Alterations in the Neural and Connective Tissue Components of Glaucomatous Cupping After Glaucoma Surgery Using Swept-Source Optical Coherence Tomography

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PURPOSE. To visualize changes in deep optic nerve head (ONH) structures following glaucoma surgery using (3-dimensional [3D]) swept-source optical coherence tomography (SS-OCT) and to determine the clinical and structural factors associated with postoperative lamina cribrosa (LC) and prelaminar neural tissue (PLT) changes.

METHODS. In this prospective observational case series, SS-OCT thin-sliced datasets of the ONH covering a 3 × 3-mm area comprised of 256 B-scans (interval between scans = ~12 μm) were obtained before and 3 months after the surgery and evaluated in 73 eyes of 73 patients with glaucoma. Bruch’s membrane opening (BMO) and anterior LC boundary were manually delineated by two methods; one in every four B-scans (64 B-scans per eye) and 15 equally spaced horizontal B-scans in BMO area, excluding both ends (interval between scans = 96–120 μm). After former delineation, the point with maximum LC depth among 64 B-scans was automatically calculated, and LC depth and PLT thickness were averaged among 5 points adding 4 points 100 μm apart from this point vertically and horizontally. Associations between the percent change in LC depth and other clinical and structural parameters were tested for statistical analysis.

RESULTS. Lamina cribrosa depth and axial length significantly decreased and PLT thickness significantly increased after surgery. The percent change of maximum LC depth correlated significantly with the percent change of IOP (P = 0.008), baseline LC depth (P = 0.032), and visual field mean deviation (P = 0.035; at the point with maximum LC depth), while the percent change of axial length correlated with IOP reduction (P = 0.002) but not with visual field mean deviation.

CONCLUSIONS. Swept-source optical coherence tomography enables 3D analysis of deep ONH structures, and the change in LC depth after glaucoma surgery have association with IOP change and the severity of glaucomatous optic neuropathy.

Keywords: swept-source optical coherence tomography, lamina cribrosa, trabeculectomy, trabeculotomy

The lamina cribrosa (LC), which is a lattice-like structure of successively perforated cribiform plates, is thought to be the key structure around which obstruction of axoplasmic transport has been noted by various previous reports.\(^1\) Many previous reports have been noted by various previous reports.\(^1\)–\(^5\) The lamina cribrosa is difficult to observe in vivo because neural tissue and many vessels exist in front of it. The advent of spectral domain (SD)-optical coherence tomography (OCT) has enabled 3-dimensional (3D) visualization of human deep optic nerve head (ONH) structures including LC in vivo.\(^6\)–\(^8\) Furthermore, the visualization of deeper laminar structures was improved by the enhanced depth imaging (EDI)-OCT technique introduced by Spaide et al.\(^9\) Several earlier studies reported qualitative and quantitative findings of the LC structure using this technique in eyes with glaucoma.\(^10\)–\(^14\)

Intraocular pressure (IOP) is considered the most important risk factor for the development and progression of glaucoma.\(^15\)–\(^16\) Since large randomized clinical trials have indicated that the lowering of IOP can reduce the progression of visual field defects in glaucoma patients, control over IOP has been a primary goal of current glaucoma treatments.\(^16\)–\(^17\) However, the mechanism by which the lowering of IOP reduces glaucoma progression remains uncertain.

The change in LC depth following IOP reduction is a candidate mechanism for the protective effect of IOP reduction, which is known to lead to the reversal of optic disc cupping after successful glaucoma surgery in children,\(^18\)–\(^19\) and to a lesser extent in adults.\(^20\)–\(^21\) Recently, Lee et al.\(^15\) and Reis et al.\(^22\) reported significant reduction in LC depth after glaucoma surgery using EDI-OCT. However, these two studies disagreed with regard to the association between the amount of reduction in LC depth and the degree of IOP reduction. To date, the relationship between this newly identified morphological change and clinical parameters associated with glaucoma has yet to be elucidated.
A further advance in ocular imaging has come with swept-source (SS)-OCT, which uses a light source at the 1-μm wavelength region and enables a high-speed scanning rate and low-sensitivity roll-off versus depth compared with SD-OCT. SS-OCT allows high-penetration imaging of the deep fundus structure without multiple B-scan averaging, which is required in EDI-OCT, and its high-speed scanning rate enables acquisition of thin sliced images of the deep tissue comprised of 256 × 256 A-scans in only 0.8 seconds. It has recently been applied to the visualization of choroid, sclera, ONH structure, and peripapillary structure in vivo, and we think that this technique potentially enables detailed description and analysis of the deep optic disc structures, which was fully examined in glaucomatous monkey eyes through the analysis of histomorphological change of laminar and prelaminar tissue change by Yang et al. also in vivo.

