Introduction: DTI [1] has become a preferred method to rapidly and noninvasively quantify the 3D myofiber structure of the heart, and atlases representing group averages of hearts in humans [2] and some animal species [3,4] have been constructed from DTI data using computational anatomical techniques and voxel-based statistics. Besides being sensitive to image noise, a key assumption in the latter is that fiber orientations in different voxels are independent of one another. Moreover, few studies have directly investigated the intra-species variability of the myocardial fiber structure [5]. Given the known structural and functional interconnectivity of the myocardium, intuitively, a pattern-based analytical approach may better reflect the individual anatomy and capture the group similarity and variability. The present study developed a computational framework and applied it to perform parametric modeling and variability analysis of the mouse heart myofiber structure. The results underscore the advantages of the proposed framework, including accuracy and simplicity of the description, which have implications for current and future constructions of myocardial fiber atlases.

Methods: DTI of formalin-fixed hearts isolated from 3 month-old male C57B/L6 mice (n = 6) was performed using 3D spin-echo EPI acquisition (100 μm resolution, 192 directions of b = 1000 s/mm^2, 4 b0 volumes) on a Bruker 70/30 instrument. Fiber orientation helix angles α_H were obtained as described previously [6] for the left ventricular myocardium, and registered onto a prolate hemisphere, using μ, φ and υ to denote the radial, azimuthal and zenithal coordinate variables. The fiber angles were then modeled by the parametric function $\alpha_H(\mu,\varphi,\upsilon) = (a_0 + a_1 f(\mu) + a_2 f^2(\mu) + \cdots)(b_0 + b_1 g(\varphi) + b_2 g^2(\varphi) + \cdots)(c_0 + c_1 h(\upsilon) + c_2 h^2(\upsilon) + \cdots)$, using various basis functions (e.g., polynomial, sinusoidal, hyperbolic, etc) for f, g and h. The specific basis function of each coordinate variable, and its order, were empirically determined for the group using F-tests. Subsequently, least squares fit was used to determine the modeling function coefficients for each heart, and principal component analysis (PCA) was performed on the coefficients to characterize the nature and behavior of myofiber structural variability in the group.

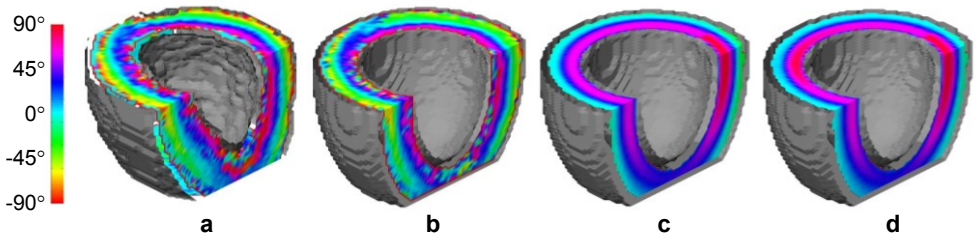

Figure 1. Cut-open view of 3D falsecolor-coded left ventricular myofiber helix angle maps. Fiber angles of a representative heart in (a) original and (b) registered prolate spheroidal spaces are shown. Compared to the group average (c), the mean plus one standard deviation of the first PCA component (d) has noticeably thickened right-handed endocardium.

Results: Figure 1 shows the 3D fiber orientation helix angle maps obtained for a typical heart. F-tests indicated that the best individual functions for the group of hearts along μ, φ and υ dimensions are third-order polynomial, fifth-order sine and fifth-order hyperbolic tangent, respectively. Fitting of fiber angles of individual hearts to the modeling function yielded root-mean-square (RMS) residual error that ranged from 18° to 25°. PCA revealed that there existed only 3 significant principal components or modes of variations of the modeling function coefficients, with the first, second and third components capturing 55%, 35%, and 6% of the variance, respectively. Visual examination of the PCA results suggests that the first component (also see Fig. 1) is largely linked to concentric variability of the helix angle in the radial dimension, which relates to the transmural rotation of the fiber angle and thicknesses of the right-handed and left-handed LV myocardium. Likewise, the second component (not shown) is associated mostly with variability of the fiber structure in the circumferential (or azimuthal) direction.

Discussion and Conclusions: Parametric modeling offers the benefit of reducing the dimensionality of an otherwise highly complex function. Current results indicate that the patterns of LV myofiber orientation can be characterized by the combination of 16 polynomial, sine and hyperbolic tangent terms of the coordinate variables. As a goodness-of-fit metric, the RMS residual deviation (18° to 25°) is comparable to the 15° reported previously for another modeling study [7]. PCA results reveal that fiber structures among hearts vary only in a few specific ways, where most of the variability exists in the concentric radial or transmural behavior of the fiber angle. Although the familiar myocardial fiber structural patterns (e.g., counterclockwise rotation of the fiber angle) in hearts are well-known, the current study demonstrates that the whole-heart structural patterns, and importantly their variability, can be well captured via relatively simple parametric modeling. The findings are useful both as practical design guide and justification for characterizing the myocardial fiber structures of both normal and diseased hearts (e.g., extrapolating the whole-heart fiber structure from few slices of DTI acquisition), and for constructing cardiac structural atlases.

References: [1] Basser PJ et al, Biophys J. 1994; 66: 259. [2] Lombaert H et al, IEEE Trans Med Imaging. 2012; 31: 1436. [3] Peyrat JM et al, IEEE Trans Med Imaging. 2007; 26:1500. [4] Piuze E et al, LNCS, 2013; 7945: 442. [5] Lombaert H et al, LNCS, 2013; 8150: 492. [6] Toussaint N et al, MICCAI. 2010; 13: 418. [7] Vadakkumpadan F et al, IEEE Trans Med Imaging. 2012; 31:1051