Impaired cone function in drusen regions revealed by phase-sensitive adaptive optics OCT

Zhuolin Liu, Furu Zhang, and Daniel X. Hammer
Center for Devices and Radiological Health (CDRH), Food and Drug Administration, Silver Spring, MD, USA, Zhuolin.Liu@fda.hhs.gov

Abstract

Phase-sensitive adaptive optics – optical coherence tomography (PhS-AO-OCT) is an optical technique to quantify photoreceptor function. The current study investigates how cone function is affected by drusen. Our results indicate cones above drusen have a weaker response compared to cones in healthy regions. This capability can be used as a precise biomarker for early disease detection and to aid new therapies.

Introduction

PhS-AO-OCT is a technique that quantifies individual photoreceptor function via phase changes in back-reflected light. Using this unique optical signature, previous investigations have demonstrated cone classification, as well as cone responsivity in normal eyes and eyes with inherited disease [1-4]. OCT provides cross-sectional retinal views while AO provides cellular-level lateral resolution.

The current study extends this capability to photoreceptors near small drusen that indicate retinal disruption and may eventually develop into more serious diseases like age-related macular degeneration (AMD). This capability may be used as a more precise (single-cell-scale) biomarker or clinical endpoint for early retinal disease detection and to aid new therapies.

Materials and Methods

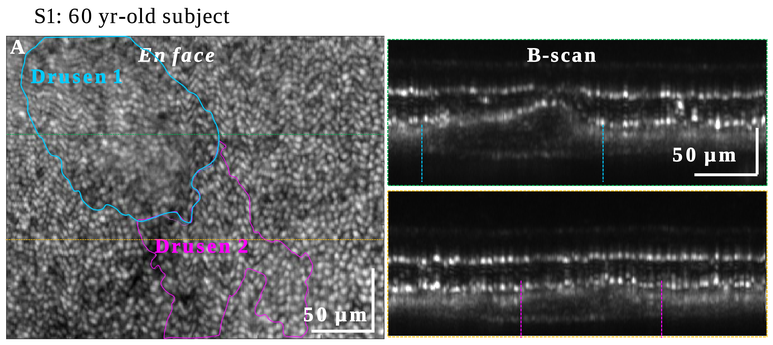
Participants: Three subjects (ages: S1, 60; S2, 36; S3, 53 yrs-old) with no diagnosed ocular diseases were imaged with the FDA adaptive optics (AO) imager [5]. Two subjects (S1, S2) had macular drusen found from previous AO imaging.

Visual stimulation: Brief synchronous visible stimuli were delivered to the retina with a Maxwellian view illumination channel co-aligned to the AO-OCT beam. Two stimulus sources (530 nm and 625 nm) were selected to probe the relative response of cones.

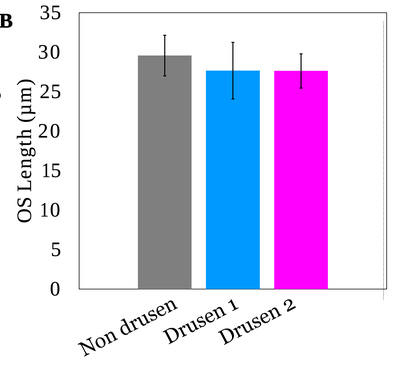
Imaging acquisition: Seven 1° field-of-view AO-OCT videos were acquired with each stimulus with A-line speed of 210 kHz and volume rate of 2.3 Hz.

Data processing and analysis: The phase difference between cone inner segment/outer segment junction (IS/OS) and cone outer segment tip (COST) signals was calculated and converted to optical path length change (ΔOPL). Cone response was determined using principal component analysis following the methods described by Zhang et al. [2]. The cone response is measured as the vector length from the origin to the centroid of each cone cluster on the PCA plots. To avoid inter subject variability, cone responsivity and outer segment (OS) length were compared between non-drusen and drusen regions.