The purpose of this study was to visualize changes in the deep ONH structures of glaucomatous eyes following glaucoma surgery using thin-sliced SS-OCT imaging, and to determine the clinical factors that are associated with postoperative structural changes of the eye.

**METHODS**

This prospective observational study was approved by the Institutional Review Board and Ethics Committee of Kyoto University Graduate School of Medicine and adhered to the tenets of the Declaration of Helsinki. According to the guidelines, we obtained written informed consent from all patients for a prospective study.

**Participants**

For this study, 83 Japanese adults with glaucoma who underwent glaucoma surgery at Kyoto University Hospital between June 1, 2010, and August 30, 2012 were recruited. All patients underwent a comprehensive ophthalmologic examination, including measurement of best-corrected visual acuity with the 5-m Landolt chart, slit-lamp biomicroscopy, gonioscopy, Goldman applanation tonometry, dilated stereoscopic examination of the ONH and fundus, stereo disc photography (3-Dx simultaneous stereo disc camera; Nidek, Gamagori, Japan); axial length measurement using ocular biometry (IOLMaster; Carl Zeiss Meditec, Dublin, CA); and achromatic threshold algorithm standard program (Humphrey Visual Field Analyzer; Carl Zeiss Meditec, Inc., Dublin, CA). Optic nerve head 3D imaging was performed before and 3 months after the surgery.

Patients who underwent glaucoma surgery to treat open angle glaucoma and secondary glaucoma including steroid-induced glaucoma and exfoliation glaucoma were included. Eyes with opaque media, poor OCT image quality, previous glaucoma surgery, or other ocular diseases that could affect the visual field results were excluded from this study. Eyes that underwent additional glaucoma surgery within 3 months were excluded.

**1050-nm Swept-Source Optical Coherence Tomography System**

For thin-sliced imaging of the ONH, we used a prototype SS-OCT system originally developed by Topcon Corp. (Tokyo, Japan). This OCT system has an axial scan rate of 100,000 Hz and was operated as reported previously. The current prototype SS-OCT system used a wavelength sweeping laser with a tuning range of approximately 100 nm centered at 1050 nm, yielding 8-μm axial resolution in tissue. Transverse resolution was set to approximately 20 μm. A single B-scan OCT image consisting of 1000 A lines can be acquired in 10-ms SS-OCT imaging at 1050 nm was conducted at ~1 mW on the cornea, which is well below the safe retinal exposure limit established by the American National Standards Institute. Sensitivity was measured at ~98 dB at this input power.

Swept-source optical coherence tomography examinations were performed by trained examiners after pupil dilation. Thin-sliced imaging data sets were acquired for each eye using three-dimensional scan mode of a raster scan protocol of 256 × 256 A-scans per data set (total 65,536 axial scans/volume) in 0.8 seconds. The scanning laser light source at 1050 nm is invisible, which prevent eye movement in response to the scanning light.

