

12. PET/CT in Cardiology

Michael W. Hanson and Salvador Borges-Neto

The high incidence of cardiovascular disease and the resultant morbidity associated with the sequelae of acute cardiovascular events continue to be major issues of medical concern. To assist in the clinical evaluation of patients with known or suspected cardiovascular disease, several methodologies of investigation have been developed to detect the presence of disease and to provide an assessment for prognosis, effects of therapy, and risk stratification of patients. These diagnostic modalities include exercise and/or pharmacologic stress testing, nuclear cardiac imaging, echocardiography, cardiac catheterization/coronary angiography, and magnetic resonance imaging. These patients frequently require an anatomic, physiologic, and functional assessment of their cardiovascular status to determine optimal clinical management. Nuclear cardiac imaging techniques lend themselves more to physiologic and functional assessments. Techniques used in nuclear cardiology can be broadly divided into those that rely on standard single photon emitting radiopharmaceuticals (e.g. multi-gated blood pool imaging, first pass radionuclide ventriculography, and planar and/or single photon emission computed tomographic (SPECT) myocardial perfusion and metabolic imaging) and those that rely on positron emitting radiopharmaceuticals (e.g. rubidium-82, nitrogen-13 ammonia, and oxygen-15 water for myocardial perfusion imaging and ^{18}F fluorodeoxyglucose for metabolic imaging).

Cardiovascular nuclear imaging for the assessment of myocardial blood flow has been available for over 30 years. The clinical use of thallium-201 for myocardial perfusion imaging was approved in 1973. The two technetium-99m labeled radiopharmaceuticals currently in use for myocardial perfusion imaging were both approved in the 1990s. The predominant cardiac applications of nuclear imaging during this time have been evaluation of myocardial perfusion and assessment of myocardial viability. These investigations have traditionally been performed in conventional nuclear cardiology with planar and/or SPECT imaging in most clinical practices. Although PET imaging techniques for the assessment of myocardial perfusion and viability were also developed many years ago [1,2], the utilization of cardiac PET imaging has suffered predominantly from the lack of widespread availability of PET scanners and radiopharmaceuticals, expense of the technology with limited reimbursement, and limited approval of cardiac PET radiopharmaceuticals by regulatory agencies. However, in recent years, there has been significant improvement of these limitations. The recent proliferation of PET scanners has made them more widely available, thus allowing greater patient access to this technology. In addition, ^{15}N ammonia has been added to ^{82}Rb as an approved radiopharmaceutical for myocardial perfusion imaging for reimbursement by the Centers for Medicare and Medicaid

Services. Cardiac PET imaging with ^{18}F fluorodeoxyglucose (FDG) is also approved for reimbursement for the assessment of myocardial viability. Another factor of importance for myocardial viability imaging has been the development of regional delivery systems for same day shipment of ^{18}F FDG, which precludes the need for on-site cyclotrons and radiopharmacies for the production of ^{18}F FDG. A recent major improvement related to cardiac PET imaging is the development of the combined PET/CT scanner. In a single study, with the use of intravenous contrast, stress testing and PET imaging, patients with known or suspected coronary artery disease can undergo anatomic assessment of coronary anatomy, evaluation of stress-induced ischemia (or evaluation of coronary flow reserve) and evaluation of left ventricular function.

Cardiac imaging with PET offers selected advantages over cardiac imaging with planar or SPECT modalities. PET imaging provides a high degree of diagnostic accuracy. In comparison to conventional planar or SPECT imaging, PET provides a higher temporal and spatial resolution, and a well-established methodology for attenuation correction. PET images can be analyzed qualitatively or semi-quantitatively. Unlike conventional cardiac imaging, PET studies can also provide absolute quantification of myocardial blood flow and ^{18}F FDG utilization.

Overall, the combination of the technological advantages of PET imaging, relative to SPECT imaging, the progress and improvements in the availability of PET scanners and PET radiopharmaceuticals, the ability to assess coronary anatomy, myocardial perfusion, and ventricular function with a combined PET/CT scanner, and the progress in reimbursement policies should lead to an increase in myocardial assessment by cardiac PET imaging.

Positron Emission Tomography Assessment of Myocardial Ischemia

Tracers for Myocardial Perfusion Imaging in Positron Emission Tomography

There are primarily three tracers that are currently used to assess myocardial perfusion with PET imaging, each of which has certain advantages and disadvantages. These tracers include oxygen-15 water, nitrogen-13 ammonia, and rubidium-82 chloride.

Oxygen-15 labeled water is a nearly ideal, freely diffusible tracer for the evaluation of myocardial perfusion, relative to its linear uptake in relation to increasing myocardial blood flow. Its uptake and clearance are related directly to perfusion and unrelated to metabolic considerations. However, image quality can be adversely affected because of the presence of ^{15}O water in the blood pool; the myocardial perfusion image must be corrected for this vascular activity, which is accomplished by obtaining a blood pool image with ^{15}O labeled carbon monoxide [3]. In addition, the very brief physical half-life of ^{15}O of only 2.1

minutes requires its production from an on-site cyclotron, which limits its availability. Research studies have been performed with ^{15}O water, but the issues of limited availability and somewhat demanding and cumbersome methodology have precluded its use for routine clinical studies.

Nitrogen-13 ammonia is a PET tracer that is extracted from the blood and distributed in the myocardium in relation to blood flow. Its uptake and retention, however, are dependent on metabolic processes in the myocardium. It demonstrates high single pass extraction of approximately 90% and subsequent long retention in the myocardium, which results in high contrast images, relative to blood pool activity. Unlike ^{15}O water, uptake of ^{13}N ammonia is non-linear and plateaus at blood flows greater than around 2 ml/gram per minute. Its uptake and retention depends on conversion of ammonia to glutamine [4]. The availability of ^{13}N ammonia is also somewhat limited due to the 10-minute physical half-life of ^{13}N , which must also be produced by an on-site cyclotron. Where available, however, the overall favorable characteristics of this agent make it suitable for routine clinical studies, which can be performed relatively efficiently.

Rubidium-82 chloride is also a PET tracer that is extracted from the blood and distributed in the myocardium in relation to blood flow. Rubidium-82 is similar to thallium-201 in that it acts as a potassium analogue. Its myocardial extraction is approximately 65% at normal resting blood flow, and like ^{13}N ammonia is also non-linear at higher flow rates. Unlike ^{15}O and ^{13}N , ^{82}Rb is produced from a free-standing generator (strontium-82 parent), which avoids the need for an on-site cyclotron and radiopharmacy, thereby making this radiopharmaceutical more readily and widely available. The half-life of ^{82}Rb is only 76 seconds, which, in general, allows for a shorter imaging time for a rest and stress perfusion study than is required for ^{13}N ammonia.

Most clinical PET studies are performed with either ^{13}N ammonia (Figure 12.1) or ^{82}Rb chloride. Both of these tracers have been found to be highly accurate for evaluating patients with known or suspected coronary artery disease [5–12]. The overall averages of reported sensitivity and specificity of myocardial PET perfusion imaging with ^{82}Rb or ^{13}N ammonia for the detection of coronary artery disease are 94% and 95%, respectively (Table 12.1) [13].

Comparison of Positron Emission Tomography and Single Photon Emission Computed Tomographic Myocardial Perfusion Imaging

In comparing PET and SPECT for myocardial perfusion imaging, there are several issues to be considered. If patients are able, the preferred modality for stress testing for myocardial perfusion imaging is physical exercise, while pharmacologic stress testing with either vasodilators (i.e., adenosine or dipyridamole) or catecholamine stimulation (i.e., dobutamine) is considered an alternative modality. Any of these modalities lend themselves well to SPECT imaging technology. For PET imaging, pharmacologic stress is usually preferred, although

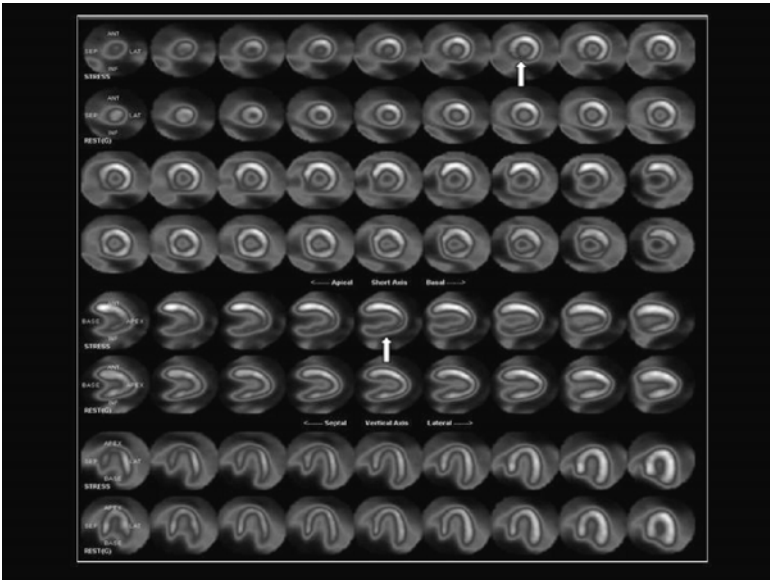


Figure 12.1. ^{13}N ammonia PET scan on a 70-year-old man with recurring chest pain, which demonstrates reversible ischemia in the inferior and inferoapical segments of the left ventricle (arrows).

exercise is feasible, particularly in conjunction with ^{13}N ammonia. PET offers advantages in spatial resolution and in accepted methodology for attenuation correction, which in turn, can result in improvement in specificity in patients being evaluated for known or suspected coronary artery disease. The higher photon

Table 12.1. Detection of coronary artery disease with ^{13}N ammonia and ^{82}Rb chloride

Radiopharmaceutical	Investigator	<i>n</i>	Sensitivity	Specificity
^{13}N ammonia	Yonekura [5]	49	97%	100%
^{13}N ammonia	Schelbert [6]	32	97%	100%
^{13}N ammonia	Tamaki [7]	46	98%	—
^{82}Rb	Gould [8]	50	95%	100%
^{82}Rb	Williams [9]	146	98%	100%
^{82}Rb	Demer [10]	193	82%	95%
^{82}Rb	Stewart [11]	81	84%	88%
^{82}Rb	Go [12]	132	95%	82%
Total		729	94%	95%

Source: Adapted from Schwaiger, Ziegler, Bengel [13], by permission of Lippincott Williams and Wilkins.

energy of PET tracers and the attenuation correction capability of PET imaging offer advantages over SPECT for evaluating obese patients. In addition to improvement in image quality, a myocardial perfusion study in an obese patient that would require a two-day protocol with SPECT imaging due to body habitus can frequently be completed in one day with PET imaging. Overall, there is high sensitivity and specificity for detection of coronary artery disease with PET perfusion imaging.

