Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT

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Background. **Although single photon emission computed tomography (SPECT) and positron emission tomography (PET) myocardial perfusion imaging (MPI) have evolved considerably over the last decade, there is no recent comparison of diagnostic performance. This study was designed to assess relative image quality, interpretive confidence, and diagnostic accuracy by use of contemporary technology and protocols.**

Methods and Results. **By consensus and without clinical information, 4 experienced nuclear cardiologists interpreted 112 SPECT technetium-99m sestamibi and 112 PET rubidium-82 MPI electrocardiography (ECG)–gated rest/pharmacologic stress studies in patient populations matched by gender, body mass index, and presence and extent of coronary disease. The patients were categorized as having a low likelihood for coronary artery disease (27 in each group) or had coronary angiography within 60 days. SPECT scans were acquired on a Cardio-60 system and PET scans on an ECAT ACCEL scanner. Image quality was excellent for 78% and 79% of rest and stress PET scans, respectively, versus 62% and 62% of respective SPECT scans (both $p < .05$). An equal percent of PET and SPECT gated images were rated excellent in quality. Interpretations were definitely normal or abnormal for 96% of PET scans versus 81% of SPECT scans ($p = .001$). Diagnostic accuracy was higher for PET for both stenosis severity thresholds of 70% (89% vs 79%, $p = .03$) and 50% (87% vs 71%, $p = .003$) and was higher in men and women, in obese and nonobese patients, and for correct identification of multivessel coronary artery disease.**

Conclusion. **In a large population of matched pharmacologic stress patients, myocardial perfusion PET was superior to SPECT in image quality, interpretive certainty, and diagnostic accuracy. (J Nucl Cardiol 2006;13:24-33.)**

Key Words: Single photon emission computed tomography • positron emission tomography • myocardial perfusion imaging

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Radionuclide myocardial perfusion imaging (MPI) is performed worldwide for assessing patients with known or suspected coronary artery disease (CAD). Most commonly, either thallium-201 or a technetium-99m perfusion tracer is used via single photon emission computed tomography (SPECT). An alternative is myocardial perfusion positron emission tomography (PET) using either cyclotron-produced ammonia or generator-produced rubidium 82.[1] There are several potential advantages of PET MPI, such as higher spatial resolution, greater counting efficiencies, and robust attenuation correction. All of these factors presumably form the basis of improved diagnostic accuracy in comparison to SPECT in studies performed more than a decade ago.[2-6] Although these studies were instrumental in shaping

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expert opinion about the relative performance of SPECT and PET,[7] they did not influence practice patterns, perhaps because of the widespread availability of SPECT relative to PET.

The past few years have seen substantial dissemination of PET instrumentation and a concomitant increase in MPI. Both PET technology and SPECT technology have advanced considerably since the comparative studies referenced previously.[8] This investigation is a comparison of image quality, interpretive certainty, and diagnostic accuracy derived from a consensus blinded read of statistically matched populations undergoing either pharmacologic Tc-99m sestamibi SPECT or Rb-82 PET MPI.

METHODS

The objective of this study was to compare the relative quality of contemporary electrocardiography (ECG)–gated myocardial perfusion SPECT and PET scans, the ability of interpreters to be definite about their diagnoses, and the diagnostic accuracy in comparison to accepted standards. This was accomplished through a consensus read of a large population of patients who were matched by gender, body mass index (BMI), and presence and extent of CAD and who underwent imaging in a single laboratory (Cardiovascular Consultants, PC, Kansas City, Mo). Because all PET studies were performed with vasodilator stress, the SPECT patients were also restricted to those who had vasodilator stress. Two broad groups of patients were eligible: those who underwent coronary angiography within 60 days of scintigraphic testing and a low-likelihood cohort. Eligible patients were identified retrospectively from an electronic nuclear cardiology database and were excluded only if the study was designated as technically compromised (uncorrectable lateral motion resulted in exclusion of 3 SPECT patients and uncorrectable misregistration of emission and transmission scans or poor signal-to-noise ratios due to excessive blood pool activity excluded 3 PET patients) or if the patients met clinical exclusionary criteria (as discussed later). The angiography and low-likelihood patients were then separately matched to arrive at a final data set. The study was approved by the Institutional Review Board of Saint Luke's Hospital of Kansas City, Kansas City, Mo.

Patients

Low-likelihood patients. A low-likelihood cohort of SPECT and PET patients was identified from the same clinical database, from which a matched group was derived. Low likelihood was defined as no known CAD, no chest pain, normal electrocardiogram, no stress-induced ECG changes, no diabetes, and database classification as a clinically normal image interpretation. From this cohort, male and female PET and SPECT patients were combined in separate PET and SPECT data sets with a uniformly distributed random number generated for each patient. Each group of data was then sorted by gender. This created a random listing of patients within each gender cell. The data were then merged on gender, by taking the smaller number in each cell between the groups.[9] There were originally 27 SPECT and 30 PET low-likelihood patients. After matching on gender, there were 27 patients in each group (13 women and 14 men).

