Nerve fibre layer thickness measurements derived by scanning laser polarimetry: the jury is out

The morphological impact of glaucomatous optic neuropathy includes a loss of retinal ganglion cells which is clinically manifested as optic nerve head damage and localised, or diffuse, dropout of the retinal nerve fibre layer (RNFL).[1] There is considerable variability in, and overlap of, the current clinical variables used to differentiate normal from glaucomatous populations. Optic nerve head damage can also be clinically observed before manifest visual field loss.[2 3] Indeed, histological evidence gained from the retinal ganglion cell counts of three human postmortem eyes which had also recently undergone automated perimetry has suggested that substantial ganglion cell loss can occur before a manifest and repeatable reduction of static perimetric sensitivity.[4] Consequently, the development of non-invasive, objective techniques which measure those retinal structures most likely to suffer glaucomatous damage has been proposed to aid the diagnosis of glaucoma and improve the monitoring of progressive glaucomatous damage. Scanning laser polarimetry is an example of such a technique.[5]

Scanning laser polarimetry purports to measure, in vivo, the thickness of the RNFL. The technique utilises a confocal scanning laser ophthalmoscope in conjunction with an integrated polarimeter to project a polarised spot of laser light onto the retina. The polarised laser light penetrates the RNFL and is partially reflected back towards the instrument from the deeper retinal layers. In effect, a double pass of the RNFL is made before the laser light emerges from the eye. The parallel intracellular organelles within the retinal ganglion cell axons are thought to induce a change in the state of polarisation (that is, retardation) of the laser light. The magnitude of retardation has been demonstrated to correspond with the histological assessment of RNFL thickness when applied to monkey eyes,[5] and human postmortem eyes,[6] with the cornea and crystalline lens removed. However, the cornea and crystalline lens also represent significant sources of birefringence within the human eye.[7] Commercial versions of the original laboratory prototype instrument include a 'cornea polarisation compensator' which is designed to neutralise anterior segment polarisation effects. The magnitude of retardation represents a relative, rather than an absolute, measure of RNFL thickness.[8] Scanning laser polarimetry is independent of the optical resolution of the human eye,[6] is independent of a reference plane or magnification effects,[9] and provides rapid, objective data.

In this issue of the *BJO* (p 350), Poinoosawmy *et al* present a clinically based study which investigated the influence of age and ethnic origin on scanning laser polarimetry derived RNFL thickness measurements in 150 normal subjects. The study found that the thickness of the superior and inferior quadrants of the peripapillary RNFL was greater than either the nasal or temporal quadrants, and the RNFL thickness was found to be inversely correlated with age. In addition, the study showed that white subjects exhibited a significantly greater RNFL thickness than subjects of Afro-Caribbean origin, suggesting an ethnic difference in the number of nerve fibres in the normal population. The results of Poinoosawmy *et al* are in overall agreement with the evidence gained from histological studies. Other clinical studies have gathered evidence from normal subjects which further validate the technique of scanning laser polarimetry based upon comparison with the known topographical characteristics of the primate RNFL—namely, the peripapillary retina exhibits the greatest RNFL thickness in the superior and inferior quadrants[8 10 11]; RNFL thickness decreases with increasing distance from the optic nerve head[8]; RNFL thickness decreases with increase in age for a given population[8 10 11]; and the RNFL thickness is reduced immediately above retinal blood vessels.[8] In addition, group mean RNFL thickness has been shown to be significantly higher in normal subjects than in patients with glaucoma,[9 10] and RNFL thickness has been demonstrated to correlate with glaucomatous visual field loss.[9]

Substantial uncertainties remain, however, about the underlying principles and assumptions, and the potential clinical application of scanning laser polarimetry. Firstly, scanning laser polarimetry derived RNFL thickness measurements exhibit considerable interindividual variation for both normal and glaucomatous populations when compared with the size of the measured effect.[8 10–12] Indeed, histological postmortem human optic nerve ganglion cell counts,[13–15] and postmortem human retinal ganglion cell counts,[16] indicate an approximate twofold interindividual range (0.7 to 1.5 million) in the total number of ganglion cells (based upon relatively small sample sizes). Such variability will necessitate substantial retinal ganglion cell loss before statistical significance is reached.[17] Secondly, despite claims of exceptionally high sensitivity and specificity of scanning laser polarimetry,[12] visual examination of all the published data reveals considerable overlap between normal and glaucomatous populations of scanning laser polarimetry derived RNFL thickness measurements.[8 11 12] The potential of scanning laser polarimetry, when considered as a single factor, to differentiate between normal and glaucomatous eyes will be limited.[8] Thirdly, although the scanning laser polarimeter measures, and corrects for, the birefringence associated with anterior eye structures, the accuracy of the 'cornea polarisation compensator' will undoubtedly influence the derived RNFL thickness measurements.[8 18] In particular, retinal fixation is known to influence corneal birefringence values.[7] Finally, the derived RNFL thickness values in micrometres are based on histological studies of monkey eyes with the cornea and crystalline lens removed.[5] A recent histological study of normal human eyes has revealed that the peripapillary RNFL thickness is thicker than that of monkeys and that the difference in RNFL thickness between the temporal peripapillary quadrant relative to the superior and inferior quadrants seems to be exaggerated by scanning laser polarimetry.[19] If scanning laser polarimetry derived RNFL thickness measurements are required in absolute units (micrometres), correlation with histological studies of normal human eyes is necessary.

In summary, the obvious and exciting potential of scanning laser polarimetry should not overshadow the uncertainties which still remain concerning the underlying principles and assumptions of the technique.

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