In comparing rubidium-82 PET and thallium-201 SPECT in the same patient population (132 patients without previous therapeutic interventions), Go et al. demonstrated a higher sensitivity with PET (95% vs. 79%) and a slightly higher specificity with PET (82% vs. 76%) [12], while Stewart et al. demonstrated no significant difference in sensitivity (84% vs. 84%) with a higher specificity for PET (88% vs. 53%) [11].

Finally, one of the major advantages of PET is the ability to measure myocardial blood flow in absolute terms (ml/gram per minute), which cannot be determined by SPECT imaging.

Assessment of Myocardial Viability

Recent estimates suggest that there are 4–5 million people in the United States who have chronic heart failure, with 400,000 new cases and one million hospitalizations occurring each year; as many as 70% of these patients may have underlying coronary artery disease as the cause of their left ventricular dysfunction [14]. The left ventricular ejection fraction (LVEF) is a major prognostic indicator for survival in patients who have coronary artery disease, particularly in patients who have severe depression of LVEF [15]. Patients who have left ventricular dysfunction as a result of coronary artery disease may demonstrate improvement of their left ventricular ejection fraction after a revascularization procedure [16]. Surgical revascularization has shown a significant survival benefit, as compared to medical therapy in patients with coronary artery disease and depressed left ventricular function; a 7-year survival rate of 63% has been shown for patients who had revascularization, as compared to a 34% survival rate after medical therapy [17]. The improved survival may relate, at least partially, to an improvement in left ventricular ejection fraction. However, revascularization presents a high clinical risk for intervention in these patients [18]. Therefore, it is clinically important to prospectively determine whether a patient has evidence of reversible left ventricular dysfunction prior to submitting the patient to a revascularization procedure, and to identify those patients who are likely to benefit most from revascularization. The most benefit appears to occur in those patients who have moderate to severe left ventricular dysfunction and evidence of significant viability. A recent study has shown an 80% reduction in annual mortality among patients with viable myocardium identified by non-invasive testing who were treated with revascularization, while there was no significant difference in mortality between revascularization and medical therapy in patients who did not demonstrate viable myocardium. In addition, patients with viable myocardium demonstrated a direct relationship between the magnitude of benefit from revascularization and the severity of left ventricular dysfunction [19].

Table 12.2. Detection of ventricular functional recovery after revascularization: weighted mean values from pooled analysis of reported non-invasive imaging studies

Modality	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Echocardiography (low-dose dobutamine)	82%	79%	78%	83%
²⁰¹ Tl rest-redistribution	86%	59%	69%	80%
¹⁸ F FDG-PET	93%	58%	71%	86%

Source: From Bax, Poldermans, Elhendy et al. [20], by permission of *Current Problems in Cardiology*.

In patients with coronary artery disease, dysfunctional myocardium can occur from variable etiologies that result in segmental wall motion abnormalities and diminished left ventricular function. A completed myocardial infarction may result in left ventricular dysfunction due to a segmental scar that represents irreversible, non-viable myocardial tissue. An acute, reversible ischemic event (“stunned” myocardium) or chronic myocardial ischemia (“hibernating” myocardium) may also result in left ventricular dysfunction with segmental wall motion abnormalities, but the affected myocardial segment may contain myocardial tissue whose function can be improved by revascularization, and is thus characterized as viable myocardium. Diagnostic studies that can define left ventricular dysfunction, but examine only wall motion at rest, cannot distinguish whether a wall motion abnormality is caused by potentially reversible or irreversible myocardial damage. Therefore, several imaging modalities have been devised or modified to assess myocardial viability (Table 12.2). These techniques rely on the ability to stimulate improvement in myocardial contractility or the ability to interrogate certain physiologic aspects of the myocardium to distinguish viable from non-viable tissue.

Echocardiography

Echocardiography is a technique that can assess wall motion at rest. In order to assess for viability, echocardiography requires a stress agent, which most often is dobutamine; vasodilator stress, such as dipyridamole, is less often employed. Viability is determined by assessing for stress-induced myocardial contractile reserve. As dobutamine is administered in increasing dosage, tissue that is viable demonstrates improvement in contractility at a lower dose, but becomes dysfunctional again at higher doses as the heart is further stressed. From a pooled analysis of reported studies in the medical literature, the weighted mean sensitivity and specificity of low-dose dobutamine echocardiography for predicting functional recovery after revascularization were 82% and 79%, respectively [20].