Coronary angiography patients. Any patient who had vasodilator pharmacologic stress via either a same-day rest/stress Tc-99m sestamibi SPECT protocol or a same-day rest/stress Rb-82 PET protocol was eligible, providing that the following criteria were met: no history of intervened myocardial infarction, no prior coronary artery bypass surgery, no coronary interventions within the prior 6 months, and BMI of less than 50 kg/m^2. Patients with a left ventricular ejection fraction of 40% or less based on their respective SPECT or PET study were also excluded because of the known impact of cardiomyopathy on myocardial perfusion independent of epicardial coronary disease. The male and female SPECT and PET patient studies were combined in separate SPECT and PET data sets, and a uniformly distributed random number was generated for each patient. Each group of data was then sorted by gender, the random number, and the number of diseased vessels. This created a random listing of patients within each gender cell and diseased vessel cell. The data were then merged on gender and number of diseased vessels, only taking the smaller number in each cell between the groups. For example, if there were 15 female PET studies with 0 diseased vessels and 20 in SPECT, the final data set would have the randomly matched 15 from each group. The original angiographic data set included 110 SPECT and 94 PET patients. After matching on gender and number of diseased vessels, there were 85 patients in each group.

The presence or absence of CAD was determined from the clinical coronary angiogram reports, with luminal diameter narrowing of the 3 main coronary arteries or their major branches of both 70% or greater and 50% or greater being used as the criteria for significance.

Clinical Tc-99m Sestamibi SPECT Protocol

Patients were instructed to fast and to abstain from caffeine- and methylxanthine-containing substances for 24 hours before testing. Approximately 370 MBq Tc-99m sestamibi was injected at rest. After 45 to 60 minutes, ECG-gated SPECT was acquired with a dual-detector 90° Cardio-60 system (Philips Medical Systems, Milpitas, Calif). All studies used the following parameters: 64 total projections; 180° right anterior oblique–left posterior oblique orbit; 64 × 64 matrix; 0.6-cm pixel size; 8 frames per cardiac cycle; low-energy, high-resolution collimation; and 30 seconds per stop. For the stress study, adenosine infusion was administered at 140 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 6 minutes.[10] At the end of the third minute of the infusion, a weight-adjusted dose of Tc-99m sestamibi (925 MBq for <102.2 kg and 1110 MBq otherwise) was administered. After 30 to 45 minutes, patients underwent imaging by use of the following parameters: 64 total projections; 180° right anterior oblique–left posterior oblique orbit; 64 × 64 matrix; 0.6-cm pixel size; 8 frames per cardiac cycle;

low-energy, high-resolution collimation; and 25 seconds per stop.

SPECT Reconstruction Protocol

For the gated frames, each projection was prefiltered with a radially symmetric Butterworth prefilter (order, 5; cutoff, 0.4 Nyquist) and reconstructed with frequency-based ramp filtering and filtered backprojection. To obtain summed (perfusion) images, all temporal frames at each angle were summed to form an integrated projection set and reconstructed with filtered backprojection by use of a Butterworth filter (order, 5; cutoff, 0.46 Nyquist).

Clinical Rb-82 PET Protocol

All Rb-82 PET studies were performed on a ACCEL PET scanner (CTI, Knoxville, Tenn). Perfusion data were acquired by use of a 2-dimensional (2D) (septa-extended) dynamic protocol. For increased sensitivity, ECG-gated data were acquired in a 3-dimensional (3D) mode.[11,12]

Rest acquisition. The first acquisition was a 4-minute nongated transmission scan by use of the rotating germanium 68 line sources for the attenuation map and as a scout for positioning the heart in the field of view. Then, 2220 MBq Rb-82 was infused over a period of 30 seconds. After a 90-second delay for blood pool clearance, 2D tomographic images were acquired in 3 successive 30-second frames, followed by a single 210-second frame, for a total acquisition time of 5 minutes. The detector septa were then retracted for 3D acquisition, and 1480 MBq Rb-82 was infused via an identical timing and injection protocol. After a 150-second delay, a 3-minute ECG-gated acquisition was performed.

