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3D late gadolinium enhanced cardiovascular MR with CENTRA-PLUS profile/view ordering: Feasibility of right ventricular myocardial damage assessment using a swine animal model

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Abstract

Aims—To develop a high-resolution, 3D late gadolinium enhancement (LGE) cardiovascular magnetic resonance imaging (MRI) technique for improved assessment of myocardial scars, and evaluate its performance against 2D breath-held (BH) LGE MRI using a surgically implanted animal scar model in the right ventricle (RV).

Methods and Results—A k-space segmented 3D LGE acquisition using CENTRA-PLUS (Contrast ENhanced Timing Robust Acquisition with Preparation of Longitudinal Signal; or CP) ordering is proposed. 8 pigs were surgically prepared with cardiac patch implantation in the RV, followed in 60 days by 1.5 T MRI. LGE with Phase-Sensitive Inversion Recovery (PSIR) were performed as follows: 1) 2DBH using pneumatic control, and 2) navigator-gated, 3D free-breathing (3DFB)-CP- LGE with slice-tracking. The animal heart was excised immediately after cardiac MR for scar volume quantification. RV scar volumes were also delineated from the 2DBH and 3DFB-CP-LGE images for comparison against the surgical standard. Apparent scar/normal tissue signal-to-noise ratio (aSNR) and contrast-to-noise ratio (aCNR) were also calculated.

3DFB-CP-LGE technique was successfully performed in all animals. No difference in aCNR was noted, but aSNR was significantly higher using the 3D technique ($p < 0.05$). Against the surgical reference volume, the 3DFB-CP-LGE-derived delineation yielded significantly less volume quantification error compared to 2DBH-derived volumes ($15 \pm 10\%$ vs $55 \pm 33\%$; $p < 0.05$).

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Conclusion—Compared to conventional 2DBH-LGE, 3DFB-LGE acquisition using CENTRA-PLUS provided superior scar volume quantification and improved aSNR.

Keywords

myocardial infarction; late gadolinium enhancement MRI; viability imaging; navigator; breath-hold

1. INTRODUCTION

Cardiovascular magnetic resonance imaging (MRI) using gadolinium-based (Gd) contrast agent injection and late gadolinium enhancement (LGE) has been established as a non-invasive imaging standard for the identification of myocardial infarction or scar and the assessment of myocardial viability in patients with non-ischemic and ischemic heart diseases (1-5). Conventional LGE is performed using an inversion-recovery (IR) magnetization preparation followed by fast field echo (FFE) or spoiled gradient echo (SPGR) imaging under multiple breath-holds in 2D (2DBH). Recently, free-breathing 3D (3DFB) LGE sequences have been proposed as an alternative to the 2DBH approach, as they provide significantly higher spatial resolution, especially in the through-plane direction (6,7). These acquisition strategies employ 1D pencil-beam navigator echoes to monitor the diaphragm motion to address respiratory motion. Nguyen et al. has compared the 3D navigator-gated IR-LGE sequence directly with standard 2DBH-IR-LGE, and have shown good agreement in scar volume quantification (6).

3D LGE acquisitions are sensitive to contrast washout in the myocardial scar region during the acquisition, which may last as long as several minutes. Therefore, the order of k-space acquisition with respect to the total 3D volumetric imaging time requires additional consideration with respect to the timing in acquiring such k-space using a custom view or profile ordering scheme.

One particular view/profile order implementation, known as CENTRA-PLUS: the acronym for Contrast ENhanced Timing Robust Acquisition with Preparation of LongitUdinal Signal, was originally designed as a dynamic key-hole approach for liver imaging (8), and was customized as a k-space segmented acquisition for use in a high-resolution coronary MR angiography (9). This 3D Cartesian k-space acquisition ordering may be suitable for other high-resolution, ECG triggered and k-space segmented acquisitions, such as 3D-LGE-MRI, which may benefit from rapid acquisition of central k-space within a short duration subset of the entire scan, and the acquisition of the remaining peripheral k-space over the duration of the scan – minimizing any averaging effects of the LGE contrast over scan duration due to gradual washout from the myocardium ~12-20 min post-Gd injection.

