Ellipsoid Zone Change According to Glaucoma-Stage Advancement

EDITOR:

THE FINDINGS OF HA AND ASSOCIATES[1] OF REDUCED RELATIVE ellipsoid zone (EZ) intensity in spectral-domain optical coherence tomography (SD-OCT) scans in more advanced stages of glaucoma are of great interest. The authors speculate elegantly regarding possible mechanisms, including trans-synaptic retrograde degeneration or Müller cell dysfunction, leading to alterations in photoreceptor mitochondria. One issue that deserves consideration is potential confounding owing to optical effects. It is a common finding on SD-OCT that an overlying hyperreflective structure (such as a blood vessel[2] or exudate[3]) will result in a shadowing effect, whereby the reflectivity of structures underneath is diminished. Similarly, incremental loss of the overlying ganglion cell and nerve fiber layer, as occurs in more advanced glaucoma, would be expected to incrementally increase the intensity of the EZ and the external limiting membrane (ELM).

The authors calculated relative intensity by dividing EZ intensity by that of the ELM, as described in a recent study evaluating these bands in intermediate age-related macular degeneration (AMD).[4] However, it is plausible that an equal increase in intensity of both bands, owing to loss of the overlying ganglion cell complex, will result in a numerically smaller relative EZ intensity. For example, if, using arbitrary intensity units, the intensity of the EZ is 3 and the intensity of the ELM is 1, the relative EZ intensity will be 3. Supposing that, after loss of overlying reflective structures, the intensity of both lines increases by 0.2 units (giving intensities of 3.2 and 1.2 for EZ and ELM, respectively), the relative EZ intensity then appears to fall, as the ratio is now 2.67. In fact, it can be shown mathematically that any absolute (not proportionate) increase in reflective intensity that is the same for both the EZ and ELM will result in an apparent increase in relative EZ intensity, provided the EZ intensity is greater than ELM intensity, which is indeed the case. Such an effect would not occur in the AMD investigation,[3] as in that study the structural alterations are beneath (more scleral to) the photoreceptors and so would not cause a shadowing effect.

Thus, it is possible that the findings of the glaucoma study[1] could be explained, at least partly, by optical factors without retrograde degeneration. It would be useful to know the absolute intensities of the EZ and ELM lines, prior to calculating the ratio, in the different groups. Other methods of adjustment could be attempted, such as first subtracting any absolute increase in ELM intensity from the EZ value, or dividing instead by the intensity of the retinal pigment epithelium line (which is of a more comparable intensity to the EZ line), to see if the findings differ. Nevertheless, we applaud the authors for raising the possibility of trans-synaptic degenerative processes and Müller cell dysfunction in this condition.

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REFERENCES

1. Ha A, Kim YK, Jeoung JW, Park KH. Ellipsoid zone change according to glaucoma-stage advancement. *Am J Ophthalmol* 2018;192:1–9.
2. Golzan SM, Avolio A, Graham SL. Minimising retinal vessel artefacts in optical coherence tomography images. *Comput Methods Programs Biomed* 2011;104(2):206–211.
3. Vujosevic S, Bini S, Torresin T, et al. Hyperreflective retinal spots in normal and diabetic eyes: B-scan and en face spectral domain optical coherence tomography evaluation. *Retina* 2017;37(6):1092–1103.
4. Gin TJ, Wu Z, Chew SK, Guymer RH, Luu CD. Quantitative analysis of the ellipsoid zone intensity in phenotypic variations of intermediate age-related macular degeneration. *Invest Ophthalmol Vis Sci* 2017;58(4):2079–2086.

REPLY

WE APPRECIATE THE COMMENTS FROM MAHROO AND ASSOciates regarding our recently published article. Our study demonstrated relative ellipsoid zone (EZ) intensity reduction in the mild-to-moderate and severe glaucoma stages on spectral-domain optical coherence tomography (SD-OCT), and the extent of reduction was positively associated with glaucoma severity.

We are in total agreement with the point noted, that incremental loss of the overlying ganglion cell and nerve fiber layer would incrementally increase the intensity of both the EZ and the external limiting membrane (ELM). We would like to emphasize, however, that the degree of intensity increase is more likely to be *proportional* in both bands.

As light passes through media, its intensity decreases exponentially according to the depth of the media, as follows[1]:

$$I_{(z)} = I_0 e^{-\alpha z}$$

where α is a constant determined by the optical property of the media, and z is the depth of the media. After the light is reflected from the ELM (or EZ) and passes back through the media again, its intensity as detected by the OCT detector can be represented as: