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Feasibility Study of a Single Breath-hold, 3D mDIXON Pulse Sequence for Late Gadolinium Enhancement Imaging of Ischaemic Scar

BACKGROUND

Late gadolinium enhancement (LGE) imaging is well validated for the diagnosis and quantification of myocardial infarction (MI). 2D LGE imaging involves multiple breath-holds for acquisition of short axis slices to cover the left ventricle. 3D LGE methods cover the left ventricle in a single breath-hold; however, breath-hold duration is typically long with images susceptible to motion artifacts.

PURPOSE/HYPOTHESIS To assess a rapid single breath-hold 3D mDIXON LGE pulse sequence for image quality and quantitation of MI.

STUDY TYPE

Prospective.

POPULATION

92 patients with prior MI.

FIELD STRENGTH/SEQUENCE

Patients underwent identical 1.5T Cardiac MRI protocol using conventional 2D PSIR and 3D mDIXON LGE imaging 10 minutes following contrast administration in a random order to avoid bias.

ASSESSMENT

Data were analysed qualitatively for image quality by 3 observers. Quantitative assessment of myocardial scar mass (full-width half-maximum), scar transmurality and contrast-to-noise ratio measurements were performed. Time taken for 2D and 3D LGE imaging was recorded.

STATISTICAL TESTS

Paired student t-test, Wilcoxon rank test, Cohen κ statistic, Pearson correlation, linear regression and Bland-Altman analysis.

RESULTS

Image quality scores were comparable between 3D and 2D LGE (1.4±0.6 vs. 1.3±0.5; P=0.162). 3D LGE was associated with greater scar tissue mass (3D: 18.9±17.5g vs 2D: 17.8±16.2g P=0.03), although this difference was less pronounced when scar tissue was expressed as %LV mass (3D: 13.4±9.9% vs 2D: 12.7±9.5% P=0.07). For 3D vs. 2D scar mass there was a strong and significant positive correlation; Bland-Altman analysis showed mean mass bias of 1.1g (95%CI: -5.7 to 7.9). Segmental level agreement of scar transmurality between 3D and 2D LGE at the clinical viability threshold of 50% transmural extent was excellent (κ=0.870). Time taken for 3D image acquisition (15.6±1.4 seconds) was just 5% of time required for 2D images (311.6±43.2 seconds) P<0.0001.

DATA CONCLUSION

Single breath-hold 3D mDIXON LGE imaging allows quantitative assessment of MI mass and transmurality, with comparable image quality, in vastly shorter overall acquisition time compared to standard 2D LGE imaging.

Key Words:

Late Gadolinium enhancement, myocardial infarction, ischaemic heart disease, 3D, Gadolinium, LGE

Abbreviations:

FOV	Field of view
IR	Inversion Recovery
LGE	Late gadolinium enhancement
MRI	Magnetic Resonance Imaging
NSA	number of signal averages
PSIR	Phase sensitive inversion recovery
ROI	Region of interest
TE	Echo time
TR	Repetition Time
MI	myocardial infarction
CNR	contrast-to-noise ratio

Introduction

Late gadolinium enhancement imaging (LGE) is the reference standard for myocardial scar assessment by cardiac Magnetic Resonance Imaging (MRI).(1) LGE imaging is both diagnostic for myocardial infarction, and confers prognostic information in patients with ischaemic heart disease.(2, 3) The transmural extent of myocardial infarction delineated by LGE imaging has been shown to accurately identify the likelihood of myocardial functional recovery following revascularisation therapy and is the cornerstone of viability assessment by cardiac MRI.(3)

LGE imaging relies on the altered washout kinetics of gadolinium contrast agents caused by expansion of the interstitial space of damaged myocardium, with a consequent higher signal intensity compared to healthy myocardium demarcating scarred territories. Typically, LGE imaging is performed 10-20 minutes following gadolinium contrast administration by a two-dimensional (2D) inversion recovery (IR) or phase sensitive inversion recovery (PSIR) spoiled gradient echo sequence. 2D IR and PSIR imaging involves a series of repetitive breath holds for the acquisition of each short axis slice to cover the entire left ventricle. Three-dimensional (3D) acquisition methods have been developed in recent years that cover the entire left ventricle in a single breath hold (4–8) or via navigator based free breathing sequences.(9–13) Studies evaluating 3D techniques have suggested the potential use of 3D LGE imaging in a variety of different patient groups.(6, 11, 14–16) Thus far, single breath hold 3D LGE techniques have typically reported a compromise in image quality, mainly due to movement artefacts resulting from the very long breath hold durations required.(4–8) Additionally, typical 3D breath hold durations (>20s) are not possible for some patient populations. Navigator gated methods, where the scan is triggered to synchronise with the patient's breathing pattern, require scan times in the order of minutes and yield no observed improvement in image quality.(9–13) Cardiac MRI scans are typically of long duration and require multiple breath holds, this is both challenging for patients and impacts clinical workflow. Faster scans with less breath holds are sought as

