In Vivo Quantification of Lamina T1, T2, and Apparent Diffusion Coefficient in the Mouse Retina at 11.74T

J. Chen[1], Q. Wang[1], H. Zhang[1], X. Yang[1], J. Wang[2], B. A. Berkowitz[3], S. A. Wickline[1], and S-K. Song[1]

[1]Washington University, St. Louis, MO, United States, [2]Chinese Pharmaceutical Association, Beijing, China, People's Republic of, [3]Wayne State University, Detroit, MI, United States

Introduction

MRI has recently been used for non-invasive examination of retinal structure and function in small-animal models. However, the quantitative MR parameters of retina from mice have not yet been reported. The objective of the present study is to quantitatively measure the thickness, T_1, T_2, and ADC in the mouse retinal layers *in vivo* at 11.74T. .

Material and Methods

Animal Model: Adult male C57/BL6 mice were anesthetized with ketamin/xylazine cocktail for MRI on a Varian 11.74T scanner using a custom-built solenoid coil. A transverse slice through the optic nerve head of the mouse eye were selected for imaging. T1-weighted spin-echo images (n = 5) were acquired with: TR, 0.5, 1.0, 2.0, 4.0, and 8.0s; and TE, 21 ms. T2-weighted spin-echo images (n = 10) were acquired with: TR, 1.5s; and TE, 21, 28, 38, and 50 ms. Diffusion weighted images (n = 5) were acquired with: TR, 1.5 s; TE, 35 ms; and b-values of 0 and 955 s/mm^2 at three orthogonal diffusion weighting directions, i.e., in-plane parallel to the optic nerve (∥), in-plane perpendicular to the optic nerve (⊥), and out-of-plane perpendicular to the optic nerve (⊙). Gd-DTPA enhanced T_1-weighted images were acquired (n = 3) with: TR, 500 ms; and TE, 21 ms. Other acquisition parameters used for all images were: slice thickness, 400 μm; FOV, 6×6 mm^2; in-plane resolution, 47×47 μm^2 interpolated to 23×23 μm^2; and number of averages, 4.

Data Analysis: Three MR-detected retina layers and a choroid layer were manually segmented based on signal intensities from the non-diffusion-weighted images. A pair of retina segments, each residing between ~250 μm and ~800 μm away from the center of the optic nerve head, composed the region of interest for quantitative analysis. T_1, T_2, and directional ADC (ADC∥, ADC⊥, and ADC⊙) maps were estimated using least-square fitting.

Histology: Mouse eyes (n=8) were enucleated for histological analysis. Paraffin-embedded tissues were prepared for morphological analysis. Frozen-cut tissues with minimal tissue distortion were prepared for accurate measurement of retina thickness.

Statistical Analysis: Data are expressed as mean ± SD. Unpaired student *t*-test, one-way analysis of variance (ANOVA), and two-way ANOVA were employed for statistical analysis. A p-value < 0.05 was taken to indicate statistically significant difference.

Results

The combined layer of retina/choroid was hyper-intense in the diffusion weighted image (Fig. 1A). Choroid adjacent to the sclera was hyper-enhanced by Gd-DTPA (Data not shown). Three MR-detected retina layers were observed on both T_1-and T_2-weighted images (Figs. 1 B - D). The three MR-detected retina layers were tentatively assigned to retina neural cell layers (Fig. 1E) based on the measured relative retina thickness (Fig. 2). The three MR-detected retina layers were also observed in the calculated T_1, T_2, and ADC maps (Fig. 3). Figure 4 shows the quantified T_1, T_2, and ADC in the vitreous, choroid, retina, and three MR-detected retina layers.

Conclusion

Three MR-detected retina layers were observed in the mouse eye. The thickness, T_1, T_2, and directional ADC of each MR-detected retina layer were quantified. The significant gain in signal-to-noise ratio is the great advantage of ultra-high field strength for MRI of the mouse eye. However, the change in MR relaxation properties and the increased susceptibility associated with the ultra-high field strength also need to be considered in experimental design.

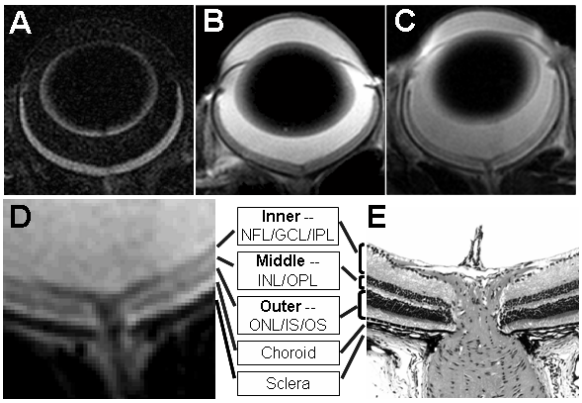

Figure 1. A diffusion-weighted (A), T_1-weighted (B), and T_2-weighted (C) image of the mouse eye. The expanded view of T_2-weighted image (D) and an H&E stained slice (E) show the tentative assignment of the three MR-detected retina layers to retinal neural cell layers.

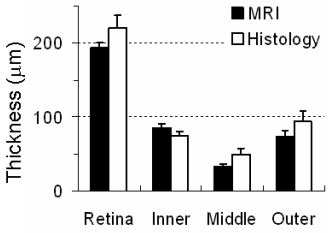

Figure 2. Thickness of the overall retina and individual retinal layer determined by MRI and histology.

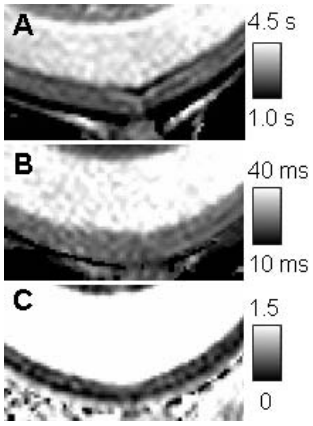

Figure 3. Expanded views of the calculated T1 (A), T2 (B), and ADC⊙ (C) maps of the mouse eye. The unit for ADC is 10^{-3} mm^2/s.

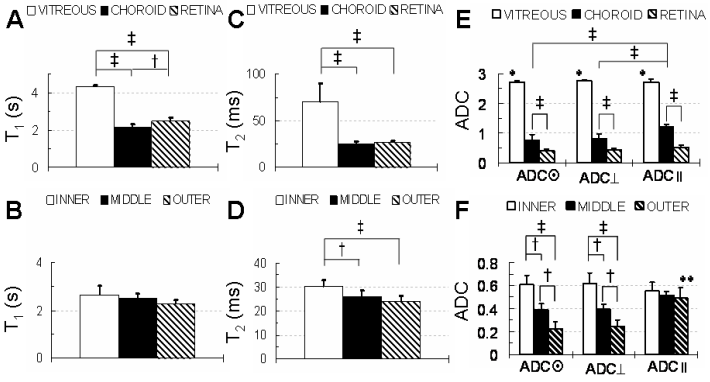

Figure 4. Quantified T1 (A and B), T2 (C and D), and ADC (E and F) in the vitreous, choroid, retina, and the three MR-detected retina layers. The unit for ADC is 10^{-3} mm^2/s. †, p<0.05; ‡, p<0.0001; *, p<0.05 compared to the choroid or retina; **, p<0.05 compared to ADC⊥ or ADC⊙.