In Vivo Delineation of Myocardial Infarction Using the Tractographic Propagation Angle Correlates Strongly with Delayed Gadolinium Enhancement

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Introduction: Delayed Gadolinium enhancement (Gd-DE) is able to detect regions of fibrosis due to myocardial infarction **[1]**. Gadolinium, however, cannot be given to patients with cardiac disease who also have renal impairment. A strong need thus exists to develop novel techniques, using endogenous contrast mechanisms, to detect myocardial infarction by MRI. We have recently defined the tractographic propagation angle (PA) as a tool for measuring changes in myocardial architecture using diffusion tensor MRI (DTI) **[2]**. Here we study whether image segmentation based on the tractographic PA can be used to delineate myocardial infarcts without the need for exogenous contrast agents. Normal human hearts (n=5) and infarcted sheep hearts (n=5) were studied ex vivo. Infarcted mice (n=5) were imaged in vivo.

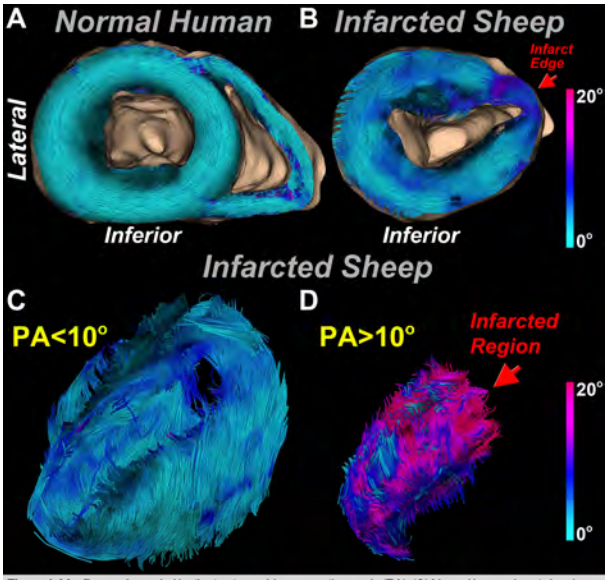

Figure 1. Myofibers color-coded by the tractographic propagation angle (PA). (**A**) Normal human heart showing a low and homogeneous PA. (**B**) Sheep heart showing an increase in PA at the edge of an anteroseptal infarct. The hearts in panels **A** and **B** are being viewed from the base towards the apex. (**C, D**) Infarcted sheep heart viewed in its long axis. (**C**) A lowpass PA value of 10 degrees delineates the normal myocardium and creates a void in the infarct. (**D**) Conversely, a highpass PA value of 10 degrees robustly delineates the infarcted myocardium.

Material and Methods: Myocardial infarction was produced in five C57BL6 mice via permanent ligation of the left coronary artery. In vivo DTI of the infarcted mice (n=5) was performed on a 9.4T scanner (Bruker) 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/mm2 with 24 gradient-encoding directions, and isotropic resolution of 280 µm. The human and sheep hearts were imaged on a clinical 3T scanner with an isotropic resolution of 2mm and a b-value of 700 s/mm^2. The tractographic propagation angle PA was defined as the angle between two adjacent principal eigenvectors ($\hat{e}_{ij}$, $\hat{e}_{ij+1}$) relative to a given fiber, and is thus a measure of tract coherence. PA values were computed along myofiber trajectories within the principal eigenvector field using a fourth-order Runge-Kutta integration method. Delayed Gd enhancement imaging was performed 10 minutes after the injection of 0.2 mmol Gd-DTPA/kg. A short axis slice through the infarcted myocardium was acquired using a cardiac-gated inversion recovery gradient echo sequence. Infarcted regions were segmented automatically on the Gd-DE images using a threshold of 2 standard deviations above normal. A PA threshold value of 10 degrees was used to automatically segment normal and infarcted myocardium. Percent infarct size was calculated with both techniques and correlated.

Results: PA maps of a normal human and an infarcted sheep heart are shown in Figure 1A and 1B respectively. The hearts are being viewed from the base towards the apex. PA in the normal myocardium of both species is highly homogeneous and averages between 2 and 4 degrees. PA in the sheep infarct is significantly elevated and allows the infarct zone to be differentiated from the rest of the myocardium (Figure 1 C-D). PA was significantly increased in the infarct zone of all the mouse hearts imaged (Figure 2A). A PA threshold of 10 degrees robustly segmented the infarct zone (Figure 2 A-C), and an excellent correlation (R^2=0.95) was seen between percent infarct size by Gd-DE and tractographic PA (Figure 2D).

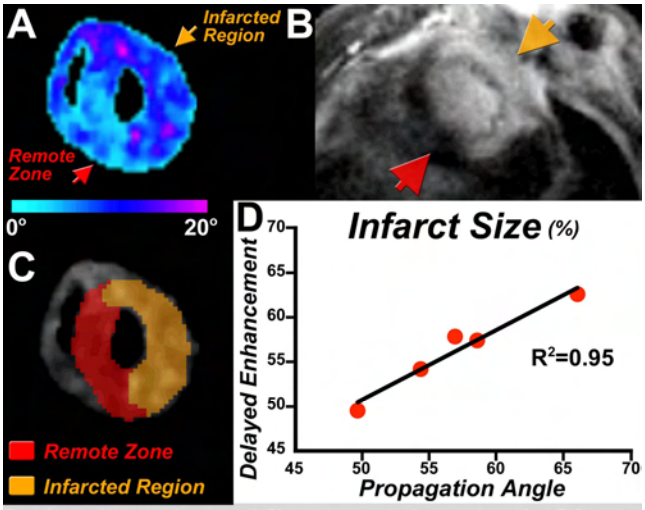

Figure 2. *In vivo* PA maps in infarcted mice. (**A**) PA map in a mouse with a large anterolateral infarct. (**B**) Delayed enhancement image at the corresponding location. It should be noted that the PA maps were acquired in mid-systole and the delayed enhancement images in mid-diastole. (**C**) Segmentation of the PA map using a threshold value of 10 degrees robustly segments normal from infarcted myocardium. (**D**) Percent infarct size calculated from the *in vivo* PA maps correlates very strongly with percent infarct size by delayed gadolinium enhancement.

Conclusion: PA detects the loss of tract coherence in infarcted myocardium and robustly delineates myocardial infarcts in vivo. Infarct size by PA correlates very strongly with infarct size by delayed gadolinium enhancement. The PA approach does not require exogenous contrast and can thus be used in all patients with cardiovascular disease. Moreover, the use of DTI, and specifically PA, can provide additional and highly complementary information in those patients in whom Gd-DE is possible. The tractographic PA provides a new, robust and highly translatable metric for the characterization of myocardial tissue integrity in a range of cardiovascular diseases.

References: [1] Kim R. *et al*. NEJM 2000, **[2]** Mekkaoui C. *et al*. ISMRM 2011. **Funding:** R01HL093038