**Clinical Investigation and Reports**

**[18F]Fluorodeoxyglucose Single Photon Emission Computed Tomography**

**Can It Replace PET and Thallium SPECT for the Assessment of Myocardial Viability?**

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**Background**—New high-energy collimators for single photon emission computed tomography (SPECT) cameras have made imaging of positron-emitting tracers, such as [18F]fluorodeoxyglucose ([18F]FDG), possible. We examined differences between SPECT and PET technologies and between [18F]FDG and thallium tracers to determine whether [18F]FDG SPECT could be adopted for assessment of myocardial viability.

**Methods and Results**—Twenty-eight patients with chronic coronary artery disease (mean left ventricular ejection fraction [LVEF] = 33 ± 15% at rest) underwent [18F]FDG SPECT, [18F]FDG PET, and thallium SPECT studies. Receiver operating characteristic curves showed overall good concordance between SPECT and PET technologies and thallium and [18F]FDG tracers for assessing viability regardless of the level of [18F]FDG PET cutoff used (40% to 60%). However, in the subgroup of patients with LVEF ≤ 25%, at 60% [18F]FDG PET threshold value, thallium tended to underestimate myocardial viability. In a subgroup of regions with severe asynergy, there were considerably more thallium/[18F]FDG discordances in the inferior wall than elsewhere (73% versus 27%, P < .001), supporting attenuation of thallium as a potential explanation for the discordant observations. When uptake of [18F]FDG by SPECT and PET was compared in 137 segments exhibiting severely irreversible thallium defects (scarred by thallium), 59 (43%) were viable by [18F]FDG PET, of which 52 (88%) were also viable by [18F]FDG SPECT. However, of the 78 segments confirmed to be nonviable by [18F]FDG PET, 57 (73%) were nonviable by [18F]FDG SPECT (P < .001).

**Conclusions**—Although [18F]FDG SPECT significantly increases the sensitivity for detection of viable myocardium in tissue declared nonviable by thallium (to 88% of the sensitivity achievable by PET), it will occasionally (27% of the time) result in falsely identifying as viable tissue that has been identified as nonviable by both PET and thallium. (Circulation. 1998;97:843-850.)

**Key Words:** myocardium ■ coronary disease ■ tomography ■ radioisotopes ■ nuclear medicine

In many patients with chronic coronary artery disease, impaired left ventricular function at rest arises, in part, from regions of ischemic or hibernating myocardium rather than scarred myocardium.1,2 Such asynergic but viable myocardial regions can be identified with radionuclide imaging techniques such as [18F]FDG metabolic imaging or thallium scintigraphy.3 Preserved or enhanced [18F]FDG uptake in asynergic myocardial regions identifies viable myocardium, which has been shown to predict not only improved regional and global function after revascularization but also improved survival compared with patients treated with medical therapy alone.4–6 The clinical application of [18F]FDG has been hampered by the limited availability and high cost of PET and cyclotron technology. Recently, because of the relatively long physical half-life of [18F] (110 minutes), off-site production of [18F]FDG and subsequent transport to satellite nuclear cardiology laboratories has been proposed. This, combined with the advent of high-energy gamma camera collimators for SPECT, has made possible the use of [18F]FDG SPECT for detection of myocardial viability.7 Recent studies have shown that when SPECT flow tracers, such as 99mTc-sestamibi8 or early resting thallium,9 are used in combination with [18F]FDG SPECT, detection of myocardial viability is similar to that with PET. In routine clinical studies, stress-redistribution-reinjection thallium studies provide assessment of the presence and extent of coronary artery disease as well as myocardial viability.10,11 However, because of its low photon energy, soft-tissue attenuation of thallium may yield technically suboptimal images. The question arises, therefore, as to whether [18F]FDG SPECT could be used alone, without a perfusion agent, to replace thallium for routine clinical assessment of myocardial viability.

To address this question, we examined regional differences in [18F]FDG uptake as measured by SPECT and PET as well as the...
differences between thallium and 18FDG tracers. For the detection of viability, we used ROC analysis, thereby minimizing the difficulty of selecting arbitrary threshold values of viability for 18FDG SPECT or thallium SPECT. To correlate regional function with perfusion and/or metabolism, we applied gated tomographic radionuclide angiography, which allowed direct comparison of tomographic regional function with the assessment of myocardial viability by 18FDG SPECT, thallium SPECT, and 18FDG PET. The results of viability assessment are most relevant in patients with severe global left ventricular dysfunction and in regions with severe resting wall motion abnormalities. We therefore examined the ability of 18FDG SPECT to detect viable myocardium in all regions in such patients, especially in regions determined to be scarred by thallium.

