Chapter

20 Nuclear Cardiology Imaging: Utility and Limitation for Decision Making in Coronary Interventions

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INTRODUCTION

"Less Anatomy—More Physiology" is the message given by nuclear cardiac imaging. Exercise imaging with radionuclide image is a better predictor of morbid events and of prognosis then coronary angiography and exercise testing. Quantitative approaches of myocardial perfusion imaging are of utmost importance for the speedy assimilation of assessment of infarction, myocardial viability on decision making for therapeutic intervention. Incorporating radionuclide techniques in follow-up of patients after coronary intervention permits detection of restenosis following percutaneous coronary intervention (PCI) or graft occlusion after Coronary Artery Bye-pass Graft Surgery (CABG), thus allowing resources to be allocated in a cost effective manner and an unnecessary expensive intervention to be avoided.

I. MYOCARDIAL PERFUSION IMAGING—IMAGE INTERPRETATION

A. Planar Myocardial Perfusion Images

In planar imaging, perfusion is visualized as the projection, of myocardial radioactivity on a plane parallel to the crystal surface of the gamma camera. The "left ventricular cavity" as it appears on planar images is in part an optical illusion[1], because of over projection of myocardial regions in one plane, it is necessary to obtain multiple planar images from different angles to visualize all segments of left ventricular myocardium.

1. Normal Variations of Planar Myocardial Perfusion Images

There are several variations in the pattern of normal radiotracer uptake on planar images description are:

i. **Apex:** Decreased tracer activity at the apex of the left ventricle is normal. In patients with a vertical position of the heart, this feature may be prominent. A typical apical variant appears as a narrow slit or cleft-like area aligned with the long axis of the left ventricle.

ii. **Aortic Valve Plane:** On the LAO view, the membranous septum and aortic valve plane are projected at the open end of the horse shoe, which at times may appear to be causing a high septal defect. This variation may be seen prominently in patients with a horizontal position of the heart.

iii. **Mitral Valve Plane:** The mitral valve plane is seen as the open end of the horse shoe in all three views.

2. Artifacts on Planar Images

i. **Inferior Attenuation:** Attenuation of the inferior left ventricular wall is a common artifact on myocardial perfusion images and occurs in approximately 25 percent of patients[1]. Recognition of this artifact is relevant for an understanding of SPECT imaging. When a patient is imaged in the supine position, planar left lateral images may appear to reveal inferior wall defects. These defects are artifactual and caused by attenuation of inferior wall activity by the left hemi diaphragm. When the patient is turned on the right side, the defect is no longer present. This disappearance of the defect can be explained by a change in position of the heart and the left hemi-diaphragm. By moving to the right side, the heart shifts to a vertical position and the left hemi diaphragm moves caudally, thereby resulting in less attenuation of the inferoposterior wall. Since patients are usually in the supine

position for SPECT imaging, inferior attenuation artifacts are common.

ii. **Obesity / Large Breasts—**Attenuation artifacts in obese patients or patients with large pendulous breasts may render planar images almost uninterruptible. These artifactual defects on different planar views are often multiple and occur in a pattern that is inconsistent with known coronary artery territories. Superimposition of breast tissue over the heart may also result in linear areas of relatively increased activity, which is believed to be caused by small angle scatter from the breast tissue fold. Breast artifacts are the most frequent cause of falsepositive planar images.

B. NORMAL VARIATIONS OF SPECT MYOCARDIAL PERFUSION IMAGES

SPECT images are reconstructed as multiple slices oriented along the anatomical axis of the left ventricle. For interpretation of short-axis slices, it is convenient to divide the slices into three groups: apical slices, midventricular slices, and basal slices. To avoid apical artifacts from tangential cuts, only apical slices that clearly show the ventricular cavity should by analyzed. When interpreting basal slices, slices showing the membranous septum are excluded.

