Beyond Qualitative Tractography: A Novel and Reproducible Technique for the Quantitative Analysis of Cardiac Diffusion MR Tractography Datasets *In Vivo*

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Introduction: Diffusion MRI can be used to visualize myofibers as continuous 3D tracts in the heart.[1] However, current techniques to analyze these tractograms are purely qualitative. Here we present a quantitative framework to measure normal variation and measurement error in diffusion MRI tractographic datasets of the heart. Validation of the technique was performed in human and sheep hearts *ex vivo*, and mouse hearts *in vivo*.

Material and Methods: DTI of the human (n=4) and sheep (n=4) hearts was performed on a 3T scanner using 6, 12, and 32 gradient-encoding directions; a b-value of 2000s/mm^2; voxel-size=2x2x2mm^3; TR/TE=8430/96ms; and a constant acquisition duration of 30 minutes.

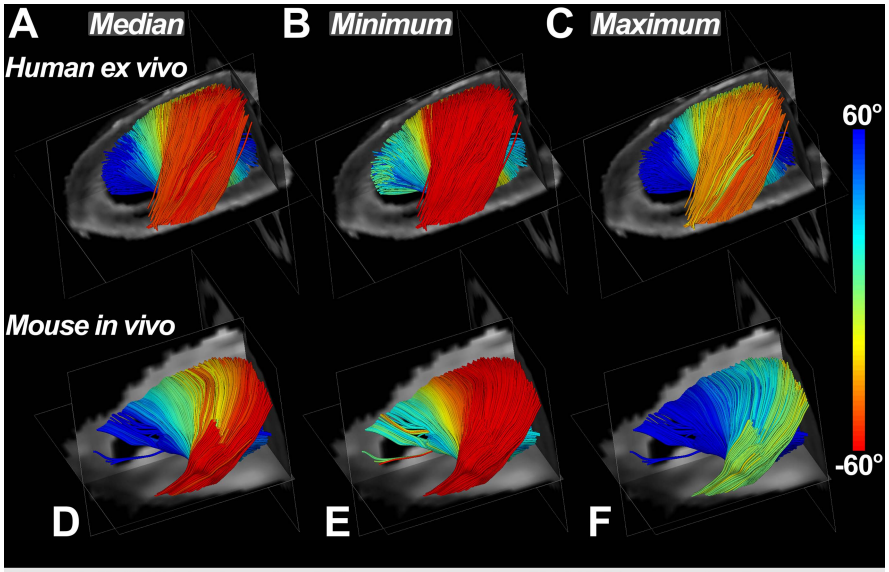

Figure 1: (A-C) DTI tractography of a human heart *ex vivo*. (D-F) DTI tractography of a mouse heart *in vivo*. Fibers passing through a region of interest (ROI) in the lateral wall have been classified by their median (left column), minimum (middle column) and maximum (right column) helix angles.

In vivo DTI of the mouse hearts (n=6) was performed on a 9.4T scanner with a 1500 mT/m gradient and a 3D fat-suppressed single-shot 3D spin echo EPI sequence. Motion-compensated bipolar diffusion-encoding gradients were applied on either side of the 180° RF pulse. Other parameters of the *in vivo* sequence included: TR/TE=2000/13.5 ms, b-value 500 - 700 sec/mm^2 with 24 gradient-encoding directions, and isotropic resolution of 280 µm. Fiber tracking was performed with a fourth-order Runge-Kutta approach and the fibers were classified according to the helix angle.[2] The helix angle assigned to each continuous tract in the dataset was defined by either the maximum, minimum or median helix angle along the tract. The normalized quadratic error (NQE) of the dataset was then defined as the quadratic error between the median, minimum and maximum helix angle profiles summed across the myocardium (**Fig. 2**).

Results: Fiber tracts in the lateral wall of a human and mouse heart are shown in **Fig. 1**. The tracts were limited in length to half the circumference of the left ventricle. High quality tractograms were obtained ex-vivo as well as in the mouse hearts *in vivo*. The helix angle profiles for the NQE calculation represented the averaged profile from 3 adjacent planes in a ROI in the lateral wall (**Fig. 2A**). The mean NQE in the human hearts was 2.3 ± 0.21, 2.8 ± 0.26, and 2.6 ± 0.07 for 6, 12 and 32 directions respectively, and 1.6 ± 0.36 in the mouse hearts (**Fig. 2B**). Tractography of the infarcted sheep revealed severe disarray in the infarct and a right-handed (more positive) rotation in helix angle in the remote zone (**Fig. 2C**). NQE, in the remote zone of the infarcted sheep, was consistently less than 5 (**Fig. 2D**), indicative of high quality data with little noise. This lends confidence to our observation of fiber realignment in the remote zone of the infarcted hearts.

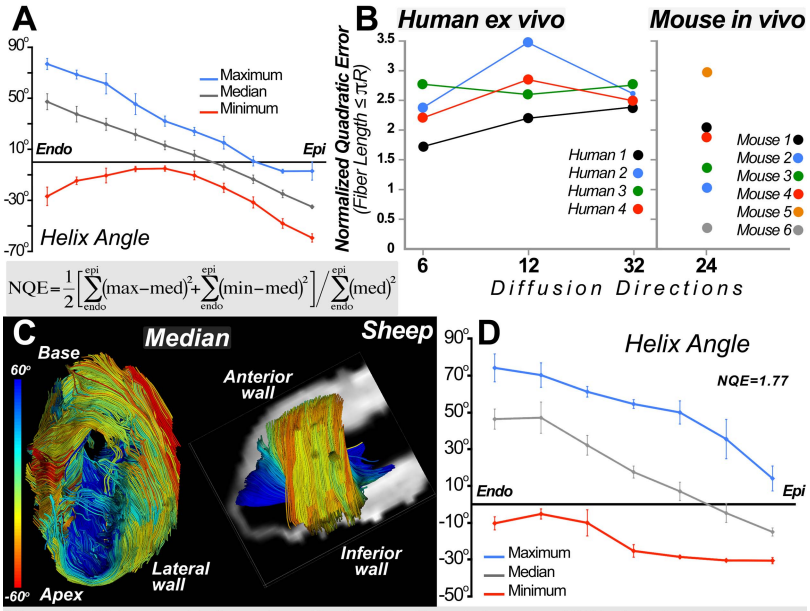

Figure 2: (**A**) Averaged helix angle profiles from 3 adjacent planes in a ROI in the lateral wall of a human heart. The NQE is calculated as shown. (**B**) NQE values in the lateral wall of human hearts *ex vivo* and mouse hearts *in vivo*. (**C**) Sheep heart with a large anterospetal infarct. Fiber architecture in the anterior wall has been lost due to the infarct. (**C**, **D**) The fibers in the remote zone (lateral wall) have undergone a righthand rotation (predominance of positive helix angles). The NQE is the remote zone is low, providing a high level of confidence in the findings.

Conclusion: A new metric (NQE) for quantifying the physiological variation and noise in tractography datasets in the myocardium is presented. The utility of the measure is shown *ex vivo*, in normal and remodeled hearts, as well as *in vivo*. The NQE is a reproducible and generalizable index that can be calculated from any tractographic dataset. NQE calculation has the potential to facilitate the standardization and comparison of tractography datasets, and constitutes an important step towards quantitative tractography in the heart.

References: 1. Sosnovik D *et al*. Circ. Cardiovasc Imaging, 2009 ; 2: 206-212. 2. Scollan DF *et al*. Am. J. Physiol, 1998.
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