Stress acquisition. Dipyridamole was used for pharmacologic stress in all studies, with patients being instructed to fast and to abstain from caffeine- and methylxanthine-containing substances for 24 hours before testing. The dose of dipyridamole was calibrated in 30 mL of normal saline solution according to the patient's weight (0.71 mg/kg; maximum total dose, 70 mg) and administered at the rate of 6 mL/min over a period of 5 minutes.[10] Beginning 2 minutes after initiation of dipyridamole infusion, a 4-minute Ge-68 transmission scan was acquired with the Ge-68 line sources for attenuation correction. Immediately thereafter, 2220 MBq Rb-82 was infused over a period of 30 seconds. After a 90-second postinjection delay for blood pool clearance, 2D tomographic images were acquired in 3 successive 30-second frames, followed by a single 210-second frame. The scanner was then configured to the 3D mode, and images were acquired via the same protocol and parameters as the resting acquisitions. Immediately thereafter, 100 mg aminophylline was administered to reverse the dipyridamole-induced vasodilation and any associated symptoms.

PET image reconstruction protocol and display. The sinograms from each dynamic 2D (framed) acquisition were corrected for dead time, scatter, and randoms and then summed to form a single static perfusion sinogram. These were then reconstructed with an ordered-subset expectation maximization (OSEM) algorithm by use of 6 iterations and 8 subsets.[13] Transmission data were first reconstructed by use of filtered backprojection; the reconstructed images were then segmented and reprojected to create the transmission sinograms, used to correct the emission data for attenuation. A postreconstruction fifth-order low-pass Butterworth filter with a 15-mm kernel was applied to the reconstructed images before reorientation to the short, vertical, and long horizontal planes.

ECG-gated data were reconstructed by use of 2 iterations and 8 subsets of the OSEM algorithm and a postreconstruction fifth-order low-pass Butterworth filter with an 18-mm kernel applied to the reconstructed gated tomograms. Stress and rest images were displayed for the nuclear cardiologists by use of Quantitative Perfusion SPECT/Quantitative Gated SPECT (QPS/QGS) software (Cedars-Sinai Medical Center, Los Angeles, Calif). The 2D framed Rb-82 images were used to examine key measures such as perfusion defect size, extent, and normal segment uniformity. The 3D ECG-gated Rb-82 images were used to evaluate functional parameters such as ejection fraction, ventricular volumes, and regional wall motion.

Scan Interpretation

The scans were presented in random sequence to the 4 reviewers for their consensus interpretation. Two of the readers had extensive SPECT experience but no PET experience, and two had experience with both SPECT and PET. The readers were shown the following image data: rotating rest and stress projection images, rest and stress emission images, and rest and stress ECG-gated images for SPECT and rest and stress emission images and rest and stress ECG-gated images for PET. No clinical data were provided so that the readers were not aware of gender, symptoms, results of the ECG stress test, or patient group.

Study interpretation was performed in 3 categories: image quality, interpretive certainty, and final diagnosis. For image quality, the rest and stress emission and gated data were separately graded on a 4-point scale: excellent, good/average, fair, and poor (not interpretable). Sources of potential artifact (breast attenuation, liver and bowel activity, low myocardial counts, poor signal-to-noise ratio) were scored as absent, visible but mild and not affecting interpretation, significant and believed to be affecting interpretation, and major (precluding interpretation). Radionuclide counts used in the reconstructions were compared for a subset of 5 male and 5 female low-likelihood PET patients and 5 male and 5 female low-likelihood SPECT patients. Sinograms containing only "true" events from the Rb-82 stress perfusion images were summed over the angular projections to produce a single composite image. A region of interest was manually drawn over the heart region for each subject, and total counts were calculated. A similar procedure and calculation were performed for the Tc-99m sestamibi stress perfusion SPECT projections. The categories for interpretive certainty were definitely normal, probably normal, equivocal, probably abnormal, and definitely abnormal. Images were scored by use of a 17-segment model,[14] with each

Table 1. Comparison of SPECT and PET patients

Variable	SPECT (n = 112)	PET (n = 112)	*p* Value
Age (y)	65	66.7	.248
Male	61 (52%)	61 (52%)	—
BMI (kg/m^2)	32.5 (16–50)	31.7 (17–50)	.329
Angina	54 (48%)	61 (55%)	.349
Prior myocardial infarction	24 (21%)	28 (25%)	.53
Prior percutaneous coronary intervention	39 (35%)	50 (45%)	.13
Smoker	12 (11%)	14 (13%)	.68
Diabetes	41 (37%)	37 (33%)	.57
Hypertension	84 (75%)	86 (77%)	.75
Hyperlipidemia	99 (88%)	92 (82%)	.19
Abnormal electrocardiogram	87 (78%)	90 (80%)	.62
50% Angiography group	85 (76%)	85 (76%)	—
0-Vessel disease	11 (13%)	11 (13%)	
1-Vessel disease	14 (16%)	14 (16%)	
Multivessel disease	60 (71%)	60 (71%)	
70% Angiography group	85 (76%)	85 (76%)	—
0-Vessel disease	18 (21%)	15 (18%)	.56
1-Vessel disease	23 (27%)	28 (33%)	.40
Multivessel disease	44 (52%)	42 (49%)	.76
Low-likelihood group	27 (24%)	27 (24%)	—

segment scored on a scale of 0 (normal) through 3 (severe defect).

