

Measuring Macular Thickness in Glaucoma

Clinicians must be aware of important differences in the macular imaging protocols of the commercially available optical coherence tomography systems.

BY AHMAD A. AREF, MD

Glaucomatous optic neuropathy results in the death of retinal ganglion cells (RGCs), which are most densely populated in the macular region. On the basis of this anatomic relationship, Zeimer and colleagues reported large losses in total macular thickness in patients with known glaucomatous damage.¹ In a later study, Greenfield et al reported a correlation between total macular thickness, as measured by time-domain optical coherence tomography (OCT), and visual field mean deviation.² Supporting a structure-function relationship, glaucomatous eyes with visual field loss localized to one hemifield were found to have macular thickness measurements that were significantly less in the retinal quadrant associated with the defect.

Since the performance of these initial studies, the advent of spectral-domain OCT (SD-OCT) technology has permitted the more rapid acquisition of retinal images at a higher axial-image resolution, allowing the discrimination and measurement of individual retinal layers.³ The relevance of macular thickness measurement in glaucomatous disease re-emerged with the recent release of OCT software upgrades capable of measuring macular thickness parameters for the purposes of diagnosing and monitoring glaucoma. This article focuses on three of the commercially available systems, with an aim of helping clinicians to recognize the important differences between the technologies in terms of image acquisition and interpretation.

RTVue GANGLION CELL COMPLEX ANALYSIS

The RTVue FD-OCT system (Optovue, Inc.) performs macular analysis in glaucoma by segmenting the ganglion cell complex (GCC) from the remaining retinal layers. The GCC is defined as the three innermost retinal layers: the retinal nerve fiber layer (RNFL), RGC layer, and inner plexiform layer.⁴ The measurement of GCC thickness, as opposed to total macular retinal thickness, has been shown to improve diagnostic accuracy in glaucoma.⁵

The device measures GCC thickness within an automatically rendered 7-mm² area, centered 1 mm temporal to the fovea. The system then produces a color-coded GCC

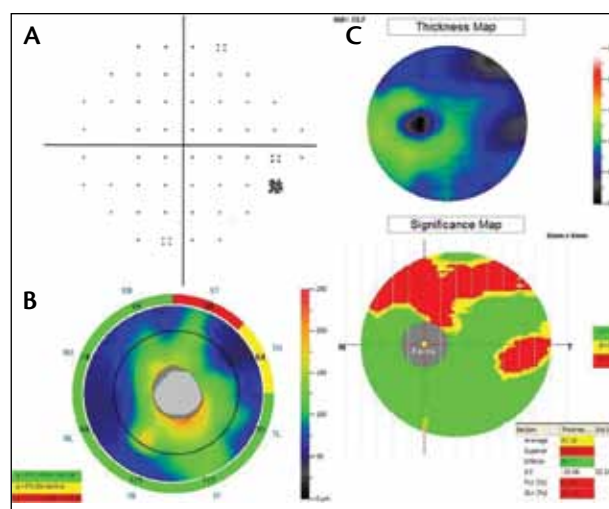


Figure 1. Automated visual field pattern deviation plot (A), RNFL analysis (B), and GCC analysis (C) printouts obtained by the RTVue FD-OCT system in a 33-year-old man with secondary open-angle glaucoma in his left eye. The inferonasal visual field defect did not meet Hodapp-Anderson-Parrish criteria for a minimal glaucomatous visual field abnormality yet showed an excellent correlation with superior RNFL and GCC defects detected by OCT.⁶ The data table reveals abnormalities of the superior and focal loss volume parameters.

thickness map for interpretation by the clinician. On this map, thicker regions of the GCC are displayed as yellow and orange, whereas thinner regions are displayed as blue and green. Acquired GCC thicknesses are also compared with values from a normative database and displayed as a significance map. The color-coded map shows corresponding probabilities of deviation from the normal range for each acquired pixel in the GCC map based on a comparison with an age-matched control group of nonglaucomatous individuals. A color-coded data table also supplies the clinician with detailed quantitative data, including average, superior, and inferior GCC thickness values. The focal loss and global loss volume parameters are calculated based on the specific pattern of GCC loss. Figure 1 displays RNFL and GCC analy-