they are more tolerable for patients, and enable more patients to be scanned per list; the challenge though is to retain the excellent image quality that is the strength of cardiac MRI.

A shorter breath-hold 3D LGE acquisition can be enabled by additional acceleration (undersampling) of data acquisition, such as the use of increased parallel imaging factors. However, this naturally yields a loss of signal-to-noise ratio (SNR) which can negatively affect image quality. Therefore, a data acquisition method is needed which provides more SNR so that additional acceleration may be applied whilst maintaining sufficient image quality. In this work, we propose use of the modified Dixon (mDIXON) method for the specific purpose of enabling a 3D acquisition via the additional SNR mDIXON provides.(17)

The Dixon method is an MRI imaging technique that acquires a minimum of two echoes per repetition time (TR) in which fat and water signals are in-phase and opposed-phase. From the two corresponding images, water-only and fat-only images may be calculated.(18) The original Dixon method is limited by B0 field heterogeneity and long scan times. Subsequent three (or more) echo methods were developed that are more robust to field inhomogeneity, and are used in many applications, such as musculoskeletal imaging and in tissue characterisation.(19) However, such Dixon techniques are not routinely used in cardiac imaging (20) because they do not accommodate reasonable breath hold durations.(17, 21) mDIXON (17) was used which has only two echoes per TR allowing shorter scan times, and flexible echo times, both of which make it suitable for cardiac MRI acquisitions with reasonable breath hold durations. In addition to the increase in SNR by moving from 2D to 3D, mDIXON acquisition allows an additional SNR boost – stated as an equivalent number of signal averages (NSA) as described by Reeder et al (22) – which can be traded for higher sensitivity encoding (SENSE) acceleration factors to reduce the breath hold duration. In this work only the water image is used, and additional

clinical utility derived from the presence of the other contrast types (water image, fat image, in-phase image, out-of-phase image) is not assessed.

The aim of this study was to prospectively evaluate a novel mDIXON 3D-LGE imaging sequence (in terms of image quality and acquisition duration) and compare it to a standard 2D sequence for the detection and quantification of myocardial scar in the setting of ischaemic heart disease.

Material and Methods

Study population

Patients with prior myocardial infarction were recruited between June 2016 and June 2017. Myocardial infarction was diagnosed by cardiac biomarkers, electrocardiography and acute coronary angiography at the time of primary PCI. Inclusion criteria were ≥18 years of age, no contra-indication to contrast-enhanced Cardiac MRI, glomerular filtration rate ≥ 60mL/min/1.73m^2. Patients with atrial fibrillation, non-MR compatible implants, renal failure or claustrophobia were excluded. Acute myocardial infarction was defined as occurring within 7 days of the acute coronary syndrome. Chronic myocardial infarction was at least 3 months following the initial presentation of the acute coronary syndrome. The study had appropriate ethical approval and was performed in accordance with the Declaration of Helsinki, and all patients provided informed written consent.

Cardiac MRI data acquisition

Cardiac MRI was performed on a 1.5 Tesla Philips Ingenia system (Philips Healthcare, Best, The Netherlands) equipped with a 24 channel digital receiver coil and patient-adaptive RF

shimming. Imaging acquisition included survey images, assessment of myocardial function using standard SSFP cine imaging (spatial resolution 1.09x1.09x8mm^3, 30 cardiac phases TR/TE 3.0/1.48ms, flip angle 40^o, field of view 360-360mm, SENSE acceleration) and 2D-LGE and 3D-LGE imaging. For LGE imaging, an intravenous bolus of 0.15mmol/kg gadobutrol (Gadovist®, Bayer Inc.) was administered. The optimal inversion time to null the myocardium was determined by a Look-Locker sequence. 2D and 3D LGE imaging were performed 10 minutes following contrast administration. 2D and 3D sequences were performed separately in random order to avoid bias and systematic error caused by contrast washout. Times taken for the 2D and 3D acquisition sequences were recorded. Imaging parameters were:

(i) 2D breath-hold phase sensitive inversion recovery (PSIR) sequences with 12 short-axis slices covering the full LV, thickness 10mm, no gap, repetition time 6.1ms, echo time 3.0ms, flip angle 25^o, field of view 300 x 300mm, matrix 127/256, acquired in-plane resolution 1.59x2.20mm^2 reconstructed to 0.91x0.91mm^2, effective SENSE factor 2.2. The turbo factor was 20 (7 shots) with an acquisition duration of 123.3ms. The receiver bandwidth was 250.2 Hz/px;

(ii) 3D mDIXON sequences with 24 short-axis slices, slice thickness 5mm, repetition time 4.0 ms/echo times 1.21ms and 2.5ms, flip angle 15^o, field of view 300 x 300 x 120mm, matrix 169/384, acquired in-plane resolution 1.83x2.00mm^2 reconstructed to 1.17x1.17x5mm^2, SENSE factors in phase and slice directions were 3 and 2 respectively with effective overall factor 6.86 after oversampling taken into account. The equivalent NSA provided by mDIXON compared to an identical single-echo protocol was 1.52.(22) The turbo factor was 30 (16 shots) with a shot acquisition duration of 148 ms, one shot per heartbeat over 18 beats. The receiver bandwidth was 866 Hz/px. Saturation bands were not used.

Additional 4 Chamber and 2 Chamber 2D LGE images were acquired but not used for analysis/interpretation.

Cardiac MRI data analysis

Cardiac MRI data were analysed quantitatively using commercially available software (CVI42, Circle Cardiovascular Imaging Inc. Calgary, Canada). MR data analysis of 2D and 3D LGE images was performed blinded in random order by a cardiologist (JF with 6 years in cardiac imaging). For 15 patients, quantitative analysis was performed again 4 weeks later to assess intra-observer variability, and to assess interobserver variability by a second (GF with 6 years in cardiac imaging) and third cardiologist (LB with 8 years in cardiac imaging). For volumetric analysis, endocardial borders were traced on the LV cine stack at end-diastole and end-systole to calculate end diastolic volume, end systolic volume (ESV), stroke volume (SV) and ejection fraction (EF). Contours were traced to exclude papillary muscles and trabeculations.

Qualitative LGE assessment

Image quality was defined on a scale of 1-4 (4=non-diagnostic, 3=acceptable diagnostic quality, 2=good quality, 1=excellent quality). For scores other than 1, the reason for impaired quality was categorized as a) motion or blurring artefacts, b) low contrast or high noise, c) inadequate myocardial nulling, or d) wrap around/folding artefacts. Additionally, both 2D and 3D LGE images were evaluated for the presence of ventricular cavity thrombi.

Quantitative LGE assessment

Quantitative assessment of the myocardial scar burden was performed using the semi-automated full-width half-maximum method (threshold of 50% of the maximum intensity within the scar) which has been proposed as the most reproducible method (23, 24). On both the 2D and 3D LGE short-axis images endocardial and epicardial contours were manually outlined (excluding papillary muscles); manual delineation of two separate user-defined

regions of interest (ROIs) were then made on an LGE short axis slice where infarcted myocardium was present. One ROI was drawn in remote myocardium (where no scar was present); a second ROI was drawn around hyperenhanced myocardium where infarcted myocardium was present. Automated calculations for the remaining LV short axis LGE stack based on these two ROIs were then performed. Scar tissue mass was calculated (grams). Scar tissue percentage and transmurality were calculated automatically for each segment of 16 segments of the 17 segment model proposed by the American Heart Association (excluding the apex).(25) Infarct transmurality was automatically calculated by the analysis software and then graded using a 5-point scale from the derived quantitative result (0=no scar, 1=1-25% transmural extent, 2=26-50% transmural extent, 3=51-75% transmural extent and 4=76-100% transmural extent). Time taken for image acquisition of the entire LV for 2D and 3D was recorded (this included time taken for pauses between breath holds for each LV slice).