In this study, we propose a free-breathing (FB), high-resolution 3D-LGE-MRI sequence that employs navigator slice-tracking and a k-space segmented CENTRA-PLUS (CP) profile ordering for LGE imaging, and evaluate this sequence's ability to quantify scar tissues implanted in the right ventricle (RV) in 8 surgically prepared porcine hearts. This 3DFB-CP-PSIR-LGE approach, which yields a significantly higher through-plane resolution, is compared against the conventional 2DBH-PSIR-LGE sequence in its ability to detect and

quantify scar volume measurements against a surgically-measured animal model reference standard.

2. METHODS

This study protocol was approved by the Institutional Animal Care and Use Committee of the University of Chicago. All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals, published by the National Institutes of Health (1996).

2.1 Porcine Model Preparation

Eight female mixed breed of Yorkshire and Landrace swine (20-30 kg) were anesthetized and placed in a left recumbent position, exposing the RV via a right anterolateral thoracotomy in the fourth intercostal space. A tangential clamp was placed on the RV free wall, and a circular region was incised in full thickness and substituted with a Dacron-based cardiac patch (25-30 mm in diameter), affixed onto the RV by suturing (10). Routine chest closure was performed after this procedure.

2.2 Cardiac MR Protocol

Cardiovascular MRI was performed 7-9 weeks (59 ± 7 days) after RV patch implantation. Fibrotic scar tissue was allowed to grow over the patch during this period. The animals were imaged on 1.5T clinical MRI hardware (Philips Achieva, Best, The Netherlands) using a Cardiac MR (CMR) protocol which included the following techniques: 1) Stack of cine-CMR images acquired in the short axis plane; 2) First-pass perfusion images acquired on 6 short axis (SA) slices each over 2R-R (~1200-1500 ms) ECG-gated intervals. Contrast injection was performed using 0.1 mmol/kg of gadobenate dimeglumine (Gd-BOPTA) (Multihance; Bracco Diagnostics, Inc. Princeton, NJ) during this acquisition. 3) LGE Look-Locker inversion time (TI) scout performed 12-15 min after the contrast injection, followed by 4) 2DBH-LGE, and immediately by 5) the proposed 3D-LGE with a 10-30 ms adjustment of TI.

The optimal TI for nulling healthy myocardium (range 260-350 ms) was determined by visual inspection on the scout Look-Locker prior to 2DBH imaging. This ballpark approximation is consistent with the kinematics associated with Gd-BOPTA, which has a reported blood-pool half-life of 1.2-2 hours post injection (11), and has been previously shown to yield an approximate 20-30 ms increase in myocardial TI per 5-minute increments during the 10-25 minutes post-injection period (12) for the injected concentration. No separate LL scout was played out immediately prior to the 3D acquisition.

2.3 3D Free-Breathing CENTRA-PLUS (FB-CP) LGE Sequence Acquisition

Figure 1a shows the schematics of the implemented ECG-triggered, navigator-gated, phase-sensitive inversion recovery (PSIR) LGE sequence (14), which enforced a 2R-R interval between each inversion pulse, and acquired a second volume to determine the sign of the magnitude image. The segmented, free-breathing CENTRA-PLUS (further abbreviated to FB-CP onwards) ordering has two design considerations. First, this ordering allows

acquisition of central k-space data timed to be concentrated at a specific subset of the 3D volumetric acquisition (eg. during the first 10% of the scan), thereby minimizing the effect of any dynamic change in LGE contrast over the scan duration. Second, the ordering synchronizes the acquisition of true k-space center to the initial FFEs, or the beginning of the acquisition window. This results in the acquisition of a centric-and-out acquisition from the ky-axis towards higher kz-encoding regions through the segmented acquisition window. This is achieved by separating out the inner and outer elliptical k-space into two separate regions, whose sizes are determined by the operator-specified inner ratio against the total (inner + outer) region (**Figure 1b**). The CP profile ordering approach acquires the inner ellipse in a centric order from the true center and outwards for each quadrant of the ky-kz coordinate table, for which the k-space acquisition always starts from the ky-axis at the beginning of the acquisition window (**Figure 1c**). Here, the color jet (1c left image) corresponds to the segment within each acquisition window comprised of ~20 FFE readouts. The middle image in 1c shows the representative acquisition for each of the inner and outer k-space regions. The rightmost image in 1c shows the full color scheme of the 3D volume with respect to the timing within the acquisition window. This CENTRA-PLUS approach can be combined with different navigator gating strategies for each of the inner and peripheral elliptical regions (eg. a conservative window for the inner k-space, and a more relaxed window for the outer region). The additional animation file available on-line demonstrates this k-space segmented CP-profile ordering over the scan duration.

