EXTENDED REPORT

Analysis of bleb morphology after trabeculectomy with Visante anterior segment optical coherence tomography

Christopher Kai-shun Leung, Doris Wai-fong Yick, Yolanda Yuen-ying Kwong, Felix Chi-hong Li, Dexter Yu-lung Leung, Shaheeda Mohamed, Clement Chee-yung Tham, Chi Chung-chai, Dennis Shun-Chiu Lam

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See end of article for authors' affiliations

Correspondence to: Dr Christopher Kai-shun Leung, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong Eye Hospital, 147K Argyle Street, Kowloon, Hong Kong; tlms00@hotmail.com

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Background: To describe the use of anterior segment optical coherence tomography (OCT) in imaging intrableb morphology after trabeculectomy.

Methods: 14 post-trabeculectomy eyes from 11 primary open angle glaucoma and 3 primary angle closure glaucoma subjects were studied. The blebs were classified with reference to slit lamp morphology and bleb function. They included diffuse filtering (n=7), cystic (n=2), encapsulated (n=2) and flattened (n=3) bleb types. One eye in each patient was imaged with the Visante anterior segment OCT. A vertical scan line of 10 mm consisting of 512 A-scans was positioned at the centre of the bleb. The images were then analysed by built-in software. Intrableb morphologies and structures, including bleb wall thickness, subconjunctival fluid collections, suprascleral fluid space, scleral flap thickness, intrableb intensity (low, medium or high) and the route under the scleral flap were characterised and measured.

Results: Diffuse filtering blebs were found by subconjunctival fluid collections. Suprascleral fluid space and the route under the scleral flap were identified in four of the seven cases. Cystic blebs were composed of a large hyporeflexive space with multiloculated fluid collections covered by a thin layer of conjunctiva. Encapsulated blebs had a thick bleb wall with high reflectivity and an enclosed fluid filled space. Flattened blebs demonstrated high scleral reflectivity and no bleb elevation.

Conclusions: Visante anterior segment OCT can be used for bleb imaging. The different patterns of intrableb morphology identified by OCT were related to slit lamp appearance and bleb function. This information may be useful to study the different surgical outcomes and the process of wound healing in trabeculectomised eyes.

Trabeculectomy has been widely accepted as the procedure of choice in the surgical management of glaucoma since its introduction by Cairns in 1968.¹ Various factors, including age, race, history of previous filtration surgery and type of glaucoma can influence the outcome of trabeculectomy and a successful procedure relies on the formation of a filtering bleb. In general, bleb appearance can be classified clinically as diffuse, cystic, encapsulated and flattened. Good intraocular pressure (IOP) control (<21 mm Hg) after filtration surgery was commonly found to be associated with low lying diffuse blebs.² In recognition of the importance of bleb appearance in relation to surgical outcome and complications, a number of classification systems have been proposed to characterise bleb morphology based on slit lamp grading.^{3–4} Although some of these grading systems have been found to be clinically useful and achieved high levels of interobserver agreement, slit lamp assessment remains essentially subjective and qualitative. The internal morphology of filtering blebs, which could play an important part in determining surgical outcome, cannot be evaluated under slit lamp.

Visualisation of intrableb morphology was first reported with ultrasound biomicroscopy (UBM).⁵ Some of the internal features of filtering bleb, such as formation of the cavernous fluid filled space and intrableb reflectivity have been characterised by UBM. However, UBM is limited by the need for contact and axial resolution is only up to 25 µm. With the advent of anterior segment optical coherence tomography (OCT), non-contact, high resolution tomographic cross sectional imaging of anterior segment structures has become possible. In this study, we used the recently launched commercial model of anterior segment OCT (ZEISS Visante OCT Model 1000; Carl Zeiss Meditec, Dublin,

California, USA) to image and characterise the internal morphology of different types of functioning and non-functioning blebs after trabeculectomy.

