A Study of Variability of the Mouse Myocardial Fiber Structure Obtained by MR Diffusion Tensor Imaging

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Introduction. MR diffusion tensor imaging (DTI) (1) has emerged as a convenient and viable method for quantifying the 3D myocardial fiber structure. However, due to the challenges in group analysis of DTI datasets, which necessitates precise co-registration and appropriate descriptive statistics across specimens (2), little information is available on the representativeness of a "typical" heart. A first step toward fiber structure group statistics is to determine the degree of variability among like datasets. In the present study, principal component analysis (PCA) was applied to investigate the intra-group variability of the normal mouse myocardial DTI datasets, as well as the detectability of structural differences in hypertrophic hearts.

Methods. DTI (3D acquisition, 100 μm isotropic-resolution) of fixed mouse (7 normal and 2 hypertrophic) hearts was performed on a 9.4 T MRI instrument (3). The myocardial fiber structure was represented by the local cylindrical-coordinate helix angle (4) and the fractional anisotropy (FA) index. All normal specimens were mapped onto a common template using an unbiased diffeomorphic registration technique. PCA using a leave-one-out strategy (5) was performed on the central 75% left ventricular volume of each subgroup of 6 normal hearts. Variability was quantified by the projection of the left-out dataset on the subgroup PCA space, and normalized distance (divided by twice the standard deviation along each principal axis) of greater than unity was taken as significant difference. To evaluate the detectability of pathologic hearts, the two hypertrophic hearts were each registered and projected onto the PCA space constructed from all 7 normal hearts.

Results. Figure 1 shows the mean myocardial fiber helix angle and FA maps obtained for the normal mouse hearts (n = 7) in their common coordinates. Leave-one-out PCA of the normal hearts revealed that each excluded dataset consistently lies within the 95% confidence interval of the principal components (i.e., normalized distance < 1.0) of the subgroup datasets. Figure 2 shows the relative locations of the normal and hypertrophic hearts on the space spanned by the first 3 principal components. That the locations of the 2 hypertrophic hearts are outside the 95%-confidence ellipsoid indicates significant difference from the normal heart population. In contrast, only isolated differences of significance are observed in pixel-by-pixel comparisons of the fiber helix angles (Fig. 3).

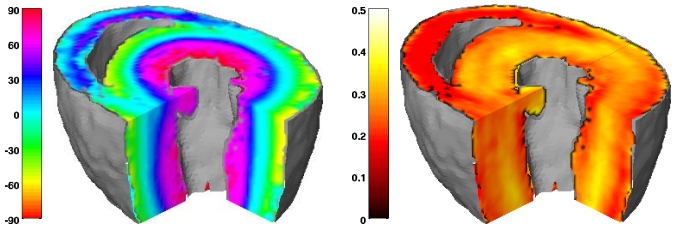

Figure 1. Group-averaged myocardial fiber helix angle (left) and FA (right) of normal mouse hearts (n = 7) shown on their template coordinates.

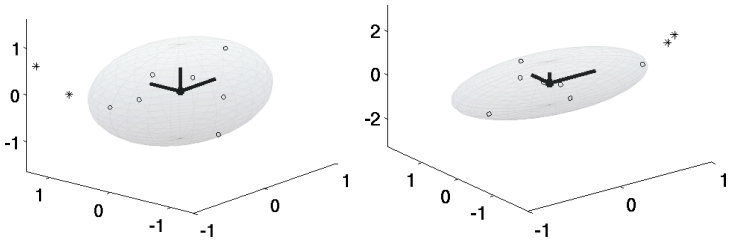

Figure 2. Relative locations of the normal (open circles) and hypertrophic (asterisks) hearts on the spaces spanned by the first 3 principal components of myocardial fiber helix angle (left) and FA (right). The ellipsoids represent the 95%-confidence interval.

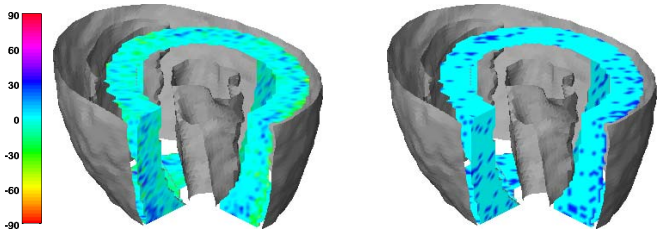

Figure 3. Pixel-wise difference (left) between myocardial fiber helix angles of a hypertrophic heart and the averaged normal heart, and matching statistical significance (right; dark blue indicates significance).

Discussion and Conclusions. Results of the leave-one-out PCA tests suggest that as few as 6 DTI datasets were sufficient to capture the group variability, indicating a rather low intra-group variability of normal mouse myocardium. Previous comparisons of myocardial structure were done largely on a pixel-wise or region-of-interest basis. In the current study, PCA of the left ventricular volume, which is sensitive to the hierarchical organization of the myocardial structure, detected significant differences in the fiber structures of the hypertrophic hearts that are likely missed in pixel-wise comparison (Fig. 3). The above findings are extremely encouraging and pave the way for atlas-based representation and modeling of myocardial fiber structures.

References. 1. Basser PJ, Pierpaoli C. J Magn Reson B 1996;111:209-219. 2. Beg MF, Helm PA, McVeigh E, Miller MI, Winslow RL. Magn Reson Med 2004;52:1167-1174. 3. Jiang Y, Pandya K, Smithies O, Hsu EW. Magn Reson Med 2004;52(3):453-460. 4. Streeter DDJ, Spotnitz HM, Patel DP, Ross J, Sonnenblick E. Circ Res 1969;24:339-347. 5. Vik T, Heitz F, Armspach JP. Lecture Notes in Computer Science 2003;2879:838-845.

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