Published in final edited form as:

J Magn Reson Imaging. 2013 November ; 38(5): . doi:10.1002/jmri.24037.

Volumetric Late Gadolinium-Enhanced Myocardial Imaging with Retrospective Inversion Time Selection

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Abstract

Purpose—To develop and validate a novel free-breathing three-dimensional radial late Gadolinium-enhanced magnetic resonance imaging technique (3D LGE-MRI) with isotropic resolution and retrospective inversion time (TI) selection for myocardial viability imaging.

Materials and Methods—The 3D LGE-MRI featuring an interleaved and bit-reversed radial k-space trajectory was evaluated in twelve subjects that also had clinical breathhold Cartesian 2D LGE-MRI. The 3D LGE-MRI acquisition requires a predicted TI and a user controlled data acquisition window that determines the sampling width around the predicted TI. Sliding window reconstructions with update rates of 1x the repetition time (TR) allow for a user selectable TI to obtain the maximum nulling of the myocardium. The retrospective nature of the acquisition allows the user to choose from a range of possible TI times centered on the expected TI. Those projections most corrupted by respiratory motion, as determined by a respiratory bellows signal, were re-sampled according to the diminishing variance algorithm. The quality of the left ventricular myocardial nulling on the 3D LGE-MRI and 2D LGE-MRI was assessed using a 4-point Likert scale by two experienced radiologists. Comparison of image quality scores for the two methods was performed using generalized estimating equations.

Results—All 3D LGE-MRI cases produced similar nulling of myocardial signal as the 2D LGE-MRI. The image quality of myocardial nulling was not significantly different between the two acquisitions (mean nulling of 3.4 for 2D vs. 3.1 for 3D, and $p=0.0645$). The average absolute deviation from mean scores was also not determined to be statistically significant (1.8 for 2D and 0.4 for 3D and $p = 0.1673$). Total acquisition time was approximately 9 minutes for 3D LGE-MRI with voxel sizes ranging from 1.6^3 to 2.0^3 mm³. Conversely, the total imaging time was twice as long for the 2D DCE-MRI (>17 minutes) with an eight times larger voxel size of $1.4 \text{ mm} \times 2.2 \text{ mm} \times 7.0 \text{ mm}$.

Conclusion—The 3D LGE-MRI technique demonstrated in this study is a promising alternative for the assessment of myocardial viability in patients that have difficulty sustaining breath holds for the clinical standard 2D LGE-MRI.

Keywords

Delayed Contrast imaging; Myocardial Viability; Non-Cartesian; Radial k-space trajectory; Inversion recovery (IR); Volumetric Imaging; Left Ventricle

INTRODUCTION

Late Gadolinium (Gd) enhanced magnetic resonance imaging (LGE-MRI) can distinguish infarcted from healthy myocardium by exploiting differential Gd based contrast agent concentrations in the regions of infarction (1). LGE-MRI is a unique and powerful tool for the assessment of tissue viability; however, LGE-MRI presents some challenges. Imaging is typically performed with a breathheld two dimensional (2D) inversion recovery (IR) sequence. This sequence requires selection of inversion time (TI) to null healthy myocardium, which varies considerably depending on Gd contrast agent relaxivity and patient specific contrast kinetics (2). Thus, TI scout scans must be performed prior to imaging to determine the optimal TI in each patient. Skilled technicians can typically predict the optimal TI to within 20 -30 ms when a standard protocol consisting of a specific concentration and type of contrast agent as well as the time since administration of agent is used. Complete coverage of the heart requires approximately 12-16 short-axis slices, each requiring a 10-20 second breathhold. Even in the most cooperative patients, this requires 8-10 minutes when recovery time in between breath holds is accounted for. During a typical session lasting 8-10 minutes, Gd concentration washout is minimal. However, when several slices need to be reacquired due to image quality degradation due to the patient's inability to maintain breathholds, considerable Gd concentration washout can occur (2). This in turn requires the operator to heuristically increase the TI to achieve optimal myocardial nulling and limit the amount of "etching" artifact in the myocardium. Individual slices must be repeated in cases of suboptimal nulling, further extending scan time and increasing patient fatigue. Due to these challenges, LGE-MRI images acquired towards the end of the scan session are often corrupted by respiratory motion and/or have incomplete myocardium nulling.

