# Wallerian Degeneration in Visual Pathway Detected Using Diffusion Tensor Imaging

S-W. Sun[1], H-F. Liang[1], A. H. Cross[2], S-K. Song[1]

[1]Radiology, Washington University, Saint Louis, MO, United States, [2]Neurology, Washington University, Saint Louis, MO, United States

## Introduction

Optic nerve, chiasm, optic tract, and optic radiation are components of the white matter tracts of the visual pathway. The optic nerve and tract consist of the axons originating from the retinal ganglion cells before and after the chiasm. The injury to retinal ganglion cells results in axonal and myelin damages of optic nerve and tract as a consequence of Wallerian degeneration. After retinal ischemia, *in vivo* DTI has been applied to characterize optic nerve degeneration detecting and differentiating axonal and myelin damage (1). Briefly, axial ($\lambda_{\parallel}$) and radial ($\lambda_{\perp}$) diffusivities were used as the surrogate markers for axonal and myelin injury *in vivo*. Decreased $\lambda_{\parallel}$ and increased $\lambda_{\perp}$ corresponding to axonal and myelin injury were confirmed using histology (1). In the present study, the extent of Wallerian degeneration in mouse of retinal ischemia was examined using DTI. It is expected that the axonal damage resulting from retinal ischemia will progress through chiasm reaching the contralateral optic tract (2). Transient retinal ischemia was induced in the right eye of mice. The optic nerve and tract were examined using DTI at 14 days after the retinal ischemia.

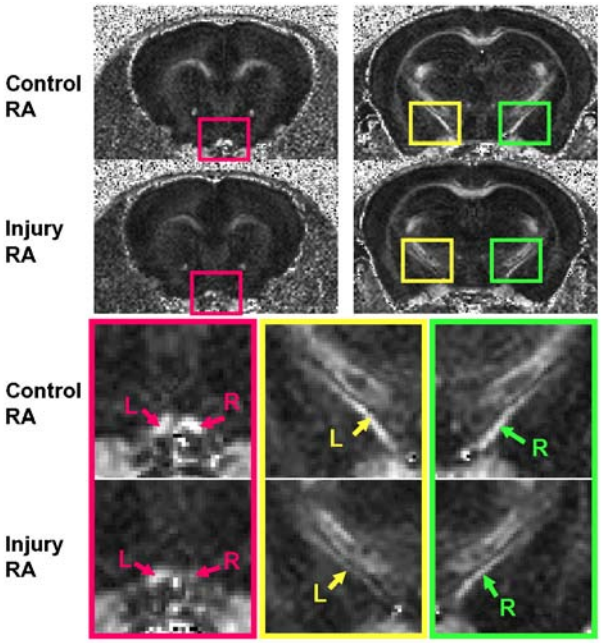


Fig. 1 RA of healthy and injured mice (R: right and L: left sides). The right optic nerve and left optic tract show reduced anisotropy suggestive of injury caused by retinal ischemia.

## Materials and Methods

***Retinal ischemia***

Six male Swiss Webster mice, 6 – 8 weeks of age, underwent the retinal ischemia preparation (1). Briefly, the intraocular pressure (IOP) of the right eye of each mouse was raised above systolic blood pressure by cannulation of the anterior chamber with a 32-gauge needle connected to a saline reservoir placed above the eye resulting in the applied pressure of 100 – 120 mmHg. The elevated IOP was maintained for one hour. Ischemia was confirmed by ophthalmoscopic observation of the blanched fundus. The contralateral eye, which serves as the control, was not cannulated. Reperfusion started immediately after removal of the cannula. At 14 days after the ischemia, *in vivo* DTI was performed. Four age-matched mice were used as controls.

***Diffusion Tensor Imaging***

Data were acquired using spin-echo diffusion weighted imaging sequence with TR 1.6 sec, TE 50 msec, Δ 25 msec, δ 8 msec, NEX 4, slice thickness 0.5 mm, field-of-view 3 cm, and data matrix 256 × 256 (zero filled to 512 × 512). Diffusion sensitizing gradients were applied along six directions: [Gx,Gy,Gz] = [1,1,0], [1,0,1], [0,1,1], [-1,1,0], [0,-1,1], and [1,0,-1]. Two diffusion sensitizing factors or b-values (0 and 0.768 ms/μm$^2$) were used. Relative anisotropy (RA), $\lambda_{\parallel}$ ($\lambda_{\parallel}=\lambda_1$), and $\lambda_{\perp}$ ($\lambda_{\perp}=(\lambda_2+\lambda_3)/2$), were measured in left and right optic nerves and tracts (1). t-test was performed, and $p < 0.05$ was considered significant.

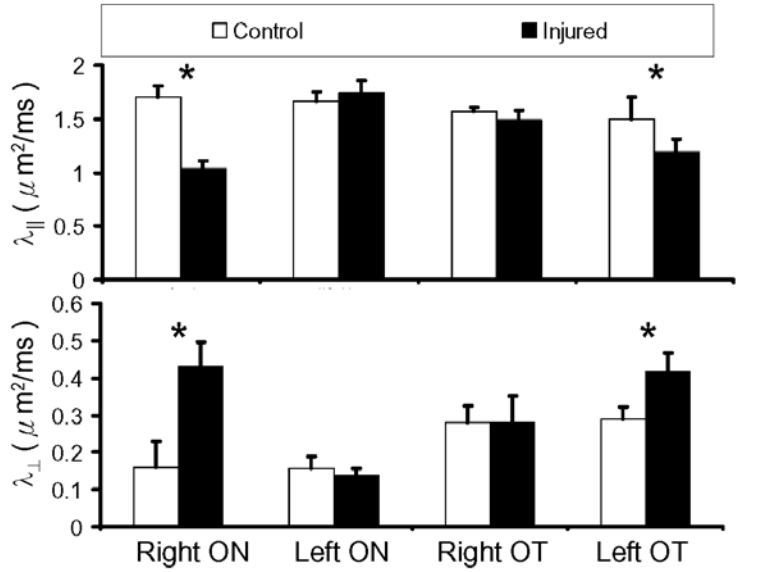


Fig. 2 $\lambda_{\perp}$ and $\lambda_{\parallel}$ of optic nerve (ON) and optic tract (OT) in control and injured mice. Comparing to the controls, right ON and left OT show reduced $\lambda_{\parallel}$ and increased $\lambda_{\perp}$ suggestive of axonal and myelin damage in both regions. *: p<0.05

## Results

The ipsilateral optic nerve and the contralateral optic tract exhibit both axonal and myelin damages at 14 days after retinal ischemia. The damage can be seen as reduced RA in both optic nerve and the contralateral optic tract (Fig. 1), consistent with the expected pathology of Wallerian degeneration after retinal ischemia and ganglion cell loss. Measurements of $\lambda_{\parallel}$ and $\lambda_{\perp}$ in the control and injured optic nerves and tracts are summarized in Fig. 2. Decreased $\lambda_{\parallel}$ and increased $\lambda_{\perp}$ in right optic nerve and left optic tract suggest the coexistence of axonal and myelin damage in these injured white matter tracts.

## Discussions and Conclusions

Unlike the binocular species such as human, the visual system in mice is primarily monocular, with each retina mapping topographically to its contralateral target (2). The present study suggests that at 14 days after lateral retinal ischemia, the damage in optic nerve progresses to the contralateral optic tract resulting in both axonal and myelin damage. *In vivo* DTI provides a new insight to characterize the Wallerian degeneration in the central nervous system.

## References

(1) Song et al., Neuroimage 2003; 20:1714-1722.

(2) Lambot et al., The Journal of Neuroscience 2005; 25(31):7232–7237.