Measurement of myocardial mechanics in mice before and after infarction using multislice displacement-encoded MRI with 3D motion encoding

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THE WIDESPREAD USE OF TRANSGENIC and knockout mice in studies of cardiovascular disease has created a demand for noninvasive imaging modalities capable of accurately assessing heart anatomy and function. These techniques not only allow serial studies of disease progression but may also improve the accuracy of measurements by minimizing the physiological or anatomic changes induced by more invasive methods. A number of imaging modalities have been explored for this purpose, including computed tomography (9), positron emission tomography (16), single photon emission computed tomography (22), ultrasound (5, 14, 20), and magnetic resonance imaging (MRI).

MRI in particular has proven to be a versatile modality for imaging the mouse heart. The three-dimensional (3D) cardiac anatomy can be assessed with multislice cine MRI (6, 15, 21), and the infarcted myocardium can be detected with contrast-enhanced techniques (23). Cardiac MRI has recently been used to serially assess left ventricular (LV) volumes, ejection fraction, and wall thickening in transgenic and knockout mice to probe the molecular mechanisms underlying postinfarct LV function and remodeling (21, 24, 25). Furthermore, tissue-tracking techniques, including myocardial tagging, velocity-encoded imaging, and displacement-encoded imaging, can quantify intramyocardial function and may provide further insight into the basic mechanisms underlying dysfunction in ischemic and other forms of heart disease.

To date, two-dimensional (2D) myocardial tagging (4, 10, 27), 2D velocity-encoded imaging (18), and single-slice 2D displacement-encoded imaging using stimulated echoes (DENSE) (8) have provided the first MRI-derived measurements of myocardial displacement, velocity, and strain in mice. However, each of these techniques has important limitations. 2D myocardial tagging does not account for the 3D motion of the heart, has relatively poor spatial resolution of myocardial strain, and typically requires time-consuming manual intervention to detect tag lines for strain analysis. Although 2D velocity-encoded imaging has improved spatial resolution, it is also not 3D and strain analysis is subject to error propagation when integrating successive velocity measurements (28). The limitations of existing DENSE techniques in mice include not accounting for 3D motion and poor slice coverage. The present study describes the development and application of a multislice DENSE MRI pulse sequence with 3D displacement encoding, which provides a fairly comprehensive measurement of systolic myocardial mechanics in mice with only 50 min of scan time.

MATERIALS AND METHODS

MRI pulse sequence. A previous implementation of DENSE in mice (8), which simultaneously measured myocardial displacement using phase-reconstructed images and infarct area using contrast-enhanced magnitude reconstructed images, acquired a 2D displacement-encoded image for a single short-axis slice and required a 35-min total acquisition time. This technique was modified for multislice imaging with 3D displacement encoding as depicted in Fig. 1. On detection of an electrocardiogram (ECG) trigger pulse at end diastole, nonselective displacement encoding was performed with two 90° radiofrequency (RF) pulses separated by a gradient pulse to spatially modulate the magnetization and store it longitudinally. The composite pulse duration was 1.4 ms. After a delay time to end systole (which was determined from cine imaging of the midventricular slice), a slice-selective RF pulse followed by a gradient echo readout with a DENSE unencoding gradient was used to sample the displacement-encoded stimulated echo of a basal slice. At end systole during...
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The next two cardiac cycles, the displacement-encoded stimulated echoes of the midventricular and apical slices were acquired, respectively, by use of a similar excitation and readout scheme. Three slices are imaged after a single displacement-encoding module because the RR-interval in mice is ~120 ms, the relaxation time (T1) of myocardium at 4.7 T is 1,300 ms, and the displacement-encoded stimulated echo decays with time constant T1, leading to adequate signal intensity at excitation times occurring ~60, 180, and 300 ms after application of the displacement-encoding pulses. The displacement-encoding gradient was applied in the frequency-encoding direction for in-plane imaging and along the slice-select direction for through-plane imaging in sequential acquisitions. For in-plane imaging, displacement encoding was performed in two orthogonal directions by rotating the direction of frequency encoding by 90°. Phase reference data with no displacement encoding were also acquired to correct for background phase errors.

