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Chapter 3

Free-Breathing MRI for the Assessment of Myocardial Infarction: Clinical Validation

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Abstract

Objective
The objective of our study was to validate free-breathing 2D inversion recovery delayed-enhancement MRI for the assessment of myocardial infarction compared with a breath-hold 3D technique.

Subjects and Methods
Institutional review board approval and written informed consent were obtained. Thirty-two patients (25 men, seven women; mean age, 68 years; age range, 39–84 years) underwent breath-hold gradient-echo 3D inversion-recovery delayed-enhancement MRI and free-breathing respiratory-triggered 2D inversion-recovery delayed-enhancement MRI of the heart (scanning time, 50–80 seconds). Infarct size was quantitatively analyzed as a percentage of the left ventricle. The location and transmural extent of myocardial infarction were assessed by visual scoring. Intraclass correlation and Bland-Altman analysis were used to evaluate the agreement between the techniques for infarct quantification. Kappa statistics were used to analyze the visual score.

Results
Excellent agreement between the two techniques was observed for infarct quantification (intraclass correlation = 0.99 [$p<0.01$]; mean difference ± SD = 0.32% ± 2.4%). The agreement in assessing transmural extent of infarction was good to excellent between the free-breathing technique and the 3D breath-hold technique (kappa varied between 0.70 and 0.96 for all segments). No regions of infarction were missed using the free-breathing approach.

Conclusion
The free-breathing 2D delayed-enhancement MRI sequence is a fast and reliable tool for detecting myocardial infarction.

Introduction

In recent years MRI has gained widespread acceptance for assessing ischemic heart disease. In particular, the assessment of myocardial infarction using delayed-enhancement MRI is now routinely used for predicting recovery of left ventricle function after revascularization therapy.[1,2] Delayed-enhancement MRI provides the opportunity to evaluate the transmural extent of infarcted myocardium with superior spatial resolution compared with nuclear medicine techniques.[3–5]
Validated techniques for delayed-enhancement MRI include breath-hold approaches using a segmented 2D fast low-angle shot inversion-recovery sequence and a rapid 3D inversion-recovery acquisition.[6] Previous studies have shown good correlation between the two techniques for showing myocardial infarction and viability.[7,8]
A potential drawback of the segmented 2D fast low-angle shot inversion-recovery approach is the relatively long acquisition time. Images are acquired during 10–16 breath-holds of at least 10 heartbeats to cover the entire left ventricle in the short-axis orientation. Inability to perform adequate breath-holding and image misregistration may result in suboptimal results using this 2D approach.
The advantage of the 3D technique is that the acquisition of images encompasses the entire heart in a single breath-hold.[8] However, depending on the patient's heart rate, the 3D approach requires a breath-hold time of more than 20 seconds. Not all patients are able to perform such long breath-holds during acquisition, for example, patients with heart failure or respiratory discomfort. Therefore, it would be clinically desirable to have a delayed-enhancement MRI technique available that is not dependent on the ability of patients to hold their breath repetitively or for relatively long periods of time.
Recently, several new free-breathing delayed-enhancement MRI sequences in combination with navigator technology have been reported.[9,10] However, the use of navigator echo-gated techniques requires scanning times of several minutes, causing possible respiratory artifacts because of diaphragmatic drift and gross patient movement. Another limitation of the navigator approach is that the entire acquisition should be completed in less than 2 minutes to minimize changes in contrast concentration over time.[9] In addition, averaged, motion-corrected free-breathing delayed-enhancement MRI may suffer from artifacts because of through-plane motion, especially for acquisitions in the long-axis orientation.[11]
Most recently, the use of a 2D single-shot inversion-recovery steady-state free procession (SSFP) delayed-enhancement MRI sequence acquired during a single breath-hold has been reported for viability imaging.[12] This fast, 2D single-shot delayed-enhancement MRI sequence in conjunction with respiratory triggering using a respiratory belt allows the acquisition of delayed-enhancement MR images during free breathing.

