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Letters to the Editor

Author Response: Expected Improvement in Structure-Function Agreement With Macular Displacement Models

We thank Drs. Montesano, Garway-Heath, and Crabb for their interest in and insights into our work. Of particular interest is their presented comparisons of displaced and non-displacement visual field locations relative to retinal nerve fiber layer defects of various widths. It is reassuring to note that the results of their modeling exercise indicates little difference between displacement and no displacement for retinal nerve fiber layer defects greater than 20 degrees in width, overall consistent with our rationale for the findings presented in our paper.[1]

We also agree that the limited differences in structure-function concordance between displacement and no displacement, as observed in our study and the modeling exercise described by Montesano et al., suggest that there are other components confounding the relationship between structural and functional measurements. The existing literature assessing microperimetry versus standard automated perimetry in structure-function analyses variably report little improvement with microperimetry to no significant differences between perimetry modalities.[2–4] Differences in perimetric algorithms aside, this suggests that correction for microsaccadic eye movements and potential errors in fixation while performing visual fields testing alone does not notably improve the relationship between structure and function, analogous to our findings when comparing displacement and no displacement.

The authors also highlight the possibility of inaccuracies in histological data used to develop displacement models, such as the Drasdo model.[5] Interestingly, our recent publication[6] reported a slight underestimation in midget retinal ganglion cell-to-cone ratio at peripheral macular locations in the asymmetric implementations of the Drasdo model relative to the Sjöstrand model.[7] As the Sjöstrand model only extends to 2 mm from the foveal center, this could indicate an overestimation in displacement by the Drasdo model at relatively peripheral locations. Nonetheless, given the little difference between displacement and no displacement outside of the parafovea, as identified in this study, the displacement model choice is unlikely to have a significant impact on the study results.

With respect to the highlighted methodological issues, our study was designed to resemble analyses readily available in clinical settings, so the chosen implementations may result in small errors, as identified by Montesano et al. We recognize that axial length contributes to transverse magnification and in turn can alter projected location of visual field stimuli,[8–10] however, commercially available instrument software do not have the function of incorporating axial length measurements. Furthermore, only 23 participants (7.78% of the total study cohort) had myopia greater than or equal to -6.00 diopters, so inaccuracies related to transverse magnification in high myopia are likely to have little impact on the reported results. Moreover, the symmetrical implementation per figure 6 of Drasdo et al.[5] is the displacement model presented in the Heidelberg Eye Explorer structure-function analyses (Heidelberg Engineering, Heidelberg, Germany), consistent with it being by far the most common displacement model applied across studies of the macular structure-function relationship.[11–15] Finally, differences between displacement applied to the visual field stimulus circumference versus center only would impact the ganglion cell inner plexiform layer thicknesses averaged over projected locations less than the retinal ganglion cell counts, where the calculated number of cells would vary more widely over different projected areas.

Overall, we agree that whereas the findings of our study indicate that application of displacement in isolation appears to contribute little to clinical interpretations of structure-function concordance, this does not discount the anatomic correctness of retinal ganglion cell displacement relative to underlying photoreceptors. Moreover, various aspects of the study design resembling current clinical implementations may be outdated with respect to the latest advances in research in this area, however, it is within the realm of the natural evolution of science that future knowledge builds from gaps in prior research.[16]

With ongoing developments in various aspects of the structure-function space, the subtleties underpinning this relationship can be further elucidated and hopefully translate to improved clinical detection and outcomes in patients with glaucoma.

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