A useful practical rule of thumb for interpreting a SPECT study is that a perfusion defect should be clearly seen on at least three consecutive slices to be considered a true abnormality. The *vertical longaxis* slices and the *horizontal longaxis* slices contain the same information shown on the short-axis slices. However, the apex and base of the heart can be analyzed in these longaxis slices without partial volume artifacts. Only slices that clearly show the left ventricular cavity should be analyzed. Slightly less inferoseptal uptake can be noted in male patients as a normal variant. In females, radiotracer distribution is usually more homogeneous. The basal short-axis slices generally show a septal defect, which is a normal finding and represents the membranous portion of the septum.

1. Image Interpretation

Myocardial perfusion images are interpretated qualitatively by visual analysis, often aided by computer quantification. Image interpretation can be described as follows:

(i) **Normal:** Homogeneous uptake of the radio pharmaceutical throughout the myocardium is considered normal

(ii) **Defect:** A defect is a localized myocardial area with relatively less radiotracer uptake than normal. Defects may vary in intensity from slightly reduced activity to almost absent activity.

a. *Reversible defect:* A defect present on the initial stress images and no longer present or present to a lesser degree on resting or delayed images is a reversible defect. This pattern indicates myocardial ischemia. Improvement over time on 201TI imaging is referred to as "redistribution." It is not appropriate to use this terminology for ^{99m}Tc-labeled agents.

b. *Fixed defect:* A defect that is unchanged and present on both exercise and rest (delayed) images is a fixed defect. This pattern generally indicates infarction and scar tissue. However, in some patients with fixed^{201}TI defects on 2 to 4-hour delayed imaging, improved uptake can be noted on 24-hour redistribution imaging or after a new resting injection[2]. Similarly, a fixed defect with^{99m}Tc-labeled agents (which involves injection at rest) may at times underestimate myocardial viability.

c. *Reverse Redistribution:* This pattern occurs mainly with 201TI imaging. However, a "reverse defect" is observed occasionally with 99mTc-labeled agents. The initial stress images are either normal or show a defect, whereas the delayed or rest images show a new defect or a more severe defect. This pattern is frequently observed in patients with infarction who are undergoing thrombolytic therapy or percutaneous coronary intervention. The phenomenon is thought to be caused by initial *excess* of tracer uptake in a reperfused area with a mixture of scar tissue and viable myocytes. Initial accumulation is followed by rapid clearance from scar tissue. With PET using fluorine-18-labeled fluorodeoxyglucose (FDG), the presence of residual viable myocardium has been demonstrated within areas with reverse redistribution.

(iii) **Radiotracer Lung Uptake:** Normally, no or very little radiotracer is noted in the lung fields on postexercise images. Increased lung uptake can be quantified as a lung/ heart ratio (normal, < 0.5 for 201Tl, < 0.45 for ^{99m}Tc-sestamibi). This abnormal image pattern indicates stress induced left ventricular dysfunction and severe coronary artery disease, a powerful predictor of adverse outcome.

(iv) **Transient left ventricular dilation:** Occasionally, the left ventricular can be noted to be larger following exercise than on the rest or delayed image. This pattern of transient dilation probably indicated exercise induced left ventricular dysfunction. It has been suggested that, rather than a true increase in volume of the left ventricular, this image pattern caused by decreased subendocardial radio tracer uptake and, consequently, apparent thinning of the myocardium on the stress image.

(v) **Right ventricular visualization:** Usually, the right ventricle is only faintly visualized on rest or stress SPECT myocardial perfusion images. Right ventricular myocardial mass and blood flow are approximately 50 percent less than that of the left ventricle. Marked visualization of the right ventricle at rest is abnormal and in most cases indicates right ventricular hypertrophy. Markedly increased right ventricular uptake on exercise SPECT images is an abnormal pattern that has been associated with severe coronary artery disease[3].

(vi) **Global and regional contraction on ECG-gated images:** The ECG-gated image should be analyzed in color display. Regional myocardial wall thickening can be appreciated as a regional increase in the brightness of color. Wall thickening can be scored subjectively as normal, hypokinetic, or absent.

