Comprehensive Assessment of Systolic Function in the Mouse Heart using Volumetric DENSE MRI

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Introduction: The recent application of cardiac MRI to transgenic and knockout mouse models of coronary heart disease has already provided new findings regarding the basic mechanisms that underlie post-infarct left-ventricular (LV) dysfunction and remodeling (1). While cine MRI, myocardial tagging, and two-dimensional DENSE have previously been demonstrated in the mouse heart, the present study aimed to develop a volumetric DENSE sequence with three-dimensional displacement encoding to comprehensively measure regional systolic function over the entire left ventricle in mice.

Methods: A 3D DENSE sequence was implemented on a 4.7T Varian MR scanner and used to image normal C57Bl/6 mice. Displacement-encoding was applied upon detection of an ECG trigger in either of two orthogonal short-axis directions or along a third orthogonal long-axis direction. Displacement encoding frequencies of 0.85 cycles/mm and 0.34 cycles/mm were used for measuring in-plane and through-plane motion, respectively. In addition to displacement-encoded data, a 3D phase reference data set without displacement encoding was acquired. Cosine and sine modulation were used to eliminate (CANSEL) artifact generating echoes by cycling the phase of the second RF pulse in the displacement encoding module as previously described (2). The displacement-encoded longitudinal magnetization was sampled at end systole using a double-oblique slab-selective 3D gradient-echo sequence. Two lines of k-space were acquired for each application of displacement encoding pulses. Specifically, a centric phase-encoding order was used to sample the central half of k-space in the k_y direction during the first heart beat following the displacement encoding pulses and the two outside quarters of k-space during the second heart beat following the displacement encoding pulses. The slab thickness was 5.5 mm and covered the full length of the mouse heart longitudinally. The 3D matrix size was 128 x 96 x 12 and the 3D field of view was 30 x 22 x 7 mm^3, leading to a voxel size of .23 x .23 x .58 mm^3, where the higher spatial resolution was in the short-axis planes and the lower spatial resolution was along the long-axis direction. The echo time was 3.1 ms, and a repetition time of 800 ms was used between each displacement-encoding pulse set to enable sufficient relaxation of the longitudinal magnetization.

Image reconstruction and data analysis were conducted off-line using Matlab. Specifically, reordering of the phase-encode lines was performed and a linear phase shift was applied in the k_z direction to center the image volume in the slab-select direction. CANSEL artifact suppression was achieved by linear combination of multiple data sets as described previously (2). A 3D-inverse Fourier transform was then performed, and the resulting volumetric data were phase corrected using the phase reference data. After manual segmentation of the left ventricle from the magnitude-reconstructed 3D volume, a comprehensive assessment of LV systolic function was automatically computed from the segmented phase-reconstructed 3D volume including 3D displacement, myocardial strain, twist and torsion. Also, SNR was measured for the LV myocardium.

Mice were scanned in accordance with protocols approved by the animal care and use committee at our institution. During MRI, mice were anesthetized with 1% isofluorane in O_2, temperature was maintained at 37°C using circulating hot water and ECG was monitored for use in cardiac gating. A birdcage RF coil was used to transmit and receive.

Results: The total scan time was between 2 and 2.5 hours. The SNR of the LV myocardium was 13.5 ± 0.7. Example images demonstrating the 3D measurement of regional systolic function are shown in Figs. 1-3. Specifically, Fig. 1 is a color surface plot of the mid-wall longitudinal displacement demonstrating approximately 1 mm of base-to-apex motion near the base of the heart, a gradient of longitudinal motion along the long axis, and around 0.25 mm of apex-to-base motion near the apex. In Fig. 2, radial displacement is color-coded and the 3D data are displayed as a stack of 2D short-axis slices. Here a gradient of radial displacement can be seen, particularly in the mid-ventricular slices. In Fig. 3, regional twist is color-coded in a stack of 2D short-axis slices, and systolic longitudinal torsion is visualized as a change in twist angle along the longitudinal direction. Mean circumferential strain throughout the mid-ventricle was -0.13 ± 0.004.

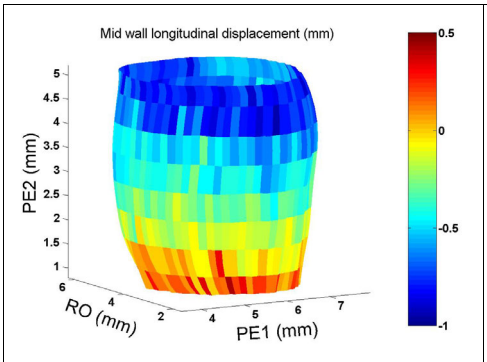

Fig. 1. Color surface map of systolic longitudinal displacement (mm).

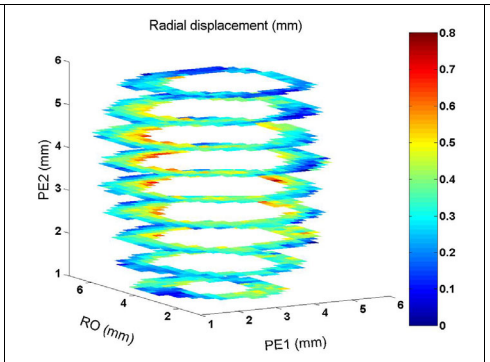

Fig. 2. Stack of 2D short-axis slices color-coded for radial displacement (mm).

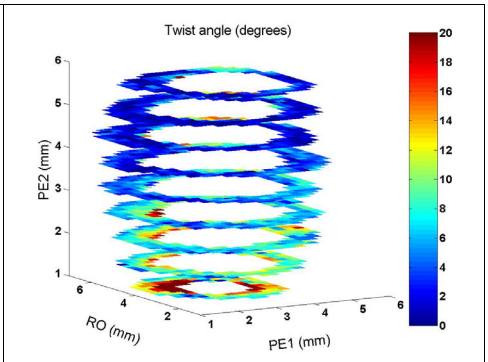

Fig.3. Stack of 2D short-axis slices color-coded for twist angle (°).

Conclusions: 3D DENSE enables a comprehensive evaluation of the systolic function throughout the entire mouse heart. This technique may be used to assess basic mechanisms underlying regional LV dysfunction in transgenic and knockout mouse models of ischemic heart disease.

(1) Gilson WD, Epstein FH, Yang Z, Laubach VE, Berr SS, French BA, Circ 2003 ;108 :IV-700 ;
(2) Epstein FH, Gilson WD. Proc Int Soc Magn Reson Med 2003;11:1645.