Three distinct echoes are present in a DENSE experiment: the desired displacement-encoded stimulated echo and two artifact-generating echoes (a complex conjugate echo and an echo due to T1 relaxation) (8). Our multislice DENSE sequence employed a phase cycling method that utilizes cosine and sine modulation to eliminate CANSEL artifact-suppression technique are designated by dashed lines. Phases of the radiofrequency (RF) pulses for the cansel technique are indicated by x, -x, y, and -y. A: after an ECG trigger pulse and displacement encoding, 3 short-axis slices are acquired at end systole in subsequent heartbeats.

Fig. 1. A: pulse sequence timing diagram for multislice displacement-encoded imaging using stimulated echoes (DENSE) with three-dimensional (3D) displacement encoding. In-plane displacement encoding was performed along the frequency-encoding (FE) direction, and through-plane encoding was performed in the slice-select (SS) direction. Displacement-encoding gradients are highlighted with dashed lines. Phases of the radiofrequency (RF) pulses for the CANSEL artifact-suppression technique are designated by x, -x, y, and -y. B: after an ECG trigger pulse and displacement encoding, 3 short-axis slices are acquired at end systole in subsequent heartbeats.

Animal care and surgical procedure. For animal studies, we used protocols in accordance with the Guide for the Care and Use of Laboratory Animals (NIH publication no. 85-23, Revised 1996); protocols were also approved by the Animal Care and Use Committee at our institution. Seven wild-type male C57Bl/6 mice (11–14 wk old; Jackson Laboratories, Bar Harbor, ME) were assessed by cardiac MRI at baseline (Bsl) and 1 day (D1) after experimental myocardial infarction (MI).

MI was induced by a 1-h occlusion of the left anterior descending coronary artery followed by 24 h of reperfusion. The details of the surgery have previously been described (26). Briefly, mice were anesthetized with intraperitoneal injection of 100 mg/kg pentobarbital sodium and artificially respirated (SAR-830/P ventilator) with an inspired O2 fraction of 0.80, a frequency of 100 strokes/min, and a tidal volume of 2.0 to 2.5 ml. A parasternal incision was made to open the chest, and the LV was located and exposed. Coronary artery occlusion was achieved by passing a 7-0 silk suture beneath the left anterior descending coronary artery just inferior to the left auricle and then tightening it over a length of PE-20 tubing. Widening of the QRS complex and elevation of the ST segment from ECG measurements, as well as color changes of the area at risk, were used to verify successful occlusion. Reperfusion was achieved 60 min later by removing the short length of PE-20 tubing. The chest was closed, and 1–1.5 ml of 5% dextrose were injected intraperitoneally to replace fluids. Throughout the surgery, the mouse body temperature was monitored and maintained between 36.5 and 37.5°C.

Animal preparation and physiological monitoring for MRI. Anesthesia was induced by 3% isoflurane in O2 and was maintained during imaging using 1% isoflurane in O2. Pediatric ECG leads (Blue Sensor, BRS-50-K/US; Ambu, Linthicum, MD) were attached to the shaved forelimbs of the mice for cardiac gating. For D1 imaging, a length of PE-20 tubing was surgically inserted into the peritoneal cavity for the automatic fluid replacement system. Magnetic resonance imaging. MRI was performed on a 4.7-T Varian INOVA MR scanner (Varian, Palo Alto, CA), using a quadrature birdcage RF coil (RF Design Consulting, Gainesville, FL). The magnet was equipped with a gradient insert capable of 800 mT/m maximum gradient strength and 666 mT·m⁻¹·ms⁻¹ slew rate.

Localizer imaging was performed to identify double-oblique long- and short-axis views of the heart. A midventricular short-axis slice...
was chosen by bisecting a chord drawn between the mitral valve and the apex on a long-axis image. An ECG-triggered 2D double inversion recovery black-blood cine fast low-angle shot (FLASH) pulse sequence was used for short-axis imaging to determine the time to end systole as a percentage of the cardiac cycle. Using this percentage, we adjusted the delay time for DENSE for each acquisition (approximately every 3–4 min) to maintain accurate timing to end systole. The multislice DENSE pulse sequence was used to image in-plane and through-plane systolic motion for three short-axis slices positioned at basal, midventricular, and apical levels (Fig. 2) spanning approximately two-thirds of the midventricle. The basal and apical slices were prescribed from the midventricular slice with the use of a 0.5-mm slice gap. No additional registration or normalization was used because all mice had similar body weights and heart sizes at Bsl, and remodeling of the LV has been shown to be insignificant at D1 post-MI in reperfused mice (15). On D1, additional end-systolic heavily T1-weighted short-axis FLASH images were acquired 20 min after intraperitoneal injection of 0.6 mmol/kg Gd-diethylene triamine pentaacetic acid for identification of infarcted tissue (12).

