Myocardial Vasculature: A major contributor to cardiac MR diffusion

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Introduction:
The coronary circulation is a pivotal component of the myocardium due to high energetic demand in the life-long pump – the capillary surface area in the heart occupies 14-22 % (significantly larger than one in the brain, 4~5 % [1]). The myocardial diffusion tensor imaging (DTI) may reveal the electromechanical activation mechanism innovatively as well as the viability of the cardiac tissue non-invasively. Thus, vascular spaces may need to be weighted as much as interstitial and intracellular spaces in order to understand the physiological compartments responsible for the DTI signals. In this experimental study using 11T magnet, we investigated the contribution of vasculature to the MR water diffusion signal observed in isolated rabbit heart 1) by replacing the vascular space with perfluorocarbon-emulsion (PFC) and 2) by changing the vascular flow rate of a modified St. Thomas' Hospital cardioplegic solution (STH).

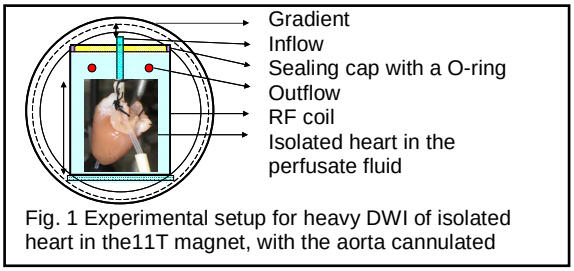

Fig. 1 Experimental setup for heavy DWI of isolated heart in the11T magnet, with the aorta cannulated

Materials and Method: Isolated heart preparation: Isolated perfused hearts (n=12) of New Zealand White male rabbits (2-4kg) were prepared according to the animal protocol approved by the UF Institutional Animal Care and Use Committee [2]. Due to the sensitivity of diffusion weighted images to motion, the hearts were arrested prior to imaging by switching perfusate to the STH. Experiments were run at room temperature.
MRI: MR experiments were performed on an 11.1 T/ 40 cm clear bore magnet (Bruker Instruments, Inc., Billerica, MA). Diffusion weighted images were acquired by applying the gradients to give 14 b values up to 6500 s/mm^2 in 6 directions with a pulsed gradient spin echo sequence (see Fig.1). Imaging parameters were TR = 1.5 s, TE = 27.3 ms, NA=1, Δ = 11.59 ms, δ = 3.8 ms. Slice thickness was 2 mm with an in-plane resolution of 0.5 × 0.5 mm^2. Five hearts underwent substitution of the STH in the coronary vascular space with 15cc of perfluorocarbon-emulsion (PFC) and the DTI measurement was repeated. Three hearts served as time-varying controls, and were measured continuously in order to estimate changes in ADC due to the intermittent ischemic condition. Four hearts underwent variation of flow from 0 mL/min to 5 mL/min, and ^{1}H DWI was repeated after each flow rate change. Viability was maintained in the zero flow rate state by brief periods of perfusion in between image acquisitions.

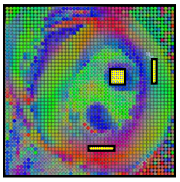
Fig. 2 Manual selection of ROIs: based on the primary eigen vector map on a short axis view of the isolated heart. Diffusion was encoded horizontally in the plane. (right: & bottom: Free Wall-1 & Free Wall-2 in the LV, middle: Papillary Muscle.)

Data analysis: Pixel by pixel analysis was conducted on a map of the primary eigen vectors of diffusion tensor following myocardial fibers using FLTView™ (©2007, Barmpoutis) (see Fig 2). Calculation of normalized diffusion-weighted signal intensity with b values and linear regression analysis were performed in Matlab (MathSoft, Cambridge, MA), to derive apparent diffusion coefficients (ADCs) under vascular replacement with the PFC. Similarly, the normalized signal intensity with vascular flow change was fitted to a biexponential function.

