# Thallium-201 Versus Technetium-99m Pyrophosphate Myocardial Imaging in Detection and Evaluation of Patients With Acute Myocardial Infarction

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**Thallium-201 myocardial imaging is of value in the early detection and evaluation of patients with suspected acute infarction. The extent of a thallium defect in an initial myocardial image may have important prognostic value. Tomographic imaging techniques hold promise for increased diagnostic sensitivity and more accurate quantitation of both infarcted and residual viable myocardium. Thallium imaging may have a special value in characterizing patients with cardiogenic shock and in detecting patients at risk for subsequent infarction or death or both, before hospital discharge.**

**Approximately 95 percent of patients with transmural or nontransmural myocardial infarction can be detected with technetium-99m pyrophosphate myocardial imaging if the imaging is performed 24 to 72 hours after the onset of symptoms. Pyrophosphate imaging has been useful in localizing the site and determining the extent of acute myocardial infarction. The "doughnut" pattern is associated with a relatively large incidence of subsequent congestive heart failure and death. However, the clinical utility of this information is limited because it is usually not available when it is most needed, on admission to the coronary care unit. Pyrophosphate imaging may have an important role in the evaluation of patients during the early follow-up period after hospital discharge from an episode of acute infarction. The finding of a persistently positive pyrophosphate image suggests a poor prognosis and is associated with a relatively large incidence of subsequent myocardial infarction and death.**

Both thallium-201 and technetium-99m pyrophosphate myocardial imaging are increasingly being used to evaluate patients with acute myocardial infarction. Since the introduction of these tracer techniques in the mid 1970s, they have excited the interest of the clinical investigator and have rapidly been applied in university and community hospitals throughout the world. In this report we review their current status in detecting and evaluating patients with acute myocardial infarction and to place these methods in perspective as we enter the 1980s.

## Thallium-201 Myocardial Imaging

**Physiologic and anatomic principles:** Thallium-201 is taken up by normal myocardial cells in proportion to blood flow.[1] Within the physiologic range of blood flow the extraction of thallium by the myocardium is approximately 88 percent.[2] Only at the extremes of the physiologic range of myocardial flow does the relation of thallium uptake by the myocardial cell and blood flow deviate. At low flows relatively more and at high flows relatively less thallium is extracted from the blood.

*In normal persons,* thallium-201 is relatively uniformly distributed throughout the myocardium. The normal myocardial thallium image may show an area of relatively diminished uptake at the apex, because the apex is normally thinner than the left ventricular free wall and septum.[3] The right ventricle is usually not well defined in a left anterior

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oblique thallium myocardial image obtained at rest because the mass and blood flow per gram of the right ventricle are less than those of the left ventricle. However, during exercise, tachycardia and acute pulmonary hypertension (conditions that result in an increase in right ventricular blood flow and mass), the right ventricle can be detected easily.[4]

*Areas of myocardial ischemia or infarction,* or both, can be detected on thallium-201 myocardial imaging by the relative absence of tracer uptake in a region of the myocardium. Ischemia or infarction, or both, can be detected immediately after experimental coronary arterial ligation because blood flow, and hence thallium uptake, will be diminished. Ischemia can be differentiated from infarction by serial myocardial imaging and quantification of the redistribution of thallium-201.[5] If myocardial imaging is repeated 1 to 6 hours after the injection of tracer, normal areas of myocardium will lose thallium activity. In contrast, areas of myocardial ischemia will have a relative increase in activity as thallium distributes in time according to myocardial mass. Areas of permanent myocardial damage after myocardial infarction will show diminished thallium-201 activity in both initial and delayed serial images.

*The location of the defect in a thallium-201 image* is also of interest because it can be used to predict the underlying anatomic disease.[6] For example, defects in thallium uptake in the anterior apical region in an anterior view or defects in the area of the interventricular septum in the left anterior oblique image indicate significant disease of the left anterior descending coronary artery. Lesions of this artery above the first septal perforator can be distinguished from those below this branch. Lesions above this branch can be detected by the finding of a defect in thallium-201 uptake involving the septum in a left anterior oblique view; lesions below this branch involve the anterior apical region in an anterior view, but not the septum in the left anterior oblique view. This differentiation may be of clinical importance because it has recently been pointed out that lesions of the left anterior descending coronary artery above the first septal perforator are associated with a large incidence of ventricular fibrillation or sudden cardiac death, or both.[7] Lesions in the right coronary artery may be detected by finding a defect on the diaphragmatic surface or apex in the right anterior oblique view; however, occasionally, because of anatomic variation, lesions of the left circumflex coronary artery may also project there. Lesions of the latter artery can be detected by the finding of a tracer defect on the high lateral wall in a left anterior oblique or left lateral image. These physiologic and anatomic principles provide the basis for the use of thallium-201 myocardial imaging in the detection and evaluation of patients with acute myocardial infarction.

