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**Title:** Novel insights into cardiac imaging in cardiovascular disease  
**Date:** 2012-06-14
Chapter 13

123-I MIBG/perfusion Scintigraphy in Comparison with Contrast-enhanced Magnetic Resonance Imaging for Assessment of Infarct Size and Infarct Border Zone

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Abstract

**Background:** Contrast-enhanced magnetic resonance imaging (MRI) allows assessment of total infarct size and infarct border zone, which can be used as markers of vulnerable myocardium for ventricular arrhythmias. Combined 123-iodine metaiodobenzylguanidine (123-I MIBG) and myocardial perfusion scintigraphy may also be used for infarct tissue characterization. However, at present, contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy have not been compared for characterization of infarct tissue. Accordingly, this descriptive study evaluated the relation between contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy for assessment of infarct size and infarct border zone.

**Methods:** Ischemic heart failure patients who underwent contrast-enhanced MRI and 123-I MIBG/myocardial perfusion scintigraphy were included. Contrast-enhanced MRI and myocardial perfusion scintigraphy were compared for assessment of infarct size. Infarct tissue was defined as myocardium with signal intensity (SI) ≥50% of the maximum SI on contrast-enhanced MRI. The total perfusion defect score was used to assess infarct size on myocardial perfusion scintigraphy. Additionally, contrast-enhanced MRI was compared to 123-I MIBG/perfusion scintigraphy for assessment of infarct border zone. On contrast-enhanced MRI, a significant infarct border zone (myocardium with ≥35% SI <50% of the maximum SI) was defined as an infarct border zone of >16.7 grams. On 123-I MIBG/perfusion scintigraphy, the total 123-I MIBG SPECT defect score and the innervation/perfusion mismatch score (infarct border zone) were used to assess vulnerable myocardium for ventricular arrhythmias.

**Results:** Forty patients (29 men, mean age 66±10 yrs) with ischemic heart failure were included. Contrast-enhanced MRI and myocardial perfusion scintigraphy showed good correlations for infarct size (r=0.72, p<0.01). In addition, patients with a significant infarct border zone on contrast-enhanced MRI showed a significantly higher total 123-I MIBG SPECT defect score (48.2±12.5% vs. 32.1±9.5%, p<0.05) and innervation/perfusion mismatch score (13.9±11.0% vs. 6.8±6.0%, p<0.05) than patients without a significant infarct border zone.

**Conclusions:** Contrast-enhanced MRI and myocardial perfusion scintigraphy showed good correlations for infarct size. Importantly, patients with a significant infarct border zone on contrast-enhanced MRI showed significantly larger areas of infarct border zone on 123-I MIBG/perfusion scintigraphy.
Chapter 13: 123-I MIBG/perfusion scintigraphy in comparison with MRI for assessment of infarct tissue

Introduction

Assessment of myocardial infarct tissue has shown to play an important role to risk stratify patients for adverse cardiac events.\(^1,2\) Infarct tissue may show considerable spatial heterogeneity due to the presence of necrotic areas that are intermingled with bundles of viable cardiomyocytes.\(^3,4\) These regions of infarct tissue heterogeneity are primarily present in the periphery of the infarcted myocardium, which is commonly referred to as the infarct border zone or peri-infarct region. Previous studies have postulated that peri-infarct regions may serve as an important substrate for the development of potential life-threatening ventricular arrhythmias through the presence of reentrant circuits originating from slow-conduction pathways.\(^4-7\)

With its high spatial resolution and signal-to-image noise ratio, contrast-enhanced magnetic resonance imaging (MRI) allows an accurate delineation of myocardial infarct tissue.\(^3-6,8\) More specifically, contrast-enhanced MRI enables the discrimination between myocardial infarct core and peri-infarct regions using marked differences in contrast-media hyperenhancement.\(^3-6,8\) Accordingly, contrast-enhanced MRI permits the assessment of vulnerable myocardium at risk for ventricular arrhythmias by assessment of infarct border zone.\(^4-6\)

In addition, nuclear imaging can be used for evaluation of myocardial infarct tissue.\(^9\) Myocardial perfusion scintigraphy can be used for assessment of infarct size, whereas cardiac 123-iodine metaiodobenzylguanidine (123-I MIBG) imaging permits assessment of myocardial sympathetic denervation.\(^9-11\) It has been shown that viable myocardium may already exhibit areas of sympathetic denervation, as sympathetic nerve fibers are more prone to the detrimental effects of myocardial ischemia than cardiomyocytes.\(^10,12\) Thus, regions with deprived sympathetic innervation may reflect the total extent of injured myocardium, rather than the myocardial perfusion defect alone.