On the basis of these scores, each coronary territory was defined as normal if the stress/rest score for relevant segments was 0/0 or 1/0 and as abnormal if the score was 2/0, 2/1, 2/2, 3/0, 3/1, 3/2, or 3/3. The specific coronary arteries were identified according to the region of abnormality: anterior, anteroseptal, and apical (left anterior descending artery); inferior and inferoseptal (right coronary artery); and anterolateral and inferolateral (left circumflex artery).

Statistical Analysis

In comparisons of patients within groups, categoric variables were calculated as percentages and then compared by use of a 2 sample *t* test or χ^2 test.[15] Diagnostic accuracy for CAD was determined with definitely or probably normal or abnormal being correct responses; a positive diagnosis was defined as a study that was probably or definitely abnormal, and a negative diagnosis was defined as a study that was probably or definitely normal. Sensitivity, specificity, and accuracy were calculated within the angiography group and compared at a cutoff disease severity of both 50% and 70% luminal diameter narrowing. The individual coronary territories were compared in the same manner. The percent of definitely normal interpretations within the low-likelihood patients was used to calculate the normalcy rates. The Fisher exact test was used to compare the two scan types.[15] Statistical significance was denoted by p values $<$ .05.

RESULTS

A total of 112 rest/stress ECG-gated SPECT Tc-99m sestamibi and 112 rest/stress ECG-gated PET Rb-82 studies in patients matched by gender, BMI, and presence and extent of CAD were included. Of these, 27 in each group were low-likelihood patients, and the remainder had coronary angiography (Table 1). The time between perfusion imaging and coronary angiography was 24 $\pm$ 21 days. The coronary angiography patients included 13% of PET patients and of SPECT patients who had no significant CAD, 16% of PET patients and of SPECT patients with single-vessel CAD, and 71% of each with 2 or 3 diseased coronaries (by use of a cutoff of 50%).

A comparison of image quality between SPECT and PET is shown in Figure 1. The PET perfusion images were significantly better in quality than the SPECT perfusion images. Image quality was considered excellent for 78% (87/112) and 79% (89/112) of the rest and stress PET perfusion images, respectively, compared with 62% (69/112) ($p < .05$) and 62% (69/112) ($p < .05$) of the rest and stress SPECT images, respectively. The gated images were graded of equal quality: 78% (87/112) and 83% (93/112) of rest and stress gated PET images, respectively, were excellent compared with 75% (84/112) (p = not significant) and 79% (89/112) (p = not significant) for SPECT scans. Fair or poor (noninterpret-

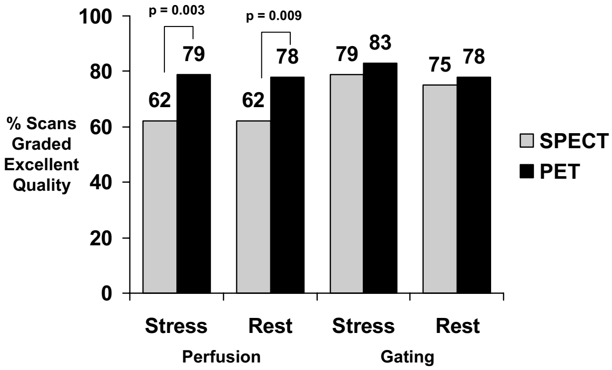

Figure 1. Image quality scores for PET and SPECT perfusion and ECG-gated scans.

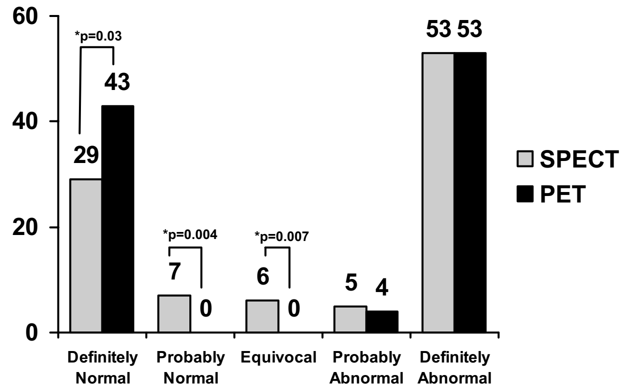

Figure 2. Comparison of degrees of interpretive certainty of SPECT and PET studies.