**Patients with suspected myocardial infarction or ischemia:** Thallium-201 myocardial imaging has been shown to be of value in the early detection and evaluation of patients with suspected acute myocardial infarction. Patients with a diagnosis of "rule out myocardial infarction" remain a major problem in most medical centers. Approximately half of the patients admitted to the coronary care unit for suspected infarction are shown not to have infarction. These patients include those with unstable angina pectoris or coronary insufficiency, patients with previously known ischemic heart disease and acute chest pain of noncardiac origin, and those with chest pain of noncardiac origin without underlying ischemic heart disease. If techniques could be developed to triage accurately patients with suspected acute myocardial infarction, great savings in cost and increased effectiveness of diagnosis and therapeutic interventions could be realized. Although thallium-201 myocardial imaging cannot be expected to solve this problem entirely, there is accumulating information to suggest that it may be of value under special circumstances.

*During the early hours of myocardial infarction,* the electrocardiogram may not be diagnostic of acute myocardial infarction. Similarly, serum creatine kinase may not be elevated for the first few hours after myocardial damage. In these early hours serial thallium-201 myocardial imaging may be of value.[8] If a defect in thallium uptake is seen in an initial myocardial image, myocardial infarction should be suspected and the patient admitted to the coronary care unit for routine monitoring and therapy of acute myocardial infarction. If the defect in thallium uptake can no longer be detected on reimaging 2 to 3 hours later, acute myocardial ischemia without infarction or only minor infarction should be suspected. Patients with these findings should also be admitted to the coronary care unit, but mobilization and the application of diagnostic and therapeutic interventions for myocardial ischemia can be accelerated. In patients who have normal thallium myocardial uptake on both initial and serial imaging, myocardial ischemia or infarction is less likely, and chest pain of noncardiac origin should be considered. One limitation of this approach is that patients with prior myocardial infarction and scarring may have residual defects in thallium uptake indistinguishable from defects secondary to acute infarction even with serial imaging. A documented history of prior myocardial infarction should alert the clinician to this possibility.

**Patients with right ventricular infarction:** Another limitation of this approach is that right ventricular infarction may not be detected and a misdiagnosis of chest pain of noncardiac origin may be made because the right ventricle is often not seen in a thallium-201 image obtained at rest. To eliminate the possibility of right ventricular infarction as a cause of the patient's symptoms, a gated blood pool image can be obtained. If right ventricular infarction is present, it will be manifested by a poorly contracting large ventricle with or without concomitant left ventricular dysfunction.[9] In our experience, right ventricular infarction can often be diagnosed with blood pool imaging before the development of characteristic hemodynamic findings. Early in the course of right ventricular infarction, right ventricular filling pressure may be only slightly elevated although the right ventricle is markedly dilated because this chamber is more compliant than the left ventricle.

Only after volume challenge or loading will the right ventricular filling pressure increase in disproportion to left ventricular filling pressure. If both right and left ventricular infarction can be excluded within the first few hours of onset of symptoms, patients could undergo appropriate diagnostic studies more quickly to determine the cause of the chest pain without the expense and stigma often associated with admission to the coronary care unit.

**Early diagnosis of acute myocardial infarction:** Once a patient is in the coronary care unit, thallium-201 myocardial imaging has proved a highly sensitive technique to detect the presence of infarction. Wackers et al.[10,11] in an early study in Amsterdam found that 100 percent of patients with either transmural or nontransmural infarction could be detected by the finding of a defect in thallium uptake in the initial image made within 6 hours of onset of symptoms. With increasing time from the onset of symptoms, the sensitivity for detecting infarction, especially nontransmural infarction is diminished. In the series of Wackers et al. the sensitivity for detecting infarction was 58 percent after 24 hours.

Because sensitivity decreases with time, prompt application of thallium-201 is important for this approach to be effective. The 74 hour physical half-life of thallium-201 is long enough to permit storage of the tracer in the hospital nuclear pharmacy for emergency use. In large metropolitan areas the tracer is increasingly accessible from centralized pharmacies.

**Diagnosis of remote infarction:** Although the sensitivity for detection of infarction by thallium-201 myocardial imaging diminishes with time, the detection of remote infarction remains greater than that for the electrocardiogram. In an early study of 101 patients with a documented old myocardial infarction (from 3 months to 10 years), a definite diagnosis could be made in 61 patients using electrocardiographic criteria and in 76 by the finding of a defect in a thallium image obtained at rest ($p < 0.01$).[12]

**Predicting prognosis:** Thallium-201 myocardial imaging may also be of value in predicting prognosis. The extent of the thallium defect has been shown to correlate with pathologically determined infarct size and with the contrast angiographic extent of asynergy.[13,14] Thallium defects have been found in more than 90 percent of patients with asynergic segments greater than 60 percent of the left ventricular circumference.[15] The extent of the thallium defect in an initial myocardial image in the coronary care unit has also been shown to have important prognostic value and to be a better prognostic indicator of subsequent survival than the extent of left ventricular dysfunction in a blood pool image.[13] The extent of a thallium defect may be defined by relatively simple computer programs. The myocardial image can be circumscribed by a light pen or edge detection routine and radi drawn from the center of activity to the perimeter of the image. In a normal person there is relatively uniform activity along each radius. This information can be displayed graphically from 0 to 360°. In patients with myocardial ischemia or infarction, or both, the extent of the defect in thallium uptake can be quantitated by determining the number of degrees around the perimeter with decreased thallium-201 activity. With this technique it is possible to define a group with a relatively high mortality rate after myocardial infarction and one with a low risk of subsequent mortality.[13]

