

# Diffusion MRI of Choroid Melanoma Tumor in Mouse Eye

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## Introduction

Choroidal melanoma is the most common intraocular malignancy<sup>[1]</sup>. Diffusion weighted MRI (DWI) and the derived apparent diffusion coefficient (ADC) map has proven to be useful in tumor identification and treatment response monitoring<sup>[2]</sup>. However, DWI of intraocular tumor, such as choroidal melanoma, has not been reported to date. The objective of the present study is to quantify ADC of choroidal melanoma for tumor identification in mice.

## Materials and Methods

**Animal Model:** 7-8 weeks old adult male C57BL/6 mice (n=9) underwent intraocular inoculation of  $50 \times 10^3$  B16F10 cells in 1.0  $\mu$ L cell culture medium into choroidal space. Mice were anesthetized with ketamine/xylazine and body temperature was maintained at 37°C during MRI.

**MRI:** MRI of the mouse eye was performed using a Varian 11.74T UNITY-INOVA spectrometer employing a custom-built solenoid coil for transmission and receiving. Mice were divided into two groups: Group1 (n=6) for imaging on day 4 and Group2 (n=3) for imaging on day 10 after tumor cell inoculation. A transverse slice through the optic nerve head of the mouse eye was planned for imaging. A spin-echo sequence incorporating a pair of diffusion sensitizing gradients was used for DWI with the following parameters: TR, 1.5 s; TE, 35 ms;  $\Delta$  25 ms,  $\delta$  8 ms, NEX 4, slice thickness 400  $\mu$ m, field-of-view 6 $\times$ 6 mm<sup>2</sup>, and in-plane resolution, 47 $\times$ 47  $\mu$ m<sup>2</sup>, interpolated to 23 $\times$ 23  $\mu$ m<sup>2</sup>; and b-values of 0 and 955 s/mm<sup>2</sup> at three orthogonal diffusion weighting directions. All diffusion weighted images were acquired with respiratory gating.

**Data Analysis:** ADC map was calculated from the diffusion weighted images. ROIs of tumor and retina were manually segmented based on the contrast difference on T2 weighted  $B_0$  image and diffusion weighted images, and ADC map (Fig. 1 A-C).

**Histology:** Eyes were enucleated, flash frozen, and sliced at 8- $\mu$ m thick through optic disk and perpendicular to retina and stained with Hematoxylin and Eosin (H&E).

**Statistical Analysis:** Data were expressed as mean  $\pm$  standard deviation. Unpaired student t-test was employed for statistical analysis. The statistically significant difference was accepted as p-value < 0.05.

## Results

Melanoma tumor and retina were hypo-intense on T2-weighted image and hyper-intense on diffusion weighted image as compared to vitreous, subretinal fluid, and choroid (Fig. 1 A&B). Melanoma tumor and retina could be further distinguished by the higher signal intensity of tumor mass on the ADC map (Fig. 1C). The MRI detected tumor mass and subretinal fluid accumulation is in agreement with that delineated by histology (Fig. 1D).

At day 4, the ADC of remote intact retina was consistent with that measured previously in normal mouse retina<sup>[3]</sup>. The ADC of choroidal melanoma tumor was about 60% higher than that of remote intact retina (Fig. 2). Tumor ADC has no statistical difference between days 4 and 10 (data not shown).

## Discussion and Conclusion

Tumor mass could be clearly identified on the ADC map due to the significantly higher ADC of melanoma tumor than that of the retina. Thus, diffusion weighted MRI may be used to identify melanoma tumor in vivo.

**References** 1. Albert DM et al. Principles and Practice of Ophthalmology. 1994; p.3197-8. 2. Koh, D.-M. et al. AJR Am J Roentgenol 2007 Jun;188(6):1622-35. 3. Chen et al., Magn Reson Med 2008; 59, p 731-8

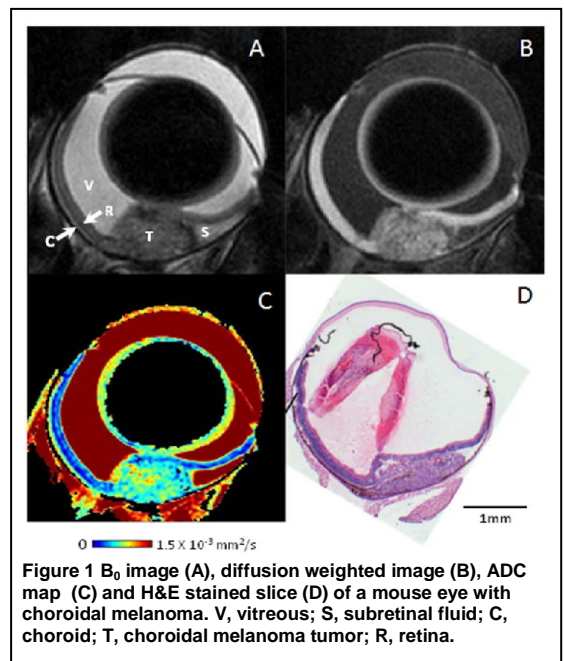


Figure 1  $B_0$  image (A), diffusion weighted image (B), ADC map (C) and H&E stained slice (D) of a mouse eye with choroidal melanoma. V, vitreous; S, subretinal fluid; C, choroid; T, choroidal melanoma tumor; R, retina.

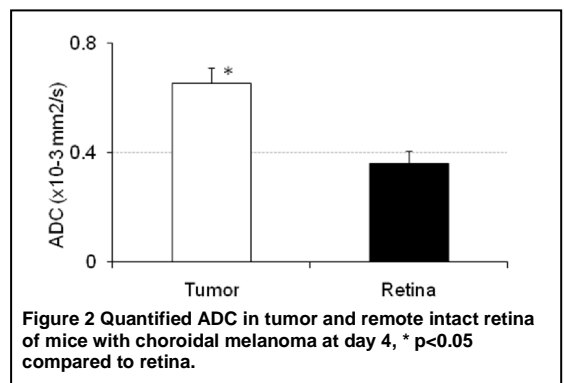


Figure 2 Quantified ADC in tumor and remote intact retina of mice with choroidal melanoma at day 4, \* p<0.05 compared to retina.