C. CLINICAL USE OF QUANTIFICATION OF MYOCARDIAL PERFUSION IMAGING

Computer quantification of myocardial perfusion enhances the overall accuracy of detection of coronary artery disease and also enhances the reproducibility of interpretation[4]. However, quantification should be used; astutely. In general, from the standpoint of diagnostic interpretation quantification should confirm impressions derived from visual analysis of images. However, sometimes artifacts may cause abnormal quantitative results. The process of integrating visual, and quantitative information can be referred to as "quantitative analysis with visual over read." It is important to realize that artifacts, such as those caused by attenuation from the overlying soft tissue or diaphragm or resulting from patient motion, often have an unpredictable effect on the appearance of reconstructed slices.

Myocardial perfusion images are relatively difficult to interpret. As with visual interpretation of any image data, considerable intraobserver and interobserver variability in subjective interpretation is noted, even among experienced readers[4]. Reproducibility of interpretation is related to a number of factors: (1) the overall quality of raw data, (2) image display quality, (3) the degree of abnormality, (4) the degree of change between exercise and rest images, and (5) familiarity with normal variations.

II. CLINICAL APPLICATIONS OF MYOCARDIAL PERFUSION IMAGING

A. Acute Coronary Syndromes

1. Acute Myocardial Infarction

a. Detection: Myocardial perfusion imaging with either 201Tl or 99mTc-labeled compound is a very sensitive and reliable means for the early detection of acute myocardial infarction. The timing of imaging after the onset of acute chest pain is relevant to the results of imaging. Images obtained during the first 6 hours after the onset of myocardial infarction show without exception perfusion ab-normalities at the anatomical location of infarction. However, as the time interval after the onset of chest pain increases, some patients may have normal perfusion images. Serial imaging in patients with acute myocardial infarction has revealed that in some patients the size of a myocardial perfusion defect may decrease over time. Endogenous thrombolysis occurs in approximately 20 percent of patients with acute infarction, which may explain the observed spontaneous improvement in myocardial perfusion images over time.

b. Thrombolytic Therapy: During the early hours of acute myocardial infarction, serial myocardial perfusion imaging with ^{99m}Tc-labeled compounds can be used to visualize the effectiveness of thrombolytic therapy. Because of the lack of significant redistribution, 99mTc-labeled compounds can be injected *before* the initiation of thrombolytic therapy, and imaging of myocardial perfusion can be performed later[5]. This imaging modality allows for noninvasive assessment of the area at risk and the amount of salvaged myocardium.

A decrease in myocardial perfusion defect size between images obtained before and after thrombolytic therapy reliably predicts subsequent improvement in left ventricular regional wall motion, Serial myocardial perfusion imaging has further shown that in many patients (approximately 40 percent), myocardial perfusion defect size continues to decrease during the days after administration of thrombolytic therapy. The delayed

recovery from micro vascular damage after acute infarction, could be a potential explanation for late improvement in defect size.

c. **Early Risk Stratification:** Patients with large resting myocardial perfusion defects had a significantly poorer prognosis and survival than did patients with small myocardial perfusion defects. This outcome appeared to be independent of other clinical parameters. Visualization of the right ventricle at rest and increased lung uptake of 201Tl at rest in patients with recent infarction are indicators of an unfavorable course after acute myocardial infarction.

   Early vasodilation myocardial perfusion imaging was safe and predicted inhospital and late cardiac events (cardiac death and recurrent infarction) better than did submaximal exercise imaging at hospital discharge. The ability to perform early risk stratification after infarction with nuclear imaging is of clinical importance. Management decisions regarding discharge or intervention can be made on days 2 after acute infarction rather than on days 5 to 7 at the time of predischarge stress testing with the conventional approach. Such earlier risk stratification may result in the prevention of in-hospital events and will definitely result in shorter in-hospital length of stay. The potential economic impact of this approach still needs to be evaluated.

