Regional Left Ventricular Wall Thickening
Relation to Regional Uptake of $^{18}$Fluorodeoxyglucose and $^{201}$Tl in Patients With Chronic Coronary Artery Disease and Left Ventricular Dysfunction

Pasquale Perrone-Filardi, MD; Stephen L. Bacharach, PhD; Vasken Dilsizian, MD; Simone Maurea, MD; Joseph A. Frank, MD; and Robert O. Bonow, MD

Background. In previous studies comparing regional $^{201}$Tl ($^{201}$Tl) and $^{18}$fluorodeoxyglucose (FDG) activity in patients with chronic coronary artery disease and left ventricular dysfunction, we hypothesized that regions with mild-to-moderate reduction in FDG activity and regions with mild-to-moderate irreversible $^{201}$Tl defects after 3- to 4-hour redistribution represent viable myocardium. In the present study, regional FDG and $^{201}$Tl activities were compared with regional systolic wall thickening by gated magnetic resonance imaging (MRI) to confirm the presence of viable myocardium in these territories.

Methods and Results. Twenty-five patients with chronic stable coronary artery disease and left ventricular dysfunction (ejection fraction, 28±10) underwent exercise $^{201}$Tl tomographic imaging (SPECT), using a reinjection protocol, positron emission tomography (PET) with FDG and H$^{15}$O, and gated MRI. Matched SPECT, PET, and MRI tomograms were analyzed. From the PET data, 105 regions had matched reduction in FDG and blood flow, of which 69 regions had moderately reduced FDG uptake (50–79% uptake relative to a normal reference region) and 36 had severely reduced FDG uptake (<50% of normal activity). Regions with moderately reduced as compared with severely reduced FDG activity had greater end-diastolic wall thickness (9.4±2.6 versus 8.0±3.7 mm; p<0.05) and regional systolic wall thickening (1.7±2.7 versus 0.7±2.1 mm; p<0.01). From the SPECT data, 169 irreversible $^{201}$Tl defects after 3–4-hour redistribution were identified, of which 70 were mild (>65 to <85% of maximal $^{201}$Tl activity), 52 were moderate (50–65% of maximal activity), and 47 were severe (<50% of maximal activity). Regional systolic wall thickening was greater in regions with normal $^{201}$Tl uptake (3.3±2.3 mm) as compared with all other regions. Regions showing only mild or moderate irreversible defects at redistribution, however, showed wall thickening (2.4±2.4 and 2.2±2.5 mm, respectively), which was similar to that observed in regions with reversible $^{201}$Tl defects (2.1±2.2 mm). Only regions with severe irreversible defects at redistribution showed absence of thickening (<0.1±2.9 mm, p<0.01 versus all other groups). After $^{201}$Tl reinjection, 12 of 47 (26%) regions with severe irreversible defects showed enhanced $^{201}$Tl uptake. The impairment in regional systolic wall thickening was not significantly different between $^{201}$Tl defects with and without enhanced $^{201}$Tl uptake after reinjection. FDG activity, however, was present in all 12 regions (100%) with enhanced $^{201}$Tl uptake after reinjection as compared with only five of 35 (14%) that were unchanged after reinjection (p<0.01).

Conclusions. Therefore, preserved wall thickness and systolic wall thickening in regions with moderate reduction in blood flow and FDG activity, and in irreversible $^{201}$Tl defects that are only mild-to-moderate, provide additional evidence that such regions represent viable myocardium. Moreover, the finding of metabolic activity and $^{201}$Tl uptake in regions with reduced blood flow and absent wall thickening provides clinical evidence of hibernating myocardium in humans. (Circulation 1992;86:1125–1137)

Key Words • systolic function • myocardium • $^{201}$Tl • scintigraphy • coronary artery disease • tomography, positron emission

Myocardial revascularization may improve both regional and global left ventricular systolic function in patients with coronary artery disease (CAD) and left ventricular dysfunction.1–3 Therefore, the distinction between ischemic but viable myocardium and nonviable tissue is a critical issue for such patients in whom coronary revascularization is considered. In this evaluation, stress-redistribution $^{201}$Tl scintigraphy is an important technique, as the uptake of $^{201}$Tl indicates viable myocardium.4,5 In recent years, however, the limitation of conventional stress-redistribution $^{201}$Tl imaging in identifying viable myocardium has been widely recognized, as many defects that remain irreversible on redistribution studies have been shown to represent viable instead of nonviable myocardium.6–12 To overcome this limitation, exercise $^{201}$Tl scintigraphy with either delayed redistribution imaging8–10 or with the reinjection of a second dose of the iso-
In particular, the identification of viable myocardium from PET studies is based on the presence of either normal 18fluorodeoxyglucose (FDG) uptake or FDG: blood flow mismatch, whereas the identification of viable myocardium from 201TI scintigraphy is based on the presence of either normal 201TI uptake or reversible 201TI defects (after either redistribution or reinjection). The accuracy of these criteria to predict an improvement in regional function after revascularization has been evaluated, for both PET and 201TI scintigraphy with rest-reinjection, in a relatively small number of patients. The results of these studies indicate that the current PET and 201TI criteria used to identify viable myocardium are quite accurate but not perfect, as they may underestimate viability in up to 22% of the myocardial segments classified as nonviable. In a recent study, using a quantitative analysis of regional FDG and 201TI uptake, we hypothesized that regions with reduced blood flow and mild-to-moderate reduction in FDG activity (without FDG: blood flow mismatch), as well as regions with mild-to-moderate irreversible 201TI defects (after redistribution and/or reinjection), represent viable myocardium. The goal of the present study was to provide confirmatory evidence that these patterns of FDG and 201TI uptake do indeed represent viable myocardium. To confirm these hypotheses, we used as a "gold standard" for viability the presence of preserved regional anatomy and systolic function evaluated by gated magnetic resonance imaging (MRI), in relation to regional 201TI and FDG activity, in patients with CAD and left ventricular dysfunction.

Methods

Patient Selection

We studied 25 patients with angiographically proven CAD and left ventricular dysfunction. There were 24 men and one woman, ranging in age from 38 to 78 years (mean, 58±9 years). Left ventricular ejection fraction by radionuclide angiography ranged from 11% to 47% (mean, 28±10%) at rest. Although all patients had evidence of previous myocardial infarction, we studied only patients with chronic stable CAD; no patient had an acute myocardial infarction or unstable angina within 6 months of the study. One patient had diabetes mellitus. In the 24 nondiabetic patients, plasma glucose levels before the FDG study were in the normal fasting range (93±18 mg/dl). Coronary arteriography (performed within a mean interval of 8±13 months from the PET study) demonstrated significant stenosis (≥50% reduction in luminal diameter) of all three major epicardial coronary arteries in 17 patients and of two coronary arteries in five patients; 21 patients had at least one totally occluded epicardial coronary artery. In 20 patients, all cardiac medications were discontinued for at least 48 hours before radionuclide angiography, 201TI scintigraphy, PET, and MRI were performed. The remaining five patients underwent all the imaging studies while receiving the same medical regimen for each study; these included nitrate compounds alone (one patient) or a combination of nitrates, digitalis, and calcium channel blockers (four patients). An average of 23±26 days (range, 1–83 days) elapsed between performance of the first and the last of these tests. PET and 201TI data have been reported previously in 11 of the 25 patients.