At present, regions with cardiac sympathetic denervation as assessed with 123-I MIBG imaging have been marked as myocardium at risk for ventricular arrhythmias.\(^11,13,14\) Areas of sympathetic denervation may show an enhanced triggering and automaticity when compared to adjacent regions with preserved sympathetic innervation.\(^14\)

Furthermore, it has been shown that the mismatch between cardiac sympathetic innervation and myocardial perfusion, which is referred to as the innervation/perfusion mismatch or infarct border zone, may be used as a marker of pro-arrhythmogenic myocardium.\(^15-17\)

Contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy have currently not been compared for characterization of infarct tissue. More specifically, the relation between contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy for assessment of infarct border zone as a marker of vulnerable myocardium for ventricular arrhythmias has not been evaluated. Accordingly, this descriptive study aimed to explore the relation between
contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy for assessment of infarct size and infarct border zone, as markers for vulnerable myocardium for ventricular arrhythmias.

Materials and Methods

Patient Population and Protocol

The patient population consisted of patients with ischemic heart failure who were clinically referred for cardiac MRI, myocardial perfusion single photon emission computed tomography (SPECT) and cardiac 123-iodine metaiodobenzylguanidine (123-I MIBG) imaging for risk stratification of heart failure. Patient data were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, the Netherlands) and retrospectively analyzed. All patients were treated according to the MISSION! - Heart Failure care track operational at the LUMC. Patients with unstable angina or acute coronary syndromes were excluded from study analysis.

Ischemic etiology was based on the presence of previous (1) myocardial infarction, (2) percutaneous coronary intervention, (3) coronary artery bypass grafting or (4) evidence of coronary artery disease (CAD) on previous diagnostic tests. Risk factors for CAD were derived from patient medical record data.

First, contrast-enhanced MRI and myocardial perfusion scintigraphy were compared for the assessment of myocardial infarct size. On contrast-enhanced MRI, infarct size was assessed with signal intensity (SI) analyses on short-axis images, in which infarct tissue was defined as myocardium with SI ≥50% of the maximum SI. On myocardial perfusion scintigraphy, the total perfusion defect score was used to assess myocardial infarct size (Table 1).

Consecutively, contrast-enhanced MRI and nuclear imaging were compared for assessment of infarct border zone (Table 1). Contrast-enhanced MRI was used to assess infarct border zone which was used as a marker of vulnerable myocardium for ventricular arrhythmias (pro-arrhythmogenic myocardium). As previously reported, a cutoff value of 16.7 grams of infarct border zone allows identification of patients at risk for potential lethal ventricular arrhythmias. Accordingly, patients with >16.7 grams of infarct border zone were considered to have a significant infarct border zone on contrast-enhanced MRI.

In addition, both total 123-I MIBG SPECT defect score as derived from late 123-I MIBG SPECT and the mismatch between cardiac sympathetic innervation and myocardial perfusion (the innervation/perfusion mismatch) were used to identify the infarct border zone (Table 1).

Thereafter, the total 123-I MIBG SPECT defect score and the innervation/perfusion mismatch score (infarct border zone) were evaluated in patients with (>16.7 grams) and without (≤16.7 grams) a significant infarct border zone on contrast-enhanced MRI.
Magnetic Resonance Imaging