Table 2. Prevalence of artifacts

	SPECT	PET	*p* Value
Any artifact			
None	19 (17%)	49 (44%)	.00001
Minor	26 (23%)	28 (25%)	.75
Significant	64 (57%)	33 (29%)	.00003
Major	3 (3%)	2 (2%)	.32
Liver or bowel			
None	45 (40%)	100 (89%)	< .00001
Minor	19 (17%)	5 (4%)	.002
Significant	46 (41%)	6 (5%)	< .00001
Major	2 (2%)	1 (1%)	.32

able) studies were observed for 9 SPECT and 3 PET stress scans. Stress myocardial counts for the 10 low-likelihood PET patients in whom counts were measured were 2.4 times those on the 10 low-likelihood stress SPECT scans, with a mean of 5,374,952 ± 1,633,133 counts on the PET images compared with 2,220,912 ± 921,892 on the SPECT scans ($p < .001$).

There were marked differences in the prevalence of image artifacts (Table 2): 44% of PET studies had no artifacts compared with 17% of SPECT studies ($p < .0001$). Liver uptake and bowel uptake were believed to affect the interpretation of 5% of PET studies compared with 41% of SPECT studies ($p < .0001$).

A comparison of interpretive certainty between SPECT and PET studies is shown in Figure 2. A significantly lower percent (81%) of SPECT scans were able to be interpreted as definitely normal or abnormal compared with 96% of PET images ($p = .0008$). Neither image quality nor interpretive certainty differences between SPECT and PET were influenced either by patient gender or when patients were subclassified into obese (BMI >30 kg/m^2) and nonobese.

In the low-likelihood patients, the normalcy rate was 81% for SPECT versus 100% for PET ($p = .02$). Overall diagnostic accuracy was determined by including all patients, those undergoing angiography, and low-likelihood patients. Given the small number of angiographically normal patients, "specificity" in this analysis included the low-likelihood patients, as well as angiographically normal patients. At the 70% stenosis severity threshold, sensitivity was 82% for SPECT and 87% for PET ($p = .41$). Specificity was significantly lower for SPECT (73%) compared with PET (93%) ($p = .02$), with a resulting significant improvement in overall accuracy by PET (89% vs 79%, $p = .03$) (Figure 3*A*). By use of a 50% threshold, the respective comparative accuracy was 71% for SPECT versus 87% for PET ($p = .003$) (Figure 3*B*).

PET was superior for localizing disease to individual coronary arteries (Figure 4) for both stenosis severity thresholds. Table 3 shows the results for each of the 3 coronary arteries.

When accuracy was examined in relation to patient gender, PET was significantly superior to SPECT. For men, SPECT accuracy was 69% (sensitivity of 78% and specificity of 50%) compared with 84% for PET (sensitivity of 81% and specificity of 89%) ($p = .055$), whereas the comparison values for women were 67% (sensitivity of 69% and specificity of 64%) for SPECT and 88% (sensitivity of 81% and specificity of 86%) ($p = .009$) for PET. Likewise, comparative accuracy computed by BMI also favored PET. For patients with a BMI of 30 kg/m^2 or less, the accuracy by SPECT versus PET was 70% versus 87% ($p = .05$), and for obese patients, the respective accuracy was 67% versus 85% ($p = .02$).

PET was more sensitive than SPECT for correctly identifying the presence of multivessel coronary disease. PET correctly classified 30 of 42 patients (71%) with multivessel CAD compared with 21 of 44 (48%) for SPECT ($p = .03$).

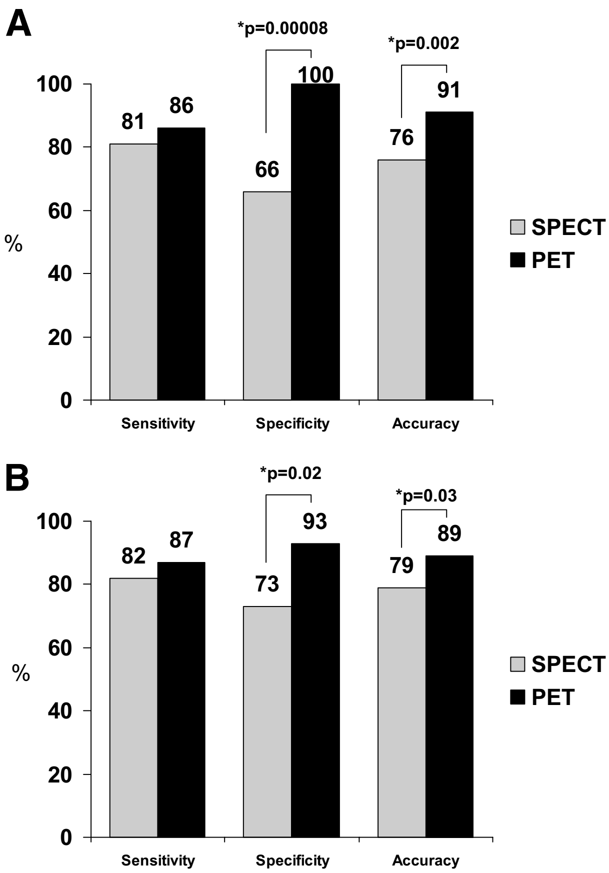

Figure 3. Overall diagnostic accuracy for PET and SPECT: 50% coronary stenosis threshold (**A**) and 70% stenosis threshold (**B**).

