Trabeculectomy Bleb Assessment via Three-dimensional Anterior Segment Optical Coherence Tomography

Takahiro Kawaji*, Toshihiro Inoue, Riyo Matsumura, Utako Kuroda, Kei-Ichi Nakashima and Hidenobu Tanihara
Department of Ophthalmology, Kumamoto University, Japan

INTRODUCTION

Trabeculectomy is the surgical treatment most often used for patients with medically uncontrolled glaucoma [1]. Because of fundamental difficulties with trabeculectomy, changes in the procedure have attempted to improve it since its introduction. These changes include using releasable sutures [2] and laser suture lysis [3]; using antifibrosis agents [4-5]; and shifting, by some surgeons, from utilizing Limbus-Based Conjunctival Flaps (LBCF) to Fornix-Based Conjunctival Flaps (FBCF) [6,7].

Many clinical investigators have shown that the existence of filtration blebs is correlated with intraocular pressure (IOP) values after trabeculectomy [8-18]. To evaluate bleb morphology, some grading methods have included slit-lamp examinations and color photography [8,9], ultrasound biomicroscopy [10], confocal microscopy [11], conventional retinal Optical Coherence Tomography (OCT) [12], time-domain Anterior Segment OCT (AS-OCT) [13-16], and three-dimensional (3D) AS-OCT [17,18].

The recent development of AS-OCT, particularly 3D AS-OCT, has enabled us to obtain more precise information on internal bleb morphology in a noninvasive and safe manner. We need to identify a complete scleral flap in the C-scan image (tomographic image of the slice plane perpendicular to the depth direction) to evaluate a precise internal bleb structure. However, it was relatively easy for us to identify the complete scleral flap when the flap was created at the uppermost region, but not in the temporal (or nasal) scleral flaps, because the C-scan image plane does not always agree with the scleral plane. Therefore, we developed new custom software for rotation of the data that we obtained. The software allowed us to approve arbitrary cross-section images from the restructured 3D data, and thereby we could identify the complete scleral flap.
custom software, we have recently found that, in most cases with functional filtration blebs, filtration openings can be identified as pits and/or troughs in fluid-filled cavities in both horizontal and vertical raster and corresponding C-scan images of scleral flap margin in the blebs [19].

Thus, this 3D technique allows more precise evaluation of internal structures of the filtration blebs than currently in use. This study aimed, therefore, to investigate the morphological features of filtering blebs after trabeculectomy and to assess the relationship between Intraocular Pressure (IOP) and the quantitative bleb parameters by means of 3D AS-OCT and custom software.

METHODS

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board and Ethics Committee of the Faculty of Life Sciences of Kumamoto University. Informed consent was obtained from all patients included in the study.

We retrospectively examined 47 glaucomatous eyes of 47 patients who underwent trabeculectomy with mitomycin C at Kumamoto University Hospital. All patients were Asians; the 26 men and 21 women had an age range from 46 to 90 years (mean ± Standard Deviation [SD], 71.3 ± 11.2 years). The diagnoses included primary open-angle glaucoma in 21 eyes and pseudoexfoliation glaucoma in 26 eyes. All eyes had had trabeculectomy with the intraoperative use of topical 0.04% mitomycin C for 4 minutes. LBCF was used in 12 eyes and FBCF was used in 35 eyes. All IOP measurements were obtained via Goldman applanation tonometry before the surgery and at the time of 3D AS-OCT imaging.

We utilized 3D AS-OCT (Casia; Tomey, Nagoya, Japan) to assess internal bleb structures. Patients were asked to look down, and an examiner used a finger to gently elevate the upper lid to expose the filtration bleb. For each bleb, at least two ways of scans were obtained as horizontal and vertical raster, and each raster consisted of 512 scans. Each bleb was scanned at least twice, and the examined area was chosen to include the entire scleral flap and bleb. We analyzed the OCT images that we obtained quantitatively with our newly developed software. This software, by which we could rotate and tilt the 3D images, allowed us to easily evaluate, in minute detail, the internal bleb structure of 3D and en face images of the scleral flap (Figure 1) and drainage route, and to quantify the intensity of the bleb structures.