Acquisition and Analysis

Contrast-enhanced images were acquired with a 1.5-T Gyroscan ACS-NT/Intera MRI scanner (Philips Medical Systems, Best, the Netherlands) equipped with powertrack 6000 gradients in combination with a 5-element cardiac synergy coil. Using vector electrocardiographic (ECG) gating, cardiac images were acquired in supine position during breath holds of approximately 15 seconds. Using 10-12 imaging levels (one slice per breath hold), the entire heart was imaged from apex to cardiac base in short-axis view with the use of a balanced turbo-field echo sequence with parallel imaging (SENSE, acceleration factor 2). Subsequently, contrast-enhanced imaging was performed 15 minutes after bolus infusion of 0.15 mmol/kg of gadolinium diethylenetriamine penta-acetic (Magnevist, Schering/Berlin, Germany) using an inversion-recovery 3D turbo-field echo sequence with parallel imaging (SENSE, acceleration factor 2). The entire heart was imaged in short-axis view during one breath-hold with 20-24 imaging levels. The number of imaging levels was dependent on the size of the heart. The inversion time was assessed by real-time plan scan to null normal myocardial signal. The cardiac images were send to a remote off-line workstation with dedicated in-house developed MASS research software (Mass V2008-EXP, LKEB, Leiden, the Netherlands).

At first, contrast-enhanced short-axis images were evaluated by an independent observer to assess infarct size as well as infarct border zone, as shown in Figure 1. For this purpose, endocardial and epicardial contours were manually outlined on contrast-enhanced short-axis images. After the contour detection, the region with maximal SI within the scarred myocardium was defined on short-axis images. Myocardial infarct tissue was defined as myocardium with SI ≥50% of the maximum SI, whereas the infarct border zone was defined as myocardium with ≥35% SI <50% of the maximum SI. The full-width at half maximum (FWHM) criterion was used to define myocardial infarct tissue. As previously reported,
the threshold for infarct border zone was based on the ratio of 2:3 for threshold SI of infarct border zone versus infarct core. Myocardial infarct size and infarct border zone were expressed in percentages of the myocardium. Patients with >16.7 grams of infarct border zone were classified as patients with a significant infarct border zone, whereas patients with ≤16.7 grams of infarct border zone were classified as patients without a significant infarct border zone. As previously reported, a cutoff of 16.7 grams of infarct border zone allows identification of patients at risk for potential lethal ventricular arrhythmias.

**Sympathetic Nerve Imaging with 123-I MIBG**

**Acquisition and Analysis**

One hour prior to intravenous administration of 185 MBq 123-I MIBG (AdreView, General Electric Healthcare, United Kingdom), patients were pretreated with 120 mg sodium iodide to block the thyroid uptake of free iodine-123. In all patients, 123-I MIBG SPECT was performed on a dual-head camera system (GCA-7200, Toshiba Corp., Tokyo, Japan) equipped with low-energy, parallel-hole high-resolution collimators. SPECT images were acquired using a step and shoot mode (90 projections, imaging time 30 minutes). A 128 x 128 matrix was used for SPECT studies and the energy window was symmetrically centered to 20% of the 159-keV energy peak of 123-I MIBG. SPECT was repeated 3-4 hours after intravenous injection of 123-I MIBG. After the SPECT studies were processed with iterative reconstruction, they were reconstructed into short-, vertical and horizontal long-axis according to the standard recommendations.
The late 123-I MIBG SPECT images were used to calculate the total 123-I MIBG SPECT defect score by two independent observers. Using the 17-segment model, each myocardial segment was scored using the following tracer uptake scale: 0 = normal tracer uptake, 1 = mildly reduced tracer uptake, 2 = moderately reduced tracer uptake, 3 = severely reduced tracer uptake, 4 = no tracer uptake. The total 123-I MIBG SPECT defect score was calculated by the summation of each segmental uptake score. Accordingly, the total 123-I MIBG defect score could range from 0 to 68 (0-100%). As previously reported, a low intra-observer (ICC 0.98, 95% CI 0.95-0.99) as well as a low inter-observer (ICC 0.98, 95% CI 0.96-0.99) variability was demonstrated for late 123-I MIBG SPECT defect score. The total 123-I MIBG SPECT defect score (%) was used as a measure of vulnerable myocardium for ventricular arrhythmias, as shown in Table 1.

