Biexponential diffusion tensor analysis of myocardial structural alteration in rabbit models with myocardium infarction

Yin Wu[1,2], Chao Zou[1,2], Wei Liu[1,2], Wei Yang[1,2], Ke Jiang[1,2], and Ed X. Wu[3,4]

[1]*Paul C. Lauterbur Research Center for Biomedical Imaging, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guangdong, China, People's Republic of,* [2]*Key Lab of Health Informatics, Chinese Academy of Sciences, Shenzhen, Guangdong, China, People's Republic of,* [3]*Laboratory of Biomedical Imaging and Signal Processing, The University of Hong Kong, Pukfulam, Hong Kong,* [4]*Department of Electrical and Electronic Engineering, The University of Hong Kong, Pokfulam, Hong Kong*

Introduction Diffusion tensor imaging (DTI) has been successfully applied in investigation of infarcted myocardial structural alteration [1-2]. All these previous studies assumed the water diffusion behavior followed Gaussian manner, resulting in monoexponential decay of diffusion-weighted signal. However, significant deviation from the decay model was observed with increase of diffusion strength in some biological tissues [3], leading to diffusion strength dependence of DTI indices characterization [4]. Biexponential model based on two components was proposed for better fitting of diffusion signal decay then [3]. Although the model may not precisely represent all possible physical compartments [5-6], biexponential diffusion behavior was regarded to be applicable in myocardium, typically with intracellular compartment contributing to slow diffusion and extracellular and microvascular spaces dominating fast diffusion in perfused heart [6-7]. In this study, left ventricular heart structure after acute MI was analyzed with biexponential diffusion model for the first time to investigate the diffusion behavior, which may provide more insights into myocardial structural degradation than conventional monoexponential model.

Method Imaging experiments were conducted on a 3T MR imager. LCX coronary artery ligation was performed on 6 New Zealand adult rabbits with infarctions typically induced at lateral wall. Infarcted animals together with 6 controls were sacrificed at 5 days after infarct surgery. The excised hearts were fixed with formalin and segmented EPI-DTI [8] was performed along the short-axis of LV using the following parameters: TR/TE = 4000/95 ms; slice thickness = 1.2 mm, slice gap = 0.2 mm; gradient direction = 6; number of slices = 6; in-plane resolution of 0.78 mm^2; non-zeros b values of 500 to 3000 s/mm^2 with a step of 250 s/mm^2; and NEX = 4. The scan time was ~2.5 hr per sample. DTI data at all b-values was fitted to biexponential model of $S(b)/S(0) = A_f*\exp(-bD_f)+A_s*\exp(-bD_s)$ [9] with a home-written MATLAB program. Pixel-based fractional anisotropy (FA), mean diffusivity (MD), axial and radial diffusivities of fast and slow diffusion were calculated from D_f and D_s, respectively. Each slice was segmented into septum, anterior, lateral and posterior [1]. In infarct group, segment with the center of infarction located was identified as infarct region, of which the bilateral segments were adjacent region, and the remaining part was remote region. For control group, lateral wall was arbitrarily regarded as sham infarct region with sham adjacent and sham remote regions subsequently defined (Fig. 1). For each sample, 6 representative slices covering infarction were selected, from which DTI indices were measured and averaged among slices and six samples of a group at three regions. Student's t-test was performed to exam the statistical difference of DTI indices between infarct and control groups with $p<0.05$ regarded as significant. Masson's trichrome stain were performed to examine myocardial microstructural degradation.

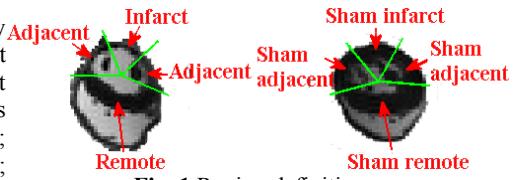

Fig. 1 Region definition.