For all imaging, field of view of 30 mm and matrix of 128 × 128 provided an in-plane resolution of 0.23 × 0.23 mm². The imaging parameters for DENSE included slice thickness of 1 mm, flip angle of 90°, echo time of 3.1 ms, repetition time of 800 ms, and averages of 2. The displacement-encoding frequency was 0.64–0.85 cycles/mm for in-plane encoding and 0.5 cycles/mm for through-plane encoding. These encoding frequencies were determined empirically to optimize the tradeoff between SNR and sensitivity to motion (3). For reference scans, the displacement-encoding frequency was set to zero. For D1 Gd-enhanced FLASH, we used repetition time of ~200–300 ms (2 R–R cycles), echo time of 3.2 ms, and flip angle of 90°.

**Image reconstruction and data analysis.** We combined DENSE raw data off-line using MATLAB (The Mathworks, Natick, MA) as described previously (3) to suppress the complex conjugate and T1 echoes. Magnitude- and phase-reconstructed images were computed from the combined raw data. The magnitude-reconstructed images were used to segment the LV. The phase-reconstructed images were corrected for background phase errors using phase-reconstructed reference images and then combined to compute the 3D end-diastolic to end-systolic tissue displacement. From the in-plane 2D displacement fields, first principal (E₁), second principal, radial (E₉), and circumferential (Eᵥ) strains were computed by use of the finite element analysis method as described previously (8). Twist angles and normalized torsion were also computed for each data set. Local twist angles were computed for each pixel using the epicardial center of mass and calculating the angle subtended by the local displacement vector. Twist angle for each slice is reported as the mean local twist angle. Normalized torsion was computed by linear regression of the twist angle as a function of longitudinal position. These definitions for twist angle and normalized torsion are consistent with recent cardiac MR studies (10, 27). For D1 data analysis, Gd-enhanced T1-weighted images were used to classify infarcted and noninfarcted myocardium. SNR was also measured for each slice and is reported as the mean SNR of images encoded for in-plane motion.

**RESULTS**

All animals completed the imaging and surgical procedures. Two D1 apical slices were excluded because of inadequate image SNR. The mean heart rate during imaging was 435 ± 18 beats/min at Bsl and 553 ± 39 beats/min at D1. Heart rate ranged from 396 to 460 beats/min at Bsl and from 495 to 620 beats/min at D1. The average difference from the mean heart rate during the DENSE scan was 6.4 ± 4.3 beats/min at Bsl and 10.1 ± 7.7 beats/min at D1. As a result, the average error in the time to end systole was 2.2 ± 1.4 ms for a mean R–R interval of 137.9 ± 2.6 ms at Bsl and 2.0 ± 1.6 ms for a mean R–R interval of 108.5 ± 2.6 ms. Temperature during imaging was 37.0 ± 0.1°C. SNR for the basal, midventricular, and apical slices is graphed in Fig. 3, which shows that sufficient SNR was achieved to image three heart slices with multislice DENSE, although SNR decreases with slice location. The decrease in SNR occurs due to T1 decay of the stimulated echo and reduced recovery time for the midventricular and apical slices. From D1 Gd-enhanced images, infarcted regions comprised 37.2 ± 17.8%, 56.7 ± 8.1%, and 71.8 ± 4.6% of the LV mass assessed in basal, midventricular, and apical imaging planes, respectively. Example Gd-enhanced images are shown in Fig. 4.

Example baseline DENSE images and function maps are shown in Fig. 5. Specifically, a twofold spatially subsampled vector map of 3D systolic displacement in basal, midventricular, and apical short-axis slices of the heart is shown in Fig. 5A.
Fig. 5: A: 3D end-diastolic to end-systolic myocardial displacement measured by DENSE MRI in basal, midventricular, and apical levels for the Bsl mice. As shown in Table 1, the high spatial resolution of this technique is evidenced by the detection of greater strain ($E_{rr}$ and $E_{cc}$) in the subendocardium compared with the subepicardium ($P < 0.05$). End-systolic torsion from linear regression of twist angles was $1.35 \pm 0.27^\circ$/mm at Bsl ($R = 0.99$).