Methods

Patient Selection

We prospectively studied 28 patients (25 men and 3 women, 36 to 78 years old; mean, 62±12 years) with chronic coronary artery disease undergoing evaluation for myocardial viability. Eighteen patients had documented prior myocardial infarction, 11 had symptoms of angina, and 7 had heart failure symptoms. LVEF assessed by radionuclide angiography ranged from 8% to 61% (mean, 33±15%) at rest. All patients had either impaired left ventricular systolic function at rest or a regional wall motion abnormality. No patient with recent (<1 month) acute myocardial infarction was included in the study. Coronary angiography demonstrated significant stenosis (>50% reduction in luminal diameter) of all three major epicardial coronary arteries in 17 patients, of two coronary arteries in 9 patients, and of one coronary artery in 2 patients. This study was approved by the Institutional Clinical Research Subpanel of the National Heart, Lung, and Blood Institute, and all patients gave informed consent.

18FDG PET

Three-dimensional PET studies were performed on a General Electric whole-body camera (35 contiguous transaxial slices 4.25 mm apart; in-plane and axial reconstructed resolution of ∼6.5 mm). All patients were studied after an overnight fast. Approximately 1 hour before the injection of 18FDG, an oral dose of 0.5 to 1 g of glucose was administered. After the patient was positioned, an 8-minute attenuation correction scan was performed with 2 rotating 68Ge/68Ga line sources. Immediately thereafter, 5 mCi of 18FDG was injected, and data acquisition was begun. Transaxial tomographic images of 18FDG uptake were created by summing the data acquired during the 30- to 45-minute interval beginning 30 minutes after injection. Of the 28 patients studied, 6 had diabetes mellitus and 5 received insulin during the imaging procedure. Only patients with technically adequate PET studies were included in the 18FDG SPECT protocol.

18FDG SPECT

Patients underwent 18FDG SPECT studies after completion of PET studies. Imaging was performed with a dual-headed (180° apart) SPECT camera (Vertex Genesys, ADAC Laboratories) equipped with a special high-energy collimator (resolution, 12 mm at 10 cm and 16 mm at 15 cm). Data were acquired in 120 steps over 360° (45 seconds per step) and reconstructed into transaxial slices (3.13 mm apart, 3.13-mm pixel size, reconstructed in-plane and axial resolution of ∼15 to 20 mm as measured with a line source in an elliptical chest phantom with lung inserts). Seventeen patients underwent SPECT imaging immediately after PET acquisition (mean time from injection to start of SPECT scan, 85±17 minutes). Because acquisition of 18FDG SPECT images so long after the completion of 18FDG PET studies raises the potential of unintentional bias against 18FDG SPECT because of isotope decay, a second injection of 10 mCi of 18FDG was given at rest in 11 patients immediately after PET imaging was completed, and SPECT images were acquired ∼40 minutes thereafter.

Thallium Scintigraphy

All patients underwent stress-redistribution-reinjection 201TI SPECT, as previously described,10 within a mean of 2.7±4.8 weeks from 18FDG SPECT and PET studies. At peak stress (exercise or pharmacological), 3 mCi of thallium was injected intravenously. Thallium images were obtained with a three-headed rotating gamma camera equipped with a high-energy, medium-resolution, high-sensitivity collimator centered on the 68-keV photo peak with a 20% window. All images were reconstructed from projection data acquired over a 360° elliptical orbit around the patient’s thorax at 3° increments for 40 seconds each.

Data Analysis

In each of these studies (thallium, 18FDG SPECT, and 18FDG PET), the transaxial images were resliced into a series of short-axis images, as previously described.12 These short-axis images were then sliced longitudinally, starting at 22.5° from midline, in 45° increments (top left), to yield four long-axis slices per patient (two horizontal long-axis and two vertical long-axis images), encompassing the entire left ventricle (top right). Bottom, Schematic representations of four long-axis slices, patient image examples, and segmentation scheme.