Informed written consent for the study protocol was obtained from each patient.

Gated Blood Pool Cardiac Scintigraphy

Gated equilibrium radionuclide angiography was performed at rest with the patients in the supine position using red blood cells labeled in vivo with 20–25 mCi of Tc 99m. High temporal resolution (20 msec per frame) time-activity curves were generated, from which the left ventricular ejection fraction was computed as described previously. Regional wall motion analysis demonstrated the presence of regional akinesia or dyskinesia in one or more vascular territories in 17 patients and hypokinesia in the other eight patients.

201TI Imaging

All patients underwent exercise 201TI single-photon emission computed tomography (SPECT) as previously described. In brief, after an overnight fast, patients underwent treadmill exercise according to a standardized multistage exercise protocol, with continuous monitoring of heart rate and rhythm, blood pressure, and symptoms. Nineteen (76%) of the 25 patients achieved ≥85% of predicted maximal heart rate during exercise. Angina developed in 12 patients during exercise and was accompanied by ST segment depression in six patients. Nine additional patients showed ischemic ST changes during exercise without angina. At peak exercise, 2 mCi 201TI was injected intravenously, and the patients continued exercise for an additional 45–60 seconds. Approximately 10 minutes after termination of exercise, 201TI images were obtained using a wide-field-of-view rotating gamma camera equipped with a high-sensitivity, medium-resolution, parallel-hole collimator centered on the 68-keV photo peak with a 20% window. The camera was rotated in a 180° arc in an elliptical orbit about the patient’s thorax from a right anterior oblique angle of 40° to a left posterior angle of 40° at 6° increments for 30 seconds each.

Redistribution images were obtained 3–4 hours after stress, while the patients were resting. Immediately thereafter, all patients received an additional 1 mCi 201TI, and SPECT images were acquired 10–15 minutes later. The exercise, redistribution, and reinjection data were reconstructed as a series of whole-body transaxial tomograms for direct comparison with the corresponding PET and MRI images as described below. SPECT in plane and z-axis resolution was approximately 12 mm. Data were reconstructed with 6.88 mm per pixel sampling and with a 6.88-mm separation between slices.

Positron Emission Tomography

PET imaging was performed, as previously described, to assess regional myocardial perfusion with 15O-water and exogenous glucose utilization with FDG: a whole-body PET camera was used, which produced 21 contiguous tomograms spaced 5.1 mm apart with a slice thickness of 13 mm and an in-plane reconstructed resolution of 6.5 mm. Images were obtained perpendicular to the long axis of the body to create a series of...
transaxial tomograms. To prevent chest movement artifacts, two seat belts were fastened around the patient's thorax during the acquisition of the study and patient positioning was checked periodically by a laser marker. All PET studies were performed after an overnight fast. One hour before the FDG study, all patients received 50 g oral glucose. After an attenuation scan, two separate bolus injections of 12–15 mCi 15O-water were administered intravenously 12 minutes apart, and 15 minutes later 5 mCi FDG was administered. Data were acquired for 5 minutes in list mode after each water injection and for 60 to 75 minutes in list mode after the FDG injection. The data beginning at 30 minutes after FDG injection, corresponding to the final 30–45 minutes of data acquisition, were reconstructed to create tomographic images of regional myocardial FDG uptake.

MRI
ECG gated MRI was performed using a 1.5-T scanner. A 15- to 20-minute scan allowed acquisition of four or five slices at four or five time points in the cardiac cycle from end diastole to end systole using spin-echo imaging (echo time, 20 msec; repetition time, R wave–to–R wave time, two excitations). Each slice was 10-mm thick, with a center-to-center slice distance of 20 mm. Immediately after this acquisition, a second acquisition was begun, which again consisted of four or five slices at four or five time points, to fill in the gaps between slices. The final image sequence therefore consisted of eight or 10 contiguous slices (10-mm thickness, 10-mm center-to-center interslice distance) at four or five time points in the cardiac cycle from end diastole to end systole. Total imaging time was 30–45 minutes.

The time to end systole was determined before MRI from the left ventricular volume curve obtained from the radionuclide ventriculogram acquired at a similar heart rate (73±11 beats per minute for MRI and 70±11 beats per minute for the gated radionuclide study). The intersequence delay of the MRI scan (i.e., time between successive time points) could then be adjusted so that the last (fourth or fifth) time point of the MRI scan occurred at end systole as determined from the radionuclide study.

Data Analysis
In each patient, corresponding transaxial tomograms from the three sets of 201Tl images representing the exercise, redistribution, and reinjection studies were visually aligned for direct comparison.20 These were then aligned with the corresponding transaxial tomographic images of myocardial FDG uptake from the PET study. Because of the limitation of the transaxial view in assessing the inferior myocardial wall, only midventricular myocardial tomograms were used for the analysis. To objectively compare relative regional FDG and 201Tl activity, five myocardial regions of interest (ROIs) representing the posterolateral, anterolateral, anteropapical, anteroseptal, and posteroseptal myocardium were drawn on each FDG tomogram and on each of the three corresponding 201Tl images. Regional FDG and 201Tl activities were then computed within each region of interest.20 The size of the ROIs ranged from 40 to 130 pixels, which corresponds to 4.6–15 cm2 (with a z-axis resolution of 12.5 mm).

Regional myocardial 201Tl activity. In each patient, the myocardial region of interest showing the maximum counts over the entire myocardium on the exercise 201Tl study was used as the normal reference region for that patient.20 The choice of these regions to represent the normal reference region for each patient is supported by the PET and MRI data. The reference regions in the 25 patients showed normal blood flow by H215O (1.0±0.2 ml/g per minute; range, 0.70–1.70 ml/g per minute) and normal wall thickening by MRI (3.7±2.7 mm; range, 1.0–8.2 mm). The corresponding anatomic regions in the redistribution and reinjection studies were identified and used as the reference regions for those studies. The 201Tl activity in all other myocardial regions was then expressed as a percent of the activity measured in the reference region for each of the exercise, redistribution, and reinjection image series.

