Contribution of myocardial vascular compartment to water diffusion

M. Hwang[1], M. Clark[1], A. Barmpoutis[1], and J. Forder[1]
[1]University of Florida, Gainesville, FL, United States

Introduction

The use of diffusion weighted magnetic resonance imaging (DWI) as a useful tool to probe microstructure of myocardium has emerged as a result of strong correlation between molecular movements and the organization and geometry of the microscopic environment. Diffusion tensor imaging (DTI) has been used to characterize fiber architectures of the myocardium and to observe its non-mono-exponential behavior of MR diffusion [1-2]. Even though interstitial, intracellular and vascular spaces in the tissue mainly contribute to water diffusion composed of the fast and slow components, the physiological compartments that are responsible for myocardial DTI signals still remain to be identified. In this experimental study, DTI from isolated rabbit heart perfused with St. Thomas' Hospital solution (STH) and/or perfluorocarbon (PFC) emulsion was used to investigate the contribution of vascular compartment to the fast component of the multi-exponentional diffusion, since freely diffusing water has potential to influence the fast component. Since most myocardial diffusion experiments are performed on fixed or cardioplegic-arrested preparations, the contribution of the vascular compartment to the measured diffusion may be substantial. As a result, pathologies that result in altered vascular architecture may lead to incorrect assumptions about myocardial fiber orientation if contributions from this compartment are ignored.

Materials and Method

Isolated heart preparation: New Zealand White male rabbits (2-4kg) were anesthetized using a mixture of ketamine/xylazine (40mg/kg:10mg/kg, i.m.) followed by heparin (1000 U/kg, i.v.) and were then exsanguinated. The excised heart and lungs were placed in a bath of cold cardiopledgic solution (4°C). The heart was transferred to a Langendorff apparatus and perfused retrogradely. After the descending aorta was cannulated, the lungs were ligated and removed rapidly. The initial perfusate was a modified Krebs Henseleit buffer to permit the heart to contract normally, and the aortic valve to seat properly. A thin (1mm-OD) polyethylene tube was inserted in the left ventricle (LV) serving as a vent to avoid excess hydrostatic pressure accumulation and distension of the LV from Thebesian flow. The heart was arrested by switching perfusate to a modified St. Thomas' Hospital cardioplegic solution (STH) before imaging. To prevent the vascular compartment from collapsing, the pulmonary artery was cannulated, and elevated to produce 10 cm of venous hydrostatic pressure. These experiments were run at room temperature (24 - 25°C).

DTI: MR experiments were performed on an 11.1 T/ 40 cm clear bore magnet (Magnex instrument Inc. UK, Bruker instrument console) with the loop-gap coil (32 mm diameter) dual tuned to $^{1}H/^{19}F$ resonances. The temperature in the magnet was 28 -29°C. Proton diffusion weighted image of the arrested rabbit heart with the STH were acquired by applying the gradients to give diffusion sensitizing factors (b values), 80, 160, 250, 350, 460, 580, 710, 850, and 1000, in 6 directions with a standard spin echo pulse sequence. Imaging parameters were TR = 1.5 s, TE = 29 ms, 1 average for all scans using Δ = 16.5 ms, δ = 5.5 ms. Thus a total of 55 scans were obtained per slice of 2 mm thickness, each with in-plane resolution of 0.5 × 0.5 mm^2 and, data matrix of 80 × 80. ^{1}H DWI was repeated after 15cc of PFC was administered through the cannulated aorta to replace the STH in the vascular compartment.

Data analysis: Pixel by pixel analysis was conducted after the primary eigen vectors of diffusion tensor were generated on the Fractional Anisotropy (FA) map derived with FLTView™ (developed at UF) (Fig 1). Calculation of normalized diffusion-weighted signal attenuation data with b values and linear regression analysis were performed in Matlab (MathSoft, Cambridge, MA), to derive apparent diffusion coefficients (ADCs).

