Comparison of the Pattern of Retinal Ganglion Cell Damage Between Patients With Compressive and Glaucomatous Optic Neuropathies

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PURPOSE. To compare the patterns of retinal ganglion cell (RGC) damage in the macular and peripapillary areas in compressive optic neuropathy (CON) and glaucomatous optic neuropathy (GON) using spectral-domain optical coherence tomography (SD-OCT), and to determine the usefulness of SD-OCT macular and peripapillary analysis in discriminating between CON and GON.

METHODS. Sixty-three eyes with CON, 68 eyes with GON, and 73 healthy control eyes were included. Spectral-domain OCT scanning of the circumpapillary and macular area was performed to measure the global and six-sector thicknesses of the circumpapillary retinal nerve fiber layer (cpRNFL), and the macular retinal nerve fiber layer (mRNFL) and macular ganglion cell layer (mGCL) thicknesses in the nine macular subfields as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS).

RESULTS. Compared to the healthy eyes, the mRNFL was significantly thinner in six ETDRS subfields (inner and outer subfields of superior, nasal, and inferior areas) in CON, but in only two subfields (outer-inferior and outer-temporal subfields) in GON. The mGCL was thinner in all nine subfields in CON, but in only four subfields (inner and outer subfields of inferior and temporal areas) in GON. The temporal cpRNFL was significantly thinner in CON but was not involved in GON. The macular parameters performed better than cpRNFL parameters in discriminating between the CON and GON.

CONCLUSIONS. Distinct differences in the patterns of RGC damage in the macular and peripapillary areas were found between CON and GON. Evaluation of the macular RGC damage may be a useful adjunct for distinguishing CON from GON when optic disc and visual field examinations are inconclusive.

Keywords: glaucomatous optic neuropathy, compressive optic neuropathy, optical coherence tomography, retinal ganglion cell, retinal nerve fiber

Optic disc cupping and neuroretinal rim pallor are, respectively, considered the hallmarks for glaucomatous optic neuropathy (GON) and nonglaucomatous optic neuropathies such as hereditary, traumatic, and compressive optic neuropathies.1–3 However, it is not uncommon for both characteristics to be combined: glaucomatous optic discs sometimes accompany pale neuroretinal rim,4,5 while some eyes with nonglaucomatous optic neuropathies show an enlarged optic cup.6–15 The visual field defect respecting the vertical meridian is a characteristic feature of compressive optic neuropathy (CON), while glaucoma patients typically present with an arcuate scotoma. However, an arcuate scotoma can also be found in patient with CON1,14,15 (which is sometimes due to patient error during the visual field testing). Moreover, the visual field damage in advanced CON is not distinguishable from that in advanced GON. Because of these factors, the differentiation between GON and CON is not always clear-cut.

Danesh-Meyer et al.16 showed that evaluating the circumpapillary retinal nerve fiber layer (cpRNFL) thickness using optical coherence tomography (OCT) can distinguish the differing patterns of retinal ganglion cell (RGC) damage between CON and GON.16 They found that the cpRNFL profile differed distinctively between the two diseases, with the damage occurring predominantly in the temporal and nasal sectors of the optic nerve head (ONH) in GON, but in the superior and inferior sectors in CON.

The advent of spectral-domain (SD) OCT has made it possible to evaluate RGC damage in the macular area. Evaluation of macular RGCs is vitaly important since the macular area contains more than 50% of all the RGCs and is directly related with visual function. Various studies have shown that assessments of the macular ganglion cell layer (mGCL) thickness can not only detect structural damage but also predict the functional damage present in both CON17–21 and GON.22–27 However, to the best of our knowledge, the
usefulness of measuring the mGCL thickness in differentiating between these two diseases has never been evaluated.

Differentiation between CON and GON is of utmost importance because the treatment approach for each disease is completely different, and timely diagnosis and treatment is often critical for visual prognosis of CON. The aim of this study was to characterize the patterns of RGC damage in the macular and peripapillary areas using SD-OCT between patients with CON and GON and to determine the usefulness of SD-OCT macular and peripapillary analysis in discriminating between CON and GON.