To our knowledge, no previous study has been performed to validate this free-breathing 2D single-shot inversion-recovery SSFP delayed-enhancement MRI sequence approach for assessing myocardial infarction. Accordingly, the purpose of our study is to validate the free-breathing respiratory-triggered 2D single-shot inversion-recovery SSFP delayed-enhancement MRI sequence for the assessment of myocardial viability compared with the accepted 3D technique with breath-holding.

Subjects and Methods

Patients

In this study, 33 consecutive patients with clinically suspected chronic myocardial infarction were included. All patients were referred for MRI for evaluation of possible ischemic cardiomyopathy. The study was approved by the medical ethics committee and written informed consent was obtained from each patient. In one patient, the MR examination was terminated because of claustrophobia. Therefore, in 32 patients (25 men and seven women; mean age, 68 years; age range, 39–84 years) the MRI protocol was successfully completed.

Imaging was performed with the patient in the supine position on a 1.5-T MR system (Achieva, release 10.3; Philips Healthcare) with master gradients (maximum amplitude, 30 mT/m) using a dedicated 5-element phased-array cardiac coil and vector cardiographic triggering.

Delayed-Enhancement MRI Protocols

All patients were imaged using a free-breathing respiratory-triggered 2D single-shot inversion inversion-recovery SSFP delayed-enhancement MRI sequence and a breath-hold 3D fast-field echo (FFE, gradient-echo) inversion-recovery delayed-enhancement MRI sequence. The order in which the two different delayed-enhancement techniques were performed alternated in successive patients. Both delayed-enhancement MRI sequences were acquired in the short-axis orientation covering the entire left ventricle from base to apex. Delayed-enhancement MR images were acquired 10-15 minutes after IV contrast injection of gadoteridol (ProHance, Bracco) at 0.2 mmol per kilogram of body weight. Nulling of normal myocardium was accomplished by defining the optimum inversion time on scout images, which were performed before delayed-enhancement MRI examinations. ECG gating was used and acquisition was performed after every R wave trigger.

The free-breathing 2D approach consisted of a single-shot inversion-recovery SSFP delayed-enhancement MRI technique. Respiratory motion was triggered using a respiratory belt. Typical imaging parameters were as follows: TR/TE, 3.0/1.49; flip angle, 45°; sensitivity encoding (SENSE)[13] factor, 1.5; acquired voxel size, 1.68 × 1.68 × 10.0 mm. The scanning time was between 50 and 80 seconds depending on the frequency of respiration. Images were acquired at end-diastole during an acquisition window of 292 milliseconds.

The breath-hold 3D technique consisted of a gradient-echo (FFE) inversion-recovery delayed-enhancement MRI sequence. The entire left ventricle was imaged during end-expiratory breath-hold. Typically, the breath-hold time was 24 seconds for a heart rate of 70 beats per minute. The imaging parameters were 3.7/1.15; flip angle, 15°; SENSE factor, 2.0; acquired voxel size, 1.71 × 1.71 × 10.0 mm. By radiofrequency excitation, one echo was acquired during an acquisition window of 217 milliseconds at end-diastole.

Qualitative and Quantitative Data Analysis

Delayed-enhancement MR images were presented in the same random order as acquired (the order in which the two different delayed-enhancement techniques were performed alternated in successive patients), and observers were blinded to the type of MRI sequence and patient information.

Image quality analysis

Image quality of the free-breathing 2D and the breath-hold 3D techniques was assessed by visual grading in consensus by two experienced cardiac MR radiologists, one with 10 years of experience and the other with more than 20 years of experience in cardiac MRI. Overall image quality was rated per scan per patient according to the following 4-point scale: 1, nondiagnostic; 2, diagnostic but with suboptimal image quality or motion artifacts; 3, good image quality but with some blurring or motion artifacts; and 4, excellent image quality with little or no motion artifacts.

