Ex-vivo Study of the Human Heart with Diffusion Tensor Imaging: Sensitivity to Cardiovascular Risk Factors

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Introduction: Diffusion tensor imaging (DTI) holds the promise of providing structural information to complement data from perfusion studies. The human myocardium is known to exhibit complex spatial organization where the orientation of the fibers changes as a function of transmural location. This fiber structure undergoes remodeling in the disease state. To-date, most ex-vivo studies have been performed on animal hearts although a few human heart studies have been done. These studies have shown differences in certain measured DTI parameters between normal and infracted myocardium [1] or in heart failure patients [2]. However, other MRI techniques such as delayed enhancement (MDE) can depict infarction while T1 mapping can be used to study heart failure. Here, we study the sensitivity of DTI to heart disease using a graded approach to cardiac disease. To our knowledge, such a study has not been carried out before. In addition, global analysis of DTI tractography was performed. Such an analysis makes post-processing more amenable to automation.

Materials and Methods: Human hearts (n=8) were procured through the National Disease Research Interchange (NDRI, Philadelphia, PA). Our inclusion criteria for whole hearts was donors between the ages of 50 and 100 years. The tissue post mortem recovery interval was 12 hrs and delivery time was 72 hrs. The hearts were fixed in 10% formalin post recovery. The hearts were imaged using reduced FOV [3] with single-shot spin-echo EPI on a 3T Philips Achieva scanner with the following parameters: FOV=15×11.5cm; TR/TE=4780/50ms, res.=1.25mm^3, partial k_y=0.67, NSA=10, b-value=1000s/mm^2, 33 directions, SENSE factor=2, scantime≅8hrs. Post-processing was performed on the left ventricle (LV) using the Philips fiber tracking tool based on FACT [4]. Since fiber tracking results can vary depending on the choice of thresholds [5] used for the tracking algorithm, set values of minimum FA=0.15, maximum angle change = 27º and minimum fiber length = 10mm were employed in all the measurements. Probability of cardiac disease (0=normal, 1=disease) based on Framingham risk scores (FRS) [6] were calculated. Risk factors such as hypertension, diabetes mellitus, dyslipidemia and history of cardiac disease and smoking were used to calculate the score.

Results: Figure 1 shows apical views of tractography from two hearts with scores 0.29 (low risk) and 1 (high risk), respectively. The helical nature of the fibers is conspicuous in this zone with the relatively normal heart exhibiting improved organization of fibers compared with the diseased heart. Table 1 shows the mean FA, ADC ($\times 10^{-3}$mm^2/s) and fiber length (FL) in mm for the hearts along with FRS scores. The mean intergroup distance in scores was 0.18±0.11. The non-parametric Spearman's rank correlation was calculated to assess trends between the risk score and DTI derived values. Rank correlation indicates that fiber length shows marginal correlation with FRS (p=0.086) but no significant correlations between FA, ADC, λ_1 (primary eigenvalue) and the FRS. However, when FRS is categorized into two classes (FRS≤0.5 and FRS>0.5), Student's t-test gave a significant difference between the FAs for the two classes (p=0.001); ADC (p=0.28) and λ_1 (p=0.58) still showed no correlation.

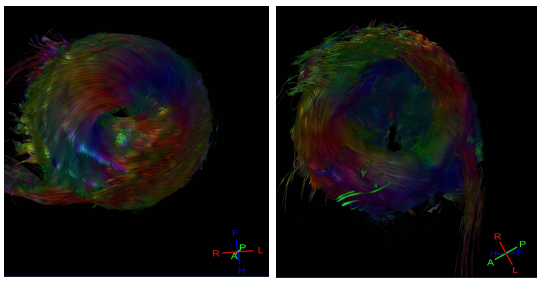

Figure shows apical view of tractography for a relatively normal heart (FRS = 0.29) (left) and for a heart with atrial fibrillation (FRS = 1) (right).

FRS	FA	ADC	FL	λ_1
0.29	0.293	0.517	152	0.67
0.40	0.286	0.551	40.3	0.68
0.57	0.239	0.527	82.4	0.66
0.66	0.239	0.476	36.6	0.59
1	0.253	0.6	37.3	0.75
P value	0.45	0.4	0.086	0.57

Discussion: In our study, fiber length showed the best sensitivity to different grades of cardiac disease. Note that the mean fiber length reported here is not necessarily related to the true myofiber length but is a reflection of fiber integrity under conditions of a set threshold for FA and maximum allowed change in fiber orientation. An earlier work had conjectured that fiber length could provide supplemental information [7]. Heart size variation could not account for the FL differences. Other measures of fiber integrity have been proposed [8] and may also prove discriminatory. FA showed differentiation in normal versus diseased hearts but not to the different nuances of disease. Some studies have shown that fibers in the endocardium undergo greater remodeling than in other regions [9]. Although values were different in the endocardium, significance results remained unchanged. In addition to threshold values, SNR and artifacts can affect fiber length measurements. SNR parity was achieved by using the same rigid 8-channel head coil and with use of the same scan parameters. Fat artifacts in EPI are prominent along the phase encoding (PE) direction. Effort was made to reduce pericardial fat signal through suppression and careful placement of the hearts in relation to the PE direction. There is some evidence that DTI values in ex-vivo hearts show temporal variation [10]. The temporal stability of the measured parameters was assessed by performing repeat experiments on three of the hearts within 40±21 days of each other. Only ADC values showed a non-trivial change but FA values were unchanged. This difference could possibly be due to the use of agar in [10]. The heart with FRS value of 0.4 took a longer time to fix and showed differences in FA and ADC with repeated scans.

References: [1] Wu MT *Circulation* 2006 :1036-1045. [2] Abdullah O et al. *ISMRM* 2011 :3398. [3] Wilm BJ et al. *MRM* 2007 ;57 :625-630. [4] Mori S. et al. *Ann. Neurol.* 1999; 45:265-269. [5] Song X et al. *Procs IEEE Signal Proc*., 2010 ;724-727. [6] Pencina MJ et al. *Circulation* 2009; 119:3078-3084. [7] Wu Y. et al. *Procs IEEE Eng Med Biol* 2005 ;7004-7007. [8] Mekkaoui C et al. *ISMRM* 2011 ; 17. [9] Tezuka F. *Tohoku J. Exp. Med.* 1975;117:289-297. [10] Hales P et al. *ISMRM* 2009;1764.