**Gated Myocardial Perfusion SPECT**

**Acquisition and Analysis**

Resting ECG-gated myocardial perfusion SPECT with 99mTc-tetrofosmin (500 MBq, injected at rest) was performed using a triple-head SPECT camera system (GCA 9300/HG; Toshiba Corp., Tokyo, Japan) equipped with high-resolution, low-energy collimators. A 20% window was centered around the 140-keV energy peak of 99mTc-tetrofosmin. Ninety projections were acquired according to the step and shoot method (35 s/projection, 64 x 64 matrix, total imaging time 23 minutes) over a 360-degree circular orbit. ECG gating was applied on the cardiac cycle with 16 frames per cardiac cycle using a tolerance window of 50%. After the pre-filtration was performed using a Butterworth filter, images were reconstructed into long- and short-axis projections perpendicular to the heart axis using a filtered back projecting algorithm. No attenuation correction was used.

Thereafter, resting myocardial SPECT images were evaluated by two independent observers who were unaware of the 123-I MIBG and contrast-enhanced MRI data. Based on the 17-segment model, each myocardial segment was scored using the similar tracer uptake scale as applied for 123-I MIBG SPECT images. Subsequently, patient’s segmental scores were summed, yielding a total perfusion defect score per patient, which could range from 0 to 68 (0-100%). As shown in Table 1, the total perfusion defect score was used as a measure of myocardial infarct size.

Finally, the innervation/perfusion mismatch score (infarct border zone) was assessed by subtracting the total perfusion defect score from total 123-I MIBG SPECT defect score. The innervation/perfusion mismatch score was used as a measure of vulnerable myocardium for ventricular arrhythmias (Table 1). The innervation/perfusion mismatch score could vary between 0 and 68 (0-100%). Figure 2 provides an example of a patient with a considerable innervation/perfusion mismatch, in which the sympathetic nerve defect as assessed with late
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123-I MIBG SPECT (panel B) was significantly larger than the myocardial perfusion defect (panel A).

Statistical Analysis

Continuous variables were expressed as mean ± SD, and categorical data as numbers or percentages. Kolmogorov-Smirnov tests were used to evaluate the distribution of the data. When non-normally distributed, data were presented as medians and 25th and 75th percentiles. Contrast-enhanced MRI and myocardial perfusion scintigraphy were compared for assessment of infarct size using Pearson’s linear regression analyses and paired t tests. Paired t tests were used to compare contrast-enhanced MRI with 123-I MIBG imaging and myocardial perfusion scintigraphy for assessment of infarct border zone.

Furthermore, patients were stratified according to the prospectively selected cutoff value of 16.7 grams of infarct border zone on contrast-enhanced MRI into patients with (>16.7 grams) and without (≤16.7 grams) significant infarct border zone. As previously reported, a cutoff value of 16.7 grams of infarct border zone allows identification of patients at risk for potential lethal ventricular arrhythmias. Student’s t tests were used to evaluate the total 123-I MIBG SPECT defect score and the innervation/perfusion mismatch score in patients with (>16.7 grams) and without (≤16.7 grams) a significant infarct border zone on contrast-enhanced MRI. All p-values were two-sided and a p-value <0.05 was considered to indicate statistical significance. Statistical analyses were performed with the use of dedicated software (SPSS version 16.0, SPSS inc., Chicago, Illinois, USA).

Figure 2. Nuclear imaging techniques were used for assessment of myocardial infarct size as well as myocardium at risk for ventricular arrhythmias.

A. Myocardial scar tissue was assessed with 99mTc-tetrofosmin resting myocardial perfusion single photon emission computed tomography (SPECT). The total perfusion defect score on myocardial perfusion scintigraphy was used as a marker of myocardial infarct size.

B. The total 123-iodine metaiodobenzylguanidine (123-I MIBG) SPECT defect score as derived from late 123-I MIBG SPECT as well as the innervation/perfusion mismatch score (the difference between resting perfusion imaging and late 123-I MIBG SPECT) were used as markers of myocardium at risk for ventricular arrhythmias.
Results

Patient Population

A total of 40 patients (29 men, mean age 66±10 yrs) with ischemic heart failure were enrolled. Baseline characteristics of the patient population are summarized in Table 2. The mean New York Heart Association (NYHA) functional class was 2.6±0.7. Medication consisted of diuretics (78% of patients), angiotensin converting enzyme - inhibitors (ACE-I) or angiotensin II (AT II) antagonists (88% of patients) or beta-blockers (68% of patients). Contrast-enhanced MRI and 123-I MIBG imaging were performed within a mean period of 8.1±47.3 days. No acute coronary events or change in medication was documented between both examinations. Contrast-enhanced MRI showed a mean LV mass of 149.7±55.1 grams.