CNR measurements

In 25 consecutive patients CNR measurement was performed, a single slice containing both hyperenhanced and healthy myocardium was selected and for this corresponding slice a dedicated noise scan (identical pulse sequence without excitation pulses) was performed immediately afterwards in order to assess the noise levels.(26) Regions of interest (ROI) were drawn on the normal 3D and 2D LGE images in areas of hyper-enhancement, a remote area of normal appearing myocardium, and in blood pool. ROIs contained at least 30 pixels, aside from the areas of hyper-enhancement where size of the ROI was governed by the size of the scar. A further ROI covering the entire LV myocardium was drawn on the corresponding noise image, the standard deviation of this measurement was then used to calculate contrast-to-noise (CNR) measurements. CNR was calculated as the ratio of the difference in mean signal intensity between ROIs on the LGE images to the standard deviation of signal intensity in the whole LV

ROI from the separate noise image. (The MR system noise level is measured and not organ/image level).

Statistical analysis

Continuous variables are expressed as mean±SD. Categorical variables are expressed as N (%) or proportions. Normality of data was tested using a Shapiro-Wilk test. Paired two-tailed student t-test and the Wilcoxon signed rank test were used as appropriate to compare continuous variables. $P<0.05$ was considered statistically significant. Pearson correlation, linear regression and Bland-Altman analysis were used to show agreement between the 2D and 3D acquisition sequences for scar tissue mass and scar tissue percentage of LV mass. Coefficient of variation was used to assess interobserver and intraobserver variability for scar tissue mass. Cohen κ statistic was used for interobserver agreement for the image quality score. Cohen κ statistic was also used to measure agreement between the 5 point grading of transmurality and the agreement for the binary detection of viable/non-viable segments. Statistical analysis was performed using IBM SPSS® Statistics 22.0 (IBM Corp., Armonk, NY).

Results

Demographics

A total of 92 patients (80/92 male, mean age 60.9±11.0 years; BMI 26.7±4.2kg/m^2; LVEDV 175.3±60.8ml; LVEDVi 90.5±31.2ml/m^2; LVESV 97.1±55.2ml; ejection fraction 47.2±12.3%) were prospectively examined. Of these, 53 patients had chronic (46/53 male, mean age 59.9±10.9 years; BMI 26.7±4.2kg/m^2; ejection fraction 47.9±13.9%) and 39 patients had acute (male 34/39, mean age 62.3±11.2 years; BMI 26.8±4.25kg/m^2; ejection fraction

46.3±9.9%;) myocardial infarction. All 92 patients were scanned with both 2D PSIR and 3D mDIXON LGE acquisitions without complication resulting in a total of 1,472 segments per technique.

Image quality

Image quality was graded as excellent for 65/92 (70.6%) of the PSIR images, and 63/92 (68.5%) of the 3D images. No dataset was deemed non-diagnostic in either 3D mDIXON or 2D PSIR images (score of 4). There was no statistically significant difference in image quality between 3D and 2D LGE (1.4±0.6 vs. 1.3±0.5, P=0.162) (Figure 1). Table 1 shows the reasons why image quality was scored other than excellent for LGE sequence. Image quality impairment was predominantly attributed to blurring/motion (15/27) in the 3D datasets. Interobserver agreement for image quality was good for both observers (between 1 and 2 κ = 0.615 and between 1 and 3: 0.706).

CNR

The CNR of scar to blood was not significantly different between 3D and 2D LGE techniques respectively (16.1±10.5 vs. 18.8±12.4, P=0.337). The CNR of scar to remote myocardium (36.4±19.8 vs. 56.6±20.8, P=0.001) and CNR of remote myocardium to blood (21.3±12.9 vs. 41.0±17.0, P<0.001) were significantly lower by 3D mDIXON compared to 2D PSIR.

Quantitative LGE Analysis

3D mDIXON compared to 2D PSIR identified statistically significantly more absolute scar tissue mass (18.9±17.5g vs. 17.8±16.2g, P=0.03) but no significant difference in scar tissue when expressed as a percentage of LV mass (13.4±9.9% vs. 12.7±9.5%, P=0.07). Bland-Altman analysis of absolute 3D scar tissue mass compared to 2D scar mass showed a small

positive bias of 1.1g (95%CI: -5.8 to 8.0); likewise for percentage scar tissue mass of 0.7% (95%CI: -4.0 to 5.5) (Figure 2a and 2b).