For each exercise study, the presence of a 201Tl defect in any myocardial region was defined arbitrarily when 201Tl activity was <85% of the normal reference region.20 Based on previous reproducibility studies from our laboratory, a regional 201Tl abnormality during exercise was considered reversible if the relative 201Tl activity increased by ≥10% on the subsequent redistribution or reinjection images. A defect was considered completely reversible if this increase resulted in 201Tl activity that was ≥85% of the activity in the reference region. Similarly, 201Tl abnormalities during exercise were considered irreversible if the relative 201Tl activity was unchanged or increased <10% on the subsequent redistribution and reinjection images. In addition, a defect on exercise images was also considered irreversible if the activity in that region remained <50% of the activity in the normal reference region after redistribution and reinjection. Based on the relative regional 201Tl activity on the exercise images, 201Tl defects that were irreversible on the 3- to 4-hour redistribution images were classified as 1) mild (201Tl uptake, >65% of maximal activity), 2) moderate (201Tl uptake, 50–65% of maximal activity), and 3) severe (201Tl uptake, <50% of maximal activity), as previously described.20

Regional myocardial FDG uptake. The myocardial region on the FDG series that corresponded to the normal reference regions on the 201Tl exercise image series was used as the normal reference region for relative FDG uptake. FDG uptake in all other myocardial regions was expressed as a percent of the activity in this reference region.20

Regional myocardial blood flow. We computed absolute regional myocardial blood flow from the dynamic 15O-water data.22 The myocardial ROIs previously constructed on the FDG images for measurement of regional FDG activity were applied to the tomographic 15O-water data to derive regional myocardial H215O time-activity curves. Absolute regional myocardial blood flow was calculated by fitting the myocardial H215O time-activity curve, M(t), to the equation:

$$M(t) = (PV) \cdot F \cdot (LV(t) \cdot e^{-\left(F/PV\right)}) + (SO) \cdot LV(t)$$

where the parameters of the fit are PV (a partial volume correction factor), F (flow in ml/g per minute), and SO (a spillover correction factor, indicating the fraction of counts spilling from the left ventricular cavity into the myocardium). x is the convolution operation. The par-
tition coefficient $p$ was assumed fixed at 0.92, and the arterial input function, $LV(t)$, was measured directly from the left ventricle, using the PET data. Contamination from the myocardium was carefully avoided by looking at both the end diastolic and end systolic corresponding MRI tomograms. This is similar to the method of Iida et al., Bergmann et al., and Herrero et al., with the exception that our fitting was weighted with the data's inverse variance as determined from total counts, dead time, and random correction factors. The computation of blood flow values was repeated twice, one for each $H_2^{18}O$ study, and the results of the two measurements were then averaged together.

In each patient, myocardial blood flow measured in the reference region (previously identified as the region showing the maximum $^{201}TI$ activity during exercise) was considered as the normal value for that patient. In all other myocardial regions, blood flow values were normalized for the value measured in the reference region. Considering the minimal variability reported by Gropler et al. in normal individuals, in each patient regions with reduced blood flow were defined as those in which blood flow was <80% of the absolute blood flow value measured in the normal reference region.

Regional FDG uptake relative to blood flow. The regional FDG uptake was then interpreted in relation to regional myocardial blood flow by computing the ratio between FDG uptake (nCi per ml) and absolute blood flow (ml per g per minute) in each myocardial region. The value obtained in the myocardial region corresponding to the normal reference region was then assumed to represent the normal ratio between FDG uptake and blood flow for that patient. In keeping with the 80% threshold used to define reduced blood flow relative to the normal reference region, regional FDG uptake was defined as reduced when it was <80% of that of the normal reference region.

Based on the FDG content and on the FDG: blood flow ratio, four groups of myocardial regions were identified: 1) normal (≥80% of the FDG activity in the normal reference region associated with normal blood flow), 2) mismatch (reduced myocardial blood flow with FDG: blood flow ratio ≥110% of that of the normal reference region), 3) moderately reduced FDG uptake (50–79% of normal reference FDG activity with reduced blood flow and FDG: blood flow ratio <110% of that of the normal reference region), 4) severely reduced FDG uptake (<50% of normal reference FDG activity with reduced blood flow and FDG: blood flow ratio <110% of that of the reference region). The choice of an FDG: blood flow ratio ≥110% of that of the normal region as a cutoff to identify the occurrence of FDG: blood flow mismatch was derived from previously reported data obtained in normal volunteers in which FDG: blood flow values ranged from 1.02 to 1.12 mg/g per minute, which is similar to the 1.20 cutoff value used by Vanoverschelde et al. to define the occurrence of FDG: blood flow mismatch. In the current analysis, a region could be defined as showing mismatch if FDG activity was normal, increased, or less than normal, as long as FDG activity was disproportionately increased relative to the reduced regional blood flow, as previously described.

The calculation of blood flow using the $H_2^{18}O$ model yields the recovery coefficient for correction for partial volume effects. This recovery coefficient is valid not just for the water blood flow data but also for the FDG data extracted from the same ROIs. A similar correction, however, could not be made for the $^{201}TI$ SPECT data. To avoid biasing the results, the FDG and SPECT comparisons were made with neither data set corrected for recovery coefficient. Similarly, the FDG activity was assessed without correction for the arterial input function.

Regional wall thickness and systolic thickening. To assess regional end-diastolic thickness and absolute wall thickening, corresponding transaxial end-diastolic and end-systolic MRI images were analyzed by two independent operators unaware of $^{201}TI$ and FDG results. Alignment of the PET slice with the corresponding MRI slice was done visually, using both the PET attenuation images (which show the lung outlines clearly, the heart shadow, and the slice in which the liver first begins to appear) and the PET emission images. Because of the different interslice distance (5.1 mm for PET and 10 mm for MRI), each MRI tomogram was matched to two contiguous PET tomograms. An average of three MRI slices (range, 1–5) and six FDG and $^{201}TI$ tomographic planes (range, 2–10) were analyzed for each patient. As described above, each PET and SPECT slice had been divided into five ROIs. By appropriate resampling, the PET and MRI images were made to be of identical size (i.e., the same number of mm per pixel). The five ROIs drawn on the PET then could be superimposed visually on the MRI (with appropriate rotations and translations also determined visually). Because each ROI encompassed a relatively large amount of myocardial tissue, minor misalignments using this visual technique would not significantly alter the results. Thickness measurements were made at the center of each ROI by manually identifying a point of the epicardial and endocardial borders perpendicular to the two surfaces. The length of the line segment joining these two points was calculated and taken as the wall thickness. Systolic wall thickening was defined as the difference between end-systolic and end-diastolic wall thickness. Based on the extent of systolic wall thickening, myocardial regions were considered normokinetic (systolic wall thickening ≥2 mm), hypokinetic (systolic wall thickening <2 mm), or akinetic-dyskinetic (in case of absent wall thickening or of systolic wall thinning).

A total of 347 myocardial regions were evaluated, which averaged 14 per patient (range, 5–25).