**1050-nm Swept-Source Optical Coherence Tomography Measurements**

The optic disc structures in SS-OCT images were measured using custom-built software produced by Topcon. In this software, a magnification effect on the lateral length measurement was corrected based on modified Littman’s formula using the eye’s refractive error, corneal radius, and axial length. To improve the signal-to-noise ratio, each image was despckled by the weighted moving average of three consecutive original B-scans as previously reported. On this despckled image, we performed two different methods for measuring optic disc parameters. First, we manually delineated Bruch’s membrane opening (BMO) and anterior LC boundary in one of every four B-scans of the 3 × 3-mm dataset comprised of 256 B-scans (64 B-scans per eye). Lamina cribrosa depth was defined as the perpendicular distance from the BMO reference line to the anterior LC boundary as shown in Figure 1. Maximum LC depth was automatically calculated in each B-scan and the scan image with maximum LC depth was automatically selected from all delineated images using this software. This point, set as the reference measurement point, was marked with an axial green line on the three-dimensional and en face images (Fig. 1). We selected four additional points for measurement, which were located 100 μm apart vertically and horizontally from the reference point. Then we delineated prelaminar tissue surface in the B-scans containing these five points manually, and calculated LC depth and prelaminar tissue thickness on these five points using this software. The optic disc measurements on the five points were averaged to obtain optic disc parameters for analysis. Second, we also delineated BMO and anterior LC boundary in 15 equally spaced horizontal B-scans in BMO area excluding both ends of BMO (interval between scans = 96–120 μm). The point with maximum LC depth was determined and LC depth and PLT thickness at this point was calculated in each of 15 B-scans automatically using this software. After performing these two measuring methods, we calculated the percent change in LC depth before and after the surgery and tested for statistical analysis between the other ocular parameters. Additionally, we classified 73 patients into three groups according to the percent degree of IOP reduction (<15%, 15% ~ 30%, and >30%) and calculated the number of patients who showed significant decrease in LC depth to examined the ability to detect eye-specific postsurgical change of LC depth.

**Interobserver and Intraobserver Reproducibility**

To evaluate the interobserver reproducibility of our measuring method, 15 randomly selected imaging data sets were acquired through 3D scan mode independently evaluated by two authors (MY and TA) blinded to clinical information, and the
intraclass correlation coefficients (ICC [2, 1]) were calculated for LC depth and prelaminar tissue (PLT) thickness. To evaluate the intraobserver reproducibility and variability in SS-OCT measurements, the same datasets were evaluated in triplicate by one author (MY) to calculate ICC (1, 1) and coefficient of variation (CV). According to Fleiss, ICCs ≥ 0.75, between 0.40 and 0.75, and ≤ 0.4 were defined as excellent, moderate, and poor, respectively.

Statistical Analysis

All statistical evaluations were performed using commercially available software (SPSS version 20; International Business Machines Corp., Armonk, NY). Paired t-test was used to compare quantitative data populations with normal distributions and equal variance. Data were analyzed using Wilcoxon signed-rank test for populations with nonnormal distributions or unequal variance. To determine the ocular parameters associated with IOP reduction and the change of parameters such as LC depth and axial length, Pearson's correlation coefficient and multiple logistic regression analysis were used. Multiple logistic regression model was used to correlate age, percent IOP reduction, baseline LC depth, axial length, and visual field mean deviation (MD) with the percent change in LC depth and axial length and to correlate percent IOP reduction. P values of <0.05 were considered statistically significant; the data are presented as the mean ± standard deviation.

RESULTS

Eighty-three eyes of 83 patients (38 male and 45 female) with glaucoma were included in the study. Among these, SS-OCT thin-sliced imaging from seven eyes were not of sufficient quality to be analyzed, two eyes required additional surgery within 3 postoperative months (one needling and one bleb revision), and one patient (one eye) ceased to attend our hospital. Finally, 73 eyes (43 eyes with POAG, 38 with high-tension glaucoma [HTG], and one with normal-tension glaucoma [NTG]; and 30 eyes with secondary glaucoma, 5 with steroid-induced glaucoma, 15 with exfoliation glaucoma, and 10 with other forms) of 73 patients (33 male and 40 female) who underwent glaucoma surgery (trabeculectomy in 46 eyes and trabeculotomy in 27 eyes) were examined in this study. Patient characteristics are presented in Table 1. Four eyes showed the IOP lower than 6 mm Hg at 3 months after surgery and two of them showed choroidal detachment. There