Selected Abbreviations and Acronyms

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<th>Abbreviation</th>
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<tr>
<td>18FDG</td>
<td>[18F]fluorodeoxyglucose</td>
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<td>LVEF</td>
<td>left ventricular ejection fraction</td>
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<td>PET</td>
<td>positron emission tomography</td>
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<td>ROC</td>
<td>receiver operating characteristic</td>
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<td>SPECT</td>
<td>single photon emission computed tomography</td>
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within each segment. The myocardial segment with the maximum mean counts per pixel on the thallium stress study was used as the normal reference segment for that patient. The same segment in the redistribution and reinjection thallium studies and $^{18}$FDG SPECT and $^{18}$FDG PET studies was identified and used as the reference segment for those studies. The activity of $^{18}$FDG or thallium in all other myocardial segments was then expressed as a percentage of the activity measured in the reference segment of the corresponding $^{18}$FDG SPECT, $^{18}$FDG PET, and thallium redistribution or reinjection image.

The data were also analyzed by use of an alternate normalization scheme, in which the segment with the highest mean counts per pixel for thallium redistribution, thallium reinjection, $^{18}$FDG PET, and $^{18}$FDG SPECT was used as the reference segment for that individual study.

Myocardial segments were grouped on the basis of severity of reduction in thallium activity: normal ($\geq 85\%$ of peak activity), mildly to moderately reduced (51% to 85% of peak), and severely reduced ($\leq 50\%$ of peak) activity. On the basis of previous reproducibility measurements in our laboratory, a region with reduced activity on thallium stress was considered reversibly ischemic if the normalized thallium activity on the subsequent redistribution or reinjection images for that region increased by $\geq 10\%$. Similarly, a region with $<50\%$ activity on thallium stress was considered severely irreversible if the normalized thallium activity on the subsequent redistribution and reinjection images did not increase by 10% or if the activity on both redistribution and reinjection images remained $<50\%$ regardless of any possible increase in thallium activity.

Because misregistration of small segments might account for variation between studies performed on the same patient, the reproducibility of segmental uptake in our laboratory was assessed by having two observers repeat these measurements on a cardiac phantom and on a patient. The interobserver variability for segmental tracer uptake was determined to be $<5\%$. In addition to segmental analysis, we also grouped the 44 segments into 5 large regions per patient (anterior, apical, septal, lateral, and inferior) to allow $^{18}$FDG and thallium uptake in these large regions to be compared with regional wall motion.

### Planar and SPECT Gated Radionuclide Angiography

Planar gated equilibrium radionuclide angiography was performed with a conventional Anger camera. Red cells were labeled with $\sim 25$ mCi of $^{99m}$Tc-pertechnetate. Three standard planar views (anterior, best septal left anterior oblique, and left lateral) were acquired at rest. LVEF was computed from the left anterior oblique view.

A subgroup of 18 patients also underwent SPECT gated radionuclide angiography to better separate cardiac structures and determine regional wall motion. Blood pool SPECT images were obtained with an ADAC (two 90° heads) scanner with a high-energy, high-sensitivity collimator, a 38×38-cm field of view, and a 128×128 matrix. The images were acquired in 60 azimuths over a 180° arc from 45° right anterior oblique to 45° left posterior oblique, with 60 seconds per step. For each patient, four gated long-axis slices were generated in a manner identical to that for thallium and $^{18}$FDG images, and regional wall motion was assessed by two observers in the same five myocardial regions per patient (anterior, apical, septal, lateral, and inferior) as normal, mildly hypokinetic, severely hypokinetic, akinetic, or dyskinetic. The grade assigned to a given region was the most severe regional asynchrony within that region from all tomographic slices and views.

### Statistical Analysis

Data are presented as mean±SD. Group comparisons between $^{18}$FDG PET, $^{18}$FDG SPECT, and thallium uptake and differences between $^{18}$FDG and thallium with respect to regional wall motion were analyzed by either paired $t$ test or $\chi^2$ analysis. The ability of $^{18}$FDG SPECT and thallium SPECT to determine viability was analyzed by use of ROC curves, ie, plots of true-positive rates versus false-positive rates. Each ROC curve was produced by dividing the total range of segmental values (ie, segment maximum to segment minimum) for the study in question (thallium or $^{18}$FDG SPECT) into 100 equal intervals and computing the sensitivity and (1−specificity) at each point. Comparison of ROC curves was performed by computing $z$ scores from a comparison of the areas under the curves as in Reference 15.

