Doctoral Dissertation Defense

Rachel E. Linderman

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Committee in charge:
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Daniel M. Lipinski, MSc, DPhil
Iris Kassem, MD, PhD
Taly Gilat Schmidt, PhD
Brandon Lujan, MD

Friday, 16 April 2021, 10:00 AM (CDT)

Live public viewing:
https://mcw-edu.zoom.us/j/97255054058?pwd=TFZHQjRrNlB4MS9UbXdNY3VKOTczUT09
GRADUATE STUDIES

- Molecular and Cellular Biology
- The Biology of Vision
- Intro to Data Science
- Ethics & Integrity in Science
- Research Ethics Discussion Series
- Reading and Research (Fall 2017 – Fall 2020)
- Doctoral Dissertation (Spring 2021)
The foveal avascular zone (FAZ) is one of the more well-studied anatomical specializations associated with the human fovea. Changes to the retinal vasculature, such as vessel dropout and enlargement of the FAZ have been reported in a variety of ocular, systemic, and neurodegenerative diseases. Routine non-invasive imaging of the retinal vasculature has been made possible with the advent of optical coherence tomography angiography (OCT-A). A critical step to the translation of any new imaging technology from research into clinical settings is an understanding of how technical and biological factors impact metrics or biomarkers extracted from the images. Therefore, we investigated how different technical components related to the device and biological factors related to subjects impact an array of retinal vasculature metrics. Additionally, we also sought to calculate each metric's relative sensitivity so that metrics best suited for a given study can be identified.

In Aim 1, we sought to characterize factors that impact retinal vasculature metrics derived from OCT-A. Specifically, differences in ocular biometry across subjects were assessed to determine how FAZ area varies when OCT-A images were either scaled or unscaled (to account for individual differences in axial length). Additionally, three different segmentation methods for measuring the FAZ area and acircularity were compared, as well as interocular symmetry, image quality, device selection and scan size for various metrics. These studies highlighted how specific factors such as ocular biometry, and segmentation can impact all metrics, including robust metrics such as the FAZ area yet other factors, such as scan size and image quality impact less robust metrics such FAZ acircularity but do not impact FAZ area. Understanding which factors need to be accounted for to acquire accurate and consistent data is critical for future studies and potential meta-analyses. In Aim 2, we wanted to understand how sensitive different vasculature metrics were by simulating random vessel loss. We found that not all metrics are equally sensitivity to detecting vessel loss, which has implications for their use in clinical trials. Finally, in Aim 3, we sought to further examine the relationship between the FAZ and the fovea. While this relationship has been studied extensively, how these two anatomical features impact each other remains unclear. First, we developed a novel method for detecting abnormal or "fragmented" FAZs, which we found to be present in about 5% of individuals with normal vision. We also found that hypomorphic mutations in the TYR gene were associated with a reduction in the size of the fovea and FAZ in individuals with normal vision. Finally, in subjects with achromatopsia we observed an
inverse relationship between the size of the FAZ and the number of remnant inner retinal layers present. While this is consistent with the expected relationship between the FAZ and the foveal pit structure, the presence of an FAZ in patients with remnant inner retinal layers was in conflict with the current understanding of foveal specialization.

In summary, the results of this work provide (1) a better understanding of different factors affecting retinal vasculature metrics derived from OCT-A, (2) a greater comprehension of the relative sensitivity of retinal vasculature biomarkers, which will impact their use in clinical trials, and (3) clarification of the relationship between foveal morphology and the FAZ. These findings will expand the clinical utility of OCT-A and further our understanding and ability to use biomarkers related to the retinal vasculature for evaluating the onset and progression of ocular, systemic or neurodegenerative diseases.
CURRICULUM VITAE

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➢ Place of Birth:
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➢ Citizenship:
    USA

Education
Bachelor of Arts, Biology; Minor: Chemistry
    Magna Cum Laude
    Luther College – Decorah, IA
    2009-2013

Doctor of Medicine
    School of Medicine
    Medical College of Wisconsin, Milwaukee, WI
    2014-2016

Doctor of Philosophy, Cell and Developmental Biology
    Medical College of Wisconsin, Milwaukee, WI
    Graduate School of Biomedical Sciences
    Dept. Cell Biology, Neurobiology, & Anatomy
    2017-present

Mentoring Experience
Brit Zaro, medical student, Clinical & Translational Research Pathway
    2017 – 2019
Sarah Omoba, medical student, Clinical & Translational Research Pathway
    2017 – 2020
Jessica Kraker, medical student, Clinical & Translational Research Pathway
    2018 – 2020
Samantha Llanas, medical student, Clinical & Translational Research Pathway
    2018 – 2020
Jenna Grieshop, undergraduate, Summer Program for Undergraduate Research
    2020
Elizabeth Heffernan, undergraduate
    2019 – present
Gelique Ayala, medical student, Clinical & Translational Research Pathway
    2019 – present
Awards and Honors

- National Institute of Aging Grant (T35AG029792) Fellowship recipient 2015
- Fight for Sight – Nick Cacciola Summer Fellowship recipient 2016
- Research Training Program in Vision Science (T32EY014537) recipient 2020

Memberships in Honorary and Professional Societies

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<tr>
<th>Membership</th>
<th>Start Date - Present</th>
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<tbody>
<tr>
<td>Beta Beta Beta (TriBeta)</td>
<td>2011 - present</td>
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<td>Phi Beta Kappa</td>
<td>2013 - present</td>
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<tr>
<td>Association for Research in Vision and Ophthalmology (ARVO)</td>
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<td>International Ocular Circulation Society (IOCS)</td>
<td>2019 - present</td>
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Academic Journal Reviews

- Translational Vision Science & Technology
- Investigative Ophthalmology & Visual Science
- Public Library of Science
- Optometry and Vision Science
- Scientific Reports

International Peer-Reviewed Presentations


National Peer-Reviewed Presentations


temporal raphe in eyes with glaucomatous damage” presented virtually at ARVO Imaging in the Eye (April 2020).

Regional Peer-Reviewed Presentations
2. Russillo, M., Goldberg, M., Khan, J., **Linderman, R.**, Conner, T., Han, D., Kim, J., Carroll, J., “Comparison of fluorescein angiography and optical coherence tomography (OCT) angiography in retinal vascular disease” presented at Midwest Eye Research Symposium, University of Iowa (August, 2015).

Local Peer-Reviewed Presentation
1. **Linderman, R.**, Goldberg, M., Khan, J., Russillo, M., Carroll, J. “Examining interocular symmetry in vascular density” presented at Medical Student Summer Research Symposium, Medical College of Wisconsin (October, 2015).
2. Russillo, M., Goldberg, M., Khan, J., **Linderman, R.**, Conner, T., Han, D., Kim, J., Carroll, J., “Comparison of fluorescein angiography and optical coherence tomography (OCT) angiography in retinal vascular disease” presented at Medical Student Summer Research Symposium, Medical College of Wisconsin (October, 2015).

Refereed Journal Publications/Original Papers
   *These authors contributed equally to the work


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Abstracts