In Fig. 6A, a spatially subsampled vector map of 3D systolic displacement is shown for a D1 postinfarct mouse. Arrows in Fig. 6A are color coded to indicate the infarcted (red) and noninfarcted (black) regions as delineated by Gd-enhanced images for this mouse. All D1 apical slices had at least a small percentage of noninfarcted tissue present (range of 22–36% of the apical slice volume; mean of $28.2 \pm 4.6\%$). These data demonstrate significantly abnormal myocardial mechanics at D1. Specifically, decreased longitudinal displacement is observed throughout the heart with abnormal apex-to-base displacement in noninfarcted zones. Also, significant hypokinesis is found in the infarcted region, including akinesis at the base and dyskinesis at the midventricle and apex. Shown in Fig. 6, B–D, are a magnitude-reconstructed image, an in-plane displacement map, and an $E_1$ map of the midventricular slice, which show markedly reduced function in the infarcted anterior and lateral walls. Table 2 summarizes the D1 data. Longitudinal displacement and $E_{cc}$ were the most sensitive indicators of differences vs. Bsl. Longitudinal displacement was significantly different from Bsl in basal and midventricular infarcted zones and in all noninfarcted zones. $E_{cc}$ was significantly reduced in all infarcted zones and in the midventricular and apical noninfarcted zones. Significant changes in subepicardial and subendocardial strains were also appreciable. End-

Table 1. Assessment of myocardial mechanics in C57Bl/6 mice at baseline

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>Mid</th>
<th>Apical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial displacement, mm</td>
<td>0.35±0.04</td>
<td>0.37±0.05</td>
<td>0.33±0.05</td>
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<tr>
<td>Circumferential displacement, mm</td>
<td>0.08±0.04</td>
<td>0.17±0.05</td>
<td>0.24±0.06</td>
</tr>
<tr>
<td>Longitudinal displacement, mm</td>
<td>−0.50±0.12</td>
<td>−0.25±0.18</td>
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</tr>
<tr>
<td>Twist angles, °</td>
<td>1.30±0.60</td>
<td>2.91±0.67</td>
<td>5.35±0.80</td>
</tr>
<tr>
<td>Radial strain</td>
<td>Transmural</td>
<td>0.30±0.04</td>
<td>0.30±0.05</td>
</tr>
<tr>
<td></td>
<td>Epicardial</td>
<td>0.26±0.06</td>
<td>0.26±0.06</td>
</tr>
<tr>
<td></td>
<td>Endocardial</td>
<td>0.34±0.03</td>
<td>0.34±0.05</td>
</tr>
<tr>
<td>Circumferential strain</td>
<td>Transmural</td>
<td>−0.14±0.01</td>
<td>−0.14±0.01</td>
</tr>
<tr>
<td></td>
<td>Epicardial</td>
<td>−0.11±0.02</td>
<td>−0.12±0.01</td>
</tr>
<tr>
<td></td>
<td>Endocardial</td>
<td>−0.17±0.01</td>
<td>−0.17±0.02</td>
</tr>
</tbody>
</table>

Values are means ± SD; $n = 7$ for basal, midventricular (Mid), and apical slices.
systolic torsion was 0.07 ± 0.54°/mm \( (R = 0.96) \) at D1 \( (P < 0.01 \text{ vs. Bsl}) \).

**DISCUSSION**

This study presents the development of a multislice DENSE pulse sequence with 3D displacement encoding and demonstrates its ability to characterize the 3D systolic mechanics of normal and postinfarct mouse hearts. Numerous measures describing myocardial function can be computed from the DENSE data, including absolute 3D tissue displacement, myocardial strain, twist angle, and normalized systolic torsion. The in-plane spatial resolution of 0.23 × 0.23 mm² provides around four to six independent measurements of myocardial displacement across the heart wall in short-axis images, which allows for the measurement of transmural differences in displacement and strain.