### Results

#### Analysis of Regional $^{18}$FDG Uptake: SPECT Versus PET

To examine whether there are differences in regional $^{18}$FDG uptake between SPECT and PET technologies, a total of 977 segments were analyzed in 28 patients. There was a good overall agreement between $^{18}$FDG SPECT and $^{18}$FDG PET ($r = 0.81$, slope=0.79, SEE=0.004), with a mean difference in normalized $^{18}$FDG uptake assessed by the two techniques of 1.2% and a mean magnitude difference (ie, mean of the absolute values of the differences) of 9.6% (Fig 2). When a 50% $^{18}$FDG threshold (for both PET and SPECT) was used to differentiate viable from nonviable myocardium, $^{18}$FDG SPECT provided information concordant with that of $^{18}$FDG PET in 920 of 977 segments (94%). When data from the 11 patients in whom SPECT images were acquired after a second injection of $^{18}$FDG were compared with data from the 17 patients who did not have $^{18}$FDG reinjection, the concordance between $^{18}$FDG SPECT and PET in the two patient groups was similar (95% versus 94%, $P=NS$).

ROC curves were used to assess the ability of $^{18}$FDG SPECT to determine viability, with $^{18}$FDG PET used as the gold standard. At 50% threshold value for $^{18}$FDG PET, the area under the ROC curve for $^{18}$FDG SPECT was 0.95±0.02. This excellent concordance between $^{18}$FDG SPECT and PET persisted when 40% and 60% $^{18}$FDG threshold values were applied with areas under the ROC curve of 0.96±0.02 and 0.94±0.02, respectively (Fig 3).

#### $^{18}$FDG and Thallium Uptake

To examine whether there are differences between $^{18}$FDG and thallium for detection of myocardial viability, a 50% threshold value was used for the two tracers to differentiate viable from nonviable myocardium. Stress-redistribution-reinjection thallium SPECT provided information concordant with that for $^{18}$FDG SPECT in 883 of 977 segments (90%) and in 896 segments (92%) with $^{18}$FDG PET. Furthermore, when the data were analyzed in the 777 segments demonstrating abnormal
thallium uptake during stress, there was concordance regarding myocardial viability in 684 segments (88%) with 18FDG SPECT and 696 segments (90%) with 18FDG PET. Among the discordant segments, 21 of 85 segments that were nonviable by 18FDG SPECT and 22 of 100 segments that were nonviable by 18FDG PET were judged viable by thallium reinjection.

ROC curves were used to assess the ability of thallium to predict viability as defined by 18FDG PET. At 50% threshold value for 18FDG PET, the area under the ROC curve for thallium reinjection was 0.95 \(\pm 0.02\) for all 977 segments. This excellent concordance between thallium and 18FDG PET persisted when data were analyzed in the 777 abnormal segments with the area under the ROC curve of 0.93 \(\pm 0.02\).

When different 18FDG PET threshold values were applied, at 40%, the area under the ROC curve for thallium was 0.95 \(\pm 0.02\), and at 60%, the area under the ROC curve for thallium was 0.90 \(\pm 0.02\). There was no statistically significant difference between the areas under the ROC curve for thallium and 18FDG PET when 40% and 50% 18FDG threshold values were applied. However, the areas under the ROC curves were significantly different between thallium (0.89 \(\pm 0.02\)) and 18FDG SPECT (0.95 \(\pm 0.02\), \(P<0.02\)) in group 2 patients when a 60% 18FDG PET threshold value was applied (Fig 5).

18FDG SPECT and 18FDG PET was similar in the two groups of patients. At 50% threshold value for 18FDG PET, the area under the ROC curve for 18FDG SPECT among group 1 patients was 0.97 \(\pm 0.02\) and in group 2 patients was 0.94 \(\pm 0.02\) (\(P=\text{NS}\)). Similarly, there was no statistically significant difference for the areas under the ROC curve between thallium and 18FDG SPECT in group 1 compared with group 2 patients when 40% and 50% 18FDG threshold values were applied. However, the areas under the ROC curves were significantly different between thallium (0.89 \(\pm 0.02\)) and 18FDG SPECT (0.95 \(\pm 0.02\), \(P<0.02\)) in group 2 patients when a 60% 18FDG PET threshold value was applied (Fig 5).