**Assessing extent of myocardial damage:** The extent of myocardial damage can also be assessed with tomographic imaging techniques.[16,17] New collimators have been developed that can be applied to standard scintillation cameras to obtain tomographic images by computer reconstruction techniques. Tomographic imaging techniques have been used to estimate the extent of experimental myocardial infarction and when they are used an excellent correlation has been found between pathologically determined infarct size and estimated infarct size[18] despite the inherent "pincushion" distortion with these collimators. Although experience with tomographic imaging in patients with acute myocardial infarction is limited, this technique should allow increased diagnostic sensitivity for the detection of infarction as well as the capacity for more accurate quantitation both of the infarcted and residual viable myocardium. (Fig. 1 and 2).

**Patients with cardiogenic shock:** Thallium-201 myocardial imaging may also be of value in assessing patients with cardiogenic shock. For example, patients with cardiogenic shock due to massive left ventricular damage will have an extensive defect in left ventricular thallium-201 uptake, often involving greater than 40 percent of the left ventricular circumference. In those with persistence of a defect of this magnitude on serial imaging several hours later, the prognosis is poor regardless of therapy because the amount of residual viable myocardium is often insufficient to maintain adequate pump function over time. Redistribution of thallium into the area of the initial defect in tracer uptake suggests reversible myocardial ischemia and the possibility of improvement by intraaortic balloon pumping and possibly by coronary bypass graft surgery. Patients with cardiogenic shock and an electrocardiographic pattern of an inferior myocardial infarction may have massive left ventricular damage demonstrated by thallium imaging. Normal or almost normal left ventricular uptake of thallium suggests massive right ventricular damage. The prognosis in patients with these findings is good if the damage is limited to the right ventricle and appropriate therapy, such as plasma volume expansion, is instituted.

**Evaluation of patients for coronary bypass surgery:** Thallium-201 myocardial imaging is also of value in detecting areas of myocardium at risk during exercise for subsequent myocardial infarction and therefore for possible coronary arterial bypass graft surgery.[12] Exercise electrocardiographic testing before hospital discharge after myocardial infarction has been shown to be useful in detecting patients at high risk for subsequent infarction or death, or both.[19] The appearance on exercise of a new tracer defect outside the area of infarction detected in a thallium-201 myocardial image