Quantitative analysis of contrast-to-noise ratio (CNR)

The CNR between infarcted, enhanced myocardium and unenhanced myocardium in the same anatomic region for both MRI techniques was calculated by one reader. Regions of interests (ROI) to determine signal intensity (SI) were defined for the infarcted, enhanced myocardium and for the unenhanced myocardium in the same acquired image for both techniques. An additional ROI (± 10 cm^2) was placed in the field of view but outside the patient's body to determine the SD of noise.

The following equation was used:

$$CNR = [(SI_{infarct} - SI_{unenhanced}) / SD_{noise}].$$

Quantitative analysis of infarct size

For assessing the presence and extent of delayed enhancement representing infarcted myocardial tissue, delayed-enhancement MR images in the short-axis orientation of the left ventricle were divided into 16 segments, as recommended previously.[14] Endocardial and epicardial contours of the left ventricle and areas of hyper-enhancement within these contours were outlined manually on short-axis images. Infarct size was expressed as a percentage of left ventricular mass (% LV) by using the formula: [Σ (areas with delayed enhancement / left ventricular areas between endocardial and epicardial contours)] ×100.

Quantitative analysis of delayed-enhancement location and transmurality

Maximum transmural extent of hyper-enhancement in relation to the thickness of the myocardium was determined. The 16 segments in the short-axis orientation were graded on a 5-point scale in which the score of 0 indicated no hyper-enhancement; a score of 1, hyper-enhancement of 1–25% of wall thickness in each segment; a score of 2, hyper-enhancement of 26–50%; a score of 3, hyper-enhancement of 51–75%; and a score of 4, hyper-enhancement of 76–100% of the myocardial wall thickness.[1] Infarct location was assigned to the segmental level.

Statistical Analysis

Continuous variables are expressed as mean ± SD and range when appropriate. Agreement between both acquisition techniques (2D technique with free breathing and 3D technique with breath-holding) regarding image quality, infarct location, and transmurality was evaluated by weighted kappa statistics. Agreement in infarct size was evaluated by the two-way mixed intraclass correlation for absolute agreement. The approach described by Bland and Altman[15] was followed to study systematic differences. Mean differences and CIs were determined and statistical significance was tested using paired-samples Student's *t* tests. A *p* value of 0.05 was considered statistically significant.

Results

The free-breathing respiratory-triggered 2D single-shot inversion-recovery SSFP delayed-enhancement MRI sequence was completed successfully in all patients (100% success rate), whereas the breath-hold 3D gradient-echo inversion-recovery delayed-enhancement MRI sequence failed in two patients because of inability to perform adequate breath-holding and irregular heart rate (success rate, 94%). These two patients were excluded from the analysis.

Twenty-two of 30 patients who were evaluated with both methods showed regions of myocardial hyper-enhancement at both imaging techniques, confirming the presence of ischemic cardiomyopathy (Figure 3.1). In the remaining eight patients, no infarcted regions were identified with either technique.