18FDG Uptake in Severely Irreversible Thallium Defects

The ROC analysis above allowed assessment of overall ability to detect viable regions. Of more specific concern was the

**Relation to Severity of Left Ventricular Dysfunction**

Because assessment of viability is of particular concern in patients with left ventricular dysfunction, the data were analyzed in two groups: group 1, representing 16 patients with normal or mildly to moderately impaired left ventricular function (LVEF >25%; mean, 44±8%), and group 2, representing 12 patients with severely impaired left ventricular function (LVEF \(\leq\)25%; mean, 19±5%). The relation between

**Figure 3.** Plots of ROC curves for thallium and 18FDG SPECT to predict myocardial viability as defined by 50% (left) and 60% (right) 18FDG PET threshold values for all segments (top) and abnormal thallium segments (bottom). Area under ROC curve for 18FDG SPECT and thallium SPECT are displayed for each panel. There are no significant differences between thallium and 18FDG SPECT for detecting myocardial viability. Of all 977 segments, 877 were viable at 50% threshold (top left) and 818 were viable at 60% threshold (top right). Of 777 abnormal segments, 677 were viable at 50% threshold (bottom left) and 618 were viable at 60% threshold (bottom right).

**Figure 4.** Concordance between 18FDG SPECT, 18FDG PET, and stress-redistribution-reinjection thallium SPECT. Four radial long-axis tomograms are displayed for 18FDG SPECT and 18FDG PET, with corresponding thallium tomograms of stress, redistribution, and reinjection. On 18FDG SPECT and PET studies, 18FDG uptake is severely reduced in apical region (arrows), suggestive of scarred myocardium. As in findings on 18FDG SPECT and PET, thallium images show severe perfusion defect in apical region during stress, which persist on redistribution and reinjection images (scarred by thallium).

**Figure 5.** Plots of ROC curves for thallium and 18FDG SPECT to predict myocardial viability as defined by 60% 18FDG PET threshold value for patients with LVEF >25% (left) and patients with LVEF \(\leq\)25% (right). Area under ROC curve for 18FDG SPECT and thallium SPECT is displayed for each panel. Thallium tended to underestimate myocardial viability in patients with LVEF \(\leq\)25% but not in patients with LVEF >25%. For patients with LVEF >25% (left), 471 of 548 segments were viable, and for patients with LVEF \(\leq\)25% (right), 347 of 429 segments were viable.
detection of potentially viable regions by $^{18}$FDG in territories previously determined to be nonviable by thallium.

**Data Normalized to Peak Stress Thallium**

Of the 777 abnormal segments, 432 defects (56%) were irreversibly on redistribution-reinjection images: 295 with mildly to moderately reduced and 137 with severely reduced thallium activity. In these 137 segments, there was considerable discordance between thallium and $^{18}$FDG uptake. $^{18}$FDG PET verified 78 (57%) of these segments to be metabolically inactive and nonviable, of which 57 (73%) were also nonviable by $^{18}$FDG SPECT (Fig 6). However, in the remaining 59 segments (43%), $^{18}$FDG PET identified the segments to be metabolically active and viable, of which 52 (88%) were also viable by $^{18}$FDG SPECT ($P$<.001). Of the 59 discordant segments (between thallium and $^{18}$FDG PET), 38 (64%) were located in the inferior region. Mean thallium uptake in segments that were judged to have severely irreversible defects but preserved $^{18}$FDG uptake by PET and SPECT was significantly higher ($0.42 \pm 0.04$ on stress) than in those with abnormally reduced $^{18}$FDG uptake ($0.24 \pm 0.10$, $P$<.001).

Among the 137 segments with severely reduced thallium uptake, 55 were located in the inferior territory and 85 were located in regions in which SPECT wall motion data were available. In the 55 inferior segments, there was significantly more discordance in subjects with severely impaired left ventricular function (LVEF $\leq$25%), 27 of 30 segments (90%) compared with those with LVEF>$>$25% (11 of 25 segments, 44%), $P$<.001. A representative example of a patient demonstrating discordance between $^{18}$FDG SPECT, $^{18}$FDG PET, and thallium stress-redistribution-reinjection is shown in Fig 7. Of the 85 segments for which wall motion data were available, thallium and $^{18}$FDG PET uptake were concordant in 53 segments (62%) and discordant in 32. Of the 53 thallium/$^{18}$FDG concordant segments, 49 (92%) were located in severely asynergic regions compared with 22 of 32 thallium/$^{18}$FDG discordant segments (69%) ($P$<.02). Moreover, only 13 of 49 segments (27%) with severe asynergy and concordance between thallium and $^{18}$FDG uptake were located in the inferior region compared with 16 of 22 segments (73%) with discordant thallium and $^{18}$FDG uptake ($P$<.001).