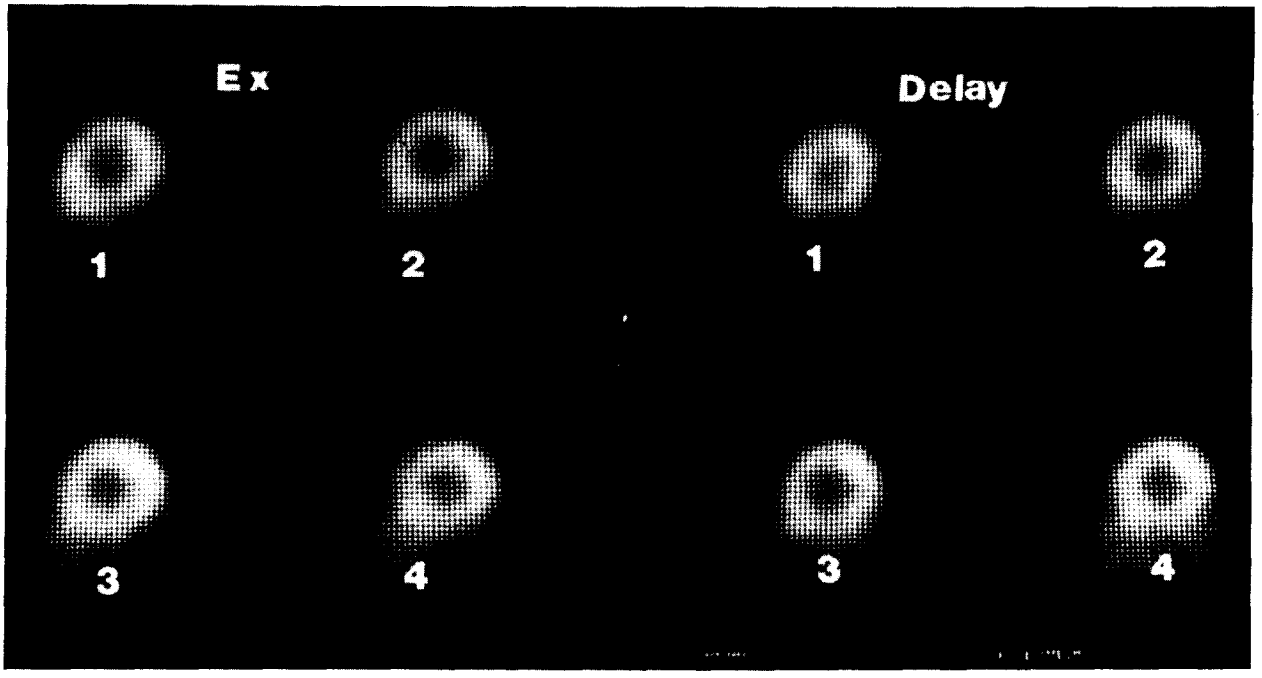


**FIGURE 1.** Tomographic thallium-201 myocardial images (1 to 4) in a patient with normal coronary arteries. Note the relatively uniform thallium-201 uptake in both the exercise (Ex) and delayed images (3 hours later).

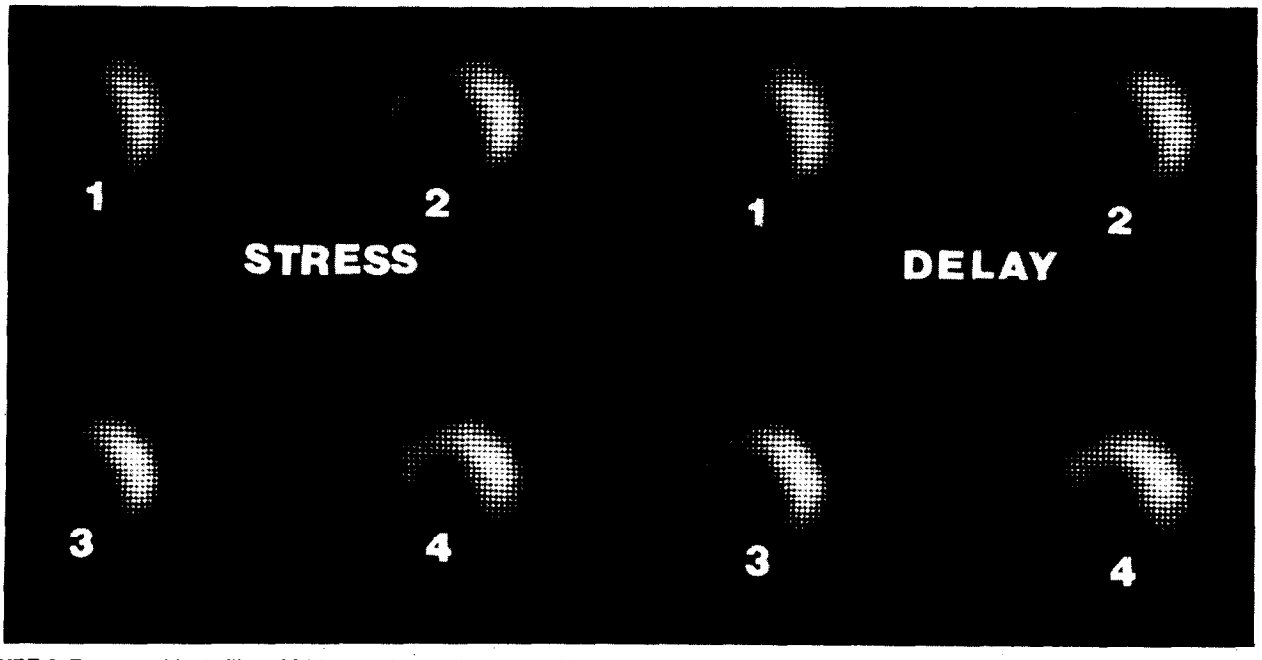


**FIGURE 2.** Tomographic thallium-201 images in a patient with a history of myocardial infarction. **Left,** the images after submaximal stress; **right,** the delayed images (3 hours later). Note that the area of decreased tracer uptake is similar in both the stress and delayed images, confirming that the area of decreased tracer uptake is due to infarction rather than ischemia.

obtained at rest indicates a "risk" segment (that is, an area of viable myocardium served by a significantly narrowed coronary artery). In a recent study more than 80 percent of "risk" segments confirmed on coronary angiography could be detected with exercise thallium-201 myocardial imaging.[20] Although experience is still limited, our current procedure is to perform rate-limited exercise electrocardiography and thallium-201 myocardial imaging before hospital discharge after an episode of myocardial infarction. Patients who do not exhibit evidence of myocardial ischemia on electrocardiography and do not exhibit a new defect in thallium uptake on exercise are assumed to be at low risk for subsequent infarction or cardiac death, or both, and are discharged to normal activity after convalescence. Patients who exhibit evidence of myocardial ischemia on

electrocardiography or show evidence of a new defect on thallium myocardial imaging are considered for early coronary arteriography in order to detect candidates for early bypass graft surgery. To determine whether this approach is correct will require further experience and carefully controlled trials.

