**Evaluation of Glaucomatous Optic Nerve using in vivo Manganese-enhanced MRI**

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**INTRODUCTION:** Glaucoma is a neurodegenerative disease of the optic nerve (ON) characterized by retinal ganglion cell (RGC) death, optic nerve head (ONH) damage, and progressive visual field loss [1]. While elevated intracranial pressure (IOP) is considered a major risk factor, the primary cause to the atrophic mechanisms is still unclear [2]. In this study, in vivo manganese-enhanced MRI (MEMRI) was applied to evaluate dynamically the Mn²⁺ enhancements along the visual pathway following an induction of ocular hypertension in rat models of chronic glaucoma. The goal is to examine the axonal transport in the glaucomatous optic nerve and to investigate into the optic nerve integrity in accordance with previous findings.

**METHODS:**

**Experimental Procedures:** Sprague-Dawley female rats (250-280g, N=11) were divided into 2 groups and were prepared to induce ocular hypertension unilaterally in the right eye by photoocoagulation of episcleral and limbal veins using an argon laser [3]. A second laser treatment in the same setting was applied 7 days later to maintain a consistent IOP elevation by about 1.5 times above the normal level. Group A (n=6) and Group B (n=5) were scanned 2 weeks and 1 month, respectively, after first laser treatment. MEMRI was performed 2 to 5 hours (Group A), and 8 & 24 hours (Group B) after intravitreal injection of 50mM, MnCl₂ solution into both eyes. Throughout the experiments, the left ON served as a control.

**3D MR Imaging:** All MRI measurements were acquired utilizing a 7T Bruker scanner. Under inhaled isoflurane anesthesia (2% induction and 1% maintenance), animals were kept warm on a heating pad at ~35°C and were imaged using an isotropic 3D MR Imaging: injection of 50mM, MnCl₂ after first laser treatment. MEMRI was performed 2 to 5 hours (Group A), and 8 & 24 hours (Group B) after intravitreal injection of 50mM, MnCl₂ solution into both eyes. Throughout the experiments, the left ON served as a control.

**RESULTS AND DISCUSSION:**

1. **ON profile near ONH:** Rectangular regions of interest (ROIs) were drawn manually 0-3mm distal to the ONH at 0.2mm intervals along the ON, and the mean and standard deviation of the ROIs were found. The ROIs were copied for each sample. In order to compensate for B₁ inhomogeneity, each value was normalized to the unaffected muscle adjacent to the ON of the same slide. Signal-to-noise ratio (SNR) was calculated from 655xSI/SD air, where SI is the normalized signal intensity of the ROI and SD represents standard deviation [4].

2. **Measurement of axonal transport rate index:** Maximum intensity projection (MIP) was performed to a segmented volume embracing the entire ON segment from the ONH to the optic foramen in both eyes (Figure 1). 6 ROIs were drawn at 1mm intervals distal to the ONH. Axonal transport rate indices were calculated from the ratio of signal intensity of an ROI to the corresponding normal ones. Significant differences between the normal and glaucomatous ONs were compared. All 3D images were reconstructed and co-registered before analysis.

**REFERENCES:**


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**Figure 1:** Typical MIP images of the optic nerves before (left) and after (right) contrast enhancement. A clear constriction was observed at the glaucomatous optic nerve head (ONH, arrow) compared to the normal one, while a brighter signal was found in the normal intraorbital optic nerve (ON, arrowhead). Image was acquired 4.5 hours after Mn²⁺ injection.