A variety of techniques have been proposed to address the challenges associated with TI selection. Some of the sensitivity to TI selection can be mitigated by utilizing a phase sensitive inversion recovery (PSIR) methods (3). PSIR uses a 2RR acquisition in which a reference image for baseline phase correction is acquired in the second RR. This lengthens scan times compared to 1RR methods (4). To speed up the acquisition of the 2D LGE-MRI, low flip angle spoiled gradient-recalled echo (SPGR) (5) and balanced steady state free precession (bSSFP) techniques (6,7) have been proposed as alternative readouts. While these sequences allow multiple TIs to be collected, they only provide a coarse selection of TIs. To improve temporal resolution, radial sampling has been proposed. Since radial techniques sample the center of k-space each TR, several TIs can be reconstructed from each acquisition (8).

Efforts have also been made to mitigate the potential for respiratory motion corruption. Single breathhold 3D Cartesian LGE-MRI with a long cardiac acquisition window has recently been proposed to reduce patient fatigue (9). This approach acquires a single 3D volume in an 18-26s breathhold, which reduces fatigue but may not be feasible for all patients. Furthermore, the extended acquisition window can lead to ghosting artifacts that are not easily distinguished from subendocardial infarct (9). Navigator gating has since been used to allow free-breathing 3D LGE in two minutes using the same approach (10). As Gd concentration changes within a single long scan, Cartesian acquisitions suffer from edge enhancement artifacts due to mismatch of high and low spatial frequency contributions (9). This prevents the use of longer scan times required for 3D imaging utilizing improved SNR, fewer views per segment, or higher spatial resolution.

Radial acquisitions have also been proposed to mitigate artifacts from incomplete breath holds. In radial imaging, motion artifact manifests as spatial blurring instead of coherent ghost artifacts (11-13) due to the sampling of the center of k-space each TR. Recently, a

hybrid radial-Cartesian acquisition to image the left atrium was proposed using respiratory averaging alone (14). In much the same way as radial imaging trades motion-induced ghosting of Cartesian acquisitions for spatial blurring, radial sampling results in T1 averaging at the central parts of k-space). This offers the potential to allow for longer scans necessary for respiratory-gated acquisitions.

In this work, a respiratory-gated, 3D radial acquisition with retrospective TI selection and isotropic spatial resolution is investigated for LGE imaging of the myocardium (3D LGE-MRI). This strategy has many advantages over current 2D LGE-MRI methods that include: retrospective selection of TI within a 3D volume, isotropic voxels, free breathing, and well-tolerated scan times. We compared this 3D LGE-MRI to 2D breathhold Cartesian LGE in a study of 11 patients with suspected coronary artery disease and 1 healthy volunteer. Image quality of the myocardium was assessed in terms of the degree of nulling of healthy myocardium and the conspicuity of infarction.

MATERIALS AND METHODS

Technique: Acquisition and Reconstruction

3D radial LGE-MRI was performed using a spoiled gradient recalled (SPGR) inversion recovery (IR) sequence as shown in Fig. 1. After detection of the cardiac trigger and a cardiac trigger delay (TD) for diastolic imaging, a non-selective adiabatic 180 degree pulse inverts the longitudinal magnetization. After a user-defined delay, N views are acquired with a fully 3D radial trajectory (11). Projections for the radial acquisition are acquired with a pseudo-random bit-reversed ordering (11) using an interleaving process (8). The N views are acquired in a bit-reversed order so that each additional view seeks to evenly divide the unit sphere into approximately equal areas. This also will divide the unit sphere into equal pieces when any subgroup of W ($W \leq N$) consecutive projections are combined. Additional interleaving is performed so that projections from identical subgroups acquired after different and consecutive inversion pulses can be combined to further subdivide the unit sphere into approximately equal areas. The interleaving also helps reduce artifacts due to inconsistent signal across regions of k-space (8). A representative example demonstrating the interleaving is shown in Fig. 2. The interleaving allows for sliding window reconstructions of arbitrary width W to be performed about any point that occurs during the data acquisition window and still results in an approximately uniformly sampled k-space. Following (15), the TI for each of the N images is given by the average time since the inversion for all the projections within each sliding window. To account for respiratory motion, a modified diminishing variance algorithm (DVA) was performed using a respiratory bellows for gating (16).

