Quantification of Myocardial Strain at Early Systole in Mouse Heart: Restoration of Undeformed Tagging Grid with Single Point HARP

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MR tagging is a valuable technique in evaluating regional ventricular function of the heart. The application of MR tagging to genetically manipulated mouse models of cardiac diseases allows the potential to elucidate the molecular mechanisms of abnormal cardiac function. Current tagging analysis frequently employs finite element method for the quantification of regional myocardial wall strains. Frequently the first tagging image, acquired immediately after the implementation of tagging sequence, is used as the reference frame, with the underlying assumption that this first image is undeformed. However, for a mouse heart, the QRS complex is typically less than 20 ms in duration, followed by a rapid phase of contraction due to the fast heart rate. As a result, the first tagging image is frequently acquired at early systole with significant tag line deformation. This deformation is even more pronounced during dobutamine stress test. Therefore, using this first frame as the undeformed reference frame can lead to significant underestimation of myocardial strains in mouse heart.

In the current study, we developed a method based on harmonic phase (HARP) method to restore the undeformed tag lines. The influence of myocardial contraction at early systole at both baseline and during dobutamine infusion was analyzed.

Theory

A SPAMM tagged image can be represented by a series of Fourier transformed harmonic peaks (1), where $I_0(\boldsymbol{p})$ is the original image without SPAMM modulation, K is determined by the tagging sequence (K=1 and 2 for SPAMM11 and SPAMM1331, respectively), c_k is a coefficient determined by the tip angles of the SPAMM sequence, and ω_k is the frequency vector determined by the strength and duration of the tagging gradients. Using the following definition of the displacement field ($\boldsymbol{u}(\boldsymbol{x},t)$) of a material point $\boldsymbol{p}$, $\boldsymbol{u}(\boldsymbol{x},t)=\boldsymbol{x}-\boldsymbol{p}(\boldsymbol{x},t)$, each harmonic peak can be expanded as (2), with the first exponential term representing a complex sinusoidal modulation with frequency ω_k. In the Fourier domain, this sinusoidal modulation will shift the center of the harmonic peak to ω_k. Therefore, selecting a single point at the center of this harmonic peak will yield a function in the form of $\delta(\omega-\omega_k)$ in k-space. Taking its inverse Fourier transform, we can thus fully recover the undeformed tag lines.

$$I(\boldsymbol{p}) = \sum_{k=-K}^{K} c_k I_0(\boldsymbol{p}) e^{j\boldsymbol{\omega}_k^T \boldsymbol{p}} \quad (1)$$

$$I_k(\boldsymbol{x},t) = c_k I_0(\boldsymbol{x},t) e^{j\boldsymbol{\omega}_k^T \boldsymbol{x}} e^{-j\boldsymbol{\omega}_k^T \boldsymbol{u}(\boldsymbol{x},t)} \quad (2)$$

Methods

MR imaging Wildtype C57BL/6 mice (n=11, 37-43 weeks old) were scanned on a Bruker 7T scanner with a volume RF coil. Mice were anesthetized with 1.5% isoflurane. ECG rising edge was used for TTL trigger signal generation. Tagged images of 3 short-axis slices were acquired from base to apex with 1 mm slice thickness. The tagging sequence was followed by gradient-echo cine sequence with the following imaging parameters: TR, R-R interval; TE, 2.2~2.5 ms; field of view, 4cm×4cm or 3.5cm×3.5cm; matrix size, 256×128; tagging resolution, 0.6 mm. Following the acquisition of the baseline tagged MR images, the mouse was continuously infused with dobutamine at a dose of 40 μg/minute/kg body weight through tail vein catheterization. After about 15 min of stabilization, the tagged images were acquired at the same short-axis positions. Regular cine images were also acquired for assessing the morphology of the heart.

Data analysis A previous in-house developed, MATLAB-based software (CVMRI) was modified for image analysis[1]. To reconstruct the undeformed tag lines, the maximum of the first-order harmonic peaks was extracted. The π iso-contours were calculated from the harmonic peaks with a HARP radius (r) of 1 pixel. The intersecting points of π iso-contour (r=1) were selected as the reference tag points for the subsequent tag tracking and strain quantification. The tag points of the first image and subsequent images were tracked semi-automatically with HARP-based approach with a HARP radius of 25 pixels (or 30 pixels, according to field of view). The strains were calculated by 2D homogenous strain analysis. Myocardial twist was computed as the rotation angle around the center of LV cavity. Positive twist indicated clockwise twist viewed from base.

