Retinal Layer Thickness Changes Associated with the Natural History of Drusen in Age-Related Macular Degeneration

Nivison-Smith L[1, 2], Zangerl B [1,2], Assaad N [2,3], Fletcher EL [4], Kalloniatis M [1,2,4]

[1]School of Optometry and Vision Science and [2]Centre for Eye Health, UNSW, Sydney, Australia; [3]Prince of Wales Hospital , Randwick, NSW, Australia and [4]Department of Anatomy and Neuroscience, University of Melbourne, Victoria Australia.

Poster: #33-A0024

Corresponding author: l.nivison-smith@unsw.edu.au

Introduction

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness worldwide.

Drusen are a hallmark of AMD and have important clinical implications.

We recently quantified drusen using OCT and found the RPE, photoreceptor and outer nuclear layer (ONL) thickness above drusen is reduced compared to drusen-free areas.

New OCT segmentation software means these changes may be more easily quantified and reveal new information on the natural history of drusen.

Purpose

To determine how retinal thinning relates to the natural history of drusen using automated segmentation software.

Methods

Drusen selection: Single druse (n=125), confluent drusen (n=45) and regressing druse (n=49) were identified from 122 early/intermediate AMD patients (Ferris et al 2013) seen at Centre for Eye Health, Sydney from 2010-15.

Automated segmentation: Layers were segmented using the segmentation algorithm provided by Spectralis SD-OCT Viewing software. Incorrect segmentation was manually adjusted when required (termed semi-automated segmentation).

Data analysis: Thickness measurements were expressed as percentage difference compared to measurements made 150µm from the drusen edge.

Results

Automated segmentation was poor for the outer retinal layers (RPE, ISe, ELM) directly above drusen. Segmentation was mostly accurate for nearby, druse-free areas except for the RPE layer (Fig. 1).

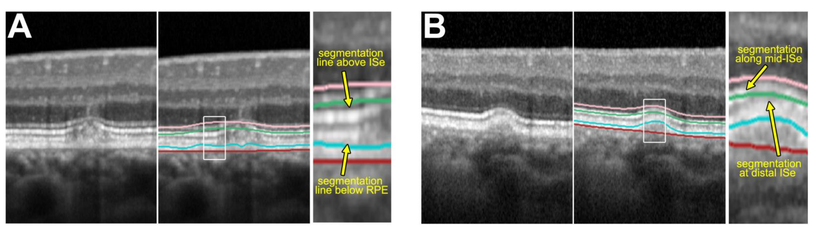

Figure 1: Examples of **(A)** Incorrect segmentation of multiple outer retinal layers or **(B) some** only part of the retinal layer at the druse site.

After incorrect segmentation was amended, we found total retinal thickness above isolated druse was reduced compared to nearby drusen-free areas (Fig. 2A). This reduction was due to thinning of the RPE, photoreceptor and ONL.

When compared to manual measurements recorded for the same lesions (Rogala, et al. 2015), semi-automated segmentation showed discrepancies between the RPE+PR and ONL measurements. However, when combined, overall loss in these 3 layers was not significantly different between the two measurement methodologies (Fig. 2C). Similar findings were seen with confluent drusen (Fig. 2B, D).

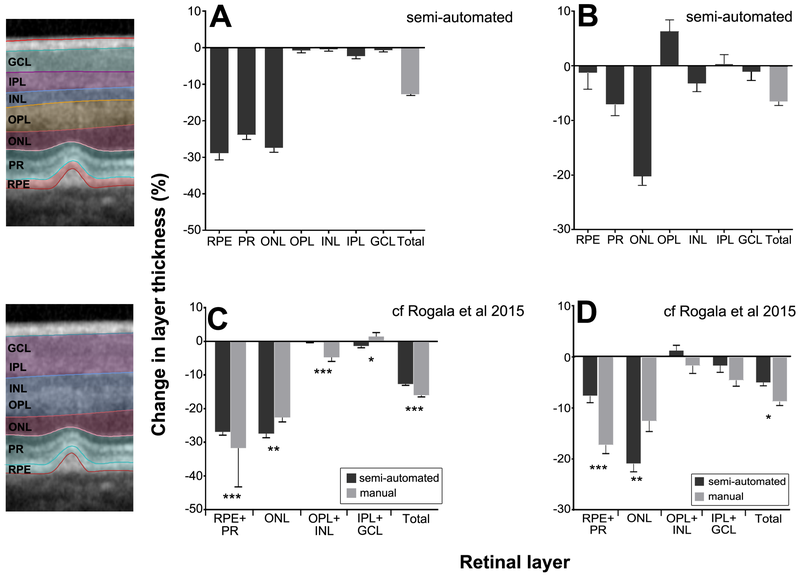

Figure 2: Percentage change in retinal layer thickness above **(A)** single, isolated druse and **(B)** confluent drusen using semi-automated segmented images. Values from semi-automated segmentation were then compared to those obtained manually for the same lesions (Rogala, et al. 2015) for **(C)** single, isolated druse and **(D)** confluent drusen. All columns represent the mean ± SEM. * = p < 0.05, ** = p < 0.01, *** = p < 0.001. Images to the left indicate the location of each layer measured. Note, some layers from semi-automated segmentation were pooled together for comparison with Rogala et al. 2015.