**METHODS**

**Participants**

This study reviewed the data of CON patients with a parasellar tumor who were referred to an ophthalmologic practice for a perioperative ophthalmologic evaluation between March 2013 and April 2015. Primary open-angle glaucoma (POAG) patients and healthy controls were recruited from the database of subjects included in the Lamina cribrosa Exploration Study (LCES) and the Investigating Glaucoma Progression Study (IGPS), which are ongoing prospective studies of glaucoma and healthy individuals at the Glaucoma Clinic of Seoul National University Bundang Hospital. Written informed consents had been obtained from all subjects included in the LCES and IGPS. The present study was approved by the Institutional Review Board of Seoul National University Hospital and conformed to the tenets of the Declaration of Helsinki.

**Ophthalmic Examinations**

Primary open-angle glaucoma patients and normal subjects underwent a complete ophthalmic examination including visual acuity assessment, refraction, slit-lamp biomicroscopy, gonioscopy, Goldmann applanation tonometry, and dilated stereoscopic examination of the optic disc. They also underwent color fundus photography, SD-OCT scanning of the macular and peripapillary areas (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany), and standard automated perimetry (Humphrey Field Analyzer II 750; 24-2 Swedish interactive threshold algorithm; Carl Zeiss Meditec, Dublin, CA, USA).

Patients who were diagnosed as having CON underwent visual acuity assessment, refraction, slit-lamp biomicroscopy, Goldmann applanation tonometry, dilated stereoscopic examination of the optic disc, color fundus photography, SD-OCT scanning of the macular and peripapillary areas (Spectralis OCT), and standard automated perimetry (Humphrey Field Analyzer II 750; 24-2 Swedish interactive threshold algorithm; Carl Zeiss Meditec).

**Criteria for Inclusion**

Patients in the CON group had an intracranial tumor compressing the optic chiasm including pituitary adenoma, craniopharyngioma, or suprasellar meningioma as confirmed with magnetic resonance imaging, and a neurologic visual field (VF) defect at the time of tumor diagnosis as confirmed by a complete neuro-ophthalmic assessment. Data obtained at least 6 months after intracranial surgery were used for analysis, because the VF loss associated with CON may not be the result of RGC loss but instead result from RGC dysfunction and so be reversible after performing decompressing surgery.10 Only subjects without any evidence of recurrent tumor confirmed by neuroradiologic examinations and with stable VF defects for at least 6 months were included. Patients with an intraocular pressure (IOP) greater than 21 mm Hg or definite glaucomatous optic nerve damage (neuroretinal rim notching or thinning, or RNFL defect) and associated VF defects without ocular disease or conditions that may elevate IOP, and had an open anterior-chamber angle. A glaucomatous VF defect was defined as (1) outside normal limits on the glaucoma hemifield test, (2) three abnormal points with a probability of <5% of being normal, one with a probability of <1% by pattern deviation, or (3) a pattern standard deviation of <5% if the VF was otherwise normal, as confirmed in two consecutive tests. Patients in the GON group were matched with those in the CON group in terms of VF mean deviation (MD), age, and refractive errors.

The inclusion criteria for the healthy control group were eyes with an IOP below 22 mm Hg without antiglaucoma medication, normal-appearing optic discs, and normal VFs. A normal-appearing optic disc was defined as the absence of CON and pallor or swelling of the optic disc. A normal VF was defined as the absence of glaucomatous VF defects and neurologic field defects. Healthy control subjects were matched with the patients in the CON and GON groups in terms of age and refractive errors.

For all subjects, eyes with a best-corrected visual acuity of <20/200, a spherical refraction of <−8.00 or >+3.00 diopters, a cylinder correction of <−3.00 or >+3.00 diopters, or unreliable VF test results (fixation loss rate > 20%, false-positive or false-negative error rates > 25%) were excluded. Subjects with a history of ocular surgery other than cataract extraction and glaucoma surgery, intraocular diseases (e.g., optic disc abnormalities such as optic disc drusen, optic disc edema, optic disc neuroretinal rim pallor not related to CON, and retinal diseases such as retinal vessel occlusion or diabetic retinopathy), or neurologic diseases (except for the intracranial tumor in the CON group) that could cause VF loss were also excluded. If both eyes were eligible, one eye was randomly selected for analysis.