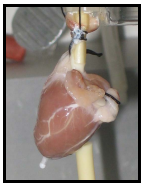
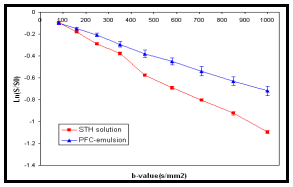

Fig 3: Replacement the STH with the PFC emulsion (left) & change of logarithmic normalized signal attenuation with the replacement. Branches of the coronary arteries are shown filled with the milky-white emulsion.

Results:
1) Replacement of vascular space with the PFC:
The ADC of control hearts decreased 12.8 ± 4.8 % over the time course of the experiment (data not shown). When the vascular space was replaced with PFC particles (~ Ø 450 nm), ADC from b value up to 1000 s/mm^2 decreased significantly by 23.1± 8.5% compared to initial measurements ($p<0.01$) (see Fig.3, right). Based on the previous reports that the PFC stays inside vasculature when administered intravenously (see also Fig 3, left), this result suggests that the ADC decrease was largely due to the vascular replacement of STH with PFC, whose isotropic ADCs were 2.23 ± 0.24 × 10^{-3} mm^2/s and 1.39 ± 0.15 × 10^{-3} mm^2/s, respectively.

2) Change of vascular flow rate of the STH:
Figure 4 demonstrates the influence of flow upon the bi-exponential decline in signal intensity plotted as a function of b values up to 6500 s/mm^2 in the selected ROIs. Free Wall-1 (where fibers are parallel to diffusion encoded direction) shows the significant changes in the ADC over the b-values with flow change, especially 1ml/min to 2ml/min. Those appear to correlate with relative change of two water pools (fast and slow components), which results from the variation of tissue compartments (extracellular/intracellular). On the other hand, Free Wall-2 and Papillary Muscle don't exhibit the same degree of change in ADC or contribution of the slow component of diffusion. The decrease of fractional anisotropy with flow rate increase (data not shown) suggests that the observed ADC change may correlate with the cell swelling toward the diffusion encoded direction at the expense of anisotropy.

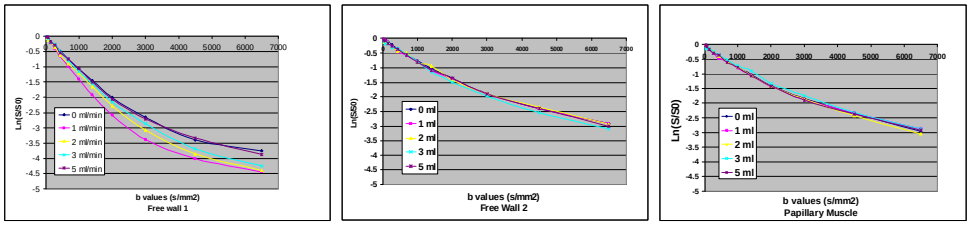

Fig. 4 Logarithmic normalized signal attenuation with changes in perfusate flow. Free Wall-1 (left panel) is parallel to the diffusion encoded direction. On the other hand, Free Wall-2 (middle panel) and Papillary Muscle (right panel) are oriented orthogonal to the diffusion encoding direction.

Conclusion:
This study demonstrates a significant contribution of vascular compartment to the myocardial MR diffusion characteristics. First, the vascular compartment may be a significant contributor to the fast component of MR water diffusion. Second, attenuation of signal intensity with b values up to 6500 s/mm^2 appears to be modulated by vascular flow. In addition, the fractional increase of the estimated fast component of ADC with flow may be from increased vascular and/or interstitial volumes. Studies to alter the interstitial volume by altered vascular permeability and/or oncotic pressure are currently underway using a fast diffusion imaging sequence. This has important implications under pathophysiological conditions, where hypoperfusion and ischemia may predominate.

References: 1. D. C Poole et al AJP-Heart 1990; 259. 2. J. R. Forder et al. AJP-Heart 2001; 28.
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