Magnetic Resonance Imaging

Cinegraphic magnetic resonance imaging (MRI) is similar to echocardiography in allowing real-time evaluation of cardiac wall motion, which then allows assessment of contractile reserve with dobutamine in a manner similar to echocardiography. In the prediction of functional recovery on an individual patient basis, dobutamine-induced systolic wall thickening evaluated by MRI has demonstrated a sensitivity of 89% and a specificity of 94% whereas assessment of preserved end diastolic wall thickness demonstrated a sensitivity of 92% and a specificity of 56% [21]. MRI can also assess myocardial viability after administration of gadolinium-DTPA contrast. Areas of completed myocardial infarction demonstrate a region of hyper-enhancement of contrast on delayed imaging. In a recent study comparing contrast-enhanced MRI to ^{18}F FDG-PET, the sensitivity and specificity of MRI for detecting myocardium characterized as non-viable by PET were 96% and 84%, respectively [22].

Thallium-201 Scintigraphy

Thallium-201 is used to assess perfusion and cell membrane integrity as markers of viability. The uptake of ^{201}Tl requires an intact and functional cell membrane. The redistribution of ^{201}Tl on delayed images in myocardial segments that demonstrated a defect on initial images is compatible with viable myocardium in that segment. From a pooled analysis of reported studies in the medical literature, the weighted mean sensitivity and specificity of thallium rest-redistribution imaging for detecting improvement in regional contractile function after revascularization were 86% and 59%, respectively [20].

Positron Emission Tomography

The most common method for evaluating myocardial viability with PET is assessing myocardial perfusion in conjunction with assessment of regional myocardial metabolism. Perfusion can be assessed with either ^{13}N ammonia or rubidium-82 chloride. Metabolism is assessed by the uptake of ^{18}F FDG, a glucose analogue that is transported into the myocardial cell and becomes metabolically trapped after intracellular phosphorylation. Image analysis relies on evaluation of the match or mismatch of segmental perfusion and metabolism. From pooled analysis of reported studies, the weighted mean sensitivity and specificity of ^{18}F FDG-PET for detecting improvement in regional contractile function after revascularization were 93% and 58%, respectively [20].

There are some nuances of cardiac PET imaging that need consideration prior to imaging, most of which relate to dietary status and blood levels of glucose and fatty acids. Under normal resting conditions, the myocardium uses free fatty acids and glucose as major sources of energy. In ischemic myocardium, however, oxidative metabolism of free fatty acids is decreased and glucose becomes the preferred substrate for energy source. The ability of the

myocardium to metabolize glucose, even though it may be inadequate for normal myocardial contractility (depending on the severity of ischemia), is indicative of viable myocardium.

Because normal myocardium uses predominantly free fatty acids and ischemic myocardium may use predominantly glucose as their respective energy substrates under normal resting conditions, one consideration for myocardial viability imaging would be to administer ^{18}F FDG in a fasting state to identify ischemic viable myocardium. The rationale of this protocol would be that ischemic viable myocardium would take up ^{18}F FDG, while normal or infarcted, non-viable myocardium would take up little, if any ^{18}F FDG. However, in that setting, overall image quality has been shown to be suboptimal for definitive evaluation [23]. The uptake of FDG into the myocardium is very dependent on dietary conditions, as particularly related to plasma levels of glucose, insulin and free fatty acids. Elevated levels of free fatty acids inhibit myocardial uptake of FDG, whereas increased levels of glucose and insulin facilitate myocardial uptake of FDG [24]. Therefore, optimizing the relative concentrations of these metabolic substrates is desired for optimal FDG cardiac imaging, and various techniques have been devised to accomplish this goal. Patients with diabetes mellitus, however, do present a challenge to obtain optimal image quality. The most demanding protocol involves the use of a euglycemic hyperinsulinemic clamping technique, which regulates these various substrates and frequently results in optimal image quality [25]. However, this procedure is time-consuming and difficult to apply in the general clinical setting. An alternative that is most frequently used in clinical practice is an oral glucose loading technique, often accompanied by the administration of intravenous regular insulin on a sliding scale, dependent upon the patient's response to the oral administration of usually 25–50 grams of oral glucose. Another alternative that has been proposed is the oral administration of acipimox, which is a derivative of nicotinic acid [26]. This agent inhibits peripheral lipolysis, which reduces the plasma level of free fatty acids, thereby indirectly stimulating cardiac uptake of glucose, and thus FDG-18. This technique has resulted in good image quality that is reported as comparable to the optimal euglycemic hyperinsulinemic technique [26].

The protocol for viability assessment includes a resting myocardial perfusion study (usually using ^{13}N ammonia or ^{82}Rb), followed by a glucose loaded ^{18}F FDG metabolic study. Myocardial segments that have been shown to be dysfunctional on wall motion analysis are then analyzed for perfusion and metabolic findings. The analysis involves evaluating the studies for areas of matched or mismatched findings (Table 12.3).

In general, viable ischemic myocardium demonstrates mismatched increased FDG activity in areas of decreased perfusion, while non-viable myocardium demonstrates matched areas of decreased FDG activity and decreased perfusion (Figure 12.2). These findings allow identification of myocardium that may benefit from revascularization. In general, any segment of the myocardium that demonstrates preservation of ^{18}F FDG uptake that is greater than 50% of normal is considered viable.