Statistical Analysis

Segmental analysis. In this analysis, each myocardial region was considered as an independent piece of information. One-way ANOVA was used to assess the overall level of significance among the four groups of myocardial regions classified according to FDG: blood flow relations and among the five groups of regions classified according to relative $^{201}TI$ activity. The two-tailed unpaired Student’s $t$ test with Bonferroni’s correction was then applied when two groups were compared. The $\chi^2$ test was used to compare percent data. All data are expressed as mean±SD. A value of $p<0.05$ was accepted as the minimal level of significance.

Patient analysis. In this analysis, each patient represented the experimental unit of interest. Therefore, for
each patient, regions were grouped as having normal 201Tl uptake, reversible 201Tl defects, or mild, moderate, or severe irreversible defects. Similarly, for the FDG data, regions were grouped for each patient as normal, mismatch, moderately reduced FDG, or severely reduced FDG activity. As more than one category of myocardial segments was present in each patient, each patient in this analysis cannot be considered as an independent unit of observation. Therefore, no statistical analysis was performed on the results obtained from the patient analysis.

Results
Regional Wall Thickness and Systolic Wall Thickening Versus FDG Activity

Of the 347 myocardial regions analyzed, 129 showed normal FDG uptake with normal blood flow. The blood flow in these regions (1.1 ± 0.3 ml/g per minute; range, 0.70–2.10 ml/g per minute;) was significantly higher than in all other groups (p<0.01). In 113 regions, reduced blood flow (0.59 ± 0.17 ml/g per minute; range, 0.20–0.91 ml/g per minute) with increased FDG: blood flow ratio was measured; these were considered to represent regions of FDG: blood flow mismatch. Among the remaining 105 regions with reduced FDG uptake, 69 showed moderately reduced FDG uptake (65 ± 12% of the normal activity) with reduced blood flow (0.70 ± 0.19 ml/g per minute; range, 0.25–1.20 ml/g per minute). The level of blood flow in these regions was significantly greater than that of regions with severely reduced FDG uptake and regions with FDG: blood flow mismatch (p<0.01). The other 36 regions had severely reduced FDG uptake (36 ± 10% of the normal activity) with reduced blood flow (0.59 ± 0.17 ml/g per minute; range, 0.20–0.90 ml/g per minute).

Segmental analysis. The end-diastolic wall thickness (Figure 1) in the 69 regions with moderately reduced FDG uptake was significantly greater than that of the 36 regions with severely reduced FDG uptake (9.4 ± 2.6 versus 8.0 ± 3.7 mm; p<0.05). Furthermore, the end-diastolic wall thickness in regions with moderately reduced FDG uptake was similar to that of regions with normal FDG uptake (10.1 ± 3.3 mm). When absolute systolic wall thickening was determined (Figure 1), myocardial regions with severely reduced FDG uptake demonstrated no wall thickening (−0.7 ± 2.1 mm) as compared with reduced but preserved systolic wall thickening in regions with moderately reduced FDG uptake (1.7 ± 2.7 mm; p<0.01). The systolic wall thickening in regions with normal FDG uptake (2.7 ± 2.3 mm) and FDG: blood flow mismatch (2.8 ± 2.4 mm) was significantly greater (both, p<0.02) than that observed in moderately reduced FDG regions.

Of the 69 myocardial regions with a moderate reduction in FDG uptake, 28 (41%) showed normal wall thickening at rest (Table 1) as compared with only two (6%) of the 36 myocardial regions with severe reduction in FDG uptake. An example of an abnormal region with moderately reduced FDG uptake but with evidence of systolic wall thickening and 201Tl uptake is illustrated in Figure 2.

Patient analysis. When, in each patient, systolic wall thickening values were averaged within each of the four groups of myocardial regions, systolic wall thickening in regions with moderate reduction in FDG uptake (1.5 ± 2.4 mm) appeared greater than that of regions with a severe reduction in FDG uptake, in which wall thickening was absent (−0.3 ± 1.8 mm). Systolic wall thickening of the myocardial regions with moderate reduction in FDG uptake did not appear different from that of regions with FDG: blood flow mismatch (2.3 ± 1.7 mm) and with normal FDG uptake (2.5 ± 1.3 mm).

Myocardial regions with a moderate reduction in FDG uptake and blood flow were observed in 20 of 25 patients. In 10 (50%) of these patients, regional systolic wall thickening was normal in these regions (Table 1). Similarly, myocardial regions with FDG: blood flow mismatch were observed in 22 of 25 patients, and in 15 patients (68%) wall thickening was normal in these regions. In contrast, myocardial regions having a severe reduction in FDG uptake were observed in 12 patients, and systolic wall thickening was normal in such regions in only one patient (8%).

Regional Wall Thickness and Systolic Wall Thickening Versus 201Tl Activity

Of the 347 myocardial regions analyzed, 66 (19%) had normal 201Tl uptake, 112 (32%) had an initial defect with either complete or partial redistribution at 3 to 4 hours, and the remaining 169 (49%) had an irreversible 201Tl defect. In these latter regions, 70 showed a mild and 52 a moderate 201Tl defect (201Tl uptake 74 ± 5 and
TABLE 1. Extent of Regional Systolic Wall Thickening in the Four Groups of Myocardial Regions Defined by 
<table>
<thead>
<tr>
<th>18 Fluorodeoxyglucose Uptake Relative to Blood Flow</th>
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<td><strong>FDG uptake</strong></td>
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| **FDG, 18 fluoroxyglucose; n*, number of patients in whom the corresponding category of myocardial regions was observed.**

58±4% of maximal activity, respectively, whereas 47 regions had a severe irreversible 201Tl defect (201Tl uptake 31±14% of maximal activity).

**Segmental analysis.** Regions with normal 201Tl uptake were significantly thicker (p<0.01) as compared with all other groups (Figure 3). No significant differences in end-diastolic wall thickness were observed among the other groups of regions. Systolic wall thickening (Figure 3) was greater in regions with normal 201Tl uptake (3.3±2.3 mm), as compared with regions with reversible 201Tl defects (2.1±2.2 mm; p<0.001), mild irreversible defects (2.4±2.4 mm; p<0.05), moderate irreversible defects (2.2±2.5 mm; p<0.01), and severe irreversible defects (−0.1±2.9 mm; p<0.01). Although systolic wall thickening was similar among regions with reversible 201Tl defects and either mild or moderate irreversible 201Tl defects, it was significantly reduced in regions with severe irreversible 201Tl defects (p<0.01, as compared with all other regions) (Figure 3). In particular, 60 (49%) of the 122 myocardial regions, with either a mild or moderate irreversible 201Tl defect after redistribution, showed normal systolic wall thickening at rest, and only 23 (19%) manifested absence of wall thickening (Table 2). In contrast, only seven (15%) of the 47 regions with a severe 201Tl defect after redistribution showed normal wall motion at rest, and in 29 (62%) systolic wall thickening at rest was absent (Table 2). An example of a myocardial region showing a moderate irreversible 201Tl defect, with preserved FDG uptake and systolic wall thickening, is illustrated in Figure 4.