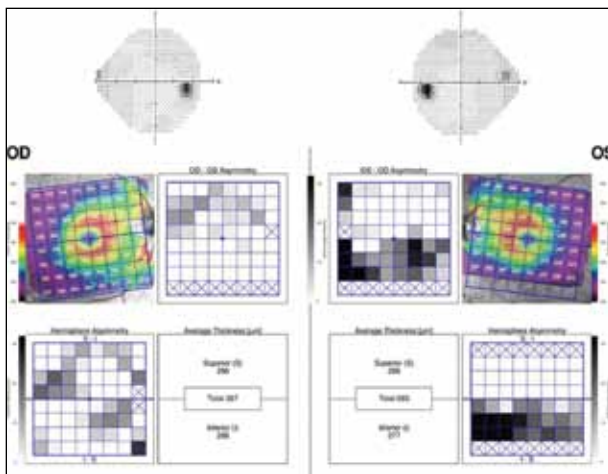


Figure 2. Automated visual field and OCT Posterior Pole Asymmetry Analysis printouts obtained by the Spectralis in a 62-year-old man referred for an evaluation of ocular hypertension. Posterior Pole Asymmetry Analysis confirmed inferior macular thinning corresponding to a borderline superonasal visual field defect in his left eye. Appropriate IOP-lowering therapy was initiated on the basis of structural and functional testing results, suggesting a diagnosis of primary open-angle glaucoma.

sis printouts obtained for a patient with known glaucoma using the RTVue FD-OCT system.

In an observational, cross-sectional study, Tan and colleagues compared the diagnostic power of macular GCC thickness measurements with peripapillary RNFL measurements obtained using time-domain OCT technology.⁴ The group found that the two technologies performed equally well with regard to diagnostic capability. Upon further analysis, however, abnormal GCC thickness parameters were found to detect additional cases of glaucoma that were not captured using RNFL measurements. The group concluded that the two parameters may be complementary in the diagnosis of glaucoma.

SPECTRALIS POSTERIOR POLE ASYMMETRY ANALYSIS

The Spectralis SD-OCT system (Heidelberg Engineering GmbH) measures total retinal macular thickness within a $30^\circ \times 25^\circ$ OCT volume scan centered on the fovea. The scanned area corresponds to 20° of the central visual field.⁷ Macular thickness values are displayed in an 8×8 -mm grid containing 65 individual $3^\circ \times 3^\circ$ square cells. An intra-eye asymmetry analysis compares each cell in a single hemisphere of one eye with corresponding cells in the opposite hemisphere and displays differences using a color-coded gray scale. The system also performs an inter-eye asymmetry analysis that compares the symmetry between the two eyes.

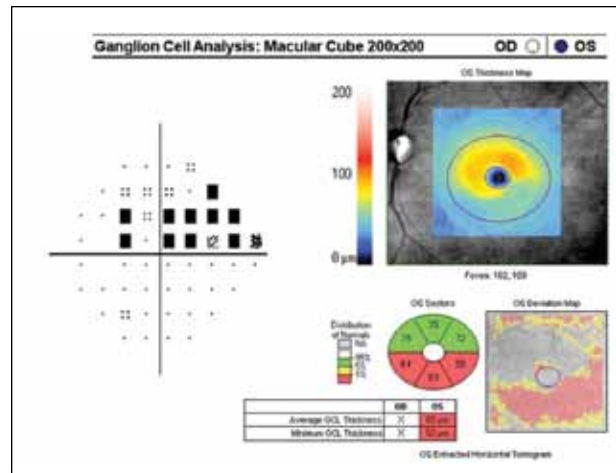


Figure 3. Pattern deviation visual field plot and GCA print-out obtained by the Cirrus HD-OCT system in a 50-year-old woman with advanced open-angle glaucoma in her left eye. The patient's superior hemifield visual field defect showed an excellent correlation with inferior GC-IPL thinning detected by the GCA scanning protocol.

Figure 2 displays a case study demonstrating the utility of this asymmetry analysis in clinical practice.

By capturing a relatively large area of macular thickness that includes peripheral retinal areas that may sustain damage early in the glaucomatous disease process, the Spectralis may allow for powerful diagnostic capabilities. The device's eye-tracking capability may reduce artifacts produced by microsaccades and thereby enhance reproducibility. Although the system does not yet allow a comparison of macular thickness measurements to an age-matched normative control group, the current analysis is useful, because early glaucomatous defects are often diagnosed on the basis of asymmetry.