**SD-OCT Scanning of the Macular and Peripapillary Areas**

The SD-OCT images of the posterior pole were obtained on the same day as cpRNFL scanning. The cpRNFL scanning was performed using the circular scan mode of the Spectralis OCT device. The scan circle was 12° in diameter, while its diameter in millimeters depended on the axial length. The software provided with the Spectralis OCT device measures the global average cpRNFL thickness and the mean RNFL thickness in each of the following six sectors relative to the fovea–disc axis: nasal-superior (NS, 90–135°), nasal (N, 135–225°), nasal-inferior (NI, 225–270°), temporal-inferior (TI, 270–315°), temporal (T, 315–45°), and temporal-superior (TS, 45–90°).

The scanning of the posterior pole was performed in the 30° perifoveal area using a 30° × 25° OCT scan. Sixty-one B-scan sections parallel to the fovea–disc axis were obtained, where each section involved averaging nine OCT frames. Images are obtainable using the Spectralis OCT device only when the quality score is >15. For lower quality scores the image acquisition process automatically stops and the image of that section is excluded. Only eyes with a quality score of >15 in all sections were included. The new software for the Spectralis OCT device automatically segments individual retinal layers, of which the macular RNFL (mRNFL) and mGCL thicknesses were used for analysis.
The accuracy of the segmentation of each retinal layer (cpRNFL, mRNFL, and mGCL) and adequate centration on the fovea were reviewed independently by masked observers (EJL and HKY). Only images that were considered adequate by both observers were included in the analysis.

The retinal thickness map used to display numeric averages of the measurements for each of nine subfields as defined by the Early Treatment Diabetic Retinopathy Study (ETDRS) was selected. Inner, intermediate, and outer rings of diameters 1, 3, and 6 mm, respectively, were used in the analysis. The average of all points within the inner 1-mm-radius circle was defined as the central (C) thickness. The intermediate ring was divided into the inner-superior (IS), inner-nasal (IN), inner-inferior (II), and inner-temporal (IT) subfields, while the outer ring was divided into the outer-superior (OS), outer-nasal (ON), outer-inferior (OI), and outer-temporal (OT) subfields. The numerical values recorded in each of the nine subfields were used in the analyses.

### Statistical Analysis

Clinical characteristics and OCT measurements were compared between groups using the independent samples t-test. The raw data for the comparison of the sector or subfield thicknesses were subjected to Bonferroni correction on the basis of the number of comparisons in each analysis. The usefulness of mRNFL, mGCL, and cpRNFL thickness measurements in discriminating between groups was assessed using the area under the receiver operating characteristic curve (AUC).

### Table 1. Patterns of RGC Damage in CON and GON

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Clinical Characteristics of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control, n = 72</strong></td>
<td><strong>CON, n = 63</strong></td>
</tr>
<tr>
<td>Age, y</td>
<td>49.5 ± 11.3 (21, 76)</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>31/41</td>
</tr>
<tr>
<td>Best-corrected visual acuity, logMAR</td>
<td></td>
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<tr>
<td>Baseline IOP, mm Hg</td>
<td></td>
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<tr>
<td>Refractive errors, D</td>
<td></td>
</tr>
<tr>
<td>Visual field MD, dB</td>
<td></td>
</tr>
</tbody>
</table>

Values in parentheses represent range. Statistically significant values are in bold. mRNFL, retinal nerve fiber layer thickness measured in the macular area; mGCL, ganglion cell layer thickness measured in the macular area; G, global.