Results

Average body weight of the mice and the heart rate during MRI scanning were 34.2±3.78 g and 419±44 BPM, respectively. The heart rate increased to 480±31 BPM upon dobutamine infusion. The LV diameter, wall thickness and wall thickness to LV radius ratio were 5.6±0.2 mm, 1.01±0.07 mm and 0.36±0.02 (n=11), respectively. The ejection fraction increased from (65±6)% (n=8) at baseline to (77±6)% (n=6, p<0.01) during dobutamine infusion.

The yellow and magenta lines in Figure 1A show the calculated π iso-contours from a HARP radius of 25 and 1, respectively. The π iso-contours from a 25 HARP radius overlap with the deformed taglines, while π iso-contours from a single point HARP overlap with the undeformed taglines of the stationary tissues. Using tag points generated from the undeformed tagging grid, the first image slice displayed obvious twist, ranging from 0.57° to 1.91° at baseline and -1.46° to 3.25° upon dobutamine infusion (Figure 1B). While dobutamine-stimulated heart displayed a trend of increased torsion at early systole (0.05±0.23 vs 0.27±0.36 °/mm), no statistical significance was detected (P=0.2). Significant circumferential strain (E_{cc}) was observed at early systole, especially in dobutamine-stimulated hearts (Figure 1C). The E_{cc} of the first image at baseline (n=8) and during dobutamine activation (n=7) were -0.005±0.011 v.s. -0.015±0.009 (Base, P=0.06); 0.001±0.010 v.s. -0.016±0.010 (Mid, P<0.01); 0.001±0.008 v.s. -0.012±0.014 (Apex, P<0.05), respectively. Peak E_{cc} at baseline (n=8) and during dobutamine infusion are -0.144±0.010 v.s. -0.159±0.008 (Mid, P<0.01); -0.117±0.011 v.s. -0.138±0.021 (Base, P<0.05); -0.134±0.014 v.s. -0.149±0.029 (Apex, P=0.23), respectively. The average E_{cc} of the first image is about 10% of the maximum circumferential strain upon dobutamine infusion.

Conclusion

In conclusion, we developed a HARP-based method to restore the undeformed tagging grid, which was shown to overlap with the undeformed tag lines in the stationary tissue. Using this grid as the reference for strain and torsion calculation, it was shown that significant circumferential strain and twist were developed at early systole upon dobutamine infusion. Therefore, for accurate strain and torsion quantification, the deformation of the first image cannot be neglected in a mouse heart.

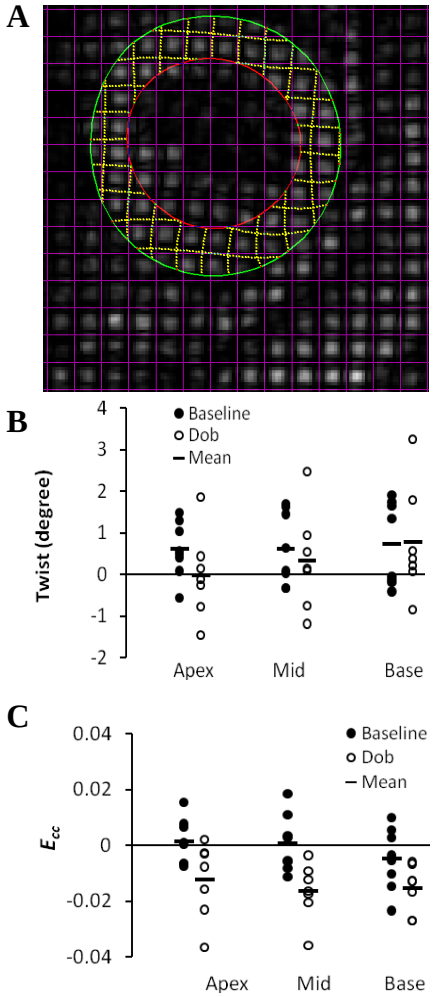

Figure 1. A. Example of π iso-contours generated from a HARP radius of 25 (dotted lines) and from a HARP radius of 1 (solid lines) from the first image frame; B. Twist angle of the first image slice; C. Circumferential strain (E_{cc}) of the first image frame.

References

1. Liu W. et al, Magn. Reson. Med., 52:1282-1290, 2004.