3D mDIXON identified significantly greater scar tissue mass compared to 2D PSIR in acute myocardial infarction (23.3±19.5g vs. 21.5±17.3g, P=0.012) and similar scar tissue mass in chronic myocardial infarction (15.6±15.3g vs. 15.0±14.9g, P=0.125).

There was strong and significant correlation in scar tissue mass (r=0.981 P<0.001) and scar tissue percentage between 3D and 2D acquisitions (r=0.970 P<0.001) (Figure 4a and b).

A total of 5 patients were identified to have interventricular thrombi in both 2D and 3D acquisitions, no thrombi were visible in only 2D or 3D images (Figure. 3).

Interobserver coefficient of variability was excellent for both 3D and 2D LGE techniques in terms of scar mass (between JF and GF 3D 7.0%; 2D 4.9%; and between JF and LB 3D: 5.8% 2D: 7.3%) and scar tissue percentage (between JF and GF 3D 7.1%; 2D 5.2% and between JF and LB 3D: 6.0% and 2D: 7.8%). Intra-observer coefficient of variability was also excellent for both 3D and 2D LGE for scar mass (3D 5.3%; 2D 4.8%) and scar tissue percentage (3D 5.4%; 2D 5.3%).

Segmental and transmurality assessment

There was excellent agreement (κ=0.870; Pearson's r=0.956, P<0.0001) between the 3D and 2D LGE techniques based upon a segmental scar transmurality threshold of 50% (the threshold typically used for clinical viability status determination); there was also good agreement between the two techniques for the overall 5-point transmurality score κ = 0.736 (Pearson's r = 0.922 P<0.0001). Results of the segmental 5 point transmurality assessment was 1±1.1 for 2D and 1±1.1 and for the binary 50% viable threshold was 0.1±0.3 for 2D and 0.1±0.3 for 3D.

Image acquisition time

Time from contrast injection to image acquisition were as follows: 2D 10.54 ±0.59minutes/seconds 3D 13.06 ±3.12minutes/seconds P<0.0001. Time taken to acquire LGE images was much shorter for 3D mDIXON compared to 2D PSIR (15.6±1.4 vs. 311.6±43.2 seconds, P<0.0001). For PSIR, 1 slice was acquired per breath hold; average breath hold duration for each PSIR slice acquisition was 10.7±1.2 seconds.

Discussion

The main findings of this study are i.) 3D mDIXON LGE offers comparable image quality for the evaluation of ischaemic scar compared to 2D LGE imaging; ii.) quantitative assessment of 3D mDIXON LGE of scar mass and transmurality has high agreement with 2D LGE imaging; iii.) 3D mDIXON LGE provides a vastly shorter overall scan duration in an acceptable single breath-hold time compared to 2D LGE.

We have used only the water-image calculated from the mDIXON-acquired data. The purpose of the study was to use mDIXON to enable 3D LGE in a reasonable breath hold duration, not to compare the utility of the various contrasts a Dixon-based scan can produce. Others have demonstrated clinical utility of Dixon fat-image, for example in detection of lipomatous metaplasia in scar.(27–29) Similar additional clinical value may be available with the 3D mDIXON method used here. Lapinskas et al. describe acquisition of a long axis 3D mDIXON LGE in a single breath hold, this however is not easily comparable to routine 2D PSIR short axis LGE imaging.(27) Short axis mDIXON LGE imaging is also described but it is limited in that it requires 2 breath holds, thus leading to increased scan duration and likely corruption of data from different breath hold positions and increasing the potential of breathing artifacts.(27)

It is possible to increase the SNR of a single-echo 3D non-Dixon scan by lowering the receiver bandwidth, which might also be considered as an enabler for a 3D LGE protocol within a sufficiently short breath hold duration. However, lowering the receiver bandwidth will also increase the TE, and thus the TR, which increases the acquisition (shot) duration, which would increase blurring due to cardiac motion. In order to shorten the shot again a higher number of readouts is needed necessitates a longer breath hold. mDIXON affords additional SNR without this consequence, which was confirmed by Bloch simulation built into the MR system.