METHODS

The study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and approved by the local clinical research ethics committee. Informed consent was obtained from 14 Chinese patients with primary open angle glaucoma or primary angle closure glaucoma who had undergone trabeculectomy with addition of mitomycin C (MMC) (0.2–0.4 mg/ml for 2–3 minutes). We imaged one trabeculectomised eye per patient with the ZEISS Visante OCT Model 1000. The Visante OCT is a high resolution tomographic and biomicroscopic device specifically designed for anterior segment imaging and measurement, with an axial resolution of 18 µm. The principle is based on low coherence interferometry using a 1310 nm superluminescent light emitting diode. Analogous to an ultrasound B-scan, Visante OCT acquires multiple A-scans and aligns them to construct two dimensional images. Scanning of the anterior segment structures employs a similar measuring principle as scanning of the retina, which has been described previously.⁶ Because of the different tissue optical properties, OCT can delineate the internal structures (eg, fluid collection, conjunctival/scleral tissue reflectivity) in fine detail. Bleb imaging is a non-contact procedure during which the subject fixates on an external fixation target. The upper lid is gently elevated by the operator

Abbreviations: IOP, intraocular pressure; MMC, mitomycin C; OCT, optical coherence tomography; UBM, ultrasound biomicroscopy

Figure 1 The diffuse filtering bleb is characterised by the presence of subconjunctival fluid filled collections and low to moderate intrableb reflectivity. The scleral flap, sclerotomy, suprascleral fluid space, the route under the scleral flap and the iridectomy site were clearly identified.

to maximise the exposure of the bleb to the camera. Scanning was performed with a vertical 10 mm linear scan consisting of 512 A-scans at the centre of the bleb. The exact position of the scanning location is shown on the real time video incorporated into the scanning panel.

All of the bleb images were measured using built-in software analysis. Figure 1 shows the various parameters measured in the study. Bleb wall thickness is defined as the distance between the first reflective signal from the conjunctiva to the top of the subconjunctival fluid space, or the suprascleral fluid space if the former is not present. As bleb wall thickness may vary along the scan, only the minimum distance was measured. The subconjunctival fluid space was measured as the maximal thickness of the signal void or hyporeflexive area directly beneath the bleb wall in the cross sectional image. The suprascleral fluid space was

measured as the maximal vertical distance in the signal void area adjacent to the sclera. One measurement was taken for each parameter in the same image and all of the images and measurements were performed by the same operator (CKL).

RESULTS

Seven diffuse filtering blebs, two cystic blebs, two encapsulated blebs and three flattened blebs were imaged by Visante anterior segment OCT. The demographic details of the patients, characteristic blebs features and measurements are presented in table 1.

Diffuse filtering blebs

Diffuse filtering blebs were characterised by multiple subconjunctival signal void areas corresponding to pockets of fluid collections and low to moderate intrableb reflectivity (see fig 1

Table 1 Demographic, clinical characteristics and anterior segment optical coherence tomography morphologies of 14 trabeculectomised eyes

Case No	Age (y)	Diagnosis	Operation	Postop (months)	Bleb type	IOP* (mm Hg)	Bleb wall thickness (mm)	Subconjunctival fluid space (mm)	Intrableb reflectivity	Suprascleral fluid space (mm)	Scleral flap thickness (mm)	Route under scleral flap†
1	50	POAG	Trab.	5	Diffuse filtering	10	0.15	0.09	Medium	0.23	0.34	+
2	73	POAG	Phaco + Trab	4	Diffuse filtering	12	0.11	0.19	Medium	0.10	0.48	+
3	31	POAG	Trab	6	Diffuse filtering	4	0.18	0.10	Low	0.16	0.31	+
4	52	POAG	Trab	1	Diffuse filtering	8	0.16	0.11	Low	0.15	0.46	+
5	82	POAG	Phaco + Trab	4	Diffuse filtering	14	0.26	0.05	Low	0.15	–	–
6	48	PACG	Trab	5	Diffuse filtering	10	0.22	0.07	Medium	–	–	–
7	71	PACG	Phaco + Trab	27	Diffuse filtering	14	0.11	0.20	Low	–	–	–
8	84	PACG	Phaco + Trab	12	Cystic	8	0.05	1.28	Low	–	–	–
9	53	POAG	Trab	38	Cystic	14	0.09	2.07	Low	–	–	–
10	73	POAG	Phaco + Trab	2	Encapsulated	32	0.46	–	High	4.02	–	–
11	27	POAG	Trab	46	Encapsulated	20	0.52	–	High	3.55	–	–
12	72	POAG	Phaco + Trab	3	Flattened	17	–	–	Scleral reflectivity	–	0.56	+
13	74	POAG	Phaco + Trab	6	Flattened	16	–	–	Scleral reflectivity	–	–	–
14	40	POAG	Phaco + Trab	6	Flattened	23	–	–	Scleral reflectivity	0.10	–	–

IOP, intraocular pressure; PACG, primary angle closure glaucoma; Phaco, phacoemulsification with implantation of intraocular lens; POAG, primary open angle glaucoma; Trab, trabeculectomy with addition of mitomycin C.