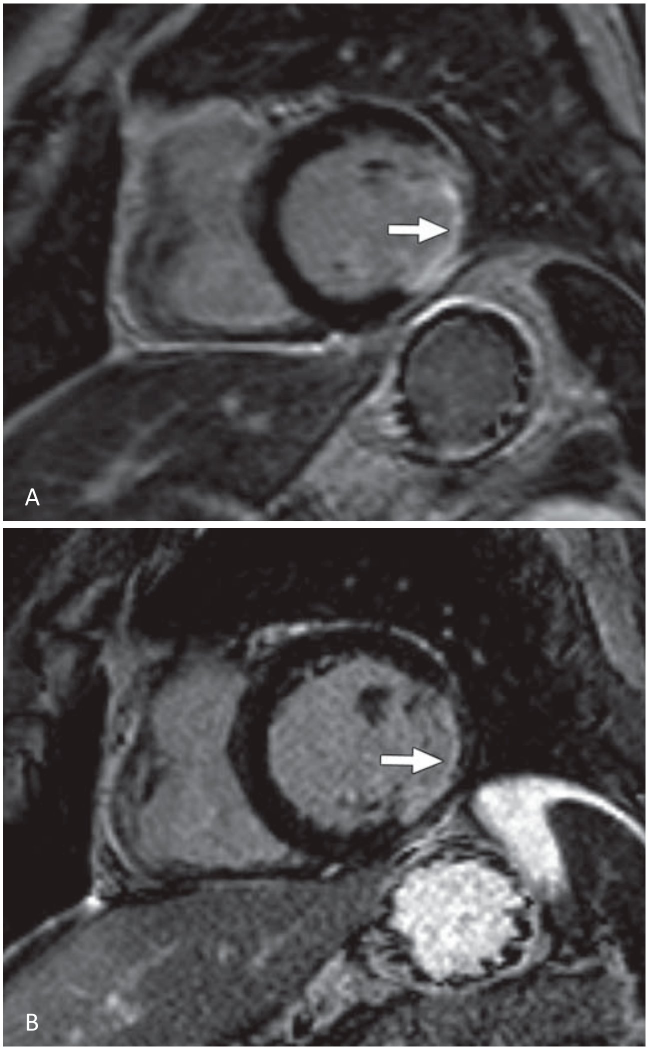

Figure 3.1 58-year-old man with myocardial infarction in inferolateral segment after occlusion of left circumflex artery. **(A)** Breath-hold 3D gradient-echo inversion-recovery delayed-enhancement MR image shows myocardial infarction (*arrow*) with hyperintense signal intensity. Extent of infarction is subendocardial. **(B)** Free-breathing 2D single-shot inversion-recovery SSFP delayed-enhancement MR image shows myocardial infarction (*arrow*) with hyperintense signal intensity. Extent of infarction is subendocardial. For both sequences area of infarction is identical.

Image Quality

Image quality was scored visually and graded on a 4-point scale. For the 2D free-breathing technique, 20 cases were scored as good and 12 cases as excellent (mean score, 3.3). For the 3D technique, two patients were not included because the data could not be obtained. In two cases, the image quality score was 2 (diagnostic but suboptimal). In 19 cases, image quality was good, and in the remaining nine cases, image quality was excellent (mean score, 3.2).

Quantitative Analysis of CNR

The CNR between infarcted, enhanced myocardium and unenhanced myocardium was significantly higher in the free-breathing 2D MRI approach compared with the breath-hold 3D MRI approach (545 ± 201 vs 327 ± 156, $p<0.001$).

Quantitative Analysis of Infarct Size

Quantitative analysis revealed excellent agreement between the two delayed-enhancement MRI techniques for the estimation of infarct size expressed as percentage of left ventricular mass. Intraclass correlation was 0.99 ($p<0.01$). Mean infarct size was 11% ± 12% with a range of 0%–65% for free-breathing 2D MRI versus 11% ± 12% with a range of 0%–61% for breath-hold 3D MRI. Differences, presented in a Bland-Altman plot (Figure 3.2), were small (0.32% ± 2.4%), not statistically significant ($p=0.46$), and nonsystematic. The 95% CI was small (−4.4% to 5.0%).