FIGURE 1. Illustration of the equally spaced 15 B-scans and determination of five measurement points including a point of maximum lamina cribrosa depth. (A) A color disc photograph showing the scan area (outlined by a red square) for 3D imaging of the optic nerve head with SS-OCT. Green lines showed equally spaced 15 B-scans used in the analysis. (B–D) 3D volume (B) and sectioned volume (C, D) images reconstructed from raster scan dataset of 256 × 256 A-scans covering a 3 × 3-mm area centered on the disc center (red square line). The point with maximum depth of LC is indicated by an axial green line, which is shown in the en face cross-sectional image at the level of the anterior surface of the LC (B), and in the scans passing through the point vertically (C) or horizontally (D) as a green bar. (E, F) A color disc photograph and an en face SS-OCT image showing a single vertical scan line and three horizontal scan lines with a 100-μm interval used for the analysis. These lines are automatically drawn so that the vertical scan and middle horizontal scan pass the point with maximum LC depth (crossing point, red point). The other four measurement points (blue points) are 100 μm from the point with maximum LC depth. (G, H) Vertical and horizontal B-scan images through the point with maximum LC depth, corresponding to each of the above sectioned volumes (C, D), respectively. The termination points of the Bruch’s membrane constituting a Bruch’s membrane opening are indicated by red dots. Yellow and blue dotted lines show the anterior surface and posterior boundary of the LC, respectively. Three lines separated by a 100-μm interval are drawn perpendicular to the white line passing the termination points of the Bruch’s membrane so that the central line passes the point with maximum LC depth. The length of the two lines between the white line and the yellow dotted line indicates the LC depth (red portion of the three lines).
The current study employed a new Fourier-domain OCT technology, SS-OCT, to visualize changes in the 3-dimensional prelaminar and laminar structures. Imaging of the optic disc with this technology successfully visualized the evident changes of optic disc structure after glaucoma surgery, such as the change in LC depth and PLT thickness. The percent change in LC depth measured by SS-OCT significantly correlated with both percent IOP change and visual field defect severity.

Earlier studies have revealed the effects of IOP reduction on ocular dimensions. Axial length decreased following IOP reduction after successful glaucoma filtration surgery. Changes of IOP have been suspected to influence the ocular dimensions following the change in choroidal thickness and scleral stretch or shrinkage. Recently, Lee et al. reported that IOP reduction after trabeculectomy induced significant change in LC depth using EDI-OCT. Consistent with these earlier studies, the current study showed that both shortening of axial length and change in LC depth were induced following IOP reduction after glaucoma surgery. Besides concomitant changes of axial length and LC depth and their significant correlation with percent IOP reduction after glaucoma surgery, the percent change in LC depth correlated significantly with baseline LC depth and visual field MD values, whereas those of axial length did not. Thus, change of LC depth after IOP reduction may not only be a simple response to IOP reduction as part of an ocular globe wall, but also be associated with pathological changes of the LC according to the severity of glaucomatous damage.

The significant correlation of the percent change in LC depth with percent IOP reduction was consistent with an earlier study and is easily understandable because IOP generates direct axial power toward the change in LC depth. By contrast, the correlation between greater percent change in LC depth and worse visual field MD value appears to indicate the greater susceptibility of the LC to IOP changes in eyes with more advanced glaucoma compared to those with milder glaucoma. However, it remains uncertain whether this susceptibility causes progressive glaucomatous damage or results from more severe glaucomatous damage.

### Table 1. Baseline Characteristics of the Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
</tr>
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<tbody>
<tr>
<td>Age, y</td>
<td>65.29 ± 15.23</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>73 (33/40)</td>
</tr>
<tr>
<td>Diagnosis, POAG/secondary</td>
<td>73 (45/30)</td>
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<tr>
<td>Spherical equivalent, diopters</td>
<td>−3.37 ± 4.68</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>24.86 ± 1.84</td>
</tr>
<tr>
<td>Visual field mean deviation, dB</td>
<td>−17.61 ± 8.51</td>
</tr>
<tr>
<td>Surgery, LET/LOT</td>
<td>73 (40/27)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or number. LET, trabeculotomy; LOT, trabeculectomy.

The effects of IOP reduction on the SS-OCT parameters of the optic disc were analyzed by univariate analysis (Table 3). The change of LC depth and PLT thickness were measured at the five locations in the maximum change. The percent change in LC depth and the percent change of axial length correlated significantly with the percent change of IOP. The percent change in LC depth correlated significantly with the percent change of IOP reduction, greater baseline LC depth, and poorer MD value, but not with axial length. The percent change of axial length correlated significantly with the percent change of IOP reduction, poorer MD value, and longer axial length, but not with baseline LC depth.