*IOP was measured on the day of imaging. For case Nos 11, 12 and 13, IOP was controlled with topical antiglaucomatous medication.

†+, present; –, absent.

Figure 2 The cystic bleb is composed of a large hyporeflective area filled with multiple fluid collections of varying size and intensity.

and fig 5A, C). Bleb wall thickness ranged from 0.11 to 0.26 mm and the thickness of subconjunctival fluid collections varied from 0.05 to 0.20 mm. The outline of the scleral flap was delineated in four cases (table 1, cases 1–4) and scleral flap thickness ranged from 0.31 to 0.48 mm. Suprascleral fluid space and the route under the scleral flap running towards the site of sclerotomy were found in each of the four cases.

Cystic blebs

Cystic blebs were composed of a large subconjunctival hyporeflective space with multiloculated fluid collections of varying size and intensity (fig 2). The blebs were covered by a thin layer of conjunctiva. Bleb wall thicknesses were 0.05 and 0.09 mm, and the thicknesses of the subconjunctival hyporeflective space were 1.28 and 2.07 mm, respectively (table 1, cases 8–9). No visible route under the scleral flap could be identified in the two cases.

Non-functioning encapsulated blebs and flattened blebs

Non-functioning blebs were characterised by the absence of subconjunctival fluid collection and high intrableb reflectivity. In the two encapsulated blebs, the bleb walls measured 0.46 and 0.52 mm (table 1). The suprascleral fluid space was surrounded by dense connective tissue, as evident by the high subconjunctival reflectivity (fig 3). In the three flattened blebs, there were only scleral reflectivities with no bleb elevation (fig 4). The route under the scleral flap and suprascleral fluid space were found in some cases (cases 12 and 14, respectively).

Case report

A 52-year-old man with primary open angle glaucoma underwent an uneventful left fornix based trabeculectomy with addition of MMC (0.2 mg/ml for 2 min). On the first operative day, IOP was 7 mm Hg. The bleb was mildly elevated, the anterior chamber was well formed and the Seidel test was negative. OCT confirmed a diffuse filtering bleb with multiple subconjunctival fluid collections in the cross sectional image (fig 5A). Anterior segment OCT showed an anterior chamber depth of 2.00 mm and a mild suprachoroidal effusion (fig 6A). However, on day 5 after operation, the anterior chamber became shallow (ACD 1.31 mm) because of a mild leakage at the conjunctival wound edge and an increase in suprachoroidal effusion (fig 6B). Bleb imaging showed reduced subconjunctival fluid collections (fig 5B). The leakage gradually resolved within a week with conservative management. Figures 5C and 6C show the OCT images on day 17 after operation. The subconjunctival fluid collections inside the bleb re-established and the anterior chamber was reformed (anterior chamber depth 2.84 mm) with resolution of suprachoroidal effusion.

DISCUSSION

Classification of bleb morphology was first described by Kronfeld in 1949.⁷ Three types of bleb were described based on bleb

Figure 3 The encapsulated bleb had a fluid filled space surrounded by connective tissue with high signal reflectivity.

appearance and function. Kronfeld's type I, type II and type III blebs represent functioning polycystic blebs, diffuse filtering blebs and non-functioning flattened blebs, respectively. Van Buskirk subsequently described the features and appearance of non-functioning encapsulated blebs.⁸ However, there are cases where bleb appearance is not correlated with bleb function. Visualising internal bleb morphology would help to better characterise the relationship between bleb structure and function and enhance our understanding of the wound healing process after trabeculectomy. Pavlin *et al* first demonstrated internal bleb morphology using UBM.⁵ They found that the filtering bleb is characterised by a patent internal ostium and is continuous with a distinct scleral split. More detailed descriptions of different bleb morphologies were then reported by Yamamoto *et al*.⁹ Based on the reflectivity inside the bleb, blebs were classified into low reflective (type L), high reflective (type H), encapsulated (type E) and flattened (type F). Good IOP control was found in type L blebs whereas type H, E or F blebs were, in general, associated with fair to poor IOP control. A recent study by Savini *et al* reported the use of the Stratus OCT (Carl Zeiss Meditec, Dublin, California, USA) to image filtering blebs.¹⁰ They classified bleb morphologies into three types based on the patterns of the OCT images. Type A had a thick wall and a single large fluid filled space; type B had a thin wall and multiple large fluid filled spaces; and type C had multiple flattened fluid filled spaces. The different types of bleb morphologies A, B and C were found to be associated with different surgical procedures corresponding to trabeculectomy without antimetabolites, trabeculectomy with MMC and phacotrabeculectomy with MMC, respectively. However, because the depth of penetration of the Stratus OCT is limited to 2 mm, deeper structures inside the bleb such as scleral flap and fluid space above the sclera were not identified.

