Doctoral Dissertation Defense Announcement

“Multimodal Assessment of Photoreceptor Structure and Function in Retinal Trauma”

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Date: Friday, November 17, 2023
Time: 3:30 PM (CST)
Defense Location: Alumni Center

Zoom: https://mcw-edu.zoom.us/j/94732467263?pwd=c09WKzFDZTNrcFV3aVpQNU1RcjE4UT09
**Graduate Studies:**

Biochemistry of the Cell
Molecular and Cellular Biology
Classical and Molecular Genetics
Fundamentals of Neuroscience
Graduate Neuroanatomy
Neuroscience Journal Club
Ethics & Integrity in Science
Research Ethics Discussion Series
Cell & Molecular Neurobiology
The Biology of Vision
Statistics for Basic Sciences
Advanced Cell Biology
Professional Development I
Clinical Human Anatomy I
Clinical Human Anatomy II
Reading and Research
Doctoral Dissertation
Many conditions either directly or indirectly interfere with normal photoreceptor function, including inherited retinal conditions, systemic diseases, neurological disorders, and traumatic injuries. Vision research has placed tremendous efforts on restorative vision treatments, but the technology required to accurately detect retinal changes and monitor retinal recovery remains limited in clinical settings. Retinal trauma is a common cause of visual defects due to associated photoreceptor disruption and degeneration. Whether the trauma results from injury or disease, optical coherence tomography (OCT) imaging is the prevailing method for diagnosis and management of retinal changes. This technique works for some cases, but for many others visual deficits persist despite having a normal appearing retina on OCT. It is important to note that a normal-appearing OCT does not mean photoreceptor structure is normal. This has been demonstrated in numerous studies comparing photoreceptor metrics from OCT with adaptive optics scanning light ophthalmoscopy (AOSLO), which enables cellular-resolution imaging of the photoreceptor mosaic. AOSLO has been used in cases of retinal trauma and disease which reveal disruptions to the mosaic that appear normal on OCT and remnant photoreceptor structure in areas of complete disruption on OCT. This suggests that OCT may be an ineffective tool for assessing the retinal origins of visual defects in retinal trauma.

There is thus a critical need to improve biomarkers for detection of retinal pathology and application of novel approaches for better understanding behind the pathophysiology of traumatic vision loss and retinal recovery. This work used OCT and AOSLO to measure photoreceptor structure in a variety of ways, identify and validate key photoreceptor metrics for either imaging modality, as well as evaluate the relationship between photoreceptor metrics acquired between devices to develop sensitive methods for describing retinal structure. In Aim 1, we sought to evaluate limitations to quantitative assessment of photoreceptor structure using AOSLO. Specifically, we assess underlying assumptions used to scale AOSLO imagery, reproducibility of quantitative metrics across human graders, and develop a method for deriving photoreceptor metrics when not all cells are visualized. This work demonstrates how biological and nonbiological factors impact quantification of photoreceptor structure, as well as offers suggested methods to mitigate bias introduced by these factors. These findings provide a basis for more accurate and accessible clinical markers of retinal structure derived from the relationship between AOSLO and OCT photoreceptor metrics, which is the focus of Aim 2. There are clinical metrics for describing photoreceptor structure from OCT, but there is an incomplete understanding of how underlying photoreceptor anatomy produces these signals. Therefore, clinical metrics of photoreceptor structure are inconsistent detectors for photoreceptor dysfunction and recovery. Evaluation of how photoreceptor...
metrics from OCT are extracted, analyzed, and compared to AOSLO measures is critical for reliable clinical markers of photoreceptor structure. Here, we review the possible photoreceptor metrics that can be derived from the second hyperreflective outer retinal band, known as the ellipsoid (EZ) band, how these metrics correlate to AOSLO-derived measures, and what factors contribute to differences observed across studies. Lastly, in Aim 3, we assess photoreceptor structure in individuals with a history of retinal trauma using a variety of imaging techniques. This work provides important insight into the etiology of visual defects in these cases and provides a foundation for modeling general relationships between OCT and other clinical tools compared to AOSLO-derived metrics of photoreceptor structure.

In summary, the results of this work provide 1) a better understanding of the underlying assumptions and models that can be applied to quantify AOSLO photoreceptor metrics, 2) a comprehensive review of OCT photoreceptor metrics extracted from the EZ band and their relationship with AOSLO metrics, and 3) characterization of retinal findings in individuals with a history of retinal trauma. These findings advance our long-term goal of developing imaging-based biomarkers of photoreceptor health for diagnosis, intervention, and management of a wide array of retinal diseases.
EDUCATION:
- The Medical College of Wisconsin, Ph.D. candidate, 08/2017 – Present
- Lake Forest College, B.A., Neuroscience & Biology, 08/2012 – 12/2015

RESEARCH GRANTS/AWARDS/CONTRACTS/PROJECTS:
- Active Peer Reviewed
  - Title: Multimodal assessment of photoreceptor structure and function in retinal trauma
  - Source: National Eye Institute (NIH; F31EY033204)
  - Role: Principal Investigator
  - Dates: 09/01/2021 – 12/01/2023

AWARDS AND HONORS:
- Retinal Degeneration Travel Award Recipient 2021
- Optica Innovation School Attendee 2022
- Graduate Student Paper of the Season Award Summer 2022

MENTORSHIP/TEACHING ACTIVITIES:
- Medical College of Wisconsin, Graduate Neuroanatomy Teaching Assistant, 2020 - 2022
- Milwaukee School of Engineering, Research mentor for Hartford High School SMART Team, 08/2019 – 05/2020
- Medical students mentored:
  - 08/2019 – 05/2021 – Karen Lee
  - 06/2020 – 05/2022 – Abigail Scheidt
  - 06/2020 – 05/2021 – Mitchell Allphin

INVITED LECTURES/WORKSHOPS/PRESENTATIONS:
- Heitkotter H. “Assessing photoreceptor structure and function in health and disease”, presented at the College of Optometry Summer Seminar Series, University of Houston, Houston, TX (August 2021).

PEER REVIEWED WORKSHOPS/PRESENTATIONS:


BIBLIOGRAPHY:

- **Heitkotter H,** *Allphin MT,* Untaroiu A, Min H, Warr E, Wynne N, Cooper RF, Carroll J. “Peak cone density predicted from outer segment length measured on optical coherence tomography” Current Eye Research, in revision (2023). *These authors contributed equally to this work

- **Heitkotter H,** *Patterson EJ,* Woertz EN, Cava JA, Gaffney M, Adhan I, Tam J, Cooper RF, Carroll J. “Extracting spacing-derived estimates of rod density in healthy retinae” Biomedical Optics Express, 14(1):473101 (2023). *These authors contributed equally to this work


- Lee KE,* **Heitkotter H,** *Carroll J “Challenges associated with ellipsoid zone intensity measurements using optical coherence tomography” Translational Vision Science & Technology, 10(12): 27 (2021). *These authors contributed equally to this work