**Data Normalized to the Segment With Highest Peak Counts per Pixel for Each Individual Study**

Because there could potentially be other approaches to normalizing the data, we repeated our data analysis, normalizing each study to its own highest segment. That is, the segment with the highest mean counts per pixel for thallium redistribution, thallium reinjection, $^{18}$FDG PET, and $^{18}$FDG SPECT was used as the reference segment for the corresponding individual study. Among 159 segments with severely irreversible thallium defects identified by this alternative normalization scheme, 74 segments (47%) were identified to be metabolically active and viable by $^{18}$FDG SPECT, of which 63 (85%) were also viable by $^{18}$FDG PET ($P$<.001). Of the 74 discordant segments (between thallium and $^{18}$FDG PET), 43 (58%) were located in the inferior region, whereas among 85 segments with concordant information, only 21 (25%) were located in the inferior region ($P$<.001). Among all 64 segments located in the inferior territory, significantly more discordance occurred in subjects with severely impaired LVEF ($\leq$25%), 31 of 36 segments (86%) compared with those with LVEF>$>$25%, 12 of 28 segments (42%), $P$<.001. Hence, the results appear to be unaffected by the normalization scheme applied.

**$^{18}$FDG and Thallium Uptake in Asynergic Regions Assessed by SPECT Gated Radionuclide Angiography**

Because assessment of myocardial viability and decisions regarding revascularization are of clinical concern predominantly in asynergic regions, we directed our attention to the five myocardial regions in which regional wall motion could be assessed (apical, anterior, septal, inferior, and lateral, representing the three major coronary vascular territories per patient). Among the 18 patients who underwent SPECT gated radionuclide angiography, a total of 90 myocardial regions were analyzed. Regional wall motion was normal in 40, mildly hypokinetic in 9, severely hypokinetic in 13, akinetic in 23, and dyskinetic in 5.

Among the 41 severely asynergic regions (severely hypokinetic, akinetic, or dyskinetic), 39 (95%) had associated ECG Q waves, a history of prior myocardial infarction in the same
vascular territory, or a critically stenosed coronary artery supplying the region. Myocardial viability was present in 23 of these 41 severely asynergic regions (56%) by thallium, 26 (63%) by 18FDG PET, and 28 (68%) by 18FDG SPECT (P = NS). 18FDG SPECT and PET provided concordant information regarding myocardial viability in 33 of 41 severely asynergic regions (80%) and discordance in 8 regions. Thallium SPECT provided concordant information with 18FDG PET in 32 of 41 asynergic regions (78%) and in 30 regions with 18FDG SPECT (73%) (Fig 8). In contrast, among the 49 normal or mildly hypokinetic regions, 45 (92%) had preserved thallium uptake, 46 (94%) had preserved 18FDG uptake by SPECT, and 46 (94%) by PET.

ROC curves were used to assess the ability of thallium and 18FDG SPECT to predict viability as defined by 18FDG PET in the 41 severely asynergic regions. At 50% threshold value for 18FDG PET, the area under the ROC curve for 18FDG SPECT was 0.91 ± 0.05 and for thallium reinjection, 0.89 ± 0.06 (P = NS). The concordance between thallium, 18FDG SPECT, and 18FDG PET persisted when different 18FDG PET threshold values were applied (40% or 60%).

Discussion

In patients with chronic coronary artery disease, we examined differences between SPECT and PET technologies and 18FDG and thallium tracers for differentiating viable from nonviable myocardium. Because in asynergic regions there may be a gradation of myocardial tissue from normal, hypoperfused but viable, to nonviable myocardium within the same region, the use of a single arbitrary cutoff value for thallium or SPECT may oversimplify this complex relationship. For example, an asynergic region with 60% 18FDG uptake would be regarded as nonviable thallium myocardium, or (2) mixed scarred and normal (nonischemic) myocardium, or (3) mixed scarred and viable (hypoperfused) myocardium. Because the precise threshold with 18FDG PET to predict recovery of function after revascularization is not known, we used ROC analysis to compare the techniques and the tracers in their ability to detect viable tissue. Our findings suggest that the overall concordance between the two technologies (SPECT and PET) and the two tracers (18FDG and thallium) was excellent regardless of the level of 18FDG PET threshold value applied (40%, 50%, or 60%).