Viability studies with ^{18}F FDG-PET have been analyzed from several perspectives to determine the ability of the studies to predict clinically useful information [27]. In addition to predicting improvement of regional left ventricular function after revascularization, ^{18}F FDG-PET has also been predictive of

Table 12.3. Wall motion and PET scan findings (perfusion and ^{18}F FDG metabolism) as related to myocardial status

Myocardium	Wall motion	Perfusion	^{18}F FDG uptake
Normal	Normal	Normal	Normal
Stunned	Decreased	Normal	Normal or increased
Hibernating	Decreased	Decreased	Normal or increased
Infarcted scar	Decreased	Decreased	Decreased

improvement in global LV function after revascularization. Cardiac FDG-PET has also been shown to be predictive of improvement in heart failure symptoms and exercise capacity. Viability assessment with FDG has also been shown to have a significant clinical impact on patient management. Based on results of an FDG-PET viability study, patient therapy can be redirected between medical and

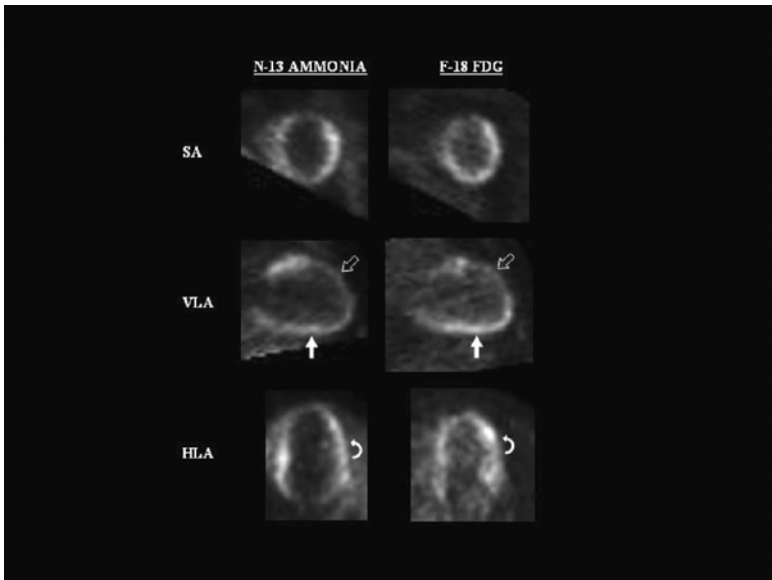


Figure 12.2. Myocardial viability study (^{13}N ammonia perfusion and ^{18}F FDG metabolism) of a 53-year-old man with coronary artery disease and ischemic cardiomyopathy being considered for coronary artery bypass graft surgery. There is a completed transmural infarct with non-viable myocardium (matched defect with severely diminished perfusion and FDG metabolism) in the anterior segment (open arrows) and segmental ischemic viable myocardium (mismatched defect with diminished perfusion, but preserved FDG metabolism) in the inferior segment (closed arrows). Normal viable myocardium (matched normal perfusion and FDG metabolism) is demonstrated in the lateral segment (curved arrows).

surgical therapy, and between heart transplant and revascularization. Therefore, patients that would be suitable for myocardial viability studies would include patients with left ventricular dysfunction and low ejection fractions as a result of sequelae of coronary artery disease who are under consideration for revascularization or cardiac transplantation.

Horizons: Positron Emission Tomography/Computed Tomography Angiography/Calcium Scoring

Scintigraphic myocardial perfusion imaging evaluates the physiology of myocardial blood flow at the cellular level, as various tracers are deposited in the myocardium in proportion to the blood flow to any given region. The usual adjunctive study to scintigraphy is the invasive coronary angiogram that is performed with contrast injection directly into the coronary arteries to evaluate the degree of potential stenosis of the epicardial coronary artery supplying a region of detected ischemia. Vice versa, myocardial perfusion scintigraphy can be utilized to determine the physiologic significance of epicardial stenoses identified on preceding coronary angiography. Currently, there is extensive interest in PET/multidetector CT scanners, which can provide a non-invasive functional and anatomical cardiac evaluation in a single setting. While the PET scanner component of these hybrid cameras can evaluate myocardial perfusion and metabolism, the CT scanner component can detect calcified and non-calcified atherosclerotic coronary artery disease, and identify suspected flow-limiting coronary artery stenoses. Thus, this combined study can provide the location and composition of atherosclerotic lesions and their physiologic significance, relative to myocardial perfusion.

The logistics for performing combined PET/CT will vary depending upon the PET radiopharmaceutical employed and the method of performing the stress test (i.e., exercise or pharmacologic stress agents). Patients are screened and prepared as per routine protocol for stress testing. Special attention to heart rate is required for optimal acquisition of the CT angiogram. For a typical ^{13}N ammonia vasodilator stress PET/CT scan, beta-blocker therapy is not withheld. If the patient is not taking an oral beta-blocker, or if the resting heart rate prior to scanning is greater than 65 beats per minute, and the resting blood pressure is greater than 90/60, oral and/or intravenous beta-blocker medication (e.g. metoprolol) can be administered prior to the CT angiogram. For exercise stress testing, beta-blocker therapy is withheld per protocol prior to the PET/CT scan. If the resting heart rate is greater than 65 beats per minute, and the resting blood pressure is greater than 90/60, a shorter-acting beta-blocker (e.g. esmolol) can be administered. After establishing an optimal heart rate of around 55–60 beats per minute, the CT angiogram is performed as the initial study. An initial non-contrast thoracic CT scan is acquired for cardiac localization. Circulation time is evaluated by giving a small bolus of intravenous contrast and determining the time to peak intensity of contrast in the root of the aorta. Subsequently, a gated contrast-enhanced scan is acquired from the ascending aorta to just below the diaphragm.