2. Unstable Angina

Patients with unstable angina but without prior myocardial infraction may have abnormal resting myocardial perfusion images. Such resting myocardial perfusion defects are demonstrable not only when the radio pharmaceutical is injected *during* chest pain but also for considerable time *after* the angina has subsided. Resting 201Tl defects in patients unstable angina are invariably reversible and indicate transient hypo perfusion of viable myocardium. 99mTc-labeled myocardial perfusion imaging agents that do not redistribute have a particular advantage in patients with unstable angina. The lack of redistribution makes it possible to inject the radiotracer during pain and acquire images at a later time when the patient is pain free and stable. The observations with myocardial perfusion imaging in patients with unstable angina imply that impaired regional myocardial blood flow persists longer than can be judged from the clinical status or ECG. Patients with reversible resting myocardial perfusion defects usually have severe multivessel coronary artery disease. Resting myocardial perfusion imaging during pain was more sensitive and more specific for the presence of significant coronary artery disease than the resting ECG.

Resting imaging in patients with recurrent chest pain after infarction or with unstable angina is useful for objectively demonstrating the presence of transient myocardial hypoperfusion and viable myocardium. This information can be very helpful when myocardial revascularization is considered. In patients with unstable angina who have been stabilized, subsequent exercise myocardial perfusion defect size reliably predicts the extent of coronary artery disease.

3. Old Myocardial Infarction

Myocardial perfusion imaging with either 201Tl or the ^{99m}Tc-labeled compounds does not differentiate between acute myocardial infarction, acute ischemia, or scar. Nevertheless, a substantial number of patients with presumably old myocardial infarction may have normal or nearnormal perfusion images. Frequently, however, prior myocardial infarction can be recognized only as "thinner" myocardial segments, particularly in patients with old inferior wall myocardial infarcts. SPECT imaging may be more sensitive than planar imaging for the detection of such small myocardial scars.

4. Myocardial Perfusion Imaging in Emergency Departments and Chest Pain Centers

Since acute myocardial ischemia can be visualized almost instantaneously with ^{201}Tl or ^{99m}Tc-labeled compounds, resting radio nuclide myocardial perfusion imaging is increasingly used as a means to triage patients with acute chest pain in emergency departments and chest pain centers. Of the numerous patients who visit emergency departments yearly with complaints of acute chest pain, many have normal or nondiagnostic ECGs. Approximately half of these patients had previously been admitted to a hospital to "rule out acute myocardial infarction." In only a small proportion of these patients (15 to 20 percent) could an acute coronary syndrome be confirmed. In the majority of pa-tients, the chest discomfort was apparently not caused by acute myocardial ischemia and hospitalization was unnecessary.

The presently available ^{99m}Tc-labeled compounds are better suited than ^{201}Tl for acute imaging of patients with chest pain, These compounds can be readily reconstituted when a patient arrives with chest pain. Moreover, the lack of redistribution of these agents provides greater flexibility with regard to the timing of

imaging. SPECT imaging also provides useful information relative to the coronary vascular territory involved and, by using ECG gating, allows for assessment of regional and global left ventricular function. Resting myocardial perfusion images are abnormal at a time when enzymes in many patients have not yet risen to diagnostic levels[6]. Furthermore, the negative predictive value of resting imaging was better than 99 percent. Thus, patients with acute chest pain, a non-diagnostic ECG, and *normal rest* SPECT images have less than a 1 percent chance of having an ongoing acute infarction. The rare patient with acute infarction who was undetected by rest SPECT imaging invariably had small and uncomplicated infarcts. On the other hand, patients with *abnormal* SPECT images had an increased risk of coronary events during hospitalization (death, acute infarction, or revascularization). Acute resting SPECT could be used as a cost-effective means to manage patients with acute chest pain and non-diagnostic ECG.

Once acute myocardial infarction has been ruled out in a chest pain center, the evaluation protocol is completed with risk stratification by stress testing. Although most patients can be evaluated with exercise ECG, a substantial number of patients are not able to perform an adequate level of physical exercise. In these patients, pharmacological vasodilation in conjunction with radio nuclide myocardial perfusion imaging is performed. Discriminative use of either resting or stress radio nuclide imaging has an important place in the efficient triaging of patients in chest pain centers.