**Patient analysis.** The results of this analysis confirmed those of the segmental analysis (Tables 2 and 3). Mild and moderate irreversible 201Tl defects after redistribution were observed in 19 and 20 of the 25 patients, respectively, whereas severe irreversible 201Tl defects were observed in 17 patients. In mild and moderate irreversible defects, systolic wall thickening appeared greater as compared with the severe irreversible defects and was similar to that observed in the reversible 201Tl defects. The mean systolic wall thickening in the mild irreversible defects was normal in 11 (58%) of the 19 patients in whom these defects were observed; similarly, in the moderate irreversible defects systolic wall thickening was normal in nine (45%) of the 20 patients with such defects. In contrast, systolic wall thickening at rest in the severe 201Tl defects was normal in only two (12%) of the 17 patients in whom these defects were observed (Table 2).
FIGURE 3. Bar graphs showing end-diastolic wall thickness and systolic wall thickening measured from magnetic resonance imaging in the five groups of myocardial regions identified according to the pattern of $^{201}$TI activity on stress-redistribution imaging. Regions with normal $^{201}$TI uptake showed greater wall thickness as compared with myocardial regions showing either reversible or irreversible defects at 3- to 4-hour redistribution. Systolic wall thickening was absent in regions with severe irreversible defects at redistribution. *p<0.01 compared with all other groups of regions.

Regional Metabolic Activity Versus $^{201}$TI Activity

Segmental analysis. A comparison of the regional FDG and $^{201}$TI activity is shown in Table 4 and Figure 5. Metabolic evidence of viable myocardium was present in 100% of regions with normal $^{201}$TI activity and in 97% of regions with reversible $^{201}$TI defects. These values were similar to those observed in regions with irreversible $^{201}$TI defects that were only mild or moderate (99% and 96%, respectively). In contrast, only 36% (17 of 47) of the regions with severe irreversible $^{201}$TI defects showed metabolic evidence of viable myocardium (p<0.01 versus all other groups) (Figure 5).

Patient analysis. Relative FDG uptake did not appear different among the reversible $^{201}$TI defects and the mild or moderate irreversible $^{201}$TI defects; all values were higher than those observed in the severe $^{201}$TI defects (Table 3). The mean relative FDG activity in the severe $^{201}$TI defects was <50% of the normal region in nine (53%) of the 17 patients with such defects. In contrast, mean FDG activity in the moderate irreversible $^{201}$TI defects after redistribution was <50% in only one (5%) of the 20 patients with such defects and in none of the mild irreversible $^{201}$TI defects, which were observed in 19 patients.

Eight of the 25 patients (32%) did not have severe irreversible $^{201}$TI defects on stress-redistribution imaging. Therefore, in one third of the patients, the interpretation of mild-moderate irreversible $^{201}$TI defects as viable myocardium indicates that stress-redistribution $^{201}$TI scintigraphy alone (without rest-reinjection) would have been of sufficient accuracy in the evaluation of myocardial viability.

Effects of $^{201}$TI Reinjection

Thallium activity relative to FDG activity. Among the regions with severely reduced FDG uptake, 32 of 36 (89%) showed an irreversible $^{201}$TI defect at redistribution imaging that remained irreversible after reinjection of $^{201}$TI. Thirty (94%) of these 32 irreversible $^{201}$TI defects were severe. In contrast, among regions with moderately reduced FDG uptake, 30 (43%) of 69 showed irreversible $^{201}$TI defects, but only four (13%) of them were severe. Thirty-six (52%) regions with moderately reduced FDG uptake showed reversible $^{201}$TI defects. Of these, eight (12%) were completely reversible, and the remaining 28 (40%) were only partially reversible. The frequency of irreversible $^{201}$TI defects in regions with normal FDG uptake (22%) was equal to that observed in regions with FDG: blood flow mis-
TABLE 2. Extent of Regional Systolic Wall Thickening in Mild, Moderate, and Severe 201Tl Defects on Redistribution Imaging

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<tr>
<th>Systolic wall thickening</th>
<th>Irreversible 201Tl defects</th>
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<td><strong>Segmental analysis</strong></td>
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<td>Hypokinesia</td>
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</tr>
<tr>
<td>Akinesia/dyskinesia</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
</tr>
</tbody>
</table>

| Patient analysis        |     |     |     |     |     |     |
| n                       | 19  | 17  | 20  | 19  |
| Normal                  | 11  | 9   | 11  | 9   |
| Hypokinesia             | 5   | 7   | 2   | 7   |
| Akinesia/dyskinesia     | 3   | 4   | 3   | 4   |

RI+, Enhanced thallium uptake after reinjection; RI−, unchanged thallium uptake after reinjection.
In the segmental analysis each myocardial region of interest was considered as an independent unit of interest, whereas in the patient analysis each patient was considered as the unit of interest (see text).

No. * Represents the number of patients in which the corresponding category of irreversible 201Tl defects was observed.

Match (22%). In the regions with normal FDG, only one (3%) of the 29 irreversible 201Tl defects was severe; no regions in the group with FDG: blood flow mismatch showed a severe irreversible 201Tl defect. Therefore, when myocardial regions with a moderate reduction in FDG uptake and blood flow were interpreted as viable myocardium and when mild and moderate irreversible 201Tl defects were also interpreted as viable, the overall concordance between 201Tl imaging and PET in identifying viable and nonviable myocardium was 97% (Tables 4 and 5). There were no patients in whom the presence of viable underperfused myocardium was identified by either PET or 201Tl imaging alone.

When relative 201Tl uptake after reinjection was averaged in each patient for each of the four groups of myocardial regions, regions with a moderate reduction in FDG uptake showed a mean 201Tl activity similar to that of regions with FDG: blood flow mismatch (72±16% versus 81±13%, respectively), with both values being greater than that observed in regions with a severe reduction in FDG uptake (35±11%). In regions with normal FDG uptake, 201Tl uptake after reinjection was greater (90±7%) as compared with all other regions.

201Tl uptake after reinjection in the myocardial regions with a moderate reduction in FDG uptake was >50% of the normal region in all 20 patients in whom this metabolic pattern was observed. In contrast, the amount of 201Tl uptake after reinjection was >50% in only one (8%) of the 12 patients with a severe reduction in FDG uptake.

201Tl reinjection in severe irreversible defects on redistribution imaging. The effects of 201Tl reinjection after redistribution imaging in regions with irreversible 201Tl defects are presented in Table 5 in relation to FDG activity, end-diastolic wall thickness, and systolic wall thickening. In mild and moderate irreversible 201Tl defects, no differences in end-diastolic wall thickness and systolic wall thickening or in the mean FDG activity were observed between regions with or without enhanced 201Tl activity after reinjection.

