Changes in Choroidal Thickness After Trabeculectomy in Primary Angle Closure Glaucoma

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PURPOSE. The purpose of this study was to evaluate changes in choroidal thickness (CT) in advanced or late-stage primary angle closure glaucoma (PACG) patients who had undergone trabeculectomy.

METHODS. This study included 23 eyes with PACG that required trabeculectomy. Enhanced depth imaging optical coherence tomography was used to measure CT before and 7 days after trabeculectomy. The relationships between changes in CT and changes in IOP and axial length were explored.

RESULTS. At all nine macular locations, CT was significantly higher after trabeculectomy, with the exception of two sites. CT at locations close to the macula exhibited a greater increase after surgery (except for the inferior location), although there were no significant differences compared to locations farther from the macula. The mean CTs (±SD) under the fovea before and after the surgery were 282.3 (±42.4) μm and 311.6 (±59.9) μm, respectively. The mean IOP (±SD) decreased from 25.9 (±11.0) mm Hg to 11.8 (±3.2) mm Hg (without antiglaucoma medications), which positively related to the shortened axial length after surgery (P = 0.019). However, the changes in CT were not correlated with either IOP or axial length.

CONCLUSIONS. Short-term CT increased following trabeculectomy in PACG, but it was not related to decreased IOP or shortened axial length. The potential role for and significance of CT increase after trabeculectomy remains to be interpreted.

Keywords: axial length, choroidal thickness, intraocular pressure, trabeculectomy

Primary angle closure glaucoma (PACG) is a widespread form of glaucoma in Asia, especially in China. It is estimated that there will be more than 10 million PACG patients in China in 2020.1 Previous studies have demonstrated that ocular biometric parameters such as shallow anterior chamber depth (ACD), short axial length (AL), and increased lens thickness (LT) are strong risk factors for PACG.2–4 Quigley et al.5 put forward a hypothesis that choroidal expansion might play an important role in PACG. Due to advances in ophthalmic imaging equipment, such as spectral-domain optical coherence tomography (OCT) with enhanced depth imaging (EDI-OCT), which noninvasively measures choroidal thickness (CT) in the posterior globe,6,7 increasing attention has been paid to CT as an important risk factor in the pathophysiology of PACG.8,9 Our previous studies have already indicated that CT in eyes with acute primary angle closure was higher than in fellow eyes diagnosed with suspected primary angle closure and that CT in both acute primary angle closure and suspected primary angle closure eyes was higher than in normal control eyes.10,11

Trabeculectomy is an effective way to decrease IOP in PACG patients, and it can also efficiently prevent progressive optic disc damage and visual field loss.12 Ocular changes, such as decreases in AL and ACD, and improvement of ocular blood flow have been observed in open-angle glaucoma patients after trabeculectomy.13–15 However, little is known about the effects of trabeculectomy on the ocular biometric parameters of PACG patients. This study explored the changes in CT, AL, and IOP following trabeculectomy as well as their relationships using EDI-OCT.

PATIENTS AND METHODS

Subjects and Enrollment Criteria

This prospective, comparative study was approved by the Ethical Review Committee of Zhongshan Ophthalmic Center, and it adhered to the provisions of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all participants involved in the study. All subjects were from a Chinese Han population, and all participants were patients at the Zhongshan Ophthalmic Center.

The study included 23 eyes of 17 PACG patients with vision sufficient to allow fixation on the eye examination. All enrolled patients met the following strict criteria: (1) PACG diagnostic criteria met; (2) advanced or late stage of the disease; (3) uncontrolled IOP after standardized maximum antiglaucoma medications and trabeculectomy required to prevent progressive glaucomatous optic neuropathy; (4) no complications after surgery and IOP reduction after trabeculectomy higher than 25% compared to baseline and postoperative IOP no lower than...
Asymmetry between fellow eyes of eyes with glaucomatous optic neuropathy (vertical cup-disc > raised IOP (defined as IOP > 21 mm Hg) and 21 mm Hg without the need of glaucoma medication postoperative IOP was reduced to the range between 5 mm Hg; and (5) with or without mild cataract to allow for clear EDI-OCT pictures. Patients with any of the following criteria were excluded: primary open-angle glaucoma (POAG), secondary glaucoma (such as lens subluxation, uveitis, iris neovascularization, trauma, tumor, or any obvious cataract leading to an intumescent lens), diabetes or systemic hypertension, a history of intraocular surgery, or inability to tolerate gonioscopy or an ultrasonographic biomicroscopy examination. Other exclusion criteria included high myopia or hyperopia (greater than +6 or –6 diopters [D] of the spherical equivalent refractive error), any retinal or retinal pigment epithelium detachment, any retinal abnormalities (such as chorial neovascularization, asymptomatic pigment epithelial detachment, or whitish myopic atrophy), clinically relevant opacities of the optic media, and low-quality images due to unstable fixation or a severe cataract.