For free-breathing swine cardiac MRI employing the 3DFB sequence with k-space segmented CP ordering, the first swine was prescribed with a 1D pencil-beam navigator in the foot-head direction, resulting in scar-mimicking artifacts. Subsequently, for swines #2-8, the protocol was modified to set up the 1D pencil-beam navigator positioned in the anterior-posterior direction across the anterior chest wall below the position of the heart to monitor abdominal chest movement, accounting for the difference in the pig anatomy that differed from human anatomy, and exhibited relatively less superior-inferior motion of the heart and substantially more anterior-posterior motion. For reference, the motion range between the pig's chest movement in the AP direction, as well as its position of the heart at the level of mid-ventricular slice, were acquired every heartbeat over a 30-60 second period prior to LGE in pigs 1-4, from which the navigator slice-tracking motion range scaling parameter was fixed to $r = 0.4$ for swines #2-8 (15) for all navigator prescription in the AP direction. A non-selective adiabatic inversion pulse was used for contrast preparation, which was followed by a navigator restoration pulse immediately after the inversion to restore the navigator signal for the subsequent navigator acquisition prior to imaging (16). An accept/reject algorithm was employed using a 3 mm gating window on the CENTRA inner profiles, while a larger 5 mm profile (#2-8), and 7mm (#1 in AP direction) were used for outer k-space acquisition.

The typical imaging parameters for the 2DBH-PSIR-LGE sequence were as follows: FOV $330 \times 330 \text{ mm}^2$; in-plane resolution: $1.4 \times 1.9 \text{ mm}^2$; slice thickness = 10 mm with no slice gap; sequential view order; interleaved PSIR acquisition of each 2D volume at every other heartbeat; 8 short-axis slices from base to apex. Repetition Time (TR) = 4.7-4.9 ms; Echo Time (TE) = 2.3-3.4 ms; number of Fast Field Echoes (nFFE) per diastolic acquisition

window = 17-21; acquisition window duration = 100 ms; flip angles (FA) = 30° (at 1st R-R), 5° (at 2nd R-R); Sensitive Encoding (SENSE) with acceleration factor R=2 was used. Each breath-hold acquisition was completed within 8 or 10 R-R cycles; sufficiently within the time of the respiratory-induced breath-hold. The 3DFB-CP-PSIR-LGE sequence was matched for coverage of the same short-axis prescription as the prior 2D sequence, and had the following parameters: FOV 330×330×80 mm³; spatial resolution: 1.9×1.9×4.0 mm³; 20 slices were acquired. Repetition Time (TR) = 4.3-4.9 ms; Echo Time (TE) = 3.4 ms; number of Fast Field Echoes (nFFE) = 21-25; acquisition window = 100 ms; flip angles (FA) = 30° (at 1st R-R), 5° (at 2nd R-R); SENSE with acceleration factor R=2 was used. The CENTRA-PLUS inner/outer k-space ratio was set to 15/85%, which corresponded to 12-15 accepted heart beats for the inner window acquisition, where a total of 90-100 heart beats were required. This variation was observed due to differences in TR that were affected by the geometry – notably the double-oblique orientation of the short-axis prescription tailored to each imaged swine, which allowed the minimal TR to vary between 4.3-4.9 ms.

2.4 Reference Volume Calculation

After the imaging protocol was completed, the pig heart was excised by the cardiac surgeon, and its scar volume was directly measured using an approximate ellipse model (**Figure 2**). Volume calculation required the major and minor axes lengths, accounting for varying thickness across the elliptical short and long axes as shown in the dotted yellow lines in this figure. In this study, this calculation was repeated three times for intra-measurement variability using both the tissue sample and photographs taken by the surgeon for measurement purposes. The final measurement was reported as the average across three independent measurements.

2.5 Data Analysis

Quantitative volume assessment of the RV scar region was performed on 2DBH and 3DFB-CP short-axis volumes by an experienced cardiovascular MR physician who was blinded to the study design (ie. 2D vs 3D LGE assessment of scar volume size) and explicitly instructed to determine the location of the scar by delineating its *volume in entirety*. Both 2D and 3D LGE images, as well as the first-pass perfusion and cine images per each case are presented to the reader to guide the manual delineation of the scar volume. The manual scar volume delineation was performed in a randomized, interleaved, or even a joint manner at the discretion of the clinician. Additionally, during this delineation step, the reader was blinded to the ex-vivo measurements from the surgical reference standard, as well as the volume display to prevent cross-matching. We note that in this study design, the reader was not blinded to the 2D and 3D imaging techniques, as it was trivial for any reader to distinguish between 2D and 3D methods; hence we provided a simple instruction to have the clinician concurrently derive the scar volumes while allowing access to all clinically available images, including the cine and perfusion images. All final tracings were performed on the PSIR image derived from the magnitude and phase images using the Philips Workstation (Best, The Netherlands).

