Taiwan Journal of Ophthalmology 6 (2016) 3–7

Contents lists available at ScienceDirect

Taiwan Journal of Ophthalmology

journal homepage: www.e-tjo.com

Review article

Macular thickness analysis for glaucoma diagnosis and management

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ARTICLE INFO

Article history:
Received 25 December 2015
Received in revised form
15 January 2016
Accepted 18 January 2016
Available online 28 February 2016

Keywords:
optical coherence tomography
macular thickness
retinal nerve fiber layer
glaucoma

ABSTRACT

There is increasing literature regarding the role of macular imaging by optical coherence tomography (OCT) in glaucoma care. Spectral domain OCT (SD-OCT) has allowed for high resolution imaging of the total macula and macular segments. With the use of asymmetry analysis, macular thickness is a measurement that can be used for the detection and progression of glaucoma. Some artifacts seen on retinal nerve fiber layer (rNFL) scans may be overcome by macular SD-OCT imaging. Also, nonglaucomatous optic neuropathies may be more easily identified on macular thickness plots than rNFL scans. Special populations, such as children or myopes, may also have improved glaucoma surveillance using macular SD-OCT. In this review we explore the advantages and pitfalls of macular OCT in glaucoma care and offer an approach on how to use macular thickness scans in clinical practice.

1. Introduction

Glaucoma is a progressive, asymptomatic optic neuropathy resulting in characteristic structural damage and associated visual field loss. In addition to ophthalmoscopy, optic nerve imaging and perimetry are used to aid in the diagnosis and surveillance of glaucoma. Automated perimetry, however, lacks the resolution to detect early glaucomatous damage as greater than 35% of the retinal ganglion cells can be lost before any visual field defects are detected.[1] This observation, that structural changes precede detectable functional deficits, has led to an increased interest in imaging technology.

To date, imaging modalities have analyzed the structure of the optic nerve head (scanning laser ophthalmoscopy) and measured retinal nerve fiber layer thickness (scanning laser polarimetry and optical coherence tomography) to aid in glaucoma diagnosis. In this review, we explore the role of macular thickness by spectral domain–optical coherence tomography (SD–OCT) in glaucoma.

2. Why macular thickness?

Retinal ganglion cells (RGCs) are the cells that die in glaucoma. RGC axons make up the retinal nerve fiber layer (rNFL) and exit the eye through the optic nerve. Progression of glaucomatous optic neuropathy can be seen by increased optic nerve cupping or peripapillary rNFL losses on SD–OCT. Within ~5mm or 16° of the fovea > 50% of RGC bodies reside.[2] Cell bodies are stacked up to six layers thick.[2] Thus, small losses of ganglion cell bodies (which along with the rNFL constitutes > 30% of the retinal thickness) are detectable by analyzing total retinal thickness. Total macular thickness is a surrogate measure of tissue thickness loss due to glaucoma in the absence of other macular pathology (which might affect other layers of the retina).

Changes in total macular thickness loss in glaucoma thus reflect the loss of the rNFL, ganglion cell bodies, and the inner plexiform layer (IPL)—tissues that are lost in glaucoma. Total macular thickness (internal limiting membrane to retinal pigment epithelium) is easily and accurately measured by optical reflective devices such as the OCT due to the high level of reflectivity from these two boundary regions of the retina. Earliest measurements of the retinal thickness were performed by the Retinal Thickness Analyzer (Talia Technologies, Neve Ilan, Israel) and subsequently by time domain OCT (Stratus, Carl Zeiss AG, Heidenheim, Germany).[3–6] The Stratus OCT measured the central 6 mm × 6 mm perifoveal area by acquiring data from six radial line scans intersecting at the fovea and created a map of macular thickness which interpolated the data in between the lines. This strategy of interpolation of data with sparse measurements in a large retinal region did not prove to be

Conflicts of interest: Dr. Gupta has no relevant financial interests, activities, relationships, or affiliations to disclose. Dr. Asrani receives lecture honoraria from Heidelberg Engineering, Inc.

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http://dx.doi.org/10.1016/j.tjo.2016.01.003

useful in the diagnosis and management of glaucoma compared with the peripapillary RNFL measurements.[6] Subsequently, SD–OCT permitted the measurements of larger areas of the retina with higher acquisition speed. This provided the ability of measuring retinal thickness with greater concentration of data points, and much less interpolation of data, thus providing a more reliable retinal (macular) thickness map. Different software strategies by different instrument makers are used for this such as a raster of lines or a grid of lines across the macular region.

Recently, software advancements have allowed the automated segmentation of the inner layers of the retina such as rNFL + RGC + IPL, collectively termed as the GCC (Ganglion cell complex). Such a strategy could be very useful in eyes with coexisting pathologies such as diabetic macular edema or age related macular degeneration, in which the total macular thickness is affected but the inner layer thickness changes due to glaucoma can be measured separately.

Various instruments measure different segmented layers such as RGCs + IPL or rNFL + RGC + IPL. Instruments such as the Cirrus (Carl Zeiss AG), RTVue (Optovue Inc., Fremont, CA, USA) and Topcon 3D OCT-2000 (Topcon Medical Systems, Oakland, NJ, USA) measure approximately the central 4–6 mm of the perifoveal area whereas instruments such as the Spectralis (Heidelberg Engineering, Heidelberg, Germany) and RS-3000 Nidek (Nidek Inc., Fremont, CA, USA) measure 9–10 mm of the perifoveal area.