In this study, PACG was diagnosed in eyes with narrow angles (eyes in which the posterior trabecular meshwork was not seen for at least 180° on indentation gonioscopy in the primary position) with peripheral anterior synechiae and/or raised IOP (defined as IOP > 21 mm Hg). Also included were eyes with glaucomatous optic neuropathy (vertical cup-disc asymmetry between fellow eyes of >0.2, a cup-to-disc ratio of >0.6, and neuroretinal rim narrowing, notches, or localized pallor), and with compatible visual field loss on static automated perimetry Swedish Interactive Threshold Algorithm (SITA) standard with a 24-2 test pattern [Humphrey visual field analyzer II; Carl Zeiss Meditec, Dublin, CA, USA]). This was defined as a glaucoma hemifield test outside normal limits, having an abnormal pattern and a P value SD of ≤5% in the normal population and fulfilling test reliability criteria (fixation losses < 20%, false positives < 15%, and/or false negatives < 15%).

All patients underwent standard trabeculectomy performed by one glaucoma surgery specialist (XZ). Seven days after trabeculectomy, patients without early complications including shallow or flat anterior chamber, hyphema, choroidal detachment, wound leakage, acute endophthalmitis, suprachoroidal hemorrhage, vitreous hemorrhage, cystoid macular edema, hypotony, or transient elevation of IOP and in whom postoperative IOP was reduced to the range between 5 mm Hg and 21 mm Hg without the need of glaucoma medication were enrolled. Before surgery and 7 days after the surgery, the patients underwent an EDI-OCT examination. To limit any potential change in choroidal structure by antiglaucoma eye drops, no medications (especially pilocarpine to constrict the pupil) were administered to the eyes that underwent the EDI-OCT examination. The adjunctive antiglaucoma medication therapy for the PACG eyes before surgery included topical β-blocker (timolol 0.5%) twice daily and/or brimonidine (Azopt; Alcon Laboratories, Elkridge, MD, USA), and/or topical 0-2 agonists (Alphagan; Allergan, Inc., Irvine, CA, USA); and/or prostaglandin analog, once daily (lutanoprost [Xalatan]; Pfizer, Inc., NY, USA); oral acetazolamide, 250 mg three times daily; oral isosorbide, 50 g twice daily; and intravenous mannitol 20%, at 1 to 2 g/kg of body weight if necessary. The number of medications was counted.

Examination and Study Measurements
All subjects’ eyes underwent a thorough ophthalmic evaluation, including slit-lamp biomicroscopy, IOP measurement (applanation tonometry), gonioscopy, fundus examination, ultrasonographic biomicroscopy, and B-scanning. They also underwent a refractive error examination with an autorefractometer (KR-8900 version 1.07; Topcon Corp, Tokyo, Japan), and AL measurements with partial optical coherence interferometry (IOLMaster; Carl Zeiss Meditec) were taken. The ACD (distance from the posterior corneal surface to the anterior crystalline lens surface), LT (distance from the anterior to the posterior lens surfaces), and vitreous chamber depth (VCD; distance from the posterior lens surface to the inner limiting membrane) were measured by A-mode ultrasonography (Cinescan; Quantel Medical, Clermont-Ferrand, France). Demographic data, such as age, sex, and blood pressure were collected. All examinations were also performed before and 7 days after surgery.