Comparison of Technologies: SPECT Versus PET

PET, with its high spatial resolution, high-count-density images, and the possibility for attenuation correction, allows accurate assessment of regional uptake using 18FDG (a glucose analogue) irrespective of weight or body habitus of patients. The clinical feasibility of imaging positron emitters such as 18FDG with high-energy collimator planar or SPECT techniques has been reported previously. In fact, imaging of 18FDG radiotracer with standard nuclear medicine equipment dates back to 1962, when attempts were made to perform bone scans by use of 18FDG.

The poorer spatial resolution of SPECT, the lower sensitivity, and the lack of attenuation correction may cause some discordance between SPECT and PET images of the same tracer. Despite these differences, relative myocardial metabolic estimates of 18FDG SPECT are comparable overall to those with PET. In previous studies by Bax and coworkers, flow measurements by thallium SPECT were combined with measurement of metabolism by 18FDG. When thallium uptake and SPECT 18FDG were taken together to differentiate viable from nonviable myocardium in regions with impaired contraction, they found an agreement between PET and SPECT of 76%. In a subsequent study, the authors acquired thallium “reinjection” images 4 hours after the infusion of high-dose dobutamine and eliminated the 3- to 4-hour redistribution images. Because apparent washout of thallium may occur between redistribution and reinjection studies, reliance on reinjection images alone might underestimate defect reversibility and hence viability. Therefore, the findings of the above study cannot be compared with our results. In patients with coronary artery disease, when 18FDG SPECT and PET images were compared with thallium redistribution acquired 3 hours after the tracer was injected at rest, ~20% of regions with severe resting thallium defects were metabolically viable by 18FDG imaging using either SPECT or PET. In the latter study, however, regional contractile function was not reported.

Our results suggest that using 40% to 60% 18FDG PET threshold values, 18FDG SPECT provides information comparable to that by 18FDG PET regarding detection of viability; concordance was found in patients with severely impaired global left ventricular function (LVEF ≤ 25%) and in patients with severely asynergic regions. Overall concordance, however, is influenced by the number of normal segments. The more clinically relevant question is how well 18FDG SPECT predicts viability in segments judged nonviable by thallium (severely irreversible defects). In segments with severely irreversible thallium defects (scarred by thallium), 18FDG PET identified 43% of these segments to be metabolically active and viable, of which 88% were also viable by 18FDG SPECT. Among the segments that were judged to be nonviable by both thallium and 18FDG PET, 73% were also nonviable by 18FDG SPECT (P < .001). Thus, 18FDG SPECT provides incremental information regarding viability, similar to 18FDG PET, in segments judged nonviable by thallium. Despite the good overall concordance between 18FDG SPECT and PET, there were noticeable discordances, especially in regions of severe left ventricular dysfunction and regional asynergy and in
regions with severely reduced $^{18}$FDG uptake on PET (27% of which appear to have more activity on SPECT). Some of these differences may be due to attenuation, others to the large counting statistical fluctuations in the data, especially with SPECT. However, the clinical significance of such discordances is unknown, especially in light of the relatively few subjects studied with severe left ventricular dysfunction.

In our study, the concordance between $^{201}$Tl SPECT and $^{18}$FDG PET was 95% among the patients studied after a second injection of $^{18}$FDG at rest and 94% among the patients in whom $^{18}$FDG was not re-injected. A possible explanation for the lack of observed difference between the two patient groups may relate to improvement in contrast between the myocardium and blood pool on delayed $^{18}$FDG images. Thus, the time delay to $^{18}$FDG SPECT imaging (performed after PET without a second $^{18}$FDG injection) may have partially offset the reduced sensitivity of SPECT and the loss of activity due to decay. In addition, the improved image quality inherent in late images may also have contributed to the good concordance between $^{18}$FDG SPECT and $^{18}$FDG PET, despite the poorer spatial resolution of $^{18}$FDG SPECT.