B. Prognostification by Stress Myocardial Perfusion Imaging—Detection of High Risk Patients

Detection of coronary artery disease is only one aspect of the clinical value of stress myocardial perfusion imaging. The greater the functional severity of coronary artery disease, the more abnormal exercise myocardial perfusion images are likely to be. Most patients (approximately 95 percent) with left main coronary disease have abnormal stress myocardial perfusion images. However, the expected typical left main pattern, i.e., defects in the anteroseptal and postero-lateral walls, is found in only a minority (approximately 14 percent) of patients with left main coronary artery disease. The majority (approximately 75 percent) of patients nevertheless have multiple perfusion defects and, frequently, abnormally increased lung uptake of 201Tl. Although most patients with triple-vessel disease have abnormal stress images, only approximately 60 percent have multiple defects in two or more vascular regions. Disease in the left circumflex coronary artery is better detected with SPECT imaging than with planar imaging.

Myocardial perfusion images of a high-risk patient can be characterized by *one or more* of the following image features: (1) multiple reversible defects in two or more coronary artery territories, (2) quantitatively large myocardial perfusion defects, (3) increased pulmonary radiotracer uptake after exercise, (4) transient dilatation of the left ventricle immediately after exercise,(5) depressed resting LVEF on either gated SPECT or first-pass angiography, and (6) increased right ventricular uptake on stress images. This high-risk pattern is highly specific (approximately 95 percent) for multivessel coronary artery disease; however, the sensitivity is only about 70 percent. Therefore, in the absence of the above-mentioned scintigraphic characteristics, multivessel disease cannot be ruled out.

C. Predischarge Stress Testing after Acute Infarction

Patients without ischemia at hospital discharge had only a 6 percent cardiac event rate (death, recurrent infarction, or unstable angina), whereas patients who had high-risk findings on predischarge 201Tl stress images (multiple defects in more than one vascular region, abnormal washout, or increased lung uptake) had a 51 percent cardiac event rate. Dipyridamole and adenosine myocardial perfusion imaging can be used for very early risk stratification during the first days after the acute event or at the time of discharge from the hospital. In the Veterans Affairs Non-Q -Wave Infarction Strategies in Hospital (VANQWISH) trial[7], invasive management (routine angiography) was compared with conservative management (noninvasive testing) in stable survivors of non-Q-wave acute infarctions. Patients in the conservative limb (who had radionuclide stress myocardial perfusion imaging) had significantly less coronary angiography (96 vs. 48 percent) but a higher revascularization rate (42 vs. 68 percent). Importantly, overall infarct-free survival was comparable in both groups. Thus, stress myocardial perfusion imaging at the time of discharge effectively identified high- and low-risk patients.

D. Prognostic Significance of Normal Stress Perfusion Images in Presence of Angiographically Documented CAD

Normal planar or SPECT stress myocardial perfusion images, even when coronary artery stenosis is angiographically documented, indicate a favorable prognosis with a low subsequent cardiac event rate. Patients

with quantitatively normal myocardial perfusion images have a yearly nonfatal myocardial infarction rate of 0.5 to 1 percent per year and a mortality rate of 0 to 0.5 percent per year.

These data on abnormal and normal stress myocardial perfusion images indicate that the extent of myocardial perfusion defects, or the lack thereof, provides significant physiological and prognostic information that surpasses the anatomical information obtained from coronary angiograms. The prognostic predictive value of stress myocardial perfusion imaging is independent of the imaging technique applied (planar or SPECT) or the radio pharmaceutical used (^{201}Tl or 99mTc-labeled agents).