EDI-OCT Examination
Choroidal thickness was detected using the Spectralis device (Heidelberg Engineering, Heidelberg, Germany), as previously reported.10,11 Choroidal imaging was averaged over 100 scans, using the device’s automatic averaging and eye-tracking

**Figure 1.** Macula choroidal thickness was measured by EDI-OCT. Subfoveal choroidal thickness, and 1 mm and 3 mm superior (S) and inferior (I) to the fovea were measured vertically, and 1 mm and 3 mm nasal (N) and temporal (T) to the fovea were measured horizontally from the outer border of the retinal pigment epithelium to the inner border of the sclera.
features. Two images (horizontal and vertical sections) were scanned using a single, 30° linear scan centered on the fovea (number of A scans/number of B scans = 1536; scan angle = 30°; scan length = 9 mm). The automatic real-time (100 frames) averaging mode was used to ensure good quality images. Image quality was judged on signal-to-noise ratio, and only scans with signal-to-noise ratios ≥ 20 dB were saved and considered for analysis. The resultant images were viewed and measured using the standard Spectralis OCT measuring software (version 1.5.12.0; Heidelberg Engineering). The choroid was measured from the outer portion of the hyper-reflective line that corresponded to the retinal pigment epithelium to the inner surface of the sclera (Fig. 1). Choroidal thickness was measured at the fovea and at 1 and 5 mm superior, inferior, nasal, and temporal from the fovea in all subjects. When using the Spectralis OCT for the EDI-OCT technique, no additional hardware or software was required, and the resultant images were viewed and measured with Eye Explorer software, version 1.5.12.0 (Heidelberg Engineering). Keratometry readings and the most recent refraction were entered into the software program to estimate optical magnification and therefore to allow for more accurate comparisons across individuals. A single experienced ophthalmologist, blinded to the clinical diagnoses of the patients, performed the EDI-OCT examinations (always at approximately 10 AM). The choroid was measured by two independent graders who were blinded to the diagnosis. If the differences in thickness measurements of the two examiners exceeded 15% of the mean of the two values, there was open adjudication with the senior author, and then the measurements were averaged for analysis.

Statistical Analysis
Data were analyzed using SPSS for Windows XP version 17.0 (SPSS, Chicago, IL, USA; Microsoft, Redmond, WA, USA). Before analysis, we used SPSS software (for the Shapiro-Wilk test) to test the normality of all data, and all variables were normally distributed. We used the “general linear model” to detect the change of overall choroid thickness. For the change of particular site of choroid thickness after surgery, a paired t-test was used. Pearson’s correlation analysis was performed to evaluate the relationships between the changes in CT and in AL and IOP at imaging after surgery. For other tests, a P value of <0.05 was considered significant.

RESULTS
Clinical Measurements Before and After Surgery
This study included 25 eyes of 19 subjects who required trabeculectomy to decrease their IOP; however, two cases had poor OCT image quality, so actually 23 eyes of 17 subjects were enrolled in the analysis. The mean age (±SD) of the enrolled patients was 53.4 (±7.1) years of age. The mean IOP (±SD) was 25.9 (±11.0) mm Hg before surgery (with 5.0 [1.2] kinds of antiglaucoma drugs) to 11.8 (±3.2) mm Hg (without antiglaucoma drugs) after surgery (P < 0.001; Table 1). The mean AL (±SD) decreased from 22.5 (±0.7) mm at the baseline to 22.4 (±0.6) mm after surgery (Table 1). The decrease in IOP was positively related to the change in AL after surgery according to Pearson’s correlation coefficient (0.487; P = 0.019; Fig. 2). There were no significant changes in ACD, LT, or VCD after surgery (Table 1).

Choroidal Thickness Changes in the Macular Region
The mean macular CT was greatest at the subfovea both before and after surgery, and it decreased away from the fovea at vertical and horizontal orientations (except at 3 mm superiorly from the fovea; Table 2), which was consistent with our previous finding.10,11 After the surgery, when we used the “general linear model” to consider the effect of trabeculectomy to the change of the CT, trabeculectomy contributed significantly to the overall increase in CT (P < 0.001). However, when we considered the effect of trabeculectomy on particular regions of CT, CT was significantly greater at seven locations around the fovea (Table 2; Figs. 3A, 3B), and the P values for the site at 3 mm from the fovea superiorly and temporally were above 0.05 and did not reach statistical significance. However, the degree of CT increase was higher at