The myocardial perfusion study is acquired after the CT angiogram. The rest perfusion study, which is preceded by a CT scan for attenuation correction, is acquired with ^{13}N ammonia, and can be gated for evaluation of left ventricular ejection fraction. The patient is then stressed as per exercise or pharmacologic protocol, followed by the stress myocardial perfusion scan and a repeat CT scan that is acquired for attenuation correction of the stress perfusion images (Figure 12.3). The combined ^{13}N ammonia stress PET/CT scan can be completed in approximately 90–120 minutes (Figure 12.4).

Calcification of the coronary artery is present in most atherosclerotic lesions, and is more likely to be found in advanced disease. CT can detect the presence of calcium in the coronary arteries, and can also quantify the extent of calcium that is detected, which can be reported in a standard scoring format (the Agatston score). Identification of coronary calcium is a sensitive, though not specific, marker for the presence of obstructive coronary artery disease (Figure 12.5). Published data from Shaw et al. suggest that the presence of coronary calcium provides independent incremental information, in addition to traditional risk factors, in predicting all-cause mortality [28]. Non-calcified atherosclerotic plaque, whether or not it is associated with hemodynamically significant luminal stenosis, can also be delineated by CT.

Active research is being conducted to evaluate the ability of CT coronary angiography to non-invasively detect the presence and extent of coronary artery

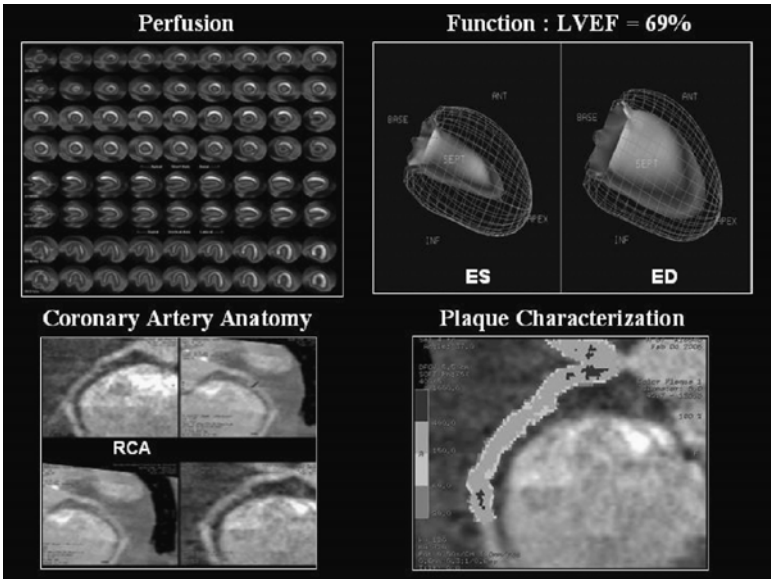


Figure 12.3. Combined PET/CT scan demonstrates inferior wall ischemia on the myocardial perfusion image. The left ventricular ejection fraction (LVEF) is normal (69%). Atherosclerotic disease is demonstrated in the proximal right coronary artery (RCA), the composition of which can be characterized by analysis of plaque density.

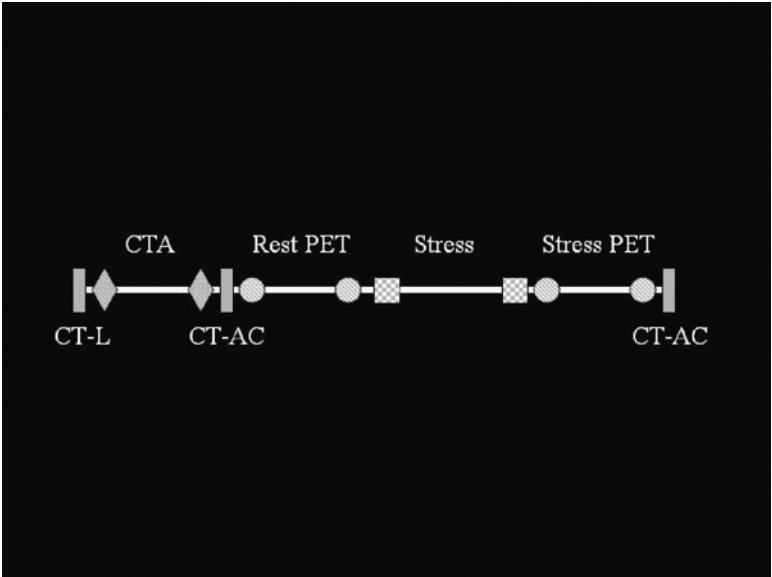


Figure 12.4. Methodology for acquisition of PET/CT scan. CT-L = localizing CT scan; CT-AC = attenuation correction CT scan; CTA = CT angiogram.