### Table 2. Comparison of mRNFL, mGCL, and cpRNFL Thicknesses Between Groups

<table>
<thead>
<tr>
<th><strong>mRNFL, μm</strong></th>
<th><strong>CON vs. Control</strong></th>
<th><strong>GON vs. Control</strong></th>
<th><strong>CON vs. GON</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control, n = 72</strong></td>
<td><strong>CON, n = 63</strong></td>
<td><strong>GON, n = 68</strong></td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td>C</td>
<td>11.4 ± 2.4</td>
<td>10.4 ± 2.6</td>
<td>11.6 ± 2.2</td>
</tr>
<tr>
<td>IS</td>
<td>26.1 ± 2.8</td>
<td>22.9 ± 4.0</td>
<td>26.5 ± 4.1</td>
</tr>
<tr>
<td>IT</td>
<td>19.3 ± 4.3</td>
<td>18.7 ± 1.6</td>
<td>18.9 ± 1.5</td>
</tr>
<tr>
<td>II</td>
<td>26.6 ± 3.0</td>
<td>24.6 ± 3.9</td>
<td>24.9 ± 4.6</td>
</tr>
<tr>
<td>IN</td>
<td>22.6 ± 2.2</td>
<td>20.5 ± 2.9</td>
<td>23.2 ± 2.5</td>
</tr>
<tr>
<td>OS</td>
<td>40.6 ± 4.8</td>
<td>54.7 ± 7.6</td>
<td>37.3 ± 8.7</td>
</tr>
<tr>
<td>OT</td>
<td>20.0 ± 2.3</td>
<td>19.8 ± 1.8</td>
<td>18.8 ± 1.8</td>
</tr>
<tr>
<td>ON</td>
<td>41.7 ± 6.0</td>
<td>38.1 ± 7.6</td>
<td>30.1 ± 9.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>mGCL, μm</strong></th>
<th><strong>CON vs. Control</strong></th>
<th><strong>GON vs. Control</strong></th>
<th><strong>CON vs. GON</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control, n = 72</strong></td>
<td><strong>CON, n = 63</strong></td>
<td><strong>GON, n = 68</strong></td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td>C</td>
<td>13.9 ± 3.8</td>
<td>11.7 ± 3.2</td>
<td>13.9 ± 3.7</td>
</tr>
<tr>
<td>IS</td>
<td>52.0 ± 4.0</td>
<td>41.9 ± 9.8</td>
<td>50.1 ± 6.6</td>
</tr>
<tr>
<td>IT</td>
<td>46.4 ± 4.8</td>
<td>40.8 ± 9.7</td>
<td>41.0 ± 8.2</td>
</tr>
<tr>
<td>II</td>
<td>50.8 ± 3.9</td>
<td>45.0 ± 9.2</td>
<td>44.1 ± 10.3</td>
</tr>
<tr>
<td>IN</td>
<td>51.1 ± 4.7</td>
<td>38.1 ± 12.8</td>
<td>49.1 ± 6.7</td>
</tr>
<tr>
<td>OS</td>
<td>34.3 ± 5.2</td>
<td>30.9 ± 4.8</td>
<td>32.6 ± 4.8</td>
</tr>
<tr>
<td>OT</td>
<td>35.3 ± 3.8</td>
<td>32.4 ± 5.9</td>
<td>28.8 ± 5.5</td>
</tr>
<tr>
<td>ON</td>
<td>31.9 ± 5.1</td>
<td>29.2 ± 3.9</td>
<td>27.5 ± 4.5</td>
</tr>
<tr>
<td>ON</td>
<td>38.2 ± 3.4</td>
<td>31.8 ± 6.9</td>
<td>36.6 ± 3.8</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>cpRNFL, μm</strong></th>
<th><strong>CON vs. Control</strong></th>
<th><strong>GON vs. Control</strong></th>
<th><strong>CON vs. GON</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control, n = 72</strong></td>
<td><strong>CON, n = 63</strong></td>
<td><strong>GON, n = 68</strong></td>
<td><strong>P Value</strong></td>
</tr>
<tr>
<td>G</td>
<td>99.3 ± 10.2</td>
<td>87.0 ± 15.5</td>
<td>83.1 ± 14.6</td>
</tr>
<tr>
<td>TS</td>
<td>138.5 ± 18.0</td>
<td>111.1 ± 29.9</td>
<td>116.2 ± 34.7</td>
</tr>
<tr>
<td>T</td>
<td>76.9 ± 11.5</td>
<td>58.8 ± 16.6</td>
<td>73.2 ± 14.8</td>
</tr>
<tr>
<td>TI</td>
<td>151.1 ± 18.1</td>
<td>125.4 ± 31.0</td>
<td>95.2 ± 35.1</td>
</tr>
<tr>
<td>NI</td>
<td>109.2 ± 22.1</td>
<td>113.9 ± 33.2</td>
<td>89.7 ± 22.3</td>
</tr>
<tr>
<td>N</td>
<td>68.6 ± 12.9</td>
<td>59.7 ± 16.7</td>
<td>60.9 ± 12.6</td>
</tr>
<tr>
<td>NS</td>
<td>104.8 ± 20.5</td>
<td>110.3 ± 28.2</td>
<td>95.7 ± 28.3</td>
</tr>
</tbody>
</table>

