Effect of Diffusion Time on Liver DWI

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INTRODUCTION

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a sensitive method to visualize microscopic motion of water molecules in biologic tissue including the molecular Brownian motion of water (true diffusion) and the microcirculation of blood (pseudo-diffusion or perfusion) by using multiple b-values [1, 2]. In fact, the DW signal decay depends on not only b-value but also the diffusion time (Δ) [3] because water molecule diffusion is hindered and restricted by cellular microstructures, such as cell membrane, cytoskeleton, and macromolecules in tissue environment [4]. However, the diffusion hindrance and restriction in liver has received little attention. In this study, we aimed to investigate the dependence of diffusion measurement on diffusion time Δ by acquiring and analyzing DW signal with various b-values at different Δ in normal rat liver in vivo.

METHODS

MRI: All MRI experiments were performed using a Bruker 7T scanner on normal adult SD rats (220-260g; 6 weeks old; N=12). During imaging, animals were anesthetized with isoflurane/air using 1.0-1.5% for maintenance via a nose cone with respiratory monitoring. Body temperature was maintained at about 36.5°C by circulating warm water in a heating pad. Each animal was placed in prone position with the abdomen fixed with adhesive tape to reduce respiratory. DW images with 5 different b-values (0, 200, 400, 800 and 1000 s/mm^2) along phase encoding (L-R) direction were acquired in one axial slice covering a large portion of the liver while avoiding inclusion of the lung with respiration-gated single shot stimulated-echo-EPI sequence. DW experiments were repeated with Δ= 15, 45 and 200ms. Imaging parameters were TR/TE=~2000/20ms, δ=3.1ms, slice thickness= 3mm, FOV=51×51mm^2, acquisition matrix=51×51, NEX=11. ***Data analysis:*** A large ROI excluding large blood vessels was drawn on liver parenchyma encompassing a large homogeneous liver region. Apparent diffusion coefficient (ADC) was obtained by fitting the equation: $SI_b/SI_0=\exp(-b\times ADC)$ with the ROI measurements of SI_b/SI_0 at all five b values (0, 200, 400, 800, 1000 s/mm^2) using a least-square nonlinear fitting in Matlab. Blood pseudo-diffusion coefficient (D_{Pseudo}) was calculated by from equation: $SI_b/SI_0=\exp(-b\times D_{Pseudo})$ using b=0 and 200 s/mm^2. True diffusion coefficient (D_{True}) was estimated by fitting the signal decay in the ROI on the images of three large b values (400, 800 and 1000 s/mm^2) to the equation: $SI_b/SI_0=(1-f)\times\exp(-b\times D_{True})$. One-way ANOVA with Turkey's multiple comparison tests was employed to compare ADC, D_{Pseudo} and D_{True} measurements of liver between different Δ, and $p< 0.05$ was considered as statistical significant.

RESULTS

Fig.1 shows the representative FLASH image, T1-weighted image, T2-weighted image and B0 EPI images of normal liver from one animal. Typical ROI used for ADC, D_{True} and D_{Pseudo} measurements is illustrated in the stimulated echo b0 EPI images obtained at Δ = 15, 45 and 200ms (Fig.1). Fig. 2 shows the liver mean DW signal decay as computed by taking the average of normalized liver DW signal (SI_b/SI_0) from 12 animals with diffusion time Δ= 15, 45 and 200ms. Error bars indicates the standard deviation among all animals. ADC was measured using all b values with a mono-exponential fit. D_{Pseudo} was measured with very small and small b values (0 and 200 s/mm^2), and D_{True} was measured with b values higher than 200 s/mm^2. It can be observed that the signal decay became slower when the diffusion time increased. Fig.3 compares the ROI measurements of liver ADC, D_{True} and D_{Pseudo} for three different Δ. ADC, D_{True} and D_{Pseudo} generally decreased with Δ, confirming the statistically significant dependency of diffusion coefficients on diffusion time. Note that the diffusion distance of water molecules in liver that can be probed by diffusion time of Δ= 15~200ms ranges approximately from 5μm to16μm as estimated from the square root of the product of diffusion time and measured D_{True} using Einstein's equation.

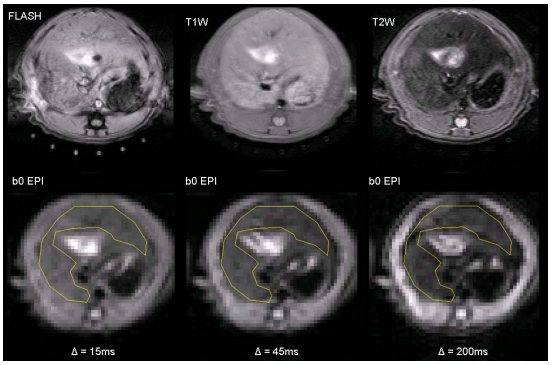

Fig. 1 Representative FLASH, T1W, T2W, non-diffusion weighted (B0) EPI liver images acquired at Δ=15, 45 and 200 ms from one normal adult SD rat. Typical ROI used for ADC, D_{True} and D_{Pseudo} measurement is illustrated in the B0 images.