Table 2. Baseline characteristics of the study population (n=40)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>66±10</td>
</tr>
<tr>
<td>Male gender</td>
<td>29 (73)</td>
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<tr>
<td>LVEF (%)</td>
<td>27±10</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>2.6±0.7</td>
</tr>
<tr>
<td>Previous MI</td>
<td>27 (68)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>17 (43)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>15 (38)</td>
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<tr>
<td>Cardiovascular risk factors</td>
<td></td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Hypertension</td>
<td>14 (35)</td>
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<tr>
<td>Hypercholesterolemia</td>
<td>18 (45)</td>
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<tr>
<td>Family history of CAD</td>
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<tr>
<td>Current smoking</td>
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<tr>
<td>Obesity</td>
<td>8 (20)</td>
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<tr>
<td>Medication</td>
<td></td>
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<tr>
<td>Diuretic</td>
<td>31 (78)</td>
</tr>
<tr>
<td>ACE-I / AT II antagonist</td>
<td>35 (88)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>27 (68)</td>
</tr>
<tr>
<td>Statin</td>
<td>36 (90)</td>
</tr>
<tr>
<td>Nitrate</td>
<td>14 (35)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation or as number (%).

ACE-I = angiotensin converting enzyme - inhibitor; AT = angiotensin; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention.
Assessment of Myocardial Infarct Size

The infarct size on myocardial perfusion scintigraphy was significantly larger as compared to the infarct size on contrast-enhanced MRI; the mean infarct size as assessed with myocardial perfusion scintigraphy and contrast-enhanced MRI were 30.6±12.6% and 16.9±11.8%, respectively (p<0.05). Contrast-enhanced MRI and myocardial perfusion scintigraphy were well-correlated for assessment of infarct size (r=0.72, n=40, p<0.01), as shown in Figure 3.

![Graph showing the correlation between infarct size assessed with contrast-enhanced MRI and myocardial perfusion scintigraphy](image)

**Figure 3.** Contrast-enhanced magnetic resonance imaging (MRI) and myocardial perfusion scintigraphy were compared for the assessment of myocardial infarct size. Contrast-enhanced MRI and myocardial perfusion scintigraphy were well-correlated for the assessment of infarct size (r=0.72, p<0.01).

Assessment of Infarct Border Zone

Contrast-enhanced MRI showed a mean infarct border zone of 16.1±7.3%. The mean total 123-I MIBG SPECT defect score was 41.4±13.8%, whereas the mean innervation/perfusion mismatch score (infarct border zone) was 10.9±9.8%. The total 123-I MIBG SPECT defect score (p<0.05) and the innervation/perfusion mismatch score (infarct border zone) (p<0.05) were significantly different when compared to the infarct border zone on contrast-enhanced MRI. Additionally, patients were stratified according to the prospectively selected value of 16.7 grams of infarct border zone (as derived from contrast-enhanced MRI) into patients with (>16.7 grams) and without (≤16.7 grams) significant infarct border zone. In total, 23 (58%) patients showed a significant infarct border zone on contrast-enhanced MRI, whereas 17 (42%) patients showed no significant infarct border zone on contrast-enhanced MRI.

As shown in Figure 4, patients with a significant infarct border zone on contrast-enhanced MRI (>16.7 grams) showed a significantly larger total 123-I MIBG SPECT defect score as
Figure 4. The infarct border zone (myocardium at risk for ventricular arrhythmias) can be assessed with contrast-enhanced magnetic resonance imaging (MRI). As previously reported, a cutoff of 16.7 grams of infarct border zone allows identification of patients at risk for life-threatening ventricular arrhythmias. Patients with a significant infarct border zone on contrast-enhanced MRI (infarct border zone >16.7 grams) showed a significantly larger total 123-iodine metaiodobenzylguanidine (123-I MIBG) single photon emission computed tomography (SPECT) defect as compared to patients without a significant infarct border zone on contrast-enhanced MRI (infarct border zone ≤16.7 grams) (48.2±12.5% vs. 32.1±9.5%, p<0.05).