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Before</th>
<th>After</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP, mm Hg</td>
<td>25.9</td>
<td>11.8</td>
<td>14.1</td>
</tr>
<tr>
<td>AL, mm</td>
<td>22.5</td>
<td>22.4</td>
<td>0.1</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>2.4</td>
<td>2.4</td>
<td>-0.0</td>
</tr>
<tr>
<td>LT, mm</td>
<td>5.0</td>
<td>4.8</td>
<td>0.2</td>
</tr>
<tr>
<td>VCD, mm</td>
<td>15.2</td>
<td>15.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

- Data are expressed as means ± SD. ACD, anterior chamber depth; AL, axial length; CI, confidence interval; LT, lens thickness; VCD, vitreous chamber depth
- *P values in boldface indicate P < 0.05, and considered significant.

FIGURE 2. Decreases in IOP were correlated positively with shortening of the axial length after trabeculectomy. Pearson’s correlation coefficient is 0.487 and P = 0.019.
locations close to the fovea, except for the inferior location, although all \( P \) values were above 0.05 (Table 2; Fig. 4).

**Relationships Among CT, AL, and IOP**

In order to explore the cause of the increased CT after surgery, we analyzed the correlations among changes in CT and the changes in IOP and AL. At all locations around the macula, there were no significant relationships between CT and IOP (all \( P > 0.05 \)) or between CT and AL (all \( P > 0.05 \)). We also calculated the mean CT at 1 and 3 mm for each study eye and analyzed the correlation between global CT at 1 mm versus IOP and AL. However, there were no significant differences (all \( P > 0.05 \)).

**DISCUSSION**

Our study found that short-term CT increased in advanced and late-stage PACG following trabeculectomy and that trabeculectomy also caused decreased IOP and AL. Trabeculectomy had no effect on other ocular biometric parameters, such as ACD, LT, and VCD. The IOP decrease following trabeculectomy was related to AL reduction. However, there were no relationships between the changes in CT and the changes in IOP or AL.

### Table 2. Choroid Thickness Before and After Surgery (\( n = 23 \))

<table>
<thead>
<tr>
<th>Location</th>
<th>Before</th>
<th>SD</th>
<th>After</th>
<th>SD</th>
<th>Difference</th>
<th>Mean 95% CI</th>
<th>( P^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFCT</td>
<td>282.3</td>
<td>42.4</td>
<td>311.6</td>
<td>59.9</td>
<td>-29.2</td>
<td>(-52.2 to 6.3)</td>
<td>0.015</td>
</tr>
<tr>
<td>S, 1 mm</td>
<td>223.4</td>
<td>70.9</td>
<td>258.2</td>
<td>66.7</td>
<td>-34.8</td>
<td>(-59.0 to 10.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>S, 3 mm</td>
<td>247.4</td>
<td>54.1</td>
<td>260.5</td>
<td>64.2</td>
<td>-13.0</td>
<td>(-34.0 to 8.0)</td>
<td>0.211</td>
</tr>
<tr>
<td>I, 1 mm</td>
<td>258.1</td>
<td>58.8</td>
<td>278.5</td>
<td>48.9</td>
<td>-20.4</td>
<td>(-39.8 to -1.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>I, 3 mm</td>
<td>210.3</td>
<td>49.3</td>
<td>253.8</td>
<td>62.4</td>
<td>-43.5</td>
<td>(-62.8 to 24.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>N, 1 mm</td>
<td>232.4</td>
<td>55.8</td>
<td>265.1</td>
<td>74.8</td>
<td>-32.7</td>
<td>(-54.5 to 10.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>N, 3 mm</td>
<td>215.7</td>
<td>77.8</td>
<td>233.7</td>
<td>90.7</td>
<td>-18.0</td>
<td>(-35.7 to 0.3)</td>
<td>0.046</td>
</tr>
<tr>
<td>T, 1 mm</td>
<td>245.9</td>
<td>53.1</td>
<td>280.3</td>
<td>58.1</td>
<td>-34.4</td>
<td>(-55.9 to 12.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>T, 3 mm</td>
<td>244.4</td>
<td>52.8</td>
<td>257.3</td>
<td>69</td>
<td>-12.9</td>
<td>(-34.9 to 9.2)</td>
<td>0.239</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD. CI, confidence interval; I, inferior; N, nasal; S, superior; SFCT, subfoveal choroidal thickness; T, temporal. * \( P \) values in boldface indicate \( P < 0.05 \), and considered significant.