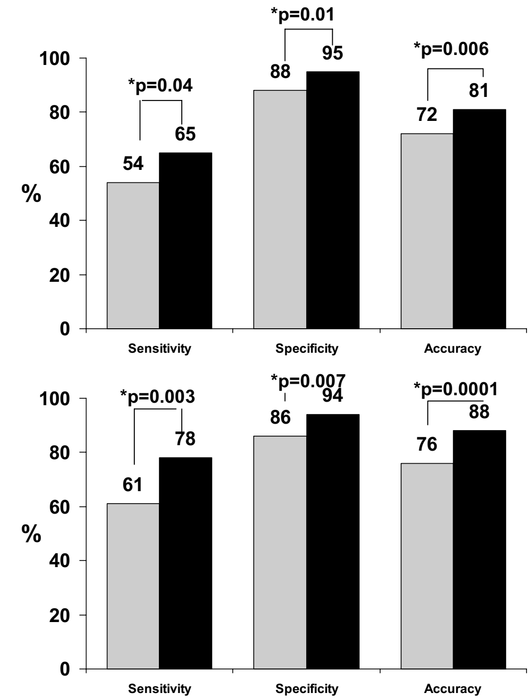

Figure 4. Diagnostic accuracy for localizing disease to individual coronary arteries: 50% stenosis severity threshold (*top*) and 70% threshold (*bottom*).

DISCUSSION

This is the first clinical study in more than a decade to compare SPECT and PET MPI. The findings, supported by a large number of patients matched by gender, BMI, and presence and extent of CAD, indicate significant benefits of vasodilator Rb-82 rest/stress ECG-gated PET MPI. The quality of the perfusion images was superior with PET, interpretive certainty was higher, and diagnostic accuracy was improved in comparison to a matched group of patients undergoing vasodilator SPECT MPI. PET performed better than SPECT in women and men and in obese and nonobese patients. Furthermore, PET improved the ability of MPI to recognize the presence of multivessel CAD, which is potentially important in subsequent management decisions.

In this study a major benefit of PET over SPECT was higher diagnostic accuracy. Combining the patients who had no significant CAD at angiography with the low-likelihood patients yielded a SPECT specificity of 58% compared with 93% with PET. There was also a trend toward higher sensitivity overall, with significantly higher sensitivity for detection of multivessel CAD and disease of the left anterior descending and left circumflex coronary arteries.

Prior PET and SPECT Accuracy Studies

To our knowledge, this is the first study that has matched patient characteristics to determine the relative performance of myocardial perfusion PET and SPECT. In addition, this study specifically compares performance in patients undergoing vasodilation stress. Prior publications of the results of blinded (no clinical information) interpretation of Tc-99m sestamibi SPECT scans reported diagnostic accuracy values similar to those in this study. Hendel et al[16] reported a sensitivity of 76% in 96 patients with CAD and a normalcy rate of 86% in 88 low-likelihood patients; Links et al[17] found a sensitivity of 78% in 27 patients with CAD and a normalcy rate of 62% in 39 patients with either normal coronary angiograms or at low statistical likelihood for CAD. Williams et al[18] published the results of a blinded consensus read of 287 dipyridamole PET scans; the sensitivity was 87%, the specificity was 88%, and the accuracy was 88%.

There have been several comparisons between SPECT Tl-201 and PET resulting from retrospective clinical analyses.[4-6] Go et al[5] reported the results of an innovative prospective study of Tl-201 versus Rb-82

Table 3. Sensitivity, specificity, and accuracy

	Sensitivity	Specificity	Accuracy
50% Disease threshold			
LAD	61%/79% (p = 0.04)	92%/95%	75%/87% (p = 0.03)
LCX	33%/58% (p = 0.03)	86%/93%	68%/79%
RCA	60%/58%	87%/100% (p = 0.007)	73%/78%
70% Disease threshold			
LAD	67%/87% (p = 0.02)	84%/91%	77%/89% (p = 0.01)
LCX	38%/71% (p = 0.007)	86%/91%	72%/85% (p = 0.02)
RCA	71%/74%	88%/100% (p = 0.003)	80%/89%

Data are presented for SPECT/PET.
LAD, Left anterior descending artery; *LCX,* left circumflex artery; *RCA,* right coronary artery.

