Improved Cardiac Tagging Resolution at 14.1 T Enables Principal Strain Measurements in the LV Wall of a Mouse Model of Regional Dilated Cardiomyopathy

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Purpose

To date, functional studies of *in vivo* mouse hearts have provided strain measurements employing tagging grids on the order of 0.7x0.7mm and tag line thicknesses of 0.2mm which limit the application for smaller regions of analysis and thus, pathophysiological wall thinning of left ventricle (LV) [1,2,3]. Improved tagging grid resolution is then required for studying the development of dilated cardiomyopathies, when LV wall thickness becomes progressively thinner than 0.9mm. Therefore, the goal of this study is high resolution tagging at 14 T for measuring regional strain in the left ventricle of dilated mouse hearts. Changes in the principle strains (E1 and E2) in the LV wall were examined in a transgenic mouse model of pure, dilated cardiomyopathy (no hypertrophy), the protein kinase Cε overexpressing transgenic mouse (PKCεTG) [3].

Method

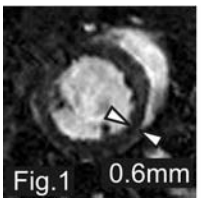
We studied two groups of mice, PKCεTG (n=6) and age- and strain-matched, wild type controls (WT, n=5) at 9 months of age, a time point corresponding to the onset of dilated cardiomyopathy in PKCεTG. Animals were anesthetized with 1.5% Isofluorane in 2L/min 100% Oxygen through a nose cone. Mice were restrained, supine, in a holder designed for a vertical bore magnet and imaging probe. ECG subdermal electrodes were inserted into the front right and rear left legs and connected to a monitoring device (Small Animals Instruments, Stony Brook, NY) enabling proper cardiac gating. Body temperature was maintained at 36.5±0.5 ^{o}C by a continuous flow of warm water through Tygon tubing, lining the mouse's body.

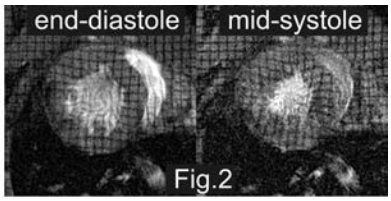
Proton anatomical and tagged cardiac images were collected from mice in an actively-shielded, 600 MHz vertical wide-bore magnet with an Avance NMR spectrometer/microimaging system (Bruker Medical, Ettlingen, Germany) with 100Gs/cm gradient coils and 600 MHz "bird-cage" resonator. All images were collected with FOV=20mm and slice thickness=1mm. Anatomical true short and long axis images were acquired using fast gradient echo (GEFI) sequence with parameters TR=100ms, TE=1.5ms, flip angle=30^{o}, matrix 128x128, NEX=2. Tagged true short axis images were obtained at midbase using a modified DANTE/GEFI sequence with tag line separation 0.45mm, tag line thickness 0.1mm, TR=200ms, TE=1.9ms, flip angle=30^{o}, matrix 256x256, NEX=4.

Images were processed with a Matlab (MathWorks, Natick, MA) based program [4]. Homogeneous strain analyses were used for calculating regional and average principle E1 and E2 strains from tagged images zero-filled to 512x512 matrix. Wall thickness at midbase was calculated from manually traced epi- and endocardial contours on standard gradient echo images.

Results

At 9 months, PKCεTG displayed significant cardiac enlargement and thinning of the LV wall, with increased thinning nearest the midbase and apex (Fig.1). LV wall thickness at diastole measured at the mid-base ranged 0.6-1.1 mm in PKCεTG compared to 0.9-1.3 mm in WT (mean ± SE: PKCεTG = 0.9 ± 0.04; WT = 1.2 ± 0.01, P<0.05). Tagging line thickness of 0.1 mm was achieved to enable strain measurements in dilated LV regions of 0.6 mm. Fig.2 illustrates a 10x10mm crop of end-diastole and mid-systole tagged cardiac images of a PKCε mouse. Images show at least 2-3 tag lines overlapping the myocardial wall, providing sufficient resolution for not only circumferential strain but more importantly, regional measurement of E1 and E2 in the thinned myocardium. Fig.3 presents average values of E1 and E2 in PKCεTG and control mice hearts where E1 in PKCεTG is 20% lower (P<0.05) than WT with similar E2 between groups.





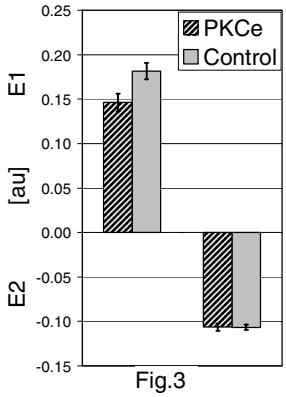


Fig.3

Conclusions

Our results show a 64% improvement in tagging grid resolution can be achieved by combining high resolution DANTE tagging (0.1 mm lines) and fast gradient echo imaging at 14.1 T. The approach enables regional strain measurements, including E1 and E2, in the thinned LV wall of dilated mouse hearts. The principle E1 strain is reduced in regions of LV wall thinning associated with the development of LV dilation. The findings demonstrate changes in E1 in the LV of a transgenic mouse model of progressive ventricular dilatation predate eventual transitioning to heart failure.

1. F.H. Epstein, Z. Yang, W.D.Gilson, S.S. Berr, Ch.M. Kramer, B.A. French MR Tagging Early After Myocardial Infarction in Mice Demonstrates Contractile Disfunction in Adjacent and Remote Regions. Magn Reson Med 48:399-403 (2002)

2. R. Zhou, S. Pickup, J.D. Glickson, C.H. Scott, V.A. Ferrari Assessment of Global and Regional Myocardial Function in the Mouse Using Cine and Tagged MRI. Magn Reson in Med, 49:760-764 (2003)

3. P.H. Goldspink, D.E. Montgomery, L.A. Walker, D. Urboniene, R.D. McKinney, D.L. Geenen, R.J. Solaro, P.M. Buttrick Protein Kinase Cε Overexpression Alters Myofilament Properties and Composition During the Progression of Heart Failure. Circulation Research 95:424-432 (2004)

4. W. Liu, J. Chen, S. Ji, J. S. Allen, P.V. Bayly, S.A. Wickline and X. You Harmonic Phase Magnetic Resonance Imaging Tagging for Direct Quantification of Lagrangian Strain in Rat Hearts After Myocardial Infraction. Magn Reson Med 52:1282-1290 (2004)