Statistically significant values are in bold. mRNFL, retinal nerve fiber layer thickness measured in the macular area; mGCL, ganglion cell layer thickness measured in the macular area; G, global.
the area under the receiver operating characteristic curve (AUC). Analyses were performed using the Statistical Package for the Social Sciences (version 20.0; SPSS, Chicago, IL, USA). Except where stated otherwise, the data are presented as mean ± standard deviation values. The cutoff for statistical significance was set at $P < 0.05$.

**RESULTS**

This study initially included 78 eyes of 78 patients with CON, of which 15 were excluded because of optic disc edema ($n = 4$), poor image quality that did not allow clear delineation of each retinal layer ($n = 5$), and being diagnosed with simultaneous glaucoma ($n = 6$). Of the remaining 63 patients, 36 were diagnosed with pituitary adenoma, 11 with craniopharyngioma, and 16 with suprasellar meningoia. Seventy-two age- and refraction-matched control eyes and 68 age-, refraction-, and VF-MD-matched GON eyes were recruited from the database of IGPS and LCES.

Table 1 lists the characteristics of the study participants. Baseline IOP was lower in CON than in the control group ($P = 0.012$). Patients with CON had worse best-corrected visual acuity than the other two groups (all $P < 0.001$). No significant differences were found between groups in terms of age, sex, and refractive errors. Visual field MD did not differ between the CON and GON groups.

Table 2 compares the mRNFL, mGCL, and cpRNFL thicknesses between the study groups. Relative to eyes in the healthy control group, the mRNFL was thinner in the CON group in six subfields [superior (OS, IS), nasal (IN, ON), and inferior (II, OI)] and in the GON group in only two subfields (OT and OI); and the mGCL was thinner in the CON group in all nine subfields and thinner in the GON group in only four subfields [temporal (IT, OT) and inferior (II, OI)]. The macular analysis did not show either mRNFL or mGCL thinning in the nasal and superior subfields in the GON group. The cpRNFL was significantly thinned globally and in the TS, T, NI, and N sectors in the CON group, and globally and in the TS, TI, NI, and N sectors in the GON group. The T-sector cpRNFL was not involved in the GON group. The patterns of thinning of the mRNFL, mGCL, and cpRNFL in CON and GON compared to the control group are also shown in Figure 1. There were significant differences between the CON and GON groups in the mRNFL thickness in the C, IS, IN, OT, and OI subfields; in the mGCL thickness in the C, IS, IN, OT, and ON subfields; and in the cpRNFL thickness in the TS, TI, NI, and NS sectors.

Figure 2 compares the percentage thicknesses of the mRNFL, mGCL, and cpRNFL in the CON and GON groups for data normalized relative to the average thickness in the control group. The diagnostic performance of each parameter for CON and GON, as well as the usefulness in discriminating between CON and GON, was assessed using the AUC (Table 3). The AUCs for diagnosing CON were largest for the IS-subfield mGCL thickness (0.878), IN-subfields, mGCL thickness (0.854), and T-sector cpRNFL thickness (0.835). The AUCs for diagnosing GON were largest for the TI-sector cpRNFL thickness (0.926), OT-subfield mGCL thickness (0.840), and OI-subfield mRNFL thickness (0.832). The best parameter for discriminating between CON and GON was the IS-subfield mGCL thickness ($AUC = 0.837$), followed by the IN-subfield mGCL thickness ($AUC = 0.819$) and IN-sector cpRNFL thickness ($AUC = 0.788$) (Table 3).
TABLE 3. AUC of mRNFL, mGCL, and cpRNFL to Discriminate Between Groups