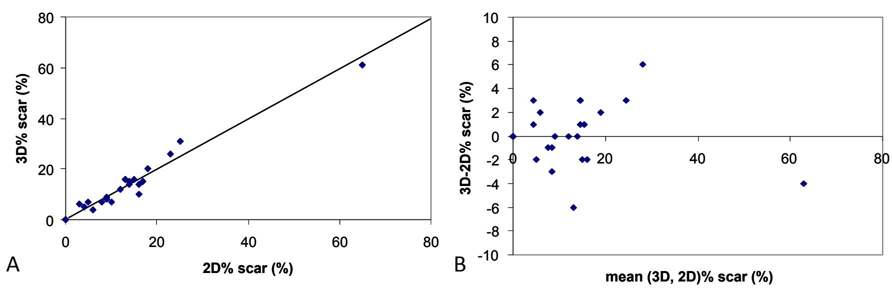

Figure 3.2 Comparison of techniques: free-breathing 2D single-shot inversion-recovery steady-state free precession delayed-enhancement MRI (2D) and breath-hold 3D gradient-echo inversion-recovery delayed-enhancement MRI (3D). **(A)** Graphic shows relation between infarct size expressed as percentage of left ventricular mass for 2D imaging versus infarct size assessed with 3D imaging. **(B)** Bland-Altman plot shows differences between 2D and 3D imaging are small (0.32% ± 2.4%), not statistically significant (p = 0.46), and nonsystematic; 95% CI is small (−4.4% to 5.0%).

Data distribution revealed a single outlier that could affect the statistical results. Removing this outlier—in this patient, the 2D technique with free-breathing revealed a scar of 65%, whereas the 3D technique with breath-holding showed 61%—shows comparable results: intraclass correlation, 0.98 ($p<0.01$); mean infarct size, 9% ± 7% (range, 0%–25%) for free-breathing 2D MRI versus 9% ± 8% (range, 0%–31%) for breath-hold 3D MRI with small (0.5% ± 2.3%), not statistically significant ($p=0.28$), and nonsystematic differences and a small 95% CI (−4.0% to 5.0%).

Location and Transmurality

In the 30 patients with diagnostic images for both scanning methods, 16-segment analysis showed good agreement in presence and transmurality of delayed enhancement. No regions of infarction were missed on the free-breathing 2D images compared with the breath-hold 3D technique.

In 468 of 480 segments, the classification of the transmural extent with the free-breathing 2D scanning showed good concordance with the breath-hold 3D technique (Figure 3.3). For all segments, the weighted kappa varied between 0.70 and 0.96. In the remaining 12 segments, the difference between the two methods was a maximum of one grade.

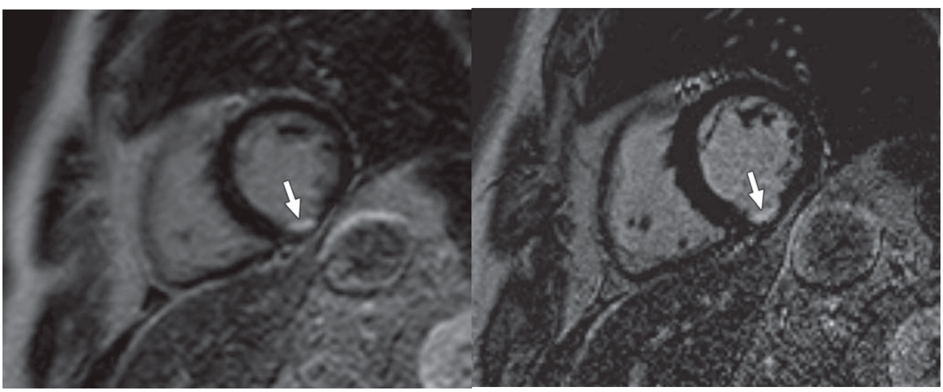

Figure 6.3 61-year-old man with myocardial infarction in inferior segment after occlusion of right coronary artery. **(A)** Breath-hold 3D gradient-echo inversion-recovery delayed-enhancement MR image shows myocardial infarction (*arrow*) with hyperintense signal intensity. **(B)** Free-breathing 2D single-shot inversion-recovery steady-state free precession delayed-enhancement MR image shows myocardial infarction (*arrow*) with hyperintense signal intensity. Both techniques show excellent agreement of maximum transmural extent of hyper-enhancement in relation to thickness of myocardium.