The workstation automatically calculated the delineated volume by summation of the delineated area on each slice accounting for both slice thickness and slice gap in multiple 2D

image slices, which was set to 0 mm in this study. In the 3D volume, the total volume was calculated as the sum of all identified voxel. A custom tool built in Matlab (The Mathworks Inc. Natick, MA) was used for additional visualization of the RV patch geometry (17). A semi-automated, threshold detection using standard region-growth was incorporated for scar volume quantification (where a standard ± 5 std region-of-interest (ROI) signal intensity cut-off) was also employed in this reformatted geometry for algorithmic refinement/validation of the manually delineated ROI measurements.

SENSE parallel imaging ($R=2$) was employed in both acquisitions, however, a dedicated fast noise scan was not obtained for the appropriate calculation of true signal-to-noise (SNR) and scar-to-myocardium contrast-to-noise (CNR) measurements (18). Therefore, apparent SNR and CNR, denoted as aSNR and aCNR, were calculated by normalizing the signal intensity values in each ROI by the standard deviation of ROI measured in a homogeneous region of the lung cavity. The clinician delineated the cavity ROIs at approximately the same lung region between the 2D and 3D. The cavity ROIs were assumed to be the sum of air signal and Gaussian white noise, which was verified on a per-ROI basis, therefore allowing its use as a sufficient surrogate to the true Gaussian noise in the SENSE-accelerated reconstructed volumes.

2.6 Statistical Analysis

All measurements are expressed as mean $\pm$ SD. Pearson's Correlation and Bland-Altman analysis were performed to compare 2D and 3D LGE-derived volume measurement data against the surgical reference volume. The signed volume differences between the surgical reference and the delineated 2D- and 3D-derived measurements, as derived from the Bland-Altman analysis would indicate a systematic over- or underestimation occurring in the derived ROIs. A one-sampled Kolmogorov-Smirnov (KS) test (19) was performed on the lung cavity ROI signal intensity to evaluate whether these pixel-wise signal distribution values satisfied a normal (ie. Gaussian) distribution at the 5% significance level. P values of less than 0.05 were considered statistically significant.

3. RESULTS

Both 2DBH-PSIR and 3DFB-CP-PSIR-LGE cardiac MR were completed successfully in all eight pigs. Every 2DBH scan was completed within 8-10 R-R pneumatic breath-hold intervals in under 8 seconds at the swine heart rate (80-116 BPM), while the acquisition time for the 3DFB-LGE scans were as follows: 317 seconds (or 5.2 minutes) for Swine #1 with the FH-direction navigator, and 217 ± 32 seconds (or 3.6 ± 0.5 minutes) for Swine #2-8 with the modified AP-direction navigator. The derived navigator gating efficiency was: 43% (Swine #1), and $58 \pm 2\%$ (Swine #2-8). We note the navigator efficiency range for #2-8: 55-62%, and its standard deviation (2%), which were consistent with the fixed breathing induced by the pneumatic control system. All acquired images were diagnostic with regard to the presence of myocardial scar tissue. **Figure 3** shows two example of the acquired PSIR-LGE at matched slice between the 2D and 3D volumes showing the scar. **Figure 4** shows another example of 2D volumes and the corresponding 3DFB-CP-PSIR-LGE

composite volumes, showing the scarred region, as well as the contour model derived from the 2D and 3D MRI data, respectively.

Table 1 summarizes the measurements between the proposed 3DFB-CP and the 2DBH PSIR-LGE acquisitions. The mean and standard deviation of the surgically derived Volume_{REF} was 4.3±3.0 mL. The measured volume error of the scar region, calculated as $100\% \cdot |\text{Volume}_{\text{MRI}} - \text{Volume}_{\text{REF}}| / \text{Volume}_{\text{REF}}$ was: 15±10% (3DFB vs surgical ref) versus 55±33% (2DBH vs surgical ref) ($P < 0.0005$ in $n=7$ visualized by both methods). The intra-observer measurement variability between the three surgical reference measurements was considered to be within the round-off error ($< 0.1 \text{ cm}^3$), as no two calculations in the same sample yielded measurement differences over 0.2 cm^3 . The semi-automated volume quantification yielded statistically comparable scar measurements as the manually delineated measurement for both 2D and 3D ROIs ($P > 0.9$ for both 2D and 3D). Measurement differences were: 2D: $0.04 \pm 0.2 \text{ mL}$, and 3D: $-0.04 \pm 0.2 \text{ mL}$, both within margin of rounding precision error. The remaining analysis was performed using the clinician-delineated measurements provided by the standard clinical workstation.