We measured the total bleb height, fluid-filled cavity height, bleb wall thickness, and intensity of the bleb wall. We defined the total bleb height as the maximum distance between the conjunctival surface and the surface of the scleral flap. We defined the fluid-filled cavity height as the maximum height of the region of significantly low-reflective fluid-filled space adjacent to the scleral flap. We measured the bleb wall thickness and intensity of the bleb wall above the internal fluid-filled cavity. At least 3 different reviewers evaluated complete images of the internal bleb structure and assessed the 3D AS-OCT images.

Statistical analyses were performed with JMP, Version 7 (SAS Institute Inc., Cary, NC). The Mann-Whitney U test and Spearman correlation coefficients were used for analyses. A P value of less than .05 was considered to be statistically significant.

RESULTS

Table 1 summarizes the demographics and baseline characteristics of the patients. The mean (±SD) duration between trabeculectomy and 3D AS-OCT imaging was 9.5 ± 6.2 months. The mean (±SD) IOP was 14.0 ± 4.3 mmHg at the time of OCT imaging.

Figure 2 shows a representative photograph and 3D AS-OCT images, and Figure 3 presents the correlation between the IOP and the quantitative bleb parameters. The IOP showed a significant negative correlation with the bleb height (Spearman correlation coefficient [r] = -0.609, P = < .0001), the fluid-filled cavity height (r = -0.381, P = 0.009), the bleb wall thickness (r = -0.503, P = 0.0004) and a significant positive correlation with the intensity of the bleb wall (r = 0.612, P = < .0001).

We also compared, via 3D AS-OCT, bleb morphologic features after trabeculectomy with the 2 different conjunctival incisions—FBCF and LBCF. The basic characteristics of the FBCF and LBCF groups showed no significant differences. Table 2 shows the results of bleb measurements. Compared with the FBCF group,

Table 1: Demographics and Baseline Characteristics of the patients.

<table>
<thead>
<tr>
<th>Patients and Characteristics</th>
<th>Total</th>
<th>FBCF</th>
<th>LBCF</th>
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<tbody>
<tr>
<td>Patients, number</td>
<td>47</td>
<td>35</td>
<td>12</td>
</tr>
<tr>
<td>Sex, M/F, number</td>
<td>26/21</td>
<td>19/16</td>
<td>7/5</td>
</tr>
<tr>
<td>Age, years</td>
<td>71.3 ± 11.2 (46–90)</td>
<td>71.2 ± 11.7 (46–90)</td>
<td>71.9 ± 9.1 (56–84)</td>
</tr>
<tr>
<td>Duration between trabeculectomy and 3D AS-OCT, months</td>
<td>9.5 ± 6.2 (4–25.1)</td>
<td>9.6 ± 5.5 (4–20.1)</td>
<td>8.9 ± 8.1 (4–25.1)</td>
</tr>
<tr>
<td>IOP at imaging, mm Hg</td>
<td>14.0 ± 4.3 (4–23)</td>
<td>14.1 ± 3.7 (6–23)</td>
<td>12.1 ± 4.6 (4–18)</td>
</tr>
</tbody>
</table>

Abbreviations: LBCF: Limbus-Based Conjunctival Flap; FBCF: Fornix-Based Conjunctival Flap; 3D AS-OCT: Three-dimensional Anterior Segment Optical Coherence Tomography; IOP: Intraocular Pressure; POAG: Primary Open Angle Glaucoma; PEX: Pseudoexfoliation Glaucoma.

Values are means ± SD (range).
the LBCF group had a higher bleb height \((P = 0.02)\), an increased fluid-filled cavity height \((P = 0.002)\), and lower bleb wall intensity \((P = 0.03)\). These groups evidenced no significant differences in bleb wall thickness \((P = 0.19)\).