Figure 5. Contrast-enhanced magnetic resonance imaging (MRI) permits assessment of infarct border zone, which was used as a marker of myocardium at risk for ventricular arrhythmias. A cutoff value of 16.7 grams of infarct border zone was used to define a significant infarct border zone. Patients with a significant infarct border zone on contrast-enhanced MRI (infarct border zone >16.7 grams) showed a significantly larger innervation/perfusion mismatch as assessed with 123-iodine metaiodobenzylguanidine (123-I MIBG) imaging and myocardial perfusion scintigraphy as compared to patients without a significant infarct border zone on contrast-enhanced MRI (infarct border zone ≤16.7 grams) (13.9±11.0% vs. 6.8±6.0%, p<0.05).
compared to patients without a significant infarct border zone on contrast-enhanced MRI (48.2±12.5% vs. 32.1±9.5%, p<0.05). Similarly, the innervation/perfusion mismatch (infarct border zone) was significantly larger in patients with an infarct border zone of >16.7 grams than in patients with an infarct border zone of ≤16.7 grams on contrast-enhanced MRI (13.9±11.0% vs. 6.8±6.0%, p<0.05) (Figure 5).

**Discussion**

The current study showed that infarct size as assessed with contrast-enhanced MRI was significantly correlated to infarct size on myocardial perfusion scintigraphy. Importantly, this descriptive study is the first showing that patients with a significant infarct border zone on contrast-enhanced MRI showed a significantly larger innervation/perfusion mismatch (infarct border zone) on 123-I MIBG/perfusion scintigraphy when compared to patients without a significant infarct border zone on contrast-enhanced MRI.

Infarct tissue may exhibit substantial heterogeneity as necrotic myocardium can be present along with different stages of healed myocardial infarction. Myocardial necrosis is primarily located in the middle of the infarct region, while bundles of viable cardiomyocytes bordered by dense fibrosis (referred to as tissue heterogeneity) can be found in the periphery of the infarct region, the so-called peri-infarct zone or border zone. Thus far, cardiac MRI and 123-I MIBG/perfusion scintigraphy have not been related for infarct tissue characterization, nor have these imaging techniques been compared for assessment of infarct border zone, which can be used as a marker of vulnerable myocardium for ventricular arrhythmias.

**Myocardial Infarct Size**

Myocardial infarct tissue can be assessed with several non-invasive imaging techniques, including contrast-enhanced MRI, echocardiography as well as nuclear imaging. Among these techniques, contrast-enhanced MRI is considered the standard of reference for evaluation of infarct tissue as it allows an accurate delineation of infarct area and border zone using marked differences in contrast-media hyperenhancement within the infarcted myocardium.

Beyond contrast-enhanced MRI, nuclear imaging is another reliable imaging technique for assessment of myocardial infarct tissue. Moreover, nuclear imaging techniques, such as myocardial perfusion scintigraphy have been used frequently for evaluation of myocardial infarct tissue in clinical practice. Previous studies have shown that myocardial perfusion scintigraphy was significantly correlated to contrast-enhanced MRI for assessment of infarct size. In 12 post-infarct patients, Lima et al. have demonstrated good correlations between contrast-enhanced MRI and myocardial perfusion imaging for myocardial infarct...
size (r=0.92, p<0.01). More recently, Ibrahim et al.\textsuperscript{25} have shown that infarct size as assessed with contrast-enhanced MRI was well-correlated with infarct size as derived from myocardial perfusion SPECT (r=0.86, p<0.05). Moreover, infarct size was significantly overestimated by myocardial perfusion SPECT (7% of the LV, p<0.03) at 42 minutes post-injection using a constant inversion time of 300 ms. Similarly, the current study has shown that myocardial infarct size on contrast-enhanced MRI was significantly correlated to infarct size as assessed with myocardial perfusion scintigraphy. Moreover, both studies showed an overestimation of infarct size on myocardial perfusion SPECT as compared to contrast-enhanced MRI. This finding may be related to differences in spatial resolution between both techniques; myocardial perfusion SPECT has a markedly lower spatial resolution than contrast-enhanced MRI, which may have introduced partial volume effects with an overestimation of infarct size. In addition, both techniques used a different approach for quantification of infarct size. In the current study, the infarct size on contrast-enhanced MRI was defined as myocardium with SI ≥50% of the maximum SI (expressed as a percentage of the total myocardium), whereas the infarct size on myocardial perfusion SPECT was assessed using the semi-quantitative resting perfusion defect score (expressed as a percentage of the total perfusion defect).