Comparison of Tracers: Thallium and $^{18}$FDG

Myocardial uptake of thallium reflects cell membrane integrity, whereas $^{18}$FDG uptake reflects the overall rate of transmembrane exchange and phosphorylation of glucose. Our data suggest that when 50% thallium threshold value was used, thallium provided concordant viability information with $^{18}$FDG SPECT in 90% of segments. Analysis of data in a dichotomous fashion is critically dependent on the exact threshold value chosen. ROC curve analysis, in particular comparison of areas under the ROC curves, has been shown to overcome this problem. When ROC analysis was applied to thallium and $^{18}$FDG data in all segments such that normal, reversible, mildly to moderately irreversible, and severely irreversible thallium defects were grouped together, regardless of the level of $^{18}$FDG PET cutoff used (40% to 60%), there was no statistical difference in ROC area between $^{18}$FDG SPECT and thallium SPECT. However, in segments with severely irreversible thallium defects (scared by thallium), 43% of these segments were identified to be metabolically active by $^{18}$FDG PET, of which 88% were also viable by $^{18}$FDG SPECT. Of the discordant segments between thallium and $^{18}$FDG PET, 64% were located in the inferior segment. Thus, there was a tendency for thallium SPECT to underestimate the extent of myocardial viability, especially in the inferior region, whereas $^{18}$FDG SPECT was less affected by such regional variation. Furthermore, a significantly larger number of inferior segment discordances occurred in subjects with LVEF $<$25% compared with those with LVEF $>$25% ($P<.001$). These findings are supported by a previous report from Altehoefer and colleagues, in which resting blood flow measurements by thallium were compared with $^{18}$FDG uptake by PET. In their study, although there was a linear relationship between thallium and $^{18}$FDG uptake in the three major coronary artery vascular territories, the correlation was lower in the right coronary artery vascular territory ($r=.52$). Furthermore, in segments with severely reduced thallium activity, there was 44% discordance between thallium and $^{18}$FDG (scared by thallium but viable by $^{18}$FDG PET) in the right coronary artery vascular territory.

In our study, because SPECT was the common technology used for acquiring both $^{18}$FDG and thallium images, at least some of the observed differences in the inferior region between thallium SPECT and $^{18}$FDG SPECT are probably explained by the attenuation differences between the two tracers. For example, only 27% of segments with severe asynergy and concordance between thallium and $^{18}$FDG uptake were located in the inferior region, compared with 73% of segments with discordant thallium/$^{18}$FDG segments ($P<.001$). Because the inferior wall is one of the most severely attenuated regions in the heart, this finding supports the greater attenuation of thallium as a potential explanation for the discordant observations. Attenuation effects might also be expected to cause discordance between thallium and $^{18}$FDG in women because of breast attenuation, but because there were only three women in our study, we were unable to examine this possible effect.

Because SPECT does not correct for soft-tissue attenuation, there is regional heterogeneity of lower limits of normal for thallium, which ranges from about 70% in the inferior region to 90% in the lateral wall. Assessment of myocardial viability is a clinical concern in patients with severely impaired left ventricular dysfunction. This group of subjects often have dilated hearts, accentuating the effects of attenuation, and our results support this concept. It remains unknown, however, how much of the observed discordance between thallium and $^{18}$FDG SPECT is related to the differences in physiological behavior of the two tracers and how much is due to the differences in their imaging properties (ie, attenuation). If the latter, then implementation of attenuation correction for SPECT might lead to greater concordance between thallium and $^{18}$FDG.

Tomographic Assessment of Regional Contractile Function

An important feature of our study is that we used SPECT radionuclide angiography for more accurate anatomic alignment of tomographic perfusion, metabolism, and regional contractile function. However, we did not have the opportunity to assess tomographic regional contractile function after revascularization. SPECT radionuclide imaging has shown improved segmental resolution, separation of overlapping structures, and localization of individual diseased coronary arteries compared with planar imaging. In the subset of patients who underwent SPECT gated radionuclide angiography, the agreement between $^{18}$FDG SPECT and PET for identifying myocardial viability in severely asynergic regions was 80%; thallium provided information concordant with that from $^{18}$FDG SPECT in 73% of these regions. In normal or mildly hypokinetic regions, thallium and $^{18}$FDG SPECT provided discordant information in 94% of the regions.

Conclusions

These data suggest that in patients with chronic coronary artery disease, there is overall good concordance between SPECT and PET technologies and thallium and $^{18}$FDG tracers for differentiating viable from nonviable myocardium. Although $^{18}$FDG SPECT significantly increases the sensitivity for detec-
tion of viable myocardium in tissue declared nonviable by thallium (to 88% of the sensitivity achievable by PET), it will occasionally (27% of the time) result in falsely identifying as viable tissue that has been identified as nonviable by both PET and thallium.

References

[18F]Fluorodeoxyglucose Single Photon Emission Computed Tomography: Can It Replace PET and Thallium SPECT for the Assessment of Myocardial Viability?
Gopal Srinivasan, Anastasia N. Kitsiou, Stephen L. Bacharach, Marissa L. Bartlett, Claiborne Miller-Davis and Vasken Dilsizian

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