**DISCUSSION**

In this study, we investigated the correlation between the IOP and quantitative bleb parameters by means of 3D AS-OCT and custom software. The three-dimensional capability of this technique allowed us to study complete surgical wounds and internal structures of filtration blebs [17,18]. With our custom software, we easily rotated and tilted 3D AS-OCT images and quantified distances, thicknesses, and optical intensity with greater precision than possible with techniques currently in use. Previous reports showed that bleb wall thickness was significantly negatively correlated with IOP \([15,16]\). Our results here also showed that bleb wall thickness was negatively correlated with IOP. Besides, IOP showed a significant negative correlation with total bleb height and fluid-filled cavity height, and a significant positive correlation with the intensity of the bleb wall in our study. Some reports in which qualitative methods were used found an association of low-reflectivity blebs with

![Figure 2](image1.png)

*Figure 2* Photograph (A) and three-dimensional anterior segment optical coherence tomographic images (B: vertical, C: horizontal, D: en face) of a post-trabeculectomy bleb. Axes: red, horizontal; blue, vertical; yellow, Z.

BW: Bleb Wall; SF: Scleral Flap; AC: Anterior Chamber; and *: internal fluid-filled cavity.

![Figure 3](image2.png)

*Figure 3* Scatter plot correlations between Intraocular Pressure (IOP) and (A) total bleb height, (B) fluid-filled cavity height, (C) bleb wall thickness, and (D) bleb wall intensity. Black and white dots indicate fornix-based and limbus-based conjunctival flap cases, respectively. Spearman correlation coefficient: \(r_s\).
good IOP control [10,16]. Our result with a quantitative method is consistent with results from those reports. Additional larger studies are needed to clarify the correlation between intrableb structural features and IOP.

We also compared bleb morphology after trabeculectomy with 2 conjunctival incisions—FBCF and LBCF. This report is the first to compare these bleb features by using quantitative methods. Our results showed that, compared with the FBCF group, the LBCF group had a higher bleb height, increased fluid-filled cavity height, and lower bleb wall intensity. No significant differences between these 2 groups were found for bleb wall thickness.

Work by previous investigators showed no significant difference in IOP-lowering ability between the 2 approaches of LBCF and FBCF [6,20,21]. However, some investigators found significant differences in postoperative bleb appearance between these approaches: limbus-based flaps were more often high and avascular [22-24]. Solus et al [22] recently reported results for large samples in which FBCF and LBCF had comparable rates of success in controlling IOP but differed in bleb morphology and in rates of undesirable late effects, although these researchers conducted a retrospective, nonrandomized study. In their study reported here, limbus-based operations resulted in more completely avascular, thin blebs and higher blebs, as suggested by previous reports [22-24]. The study of Solus et al [22], to quantify potential differences in bleb morphology between FBCF and LBCF, used a semiquantitative method, the Indiana Bleb Grading System. Our result is consistent with results from those reports. Additional larger studies are needed to clarify the correlation between intrableb morphology and the subjectivity of the grading.

CONCLUSION

In conclusion, our technique of utilizing 3D AS-OCT imaging with custom software was advantageous for evaluating morphological features of trabeculectomy blebs both quantitatively and noninvasively. Bleb height, the fluid-filled cavity height, the bleb wall thickness and the bleb wall intensity bleb wall intensity were significantly correlated with the IOP. LBCF procedures resulted in higher blebs, increased fluid-filled cavity height, and lower bleb wall intensities, but not greater bleb wall thickness, than did the FBCF procedures.

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REFERENCES


Table 2: Bleb features for different types of conjunctival incision.

<table>
<thead>
<tr>
<th>Feature</th>
<th>FBCF (n = 35)</th>
<th>LBCF (n = 12)</th>
<th>p value</th>
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<tr>
<td>Total bleb height, mm</td>
<td>0.89 ± 0.46</td>
<td>1.36 ± 0.53</td>
<td>0.02</td>
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<tr>
<td>Fluid-filled cavity height, mm</td>
<td>0.23 ± 0.25</td>
<td>0.63 ± 0.32</td>
<td>0.002</td>
</tr>
<tr>
<td>Bleb wall thickness, mm</td>
<td>0.68 ± 0.32</td>
<td>0.51 ± 0.26</td>
<td>.19</td>
</tr>
<tr>
<td>Intensity of bleb wall, optical density</td>
<td>150.3 ± 49.7</td>
<td>109.8 ± 42.6</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: LBCF: Limbus-Based Conjunctival Flap; FBCF: Fornix-Based Conjunctival Flap.