<table>
<thead>
<tr>
<th></th>
<th>CON vs. Control</th>
<th>GON vs. Control</th>
<th>CON vs. GON</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC</td>
<td>95% CI</td>
<td>AUC</td>
</tr>
<tr>
<td><strong>mRNFL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.621</td>
<td>0.523–0.719</td>
<td>0.463</td>
</tr>
<tr>
<td>IS</td>
<td>0.764</td>
<td>0.679–0.848</td>
<td>0.461</td>
</tr>
<tr>
<td>IT</td>
<td>0.490</td>
<td>0.389–0.591</td>
<td>0.451</td>
</tr>
<tr>
<td>II</td>
<td>0.681</td>
<td>0.587–0.775</td>
<td>0.578</td>
</tr>
<tr>
<td>IN</td>
<td>0.735</td>
<td>0.647–0.823</td>
<td>0.414</td>
</tr>
<tr>
<td>OS</td>
<td>0.739</td>
<td>0.651–0.827</td>
<td>0.618</td>
</tr>
<tr>
<td>OT</td>
<td>0.501</td>
<td>0.400–0.602</td>
<td>0.653</td>
</tr>
<tr>
<td>OI</td>
<td>0.644</td>
<td>0.546–0.742</td>
<td>0.832</td>
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<tr>
<td>ON</td>
<td>0.796</td>
<td>0.716–0.876</td>
<td>0.588</td>
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<tr>
<td><strong>mGCL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0.690</td>
<td>0.598–0.783</td>
<td>0.484</td>
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<tr>
<td>IS</td>
<td>0.878</td>
<td>0.781–0.959</td>
<td>0.563</td>
</tr>
<tr>
<td>IT</td>
<td>0.734</td>
<td>0.645–0.823</td>
<td>0.691</td>
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<tr>
<td>II</td>
<td>0.829</td>
<td>0.756–0.902</td>
<td>0.675</td>
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<tr>
<td>IN</td>
<td>0.854</td>
<td>0.785–0.924</td>
<td>0.560</td>
</tr>
<tr>
<td>OS</td>
<td>0.758</td>
<td>0.672–0.843</td>
<td>0.599</td>
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<td>OT</td>
<td>0.667</td>
<td>0.572–0.762</td>
<td>0.840</td>
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<tr>
<td>OI</td>
<td>0.735</td>
<td>0.649–0.821</td>
<td>0.778</td>
</tr>
<tr>
<td>ON</td>
<td>0.823</td>
<td>0.745–0.902</td>
<td>0.598</td>
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<tr>
<td><strong>cpRNFL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>0.752</td>
<td>0.668–0.836</td>
<td>0.806</td>
</tr>
<tr>
<td>TS</td>
<td>0.818</td>
<td>0.744–0.892</td>
<td>0.689</td>
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<tr>
<td>T</td>
<td>0.835</td>
<td>0.767–0.903</td>
<td>0.571</td>
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<tr>
<td>TI</td>
<td>0.805</td>
<td>0.726–0.884</td>
<td>0.926</td>
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<tr>
<td>NI</td>
<td>0.458</td>
<td>0.354–0.562</td>
<td>0.726</td>
</tr>
<tr>
<td>N</td>
<td>0.666</td>
<td>0.568–0.765</td>
<td>0.642</td>
</tr>
<tr>
<td>NS</td>
<td>0.407</td>
<td>0.304–0.510</td>
<td>0.615</td>
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</table>

mRNFL, retinal nerve fiber layer thickness measured in the macular area; mGCL, ganglion cell layer thickness measured in the macular area; G, global.

FIGURE 3. Color disc photographs (A), mRNFL (B) and mGCL (C) thickness maps, cpRNFL thickness circular diagrams (D), and grayscale plots of VF test results (E) in patients with CON (A-1–E-1) and GON (A-2–E-2) with early VF damage. The CON patient shows characteristic thinning of the mGCL in the nasal hemiretina ([C-1] white arrow indicates the border between the damaged and undamaged areas) and selective thinning of the papillomacular mRNFL ([B-1] white arrows) and in the N and T sectors of the cpRNFL (D-1). On the other hand, the GON patient shows an obvious pattern of loss in the inferotemporal arcuate fibers both in the mRNFL ([B-2] black arrow) and mGCL ([C-2] black arrow) thickness maps, and thinning in the TI sector of the cpRNFL (D-2).
Figures 3, 4, and 5 illustrate the characteristic patterns of macular and peripapillary damage in CON and GON with early, moderate, and advanced VF damage, respectively. In eyes with early to moderate VF damage, the pattern of damage was clearly distinguishable between CON and GON in all mRNFL and mGCL thickness maps and the cpRNFL diagram as follows: selective loss of the mGCL in the nasal hemiretina ([C-1] arrow indicates the border between the damaged and undamaged areas) and selective thinning in the N and T sectors of the cpRNFL ([D-1]), while mRNFL thinning is noted in the papillomacular area ([B-1] arrows). On the other hand, the GON patient shows an obvious pattern of loss in the inferotemporal arcuate fibers in both the mRNFL ([B-2] arrow) and mGCL ([C-2] arrow) thickness maps, and thinning of the cpRNFL in the TS and TI sectors ([D-2]).