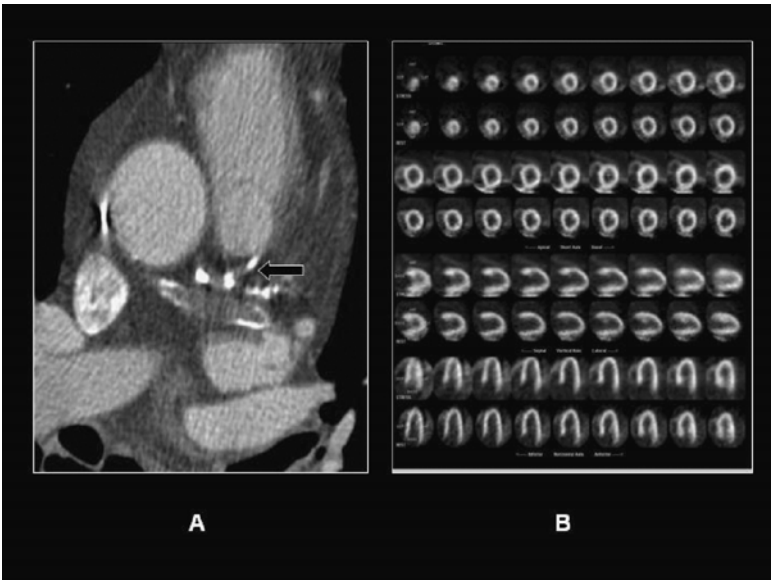


Figure 12.5. Dense calcification is noted in the coronary arteries (arrow) (A). The ^{13}N ammonia myocardial perfusion study (B) does not demonstrate any evidence of myocardial ischemia.

stenosis. The sensitivity for detection of coronary artery disease with CT can vary depending on several factors, including the location of disease (e.g. proximal versus distal vessel) and the CT scanner employed (e.g. 4-slice versus 16-slice or 64-slice scanners). Leber et al. have reported on the diagnostic accuracy of a 64-slice CT scanner to identify and quantify atherosclerotic coronary lesions in comparison to catheter-based angiography and intravascular ultrasound [29]. In this study, 59 patients with stable angina pectoris were included who had coronary angiography performed within 2 days of the contrast-enhanced CT angiogram. A subset of 18 patients had intravascular ultrasound of 32 vessels performed as part of the catheterization procedure. The 64-slice CT scanner obtained diagnostic image quality of the entire coronary artery tree (American Heart Association 15-segment model for proximal, mid and distal segments) in 55/59 patients. For all segments, sensitivity for the detection of stenosis <50% was 79%, stenosis >50% was 73%, and stenosis >75% was 80%. Specificity for all three groups was 97%. Sensitivity for the detection of stenoses that subsequently required revascularization, however, was 89%. In comparison with intravascular ultrasound, the overall sensitivity and specificity of CT for the detection of coronary lesions were 84% and 91%, respectively.

Although the full impact of PET/CT on the clinical management of patients with known or suspected coronary artery disease remains to be determined, this exciting new technology provides an attractive modality for the simultaneous non-invasive evaluation of the status of the coronary arteries, myocardial perfusion and/or metabolism, and evaluation of left ventricular function (Figure 12.6).

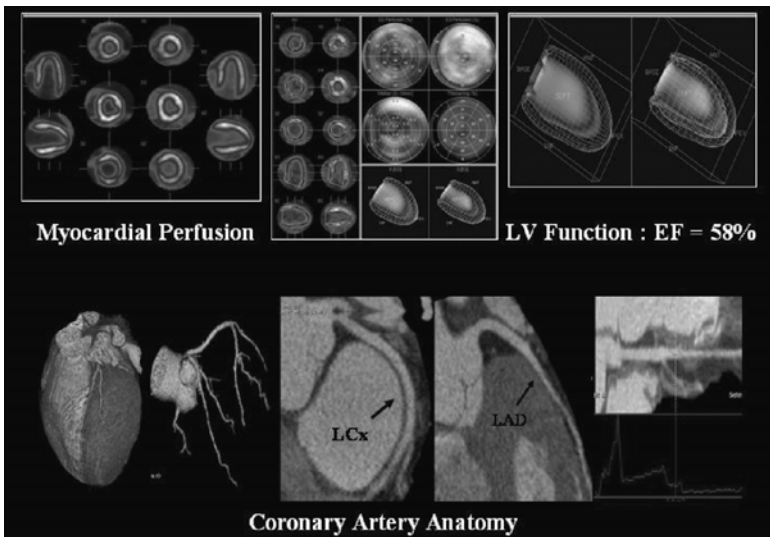


Figure 12.6. In a non-invasive, single setting, combined PET/CT demonstrates myocardial perfusion, evaluation of left ventricular function, and coronary artery anatomy, which can be displayed in various planar and three-dimensional displays.