OCT offers a better alternative for bleb imaging compared with UBM because it provides a non-contact approach for bleb assessment and requires no coupling medium or supine positioning. Unlike UBM, the position and orientation of the scan can be localised and visualised from the real time camera panel. OCT also provides higher axial resolution images (18 μ m in Visante v 25 μ m in UBM). The major advantage of Visante anterior segment OCT over Stratus OCT is its deeper tissue penetration (6 mm for

Figure 4 The flattened bleb demonstrated no bleb elevation and high scleral reflectivity. The outline of the scleral flap and the sclerotomy were identified.

Figure 5 Serial intrableb morphologies of case 4, imaged on day 1 (A), day 5 (B) and day 17 (C) after trabeculectomy with mitomycin C. See the case report for detailed descriptions.

Visante v 2 mm for Stratus) because it uses a longer wavelength of superluminescent diode for imaging (1310 nm in Visante v 820 nm in Stratus) and thus allows visualisation of deeper intrableb structures. All of these merits of anterior segment OCT translate into more accurate and reproducible images for direct and objective bleb assessment and measurement.

In this study, we described and quantified the internal features of different bleb morphologies with reference to the observed clinical appearance and bleb function. Similar to the findings of UBM in the type L bleb, low to medium intrableb reflectivity and intrableb fluid filled spaces were found in functioning blebs (the diffuse filtering and cystic blebs). A visible route under the scleral flap was also evident in some cases. In contrast with UBM, the higher scanning resolution in Visante OCT images allows us to differentiate two levels of intrableb fluid filled spaces: (1) the subconjunctival fluid collections and (2) the suprascleral fluid space. Subconjunctival fluid collections are in the vicinity of the conjunctiva, suggesting continuous aqueous drainage and therefore good IOP control. Absence of the subconjunctival fluid collections in the non-functioning encapsulated and flattened blebs are in agreement with this hypothesis. The presence of suprascleral fluid space, on the other hand, may not indicate aqueous drainage as the aqueous outflow could be impeded by the surrounding dense fibrous tissue, as seen in encapsulated blebs where high reflectivity was found surrounding the fluid filled space. Our case series demonstrated that neither the presence of suprascleral fluid space nor the route under the scleral flap is related to bleb function. Histological studies on functioning blebs showed that collagen in the conjunctival substantia propria was widely spaced and the subepithelial connective tissue was loosely arranged.¹¹ These features accounted for the low-medium reflectivity in the OCT images of functioning blebs. This is in contrast with the high reflectivity in the encapsulated blebs where the bleb wall was composed of dense collagenous connective tissue.¹²

Although the diffuse filtering and cystic blebs have different clinical features under slit lamp, little is known of the differences in internal morphology. While UBM is able to delineate the fluid filled spaces inside the bleb, its resolving

Figure 6 Serial anterior chamber images of case 4 imaged on day 1 (A), day 5 (B) and day 17 (C) after trabeculectomy with mitomycin C. See the case report for detailed descriptions.

power may not be high enough to discern detailed spatial architecture. The fact that it is a contact technique may also pose additional risks for bleb related complications, including bleb leakage and blebitis, which more commonly occur in cystic blebs.¹³ It was observed in this study that cystic blebs had a thin conjunctival wall encasing a large hyporeflective space consisting of multiloculated fluid collections of varying sizes. These intrableb morphologies were distinct from the diffuse filtering type. The thinner conjunctival wall in cystic blebs explains why these blebs are more prone to complications, and measurement of wall thickness in these blebs may provide a useful indicator to assess the risk of bleb related complications.