Feasibility Study and Comparison to 2D LGE

Using an Institutional Review Board (IRB) approved protocol, 1 healthy volunteer and 11 patients with suspected chronic myocardial infarction (MI) were scanned with a standard multi-slice 2D LGE-MRI and the new 3D LGE-MRI proposed in this study. For the patients with suspected MI, six of the exams were performed at 3T (MR 750, GE Healthcare, Waukesha, WI) and five at 1.5T (MR 450W, GE Healthcare, Waukesha). The healthy volunteer was scanned at 3T (MR 750, GE Healthcare, Waukesha, WI). The 2D LGE imaging began approximately 9 minutes after administration of 0.15 mmol/kg of Gd (Multihance, Bracco Diagnostics Inc.) and had a mean duration 17min 08s (range 9 - 33 minutes). Parameters for the clinical 2D LGE-MRI acquisition were as follows: FOV: 37×37 cm, resolution: $1.4 \times 2.3 \text{ mm}^2$, slice thickness: 8 mm, no slice overlap, flip angle: 20°, readout bandwidth: $\pm 31.25 \text{ kHz}$, TE/TR: 1.6/6.4 ms, 2 signal averages, 24-32 views per segment (154ms to 205ms temporal resolution), 1 RR between inversions for heart rates <

80 beats per minute, for heart rates > 80 beats per minute 2 RR were used, scan time 9-17 s per breathhold, TD was adjusted to the heart rate for optimal diastolic imaging REF The 3D LGE MRI acquisition was performed after the 2D LGE-MRI was completed using: FOV $48 \times 48 \times 18 \text{ cm}^3$, $(1.6 \times 1.6 \times 1.6)$ to $(2 \times 2 \times 2) \text{ mm}^3$ isotropic resolution, flip angle 15° , BW: $\pm 62.5 \text{ kHz}$, TE/TR: 0.7/3.6 ms, data acquisition window = 216 ms ($60 \times \text{TR}$). Scan time was fixed to 9 minutes. Sliding window reconstruction was used to reconstruct 60 images about each TR (TI) of the acquisition window. Except for the case of the healthy volunteer, a maximum radial viewsharing of ± 15 views ($\pm 54 \text{ ms}$) was used. Symmetric viewsharing was used except for those points near the beginning and end of the data acquisition. Coil sensitivity maps estimated from the low resolution oversampled center of k-space (17) data were used to combine individual coil images. The separate coils in the eight channel multicoil array (1.5 T) or the 32 channel array (3T) were combined according to (18) for improved SNR and artifact reduction. To reduce phase errors associated with the regrowth of the inverted longitudinal magnetization, only the last 15 views from each heart beat were used in reconstruction of the sensitivity maps.

Images from the healthy volunteer were utilized to optimize reconstruction parameters eventually utilized for the patient studies. The effects of radial view sharing were examined using the normal volunteer and the identical protocol as detailed above. Radial view sharing with window widths of $\pm 5 \text{ TR}$, $\pm 10 \text{ TR}$, $\pm 15 \text{ TR}$, $\pm 20 \text{ TR}$ and $\pm 25 \text{ TR}$ were reconstructed with update rates of 1 TR. After reformatting to short axis views, images were filtered in k-space by decimating high spatial frequency components in the kz direction to produce spatial resolution of 6.0 mm. Image quality was assessed by visual inspection and signal contrast between the healthy myocardium and neighboring blood pool of the left ventricle.

Left Ventricular (LV) image quality was assessed on 17 segments defined according to the American Heart Association (19). The 3D LGE-MRI image with best myocardial nulling, as determined by ROI measurements, were upload to a workstation for each case and manually reformatted to match the orientation of the short axis 2D LGE exams. Each segment was scored using a Likert Scale by two experienced radiologists based on myocardial nulling: 1 - incomplete- not diagnostic quality, 2 - some-diagnostically useful, 3 - good, 4 - excellent, and presence or absence of infarct (yes/no). Generalized estimating equation (GEE) models were used to model subjective nulling quality as a function of acquisition method while taking into account clustering of observations within an individual. An independent working correlation matrix was assumed and the sandwich variance estimator was used to obtain robust standard errors. Infarcted segments were considered as missing and excluded from the analysis. To compare variability of method, GEE models were also fitted to the absolute values of deviations from subject and method specific nulling scores.

RESULTS

Fig. 3 shows short axis reformats for TIs representing the null point of normal myocardium, which is defined as the image with the lowest myocardial signal, for sliding window widths of ($\pm 5 \text{ TR}$, $\pm 10 \text{ TR}$, $\pm 15 \text{ TR}$, $\pm 20 \text{ TR}$ and $\pm 25 \text{ TR}$), or equivalent reconstruction window widths of (44 ms, 81 ms, 117 ms, 154 ms, and 191 ms). Despite the averaging of the central regions of k-space, all window widths are able to effectively null the myocardium in at least one of the images from the sliding window reconstruction. As the sliding window width increases, image quality improves due to decreased streak artifacts and increased relative “SNR”. The averaging at the center of k-space increases the effective null point (TI) for myocardium from 129 ms for $\pm 5 \text{ TR}$ to 186 ms for $\pm 25 \text{ TR}$ in this example. The bottom row of Fig. 3 shows how filtering the reformatted complex images in the slice direction improve image quality by reducing undersampling artifacts and increasing SNR. For the case with

154 ms temporal resolution, reducing the slice resolution shifted the null frame to the left by 8 ms.