III. UTILITY AND LIMITATIONS

In clinical practice, diagnostic tests are generally used in conjunction with each other. The clinician usually has other clinical and diagnostic information available. Evidence for the prognostic value of stress myocardial perfusion imaging is compelling. However, if similar information can be derived from other less costly and readily available tests, it may not be cost-effective to perform radionuclide myocardial perfusion imaging. The incremental prognostic value of various diagnostic data obtained in succession (clinical data, exercise ECG, stress ^{201}Tl-myocardial perfusion imaging and coronary angiography) is complementary. The combination of clinical and exercise 201Tl variables provided greater prognostic information than did the combination of clinical and angiographic data alone.

A. Detection of Coronary Artery Disease in Women

Exercise ECG has been rep-orted to be less accurate in women than in men for the detection of coronary artery disease. Moreover, women more often have an abnormal baseline ECG, which affects accuracy of interpretation of exercise ECGs. Although breast attenuation artifacts may make the interpretation of stress myocardial perfusion images in women more difficult, experienced interpreters usually recognize artifacts and can avoid false-positive interpretations[8].

B. Detection of Coronary Artery Disease in Diabetic Patients

Patients with diabetes mellitus have an increased risk of coronary artery disease. Myocardial ischemia is frequently asymptomatic and silent in patients with diabetes. It is not uncommon that an asymptomatic patient with diabetes is referred for stress testing as part of evaluation and found to have markedly abnormal myocardial perfusion images. Clearly significant coronary artery disease is detected late in many diabetic patients, for any given degree of myocardial perfusion abnormality.

C. Myocardial Perfusion Imaging in Patients with Left Bundle Branch Block

In patients with complete left bundle branch block, the conduction abnormality precludes the use of conventional ECG criteria for the diagnosis of infarction or exercise-induced ischemia. It was expected that myocardial uptake of perfusion imaging agents would be unaffected by the ECG abnormality. Indeed, in patients with left bundle branch block without prior myocardial infarction, *resting* myocardial perfusion images are generally normal. However, the septum is frequently thin, and in older patients the left ventricle is often dilated.

D. Myocardial Perfusion Imaging for Preoperative Screening

An important clinical application of myocardial perfusion imaging involves the preoperative evaluation of patients undergoing noncardiac surgery. Such perfusion imaging has had its most meaning-full application in the study of patients prior to revascularization surgery involving the descending aorta and the lower extremities. This group of patients has a strong likelihood of the coexistence of coronary artery disease. Evidence of ischemia on dipyridamole ^{201}Tl imaging was predictive of subsequent perioperative cardiac events. Preoperative risk assessment has been extended to patients scheduled to undergo major noncardiac surgery.

E. Myocardial Perfusion Imaging before and After Revascularization in Decision Making

The main purpose for performing stress myocardial perfusion imaging is not only to detect significant coronary artery disease but also to aid in patient management decisions. Patients with markedly abnormal and high-risk stress myocardial perfusion images will usually be considered candidates for coronary revascularization.

1. Coronary Artery Bye-pass Graft Surgery

Myocardial perfusion imaging is not routinely performed after coronary bypass surgery and is only

indicated when symptoms recur. Since many patients have nonspecific ST-T segment changes on the baseline ECG after surgery, myocardial perfusion imaging is preferred over exercise ECG to evaluate these patients. Tomographic localization of perfusion abnormalities allows a determination of whether clinical ischemia is likely to be caused by coronary graft closure or by newly developed disease in other coronary arteries.

2. Percutaneous Coronary Intervention

Stress myocardial perfusion imaging may be particularly useful after percutaneous coronary intervention in patients with multivessel coronary artery disease. Often, the most severe stenosis in one vessel was dilated and questions remain whether the stenosis in other vessels are of significance. With SPECT imaging, a specified vascular territory can be evaluated readily. The optimal timing of imaging after intervention is unclear. Some investigators reported a high incidence of false-positive myocardial perfusion abnormalities early after intervention, presumably because of delayed return of coronary flow reserve within the territory of the dilated artery. Most patients have normal myocardial perfusion images within the first week after successful angioplasty. At approximately 4 weeks after coronary angioplasty, good correlation has been demonstrated between stress-induced myocardial perfusion abnormalities and the presence or absence of restenosis, independent of clinical symptoms. SPECT imaging allows one to determine whether clinical ischemia is caused by restenosis at the site of angioplasty and stenting or by progression of disease in other coronary arteries.