We then assessed whether changes in retinal thickness were linear with drusen growth. We found a weak correlation between ONL thinning and increased drusen width but a moderate correlation between ONL thinning and increased drusen height (Fig. 3).

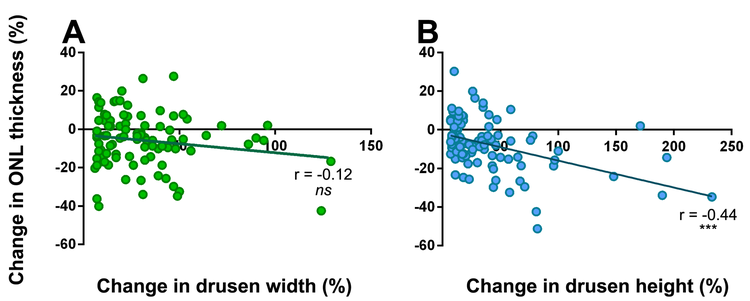

Figure 3: Percentage change in ONL thickness vs change in **(A)** drusen width and **(B)** drusen height for the same drusen which were found to increase in size between two consecutive visits (n = 45). *** = p < 0.001, r = Spearman's correlation co-efficient. Note correlation in B remains even with the removal of possible outliers (drusen with over 100% change in height).

We also assessed whether changes in retinal thickness remained following drusen regression. In the photoreceptor layer, there was a significant recovery in thickness post-regression but for the ONL, thickness post-regression was still significantly thinner than adjacent, drusen-free areas (Fig. 4).

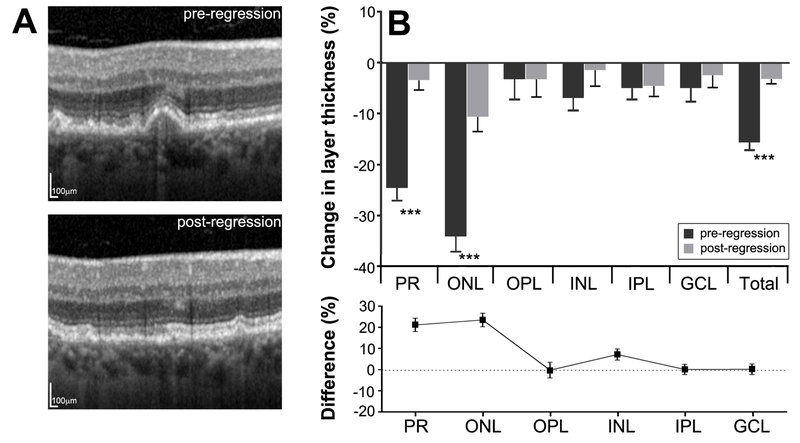

Figure 4: (A) Example of druse pre- and post-regression in a 70 year old male with intermediate AMD. **(B)** Percentage change in thickness of each retinal layer above drusen pre- and post-regression (column graph; n = 49) and the relative difference between each time-point, graphed as a difference plot. ***: p < 0.001

Conclusions

- Automated segmentation algorithms still require manual quality control when assessing drusen.
- Corrected segmentation can detect thinning of the outer retina above drusen similar to manual measurements.
- As drusen grow, they further thin the ONL and this change is best correlated with drusen height.
- The ONL remains abnormal following drusen regression suggesting drusen may have permanent structural effects on the retina.

Support

This project received support from National Health and Medical Research Council (NHMRC) Australia, grant 1009342 and University of New South Wales Early Career Researcher Grant 2015. Guide Dogs NSW/ACT are partners in the NHMRC grant and support LN-S. The authors also that S Hoang, H Ton, Y Wang and C Zangerl for technical assistance. Disclosure The authors report no conflicts of interest and have no proprietary interest in any of the instruments mentioned in this work.

References

Ferris FL, Wilkinson CP, Bird A, Chakravarthy U, Chew E, Csaky K, Sadda SR; Beckman Initiative for Macular Research Classification Committee. (2013) Clinical classification of age-related macular degeneration. Ophthalmology. 120(4):844-51.

Rogala J; Zangerl B; Assaad N; Fletcher EL; Kalloniatis M; Nivison-Smith L (2015) In vivo quantification of retinal changes associated with drusen in age-related macular degeneration, IOVS, 56 (3) 1689 – 1700.