Assessment of residual myocardial viability in patients with chronic coronary artery disease and left ventricular (LV) dysfunction is of great clinical importance (1–4). Several techniques analyzing the morphologic (5), functional (6), cellular (7), or metabolic (8) integrity of the myocardium have been introduced into clinical medicine. Each of these methods has specific advantages for the diagnosis of myocardial viability, but none allows direct visualization of the cellular (7), or metabolic (8) integrity of the myocardium. Among various resolution techniques, the size and shape of hyperenhanced areas at ceMRI were identical to areas of irreversible injury defined by tetrazolium staining (15). Moreover, ceMRI allows one to distinguish between regions with reversible and irreversible myocardial injury, depending on the transmural extent of hyperenhancement (14,15). Furthermore, the transmural extent of hyperenhancement has been shown to be predictive of recovery of segmental contractile function after myocardial revascularization in experimental studies (16) and in patients with acute myocardial infarctions and chronic ischemic heart disease (17,18).

The aim of this study was to compare ceMRI with nuclear metabolic imaging using $^{18}$F-fluorodeoxyglucose (FDG) positron emission tomography (PET) for the detection of myocardial viability in patients with chronic ischemic heart disease and LV dysfunction.

**METHODS**

**Patient population.** Twenty-six consecutive patients with LV dysfunction scheduled for myocardial viability assessment were scanned with both PET and ceMRI within three weeks of each other. All patients were in a stable clinical condition, and there were no ischemic events or mechanical
interventions in the period between the different examinations. Three patients were scanned within two weeks after an acute myocardial infarction and were excluded from the final analysis. The baseline characteristics of the patient population are given in Table 1. The Committee on Research Involving Human Subjects of the Vrije Universiteit Medical Center, Amsterdam, approved the study protocol, and all subjects gave written, informed consent.

**Imaging protocols.** MAGNETIC RESONANCE IMAGING. Images were acquired on a 1.5-Tesla whole-body scanner (Magnetom Sonata by Siemens, Erlangen, Germany) with the patient in a supine position using a four-element, phased-array cardiac coil. Scout images were acquired in long-axis and short-axis orientations for planning of the final double-oblique long-axis and short-axis views. Electrocardiographically gated cine images were acquired using a segmented steady-state free precession sequence (true FISP; echo time/repetition time [TE/TR] of 1.2/3.2 ms; resolution of $1.3 \times 1.8 \times 5$ mm). Three long-axis views and seven to 11 short-axis views 1 cm apart, covering the whole LV, were obtained during repeated breath-holds. A gadolinium-based contrast agent (Magneuve 0.2 mmol/kg; Schering AG, Berlin, Germany) was then administered intravenously using an automated injection at a rate of $3 \text{ ml/s}$. After 15 to 20 min, contrast-enhanced images were acquired in the same orientation as the cine images, using a segmented inversion-recovery, gradient-echo pulse sequence triggered to end diastole (19). The inversion time was set to null the signal of normal myocardium after contrast administration (typically 250 to 300 ms) and was adjusted in the course of the investigation if necessary. Other parameters of the sequence were TR/TE of 9.6/4.4 ms, flip angle 25°, matrix $208 \times 256$, and a typical voxel size of $1.6 \times 1.3 \times 5$ mm.

**FDG-PET IMAGING.** All patients underwent hyperinsulinemic-euglycemic clamping (20). Scans were performed in a two-dimensional mode, using an ECAT EXACT HR+ (Siemens/CTI, Knoxville, Tennessee), after an intravenous injection of $370 \text{ MBq}$ of FDG. The dynamic scan consisted of 39 frames with variable frame lengths for a total time of 60 min. All dynamic scan data were corrected for physical decay of $^{18}$F and for dead time, scatter, and random and measured photon attenuation. The images were reconstructed using filtered backprojection with a Hanning filter at the Nyquist frequency. This resulted in a transaxial spatial resolution of $~7$ mm full width at half maximum. Additionally, each patient underwent technetium-99m-tetrofosmin single-photon emission computed tomography (SPECT) for assessment of rest blood flow.

**Data analysis. SEGMENTAL MODEL.** For each imaging modality, an identical 17-segment model was used dividing the LV into six basal, six midventricular, and four distal segments, and the apex (21). The basal, midventricular, and distal segments were evaluated in short-axis images, whereas the apical cap was evaluated in the two-chamber long-axis view with ceMRI and in the vertical long-axis view with PET and SPECT. By convention, the most basal short-axis slice used for analysis was located just below and exclusive of the LV outflow tract.