The non-contact nature of OCT imaging provides a safer approach to examine the intrableb morphology in the early postoperative period, thereby offering a unique opportunity to study the healing and remodelling process inside the blebs longitudinally. In the case report, we showed that the subconjunctival fluid collections and suprascleral fluid space decreased in size and the outline of the scleral flap became less distinct from day 1 to day 17 after surgery. The changes inside the bleb indicated that there was an active remodelling process in the early postoperative period. OCT bleb imaging would thus be useful to follow the evolution of intrableb morphology and understand the development of various bleb types.

There are a number of limitations using Visante OCT for bleb imaging. Although Visante OCT is capable of providing detailed cross sectional images of intrableb structures, the software is primarily designed to image and measure anterior chamber structures. Therefore, measurements made on the bleb images may not reflect true values. Nevertheless, these measurements are still very useful to monitor bleb changes over time and to compare differences among different bleb types. Another limitation is that Visante OCT does not provide signal intensity measurements. The grading of intrableb reflectivity is essentially a subjective

assessment based on comparisons among the different bleb types. Before a validated approach for pixel intensity measurement becomes available, it is difficult to objectively comment on intrableb reflectivity. Finally, while the intrableb structures can be visualised clearly with OCT, some important parameters such as bleb vascularity and Seidel status would still rely on slit lamp assessment.

In summary, we have shown that internal bleb morphology can be visualised and analysed using Visante anterior segment OCT. Combining both clinical and imaging information could provide a new perspective towards understanding the different surgical outcomes after trabeculectomy. This knowledge could be important to refine surgical techniques and evaluate the use of different adjuvant treatments in the surgical management of glaucoma patients.

Authors' affiliations

Christopher Kai-shun Leung, Doris Wai-fong Yick, Yolanda Yuen-ying Kwong, Felix Chi-hong Li, Dexter Yu-lung Leung, Shaheeda Mohamed, Clement Chee-yung Tham, Chi Chung-chai, Dennis Shun-Chiu Lam, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, PRC

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REFERENCES

- 1 Cairns JE. Trabeculectomy. Preliminary report of a new method. *Am J Ophthalmol* 1968;**66**:673–9.
- 2 Vesti E. Filtering blebs: follow up of trabeculectomy. *Ophthalmic Surg* 1993;**24**:249–55.
- 3 Cantor LB, Mantravadi A, WuDunn D, et al. Morphologic classification of filtering blebs after glaucoma filtration surgery: the Indiana Bleb Appearance Grading Scale. *J Glaucoma* 2003;**12**:266–71.
- 4 Wells AP, Crowston JG, Marks J, et al. A pilot study of a system for grading of drainage blebs after glaucoma surgery. *J Glaucoma* 2004;**13**:454–60.
- 5 Pavlin CJ, Harasiewicz K, Foster FS, et al. Ultrasound biomicroscopy of anterior segment structures in normal and glaucomatous eyes. *Am J Ophthalmol* 1992;**113**:381–9.
- 6 Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science* 1991;**254**:1178–81.
- 7 Kronfeld PC. The mechanism of filtering operations. *Trans Pac Coast Otophthalmol Soc Annu Meet* 1949;**33**:23–40.
- 8 Van Buskirk EM. Cysts of Tenon's capsule following filtration surgery. *Am J Ophthalmol* 1982;**94**:522–7.
- 9 Yamamoto T, Sakuma T, Kitazawa Y. An ultrasound biomicroscopic study of filtering blebs after mitomycin C trabeculectomy. *Ophthalmology* 1995;**102**:1770–6.
- 10 Savini G, Zanini M, Barboni P. Filtering blebs imaging by optical coherence tomography. *Clin Exp Ophthalmol* 2005;**33**:483–9.
- 11 Powers TP, Stewart WC, Stroman GA. Ultrastructural features of filtration blebs with different clinical appearances. *Ophthalmic Surg Lasers* 1996;**27**:790–4.
- 12 Addicks EM, Quigley HA, Green WR, et al. Histologic characteristics of filtering blebs in glaucomatous eyes. *Arch Ophthalmol* 1983;**101**:795–8.
- 13 DeBry PW, Perkins TW, Heatley G, et al. Incidence of late-onset bleb-related complications following trabeculectomy with mitomycin. *Arch Ophthalmol* 2002;**120**:297–300.