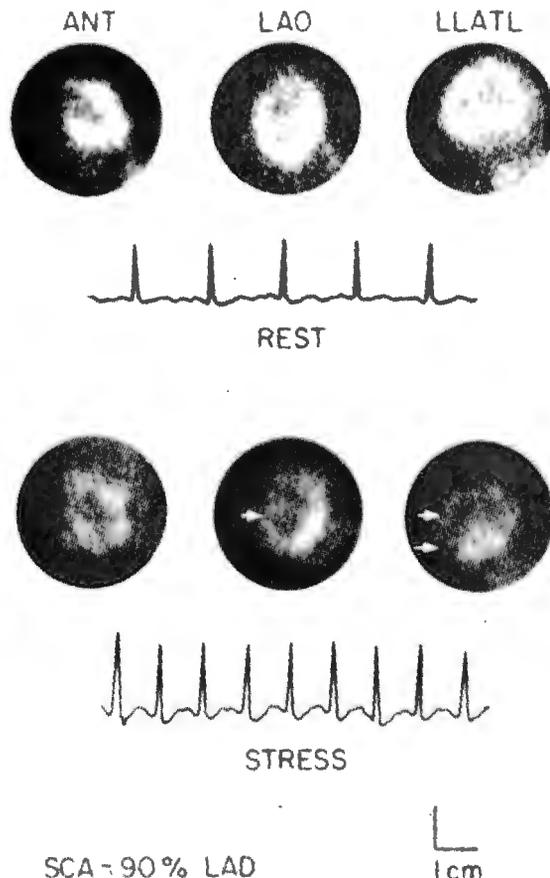


Fig 7—False-negative stress electrocardiogram. Resting (top) and stress (bottom) electrocardiogram and thallium 201 MPI in the anterior (ANT), left anterior oblique (LAO), and left lateral (LLATL) projections in a patient whose coronary angiograms (SCA) demonstrated significant left anterior descending coronary artery stenosis. The resting scintigram reveals homogeneous radioactivity. With stress, the interventricular septum and anterior left ventricular walls (arrows), the regions supplied by the stenotic vessel, are barely visible. The electrocardiogram shows no ischemic change on exercise.

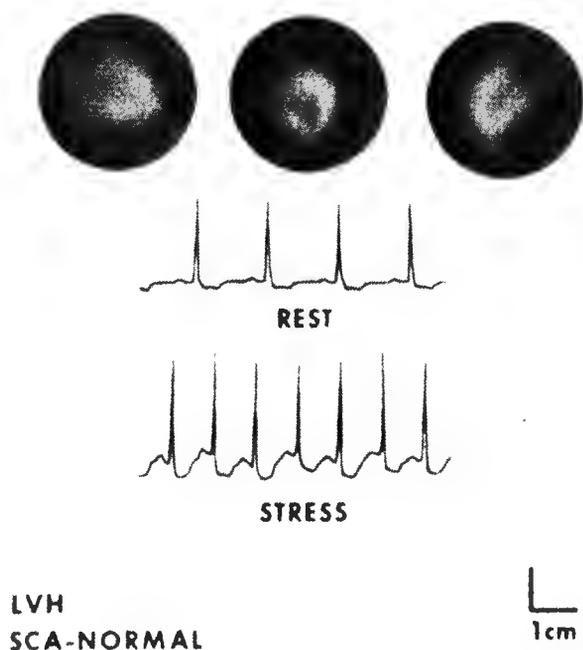


Fig 8—Normal thallium 201 MPI and equivocal stress electrocardiogram in a patient with normal coronary arteries on angiography (SCA). Resting (top) and stress (bottom) electrocardiogram and stress imaging in the anterior (left), left anterior oblique (center) and left lateral (right) projections in a patient with troublesome atypical chest pain and a history of hypertension. The full resting electrocardiogram revealed left ventricular hypertrophy (LVH). The monitored lead showed ST-segment depression that deepened with stress and was difficult to interpret in view of the depression at rest. The perfusion image was normal and clarified the stress electrocardiogram.

gina without infarction owing to severely reduced flow,¹⁵ but this can usually be clarified if delayed images are also obtained. Thallium 201 studies may also be abnormal in certain forms of noncoronary heart disease, particularly cardiomyopathy.¹⁶ For these reasons, thallium 201 MPI appears to have limited general usefulness for the diagnosis of acute infarction but can be of value to confirm infarction in situations when standard criteria are not helpful. It has been useful in screening patients for coronary care unit admission.⁹

Exercise Myocardial Imaging

Thallium 201 MPI has its greatest application when used in combination with treadmill exercise testing for the evaluation of chest pain and transient myocardial ischemia,¹⁷⁻²⁰ and it provides advantages over exercise testing alone

