Diffusion MRI Tractography of the Human Heart *In Vivo* Reveals Differences in Myofiber Organization at End-Diastole and End-Systole

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Introduction: Characterization of myocardial fiber architecture using Diffusion Tensor Imaging (DTI) has traditionally been performed *ex vivo*. *In vivo* DTI of the human heart has been described but has been limited either to single slice acquisitions at single phases of the cardiac cycle **[1,2],** or to techniques requiring large amounts of image transformation and interpolation **[3].** The 3D organization of myofiber tracts in the human heart *in vivo* thus remains poorly defined. Moreover, the impact of myocardial contraction on the 3D fiber architecture in the human heart *in vivo* remains unknown. Here, we employ a recently developed diffusion weighted (DW) stimulated echo (STEAM) single shot (SS) EPI sequence **[4],** combined with a 3D tractographic approach **[5],** to address these issues. *In vivo* DTI tractography of the heart was performed in normal volunteers in a single session without the need for data regridding, interpolation or transformation. In addition, data were acquired at end-diastole and end-systole to quantify changes in myofiber organization as a function of myocardial contraction and relaxation.

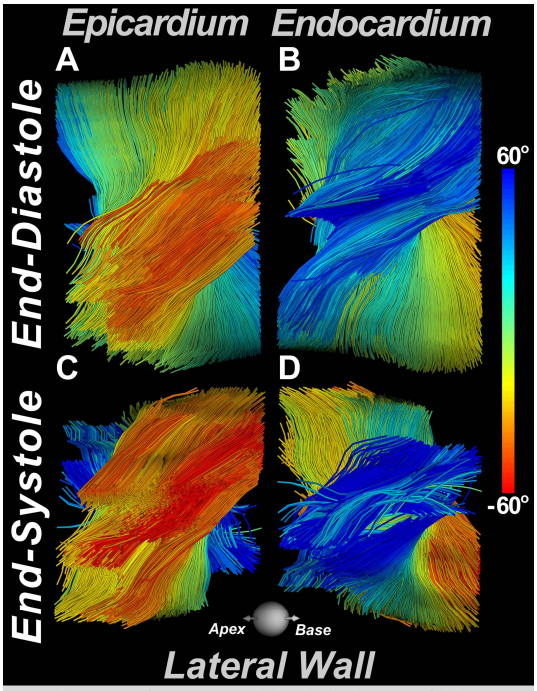

Figure 1. DTI tractography of the heart *in vivo* at end-diastole (**A, B**) and end-systole (**C, D**). Fiber tracts are viewed from their subepicardial (**A, C**) and subendocardial surfaces (**B, D**) and are color-coded by their median helix angle. Fiber tracts in the subepicardium are more oblique (red) in systole than diastole. This is likely due to the smaller LV outer circumference in systole allowing the subepicardial fibers to assume a more oblique (left-handed) orientation.

Material and Methods: DTI of eight normal volunteers (n=8) was performed on a 3T clinical scanner (Skyra, Siemens) using a diffusion-weighted STEAM sequence with the following parameters: 6 diffusion-encoding directions, b=350s/mm^2, fat saturation, TR/TE=1100/23ms, spatial resolution=2.7x2.7x8mm^3, 3 slices, 6-10 averages, multiple breathholds, scan duration 14.4±1.5min. The diffusion tensor field was determined and diagonalized to yield the principal (e1/λ1), secondary (e2/λ2) and tertiary (e3/λ3) eigenvectors/values. Fiber tracts were constructed by integrating the principal eigenvector field into streamlines using a 4th order Runge-Kutta approach. Mean diffusivity (MD), fractional anisotropy (FA) and helix angle (HA) values in 12 sectors in the anterior, lateral, inferior and septal walls of the left ventricle (LV) were derived. Myofiber tracts were color-coded by their median HA. The MD, FA and HA values from all sectors were averaged for analysis.

Results: Robust tractograms, showing the characteristic crossing helical architecture of the myocardium, could be obtained at both end-diastole and systole (Figure 1). Tractography showed that myofibers in the subepicardium of the LV assumed a more oblique orientation at end-systole versus end-diastole (Figure 1). Both MD and FA were significantly ($p<0.05$) higher at end-diastole than end-systole (Figure 2A, 2B). Further analysis revealed that all three eigenvalues were higher at end-diastole than end-systole ($p<0.05$), although the change in the principal eigenvalues (λ1) was greatest. The helix angle of fibers in the subendocardium changed little across the cardiac cycle (Figure 2C). However, HA in the subepicardium increased in its obliquity by approximately 10 degrees at end-systole versus end-diastole.

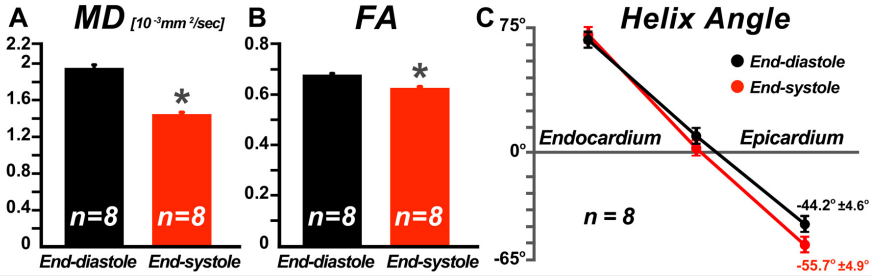

Figure 2. Bar plots of MD, FA and HA in the LV of 8 normal human volunteers. As the myocardium contracts (from end-diastole to end-systole), extracellular volume decreases and the myocytes thicken, resulting in concomitantly reduced MD and FA. In addition, the HA in the subepicardium increases in its obliquity by approximately 10 degrees from end-diastole to end-systole.

Conclusion: Here we perform DTI tractography of the human heart *in vivo* for the first time without the need for interpolation or image transformation. We show that robust tractograms can be constructed with this approach with a total scan time of less than 20 minutes. We show that fiber architecture in the myocardium is highly dynamic and is a function of both chamber geometry and LV contraction. The decrease in MD and FA observed during end-systole is likely due to myocyte thickening, which compresses the extracellular space during systole. Contraction of the LV reduces its outer circumference, thus allowing the subepicardial myofibers to assume a more oblique orientation during systole. Future experiments will be needed to determine the impact of myocardial strain on the diffusion tensor. Nevertheless, our results show for the first time that *in vivo* diffusion tensor MRI tractography of the human heart is feasible and can be performed under conditions suitable for clinical translation. Our data also show that MD, FA and fiber HA change as the myocardium contracts and relaxes, underscoring the important relationship between myocardial microstructure and function.

References: **[1]** Wu *et al*. Circulation. 2006, **[2]** Gamper U. *et al*. MRM. 2007, **[3]** Toussaint N. *et al*. MICCAI 2010, **[4]** Nielles-Vallespin S. *et al*. ISMRM. 2011, **[5]** Mekkaoui C. *et al*. ISMRM 2011. **Funding**: R01HL093038