Stepwise multiple regression analysis was applied to analyze the correlation of the percent change in LC depth and the percent change in axial length to the factors that demonstrated a significant correlation by univariate analysis (Table 3). Greater percent IOP reduction, larger baseline LC depth, and poorer MD value correlated significantly with larger percent reduction in LC depth. Greater percent IOP reduction correlated significantly with larger percent decrease of axial length, but poorer MD value did not.

In equally spaced 15 B-scans, associations of the percent change of mean LC depth to age, preoperative IOP, the percent change in IOP, AL, MD value, and baseline mean LC depth were also analyzed by univariate analysis. Age, preoperative IOP, and AL showed no correlation to the percent change in mean LC depth, and that of other factors were shown in Supplementary Table S1. Multivariate analysis were applied to the factors that showed $P$ value of lower than 0.10 by univariate analysis.

Figure 2 is a representative image of a glaucomatous eye with an advanced stage of visual field loss. The change in LC depth following 65.0% of IOP reduction was evident in this eye. By contrast, a glaucomatous eye with an early stage of visual field loss is shown in Figure 3, which did not show apparent change in LC depth regardless of 38.1% IOP reduction after glaucoma surgery.

Mean LC depth changes and regional variance of 15 equally spaced horizontal B-scans were illustrated in Figure 4. The correlation between the percent change of mean LC depth and age, preoperative IOP, the percent change of IOP, AL, MD value, and baseline LC depth were analyzed by univariate (Pearson’s rank correlation coefficient) and multivariate analysis (Supple-

### Table 2. Comparison of Ocular Parameters Before and After Glaucoma Surgery

<table>
<thead>
<tr>
<th>Ocular Parameter</th>
<th>Preoperation</th>
<th>Postoperation</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP, mm Hg</td>
<td>22.73 ± 8.95</td>
<td>13.42 ± 6.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depth of LC, μm</td>
<td>580.6 ± 152.5</td>
<td>548.4 ± 148.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLT thickness, μm</td>
<td>352.3 ± 180.8</td>
<td>390.5 ± 235.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>24.86 ± 1.84</td>
<td>24.51 ± 1.71</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD.
On the other hand, our finding is not consistent with an earlier study using EDI-OCT, which did not find a significant correlation between the percent change in LC depth and SAP MD. This discrepancy was possibly caused by the difference of the severity of glaucoma; our study subjects had worse SAP MD values (17.80 dB in the current study versus 15.52 dB and 9.61 dB in the earlier studies) and may cause this discrepancy under the assumption that the susceptibility of the LC to IOP changes could not be detectable until glaucoma progression occurred substantially. Earlier studies using histological methods and OCT imaging reported that the LC in glaucomatous eyes with severe visual field defects was significantly thinner than that in normal eyes. By contrast, thinning of the sclera including the peripapillary sclera did not significantly correlate with the presence of glaucoma. Thus, the thickness reduction of an ocular globe wall in glaucomatous eyes is specific to the LC, which is consistent with our results that SAP MD values correlated only with LC depth change, not with AL change. We speculate that compressed LC may not be susceptible to changes in posterior displacement following IOP reduction, while thinned LC due to atrophy at a later stage may be more susceptible.

We also analyzed the percent change in LC depth thoroughly in 15 equally spaced B-scans, which showed that

| TABLE 3. Univariate and Multivariate Analysis of Factors Associated With the Change in LC Depth, AL, and PLT Thickness |
|-----------------|-----------------|-----------------|-----------------|
|                 | Percent Change of LC Depth | Percent Change of AL | Percent Change of PLT Thickness |
|                 | Univariate       | Multivariate    | Univariate       | Multivariate    | Univariate       | Multivariate    |
| Age             | 0.127            | –               | 0.007            | 0.320           | 0.081            | –               |
| Preoperative IOP| 0.997            | –               | 0.971            | –               | 0.989            | –               |
| Percent IOP reduction | 0.006     | −0.325          | <0.001           | −0.459          | 0.002            | −0.375          |
| Baseline PLT thickness | 0.375  | –               | 0.986            | –               | 0.024            | 0.272           |
| Baseline LC depth | 0.025           | −0.269          | 0.728            | –               | 0.768            | –               |
| Axial length    | 0.117            | –               | 0.005            | −0.331          | 0.623            | –               |
| Visual field mean deviation | 0.004  | 0.344           | 0.040            | 0.247           | 0.168            | 0.264           |