**MAGNETIC RESONANCE IMAGING.** All MRI images were first previewed on a personal computer workstation, using commercial software (Radworks version 5.0, Applicare Medical Imaging, Zeist, The Netherlands). To compose the basal, midventricular, and distal segments, MRI data of a maximum of three short-axis slices were averaged. All short-axis slices were projected on the two-chamber long-axis view and were allocated to the different positions according to their relationship to the papillary muscles: the midventricular slices at the level of the papillary muscles and the basal and distal slices above or below the papillary muscles. Each basal and midventricular slice was divided into six equidistant sectors angulated $60^\circ$ apart starting from the posterior insertion of the right ventricular free wall into the LV myocardium. The distal slices were segmented into four equidistant sectors angulated at $90^\circ$.

**EVALUATION OF CONTRAST-ENHANCED IMAGES.** The MASS software (Medis, Leiden, The Netherlands) was used for quantitative analysis. Each myocardial sector was used for analysis was located just below and exclusive of the LV outflow tract.
excluding trabeculations and papillary muscles. The extent of contrast enhancement was expressed as a percentage of the total myocardial area (A_{hyperenhanced} / A_{myocardium} \times 100, where A denotes area) (Fig. 1). The MRI data of corresponding sectors on different short-axis slices used to compose one myocardial segment were averaged to give one final value for the segmental extent of hyperenhancement (SEH).

**ASSESSMENT OF SEGMENTAL FUNCTION.** Wall motion was assessed by visual interpretation for each myocardial sector on each cross section using a five-point scale: 1 = normal contractility; 2 = mild to moderate hypokinesia; 3 = severe hypokinesia; 4 = akinesia; and 5 = dyskinesia. The results of different sectors composing the different myocardial segments were averaged. Additionally, segmental end-diastolic wall thickness (EDWT) and wall thickening were determined by manual tracing of endocardial and epicardial borders in end-diastolic and end-systolic stop-frame images, excluding trabeculations and papillary muscles.

**FDG-PET.** Data were analyzed blinded to the MRI results and patient data, using a SUN work station (SUN Microsystems, Inc.) with Siemens/CTI software. Transaxial images were reoriented according to the anatomic axis of the heart. Reconstructed slices were displayed as short-axis slices and horizontal as well as vertical long-axis slices. Short-axis slices were oriented in the same way as described for ceMRI, using the posterior insertion of the right ventricular wall with the LV as a landmark. Regions of interest (ROIs) were defined manually on each of the short-axis slices using the same segmentation model as for ceMRI. Corresponding ROIs from a variable number of slices were grouped in each patient to compose the 17 segments. For each segment, mean tracer uptake was calculated. Uptake of FDG in each segment was normalized to the myocardial segment with maximal tetrofosmin uptake.

**DEFINITION OF VIABILITY BY PET.** Segments with normal perfusion (tetrofosmin uptake ≥50%) and metabolism (FDG uptake ≥50%) and segments with reduced perfusion (tetrofosmin uptake <50%) and normal or increased metabolism (mismatch) were considered viable. Segments with reduced perfusion and reduced metabolism (matched defect) were considered non-viable (22–25). In two patients with a left bundle branch block, dysfunctional segments in the septum demonstrating FDG uptake <50% were considered viable if tetrofosmin uptake exceeded 50%, as FDG–PET may underestimate viability in the septal region in the presence of left bundle branch block (26).

**Statistics.** Data are expressed as the mean value ± SD. To compare the segmental results for EDWT, wall thickening, SEH, and FDG uptake by PET, depending on cardiac function, and to compare the segmental results for EDWT, wall thickening, and SEH, depending on the viability status as defined by PET, the unpaired Student t test at the Bonferroni-adjusted individual significance level (0.05/24; number of comparisons = 24) was performed. Recently described non-parametric analysis of overall sensitivities and specificities, as well as areas under the receiver operator characteristic (ROC) curves, were applied (27,28). The area under the ROC curve (AUC) was considered as a measure of accuracy of ceMRI to discriminate between viable and non-viable myocardium, as defined by PET. The ROC curve analysis was also used to assess the optimal cutoff point of the increase of SEH, as determined by ceMRI for the detection of segments with myocardial non-viability. Sensitivity and specificity were determined for viability or non-viability, as defined by PET. Computations were performed using SAS version 8.02 for Windows.

