The Tractographic Propagation Angle: A Novel Tool to Detect Infarction and Characterize Myocardial Microstructure

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Introduction: Nerve and myofiber tracts can be reconstructed from 3D diffusion fields by integrating the primary eigenvectors into streamlines. A threshold value of 35 degrees between adjacent eigenvectors has traditionally been used as an upper limit of fiber continuity.[1] However, this value is based largely on the experience in the brain and its validity in the heart is unknown. The purpose of this study was thus to characterize the average angle between adjacent eigenvectors along myofiber tracts. We term this angle the tractographic propagation angle (PA). We further aimed to determine whether the PA would allow areas of normal myocardial microstructure to be differentiated from areas of infarction.

Methods: Normal human and mouse hearts, and infarcted sheep and rat hearts, were imaged. Diffusion tensor MRI (DT-MRI) of the human (n=4) and sheep (n=4) hearts was performed *ex vivo* on a 3.0T 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. *Ex vivo* DT-MRI of the rat hearts was performed at 4.7T with an isotropic resolution of 400 µm. *In vivo* DT-MRI 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. The tractographic propagation angle PA was defined as the angle between two adjacent principal eigenvectors (êij, êij+1) relative to a given fiber trajectory (**Fig. 1A**). PA values were computed along myofiber trajectories within the principal eigenvector field using a fourth-order Runge-Kutta integration method.

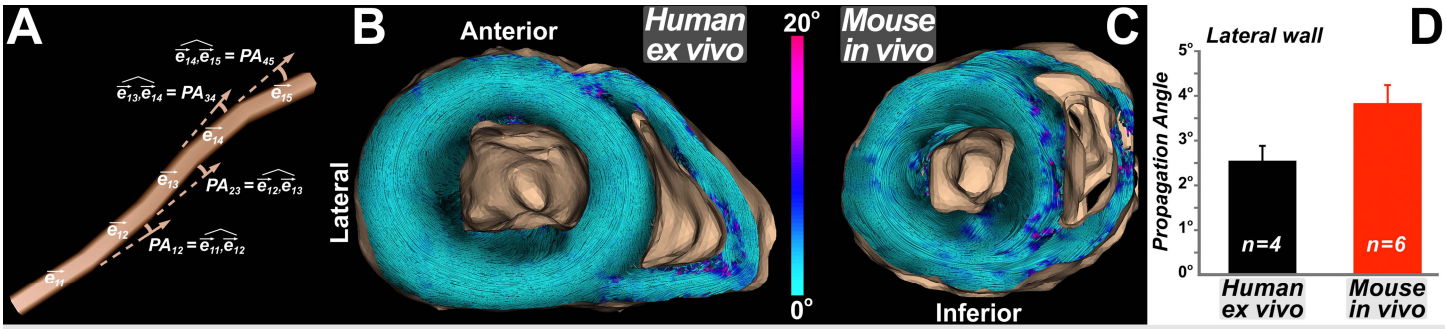

Figure 1: Tractographic Propagation angle (PA) values in normal human and mouse hearts. Similar PA values are seen in fixed human hearts *ex vivo* and in beating mouse hearts *in vivo*.

Results: PA maps of normal human and mouse hearts are shown in **Fig. 1B** and **1C** respectively. The hearts are being viewed from the base towards the apex. PA over the myocardium in both species is highly homogeneous and averages between 2 and 4 degrees (**Fig. 1D**). PA maps of infarcted sheep and rat hearts are shown in **Fig. 2**. Anteroseptal infarction was produced in the sheep hearts with balloon occlusion and anterior infarction in the rat hearts with coronary ligation. PA was significantly increased in the infarct zone of all the sheep and rat hearts imaged. The region of myocardium with increased PA is in agreement with the area of thinned infarcted myocardium.

Conclusion: A new tractographic metric, the tractographic propagation angle is introduced. This reveals that myofibers in the heart have a low and very consistent radius of curvature (2-4 degrees). The threshold value of 35 degrees used in many tractographic algorithms is thus likely excessive in the heart. In infarcted myocardium PA was significantly elevated and heterogenous. In this work, PA robustly distinguishes normal from infarcted myocardium. This novel metric has the potential to diagnose and characterize myocardial infarctions at the microstructural scale and may also be of use in other conditions such as transplant rejection.

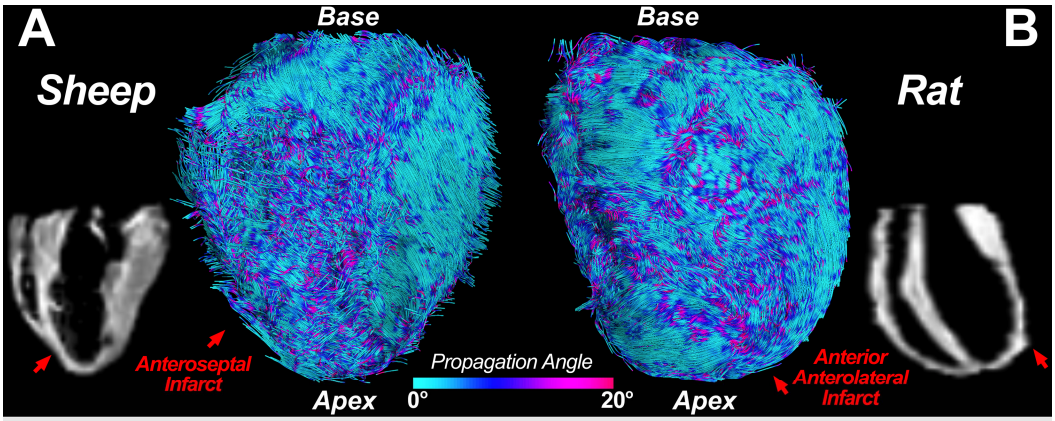

Figure 2: PA maps of infarcted sheep and rat hearts. PA robustly detects the anteroseptal infarct in the sheep heart and the anterior/anterolateral infarct in the rat heart. PA in the infarct is increased and highly heterogeneous.

References: 1. Sosnovik et al. Circ. Imaging, 2007. **Funding:** R01 HL093038 (Sosnovik), NCRR P41RR14075 (Martinos Center) and MGH-ECOR (Mekkaoui).