### Technetium-99m Pyrophosphate Imaging

**Physiologic and anatomic principles:** Myocardial infarction can also be detected with the uptake of technetium-99m pyrophosphate within an area of acute infarction.[21] This is in contrast to thallium-201 myocardial imaging in which infarction is recognized by an absence of tracer uptake. Since its introduction in 1974 by Bonte et al.[21] technetium-99m pyrophosphate myocardial imaging has found wide clinical application. Although the exact mechanism of technetium-99m pyrophosphate uptake by infarcted myocardium is still being investigated, the weight of evidence suggests that the major mechanism is the formation of complexes with tissue calcium stores within the injured cell.[22] Technetium-99m pyrophosphate may also form complexes with damaged myocardial proteins and other macromolecules, but this may not be as important as the binding to tissue calcium. Residual myocardial blood flow is also of direct importance because, if there is no residual flow, tracer cannot be delivered to the area of infarction. This is evident from the pattern of pyrophosphate uptake in patients with massive myocardial damage in which the central necrotic area with low residual flow fails to take up tracer, whereas the surviving border zone with residual collateral flow avidly takes up tracer resulting in a "doughnut" pattern.

*Areas of myocardial infarction can be detected approximately 12 hours after the onset of symptoms.* However, imaging at this time will result in a relatively low sensitivity for detection of infarction. Maximal sensitivity for detection of infarction is achieved 24 to 72 hours after the onset of symptoms.[23] After 1 to 2 weeks, pyrophosphate uptake by the myocardium is usually not detected but in some patients a positive image may persist for several weeks or months. It is important to wait at least 90 minutes and preferably 3 hours after injection of pyrophosphate before imaging. Imaging performed earlier than 90 minutes after injection may result in a low specificity due to persistence of blood pool activity and the appearance of diffuse uptake, which may be mistaken for a positive image. Wherever there is a question that apparent uptake is due to blood pool activity, further delayed views should be obtained for comparison. Several approaches have been used to grade pyrophosphate images. The most commonly used is that recommended by Willerson et al.[23] Scintigrams are graded from 0 to 4+: 0 = no activity; 1+ = minimal activity; 2+ = definite myocardial activity; 3+ = activity equal to bone activity; and 4+ = activity greater than bone activity. In this system scans with 2+ or greater activity are thought to suggest acute myocardial infarction.

**Sensitivity of test for acute infarction:** If imaging is performed during the optimal time, 24 to 72 hours after onset of symptoms of acute infarction, approximately 95 percent of patients with transmural or nontransmural infarction will be detected.[24] To obtain such a high sensitivity with a high specificity requires careful attention to imaging technique and the use of serial imaging. However, such high sensitivity for detecting infarction has not been a universal finding. For example, Lyons et al.[25] recently reported that 96 percent of patients with transmural infarction had pyrophosphate uptake, but in only 82 percent was the uptake localized. Similarly, 88 percent of patients with nontransmural infarction had pyrophosphate uptake but the uptake was localized in only 44 percent. A relatively large proportion of patients with chest pain, unstable angina pectoris, congestive heart failure or pericarditis, as well as patients studied after resuscitation, also had pyrophosphate uptake, but not a localized pattern. Therefore, if one requires a localized or focal pattern of uptake as the criterion for diagnosis of myocardial infarction, the sensitivity for detecting nontransmural infarction is relatively low, approximately 44 percent.

*Several conditions are known to cause false positive pyrophosphate images.* They include calcific valvular heart disease, left ventricular aneurysm with dystrophic calcification, inflammation or tumors of the breast, and disease of the chest wall or ribs. Cardioversion with skeletal muscle damage may also cause pyrophosphate uptake.[26]

**Limitations of method:** The major limitation of pyrophosphate imaging for detection of acute myocardial infarction is that in most instances the diagnosis has been established with serial electrocardiography and serum enzyme determination in 24 to 72 hours, the time of optimal pyrophosphate imaging. In the approximate one fourth to one third of patients with infarction in whom the diagnosis is still in doubt at 48 hours, pyrophosphate imaging is of limited value in view of the relatively low sensitivity for detecting nontransmural infarction if a localized pattern is required and the frequent occurrence of the conditions known to cause false positive images. Although only a relatively small proportion of patients with infarction will be detected during the early hours of infarction with pyrophosphate imaging, imaging 5 hours after infarction may have some value. Recent experimental studies[27] suggest that the early appearance of pyrophosphate uptake indicates reperfusion injury due to reversible coronary arterial occlusion with more rapid delivery of flow to the infarcted region than would occur by collateral channels over 48 to 72 hours in animals with a completely occluded vessel This approach may therefore be of value in detecting patients with infarction due to coronary arterial spasm.