**RESULTS**

A total of 391 segments in 23 patients were analyzed. Table 2 summarizes the results for EDWT, wall thickening, SEH, and FDG uptake by PET, depending on segmental cardiac function. Segments with normal wall motion or mild to moderate dysfunction showed normal metabolism and perfusion in 225 (99%) of 226 segments; of these, 169 segments demonstrated no hyperenhancement and 57 segments revealed subendocardial enhancement only (mean SEH 15 ± 11%). Segments with severe dysfunction (n = 165) showed normal metabolism/perfusion in 78 segments, a metabolism/perfusion mismatch in 38 segments, and a matched defect in 49 segments. Table 3 summarizes the results for SEH, EDWT, and wall thickening, depending on the viability status defined by nuclear imaging. Of 78 dysfunctional segments with normal perfusion and metabolism, 50 segments (64%) showed no hyperenhancement and 28 segments (36%) demonstrated subendocardial hyperenhancement (25 ± 13% SEH). In 38 mismatched segments, there were six segments (16%) without hyperenhancement.
and 32 segments with hyperenhancement (40 ± 23% SEH). In 49 segments with a matched defect, only one segment (2%) demonstrated no hyperenhancement, whereas 48 segments showed a large extent of hyperenhancement (82 ± 20% SEH). A strong inverse correlation was found between FDG uptake by PET and SEH by ceMRI (r = 0.20% SEH). A strong inverse correlation was found between FDG uptake and EDWT (r = 0.001). The correlation between FDG uptake and EDWT (r = −0.86, p < 0.001). The correlation between FDG uptake and EDWT (r = −0.51, p < 0.001) or wall thickening (r = −0.41, p < 0.001) was lower than that with ceMRI. Figure 2 shows mean SEH by ceMRI categorized according to FDG uptake by PET.

**Accuracy of ceMRI to predict viability by FDG-PET.**
To assess the ability of ceMRI to discriminate between viable and non-viable segments, as defined by FDG-PET, ROC analysis was performed on all segments with severe dysfunction. The AUC of ceMRI to predict myocardial viability defined by FDG-PET was 0.95 (95% confidence interval 0.93 to 0.97) (Fig. 3). A threshold of ≤37% SEH was identified to yield optimal sensitivity and specificity for the differentiation of viable and non-viable segments defined by FDG-PET. Using this cutoff value, 100 segments were assessed as viable and 65 segments as non-viable by ceMRI. Compared with FDG-PET, the sensitivity and specificity of ceMRI for the identification of non-viable myocardium were 96% and 84%, respectively. Table 4 displays different sensitivity and specificity levels derived from the ROC curve for the detection of non-viable myocardium, as defined by PET, according to different thresholds of SEH, as assessed by ceMRI.

**Relationship of viability status by ceMRI and FDG-PET.**
Table 5 relates the viability by ceMRI to the viability status by FDG-PET. Concordance between the techniques was high for segments with normal metabolism/perfusion (95%) or a matched defect (96%). Mismatched segments demonstrated SEH ≤37% in 24 segments (63%). Uptake of FDG was lower in the mismatched segments with SEH >37% compared with the mismatched segments with SEH ≤37% (54 ± 3% vs. 71 ± 9%; p < 0.001). Figure 4 shows representative images of a patient with akinnesia of the inferior wall, subendocardial hyperenhancement on ceMRI, and a metabolism/perfusion mismatch by PET and SPECT.

Complete agreement between PET and ceMRI was present in 11 patients. Figure 5 shows an example of a patient with a match between ceMRI and PET. In the remaining 12 patients, the methods differed by one segment in four patients, two segments in five patients, and three segments in three patients.

**DISCUSSION**
Previous studies have suggested that myocardial hyperenhancement by ceMRI represents irreversible myocardial injury, thus allowing determination of myocardial viability. The aim of this study was to compare assessment of myocardial viability by ceMRI with metabolic imaging using FDG-PET, which is considered the in vivo reference standard for viability determination. For this purpose, we quantitatively analyzed the segmental extent of scar tissue.