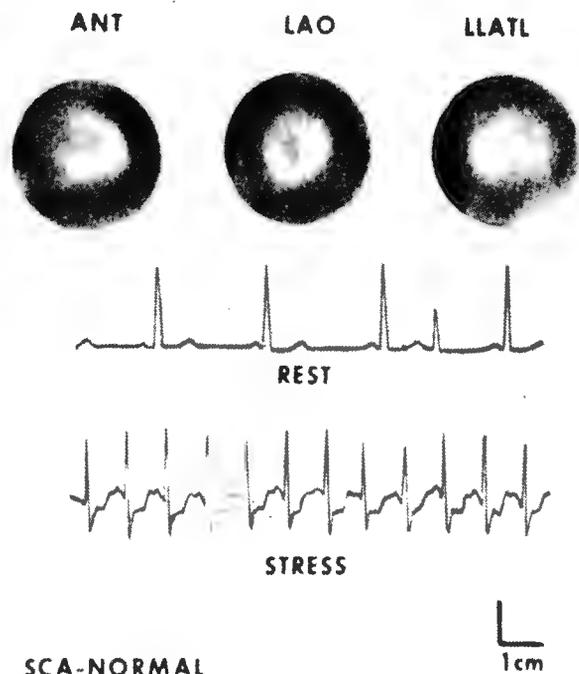


Fig 9—False-positive stress electrocardiogram. Stress thallium 201 MPI in the anterior (ANT), left anterior oblique (LAO), and left lateral (LLATL) projections (top) and the resting and stress electrocardiograms (bottom) in a patient with normal coronary arteries on angiography (SCA). Radio-nuclide distribution was normal, but the stress electrocardiogram showed distinct and significant horizontal ST-segment depression. Scintigraphy proved to be the valid clinical indicator.

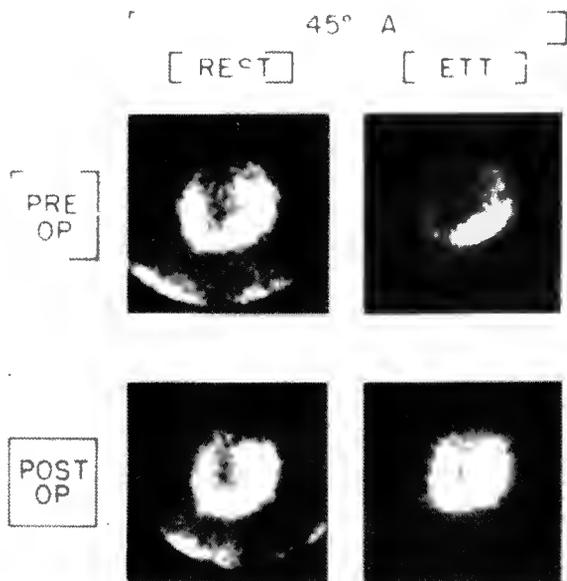


Fig 10—Preoperative (top) and post-operative (bottom) thallium 201 MPI in the 45-degree left anterior oblique (LAO) projection in a patient who underwent coronary bypass surgery. The preoperative rest image (top, left) is normal, but following exercise (ETT) there is an extensive defect in the anteroseptal region (top right) preoperatively. Postoperatively both rest (bottom, left) and exercise (bottom, right) are normal. The bypass graft was patent on angiography.

(Table 2). Thallium 201 is administered at the peak of exercise, and early images are obtained. If a normal image is recorded, further imaging is unnecessary (Fig 2). If an abnormality is present, delayed images are recorded to assess the redistribution into ischemic areas (Fig 5). When compared with standard exercise electrocardiography, thallium 201 MPI is significantly more sensitive than exercise testing in the detection of coronary artery disease. This improved sensitivity is present in patients with a normal resting electrocardiogram (ECG) in whom exercise testing is most reliable (Fig 7), and is found particularly in patients with an abnormal resting ECG, in whom ECG changes with exercise are often difficult to interpret or are uninterpretable. This is encountered in patients with intraventricular conduction defects, particularly left bundle-branch block; left ventricular hypertrophy (Fig 8); nonspecific resting ST-segment abnormalities; and in patients taking digitalis or other medications which may alter the resting and exercise ECG.

Thallium 201 also has a higher specificity in detection of coronary artery disease than standard treadmill exercise testing, as false-positive results with thallium 201 are infrequent (Fig 9).^{17,19} In contrast, the incidence of false-positive results with exercise electrocardiography may be as high as 30% in certain patient populations.²¹ Thallium 201 exercise imaging is complementary to exercise testing, and diagnostic accuracy is improved when they are used in combination. In several series, this accuracy exceeds 90% in the detection of significant coronary artery disease.^{17,19}

MPI with thallium 201 may also be of value in the postoperative evaluation of patients having coronary artery bypass graft surgery, as changes in regional myocardial perfusion with MPI have been shown to correlate well with bypass graft function,²² thereby providing a non-invasive method of determining graft patency or closure (Fig 10).

In summary, MPI with thallium 201 is a new and effective noninvasive technique in the diagnosis of ischemic heart disease. It can reliably detect myocardial infarction and may be useful when the diagnosis of acute infarction by other means is uncertain. Exercise thallium 201 imaging is the area of greatest clinical application of MPI, resulting in improved sensitivity

and specificity over exercise testing alone, and in high diagnostic accuracy in the detection of coronary artery disease when used in combination with exercise electrocardiography. Thallium 201 MPI is also of value in the evaluation of coronary artery bypass graft function.

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