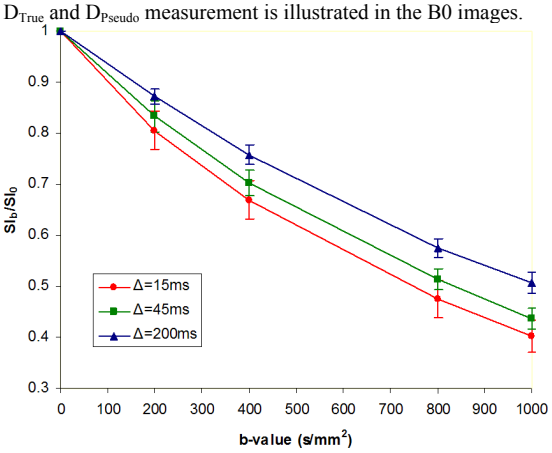

Fig. 2 Mean DW signal decays, computed as the average of all DW signal measured from 12 animals, at different Δ.

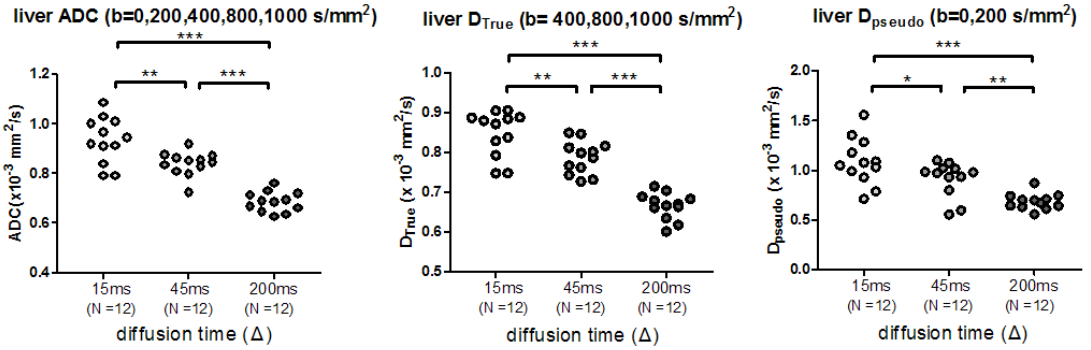

Fig.3 ROI measurement of liver ADC, D_{True} and D_{Pseudo} obtained from DWI with 3 different Δ. One-way ANOVA was performed with * for $p<0.05$, ** for $p<0.01$, *** for $P< 0.001$.

DISCUSSION AND CONCLUSION

The drop of D_{True} with increasing Δ is expected because the probability for diffusing water molecules to encounter barriers would increase with longer Δ, which leads to a smaller mean squared displacement per unit time. On the other hand, by reducing the time over which the diffusion process is observed, it may be possible to reduce the interaction with the surrounding microstructures. Therefore, the effect of restricted diffusion in liver can be magnified or minified by increase or decrease the diffusion time. Note that the D_{Pseudo} decrease with Δ is counter-intuitive as one might expect D_{Pseudo} not to change with Δ because microcirculation (perfusion) only depends on blood velocity and capillary geometry [2]. However, this might be explained by that long TM stimulated echo suppress the blood perfusion contribution to D_{Pseudo} measurement. The incoherent motion of blood during the long mixing time results in severe intra-voxel dephasing and subsequent signal loss [5, 6]. In other words, D_{Pseudo} is underestimated at long Δ. The experimental results from this study show that changes in both true diffusion and blood perfusion contribute to the observed ADC decrease with diffusion time. In summary, restricted diffusion behavior is observed in liver in vivo for the first time, demonstrating the effect of both b-value and Δ on liver DWI quantification.

REFERENCES

1. Lebihan D, et al. Radiology 1986; 161(2): 401-407. 2. Lebihan D, et al. Radiology 1988; 168(2): 497-505. 3. Horsfield MA, et al. Magnetic Resonance in Medicine 1994; 31(6): 637-644. 4. Cooper RL, et al. Biophysical Journal 1974; 14(3): 161-177. 5. Lin AP, et al. Magnetic Resonance in Medicine 2008; 60(1): 8-13. 6. Aletras AH, et al. Journal of Magnetic Resonance 1999;140(1): 41-57.