**Infarct Border Zone**

Beyond the assessment of infarct size, contrast-enhanced MRI allows evaluation of infarct tissue heterogeneity by demarcation of infarct core and border zone.\textsuperscript{4-6} The infarct border zone is considered an important infarct region as it may serve as substrate for development of ventricular arrhythmias; patients with a large infarct border zone showed an increased susceptibility for ventricular arrhythmias as compared to patients with small infarct border zone.\textsuperscript{4, 6}

Nuclear imaging may also be used for evaluation of arrhythmogenic myocardium by assessment of total denervated myocardium and the innervation/perfusion mismatch, which is referred to as the infarct border zone.\textsuperscript{11, 13, 14} Previous studies have indicated that regions with deprived cardiac sympathetic innervation as assessed with 123-I MIBG imaging may play an important role in ventricular arrhythmogenesis as they show an enhanced triggering and automaticity when compared to adjacent regions with relatively intact sympathetic innervation of the myocardium.\textsuperscript{14} In addition, the mismatch between cardiac sympathetic innervation and myocardial perfusion (innervation/perfusion mismatch) can be used as a marker for pro-arrhythmogenic myocardium as it reflects the infarct border zone.\textsuperscript{15-17} Regions with cardiac sympathetic denervation but preserved myocardial viability can be present as neural tissue exhibits an increased susceptibility to hypoxia as compared to cardiomyocytes.\textsuperscript{10} Simoes et al.\textsuperscript{16} have shown that the innervation/perfusion mismatch as assessed with 123-I MIBG imaging and 201-thallium perfusion scintigraphy was significantly correlated to prolonged ventricular repolarization and delayed depolarization in 67 patients with ischemic heart disease. Based upon these initial studies, it has been suggested that
nuclear imaging with 123-I MIBG/perfusion scintigraphy can be used to identify patients at risk for arrhythmic events.

The current descriptive study has shown that patients with a significant infarct border zone on contrast-enhanced MRI exhibited a significantly higher total 123-I MIBG SPECT defect score and innervation/perfusion mismatch score (infarct border zone) as compared to patients without a significant infarct border zone on contrast-enhanced MRI. This is an important finding as it indicates that 123-I MIBG/perfusion scintigraphy permits identification of patients with a significant infarct border zone, and for this reason may help to identify patients at risk for adverse arrhythmic events. Eventually, the assessment of arrhythmogenic substrate (infarct border zone) may be used for identification of patients indicated for implantable cardioverter-defibrillator (ICD) therapy.

Although contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy allowed identification of vulnerable myocardium for ventricular arrhythmia by assessment of infarct border zone, both techniques showed differences in the size of the infarct border zone. This may be related to the superior spatial resolution of contrast-enhanced MRI when compared to the nuclear imaging techniques. In addition, the differences between both imaging techniques for assessment of infarct border zone may be related to the fact that the infarct border zone on contrast-enhanced MRI can be calculated using several approaches. At present, additional studies are needed that determine the optimal criterion for assessment of infarct border zone.

Although the study showed that 123-I MIBG/perfusion scintigraphy can be used to assess infarct border zone, some limitations need to be acknowledged. First, the study findings are based on a relatively small patient population consisting of 40 patients with ischemic heart failure, whereas a larger patient population would have been preferred for comparison of both techniques. Moreover, the prognostic value of infarct size and infarct border zone has not been evaluated as the current study was only designed to describe the relation between contrast-enhanced MRI and 123-I MIBG/perfusion scintigraphy for assessment of infarct size and infarct border zone.

**Conclusion**

Contrast-enhanced MRI and myocardial perfusion scintigraphy were significantly correlated for infarct size. Importantly, patients with a significant infarct border zone on contrast-enhanced MRI showed a significantly larger innervation/perfusion mismatch (infarct border zone) on 123-I MIBG/perfusion scintigraphy.
Reference List