The baseline \( E_{mc} \) and \( E_{cc} \) measured in this study agree well with previous tagging \((4, 27)\) and DENSE studies \((8)\). Moreover, D1 \( E_{mc} \) values in infarcted and noninfarcted regions are consistent with the tagging results of Epstein et al. \((4)\). Our measurements of normalized systolic torsion \((1.35°/mm)\) are similar to a recent myocardial tagging study by Zhou et al. \((27)\). However, these results are quite different from those of Henson et al. \((10)\) who used tagging to measure the 0.27°/mm result. The differing results may be explained by differences in anesthesia, strain of mouse, heart rate, temperature, or imaging technique. Specifically, we and Zhou et al. \((27)\) studied C57Bl/6 mice and used isoflurane, whereas Henson et al. \((10)\) used isoflurane.

**Table 2. Assessment of myocardial mechanics in mice 1 day postinfarction**

<table>
<thead>
<tr>
<th></th>
<th>Infarct</th>
<th></th>
<th></th>
<th>Noninfarct</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal</td>
<td>Mid</td>
<td>Apical</td>
<td>Basal</td>
<td>Mid</td>
<td>Apical</td>
</tr>
<tr>
<td>Radial displacement, mm</td>
<td>0.16±0.03*</td>
<td>0.05±0.07*</td>
<td>−0.01±0.03*</td>
<td>0.31±0.12†</td>
<td>0.24±0.05†</td>
<td>0.10±0.04†</td>
</tr>
<tr>
<td>Circumferential displacement, mm</td>
<td>0.11±0.03</td>
<td>0.13±0.02</td>
<td>0.10±0.06*</td>
<td>0.10±0.03</td>
<td>0.11±0.03*</td>
<td>0.12±0.06*</td>
</tr>
<tr>
<td>Longitudinal displacement, mm</td>
<td>−0.04±0.12*</td>
<td>0.08±0.10*</td>
<td>0.18±0.07</td>
<td>−0.17±0.04†</td>
<td>0.17±0.05*</td>
<td>0.44±0.09*</td>
</tr>
<tr>
<td>Twist angles, °</td>
<td>2.25±0.65</td>
<td>2.38±0.41</td>
<td>2.21±1.11*</td>
<td>2.09±0.76</td>
<td>2.06±0.53*</td>
<td>2.63±1.19*</td>
</tr>
<tr>
<td>Radial strain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trans</td>
<td>0.15±0.05*</td>
<td>0.02±0.04*</td>
<td>0.01±0.07*</td>
<td>0.39±0.09†</td>
<td>0.37±0.10†</td>
<td>0.09±0.09</td>
</tr>
<tr>
<td>Epi</td>
<td>0.11±0.07*</td>
<td>0.00±0.05*</td>
<td>0.03±0.06*</td>
<td>0.36±0.08†</td>
<td>0.37±0.11†</td>
<td>0.07±0.08*</td>
</tr>
<tr>
<td>Endo</td>
<td>0.22±0.09*</td>
<td>0.03±0.05*</td>
<td>0.00±0.09</td>
<td>0.42±0.10†</td>
<td>0.37±0.10†</td>
<td>0.11±0.22</td>
</tr>
<tr>
<td>Circumferential strain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trans</td>
<td>0.00±0.02*</td>
<td>0.04±0.03*</td>
<td>0.05±0.03*</td>
<td>−0.14±0.02†</td>
<td>−0.11±0.02†</td>
<td>−0.05±0.07†</td>
</tr>
<tr>
<td>Epi</td>
<td>0.02±0.02*</td>
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<td>−0.03±0.05†</td>
</tr>
<tr>
<td>Endo</td>
<td>−0.03±0.03*</td>
<td>0.04±0.04*</td>
<td>0.05±0.03*</td>
<td>−0.15±0.03*</td>
<td>−0.13±0.02†</td>
<td>−0.08±0.10†</td>
</tr>
</tbody>
</table>

Values are means ± SD; \( n = 7 \) for basal and midventricular and \( n = 5 \) for apical. Trans, transmural; Epi, epicardial; Endo, endocardial. *\( P < 0.05 \) vs. baseline.
†\( P < 0.05 \) vs. infarct.