**Localizing the site and extent of infarction:** Pyrophosphate imaging has also been useful in localizing the site and determining the extent of acute myocardial infarction. For example, right ventricular infarction has been diagnosed by the finding of a characteristic pattern of pyrophosphate uptake in the left anterior oblique image.[28] As previously pointed out, patients with the electrocardiographic pattern of an inferior myocardial infarction may have a spectrum of anatomic damage involving the left or the right ventricle, or both. Al-

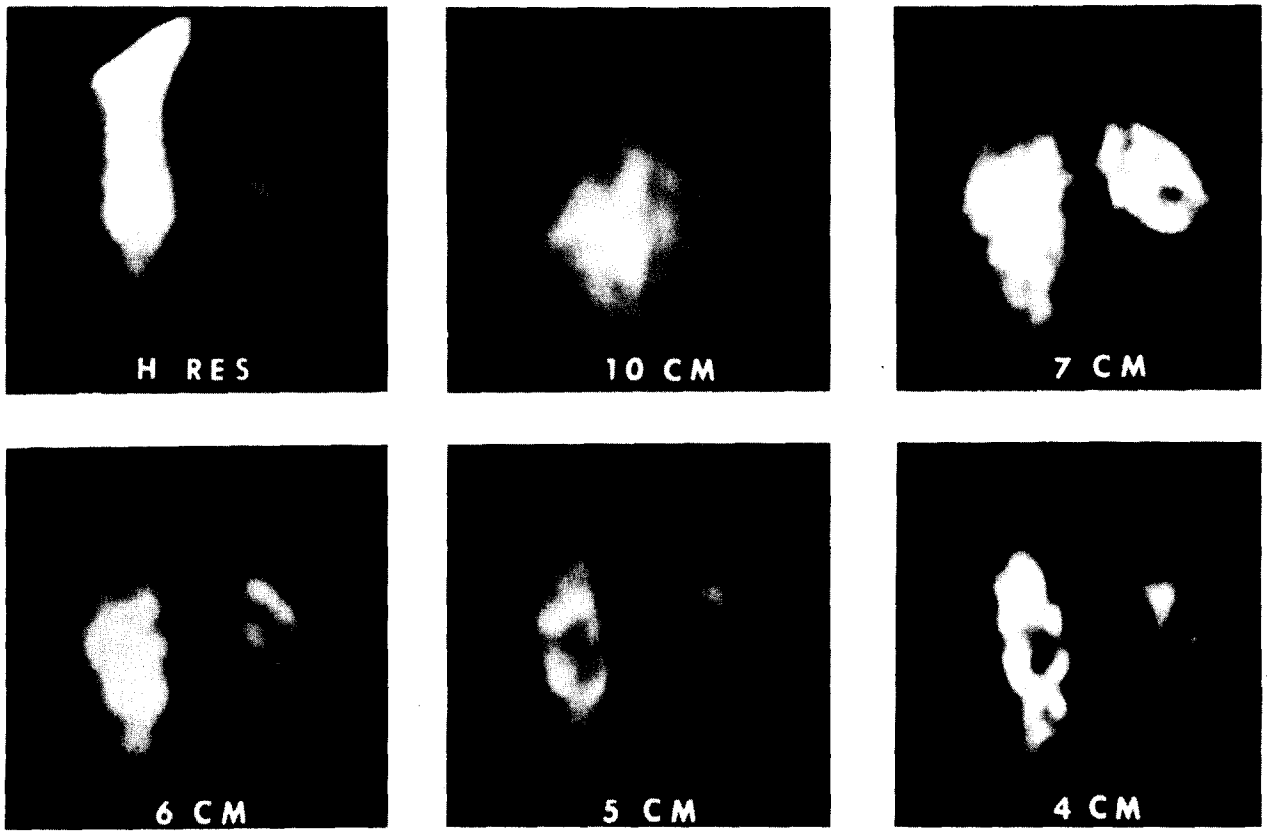


**FIGURE 3.** Technetium-99m pyrophosphate tomographic myocardial imaging. A standard planar image using a high resolution (H RES) collimator is shown in the **upper left panel** and tomographic cuts in the same patient at 10, 7, 6, 5 and 4 centimeters (CM). The tomographic images provide a better estimate of the extent of infarction than does the standard planar image.

though this differentiation has important therapeutic and prognostic implications, the information provided by pyrophosphate imaging is often too late to be of therapeutic importance.

The extent of pyrophosphate uptake has also been correlated with the extent of myocardial infarction using standard imaging techniques. Good correlations between the extent of infarct-avid agents and the extent of acute anterior transmural myocardial infarction have been found.[29,30] Less satisfactory correlations have been found in patients with inferior or posterior myocardial infarction because of inadequate projection of the area of damage when standard imaging techniques are used. Recently, this limitation has been overcome using tomographic imaging techniques[31] (Fig. 3). Excellent correlations between the extent of infarction determined pathologically and the extent of pyrophosphate uptake have been found for transmural infarction in all locations using tomographic techniques. Precise correlation between the extent of pyrophosphate uptake and infarction in patients with nontransmural infarction is less satisfactory because of the presence of the pattern of diffuse uptake in some patients. Nevertheless, some correlation with the extent of damage can be found even in patients with nontransmural infarction.