Results Monoexponential and biexponential fittings were performed on normalized diffusion-weighted signals averaged along 6 diffusion directions of a representative normal heart sample (Fig. 2). The squared 2-norm of the fitting residuals of biexponential fitting (1.9×10^{-5}) was much smaller than that of monoexponential fitting (4.3×10^{-3}). SNR was ~93 and ~24 at the smallest and largest b-values, respectively, ensuring sufficient SNR for DTI index measurement. Significant decrease of both fast and slow FA together with statistically substantial increase of fast MD and fast radial diffusivity were observed in infarct (Fig. 3a) and adjacent (Fig. 3b) regions in infarct group compared to control. Specifically, slow FA was greater than fast FA due to the contribution of highly anisotropy from intracellular space. And more substantial reduction of fast FA occurred in infarct region, indicating fast compartment becoming less anisotropic. Fast radial diffusivity increased obviously, reflecting enlargement of extracellular and microvascular space and subsequently leading to increase of fast MD. However, no significant alteration was found for slow MD, slow radial diffusivity, and volume fraction of fast and slow compartments (not shown). Compared to control, myocardium in infarct region was replaced by collagen/fibrosis stained with blue/green, where myocardial fiber lost organized structure with extracellular and microvascular space increase. In adjacent region, viable fiber bundles (in red) exhibited but tended to lose organized structure with greater extracellular and microvascular space compared to control (Fig. 4).

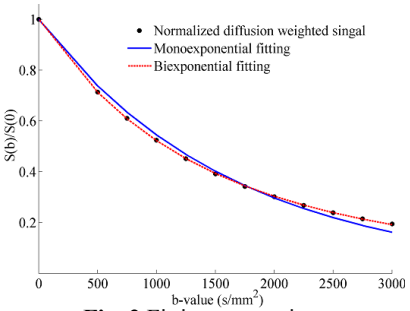

Fig. 2 Fitting comparison.

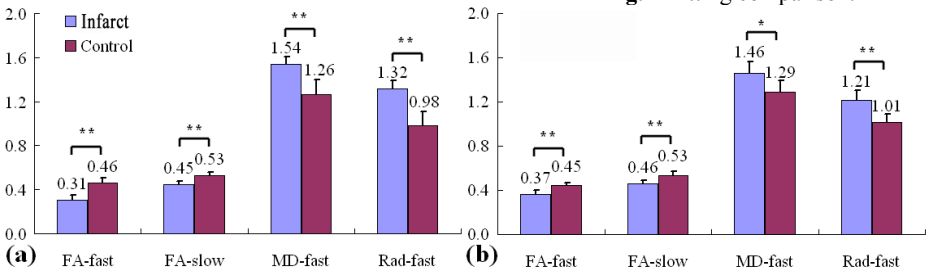

Fig. 3 Myocardial structural alteration at (a) infarct and (b) adjacent regions. *p<0.05, **p<0.01.

Discussion In this study, myocardial structural degradation 5 days after MI surgery was assessed with biexponential diffusion model, from which diffusion characteristics of two compartments were assessed. DTI results showed that fast radial diffusivity increased due to extracellular and microvascular compartment augmented along radial direction, leading to enhancement of fast MD, which was in good agreement with the histological observation. Increase of fast radial diffusivity and fiber integrity/coherence loss forced both of the two compartments to be less anisotropic, resulting in decrease of both fast and slow FA. The current study suggested that biexponential diffusion function could be utilized as a tool to monitor and detect myocardial morphological alteration and structural degradation by probing multi-compartment diffusion behavior compared to conventional used monoexponential diffusion model.

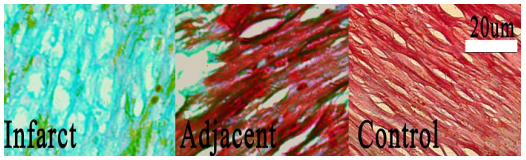

Fig. 4 Masson's trichrome stain at ×400 magnification.

References [1] Chen J et al, 2003; [2] Wu MT et al, 2006; [3] Niendorf T et al, 1996; [4] Hui ES et al, 2010; [5] Mulkern RV et al, 1999; [6] Forder JR et al, 2001; [7] Hsu EW et al, 2001; [8] Porter DA et al, 2009; [9] Maier SE et al, 2004.

Acknowledgments NSFC 30900387, GIRTF-LCHT, NSFGD 9478922035-X003050, BRPSZ JC200903170437A and JC201005270311A.