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studied CD-1 white mice and used halothane. Also, the lower spatial resolution of tagging appears to introduce greater measurement variability as seen by Zhou et al. (27), compared with our DENSE results. With the use of a normalized systolic torsion of 1.35 +/- 0.09 mm and assuming that the longitudinal length of the mouse heart is ~8 mm, a net systolic twist of ~11° is expected for the entire mouse heart. This value is essentially the same as for humans (13). Finally, although longitudinal displacement of midventricular slices is normally directed toward the apex, at D1 we observed apex-to-base motion of noninfarcted myocardium in the midventricular and apical slices, as demonstrated in Fig. 6 and Table 2. This abnormal motion may serve to preserve longitudinal shortening in the setting of large acute MI.

Multislice DENSE MRI with 3D displacement encoding is a novel and unique imaging method for noninvasively measuring mouse heart function. Catheter-based methods are traditionally used to obtain hemodynamic information, including mean arterial pressure, LV diastolic pressure, and the maximum change in pressure with respect to time. These are important physiological measurements, but they do not provide information about regional myocardial function. Echocardiographic techniques (2, 7, 14) have been used extensively to image myocardial function in mice. M-mode imaging is used to measure wall thickening and chamber diameters. However, wall thickening does not provide information about intramyocardial function, and echo measurements are typically limited in their coverage of the heart. Several studies have employed MRI tagging to study intramyocardial function in the mouse heart (4, 27). Although tagging studies can measure intramyocardial contractile function, the strain resolution in this technique is limited by the tag line separation. Furthermore, post-processing of tagged MR images is time and labor intensive, requiring extensive manual interaction for tag line detection. Velocity-encoded MR imaging is a motion-mapping technique that can quantify intramyocardial function with high spatial resolution. However, computation of strain from phase-velocity data is complicated by the need to integrate the measured velocities and can lead to the propagation of measurement errors (28). The new DENSE MRI technique offers high spatial resolution of myocardial displacement, strain, twist, and torsion data with rapid postprocessing.

This technique may be used as part of a comprehensive MR study of the mouse heart. In addition to using multislice DENSE to quantify regional contractile function, other cardiac MRI techniques can be used to assess murine cardiac structure, function, perfusion, and metabolism. Cine MRI has been used to measure the LV shape and volumes in mice (15, 17, 21, 24). Contrast-enhanced MRI has been shown to accurately locate and quantify infarction size in post-MI mouse studies (23). Perfusion studies have been performed in mouse skeletal muscle (19) and in the mouse heart. Furthermore, spatially localized 31P spectroscopy techniques have been applied to the mouse heart to study cardiac metabolism (1).

Limitations. Limitations of the present multislice DENSE technique include suboptimal slice coverage and incomplete temporal sampling. With more slices, the entire heart could be covered from base to apex without interslice gaps, and full coverage of the heart would then lend itself to computation of the 3D strain tensor. Here, we computed the 2D strain tensor describing in-plane strain. Also, instead of acquiring data only at end systole, a multiphase sequence would provide information on the temporal development of myocardial displacement, strain, twist, and torsion.

Future work may include DENSE imaging at higher magnetic field strengths, where the increased SNR and longer myocardial TI may help address the present limitations. As shown previously in humans (11), multiphase DENSE is feasible when sufficient SNR is available. On the basis of SNR measurements from our initial implementation of multiphase DENSE in mice at 4.7 T (data not shown), we estimate that a field strength of 9.4 T would provide sufficient SNR for multiphase DENSE with similar voxel sizes and scan times.

An additional limitation is the lower SNR in the most apical slices, particularly in D1 post-MI mice. The reduced SNR could be improved by reversing the order of slice acquisition or by imaging at higher field strengths. Also, much of the SNR loss can be attributed to greater artifacts from respiratory motion, as breathing is more labored in D1 post-MI mice. Future work is needed to investigate the use of respiratory gating with DENSE to reduce this problem.

In summary, multislice DENSE MRI with 3D displacement encoding can quantify numerous measures of myocardial function in basal, midventricular, and apical slices in mice using ~50 min of scan time at 4.7 T. Data analysis is straightforward, with manual intervention required only to segment the LV myocardium. This technique may provide new insights when used in murine studies to investigate the roles of individual genes in the pathophysiology of LV dysfunction.

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