![Figure 3](https:// iovs.arvojournals.org/doi/abs/10.1167/iovs.14-14686)

**FIGURE 3.** Changes in choroidal thickness before and after surgery. (A) Change of choroidal thickness at the subfoveal, 1 mm and 3 mm nasal (N) and temporal (T) to the fovea. (B) Change of choroidal thickness at the subfoveal, 1 mm and 3 mm superior (S) and inferior (I) to the fovea. * \( P < 0.05 \); ** \( P < 0.01 \); *** \( P < 0.001 \).
Changes in Choroidal Thickness After Trabeculectomy

The finding that IOP decreased after trabeculectomy and caused a reduction in AL was consistent with that in other studies.\(^{16,17}\) Leydolt et al.\(^{18}\) investigated the effects of a short-term mechanical IOP change on ocular biometrics, including the AL, and found that changes in AL correlated with changes in IOP; an IOP reduction of 5.1 mm Hg caused a significant AL shortening of 7 µm. Using A-scan biometry, another study found that AL decreased in 32 of 62 eyes after successful initial trabeculectomy.\(^{13}\) In our study, we used partial optical coherence interferometry to measure AL, and we found that a decrease in IOP was positively related to a reduction in AL after trabeculectomy, although the exact mechanism for this change remains unknown. We hypothesize that this is like gas in a balloon: Decreased pressure results in a smaller size.

An abnormal increase in CT has been hypothesized to be a contributing feature in primary angle closure.\(^{5}\) In previous studies, CT has been associated with many factors, such as older age, AL, and IOP; however, the degree of glaucoma damage has not been consistently associated with CT.\(^{7,19,20}\) There is some controversy regarding the effect of trabeculectomy on CT. Kara et al.\(^{17}\) reported that a large decrease in IOP after trabeculectomy could cause choroidal thickening and that CT changes are associated with AL reduction in POAG. However, Usui et al.\(^{21}\) reported that 6 days after trabeculectomy, the choroid was thicker, the axial length was shorter, and the IOP was lower, but the change in IOP was not correlated with the change in CT at the fovea in POAG. In our study, CT was not related to AL or IOP after trabeculectomy in PACG patients; those results are consistent with the findings of other studies.\(^{21}\) There might be some explanations for the inconsistencies between our findings and those of Kara et al.\(^{17}\) First, the patients in their study all had POAG, which has a totally different pathogenesis than PACG. Another reason for the difference may be the sample size, which was bigger than ours; the study by Kara et al.\(^{17}\) included 39 eyes from 39 patients. In addition, CT was measured 1 month after surgery, which was longer than in our study. This difference might explain why CT did not increase significantly according to the decreasing IOP in the early stages following trabeculectomy, and the expansion time of the choroid may also be different between PACG and POAG. Finally, the decrease in IOP after trabeculectomy may not directly cause the expansion of the choroid, rather, it may have increased the ocular blood flow to the choroid and changed the uveoscleral outflow, which in turn caused the thickening of the choroid.

Potential limitations of our study should be mentioned. First, we measured only the change in CT that occurred 7 days postoperatively; how CT changes after a longer period of time remains unknown. In future studies, time-dependent research might be required in order to investigate changes in CT after trabeculectomy. Moreover, whereas manual CT measurement is one of the principal drawbacks of this study; until now, no OCT equipment could provide the software for automated measurement. Finally, when considering a relatively small sample size, strict inclusion criteria for patients should be taken into account.

In conclusion, the present study found that trabeculectomy might cause an increase in CT in advanced and late-stage PACG. Our results indicated that there were no significant correlations between increased CT and decreased IOP or reduced AL. However, decreased IOP following trabeculectomy was related to reduced AL. The potential role of trabeculectomy in increased CT and the effect of this change remain to be investigated.

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References