Images with select TIs from the 3D radial LGE are shown in Fig. 4. Incomplete nulling of the myocardium is seen in images with TIs as little as 18 ms less than the optimal nulling time (158 ms), demonstrating the necessity to have a fine selection of TIs. The full range of TIs is demonstrated in Fig. 5 where the signal intensities of healthy myocardium, myocardial infarct, and blood are plotted for 60 TIs ranging from 70 to 230 ms.

Native axial views, as well as the reformatted long axis, four chamber, and short axis views from the 3D acquisitions are shown in Fig. 6 for two patients. The first patient (top) showed no areas of enhancement, while the second patient (bottom) shows myocardial infarct. The short axis view from the second patient also shows enhancement pointed by the arrow head, which was not visualized on the 2D scan (Fig. 6d) due to partial volume effects in the slice direction (8 mm).

Two dimensional (a-d) and approximately matching three-dimensional (e-h) LGE slices are shown for four patients in Fig. 7. The 3D LGE images were acquired axially and reformatted to long axis (e) and short axis (f-h) views to match the 2D LGE images. The orientation between the 2D and 3D LGE are slightly mismatched due to the different delay times used in each acquisition. 3D LGE acquisition in Fig. 7h (also visible in Fig. 6d) shows enhancement of the papillary muscle (arrow head) while the matching 2D LGE slice (Fig. 7d) did not show the papillary muscle.

Myocardial average nulling was not significantly different (3.4 for 2D vs. 3.1 for 3D, and $p=0.0645$). The average absolute deviation from mean scores was also not determined to be statistically significant (1.8 for 2D and 0.4 for 3D and $p = 0.1673$). Of the total 204 (10×17) segments, the 3D radial acquisition had only 3 segments with incomplete nulling while the 2D acquisition had 29 with incomplete nulling. Both methods detected the presence of infarct in the same 15 segments and thrombus in one segment. One or more images from 8 of the 11 patients had respiratory motion artifacts for the 2D Cartesian acquisition, resulting in motion corrupted images or the appearance of incomplete nulling (etching). Fig. 8(top) shows an example showing the typical effects from respiratory motion in the 2D breathhold Cartesian acquisitions. The respiratory-gated 3D radial acquisition, Fig. 8(bottom), did not display respiratory induced artifacts in this or any of the other cases.

DISCUSSION

In this work, we evaluated a new 3D LGE-MRI method for myocardial imaging utilizing 3D radial sampling. This method dramatically reduces sensitivity to TI, allowing long free breathing scans without the need for TI scouts. In a cohort of 12 subjects, this 3D technique was compared to a clinical standard 2D LGE protocol. Respiratory gated scans eliminated the on average 17 breath holds used in the conventional 2D DCE-MRI and reduced the total exam time (9 vs. 17 minutes). In a blinded comparison, 3D LGE-MRI was found to be statistically similar in image quality to the standard 2D LGE. For patients unable to maintain breaths, 3D LGE showed superior image quality compared to the 2D method performed during the same scanning session.

In this work, 3D LGE exams were found to be equivalent to a standard clinical 2D protocol despite study disadvantages due to performing 3D LGE scans at the end long after the 2D LGE scans to avoid interference with the clinical protocol. Radial 3D LGE exams were preceded by a comprehensive cardiac workup including multislice breathhold SSFP cardiac function and 2D breathhold LGE scans. On average, the delay between the 2D delayed enhanced imaging and 3D exams was 22 minutes (min 15, max 33). This increased patient

fatigue and resulted in considerably lower GBCA concentration in 3D LGE-MRI scans (2). This delay from injection also increased the TI required to null healthy myocardium in the 3D LGE-MRI, which resulted in stronger fat signal. In 3D radial sampling, undersampling artifacts manifest as haze for moderate amounts of angular undersampling and as streak artifacts for high levels of undersampling. With these artifacts, high intensity fat signal can cause the myocardium to artificially appear enhanced. This limits the amount of angular acceleration. Several methods have been proposed to reduce fat signal in delayed enhanced myocardial imaging (20,21); however, as currently implemented there is no special consideration for the signal from fat in the 3D LGE-MRI. Future application with fat separation techniques may allow for shorter scan times and/or improve image quality.