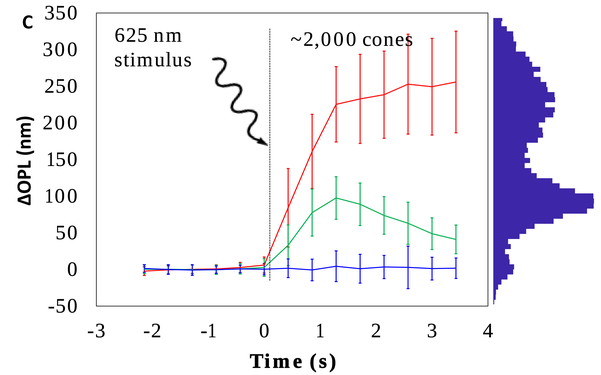
Results and Discussion



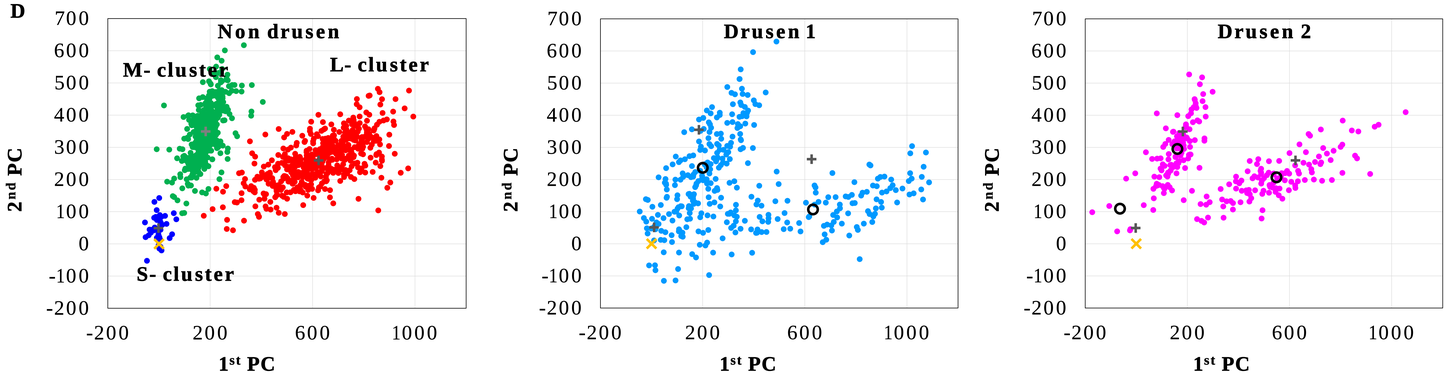
A. *En face* and B-scans show evidence of drusen delineated approximately by the blue and magenta boundaries. Drusen 1 showed clear RPE disruption and COST displacement, and drusen 2 had RPE disruption and only slight COST elevation.



B. OS length in non-drusen region is significantly longer than two drusen regions ($p<0.05$), while the measurement is similar at the two regions with drusen ($p=0.89$).



C. Cone ΔOPL between IS/OS and COST in response to 625-nm stimulus for a non-drusen region.



D. The cones' response is projected in principal component (PC) space along the two PC components for non-drusen, drusen 1, and drusen 2 regions. "+" denotes the centroid of L-, M-, and S-clusters in the non-drusen area, "○" represent the centroids of the corresponding clusters in drusen regions, and "x" indicate the origin. Cones in the drusen areas had weaker response compared to the non-drusen region. Similar results were found in S2, but no regional difference in cone functionality was evident in S3, who had no observable drusen.

Conclusion

Our early PhS-AO-OCT evidence indicates that cone photoreceptor function is affected by the presence of drusen. Drusen displaces the photoreceptors resulting in shorter OS length. Drusen also changes the normal cone response to visible stimulation. The ability to measure individual cone function in drusen regions may lead to new functional biomarkers for early AMD detection.

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References

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