Univariate analysis, Pearson’s correlation coefficient. Multivariate analysis, multiple logistic regression analysis. Percent change of LC depth and PLT thickness are measured at the five locations in the maximum change.

On the other hand, our finding is not consistent with an earlier study using EDI-OCT, which did not find a significant correlation between the percent change in LC depth and SAP MD. This discrepancy was possibly caused by the difference of the severity of glaucoma; our study subjects had worse SAP MD values (−17.80 dB in the current study versus −15.52 dB and −9.61 dB in the earlier studies) and may cause this discrepancy under the assumption that the susceptibility of the LC to IOP changes could not be detectable until glaucoma progression occurred substantially. Earlier studies using histological methods and OCT imaging reported that the LC in glaucomatous eyes with severe visual field defects was significantly thinner than that in normal eyes. By contrast, thinning of the sclera including the peripapillary sclera did not significantly correlate with the presence of glaucoma. Thus, the thickness reduction of an ocular globe wall in glaucomatous eyes is specific to the LC, which is consistent with our results that SAP MD values correlated only with LC depth change, not with AL change. We speculate that compressed LC may not be susceptible to changes in posterior displacement following IOP reduction, while thinned LC due to atrophy at a later stage may be more susceptible.

We also analyzed the percent change in LC depth thoroughly in 15 equally spaced B-scans, which showed that

Figure 2. Swept-source optical coherence tomography images of the lamina cribrosa before (A–F) and after (G–L) glaucoma surgery in the right eye of a 23-year-old man with steroid-induced advanced glaucoma. Mean deviation on static automated perimetry was −18.48 dB. Four scan lines to determine measurement points are shown on color disc photographs and en face SS-OCT images in the four left columns. (C, I) Swept-source optical coherence tomography B-scans along the vertical scan line. (D–E, J–L) Swept-source optical coherence tomography B-scans along the top, middle, and bottom horizontal scan lines. Intraocular pressure decreased from 40 mm Hg to 14 mm Hg after trabeculotomy. The LC depth changed from 927 μm to 711 μm. The point of maximum LC depth is indicated by white arrowheads. The termination points of the Bruch’s membrane are indicated by red dots. Yellow dotted line shows the anterior boundary of the LC. Red line indicates LC depth.
FIGURE 3. Swept-source optical coherence tomography images of the lamina cribrosa before (A–F) and after (G–L) glaucoma surgery in the left eye of an 81-year-old woman with pseudo-exfoliation syndrome. Mean deviation on static automated perimetry was −3.54 dB. Four scan lines to determine measurement points are shown on color disc photographs and en face SS-OCT images in the four left columns. (C, I) Swept-source optical coherence tomography B-scans along the vertical scan line. (D–F, J–L) Swept-source optical coherence tomography B-scans along the top, middle, and bottom horizontal scan lines. The point of maximum LC depth is indicated by white arrowheads. Intraocular pressure decreased from 21 mm Hg to 13 mm Hg after trabeculotomy combined with phacoemulsification and intraocular lens implantation. No apparent change was observed between preoperative and postoperative SS-OCT images in this case. The termination points of the Bruch’s membrane are indicated by red dots. Yellow dots indicate anterior boundary of the LC. Red line indicates the LC depth.