Current 2D LGE imaging techniques are highly discriminatory for the diagnosis of myocardial infarction and form the basis of myocardial viability imaging by Cardiac MRI.(1, 2) Thus, high image quality is of paramount importance when introducing a new LGE technique, as current 2D methods are so effective. The in-plane resolution of the 2D scan was higher than the 3D, in our study the 2D scan was clinically optimised and established and we wanted to directly compare with it; the 3D scan was separately optimised, balancing resolution and acceleration. Typically, 3D LGE techniques have been shown to have compromised image quality compared to 2D techniques, though differences in qualitative ratings often do not reach significance.(6, 7, 15, 30, 31) Our findings were that categorical image scoring of the 3D mDIXON sequence was in fact very comparable to the 2D LGE sequence. This is despite the lower CNR for myocardium to scar and myocardium to blood seen in the 3D images compared to the 2D images. This is likely due to the similar CNR for scar to blood seen between 3D and 2D images; this parameter is arguably more important as poor contrast between scar and blood pool can make it difficult to identify the endocardial border so consequently compromising accurate assessment of scar size and identification of sub-endocardial infarction. Furthermore, despite the CNR differences recorded this does not make an impact on the automated quantitative LGE assessment. PSIR reconstruction used in the 2D protocol mitigates sensitivity of the sequence to the precise inversion time (TI) set by the user to null normal myocardium, which varies from

patient to patient. Since the TI required to null normal myocardium changes during contrast washout over the scanning time of the 2D stack of slices, the flexibility PSIR allows is helpful. PSIR reconstruction was not used in the 3D mDIXON protocol, but since the whole stack of slices is acquired in just one breath hold, the effect of contrast washout between slice acquisitions is not an issue. There is no theoretical obstacle to combining the 3D scan we used with PSIR in further work. However, note that since PSIR requires 2 beats, a "3D mDIXON PSIR" scan duration might get significantly longer again (the second beat is used to watch the magnetisation recover and so determine whether the acquisition in the first beat was above or below the null point).

Scar burden by LGE imaging has been shown to be proportional to likelihood of major adverse cardiovascular events and offers prognostic information in patients with ischaemic heart disease.(2) Of note, the 3D mDIXON technique identified significantly more scar compared to the 2D sequence. This is likely a result of the contiguous slices which a single breath hold 3D scan affords, compared to the series of breath holds for a 2D stack of slices which can be affected by inconsistent breath hold position even in expiration as used in this work. The 5mm reconstructed slice thickness used in the 3D mDIXON technique compared to the 10mm used in the routine PSIR sequence may also aid perception of scar; a similar result was described by Yin et al who also used a thinner slice thickness in the 3D acquisition compared to the 2D.(13) The thinner slice thickness may help identify smaller infarcts and delineate the true border of the scar being imaged.

The transmural extent of infarction has been shown to directly relate to the likelihood of functional recovery following revascularisation. LGE imaging consequently has a grade A rating to determine myocardial viability prior to revascularisation in the ACCF/AHA/SCMR

appropriate use criteria and is the third highest indication for Cardiac MRI in Europe.(32, 33) Therefore, accurate discrimination of transmural scar extent is important when considering a new LGE sequence. Previous studies have showed variable results, though more recent studies have shown reasonable agreement.(5, 6, 15, 34, 35) The 3D mDIXON technique showed strong agreement with the 2D sequences. Statistical significance was seen in scar mass seen by 3D compared to 2D in the acute but not in the chronic infarctions, overall however there was no difference in viability assessment or the overall % LV mass. This is potentially a reflection of the smaller sample size of acute patients, compared to the overall study group. Furthermore, although the difference in scar tissue mass reached statistical significance, there is in fact little clinical significance in the difference between the two sequences when expressed as a percentage of LV mass (0.7% difference).