The results of 201Tl reinjection in regions with severe 201Tl defects are also shown in Table 5. Twelve (26%) of the 47 regions with severe irreversible 201Tl defects (corresponding to eight of the 17 patients in which such regions were located) showed enhanced 201Tl uptake after reinjection, and the remaining 35 regions showed no increase in 201Tl activity after reinjection. End-diastolic wall thickness was 10±2 mm in the regions that showed enhanced 201Tl uptake after reinjection and 8±4 mm (p=NS) in those who did not. A trend toward preserved systolic wall thickening was observed in regions that showed increased 201Tl uptake after reinjection (1.6±3.3 mm) as compared with those that did not (−0.6±2.6 mm; p=0.06; Figure 6). However, absence of systolic wall thickening at rest was not only observed in 24 (69%) of the myocardial regions without increased 201Tl uptake after reinjection but also in five (42%) of

TABLE 3. Analysis by Patients of Regional Systolic Wall Thickening and Relative 18Fluorodeoxyglucose Uptake in Relation to 201Tl Activity on Stress-Redistribution Imaging

<table>
<thead>
<tr>
<th>201Tl stress-redistribution</th>
<th>Reversible defects</th>
<th>Irreversible defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n=25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic wall thickening (mm)</td>
<td>3.2±1.4</td>
<td></td>
</tr>
<tr>
<td>18Fluorodeoxyglucose (%)</td>
<td>96±6</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mild (n=20)</th>
<th>Moderate (n=19)</th>
<th>Severe (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversible defects</td>
<td>2.0±1.4</td>
<td>2.0±2.4</td>
<td>0±2.2</td>
</tr>
<tr>
<td>Irreversible defects</td>
<td>2.0±1.4</td>
<td>2.0±2.8</td>
<td>0±2.2</td>
</tr>
</tbody>
</table>

n, Number of patients in whom the corresponding pattern of 201Tl activity was observed.
TABLE 4. Regional 18Fluorodeoxyglucose Activity in Relation to Regional 201TI Findings on Stress-Redistribution Imaging

<table>
<thead>
<tr>
<th>18Fluorodeoxyglucose</th>
<th>201TI stress-redistribution</th>
<th>Irreversible defects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Reversible defects</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>46</td>
<td>70</td>
</tr>
<tr>
<td>18Fluorodeoxyglucose/blood flow mismatch</td>
<td>17</td>
<td>26</td>
</tr>
<tr>
<td>Moderately reduced</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Severely reduced</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>66</td>
<td>112</td>
</tr>
</tbody>
</table>

the 12 regions with enhanced 201TI uptake after reinjection (Table 2). In contrast, FDG uptake occurred in all 12 regions with severe irreversible 201TI defects at redistribution that improved after reinjection, as compared with only five of the 35 (14%) of the severe 201TI defects that remained irreversible after reinjection (p<0.01; Figure 6). Mean FDG activity (expressed relative to that measured in the normal reference region) was also significantly higher (78±24%) in regions that showed enhanced 201TI uptake after reinjection, as compared with mean FDG activity of regions remaining unchanged after reinjection (41±19%; p<0.001) (Table 5). Myocardial blood flow was reduced in regions with and without enhanced 201TI uptake after reinjection; however, in regions with severe 201TI defects, which were irreversible after reinjection, myocardial blood flow was significantly lower (p<0.05) as compared with regions that showed enhanced 201TI uptake after reinjection (Table 5). An example of a myocardial region showing a severe 201TI defect with enhanced 201TI uptake after reinjection as well as preserved metabolic activity is illustrated in Figure 2.

Discussion

The results of the present study provide confirmatory evidence that, in patients with ischemic left ventricular dysfunction, myocardial regions with a moderate reduction in FDG uptake and blood flow, without FDG:blood flow mismatch, as well as myocardial regions with mild to moderate 201TI defects after redistribution, represent viable myocardium.

Moderate Versus Severe Reduction in FDG Uptake

The demonstration of preserved metabolic activity by PET, in which the regional uptake of FDG is an estimate of glucose utilization, has been shown in several studies to identify the presence of viable myocardial tissue in patients with CAD and left ventricular dysfunction3,15-20,30-32 and to predict reversal of regional dysfunction after revascularization.3,19 Although these findings have reasonably high predictive accuracy, they may be inaccurate in predicting functional recovery or lack of functional recovery in up to 22% of the myocardial regions analyzed.19 In these previous studies, regions with reduced myocardial blood flow were assumed to represent viable tissue only if those regions demonstrated either an absolute increase in FDG activity or a relative increase in comparison with the reduced blood flow, thereby exhibiting FDG:blood flow mismatch3,15-20,30-32; any regions with diminished FDG uptake and diminished blood flow but without the occurrence of FDG:blood flow mismatch were considered nonviable, regardless of the severity of reduction in blood flow or FDG uptake. We hypothesized that regions with only a mild or moderate reduction in FDG uptake might represent viable tissue whether or not FDG:blood flow mismatch is present because it is possible that glucose consumption might be reduced in some regions of viable tissue because of reduced perfusion and function.3,33 This hypothesis is suggested by 201TI activity in the majority of such regions.3,34 The findings of the present study confirm that the majority of regions in which FDG uptake is moderately reduced in proportion to reduced blood flow represent viable myocardium, which is evidenced by preserved regional systolic wall thickening.

Although reduced with respect to the normal regions and to regions with FDG:blood flow mismatch, the mean systolic wall thickening of the regions with moderately reduced FDG uptake was significantly greater than that observed in regions with severely reduced FDG uptake. Similarly, end-diastolic wall thickness in regions with moderate reduction in FDG activity was similar to that of normal regions but was significantly higher than that observed in the regions with severely reduced FDG activity. Moreover, when the extent of
TABLE 5. Irreversible \(^{201}\)Tl Defects on Redistribution Imaging: \(^{18}\)Fluorodeoxyglucose Uptake, End-Diastolic Wall Thickness, Systolic Wall Thickening, and \(^{201}\)Tl Uptake After Reinjection  