The Pearson's correlation plot and Bland-Altman analysis of the scar volume measurements (Surgical Reference vs 3D; Surgical Reference vs 2D) are shown in **Figure 5**. The 3DFB-CP data showed a strong correlation with the surgical reference volume ($R^2 = 0.97$; **Figure 5a**). However, the 2DBH-derived volume measurement data showed no correlation ($R^2 = 0.02$; **Fig 5c**), and demonstrated its inability to accurately capture small scar volumes less than $5\text{--}10 \text{ cm}^3$. From the Bland-Altman analysis data, the signed volume differences against the surgical reference from each of 2D and 3D ROIs were non-significant (2D: $P = 0.6$, 3D: $P = 0.7$), indicating that there was no systemic over- or underestimation by both measurements.

Apparent signal-to-noise ratio of scar and scar-to-healthy myocardium contrast-to-noise ratios, aSNR and aCNR, as measured on the composite PSIR-volumes were as follows (3DFB vs 2DBH). aSNR: 38 ± 14 vs 25 ± 13 , which was significantly higher with 3D ($p < 0.05$). aCNR: 39 ± 17 vs 25 ± 11 , which was statistically non-significant ($p = 0.06$). We note the signs of the PSIR reconstruction values were accounted for in this evaluation, which allowed negative magnitude due to negative longitudinal signal at the time of acquisition according to the PSIR scheme. All selected cavity ROIs were drawn in the same area of the lung in the composite image, and satisfied the KS test – which indicated that the measured cavity ROIs had a normal distribution of white noise signal in the selected regions.

4. DISCUSSION

In this study, we have successfully demonstrated the feasibility of the CENTRA-PLUS ordering as an effective 3D free-breathing PSIR LGE acquisition technique to detect and measure the size of surgically implanted scar tissue in a right ventricular animal scar model using cardiac patches. While the conventional 2D LGE method was unable to accurately quantify the volumes of the implanted scar tissues, the proposed 3D approach yielded measurements comparable to the surgically determined reference standard. Furthermore, the proposed 3D LGE approach had significantly better spatial resolution and higher aSNR when compared to the conventional 2D technique.

The k-space segmented CENTRA-PLUS acquisition for the proposed 3DFB LGE approach has several distinct advantages over conventional 2D acquisitions, which include higher SNR from the larger 3D coverage, as well as an improved through-plane resolution through the use of a circular k-space shutter. Compared to alternative 3D k-space acquisition approaches, the proposed profile ordering can constrain the central k-space acquisition to the initial heartbeats of the 3D scan, which can minimize changes in the contrast kinetics due to washout over a potentially long 3D image acquisition time on the order of several minutes and dependent on navigator gating efficiency. Additionally, the k-space segmented CENTRA-PLUS approach affixes the initial echo readout of the acquisition window along the ky axis for each heartbeat, and aligns the final echo readout of the acquisition window along the kz axis. This may offer additional benefits over a relatively large acquisition window in a cardiac approach triggered to mid-diastole, though such benefit can also be potentially greater in balanced SSFP-type acquisitions, where the acquisition of central k-space during the initial k-space may lead to notable improvement in overall SNR. The evaluation of k-space segmented CENTRA-PLUS ordering in 3D b-SSFP approaches that builds upon the preliminary works in both (9) and the present study warrant further investigation.

Furthermore, such CENTRA-PLUS acquisition is compatible with employing independently navigator-gated strategies for each of the inner and outer k-space regions. In this study, a conservative 3 mm gating window was used for the acquisition of the central 15% of the k-space region in the first $\sim 1/6$ th of the scan, and the window was expanded to 5-7 mm for the remainder of the scan duration. The smaller gating window was employed for the central k-space data in this study, which concurs with recent approaches proposed for several coronary MR approaches that define inner and outer gating window separately (20,21). Such flexibility in navigator gating may allow for accelerated acquisition strategies that may suit clinical patient imaging that will have additional challenges in respiratory motion correction such as drifting respiratory motion during the scan.