Macular thickness is a highly reproducible measurement on SD–OCT with intravisit and intervisit coefficients of variation of < 1%.[7–9] Segmented layers, such as ganglion cell-IPL (GCIPL), also show good reproducibility.[8] High reproducibility thus allows for easier detection of glaucomatous progression.

2.1. Correlations between rNFL thickness, visual fields, and macular thickness

Macular thickness has been shown to correlate both with optic nerve cupping and peripapillary rNFL thickness in glaucoma.[10,11] Macula thickness losses in glaucomatous eyes have correlated with estimated RGC count and Humphrey Visual Field (HVF) parameters in both glaucomatous and normal eyes.[4,10,12–14] Peripapillary rNFL scans images a ring of tissue around the optic nerve, whereas, imaging the macula allows for quantification of total macula thickness. This permits the mapping of macula thickness, and thus RGCs, to the visual field for comparison.[15]

The traditional 24-2 or 30-2 visual field has relatively few spots dedicated to the macular region and visual field deficits in this area require a greater numbers of ganglion cell loss as compared with the more peripheral retina represented in the visual field.[16] Small losses of macular thickness are thus not detectable on visual field testing, enhancing the potential for detecting early glaucoma using this modality.[2,17]

3. How to use macular thickness

3.1. Glaucoma diagnosis

Pattern recognition of arcuate losses on macular thickness maps permits early detection of disease. Ganglion cell losses in the perifoveal area are not isolated. They are accompanied by loss of the ganglion cells along the arcuate track of the rNFL extending to the optic nerve (Figure 1).[18]

3.2. Glaucoma progression

Continued glaucomatous progression is detected by worsening of existing visual field defects or by development of new visual field losses. Progression detection on macular thickness maps is similarly performed by comparison plots between maps at different time points. Glaucomatous losses are detectable by their arcuate shape in the subtraction maps (Figure 1).

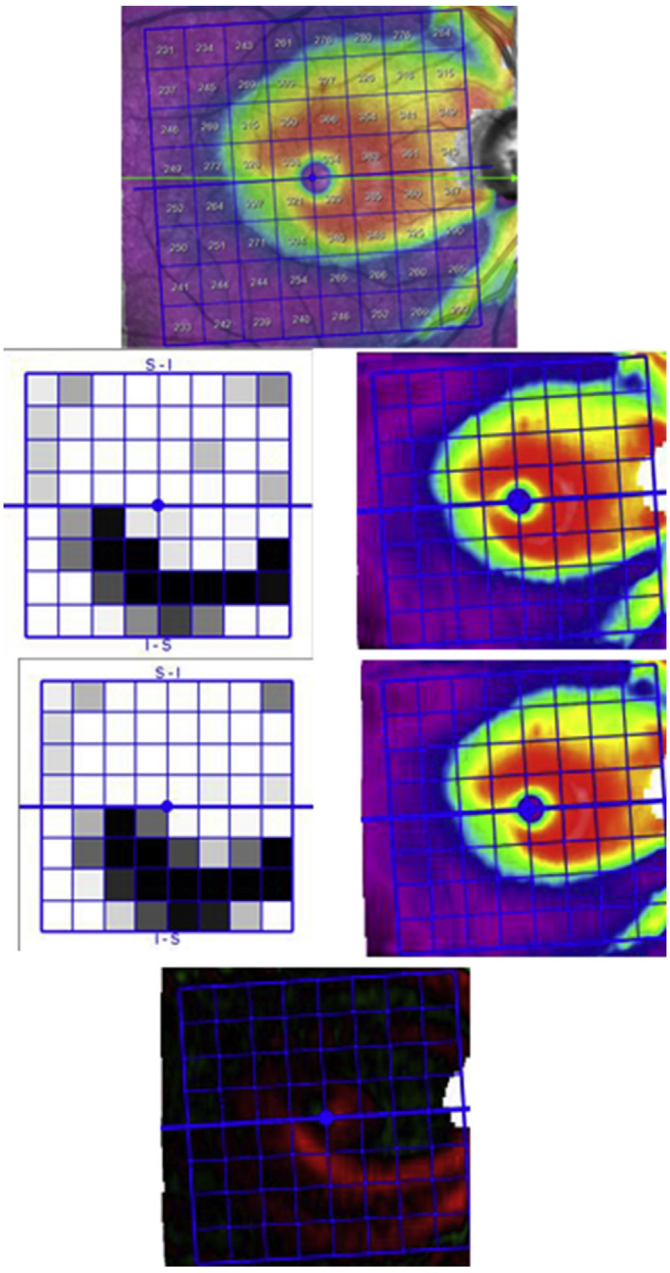

Figure 1. Glaucomatous progression on macular SD–OCT scans. A macular thickness map of the right eye (top) with arcuate thickness loss (inferior) is shown followed by macular thickness maps and superior–inferior hemifield asymmetry plots at two separate visits (middle). The bottom figure is a macula progression (change) map highlighting arcuate retinal thickness losses (red) in the inferior macula between the two patient visits.

3.3. Asymmetry of macular thickness

Glaucoma is typically a bilateral disease, but frequently asymmetric. A hallmark of glaucoma is that visual field defects respect the horizontal midline, affecting superior or inferior visual field differentially. Visual field deficits are also commonly asymmetric between the two eyes at the time of diagnosis.[19] Structurally,