Although the total imaging time for 3D LGE-MRI is one half that of a full multi-slice 2D LGE-MRI exam, the single long scan increases the chance for bulk patient motion. However, radial k-space trajectories are inherently less sensitive to motion due to the oversampling of the center of k-space (22) and have recently been used for self navigating with 100 % respiratory efficiency (12,23). Bulk patient motion was not directly observed in this study.

This was a preliminary feasibility study only and has not been subjected to rigorous quantification of the statistical variability between the differences in infarct size found using the standard 2D LGE-MRI and this new method. Furthermore, this new method was only used in normal volunteers, patients with left ventricular infarction, and patients with no findings of myocardial infarction. The method may actually be of more use for patients with right ventricular disease and non-ischemic cardiomyopathies where resolution is of critical importance. The delay time for the 2D LGE-MRI and 3D LGE-MRI were different as the new method under investigation always followed the clinical 2D LGE-MRI to avoid interference with the clinical protocol and had different imaging parameters such as flip angle, TR, and number of views acquired after each inversion pulse. Acquiring images across a range of different inversion times also opens up the door to T1 quantification. However, with this method, the inversion time is synchronized with the cardiac cycle, so motion between inversion times may be problematic. T1 quantification is beyond the scope of this manuscript and will be investigated in future studies.

In conclusion, the 3D LGE-MRI technique demonstrated in this study is a promising alternative for the assessment of myocardial viability in patients who have difficulty sustaining breath holds for the clinical standard 2D LGE-MRI. This free-breathing 3D LGE-MRI, which allows retrospectively choosing the TI and reformatting to arbitrary orientations without loss of spatial resolution, simplifies the whole LGE exam, is shorter, and reduces patient discomfort compared to 2D LGE-MRI.

Acknowledgments

Grant Support: NIH HL86975

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Figure 1.

Three dimensional spoiled gradient echo (SPGR) inversion recovery (IR) sequence with 3D radial k-space sampling. The inversion pulse occurs at a delayed time (TD) after the R-wave is detected to position the data acquisition (DAQ) is late diastole. The reconstruction window (blue rectangle) can have arbitrary width and be positioned anywhere inside the DAQ. The TI is defined as the time from the IR pulse to the center of reconstruction window.

Figure 2.

A schematic showing angular interleaving for radial LGE. For simplicity in illustration purposes, interleaving is demonstrated for a 2D radial acquisition, although the actual acquisition used a 3D radial acquisition with the end points of spokes distributed across the unit sphere. In this schematic, there are $N=8$ views acquired after each of the 2 inversion pulses. The 8 views are acquired in a bit-reversed order so that each additional view seeks to evenly divide the unit circle (sphere) into approximately equal pieces. This also will divide the unit circle (sphere) into equal pieces when any subgroup of W ($W \leq N$) consecutive projections are used. Additional interleaving is performed so that projections from identical subgroups acquired after different and consecutive inversion pulses can be combined to further subdivide the unit circle (sphere) into approximately equal pieces.

Figure 3.

The myocardial null frames from sliding window reconstructions with reconstructed TIs (rTI's) of (a) 129ms (b) 157ms (c) 165ms (d) 169 ms and (e) 186 ms (top) and 172 ms (bottom). All window widths are able to null the myocardium. Image quality generally improves as window width is increased due to increased number of projections and less angular undersampling artifacts.

Figure 4. Reformatted two (top) and four (bottom) chamber views from the 3D LGE showing transmural infarct (arrow) from 5 different reconstructed inversion times. Note the incomplete nulling of the myocardium (arrows) just 18ms before the null time (158ms).

Figure 5. Normal myocardial, blood, and infarct signals (a) and null map (b) from the case in Fig. 4 can be used to select the optimal reconstructed TI. The infarct (red arrow) nulls at an earlier TI than normal myocardium due to T1 shortening effects of the retained Gd in the scar tissue.

Figure 6.
Acquired axial, and reformatted long axis, four chamber, and short axis views from the 3D radial method for two patients.

Figure 7.

Comparison of 2D Cartesian (top) and 3D radial LGE images (bottom) for 4 different patients. The 3D were reformatted to approximately the same orientation, although slight differences occur due to the different acquisition times with respect to cardiac cycle and the thinner slice thickness of the 3D images (1.6mm for 3D vs. 8 mm 2D). The white arrows show infarcted myocardium, while the arrow head depicts enhancement of the papillary muscle.

Figure 8. Results from a patient who had difficulty maintaining the required breath holds for 2D scans. The 2D LGE images (top) show decreased spatial resolution and poor contrast between the blood and nulled myocardium due to respiratory artifacts. The respiratory gated 3D LGE shows increased contrast between blood and nulled myocardium and sharper delineation of myocardium.