Semi-automated thresholding that employed a standard ROI-based approach was additionally used to corroborate the accuracy and precision of manually delineated measurements against the acquired image reference. This assessment was performed in place of examining intra- and inter-observer variability, which was logistically complex to implement, as the reader needed to be blinded to the study design itself. Our results support the general observation in clinical practice that scar delineation in LGE MRI is straightforward; as scar regions during the delayed enhancement stage would clearly appear hyper-enhanced. By ruling out potential error with reproducibility in LGE data, we can further appreciate the superior quantitative measurements derived from the 3D MRI versus the state-of-the-art 2D approach; where both volumetric measurements were made against the surgical reference standard.

There are several limitations to this study. First, our experiments were performed on pigs in which respiratory motion was controlled using a pneumatic device under sedation, and yielded high heart rates. Accordingly, we have only incorporated a single navigator gating with slice-tracking (in the anterior-posterior direction, as opposed to the typical foot-head direction for human imaging). Human imaging will warrant a similar strategy to effectively

collect both the magnitude and phase. Second, these swine were imaged at a notably higher heart-rates than most clinical scans (80-110 BPM vs 50-90 BPM), which yielded significantly less time between the acquisition of each magnitude and phase 3D volumes in the PSIR sequence. For in-vivo applications in human subjects, a separate gating strategy for these two volumes is warranted, for example, by employing a pair of navigators before each volumetric acquisition (22), or alternatively by employing a set of three navigators in the 2R-R PSIR acquisition cycle, where the first navigator is placed prior to inversion pulse for accept/reject gating, and the two subsequent navigators are played out during the mid-diastolic phase prior to FFE readout for slice-tracking. Third, we note that 2DBH and 3DFB protocols were not randomized in this study. Future work warrants such randomization of the 2D and 3D acquisitions, which was not done in this study. This warrants further investigation; perhaps with a larger study size. Fourth, the 2DBH acquisition in this study employed a 10mm slice thickness. We acknowledge that the use of a thinner 6-8 mm slice excitation profile may have yielded potentially superior 2DBH-derived measurements; however, we additionally note here that the employed 2D animal protocol was optimized and tailored for the primary study on the specific MRI hardware. For this other cardiac MR protocol, the 2DBH-PSIR-LGE acquisition required each BH scan to complete within each pneumatically controlled breath-hold of ~4-6 seconds; our preliminary experiences showed that the anesthetized swine could force its breathing through the pneumatic control if the imaging times were any longer. The use of a 10mm-thick 2D slice ensured the limited scan duration per each breath-hold regardless of the double-oblique prescriptions of both the short-axis and long-axis slices, critical for the success of the original study onto which this 3D-LGE evaluation was inserted as an add-on evaluation. The non-significant signed volume differences from the Bland-Altman analysis also indicated that there was no evidence of consistent scar volume overestimation due to the enlarged 2D slice thickness; although we acknowledge that the sample size of $n=7$ is perhaps limited to exhaustively rule out this phenomena. We also note that in this study, in an effort to compensate for the relatively large 10mm slice thickness, our MRI hardware employed a short 0.4 ms Gaussian RF slice-excitation pulse that yielded a slight drop-off in the edge of the excited 2D slice, potentially mitigating undesirable partial volume effects. The use of superior hardware such as 3T MRI and 32-channel cardiac arrays, and evaluation in a larger study size upon migration to human imaging may warrant further investigation using thinner 2D slices. Likewise, we note the limitation that the 2DBH-PSIR-LGE protocol was acquired without fat suppression, and the 3D protocol was also chosen to match the 2D protocol: thus also performed without fat suppression. Finally, our surgical reference volume measurement approach did not incorporate the gold standard approach of triphenyl tetrazolium chloride tissue enzyme staining. The geometry-based elliptical model employed in this study was considered sufficient for the purpose of estimating the true scar volume in this study. Future work warrants a carefully controlled evaluation using histological validation.