The prognosis in patients with myocardial infarction depends on the extent of myocardial damage, both new and old. Patients with an old anterior transmural myocardial infarction may present with an acute inferior infarction or nontransmural infarction. The extent of pyrophosphate uptake and, similarly, creatine kinase release will reflect only the acute damage in these situations. Implications as to prognosis based on infarct size determined from techniques that reflect only acute damage must of necessity be misleading. Under these circumstances techniques that reflect total myocardial damage will be of greater value. Total myocardial damage can be assessed from the extent of a defect in thallium-201 uptake or from the extent of ventricular dysfunction on gated blood pool imaging. For example, in one early study[32] no significant difference could be found in creatine kinase release between survivors of infarction and those subsequently dying, whereas there was a significant difference in an index that reflected total myocardial damage, such as left ventricular ejection fraction and percent of the left ventricular wall that was akinetic on blood pool imaging.

**Significance of "doughnut" imaging pattern:** Despite these limitations pyrophosphate imaging may provide important prognostic information. The "doughnut" pattern has been found in patients with massive anterior transmural infarction. The essentially clear area without pyrophosphate uptake indicates se-

verely necrotic myocardium with inadequate myocardial blood flow for delivery of tracer. In one study[33] of 71 patients with acute anterior myocardial infarction, 45 were shown to have a doughnut pattern and 26 a "focal" pattern of uptake. Peak creatine kinase release in those with a doughnut pattern was 660 units compared with 344 units in those with a focal pattern ($p < 0.05$). Of the patients with a doughnut pattern, 67 percent had congestive heart failure and 9 percent died, whereas among those with a focal pattern, only 35 percent had congestive heart failure and none died. Similarly, Ahmad et al.[34] found late complications in all patients with a doughnut pattern of pyrophosphate imaging compared with only 43 percent of patients with a focal pattern of uptake and 12 percent of those with a diffuse pattern. The post-hospital mortality rate was 83 percent in those with a doughnut pattern, 6 percent among those with a focal pattern and 0 percent among those with a diffuse pattern. Although these early data are encouraging and identification of high risk subsets after myocardial infarction is clearly of great importance, a larger experience will be required to determine if the doughnut pattern provides prognostic information over and above that obtainable by more routine clinical techniques, including creatine kinase release.

**Persistently positive image after infarction:** One circumstance in which pyrophosphate imaging appears to provide independent prognostic information not readily obtainable by other techniques is the occurrence of persistently positive image after infarction. Olsson et al.[35] recently reported on 109 patients in whom pyrophosphate imaging was performed a mean of 31 weeks after infarction; 61 patients (56 percent) had a positive pyrophosphate image and 48 (44 percent) a negative image. These patients were followed up for a mean of 50 weeks. In those with a positive pyrophosphate image 10 percent had recurrent myocardial infarction and 16 percent died compared with a 2 percent incidence rate for both myocardial infarction and for death in those with a negative image. They also noted an increased incidence of congestive heart failure and severe angina pectoris in those with a positive image.

*The finding of a persistently positive pyrophosphate image after an episode of acute myocardial infarction may be due to unresolved calcium complexes within the infarcted region, dystrophic myocardial calcification or ongoing myocardial necrosis.* In the past we tended to think of myocardial infarction as a sudden event healing in 6 to 8 weeks. More likely, many patients with infarction have islands of viable myocardium within the distribution of the "infarct." These islands of viable myocardium are supplied by collateral flow that, although adequate to preserve myocardium initially, may be inadequate over time and during periods of increased oxygen demands required during stress. Identification of this high risk subset with a persistently positive pyrophosphate image suggests the need for new therapeutic strategies.

**Patients with unstable angina:** A similar situation has been encountered in patients presenting with unstable angina pectoris.[36] Several groups have noted that approximately one fourth of patients with unstable angina pectoris but without serial electrocardiographic or serum enzyme evidence of acute myocardial infarction have a positive pyrophosphate image. Initially it was thought that a positive pyrophosphate image under these circumstances was a false positive image. However, recent studies suggested that a positive pyrophosphate image under these circumstances may represent subclinical myocardial necrosis. Small areas of myocardial necrosis are frequently seen at postmortem examination in patients with unstable angina pectoris dying of other causes and have been correlated with a positive pyrophosphate image. Olson et al.[36] reported on 199 patients with unstable angina pectoris without electrocardiographic or serum evidence of myocardial infarction; 67 (34 percent) had a positive and 132 (66 percent) a negative pyrophosphate image. Of those with a positive pyrophosphate image 21 percent had subsequent nonfatal myocardial infarction and 22 percent had cardiac death during a mean follow-up period of 35 weeks compared with a 3 percent incidence rate of nonfatal infarction and a 6 percent incidence rate of cardiac death in those with a negative image. It is possible that those with a positive pyrophosphate image had ongoing or sporadic episodes of myocardial necrosis similar to those of patients with cerebrovascular disease and ischemic attacks.

