Correspondence

Optical effects of loss of ganglion cell and nerve fibre layer on relative intensity of ellipsoid zone

Omar A. Mahroo,[1-3] Anthony P. Khawaja,[1-3] Pearse A. Keane[1,2]

1. University College London Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL
2. Moorfields Eye Hospital, 161 City Road, London EC1V 2PD
3. Department of Ophthalmology, King's College London, St Thomas' Hospital Campus, Westminster Bridge Road, London SE1 7EH

Correspondence to Omar Mahroo at Address (1) above.

Tel: +44 207608 6800

Email: omar.mahroo@moorfields.nhs.uk

The findings of Ha et al.[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 Muller cell dysfunction, leading to alterations in photoreceptor mitochondria. One issue that deserves consideration is potential confounding due to optical effects. It is a common finding on SD-OCT, that an overlying hyper-reflective 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 fibre layer, as occurs in more advanced glaucoma, would be expected to incrementally increase the intensity of the EZ and the ELM.

The authors calculated relative intensity by dividing EZ intensity by that of the external limiting membrane (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, due 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, 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 Muller cell dysfunction in this condition.

1. Ha A, Kim YK, Jeoung JW, Park KH. Ellipsoid Zone Change according to Glaucoma-Stage Advancement. Am J Ophthalmol. 2018 May 8 [Epub ahead of print].
2. Golzan SM, Avolio A, Graham SL. Minimising retinal vessel artefacts in optical coherence tomography images. Comput Methods Programs Biomed. 2011 Nov;104(2):206-11.
3. Vujosevic S, Bini S, Torresin T, Berton M, Midena G, Parrozzani R, Martini F, Pucci P, Daniele AR, Cavarzeran F, Midena E. HYPERREFLECTIVE RETINAL SPOTS IN NORMAL AND DIABETIC EYES: B-Scan and En Face Spectral Domain Optical Coherence Tomography Evaluation. Retina. 2017 Jun;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 Apr 1;58(4):2079-2086.