Despite the above limitations, this study's aim was to compare the proposed 3DFB-CP-PSIR-LGE approach with the state-of-the-art 2DBH-PSIR-LGE clinical reference for RV imaging, and was successfully evaluated under the constraints of having the 3DFB investigative sequence performed as an add-on to a separately established animal cardiac MR perfusion protocol. Our findings in this study show that there is significant promise in

the proposed 3DFB-CP-PSIR-LGE technique when compared against the conventional 2DBH-PSIR-LGE reference for RV imaging, which warrants additional investigation of factors including: 1) choice of alternate contrast agents typically preferred by clinicians for cardiac MR studies; 2) investigation in the LV, with potential inclusion of additional LV scars >10mm through a surgically prepared infarction/ischemia animal model, and 3) randomizing the order of 2D and alternative 3D acquisition schemes to decouple the sensitivity of these techniques to the timing. All of these investigations would require a substantially larger cohort than the n=8 swine imaged in this study.

5. CONCLUSION

In conclusion, we evaluated the ability of a 3DFB-LGE sequence which utilizes a dedicated profile ordering with k-space segmented CENTRA-PLUS for the detection and quantification of myocardial scar in a thin walled structure such as the RV against conventional 2DBH approach and direct surgical measurements as the reference standard. The proposed 3DFB approach resulted in substantially improved quantification of the size of scar tissue when compared to the conventional 2DBH-LGE against direct surgical measurements. The developed 3DFB-LGE technique may prove to be a valuable tool for the detection of myocardial damage in thin walled cardiac structures such as the right ventricle, which is currently an important clinical challenge that has yet to be resolved.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

a) Schematics of the 3D PSIR-LGE Sequence. b) Schematic diagram of the CENTRA-PLUS profile ordering over the 3D scan acquisition. The k-space table shows the filled k-space trajectory table over the duration of the scan. Using this scheme, inner (blue) and outer (green) views can be acquired with different navigator gating strategies, such as using a conservative window of 3 mm (inner), and a larger 5 mm window for the remainder of the scan. c) Color scheme of the CENTRA-PLUS ordering within each acquisition table. For each 100 ms acquisition window, ~20-21 consecutively FFEs are acquired from the ky axis towards the outer kz-axis (blue → red). Supplementary animation file shows the time-course of this ky-kz acquisition table.

Figure 2.

Gold standard measurements were made using an elliptical shape assumption with heights adjusted across the major axis. In addition to the live measurements immediately in the surgical suite, two additional measurements were performed retrospectively, and the final value was calculated as an average of the 3 measurements.

Figure 3.

Acquired images from two cases (Pig #1 in top row; #4 in bottom row). Left column shows the 2DBH-PSIR-LGE cases; Right column shows the 3DFB-CP-PSIR-LGE cases. Identified patch is shown using the red arrow. We also note in swine #1 with the 3D acquisition, where the navigator was placed in the foot-head direction. This resulted in the pencil-beam RF pulse producing an artifact that mimicked LGE and excited a circular region in the chest cavity. The blinded clinician read through the artifact in this case, and the protocol was modified between swine #1 and #2,, to instead prescribe the pencil-beam navigator in the AP direction across the chest wall below the heart position.

Figure 4.

Acquired images from Pig #5 with 2.5cm^3 directly measured volume of the RV patch scar region. a) 3 slices and the corresponding geometric model view from the 2D (left) and 3D (right), respectively. The implanted patch is shown only in one slice on the 2D image, whereas it is depicted on multiple slices with the 3D sequence. The improved resolution with the 3D sequence allows a clear depiction of the circular patch and scar geometry, despite presence of bright blood infiltrating onto the surface in both models. These geometric visualization employed a maximum intensity projection approach across a 4 mm segment orthogonal to the manually delineated contour on each slice. The yellow points indicate the drawn contours. b) Reformatted view of the 3DFB-LGE sequence at 1.0mm^3 interpolated resolution allowed thickness measurements of the RV patch.

Figure 5.

Top row: 3DFB-LGE vs surgical ref volume measurements; Bottom row: 2DBH-LGE vs surgical reference volume measurement comparisons. Pearson's Correlation plot is shown on the left column, Bland-Altman Analysis on the right column. 3DFB-LGE measurements yielded good agreement with the surgical reference measurements, whereas the 2DBH-LGE measurements did not.

Table 1Scar Volume Measurements (cm³)

Pig #	Surgical Ref	2DBH LGE	3DFB LGE
1	10.0	2.7	8.8
2	2.8	5.7	3.0
3	3.0	N/A	0.9
4	7.9	5.3	6.4
5	2.5	4.2	3.3
6	3.4	2.3	3.7
7	1.7	2.8	1.7
8	3.2	3.3	3.8