Figure 6 shows the usefulness of SD-OCT in distinguishing CON when optic disc and VF findings are unremarkable. Specifically, the mGCL thickness map clearly displayed RGC damage of neurologic origin.

Figures 3, 4, and 5 illustrate the characteristic patterns of macular and peripapillary damage in CON and GON with early, moderate, and advanced VF damage, respectively. In eyes with early to moderate VF damage, the pattern of damage was clearly distinguishable between CON and GON in all mRNFL and mGCL thickness maps and the cpRNFL diagram as follows: selective loss of the mGCL in the nasal hemiretina ([C-1] arrow indicates the border between the damaged and undamaged areas) and selective thinning in the T and N sectors, with relative sparing of arcuate mRNFL and cpRNFL fibers in CON (Figs. 3, 4); versus obvious thinning of arcuate areas of the mRNFL, mGCL, and cpRNFL with relative sparing of the inner-subfield macular thicknesses in GON. However, the difference in the mRNFL and cpRNFL profiles between CON and GON was less definite in the advanced stage, while the pattern of mGCL thinning remained distinct (Fig. 5).

Figure 6 shows the usefulness of SD-OCT in distinguishing CON when optic disc and VF findings are unremarkable. Specifically, the mGCL thickness map clearly displayed RGC damage of neurologic origin.
connective tissue support in these regions. 28 passing through the superior and inferior laminar cribrosa are lamina cribrosa of the ONH. It is known that the arcuate fibers Meanwhile, the primary site of axonal injury in GON is the location and/or mechanism of damage to their axons differing in discriminating between CON and GON. Because the ONH characteristics may overlap between CON and GON, the findings of the present study provide valuable information for distinguishing CON from GON.

There was a distinct difference in the patterns of damage between CON and GON, which may be explained by the location and/or mechanism of damage to their axons differing between these two diseases. In CON, due to parasellar tumor, the mass affects the crossing fibers initially, and thus axons originating from the nasal hemiretina are selectively damaged. Meanwhile, the primary site of axonal injury in GON is the lamina cribrosa of the ONH. It is known that the arcuate fibers passing through the superior and inferior laminar cribrosa are the most susceptible to glaucomatous damage due to the lesser connective tissue support in these regions. 29

Compared to the healthy control eyes, all subfields of the mGCL were thinner in CON (Fig. 1). However, the thinning of the mGCL was more distinct in the nasal subfields than in the temporal subfields, most especially in the IN subfield relative to the IT subfield. The selective damage of the nasal hemiretina is well documented in CON. 30,31,28 and is attributable to the axons originating from the nasal hemiretinal RGCs comprising crossing fibers that are close to the chiasm-compressing mass. The temporal hemiretinal fibers can also be damaged when the mass enlarges and affects the noncrossing fibers, eventually causing total macular RGC loss. Meanwhile, the cpRNFL was thinner in the nasal and temporal sectors in the CON group (Fig. 1), which is consistent with previous findings. 32,33,34

The nasal and temporal cpRNFL thinning is consistent with the classic band atrophy of the ONH that can be seen in patients with a chiasmal tumor and preservation of uncrossed fibers. 35

