In Vivo Assessment of Myofiber Dynamics in the Human Heart Using Supertoroidal Analysis of Diffusion Tensor MRI

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Introduction: The supertoroidal approach has been used to analyze in vivo Diffusion Tensor Imaging (DTI) datasets of normal animal hearts and animal models of heart disease **[1]**. The use of supertoroids has been shown to be more sensitive to subtle changes in myocardial microstructure than conventional diffusion indices **[1]**. The effectiveness of the supertoroidal model on in vivo human data, however, remains to be determined. Here, we describe the use of supertoroids to analyze in vivo DTI data acquired in normal human volunteers. We use the supertoroidal model to assess whether subtle differences in myocardial microstructure are seen across the cardiac cycle, specifically between end-diastole and systole.

Material and Methods: In vivo DTI of eight normal volunteers (n=8) was performed on a 3T clinical scanner (Skyra, Siemens) using a diffusion-encoded STEAM sequence **[2]** with the following parameters: 6 diffusion-encoding directions, b=350s/mm^2, fat saturation, TR/TE=1100/23ms, BW=2442Hz/pixel, spatial resolution=2.7x2.7x8mm^3, 3 slices, 6-10 averages, multiple breathholds. The diffusion tensor field was determined and diagonalized to yield the principal (e1/λ1), secondary (e2/λ2) and tertiary (e3/λ3) eigenvectors/values. Mean toroidal volume (TV), toroidal curvature (TC) and as well as individual eigenvalues were computed in 12 sectors in the anterior, lateral, inferior and septal walls of the left ventricle (LV). TV and TC were calculated as follows: $TV = (\pi/3)\lambda_1\left(\lambda_2\lambda_3 + \lambda_3^2/2\right)$,

$$TC = \frac{4\beta'\gamma'^2\cos\phi_M}{\left(\alpha'+\beta'\cos\phi_M\right)\left[\beta'^2+\gamma'^2+\left(\gamma'^2-\beta'^2\right)\cos 2\phi_M\right]^2}$$

$$\begin{cases}\alpha' = \left(2\lambda_2+\lambda_3\right)/4\lambda_1, \beta' = \lambda_3/4\lambda_1, \gamma' = 1/2, \text{ where } tc(\phi) \text{ is the maximum curvature at angle } \phi.\\ \phi_M = \underset{\phi}{\operatorname{argmax}}\left\{tc(\phi)\right\}, \phi \in [0,\pi]\end{cases}$$

The TV and TC values, as well as the eigenvalues, in the 12 LV sectors were averaged for statistical analysis.

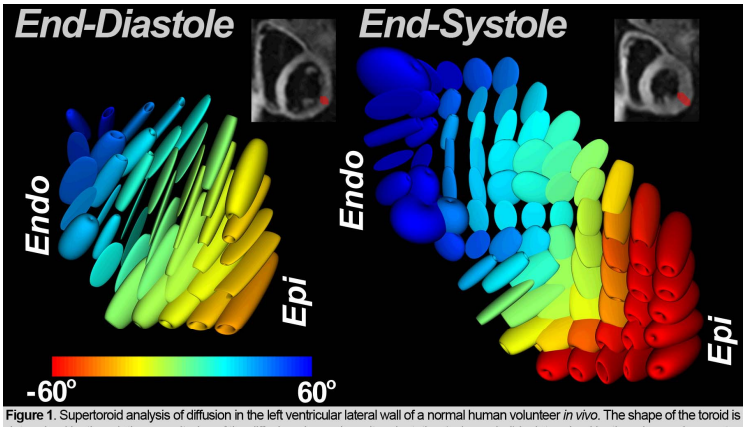

Figure 1. Supertoroid analysis of diffusion in the left ventricular lateral wall of a normal human volunteer *in vivo*. The shape of the toroid is determined by the relative magnitudes of the diffusion eigenvalues. Its orientation (color-coded) is determined by the primary eigenvector. The toroids at end-diastole are flat and elongated, indicating highly anisotropic diffusion. At end-systole, however, the toroids are thicker and more spherical indicating a reduction in diffusion anisotropy. The toroids in the subepicardium have transitioned from mustard to red as the heart contracts, indicating a more left handed orientation at end-systole.

Results: Supertoroidal fields within a region of interest in the lateral wall at end-diastole and end-systole are shown in Figure 1. A marked change in the shape of the supertoroids is seen from end-diastole to systole. In diastole the supertoroids are highly elongated, indicating highly anisotropic diffusion. In systole, the supertoroids are thicker and more spherical indicating a significant decrease in the primary eigenvalue and less anisotropic diffusion. TV and TC values in humans were similar to those previously seen in normal animals in vivo. TV and TC values in the 8-volunteers converged well and showed low standard deviation values (end-diastole: TV=0.85±0.1 and TC=76.2±2.5, end-systole: TV=0.33±0.2 and TC=50.5±1.3). Both TV and TC were significantly ($p<0.05$, Mann-Whitney) lower at end-systole than end-diastole (Figure 2). These changes robustly reflected the reductions in the individual eigenvalues, particularly the primary eigenvalue (Figure 2C), present at end-systole. The supertoroids robustly depicted the transmural gradient in myofiber helix angle (primary eigenvector) as well as the sheet structure of the myocardium (secondary eigenvector). A leftward rotation of the primary eigenvector was seen in the subepicardium at end-systole versus diastole.

Conclusion: Supertoroidal analysis of in vivo DTI data in the human heart is performed for the first time. We show that the volumetric nature of the toroidal indices makes them highly sensitive to small and dynamic changes in myocardial microstructure. The orientation of the toroids (primary diffusion eigenvector) changes little as the myocardium contracts, except in the subepicardium. However, toroidal volume and curvature both decrease significantly in systole, reflecting a reduction in diffusion anisotropy as the myocardium contracts. The supertoroidal formalism holds significant promise for the detection of myocardial pathophysiology in vivo with DTI.

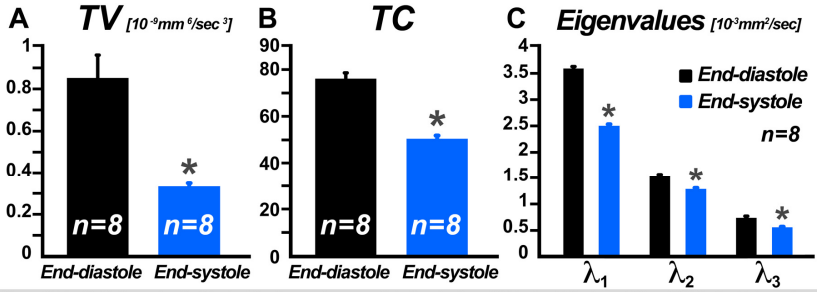

Figure 2. Toroidal indices robustly detect subtle changes in myocardial microstructure. (**A**) The toroidal volume (TV) and (**B**) the toroidal curvature (TC) are volumetric indices that are highly sensitive to small changes in the eigenvalues of the diffusion tensor (**C**).TV and TC both decrease significantly in systole reflecting a decrease in the extracellular space and more hindered diffusion as the myocytes thicken. * $p<0.05$.

References: **[1]** Mekkaoui C. *et al*. ISMRM 2011, **[2]** Nielles-Vallespin S. *et al*. ISMRM. 2011. **Funding:** R01HL093038