3. Assessment Of Myocardial Viability

For patients with angina, known coronary artery disease, previous infarction(s), and left ventricular dysfunction, a reliable method for assessing the presence, extent, and location of viable myocardium is of considerable clinical importance. It is well established that global or regional ischemic left ventricular dysfunction is not always an irreversible condition. Approximately 25 to 40 percent of patients have the potential for improvement in function after adequate revascularization. Extensive research has been conducted to establish the relative value of myocardial perfusion imaging with ^{201}Tl and ^{99m}Tc-labeled tracers for predicting myocardial viability. Initially, 18F-FDG regional uptake on positron imaging was used as a reference standard for myocardial viability, Unfortunately, in many later publications only improvement in regional dysfunction on dobutamine echocardiography has been equated with viability. This practice ignores the clinical importance of relieving ischemia in myocardial segments that are unlikely to have improved function after revascularization because of nontransmural scarring. Myocardial metabolic activity on positron 18F-FDG imaging is a more appropriate benchmark for viability[9].

Two important practical issues need to be addressed when evaluating patients with presumed ischemic dysfunc-tion: (1) assessment of the relative regional myocardial uptake of ^{201}Tl (often after rest reinjection , 99mTc-sestamibi, or ^{99m}Tc-tetrofosmin (often after rest ad-ministration of nitroglycerin). When the resting uptake of radiotracer is greater than 50 percent of normal, one can expect recovery of function after revascularization. (2) Assessment of the presence of demonstrable ischemia (i.e., partially reversible defect) in a myocardial segment with decreased uptake, even if the resting uptake is less than 50 percent.

4. Myocardial Infarct Imaging

From the early days of nuclear cardiology, myocardial infarction was visualized either as a "cold spot" (perfusion defect) or as a "hot spot." Cold spot imaging has been extensively discussed above. When a radio pharmaceutical localizes specifically in an area of recent infarction, the infarct is visualized as a "hot spot." The advantage of hot spot imaging is that it is generally easier to image the pres-ence of a tracer than its absence. The clinical usefulness of infarct imaging still requires clear definition. The diagnosis of acute myocardial infarction in the majority of patients can be readily made on the basis of simple and inexpensive tests such as the ECG and cardiac enzyme analysis

^{99m}Tc-Sn-PYROPHOSPHATE. The first clinically useful hot spot imaging of acute infarction was performed with ^{99m}Tc-Sn-pyrophosphate. This imaging agent was very sensitive for detecting acute myocardial infarction from 24 hours to 5 days after the onset of chest pain[10]. The intensity and pattern of ^{99m}Tc-Sn-pyrophosphate uptake were found to be of prognostic significance. At the present time, ^{99m}Tc-pyrophosphate infarct imaging is mainly of historical interest and is performed infrequently in most laboratories.

In occasional patients suspected of having sustained an acute infarction 2 to 3 days prior to hospital admission, ^{99m}Tc-pyrophosphate imaging may be useful to establish the diagnosis at a time when plasma enzymes levels have returned to normal. SPECT imaging appears to be more sensitive than planar imaging. At

the present time, cardiac troponins can be used for the same purpose, although the anatomical site and extent of infarction cannot be assessed by using these biochemical markers of myocardial injury.

