Monitoring Random Molecular Diffusion and Tissue Perfusion in Rat liver by Diffusion Weighted Proton MRI

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Introduction

Diffusion weighted (DW) ^{1}H MRI may be useful for diagnosis of fibrosis in diffuse liver diseases and for monitoring response of liver tumors to therapy. However, a very wide range of ADC values have been reported for the liver in both human [1,2] and animal [3,4], and some reported values are greater than the free diffusion of water [5]. In addition, on death a dramatic decrease in water ADC has been reported [6,7], which cannot be explained by ischemia induced intracellular accumulation of water. These anomalous and unexpected results may be because DW ^{1}H MRI is sensitive to both molecular diffusion of water and tissue perfusion [4]. In this study the contributions of diffusion and perfusion to DW ^{1}H MRI were separated in the normal rat liver using ten *b* values that encompass both low (< 100 s/mm^2) and high (> 100 s/mm^2) *b* values. In addition effect of mortal ischemia was examined to demonstrate that the fast ADC component results from microcapillary blood perfusion.

Methods

DW ^{1}H MRI experiments were conducted on male Wistar rats (300 g, n=8) using a Varian 9.4 T, 31 cm horizontal bore system and a 6.3 cm diameter quadrate bird cage coil. A small tube containing 54 mM NaCl was placed inside the coil and used as a reference. The anesthesia was maintained with 1.0-1.5% isoflurane delivered in medical air at 1.5-2.0 L/min during the MRI experiments. The animal core body temperature was maintained at 35-37 ^{o}C by blowing warm air through the magnet bore. A multi-slice DW ^{1}H imaging sequence with the following imaging parameters was used: 1,100 ms repetition time, 25 ms echo time, 128 × 128 data points over a 64 × 64 field of view, 0.5 mm slice thickness, 1.5 mm slice gap, and ten *b* values (0, 10, 20, 30, 100, 220, 350, 600, 1000, 1600 s/mm^2). Respiratory gating was used to minimize the effects of motion. Total imaging time was ~25 min. Mortal ischemia was produced by increasing the isoflurane to 4.5 % in medical air at 4 L/min. Respiration was monitored until it stopped, then again DW ^{1}H MR images were collected for the ten *b* values with respiratory gating turned off. DW MRI signal intensity (SI) versus *b* value data were fit to the following biexponential equation:

$$SI = SI_o\left[A_f \times e^{-b\times ADC_{fast}} + \left(1 - A_f\right) \times e^{-b\times ADC_{slow}}\right], \qquad \text{Eq. 1}$$

where SI is signal intensity for a given *b* value, ADC_{fast} and ADC_{slow} are the fast and slow ADC, and A_f is the relative contribution of ADC_{fast}.

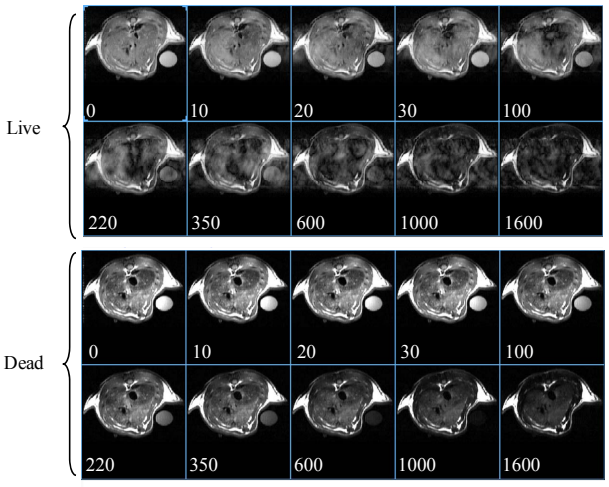

Fig.1. Representative transaxial slices of DW ^{1}H MRI of the rat liver with different *b* values before and after mortal ischemia.

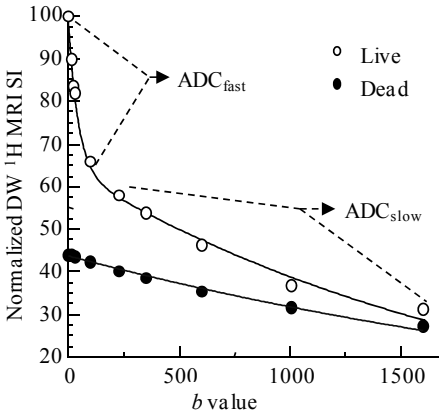

Fig.2. Effect of mortal ischemia on DW ^{1}H MRI SI vs. b value plot.

Results

Transaxial sections of DW ^{1}H MRI of the rat liver collected using ten *b* values pre- and post-mortem for a representative animal are shown in Fig 1. Image blurring due to respiratory motion is clearly visible in the live animal images, especially at high *b* values. The motion artifact disappeared after mortal ischemia. Plots of DW ^{1}H MRI SI as a function of *b* value, before and after mortal ischemia, are shown in Fig 2. The plot is bi-exponential for the live animal but mono-exponential for the dead animal. Results of curve fitting the plots to Eq. 1 are shown in Table 1. The average ADC_{fast} and ADC_{slow} for the live animals were 26 × 10^{-3} and 0.52 × 10^{-3} mm^2/s, respectively, with the fast component contributing 35 % to the total signal. On ischemia, SI from liver at *b* = 0 decreased to 44% of the pre-ischemia value, ADC_{fast} component disappeared, and ADC_{slow} decreased to 0.31 × 10^{-3} mm^2/s.

Table 1. Effects of mortal ischemia on molecular diffusion and perfusion parameters for the rat liver measured by DW ^{1}H MRI. ADC values are in 10^{-3} mm^2/s. * p < 0.05

Parameter	Live	Dead
A_o	98 ± 3	44 ± 4*
A_f	0.35 ± 0.03	-
ADC_{fast}	26 ± 4	-
ADC_{slow}	0.52 ± 0.11	0.31 ± 0.04*

Discussion

The data presented here shows that ADC_{fast}, which contributes 35% to the total signal, most likely represents microcapillary perfusion because this component disappeared after mortal ischemia. Respiratory motion may also contribute to ADC_{fast} because the motion artifact was clearly visible in live animals but not in the dead animals. The observed decrease in ADC_{slow} after ischemia may be because of accumulation of water inside the cells, where diffusion of water is more restricted than in the extracellular space. The large variations in the previously reported ADC values for the liver were because of the use of a monoexponential model and different ranges of only two to four *b* values. In the presence of perfusion, the monexponential model can result in a calculated ADC that is greater than the free diffusion of water especially when low *b* values are used. The dramatic decrease in water ADC after mortal ischemia reported in the previous studies [6,7] can be explained by the disappearance of ADC_{fast}.

Conclusion

Use of a biexponential model for analysis of DW ^{1}H MRI data provides information about molecular diffusion of water and micro-capillary tissue perfusion, both of which are important physiological parameters.

References

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