Discussion

The main findings of our study are the following: First, free-breathing, respiratory-triggered 2D single-shot inversion-recovery SSFP delayed-enhancement MRI is comparable to breath-hold 3D segmented gradient-echo inversion-recovery delayed-enhancement MRI when used for quantification of left ventricular scar. Second, the 2D technique with free breathing is well-tolerated and provides an alternative when patients are not capable of performing breath-holding. Third, CNR is higher for the 2D technique with free breathing compared with the 3D breath-hold technique. The free-breathing technique was successfully completed in all patients, whereas two patients failed to complete the 3D delayed-enhancement breath-hold examination because of inability to perform adequate breath-holding, underscoring the potential use of the 2D approach in patients who have difficulties with breath-holding during image acquisition.

The reference standard for assessing viability by delayed hyperenhancement is 2D inversion-recovery fast low-angle shot imaging.[6,16] The long acquisition time and use of multiple breath-holds to cover the entire left ventricle are considered major drawbacks. Single breath-hold imaging in conjunction with a 3D MRI sequence has been validated against the 2D reference standard as an alternative acquisition to overcome the limitations of the 2D technique.[7,8] The necessary breath-hold time for the 3D sequence is significantly shorter compared with the 2D approach, whereas the two techniques agree very closely for assessing the transmural extent of infarction. A high technical success rate for the 3D acquisition has been reported.[7,8,17]

In the current study, we compared a free-breathing 2D technique that was triggered to respiratory motion with the use of a respiratory belt to a standard breath-hold 3D technique. The acquisition time varies between 50 and 80 seconds for the free-breathing technique compared with approximately 25 seconds of breath-hold for the 3D technique, depending on respiratory frequency and the heart rate, respectively. The data for the 3D technique are acquired over several heartbeats, making this technique more sensitive to motion artifacts because of heart rate variability and arrhythmia. The free-breathing respiratory triggered 2D single-shot sequence overcomes this limitation by acquiring one slice during one R-R interval and may therefore be less sensitive to arrhythmia.

The spatial resolution was similar for both techniques. The CNR was significantly higher in the free-breathing 2D MRI approach compared with the breath-hold 3D MRI approach (545 ± 201 vs. 327 ± 156, p<0.001). In recent literature, it has been shown that a 2D single-shot inversion-recovery SSFP delayed-enhancement MRI sequence has a lower CNR compared with a segmented 2D fast low-angle shot inversion-recovery sequence. In concordance with our results, Huber et al.[12,18] have shown that assessment of the volume of infarcted myocardium is possible with excellent correlation.

The results of this study show that the visual scores of infarct location and transmural extent are very similar between both techniques, indicating the potential clinical use of the free-breathing approach. In a limited number of segments, a difference between the two techniques was found, but the difference was not more than one grade when using the 5-point scale for transmurality of infarction. No areas of infarction went undetected using the free-breathing technique compared with the reference standard. Furthermore, when comparing the quantitative analysis of infarct size, the two techniques revealed close agreement, underscoring the reliability of the free- breathing approach for infarct imaging.

The performance of inversion-recovery delayed-enhancement techniques is sensitive to the selection of the appropriate inversion time. In our study, the optimal inversion time was selected for both the breath-hold 3D approach and the free-breathing 2D approach separately. Therefore, we believe that we have minimized the possible effect of changes of infarct size over time after the administration of the contrast agent. No systematic differences regarding infarct size were observed between the two techniques.

We acknowledge some possible limitations of the current study. The use of the respiratory belt requires a relatively stable and reproducible respiration pattern that can be registered through the belt. The acquisition time of the images may therefore vary between 50 and 80 seconds depending on the breathing pattern. Furthermore, the 2D free-breathing technique was compared with the 3D breath-hold technique, whereas 2D inversion-recovery fast low-angle shot imaging with breath-holding is more commonly used as a standard of reference.[6,16]

The excellent diagnostic value and clinical success rate of the 2D free-breathing technique support its clinical application as a possible first-line or second-line technique for assessing myocardial viability, depending on patient compliance and ability to follow breathing instructions.

In conclusion, the free-breathing, respiratory-triggered single-shot inversion-recovery approach appears to be a fast and reliable technique to assess myocardial infarct size and transmurality after administration of a gadolinium-based contrast agent.

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