FIGURE 4. A line graph showing variation and changes in LC maximum depth in 15 equally spaced horizontal B-scans. Horizontal axis indicates scanning location (numbers 1–15; from upper to lower of Bruch membrane opening) and vertical axis shows LC depth. Error bar shows standard deviation (pre- and postoperation, drawing only one-sided). Lamina cribrosa depth decreased significantly in every 15 scans after the surgery. Results of univariate and multivariate analysis between the percent change in LC depth and the percent change of IOP, MD value, and baseline LC depth were shown in Supplementary Table S1.
the LC changes generally, not locally. However, significant correlations of the percent change of 15 individual LC depth to the percent change of IOP and MD value were limited only to some scans, which suggest significance of scanning ONH generally and thoroughly (data not shown). For glaucomatous nerve fiber layer defects usually show uneven distribution of the severity and have an inclination to start from some restricted areas in upper temporal or lower temporal of ONH, which could be explained by the also uneven susceptibility of LC to IOP change. If the visualization of LC further advanced and the delineation of posterior border of LC became feasible in the thorough area of ONH, advanced studies of correlating LC change, LC susceptibility, and LC thickness to glaucomatous visual field defects in detailed areas would disclose involvement of LC to glaucomatous visual field defects.

In the current study, we did not find a significant correlation between the percent change in LC depth and age, inconsistent with an earlier study, which reported the significant influence of younger age on the magnitude of reduction of LC depth using EDI-OCT. Age and severity of visual field defects can be mutually confounding factors, because progressive visual field defects occur with age. This discrepancy might result from much older age of our study patients (mean: 65.9 years; range: 22–90 years) compared with those of the earlier studies (mean: 52.6 years; range: 15–80 years; and mean: 54.1 years; range: 15–82 years). Furthermore, our study included only adult cases.

During aging, the constituents of these cribiform plates undergo various changes, including increase in the amount of collagen types 1, 3, and 4 and remodeling of extracellular matrix within the cribiform plates. These age-dependent changes are thought to decrease mechanical compliance of the LC, which was shown to occur in human cadaver LC with age, and are consistent with the clinical findings that the reversal of optic disc cupping often occurs after successful glaucoma surgery in children but is rarely observed in adults. Thus, our study results may be less affected by the effects of younger age, in which the LC has a good mechanical compliance and greater susceptibility to IOP changes.

A possible advantage of SS-OCT is the ability to acquire thin-sliced imaging dataset comprised of 256 × 256 A-scans in only 0.8 seconds, which allowed us thorough investigation of the ONH. Baseline LC depth was larger in the upper area than in the lower area of ONH, and change in LC depth also tended to be larger in the upper area. Association of the percent change in LC depth in each 15 B-scans with the percent reduction of IOP and visual field MD value were significant in the upper area of ONH, especially the area which showed larger LC depth change after operation, but did not meet statistical significance in the lower area of ONH by multivariate analysis. There was no correspondence between the area of maximum LC depth and the area of visual field defect, as was consistent with the previous reports.

**Study Limitations**

Our study has some limitations. First, the postoperative period was established at 3 months. Reduction of LC depth and thickening of LC and PLT have been demonstrated to occur largely before 3 postoperative months. Thus, we believe that evaluation of the LC change at postoperative month 3 may be sufficient if postoperative IOP is stable. Second, several types of glaucoma, such as HTG, NTG, and secondary glaucoma, were included in this study. Possibly, LC response to IOP reduction differs in these various types of glaucoma. The LC has been reported as thinner in NTG eyes than HTG eyes, and different pathophysiologic mechanisms may be involved in NTG and HTG. Further studies on a larger scale might answer this question.

Third, we used only two measuring methods concerning LC depth; maximal LC depth with surrounding four points and mean LC depth of 15 equally spaced B-scans. Although there are no established methods concerning which LC depth to be selected as a parameter for analysis, there may be a better way to represent detail of the change of LC depth. Further investigation for detection of the change of LC depth should be needed.

In conclusion, we demonstrated that thin-sliced imaging with SS-OCT technology allows clear visualization and measurement of the change of posterior displacement and prelaminar tissue after successful glaucoma surgery. Percent changes in both LC depth and axial length after glaucoma surgery were associated with percent change of IOP. However, only percent change in LC depth was associated with baseline value (LC depth) and visual field MD. Thus, the change of LC appears to have important correlation with IOP and the severity of glaucomatous optic neuropathy. Longitudinal studies are needed to determine whether greater reduction of LC depth is associated with a lower risk for glaucoma progression.

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**References**

Optic Disc Cupping After Glaucoma Surgery