Results and discussion

Figure 1 demonstrates determination of region of interest (ROI) in the free wall of LV where vascular compartments are filled with different materials, STH (a) and PFC (b). Pixels providing the same primary eigen vector, which correlates with myocardial fiber orientation, were manually selected to examine the effect of vascular compartment to the fast component of water diffusion because myocardial capillaries generally run parallel to myocardial fibers [2]. The apparent diffusion coefficient of the fast component is represented by the slope of logarithmic normalized signal attenuation data at low b-values, shown in Figure 2. The left ventricular free wall of hearts perfused with STH showed significant variation depending on the applied diffusion gradient directions (a) and slice positions (not shown). It implies that ADC may change depending on geometric relation between capillary orientation and diffusion gradient direction. An additional confounding factor is that fiber orientation changes from epicardium to endocardium and from base to apex. When the vascular space was replaced with PFC emulsion particles (200-450 nm diameter), ADC decreased up to 40% in applied directions of measured slices (Fig.3, Table 1). It has been reported that PFC emulsion stays inside vasculature when administered intravenously [3]. It may be verified with ^{19}F MR imaging planned as the following study. It suggests that PFC emulsion may not affect the interstitial space (which accounts for another 20% of myocardial volume) and suggests the vascular compartment is a major contributor to the fast component of water diffusion.

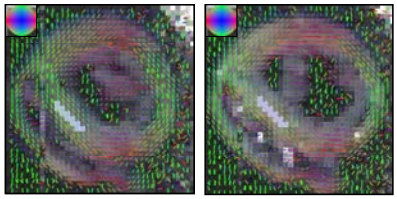

Fig. 1 manually selected ROIs based on the primary eigen vectors on FA map. Left: filled with STH, right: replaced with PFC

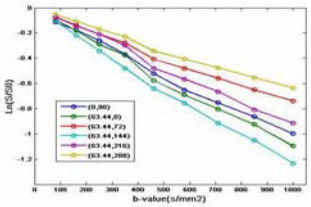

Fig.2 Logarithmic normalized signal attenuation with diffusion weighted orientations (STH)

When STH and PFC emulsion phantoms were measured with diffusion weighting (b-values 0-1000), ADC was isotropic and measured 2.23 × 10^{-3} mm^2/s and 1.39 × 10^{-3} mm^2/s, respectively. These results suggest that the significant decrease of ADC may be from replacement of STH with PFC emulsion in the vascular compartment.

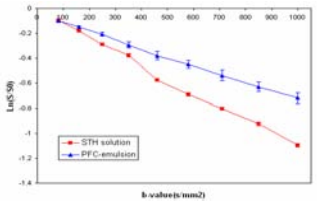

Fig 3: representative logarithmic normalized signal attenuation of STH and PFC Each point corresponds to the mean and SD of selected ROIs.

θ, φ	STH	PFC	ADC Decrease
0, 90	1.0	0.84	16 %
63.4, 0	1.1	0.67	39.1 %
63.4, 72	0.7	0.48	31.4 %
63.4, 144	1.2	0.86	28.3 %
63.4, 216	0.9	0.78	13.3 %
63.4, 288	0.6	0.36	40 %

Table 1 ADC of STH and PFC with diffusion weighted directions in spherical coordinate, × 10^{-3} mm^2/s; obtained from linear regression analysis in MATlab

Conclusion

DTI of rabbit heart at 11.1 T demonstrates that vascular compartment in the myocardium may be a significant contributor to the fast component of water diffusion. Interpretation of existing myocardial DTI data without knowledge of the source of the diffusion signals may lead to incorrect assumptions. Additional experiments to elucidate the source of the remaining fast component (as well as physiological sources for the slow components) are currently underway.

References: 1. J. R. Forder et al. AJP-Heart 2001;28. 2. E. W. Hsu et al. Magn Reson Med 2001;45. 3. R. M. Judd et al. Magn Reson Med 1992; 28.

Acknowledgement: This work was funded by seed grants (JRF) from the McKnight Brain Institute and the Department of Radiology at the University of Florida. MRI was performed at the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility in the McKnight Brain Institute (MBI) at the UF.