Thus far, a significant limitation in the utility of 3D LGE imaging has been that despite a significant reduction in overall scanning time to acquire an entire short axis stack, individual breath holds remain overly long leading to image degradation or scan failure.(6, 15) In the patient groups proposed to benefit from shorter scanning times (those with cardio-respiratory disease and those unable to perform long breath holds) this increased breath hold duration negates the perceived advantages. Goetti et al., noted a doubling of blurring artifacts due to breath hold durations of 26.7±4.4seconds compared to a routine 2D inversion recovery sequence.(6) Bratis et al., observed no increase in blurring artifacts, despite 3D acquisitions requiring a breath hold duration of 22-27seconds, however 60% of patients demonstrated no pathology and comment is made that respiratory motion was the main cause of 3D imaging failure (10/57cases).(15) Various methods have attempted to overcome the long 3D breath hold duration; Bauner et al., used a 3D acquisition sequence that used 3 consecutive slabs to cover the entire ventricle, however this only resulted in a halving of the acquisition time and

generated new artefacts due to misalignment of the 3D volume stacks as a result of variations in breath hold position.(35) Alternatively, navigator gated 3D sequences can be acquired in a free-breathing manner; however, navigator gated sequences can lead to prolonged scan times due to navigator inefficiency, with potential scan failure due to drift of respiratory pattern leading to impaired image quality as the inversion time required to null myocardium alters.(9–13) Bizino presented a free breathing motion corrected 3D sequence but this was not compared to 2D LGE for image quality, and still took over 3minutes for acquisition. (36) Recently compressed sensing techniques have been proposed as a method to reduce scanning times,(37) however recent publications of 3D LGE using compressed sensing still require scanning times between 3- 7 minutes and have not been compared to currently used 2D sequences.(38, 39) Moreover, the 3D mDIXON method described here can be combined with the product "Compressed SENSE" on the MR system used for this work for further acceleration and reduction in breath hold duration. Preliminary tests suggest a breath hold duration of just 11 seconds may still preserve sufficient image quality. More extreme methods have also been proposed to overcome the prolonged breath hold durations by increasing the patient's ability to breath hold by supplemental oxygen and hyperventilation techniques, however this approach appears incongruous if this requires training time and resources.(40) Our data showed no failed 3D scans in any of the 92 patients, some with significant left ventricular dysfunction, resulting in diagnostic quality studies (none deemed non-diagnostic) that was obtainable in a single breath hold. Our study has shown that a breath hold duration (15.57±1.361seconds) using the 3D mDIXON technique is sufficiently short to enable most patients to complete, as demonstrated in both acute and chronic MI patient groups.

A limitation of our study is the difference in slice thickness between the 2D and 3D acquisitions. We chose to use the slice thickness currently used in our 2D clinical scanning

sequence and ongoing clinical trials at our establishment, and used the default 5mm slice thickness on the 3D mDIXON sequence as it was apparent from pilot data that this achieved acceptable SNR within a sufficiently acceptable breath hold duration. Additionally, the 3D LGE scan does not employ a PSIR reconstruction, and so the image contrast is more sensitive to correct inversion time selection. A further limitation is that there is no pathology based reference standard to compare the true size and presence of myocardial infarction from the quantitative analysis of either 2D or 3D LGE approaches. A further limitation is the difference in time from gadolinium injection to image acquisition between the 2 sequences which is inherently impossible to overcome, a pragmatic approach of randomizing test order is what comparable studies on this topic have done previously (6, 7, 14, 15) and although not perfect is an attempt to reduce the effect on image quality of contrast washout from the blood pool.

In conclusion, single breath-hold 3D mDIXON LGE imaging allows quantitative assessment of scar tissue burden and transmurality, with comparable image quality, in a significantly shorter acquisition time compared to standard 2D LGE imaging.

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Tables

Table 1. Reasons for impaired subjective image quality ratings (for any rating other than excellent)

	2D PSIR	3D mDIXON
Motion /blurring	7	15
Low contrast/noise	7	4
Nulling	6	5
Folding artefact	4	3
Total	24	27

Figure Legends

Figure 1. Short axis LGE images from (A) basal, (B) mid-ventricular and (C) apical slices from 2D PSIR acquisitions, and (D) basal, (E) mid-ventricular and (F) apical slices from 3D mDIXON acquisitions of the same patient showing antero-lateral scar following a left anterior descending artery territory infarction.

Figure 2. Bland-Altman analysis of 3D and 2D LGE acquisitions (±1.96 Standard deviations – dashed lines) for assessment of (A) absolute scar tissue mass and (B) scar tissue as a percentage of LV myocardial mass.

Figure 3. Laminated thrombus in a chronic myocardial infarction in an apical slice of a (A) 2D PSIR acquisition and (B) 3D mDIXON acquisition of the same patient (red arrows demarcate the thrombus).