AN *IN VIVO* BIOMARKER TO MONITOR GLAUCOMA PROGRESSION

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INTRODUCTION

My aim is to find a new way to see damage to the retina caused by glaucoma, a condition that affects eyesight. In glaucoma, a key part of the eye called retinal ganglion cells (RGCs) gets damaged, which can lead to vision loss if not managed well. Currently, we use a method called optical coherence tomography (OCT) to check for damage, but it's not perfect. It measures the thickness of certain layers in the eye, but it doesn't directly show us the damage to RGCs.

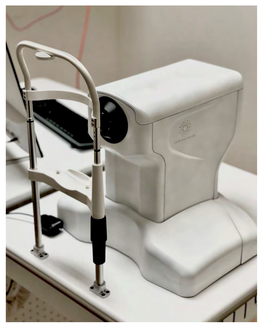
So, I'm working on a new method called visible-light Optical Coherence Tomography (OCT) fibergraphy (a.k.a. vis-OCTF) to see if we can directly see changes in the RGCs. I'll be studying this in mice with glaucoma to see if the changes in RGCs match up with vision loss. If successful, this could lead to better ways of detecting and managing glaucoma in people, helping to save their vision.

DESIGN & METHODS

Mice and tree shrews were imaged with a small animal vis-OCT system, Halo 100 (Opticent Health, Evanston, IL), as previously reported (Grannonico et al., 2023; Grannonico et al., 2021; Miller et al., 2020). The system used broadband visible light from 510 nm to 610 nm with an incident power on the cornea of 1 mW. The system was scanned with an A-line rate of 75 kHz with an integration time of 12.6 µs/A-line. Halo 100 offers a 1.3 µm axial resolution in the retina for both mice and tree shrews (Grannonico et al., 2021; Miller et al., 2020).

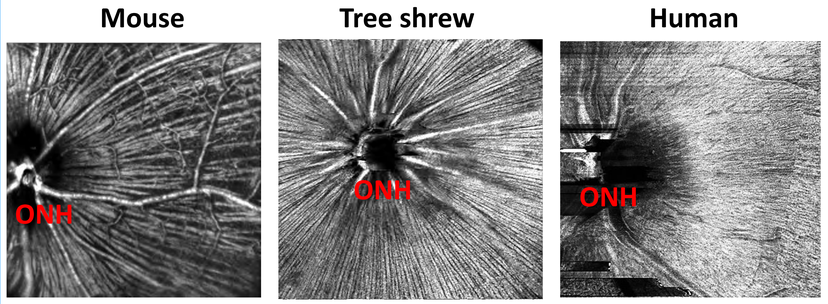
The clinical vis-OCT system used was Aurora $\mathcal{X}2$ vis-OCT system (Opticent Inc., Evanston, IL). The system generates a 3 x 3 mm^2 *en face* image with 7.0 µm of lateral resolution and 1.3 µm of axial resolution, with a 40 kHz A-line rate. The incident power was set below 250 µW on the cornea. The laser used in Aurora $\mathcal{X}2$ has been certified by the Food and Drug Administration as a nonsignificant risk device for laser safety.

Halo 100



Aurora X2

Vis-OCTF



RESULTS

1. Grannonico, M.†, Miller, D.A.†, Gao, J.†, McHaney, K.M., Liu, M., Krause, M., Netland, P.A., Zhang, H.*, and **Liu, X.*** (2023) Longitudinal analysis of retinal ganglion cell damage at individual axon bundle level in mice using visible-light optical coherence tomography fibergraphy *Transl Vis Sci Technol.* 5399, https://doi.org/10.1167/tvst.0.0.5399
2. Chang, S., Xu, W., Fan, V., McDaniel, J.A., Grannonico, M., Miller, D.A., Liu, M., Zhang, H.F., and **Liu, X.** (2023) Alignment of *in vivo* vis-OCT images with *ex vivo* confocal images of mouse retina *J. Visualized Experiments* e65237, doi:10.3791/65237.
3. Cole, J.D.†, McDaniel, J.A.†, Ban, A., Nilak, J., Rodriguez, C., Hameed, Z., Netland, P.A., Yang, H., Provencio, I.*, and **Liu, X.*** (2023) Characterization of neural damage and neuroinflammation in Pax6 *small-eye* mice *Exp Eye Res* DOI: 10.1016/j.exer.2023.109723
4. Miller, D.A.†, Grannonico, M.†, Liu, M., Savier, E., McHaney, K.M., Erisir, A., Cang, J., **Liu, X.*** and Zhang, H.* (2023) Tree Shrew Retina by Visible-Light Optical Coherence Tomography (IEEE Transactions on Medical Imaging, revision)
5. Grannonico, M.†, Miller, D.A.†, Liu, M.†, Krause, M.A., Savier, E., McHaney, K.M., Erisir, A., Netland, P.A., Cang, J., Zhang, H.*, and **Liu, X.*** (2024) Comparative *In Vivo* imaging of retinal layer structures of Tree Shrew, Human and Mouse *eNeuro* (accepted)
6. Krause, M.A.†, Grannonico, M.†, Tyler, B., Miller, D.A., Kuranov, R.V., Liu, M., Zhang, H.F., **Liu, X.*** and Netland, P.A.* (2024) Hyperreflective Dots in Central Fovea Visualized by a Novel Application of Visible-light Optical Coherence Tomography *Case Reports in Ophthalmological Medicine* (revision)
7. Fan, W.†, Miller, D.A.†, Chang, S.†, Kweon, J., Yeo, W., Grannonico,M., **Liu, X.**, and Zhang, H.F. (2024) Longitudinal imaging of vitreal hyperreflective foci in mice with acute optic nerve damage *Optics Letters* (in press)

CONCLUSIONS

- Vis-OCT is a platform which can be applied to both animal research and clinical studies.
- We validated vis-OCT findings using the acute mouse model of optic nerve crush injury.
- We established the baseline for vis-OCT imaging of tree shrews (Tupaia belangeri), diurnal para-primates that exhibit more similarities in retinal structure to that of humans compared to mice.
- We also started imaging human eyes at UVA Ophthalmology, in collaboration with Drs. Netland and Krause.

NEXT STEPS

Related proposal submission

NIH/NEI R01EY035055 07/2023 – 06/2028
Title: Establishing an in vivo biomarker for RGC Damage by vis-OCTF
MPI: Liu, Xiaorong (contact), and Zhang, Hao (Northwestern)
First submission in June 2022; Resubmitted in March 2024.

UVA Brain Institute Seed Fund 09/2024– 08/2025
Title: Advancing Personalized Diagnosis: A Novel Non-Invasive Imaging System for Glaucoma
PI: Xiaorong Liu (Biology); Co-PI: Michael Krause (Ophthalmology)
Submitted in Feb 2024.

Knights Templar Eye Foundation Career-starter Research Grant Title: *In vivo* Tracking of Developmental Damage in Aniridic Retina
PI: Marta Grannonico; **Preceptor: Liu, Xiaorong**
Funded for 07/2023 – 06/2024; Competitive renewal in Jan 2024.

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