A study performed by Seo et al found that the Spectralis SD-OCT Posterior Pole Asymmetry Analysis achieved a high diagnostic sensitivity (83.3%) and specificity (92.6%) when using three consecutive black cells to detect glaucoma with localized RNFL defects.⁸ The group reported statistically similar sensitivity and specificity values when using peripapillary RNFL parameters to detect the glaucomatous defects.

CIRRUS GANGLION CELL ANALYSIS

The Cirrus HD-OCT Ganglion Cell Analysis (GCA) protocol (Carl Zeiss Meditec, Inc.) automatically segments the ganglion cell and inner plexiform layers (GC-IPL) from the remaining retinal layers. Thereafter, the system measures the thickness of these two retinal layers within an elliptic annulus area (vertical radius of 2 mm, horizontal radius of 2.4 mm) centered on the fovea. The area of the annulus corresponds to the area of the thickest RGC layer in non-

TABLE. COMPARISON OF COMMERCIALY AVAILABLE IMAGING DEVICES FOR MACULAR ANALYSIS IN GLAUCOMA

OCT Device	Macular Imaging Protocol	Macular Area of Analysis	Macular Layers Analyzed	Normative Database?
RTVue FD-OCT	Ganglion cell complex analysis	7 mm ² , centered 1 mm temporal to fovea	RNFL, RGC, IPL	Yes
Spectralis SD-OCT	Posterior pole asymmetry analysis	8 mm ² , centered on fovea	All macular layers	No
Cirrus HD-OCT	Ganglion cell analysis	Elliptical annulus (vertical radius of 2 mm, horizontal radius of 2.4 mm), centered on fovea	GC-IPL	Yes

Abbreviations: OCT, optical coherence tomography; RNFL, retinal nerve fiber layer; RGC, retinal ganglion cell; IPL, inner plexiform layer; GC-IPL, ganglion cell and inner plexiform layers.

glaucomatous eyes.⁹ The macular GC-IPL values are displayed on a color-coded thickness map in which “warmer” colors represent thicker values and “cooler” colors represent thinner values. Additional parameters are displayed in a data table (mean and minimum GC-IPL thicknesses), deviation map, and sectoral map, each of which is color coded according to relative GC-IPL thickness compared with a normal age-matched database. A case example of the clinical use of the GCA protocol is displayed in Figure 3.

Similar to the GCC analysis obtained by the RTVue FD-OCT system but unlike the asymmetry analysis obtained by the Spectralis SD-OCT system, the GCA algorithm segments only a portion of all macular retinal layers for thickness measurement and analysis. The GCA algorithm, however, does not include a measurement of RNFL thickness, which is analyzed by the GCC protocol in addition to the GC-IPL thickness. The measurement of GC-IPL thickness alone may increase diagnostic accuracy, as prior studies have shown less variability among normal individuals compared with RNFL measurements.⁹

In a cross-sectional multicenter study, Mwanza and colleagues evaluated the diagnostic accuracy of the GCA protocol and compared it to RNFL and optic nerve head analyses obtained with the Cirrus HD-OCT device.¹⁰ The group reported similar areas under the curve for the best parameters of each algorithm.

CONCLUSION

The advent of SD-OCT technology has allowed advanced macular imaging protocols to play an important role in the diagnosis and monitoring of glaucoma. Although current studies suggest similar diagnostic capabilities compared to peripapillary RNFL and optic nerve protocols, macular imaging is likely complementary. The three imaging systems discussed in this article have all been shown to have high diag-

nostic capabilities, but there are important differences in image acquisition and analysis among the platforms (Table). The GCC analysis rendered by the RTVue FD-OCT system measures the thickness of the three innermost retinal layers for comparison with age-matched normative data. The asymmetry analysis obtained by the Heidelberg SD-OCT system measures total macular thickness over a relatively large area. Thickness measurements are not compared with normative data; rather, valuable inter- and intra-eye asymmetry analyses are performed. The GCA analysis obtained by the Cirrus HD-OCT system segments and measures the thickness of only the GC-IPL in a unique elliptical annulus for comparison with age-matched normative data. ■

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