References

1. Schelbert HR, Phelps ME, Hoffman EJ, et al. Regional myocardial perfusion assessed with N-13 labeled ammonia and positron emission computerized axial tomography. *Am J Cardiol* 1979;43:209–218.
2. Tillisch J, Brunken R, Marshall R, et al. Reversibility of cardiac wall motion abnormalities predicted by positron emission tomography. *N Engl J Med* 1986;314:884–888.
3. Bergmann SR, Fox KA, Raud AL, et al. Quantification of regional myocardial blood flow in vivo with H₂¹⁵O. *Circulation* 1984;70:724–733.
4. Bergmann SR. Quantification of myocardial perfusion with positron emission tomography. In: Bergmann SR, Sobel BE, editors. *Positron Emission Tomography of the Heart*. Mount Kisco, NY: Futura; 1992:97–127.
5. Yonekura Y, Tamaki N, Senda M, et al. Detection of coronary artery disease with ¹³N-ammonia and high-resolution positron-computed tomography. *Am Heart J* 1987;113:645–654.
6. Schelbert H, Phelps M, Huang S, et al. N-13 ammonia as an indicator of myocardial blood flow. *Circulation* 1981;63:1259–1272.
7. Tamaki N, Yonekura Y, Senda M, et al. Myocardial positron computed tomography with ¹³N-ammonia at rest and during exercise. *Eur J Nucl Med* 1985;11:246–251.
8. Gould K, Goldstein R, Mullani N. Economic analysis of clinical positron emission tomography of the heart with rubidium-82. *J Nucl Med* 1989;30(5):707–717.
9. Williams B, Jansen D, Wong L, et al. Positron emission tomography for the diagnosis of coronary artery disease: a non-university experience and correlation with coronary angiography. *J Nucl Med* 1989;30:845.
10. Demer LL, Gould KL, Goldstein RA, et al. Assessment of coronary artery disease severity by positron emission tomography. Comparison with quantitative arteriography in 193 patients. *Circulation* 1989;79:825–835.
11. Stewart R, Schwaiger M, Molina E, et al. Comparison of rubidium-82, positron emission tomography and thallium-201 SPECT imaging for detection of coronary artery disease. *Am J Cardiol* 1991;67:1303–1310.
12. Go RT, Marwick TH, MacIntyre WJ, et al. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the diagnosis of coronary artery disease. *J Nucl Med* 1990;31:1899–1905.
13. Schwaiger M, Ziegler SI, Bengel FM. Assessment of myocardial blood flow with positron emission tomography. In: Pohost GM, O'Rourke RA, Berman DS, et al., editors. *Imaging in Cardiovascular Disease*. Philadelphia: Lippincott, Williams and Wilkins; 2000:195–212.
14. Gheorghiane M, Bonow RO. Chronic heart failure in the United States. A manifestation of coronary artery disease. *Circulation* 1998;97:282–289.
15. The Multicenter Post Infarction Research Groups. Risk stratification and survival after myocardial infarction. *N Engl J Med* 1993;309:331–336.

16. Bonow RO, Dilsizian V. Thallium-201 for assessing myocardial viability. *Semin Nucl Med* 1991;21:230–241.
17. Pigott JD, Kouchoukos NT, Oberman A, et al. Late results of surgical and medical therapy for patients with coronary artery disease and depressed left ventricular function. *J Am Coll Cardiol* 1985;5:1036–1045.
18. Baker DW, Jones R, Hodges J, et al. Management of heart failure III. The role of revascularization in treatment of patients with moderate or severe left ventricular systolic dysfunction. *JAMA* 1994;272:1528–1534.
19. Allman KC, Shaw LJ, Hachamovitch R, et al. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 2002;39:1151–1158.
20. Bax JJ, Poldermans D, Elhendy A, et al. Sensitivity, specificity, and predictive accuracies of various non invasive techniques for detecting hibernating myocardium. *Curr Probl Cardiol* 2001;26:147–186.
21. Baer FM, Theissen P, Schneider CA, et al. Dobutamine magnetic resonance imaging predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. *J Am Coll Cardiol* 1998;31:1041–1048.
22. Kuhl HP, Beek AM, van deer Weerd AP, et al. Myocardial viability in chronic ischemic heart disease. Comparison of contrast-enhanced magnetic resonance imaging with ¹⁸F-Fluorodeoxyglucose positron emission tomography. *J Am Coll Cardiol* 2003;41:1341–1348.
23. Berry JJ, Baker JA, Pieper KS, et al. The effect of metabolic milieu on cardiac PET imaging using fluorine-18-deoxyglucose and nitrogen-13-ammonia in normal volunteers. *J Nucl Med* 1991;32:1518–1525.
24. Nuutila P, Koivisto VA, Knuuti J, et al. Glucose-free fatty acid cycle operates in human heart and skeletal muscle in vivo. *J Clin Invest* 1992;89:1767–1774.
25. Knuuti J, Nuutila P, Ruotsalainen U, et al. Euglycemic hyperinsulinemic clamp and oral glucose load in stimulating myocardial glucose utilization during positron emission tomography. *J Nucl Med* 1992;33:1255–1262.
26. Knuuti MJ, Yki-Jarvinen H, Voipio-Pulkki LM, et al. Enhancement of myocardial [fluorine-18] fluorodeoxyglucose uptake by a nicotinic acid derivative. *J Nucl Med* 1994;35:989–998.
27. Bax JJ, Patton JA, Poldermans D, et al. 18-Fluorodeoxyglucose imaging with positron emission tomography and single photon emission computed tomography: cardiac applications. *Semin Nucl Med* 2000;30:281–298.
28. Shaw LJ, Raggi P, Schisterman E, et al. Prognostic value of cardiac risk factors and coronary artery calcium screening for all cause mortality. *Radiology* 2003;228:826–833.
29. Leber AW, Knez A, Von Ziegler F, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005;46:147–154.