<table>
<thead>
<tr>
<th>Blood flow (ml/g per minute)</th>
<th>(^{18})Fluorodeoxyglucose uptake</th>
<th>Mean (^{18})fluorodeoxyglucose activity (% of normal reference activity)</th>
<th>Mean end-diastolic wall thickness (mm)</th>
<th>Mean systolic wall thickening (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild ((n=70))</td>
<td>Moderate ((n=52))</td>
<td>Severe ((n=47))</td>
<td>Mild ((n=70))</td>
</tr>
<tr>
<td></td>
<td>RI+ ((n=25))</td>
<td>RI− ((n=45))</td>
<td>RI+ ((n=14))</td>
<td>RI− ((n=38))</td>
</tr>
<tr>
<td>Blood flow (ml/g per minute)</td>
<td>0.86±0.26 (NS)</td>
<td>0.93±0.38 (NS)</td>
<td>0.74±0.28</td>
<td>0.82±0.35</td>
</tr>
<tr>
<td>(^{18})Fluorodeoxyglucose uptake</td>
<td>24</td>
<td>45</td>
<td>14</td>
<td>36</td>
</tr>
<tr>
<td>No (^{18})fluorodeoxyglucose uptake</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Mean (^{18})fluorodeoxyglucose activity (% of normal reference activity)</td>
<td>86±17</td>
<td>94±19</td>
<td>81±26</td>
<td>77±19</td>
</tr>
<tr>
<td>Mean end-diastolic wall thickness (mm)</td>
<td>11±4</td>
<td>9±3</td>
<td>10±4</td>
<td>9±3</td>
</tr>
<tr>
<td>Mean systolic wall thickening (mm)</td>
<td>2.4±2.7</td>
<td>2.3±2.4</td>
<td>1.9±3.2</td>
<td>2.4±2.4</td>
</tr>
</tbody>
</table>

RI+, enhanced \(^{201}\)Tl uptake after reinjection; RI−, unchanged \(^{201}\)Tl uptake after reinjection.  
*\(p<0.01\) compared with all other groups; †\(p<0.01\) compared with mild and moderate irreversible defects.

Regional wall thickening was analyzed, 41% of the myocardial regions showing a moderate reduction in FDG uptake and blood flow (corresponding to 50% of the patients in which such pattern was observed) (Table 1) demonstrated normal wall thickening at rest, as opposed to only 6% of the regions with a severe reduction in FDG uptake. In keeping with our previous observations, the presence of viable myocardium in the regions with moderately reduced FDG uptake is further supported by the scintigraphic data; 52% of myocardial regions with moderate reduction in blood flow and FDG uptake had reversible perfusion defects on \(^{201}\)Tl scintigraphy, and an additional 4% had completely normal \(^{201}\)Tl uptake. Although irreversible \(^{201}\)Tl defects were observed in the remaining regions, 87% of the irreversible defects were mild or moderate. Only 6% of all myocardial regions with moderately reduced FDG uptake corresponded to severe irreversible thallium defects, which was similar to the frequency of severe irreversible defects observed in myocardial regions with normal FDG uptake (1%) and in regions exhibiting FDG: blood flow mismatch, in which no severe irreversible \(^{201}\)Tl defects were observed. As \(^{201}\)Tl uptake is dependent on myocardial cell membrane integrity as well as perfusion, we interpret \(^{201}\)Tl activity to be an index of cellular viability. Therefore, both the functional data and the pattern of \(^{201}\)Tl uptake in regions with moderate reduction in FDG uptake indicate the presence of viable myocardium instead of irreversibly damaged tissue in these regions.

In contrast, in the regions with severely reduced FDG uptake, end-diastolic wall thickness was reduced as compared with the other regions, and systolic wall thickening was absent in 75% of these regions (Table 1), which is compatible with the presence of nonviable tissue.\(^{34-36}\)

Myocardial regions with a severe reduction in FDG uptake also had a high prevalence (83%) of severe irreversible \(^{201}\)Tl defects, which suggests the presence of nonviable myocardium in those territories. The remaining regions with severely reduced FDG uptake showed either mild or moderate irreversible \(^{201}\)Tl defects (6%) or partially irreversible defects (11%); no regions in this group had either normal \(^{201}\)Tl activity or a completely reversible \(^{201}\)Tl defect (Table 4). The discordance in a small number of regions with severely reduced FDG uptake in which \(^{201}\)Tl activity suggested viable myocardium might indicate a potential underestimation of viability by the interpretation of FDG uptake, although some error in the alignment process could also contribute to this discrepancy. The pattern of a moderate reduction in FDG uptake and blood flow, without FDG: blood flow mismatch, probably represents a region of myocardium with a mixture of viable and nonviable tissue. Although it could be argued that no improvement in wall motion would occur after revascularization in these areas, as FDG: blood flow mis-

![Graph showing effects of \(^{201}\)Tl reinjection in regions with severe irreversible \(^{201}\)Tl defects at redistribution. Regions with severe \(^{201}\)Tl defects, which reversed after reinjection, showed a trend toward preserved wall thickening with respect to regions without \(^{201}\)Tl uptake after reinjection although a large overlap was observed. The reversibility of a severe \(^{201}\)Tl defect after reinjection always corresponded to the presence of \(^{18}\)fluorodeoxyglucose (FDG) uptake in all regions. In contrast, only 14% of the severe defects, which remained unchanged after reinjection, showed presence of metabolic activity by positron emission tomography.](http://circ.ahajournals.org/)

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match was absent, the \(^{201}\text{Tl}\) findings together with the finding of preserved wall thickening strongly suggests the presence of underperfused jeopardized myocardium in these regions. Whether the extent of viable tissue in these regions is sufficient to result in improved regional function after reperfusion of blood flow will require additional studies in patients undergoing revascularization.

**Mild-Moderate Versus Severe \(^{201}\text{Tl}\) Defects**

The \(^{201}\text{Tl}\) reinjection protocol we used in this study has been recently shown to predict reliably the functional recovery of regions with apparently irreversible defects on standard exercise-redistribution imaging,\(^{11,12}\) with an accuracy similar to that reported using FDG imaging with PET.\(^ {3,19}\) Although these \(^{201}\text{Tl}\) results have been thus far validated in a relatively small number of patients undergoing revascularization,\(^ {11,12}\) the number of patients so studied is similar to those reported using PET imaging.\(^ {3,19}\) We have reported previously that the majority of irreversible \(^{201}\text{Tl}\) defects, in which the reduction in \(^{201}\text{Tl}\) activity is only mild or moderate, have FDG uptake whether or not regional \(^{201}\text{Tl}\) activity is enhanced by reinjection.\(^ {20}\) The maintenance of metabolic activity suggested that irreversible \(^{201}\text{Tl}\) defects of only mild or moderate severity represent viable myocardial tissue. The results of the present study, in which regional systolic wall thickening and end-diastolic wall thickness were assessed in relation to patterns of regional \(^{201}\text{Tl}\) uptake, provide confirmatory evidence of viable myocardium in regions with only mild or moderate irreversible \(^{201}\text{Tl}\) defects. End-diastolic wall thickness did not differ among regions in relation to the severity of irreversible \(^{201}\text{Tl}\) defects on redistribution imaging (Figure 3). Myocardial regions with mild or moderate irreversible \(^{201}\text{Tl}\) defects, however, manifested reduced but maintained systolic wall thickening, which was similar to that of regions with reversible \(^{201}\text{Tl}\) defects but was significantly greater than that of regions with severe irreversible defects (Figure 3). Moreover, 49% of the regions with mild-moderate irreversible \(^{201}\text{Tl}\) defects (corresponding to 51% of the patients in which such defects were observed) showed presence of normal wall motion at rest (Table 2), and only 19% of the mild-moderate irreversible \(^{201}\text{Tl}\) defects showed absent wall thickening. In contrast, systolic wall thickening was absent in 62% of the regions with severe \(^{201}\text{Tl}\) defects. Finally, the presence of metabolic activity, as assessed by FDG uptake, was identified in 98% of these segments (Figure 5). Therefore, the functional characteristics of these territories together with the metabolic evidence indicate the presence of viable myocardium in mild and moderate irreversible \(^{201}\text{Tl}\) defects after redistribution; this is in agreement with a previous report by Gibson et al.\(^ {6}\) These findings suggest that patients with irreversible \(^{201}\text{Tl}\) defects on redistribution imaging, in which the magnitude of the \(^{201}\text{Tl}\) defects is not severe, may not require any further investigation to assess the viability of those segments.