---

**Table 2. Results of Magnetic Resonance Imaging Parameters and uptake by Positron Emission Tomography, According to Wall Motion**

<table>
<thead>
<tr>
<th>Wall Motion</th>
<th>No. of Segments</th>
<th>EDWT (mm)</th>
<th>Wall Thickening (mm)</th>
<th>SEH (%)</th>
<th>FDG Uptake (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>156</td>
<td>7.8 ± 1.7</td>
<td>4 ± 1</td>
<td>2 ± 8</td>
<td>86 ± 12</td>
</tr>
<tr>
<td>Mild to moderate hypokinesia</td>
<td>70</td>
<td>7.1 ± 1.6</td>
<td>2 ± 1*</td>
<td>9 ± 13*</td>
<td>82 ± 15</td>
</tr>
<tr>
<td>Severe hypokinesia</td>
<td>65</td>
<td>6.7 ± 2.0*</td>
<td>1 ± 0.7*</td>
<td>14 ± 20*</td>
<td>75 ± 17*</td>
</tr>
<tr>
<td>Akinnesia/dyskinesia</td>
<td>100</td>
<td>5.5 ± 1.6*</td>
<td>0.2 ± 0.3*</td>
<td>50 ± 38*</td>
<td>54 ± 22*</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. normal. Data are presented as the mean value ± SD.

EDWT = end-diastolic wall thickness; FDG = 18F-fluorodeoxyglucose; SEH = segmental extent of hyperenhancement.

---

**Table 3. Magnetic Resonance Imaging Parameters in Severely Dysfunctional Segments (n = 165) According to the Viability Status by Positron Emission Tomography**

<table>
<thead>
<tr>
<th>Viability Status by PET</th>
<th>SEH (%)</th>
<th>EDWT (mm)</th>
<th>Wall Thickening (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n = 78)</td>
<td>9 ± 14</td>
<td>7 ± 2</td>
<td>1 ± 0.7</td>
</tr>
<tr>
<td>Mismatch (n = 38)</td>
<td>33 ± 25*</td>
<td>6 ± 2</td>
<td>0.6 ± 0.6</td>
</tr>
<tr>
<td>Non-viable (n = 49)</td>
<td>80 ± 23†</td>
<td>4 ± 1†</td>
<td>0.1 ± 0.4†</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. viable segments. †p < 0.05 vs. mismatched segments. Data are presented as the mean value ± SD.

MRI = magnetic resonance imaging; PET = positron emission tomography; other abbreviations as in Table 2.

---

**Figure 2.** Bar graph showing mean segmental extent of hyperenhancement by contrast-enhanced magnetic resonance imaging categorized according to 18F-fluorodeoxyglucose (FDG) uptake by positron emission tomography (PET).
by ceMRI and compared it with segmental FDG uptake by PET. The results demonstrate that non-viable segments by FDG-PET demonstrate a significantly larger extent of hyperenhancement compared with segments identified as viable by FDG-PET. Moreover, we found a progressive increase of scar among segments with normal perfusion/metabolism, reduced perfusion but preserved metabolism representing hibernating myocardium, and a matched perfusion/metabolism defect (Table 3). Using ROC analysis, the AUC was 0.95 for the discrimination of viable myocardium from scar, as defined by FDG-PET, reflecting high diagnostic accuracy. A cutoff value of 37% SEH was identified from the ROC curve to differentiate non-viable from viable myocardium with optimal sensitivity and specificity. Thus, ceMRI allows accurate assessment of myocardial viability in patients with ischemic heart disease and severely reduced LV function.

**Comparison with previous studies.** The results of the present study compare favorably with previous reports relating the extent of fibrosis to FDG-PET findings. Maes et al. (29) observed a similar extent of percentage volume fibrosis assessed on the basis of myocardial biopsy data (35 ± 25%) in segments showing non-viability by PET. Dakik et al. (30) demonstrated that ~30% of transmural scarring correlated with a lack of improvement in function after revascularization. In a recent animal experiment studying the relationship between ceMRI and regional inotropic response, Gerber et al. (31) demonstrated that only segments with <33% transmural extent of CE had inotropic reserve during dobutamine infusion, whereas segments with a higher (>33%) transmural extent of CE did not. The results of the present study are also in close agreement with a recent report by Klein et al. (32), who evaluated ceMRI and FDG-PET for viability assessment in a similar patient population. In their study, the AUC was 0.93, with a sensitivity of 86% and a specificity of 94% for the detection of non-viability by FDG-PET. Additionally, a high correlation was reported between semiquantitative estimates of scar severity by ceMRI and PET (r = 0.91). Similarly, we observed a strong correlation between the segmental extent of scar by ceMRI and FDG uptake by PET (r = −0.86). This finding closely agrees with the results of a previous study relating the amount of fibrosis at histologic examination with regional thallium-201 activity (r = −0.85) in patients with chronic ischemic heart disease (33). Other functional parameters that have been useful for the characterization of myocardial viability, such as regional wall thickness and wall thickening (5), correlated less well with FDG-PET, which is in line with the results reported by Klein et al. (32).