INDIUM-111-LABELED ANTIMYOSIN. The $^{111}I_n$-labeled murine monoclonal antimyosin binds selectively to irreversibly damaged myocytes. Imaging should be performed 24 hours after injection of the radio pharmaceutical to allow clearance of $^{111}I_n$ from the blood. Typical $^{111}I_n$ antimyosin images of an acute infarct demonstrate discrete up-take in the myocardium. In addition, substantial liver and spleen uptake may be seen. In addition to positive images in patients with acute myocardial infarction, uptake of $^{111}I_n$-antimyosin has been noted in patients with unstable angina. The intensity and extent of $^{111}I_n$-antimyosin accumulations were of prognostic significance both in patients with acute infarction and in those with unstable angina. Patients with extensive antimyosin uptake, i.e., greater than 50 percent of the myocardium, had a four to nine times increased risk for future cardiac events, i.e., cardiac death and nonfatal myocardial infarction, than did patients with less or no uptake. The positive uptake seen in patients with unstable angina probably represents small clinically undetectable focal areas of necrosis.

In addition to imaging acute myocardial infarction, 111In-antimyosin imaging may have a role in cardiac transplant patients for the detection of cardiac rejection.[11] Furthermore, in patients with active myocarditis, diffuse $^{111}I_n$-antimyosin uptake has been observed.

IV. POSITRON-EMISSION TOMOGRAPHY (PET)

The uniqueness of PET imaging lies in its ability to image and quantify metabolic processes, receptor occupancy, and blood flow. The main advantages of positron imaging are the ability to label and thus image biologically active compounds and drugs, the higher energy of the positron signal (allowing enhanced count statistics), and the ability to correct for body attenuation, thereby increasing specificity. Clinical indications for PET studies are for the identification of myocardial viability in patients with established coronary artery disease and regional or global left ventricular dysfunction[12] and for the noninvasive diagnosis of coronary artery disease.

Assessment of Myocardial Viability

The accurate assessment of the presence and extent of viable, yet poorly contractile myocardium and its discrimination from purely infarcted tissue are of potential clinical importance. A number of diagnostic tech-niques are available for assessing myocardial viability. Approaches to viability assessment using radionuclide techniques involved the assessment of myocardial perfusion, cell membrane integrity. or myocardial metabolism. For institu-tions without PET facilities, myocardial viability is generally assessed with resting ^{201}Tl imaging. For assessment of myocardial viability with ^{99m}Tc-sestamibi results are variable. PET imaging is generally regarded as the noninvasive "gold standard" in decisions regarding viability . Identification of viable myocardium with PET based on assessment of metabolism, although certain parameters of perfusion have been shown to be indicators of preserved viability as well.18F-FDG, a marker of glucose utilization is the most commonly used, metabolic radiotracer. Other metabolic tracers include ^{11}Cacetate and ^{11}C-palmitate as markers of oxidative metabolism.

Special Applications of PET and Future Directions—Coronary Blood Flow Reserve

The true potential of cardiac PET is its ability to label organic compounds and accurately quantitative radiotracer uptake, thereby allowing assessment of absolute myocardial and brain blood flow, coronary flow reserve, cardiac and brain receptor density, and other potential *in vivo* markers of cardiac and/or vascular physiology. Cardiac PET has added much to our understanding of a variety of cardiac disorders and will continue to do so with the future development of quantitative techniques. Quantitative cardiac PET may contribute relevant information for coronary blood flow.

The anatomical delineation of coronary artery luminal narrowing by coronary angiography may not accurately reflect the functional significance of coronary artery disease. With stress-rest dynamic PET perfusion imaging, measurements of absolute myocardial blood flow and flow reserve can be determined. The term "flow reserve" is meaningful to the extent that absolute measurement before and after pharmacological intervention is measured. Absolute flow reserve, that is, the difference between stress and rest flow, reflects the cumulative effects of physiological factors such as vasomotor tone, workload, hypertrophy, and coronary stenosis. Relative flow reserve, that is, the ratio of stress to rest flow, reflects more specifically coronary stenosis independent of these other physiological variables and is thus comparable (with regard to mechanism) to reversible/nonreversible SPECT flow tracers for the assessment of coronary artery disease. In general, stress

perfusion imaging is performed after vasodilator hyperemia with either dipyridamole or adenosine. Delineation of absolute myocardial blood flow and determination of flow reserves with PET are powerful noninvasive techniques by which to assess the effects of coronary and other cardiovascular diseases on cardiac physiology.

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