# Macular Ganglion Cell Analysis for Early Detection of Glaucoma

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***Purpose:*** To investigate the ability of Cirrus high-definition optical coherence tomography (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA) macular ganglion cell analysis (GCA) sector, deviation, and thickness maps to detect early glaucoma.

***Design:*** Cross-sectional study.

***Participants:*** We enrolled 131 eyes with early glaucoma (mean deviation >−6.0 dB) and 132 age- and refractive error−matched healthy eyes.

***Methods:*** Macular GCA maps were obtained using Cirrus HD-OCT. The location, angular distance, and width of circumpapillary retinal nerve fiber layer (RNFL) defects were investigated by using red-free fundus photographs. The presence of a structural abnormality in the GCA map was defined as (1) yellow/red color codes in the sector map, (2) yellow/red pixels (>10) in the deviation map, and (3) blue areas in the thickness map.

***Main Outcome Measures:*** The prevalence of and factors associated with the presence or absence of abnormal GCA findings were assessed.

***Results:*** Among the 131 glaucomatous eyes, 105 (80.2%), 115 (87.8%), and 104 (79.4%) showed structural abnormalities in the GCA sector, deviation, and thickness maps, respectively. The absence of abnormal findings in the GCA maps of glaucomatous eyes was associated with the presence of RNFL defects in the superior hemisphere, a greater angular distance between the fovea and the RNFL defect, a narrower width of the RNFL defect, less severe visual field defects, or an isolated peripheral nasal step (outside 10 degrees of fixation) ($P<0.05$). A greater angular distance of the RNFL defect remained significant in multivariate analyses ($P<0.05$). Among the 132 healthy eyes, 28 (21.2%), 37 (28.0%), and 20 (15.2%) had abnormal findings in the GCA sector, deviation, and thickness maps, respectively. The presence of abnormal GCA findings in healthy eyes was associated with a higher degree of myopic refractive error ($P<0.05$).

***Conclusions:*** Cirrus HD-OCT GCA maps showed a good ability to detect early glaucoma. However, GCA maps did not show abnormal findings in glaucomatous eyes when the angular distance between fovea and RNFL defect was great. These findings should be considered when diagnosing early glaucoma using GCA maps. *Ophthalmology 2014;■:1−8 © 2014 by the American Academy of Ophthalmology.*

*Supplemental material is available at www.aaojournal.org.*

Progressive thinning of the circumpapillary retinal nerve fiber layer (RNFL) is a key feature of glaucoma.[1] The retinal ganglion cells (RGCs) of the RNFL are mainly located in the central 4.5-mm−diameter region of the macula.[2] Therefore, detecting structural changes in macular RGCs is important for the assessment of glaucoma. The recently introduced Cirrus high-definition (HD) optical coherence tomography (OCT; Carl Zeiss Meditec, Dublin, CA) system provides a ganglion cell analysis (GCA) algorithm that measures the ganglion cell−inner plexiform layer (GCIPL) thickness within a 14.13-mm$^2$ elliptical annulus area centered on the fovea.[3]

It has been reported that assessment of macular GCIPL thickness by using Cirrus HD-OCT GCA maps had an excellent reproducibility and glaucoma diagnostic ability.[4−8] However, we found that GCA maps did not show abnormal findings even though circumpapillary RNFL defects were observed in some cases. In addition, we found that GCA maps showed abnormal findings in healthy eyes (false-positive findings). Previous studies investigated factors associated with misidentification of photographic RNFL defects in early glaucoma by using OCT RNFL maps[9] and factors that affect false-positive findings in the RNFL thickness measurement by using OCT.[10] However, little has been reported regarding the factors associated with the absence of abnormal GCA findings in glaucomatous eyes and the presence of abnormal GCA findings in healthy eyes. Identifying these factors may provide valuable information for glaucoma detection using GCA maps.

The current spectral-domain OCT algorithm provides deviation and thickness maps based on entire cube data and sector-based thickness values. Hwang et al[9] recently reported that RNFL deviation and thickness map analysis outperformed sector-based RNFL thickness assessment for photographic RNFL defect identification. Likewise, we hypothesized that the ability of the GCA deviation map or thickness map to detect glaucoma would differ from that of the GCA sector map. To date, little is known about the



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abilities of GCA deviation and thickness maps to detect glaucoma. This study was performed to evaluate the abilities of GCA sector, deviation, and thickness maps of Cirrus HD-OCT to detect early glaucoma and the factors associated with the presence or absence of abnormal findings in the GCA maps of glaucomatous eyes and healthy eyes.

## Methods

### Participants

The institutional review board of Kim's Eye Hospital, Seoul, Korea, approved the study protocol, and all procedures conformed to the guidelines of the Declaration of Helsinki. Participants who visited a glaucoma specialist (Y.H.H.) were recruited consecutively at the glaucoma clinic of Kim's Eye Hospital. Each subject underwent a complete ophthalmic examination that included the following assessments: visual acuity and refractive error with a model TX-20P autorefractor keratometer (Canon, Tokyo, Japan); intraocular pressure with a Goldmann applanation tonometer; anterior segment examination by slit-lamp biomicroscopy; optic nerve head (ONH) evaluation and fundus examination with a 90-diopter lens; the 24-2 Swedish Interactive Threshold Algorithm standard automated visual field (VF) test using a Humphrey Visual Field Analyzer (Carl Zeiss Meditec); red-free fundus photograph using a Kowa Nonmyd7 fundus camera (Kowa, Tokyo, Japan); and peripapillary RNFL and macular measurement using Cirrus HD-OCT.[9] A glaucomatous VF defect was defined as (1) a cluster of 3 points with probabilities of <5% on the pattern deviation map in at least 1 hemifield, including at least 1 point with a probability of <1% or a cluster of 2 points with a probability of <1%, (2) glaucomatous hemifield test results outside of normal limits, or (3) a pattern standard deviation beyond 95% of normal limits[11] as confirmed by at least 2 reliable examinations (false-positive/negatives <15%, fixation losses <15%).

The inclusion criteria for glaucomatous eyes were as follows: a best-corrected visual acuity of 20/30 or better; a normal anterior segment on slit-lamp examination; an open angle on gonioscopic examination; ONH with glaucomatous changes (i.e., an increased cup-to-disc ratio and neuroretinal rim narrowing); an RNFL defect on red-free fundus photography (a dark wedge-shaped area with its apex touching the optic disc border in the brightly striated pattern of the surrounding RNFL[12]) within 1 hemisphere; and a mean deviation of VF >−6.0 dB. Eyes with RNFL defects in both the superior and inferior hemispheres were excluded because this can confound the effect of RNFL defect location (superior or inferior hemisphere) on the ability of GCA maps to detect glaucoma. Other exclusion criteria were eyes with a mean deviation of VF ≤−6.0 dB; a history of ocular inflammation or trauma; and the presence of concurrent retinal disease (i.e., vascular disorder or macular degeneration), optic nerve disease other than glaucoma, or a brain disorder that could influence VF results.

The inclusion criteria for age-, sex-, and refractive error–matched healthy eyes were a best-corrected visual acuity of ≥20/30, a normal anterior segment on slit-lamp examination, no RNFL defects in red-free fundus photographs, no VF defects, and intraocular pressure ≤21 mmHg.

### Optical Coherence Tomography Measurement

A 200 × 200 cube optic disc scan and 512×128 macular cube scan were obtained using Cirrus HD-OCT, as described previously.[13] The subjects were seated and properly positioned, and scanning laser images were focused for image acquisition. By using the iris and fundus viewports, the alignment was properly positioned to the ONH or macula in the center of the scan. Once the ONH or macula was centered on the live scanning laser image, a 6 × 6-mm square of data was captured.

The built-in algorithms of the Cirrus HD-OCT software (version 6.5.0.772) are capable of automatically identifying the vitreoretinal interface and posterior boundary of the circumpapillary RNFL and can subsequently calculate the circumpapillary RNFL thickness. The GCA algorithm identifies the outer boundary of the macular RNFL and the outer boundary of the IPL.[3] The difference between the RNFL and the IPL outer boundary segmentation yields the GCIPL thickness.[3] The average, minimum, and sectoral (superotemporal, superior, superonasal, inferonasal, inferior, and inferotemporal) GCIPL thicknesses are measured in an elliptical annulus with a vertical outer radius of 2.0 mm and horizontal radius of 2.4 mm (Fig 1; Fig 2, available at www.aaojournal.org). The results from the comparison of the GCIPL thickness with normative data are presented as color-coded maps. Green, yellow, and red codes are used to depict GCIPL thicknesses that are in the normal range, that are abnormal at the 5% level, and that are abnormal at the 1% level, respectively. In this study, a yellow or red code in a GCA sector map from Cirrus HD-OCT was defined as an abnormal GCA finding.

A deviation map is provided in the GCA algorithm of Cirrus HD-OCT. Uncolored areas indicate a normal GCIPL thickness, and areas with a GCIPL thickness less than 5% or 1% of normative data are indicated by yellow or red areas, respectively (Fig 1; Fig 2, available at www.aaojournal.org). In this study, we arbitrarily defined the presence of an area with a size >10 pixels coded in yellow/red in the GCA deviation map as a structural abnormality. Cirrus HD-OCT also provides a GCIPL thickness map that is not based on the normative database comparison. In the GCA thickness map, an area with a thick GCIPL is indicated by red/white, and an area with a thin GCIPL is indicated by blue/black (Fig 1; Fig 2, available at www.aaojournal.org). We defined the presence of a blue/black area in the GCA thickness map as a structural abnormality. To avoid subjectivity, the examination results of other GCA maps, RNFL photographs, and VF tests were masked to the observer who was assessing the GCA thickness map.

Poor-quality images were defined as those with a signal strength <8, incorrect identification of the vitreoretinal surface detection algorithm in the peripapillary RNFL-extracted B-scan, incorrect identification of the RNFL and IPL surface detection algorithm in the macular-extracted B-scan, and prominent involuntary saccade during the scan. These images were excluded.

The angular distance and width of circumpapillary RNFL defects were evaluated as described previously (Fig 3).[9,14] In brief, the OCT image was overlaid on the red-free fundus photographs. A reference line was drawn between the center of the optic disc and the center of the macula. In addition, the location of the defect margin was marked on the Cirrus HD-OCT scan circle, and a line was drawn between this point and the optic disc center. The angular distance of the RNFL defect was defined as the angle between the reference line and the nearest RNFL defect margin.[14] The angular width of each RNFL defect was measured as the angle between the 2 lines from the center of the optic disc to the points at which the RNFL defect and scan circle converged.[9] The angular distance and width of RNFL defects and the presence of abnormal findings in GCA maps were investigated independently by 2 observers (Y.H.H. and Y.C.J.) who were masked to the clinical features of the patient and to the other observer's assessment. When the 2 observers disagreed, the disagreement was resolved by a discussion. To investigate the intraobserver repeatability, the same measurements were performed again on another day.