A high concordance was found between ceMRI and PET for assessment of the viability status of dysfunctional segments with normal perfusion/metabolism or a matched defect (Table 3). In segments with preserved metabolism but reduced perfusion (mismatch), reflecting hibernating myocardium, the results were less explicit. Sixty-three percent of segments scored viable and 37% of segments scored non-viable by ceMRI, using the threshold value of 37% SEH. The amount of enhancement averaged 33 ± 25% in this group of segments (Table 3). A similar extent of volume fibrosis at histologic examination in segments with hibernating myocardium of >6 months duration (41.9 ± 22.1%) has been reported in a previous study (34). It should be

**Table 4. Sensitivity and Specificity of Different Thresholds of Segmental Extent of Hyperenhancement for the Detection of Non-Viable Myocardium by 18F-Fluorodeoxyglucose–Positron Emission Tomography**

<table>
<thead>
<tr>
<th>SEH Threshold (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>96</td>
<td>76</td>
</tr>
<tr>
<td>35</td>
<td>96</td>
<td>80</td>
</tr>
<tr>
<td>40</td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>45</td>
<td>92</td>
<td>88</td>
</tr>
<tr>
<td>50</td>
<td>90</td>
<td>89</td>
</tr>
<tr>
<td>55</td>
<td>84</td>
<td>91</td>
</tr>
<tr>
<td>60</td>
<td>84</td>
<td>93</td>
</tr>
<tr>
<td>65</td>
<td>80</td>
<td>95</td>
</tr>
<tr>
<td>70</td>
<td>76</td>
<td>96</td>
</tr>
</tbody>
</table>

SEH = segmental extent of hyperenhancement.
considered that myocardial viability is a gradual phenomenon and that the dichotomous definition of viability used in the present study for ceMRI is related to the dichotomous definition of viability for FDG-PET. Thus, a segment with 50% SEH, although scored non-viable by ceMRI in the present study, demonstrates a large rim of viable myocardium. Even if recovery of function after revascularization is unlikely, restoration of blood flow may contribute to prevent further ischemic injury and improve the clinical status and prognosis of the patient (34,35). Moreover, while the cutoff value of 37% SEH is mathematically the best threshold, one might wish to choose a different cutoff value to minimize the chances of missing viable myocardium. Thus, as demonstrated in Table 4, a threshold of 50% would increase the specificity of detecting non-viable myocardium, thereby increasing the amount of segments scored viable by ceMRI.

Study limitations. As in all studies comparing different imaging modalities, there is the possibility of image misalignment, which may account for some of the discrepancies between the FDG-PET and ceMRI results. Moreover, variability may be associated with averaging of MRI as well as PET and SPECT data, which was performed in order to compose the 17 myocardial segments. The MRI sequence used is susceptible to artifacts associated with patient movement or imperfect breath-holding, which can be erroneously interpreted as areas of hyperenhancement. Recovery of myocardial function after revascularization was not assessed in the present study. Thus, conclusions on the functional recovery of dysfunctional segments deemed viable by ceMRI cannot be drawn from the present study. Others have shown that recovery of function after revascularization is related to the transmural extent of hyperenhancement in patients with ischemic cardiomyopathy (17), with a gradual decrease in functional recovery paralleled by an increasing transmurality of hyperenhancement. In the study of Kim et al. (17), 73% (44/60) of segments with no hyperenhancement or with <50% transmural hyperenhancement improved function after revascularization. Based on these results, one might speculate that most of the dysfunctional segments assessed as viable by ceMRI in our study might have recovered function after restoration of adequate blood flow. Nevertheless, determination of contractile function after revascularization would be helpful to establish the relative importance of ceMRI and FDG-PET to predict functional recovery, which is considered an important outcome variable. Another limitation is that although the prognostic relevance of FDG-PET to predict morbidity and mortality is well established (2,36), data on ceMRI are scarce (37). Thus, the prognostic relevance of ceMRI needs to be established in future studies.

Conclusions. In patients with chronic ischemic heart disease and LV dysfunction, ceMRI allows detection of myocardial viability with a high accuracy, as compared with FDG-PET. Therefore, ceMRI should be considered as an alternative technique for assessment of myocardial viability in patients with chronic coronary artery disease and may be an alternative imaging modality in centers where FDG-PET is unavailable or less economical. Future studies should be directed at assessing the prognostic value of ceMRI to predict morbidity and mortality in patients with chronic ischemic heart disease and LV dysfunction.
REFERENCES