*Identification of a high risk subset of patients with unstable angina has important therapeutic implications.* For example, in those with a negative image with a low risk of subsequent infarction and death, conservative medical therapy appears justified, whereas in those with a positive image more aggressive therapy, possibly medical or surgical, seems indicated. Failure to separate high and low risk subsets in any trial of therapy in unstable angina may lead to an inability to show efficacy of a therapeutic intervention and may in part account for the failure of the multicenter trial of coronary arterial bypass graft surgery to show a significant effect of surgery on survival.[37]

## Clinical Applications

**Diagnostic protocol in thallium-201 imaging:** We suggest that if, after routine clinical examination, electrocardiography and initial serum enzyme determination, there is a question as to the diagnosis of acute myocardial infarction in a patient without a previous history of infarction, serial thallium-201 imaging should be considered. This technique will be of special value when applied to patients without known previous ischemic heart disease who present to the emergency room with chest pain or symptoms suspicious of acute myocardial infarction within the first few hours of onset of symptoms. The finding of a defect in thallium-201 uptake suggests the presence of ischemic heart disease. If serial imaging 2 to 3 hours later demonstrates that the defect persists or enlarges, acute myocardial infarction should be suspected and the patient admitted for further observation. In patients with negative serial thallium-201 myocardial images but a high suspicion of infarction by clinical history, a blood pool image may

be obtained in both the right and left anterior oblique projections. The finding of a normal left ventricular ejection fraction and normal wall motion of both the right and left ventricles makes the presence of an acute infarction unlikely.

**Protocol in high risk patients to evaluate therapy:** In patients admitted to the coronary care unit with the diagnosis of acute myocardial infarction an initial thallium-201 myocardial image and quantification of the extent of thallium defect provide important prognostic information sufficient to assign patients to high or low risk subsets.[13] To evaluate the effectiveness of therapeutic interventions blood pool imaging should be considered.[38–40] Although not reviewed in this study, left ventricular ejection fraction determined with blood pool imaging is highly reproducible and correlates well with values obtained with standard contrast angiography. In patients with complicated myocardial infarction and cardiogenic shock a combination of thallium-201 myocardial imaging and blood pool imaging should be considered to identify those with massive irreversible left ventricular damage, whose prognosis is poor even with aggressive therapy, those with residual left ventricular ischemia or right ventricular damage and those whose cardiogenic shock is the result of a small strategically placed infarction (such as with rupture of a papillary muscle or of the interventricular septum).

**Role of pyrophosphate imaging in the coronary care unit:** Although there is undoubtedly still much to be learned from infarct-avid imaging, technetium-99m pyrophosphate imaging with standard imaging techniques will not find wide application within the coronary care unit. By the time the optimal sensitivity is obtained at 48 to 72 hours, the information concerning the presence of infarction and its location and extent is to a large degree superfluous. To be of clinical value, this information is necessary on admission to the coronary care unit. In those patients in whom the question of infarction is still unanswered at 48 to 72 hours and in those whose onset of symptoms is uncertain, pyrophosphate imaging may prove to be of value, but the relatively low sensitivity of detecting nontransmural infarction reported from several centers and the high but still imperfect specificity of the technique raises doubt as to its clinical utility even in these circumstances.

*Does infarct-avid imaging with pyrophosphate have any role in the evaluation of patients with acute myocardial infarction?* Pyrophosphate imaging may be useful in the detection of peri- and postoperative myocardial infarction.[41] If the early data of Olson et al.[35] can be confirmed in other centers, pyrophosphate imaging would also appear to have a most important role, not in the coronary care unit, but in the evaluation of patients seen during the early follow-up period after hospital discharge after an episode of acute infarction. The finding of a persistently positive pyrophosphate image suggests a poor prognosis and the need for therapeutic intervention, whereas the finding of a negative image appears to indicate a low risk subset of patients in whom high risk interventions should be applied cautiously, if at all. Similarly, the patient with unstable angina pectoris and a positive pyrophosphate image appears to have a different prognosis and to require more aggressive therapy than the patient with a negative image and an excellent prognosis.[36]

**Future directions:** As we enter the coming decade, thallium-201, technetium-99m pyrophosphate and blood pool imaging techniques will undoubtedly play an increasingly important role in detecting patients with ischemic heart disease, selecting high risk subsets for therapeutic interventions and evaluating the effects of therapeutic interventions, as well as providing further insight into the natural history of disease processes. New imaging techniques and improvements and developments of new radiopharmaceuticals will undoubtedly open new areas for clinical investigation. However, the challenge of the next several years is to apply more efficiently currently available techniques. We must determine where and when they are cost-effective and an aid in clinical decision-making as well as where and when they are superfluous, adding only to the cost of care without affecting clinical outcome. Although it is the role of the clinical investigator to provide this information, it is the role of the individual clinician to be satisfied that this information is available and reliable before he applies these techniques clinically. It is not enough that a new technique such as pyrophosphate myocardial imaging diagnoses the presence of myocardial infarction or estimates the size of myocardial infarction. To be clinically applicable and to justify the expense of the technique, the technique must provide information not obtained by less costly techniques and must result in clinical decisions affecting patient outcome that are otherwise not possible. If these conditions can be met, as we believe they will be, and if the techniques are intelligently applied, we can look forward to improved diagnosis and evaluation of patients with acute myocardial infarction.

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