On the other hand, the cpRNFL showed thinning in all sectors except for the T and NS sectors in GON, with the thinning being most notable in the TS and TI sectors (Fig. 1). This is consistent with the notion that superior and inferior arcuate fibers are the most susceptible to glaucomatous damage, while the temporal papillomacular fibers are the least to be damaged. 36 However, macular analysis revealed significant damage to the mGCL and mRNFL only in the inferior and temporal subfields, without significant thinning in the superior subfields. This may be explained by the distribution of RGC axons differing between the inferior and superior hemiretina. Most RGCs in the inferior and inferotemporal macular areas project their axons to the inferior quadrant of the ONH. 37 Therefore, damage to the axons entering the inferior pole of the ONH would be detected in the inferior and inferotemporal macular areas; these areas have been described as a vulnerable zone that is frequently damaged in GON. 38 In contrast, RGCs in the superior macular area project axons to the temporal quadrant of the ONH, 39 which is generally not involved until the end stage of the disease. 30 Significant thinning would therefore generally not be detected in the superior macular area. Meanwhile, axons entering the superior pole of the ONH originate from the area that is not included in the mGCL analysis. Thus, axonal damage occurring at the superior pole of the ONH might not be detected in macular analysis. 32

The macular evaluation performed better than the peripapillary evaluation in discriminating between CON and GON, with the mGCL thicknesses in the IS and IN subfields being the two best parameters for performing this discrimination. This finding suggests that the IS and IN macular subfields are the least likely to be involved in glaucoma, and so eyes with suspected glaucoma and macular RGC damage in those areas may have to be considered for neurologic evaluation.

In the present study, patients with CON had worse visual acuity than those with GON, despite a similar degree of cpRNFL and VF loss. This was because of the relatively larger number of patients having lower visual acuity in the CON group: Subjects with visual acuities <20/30 numbered 18 and 5 in the CON and GON groups, respectively (data not presented). This may indicate that low visual acuity relative to the degree of optic nerve damage can be another point to distinguish CON from GON.

Intraocular pressure was lower in the CON group than the healthy control group, which is attributable to many of the patients being on IOP-lowering treatment at the time of SD-OCT. Interestingly, IOP was also lower in the CON group than in the control group, which is consistent with the findings of Danesh-Meyer et al. 32 Although we do not have a clear explanation for this finding, we speculate that it is related to the effect of long-term hormonal imbalance in CON patients who have a parasellar tumor. It is known that the production of the aqueous humor is influenced by pituitary hormones. 40–43 Since pituitary tumors often induce hormonal changes, this may affect the IOP by modulating the amount of aqueous produced. In addition, CON patients underwent tumor removal surgery that included removal of part of the pituitary gland, which would obviously result in hormonal imbalance. 40

Temporal or incongruous hemianopia have been considered pathognomonic of chiasmal compression. The type of VF defect characteristic of glaucoma has also been well described. It is therefore infeasible to consider VF defects to be a better gold standard for differentiating between CON and GON. However, the patterns of VF defects in the two diseases are
frequently confused with one another,12,41–43 and so the evaluation of macular RGC damage using SD-OCT may a useful adjunct when the pattern of VF defect is equivocal. This study was subject to some limitations. Firstly, the macular retinal layer segmentation performed by the current version of the Spectralis OCT device does not provide normative data; we overcame this problem by including healthy control subjects. Secondly, in extremely advanced stages of both CON and GON, neither macular nor peripapillary evaluation may be valid, because nearly total RGC loss can be present in either condition. Thirdly, the mGCL thickness in the superior and inferior subfields was evaluated without separating it into the nasal and temporal hemiretina, since the Spectralis OCT device did not allow such a separation. The availability of an interhemispheric comparison of the superior and inferior mGCL analysis would provide valuable information. Nonetheless, the interhemispheric difference was readily recognizable on the mGCL map, and so clinicians need to view an mGCL map when they suspect CON. Lastly, this study included only CON patients with a parasellar tumor, so the reported results are not applicable to CON caused by central nervous system tumors at other locations.

In conclusion, this study has revealed distinct patterns of RGC damage in the macular and peripapillary areas in CON and GON. The macular evaluation showed better performance than the circumpapillary evaluation in discriminating between CON and GON, with the mGCL thicknesses in the IS and IN subfields being the two best parameters for performing this discrimination. Based on the findings of this study, assessment of macular RGC damage may be a useful adjunct for distinguishing CON from GON when the optic disc and VF evaluations are equivocal. In addition, clinicians should be aware of the characteristic pattern of RGC loss in CON so that they can avoid misdiagnosing CON as GON.

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References