PET in 202 patients who had undergone prior angiography. The patients had rest Rb-82 imaging, followed by dipyridamole infusion, PET imaging, and then an injection of Tl-201, which was followed by poststress and rest SPECT imaging. A blinded interpretation revealed a sensitivity and specificity for PET of 93% and 78% versus 76% and 80%, respectively, for SPECT. Both our PET and SPECT results are better, probably reflecting advances in both technology and radionuclides. Tl-201 is used today much less frequently than Tc-99m perfusion tracers, and the study by Go et al did not include ECG gating of either method.

Comparative Image Quality and Interpretive Certainty

Image quality was perceived to be lower for SPECT despite imaging times that exceeded those of PET by a factor of greater than 2, mainly because of excessive tracer uptake in the liver and bowel, with resulting scatter into the inferior wall of the heart. This is more of a problem with pharmacologic stress than with exercise, as well as with Tc-99m sestamibi than with Tl-201.[19] The combination of low-level exercise with vasodilator stress has been proposed to improve cardiac-to-background counts with SPECT,[20-23] but this approach was not used in this study. Interestingly, liver and bowel uptake of Rb-82 was significantly less than with Tc-99m sestamibi (again without concomitant low-level exercise), possibly because of differences in radionuclides themselves or possibly reflecting the relative resolution of the 2 different acquisition modalities. Greater spatial resolution allows improved separation of structures and therefore less overlap of the myocardium from extracardiac sources.

SPECT images also tended to be degraded in some patients because of soft-tissue attenuation artifacts. The problem of soft-tissue attenuation artifacts has long been appreciated to be a major source of interpretive errors in SPECT imaging,[24] with increasing attention to potential ways to address this.[25,26] Some newer SPECT equipment includes hardware and software solutions for attenuation correction, but this approach is not yet widely used clinically. The overwhelming majority of SPECT studies are performed with ECG gating, partly in response to data demonstrating its effectiveness in distinguishing attenuation artifacts from CAD and increasing interpretive certainty.[27-29] In our study regional function assessment was considered in relation to corresponding regional tracer uptake in the final diagnosis.

In addition to a higher percent of excellent-quality images, the PET scans were interpreted with significantly higher certainty (with more studies being definitely normal or abnormal). This probably reflects the better image quality, but importantly, the diagnostic certainty also translated into higher accuracy in both the coronary angiography patients and the low-likelihood patients.

PET Compared With SPECT Technology

There are several technologic and biologic reasons why PET might outperform SPECT for gated cardiac perfusion imaging. SPECT image quality degradation occurs with low myocardial counts, soft-tissue attenuation, and scatter of activity from adjacent structures such as the liver and bowel into the cardiac region of interest. PET technology provides greater myocardial count density in a much shorter acquisition time. Because, to our knowledge, there is no literature reference to the quantitative differences between Rb-82 and Tc-99m sestamibi counts, we performed a substudy in which we measured the poststress counts in 10 low-likelihood PET patients and 10 low-likelihood SPECT patients. The PET counts exceeded those in SPECT images by a factor of greater than 2, despite imaging times of only 5 minutes compared with 16 minutes. This difference in counts contributes to better-quality images and permits reslicing at 3 mm rather than the conventional 6-mm thickness.

Soft-tissue attenuation has been a source of reduced sensitivity and specificity for cardiac perfusion SPECT. ECG gating, additional prone-position acquisitions, and attenuation correction have all been proposed to address this issue. Although ECG gating was used in this study, the SPECT images were not attenuation-corrected. Recent publications have shown that attenuation correction can improve the specificity of exercise stress ECG-gated SPECT.[17,30] However, we chose to not compare PET against attenuation-correction SPECT in this group of pharmacologic stress patients, on the basis of our observations that the concomitant correction of cardiac-adjacent areas such as the liver and bowel adversely affects image quality.[8,31] In a recently completed study we showed that 50% of attenuation-corrected post–pharmacologic stress sestamibi SPECT images were of compromised quality because of excessive liver activity scattering into the inferior wall of the heart, with resultant unimproved diagnostic accuracy compared with non–attenuation-corrected images.[32] Because SPECT image quality and accuracy might have been better if pharmacologic stress was accompanied by low-level exercise, the conclusions of our study should be limited to patients who undergo pharmacologic stress not combined with exercise.