Among regions with mild or moderate irreversible \(^{201}\text{Tl}\) defects, no differences in systolic wall thickening, end-diastolic wall thickness, or FDG activity were observed between regions with and those without enhanced \(^{201}\text{Tl}\) uptake after reinjection (Tables 2 and 5). This observation may be accounted for by the relative nature of the \(^{201}\text{Tl}\) analysis. Regional \(^{201}\text{Tl}\) activity in each of the stress, redistribution, and reinjection images was expressed relative to that of a normal reference region. Thus, a substantial increase in absolute \(^{201}\text{Tl}\) activity within the defect after reinjection might be masked by comparable or even greater uptake of \(^{201}\text{Tl}\) in the normal region, and, therefore, result in the appearance of a persistent defect. Recent data in our laboratory, in which absolute as well as relative increases in \(^{201}\text{Tl}\) activity were assessed after reinjection, indicate that the absolute uptake of \(^{201}\text{Tl}\) is significantly greater in mild-to-moderate defects that persist after reinjection than in severe persistent defects.\(^ {37}\)

Our data also provide additional observations on severe irreversible \(^{201}\text{Tl}\) defects on redistribution images. It is in such regions that viability is an issue and in which evidence of preserved systolic function, metabolic activity, or enhanced \(^{201}\text{Tl}\) uptake after reinjection would be clinically important. Compatible with our previous observations,\(^ {20}\) there was concordance between enhanced uptake of \(^{201}\text{Tl}\) after reinjection and evidence of metabolic activity by PET in the majority of these severe irreversible defects; all regions in which \(^{201}\text{Tl}\) activity was enhanced by reinjection showed FDG uptake, whereas FDG uptake was observed in only 14% of regions without increased \(^{201}\text{Tl}\) activity after reinjection (Figure 6). The current data also indicate that evidence of myocardial viability or nonviability in such severe irreversible \(^{201}\text{Tl}\) defects cannot be obtained by analysis of regional systolic function alone. Unlike irreversible defects that are mild or moderate, in which preserved systolic wall thickening confirms the presence of viable tissue, wall thickening is markedly reduced or absent in the majority of regions in which the reduction in \(^{201}\text{Tl}\) activity is severe. Moreover, the reduction in wall thickening did not differ significantly between viable regions (as identified by FDG uptake and \(^{201}\text{Tl}\) uptake after reinjection) and nonviable regions (Figure 6). Although the analysis of the extent of wall thickening (Tables 2 and 5) indicates that some viable regions might have been identified by preserved wall thickening, the majority had severely depressed or absent wall thickening. These particular regions, with maintained metabolic activity and \(^{201}\text{Tl}\) uptake on rest reinjection despite lack of systolic thickening and with reduced blood flow, appear to provide clinical evidence of hibernating myocardium in these patients.\(^ {38-39}\)

The percentage of severe irreversible \(^{201}\text{Tl}\) defects that manifested metabolic activity (36%) in the current series is lower than in our previous experience, in which 51% of such regions showed FDG uptake.\(^ {20}\) This result probably arises from the inclusion of different patients in the two studies. Despite this lower prevalence of viable myocardium in severe irreversible defects, our data continue to demonstrate an excellent concordance between the results of FDG imaging and \(^{201}\text{Tl}\) reinjection imaging, as noted above. The two techniques provided similar information regarding viable versus nonviable myocardium in 42 of 47 (89%) severe irreversible defects (Table 5).

**Limitations of the Study**

The lack of data regarding the functional outcome after revascularization of myocardial asynergic territories identified as viable represent a limitation of the
present study. Maintenance of normal or reduced systolic wall thickening in the majority of myocardial regions with a moderate reduction in FDG uptake or with mild-to-moderate irreversible $^{201}$TI defects, however, clearly indicates viable myocardium in these territories. It is also noteworthy that as many of these myocardial regions do not show impaired wall motion at rest, they would not be expected to improve after revascularization. Nevertheless, our data must be considered preliminary until supported by a larger study of patients before and after revascularization. Whether the currently available data may be applied to management decisions regarding revascularization of the individual patient with chronic coronary artery disease and left ventricular dysfunction remains to be defined.

In the present study, no attenuation correction was performed for the $^{201}$TI data. This might affect the recovery of counts in some myocardial regions. However, because in male subjects this potential problem mainly concerns the inferior myocardial wall, which was excluded from the analysis in the present study, it is unlikely that it would substantially affect our results.

Finally, in the current study, myocardial blood flow values were not compared with a normal data base but with a “normal” reference region identified in each patient on the basis of maximal $^{201}$TI activity during exercise. Although the large variability of blood flow values reported in normal individuals makes it difficult to identify a lower limit for normal blood flow, the possibility cannot be excluded that some myocardial segments with normal absolute blood flow values may have been included in the group of segments with moderately reduced FDG and blood flow. As the vast majority of these segments demonstrated viability by regional function and $^{201}$TI criteria, this possibility probably had little influence on the conclusions of this study.

**Conclusions**

The findings of the present study confirm that regions with moderately reduced blood flow and FDG activity, as well as those with mild-moderate irreversible $^{201}$TI defects, represent viable myocardium in patients with chronic ischemic left ventricular dysfunction. Therefore, the degree of the metabolic deficit should be taken into account in viability studies using PET imaging, as should the severity of irreversible defects in $^{201}$TI scintigraphy. A quantitative analysis of regional FDG uptake as well as $^{201}$TI uptake yields important clinical information, which may further improve the accuracy of PET and of exercise $^{201}$TI scintigraphy in the identification and quantification of viable myocardium.

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Regional left ventricular wall thickening. Relation to regional uptake of 18fluorodeoxyglucose and 201Tl in patients with chronic coronary artery disease and left ventricular dysfunction.

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