PET has better spatial resolution than SPECT. Theoretic tomographic in-plane spatial resolution of PET is in the range of 2 to 4 mm, as compared with 6 to 8 mm for Tc-99m SPECT (full width at half maximum). Effective image resolution is dependent on multiple patient and processing factors and is in the range of 6 to 10 mm and 10 to 14 mm, respectively. Perhaps most importantly affecting PET effective resolution is the positron range, which contributes an inherent blur to the images not present with the gamma emissions of SPECT. Rb-82 has a relatively high positron emission energy (1.52 MeV), with a mean range of approximately 5.5 mm. One implication of the higher spatial resolution of PET is better separation of the heart from adjacent structures such that there is less scatter effect on myocardial counts. When there is hot activity in close proximity to the heart in SPECT scans, the filtered backprojection method of reconstruction can result in artifacts that appear as perfusion defects.[28] In contrast, PET reconstruction uses an OSEM algorithm,[13] which does not introduce the "ramp-filtering artifact."[31]

Tracer properties may also impact the findings in this investigation. Rb-82 chloride is highly extracted by the myocardium; in addition, its uptake is more linearly related to increases in coronary blood flow compared with the Tc-99m SPECT perfusion tracers, which plateau at relatively low flows. Especially when used with vasodilator stress, this property may be advantageous in increasing sensitivity for detection of moderate-severity CAD. Other investigators have reported on the potential advantages of using Tl-201 with pharmacologic stress for this same reason[33]; however, these properties are likely to be better realized with Rb-82, an analog of Tl-201, as a result of the higher spatial resolution, counting statistics, and attenuation correction of PET. Given the relatively subtle differences in permeability surface products and first-pass extraction fractions, it may be that PET's superior spatial and contrast resolution and count densities are more important than tracer differences. Furthermore, in this study there was less liver and bowel uptake of Rb-82 than was observed for Tc-99m sestamibi; this may have affected the relative specificity of the 2 approaches.

Patient exposure to radiation is considerably lower with Rb-82 PET compared with rest/stress Tc-99m SPECT. Package inserts indicate that the total absorbed dose for 2220 MBq Rb-82 is 0.096 rads,[34] and in the protocol used in this study the exposure is 0.302 rads. For the Tc-99m sestamibi protocol used here (370 MBq at rest followed by 925 MBq at stress), the exposure is 0.667 rads.[35]

Study Limitations

We used rigorous biostatistical techniques to ensure that the patient groups were matched for characteristics known to impact on perfusion data. Performing both tests in the same patients would be a preferred study methodology, and had each patient undergone imaging by use of both techniques, it is possible that there could be other differences than those found in this study.

The SPECT studies used adenosine for pharmacologic stress, whereas PET used dipyridamole. The longer duration of hyperemia provided by dipyridamole is currently a requisite to enable 3 separate image sets (transmission, emission, and ECG-gated scans) to be acquired under stress conditions with PET,[36] whereas adenosine is excellent for the longer-lived SPECT Tc-99m sestamibi tracer that is taken up in proportion to blood flow at the time of injection and does not redistribute. It is doubtful that the difference in accuracy that we found between SPECT and PET can be attributed to the stress agents. Adenosine and dipyridamole both act on coronary A2A receptors to increase coronary blood flow to similar degrees.[37] Prior investigations comparing adenosine and dipyridamole have shown better myocardial/background count ratios, more abnormal segments,[38] and higher diagnostic accuracy[39] with adenosine. As such, any differential effects on accuracy as a result of the different stress agents used in this study would likely disfavor PET.

The results of our study may not be generalized to other PET systems that use either different crystal technology or hardware approaches to attenuation correction than those used here. We acquired the perfusion and gated images separately, in 2D (septa-in) and 3D (septa-retracted) modes, respectively. Most published PET literature has used 2D acquisitions for perfusion imaging, whereas ECG gating is a relatively new capability facilitated by the higher count rates possible with 3D imaging. Since the completion of our study, investigations have suggested the feasibility of combined perfusion and function imaging in 3D mode, which would greatly simplify the PET protocol.[40,41]

Finally, the images in this study were interpreted by consensus; the methodology precluded an ability to assess intraobserver or interobserver agreement.

Clinical Implications

Recent data indicate that almost 50% of MPI studies are being performed by use of pharmacologic stress. Currently, Rb-82 PET perfusion imaging is performed almost exclusively with pharmacologic stress, because of the logistic challenges of obtaining image data in the immediate post-treadmill time limited by the short half-life of Rb-82. Our investigation provides evidence that for patients who require pharmacologic stress, PET imaging may be preferable to SPECT. In this study image quality was higher and the certainty of the interpretation was higher with gated PET MPI compared with gated SPECT MPI. Importantly, PET proved superior in diagnostic accuracy to SPECT for the overall population, but also for both genders, for nonobese patients and for obese patients, and for identification of those patients with multivessel CAD.

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