ORIGINAL RESEARCH

Ultrasound biomicroscopy of filtration blebs

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Abstract

Aim: To assess the internal anatomy of filtering blebs *in vivo*.

Materials and methods: We performed high-resolution, high-frequency ultrasound biomicroscopy on filtration blebs with a range of clinical appearances to evaluate the internal ostium, scleral flap, and subconjunctival space in each type of bleb.

Results: Diffuse, spongy, thin-walled and cystic, encapsulated, and failed blebs were successfully imaged without morbidity. The pattern of subconjunctival aqueous flow was assessed and sites of blockage to flow determined.

Conclusion: Improved knowledge of the internal structure of filtration blebs should allow us to recognize earlier stages of bleb failure and characteristics of nonfunctional blebs with the intent of manipulating bleb structure to establish or improve function.

Key words: Ultrasound biomicroscopy, Filtration, Trabeculectomy, Bleb

Introduction

Filtration blebs vary widely in their clinical appearance. Blebs following successful trabeculectomy characteristically have a diffuse, spongy appearance, while those following full-thickness surgery or adjunctive antifibrosis chemotherapy are typically more thin-walled and cystic.[1-9] Encapsulated blebs tend to be elevated and localized, with or without prominent surface vessels.[10-12] Failed blebs are often totally flat and vascularized.[13,14] The clinical appearance of a bleb is not always an accurate predictor of functional status.[11,15] Rather than being static structures, blebs are dynamic, and remodeling takes place over time.[16]

Relatively little attention has been paid to those characteristics of blebs in the early postoperative period that predict surgical success or failure. Similarly, the structure of established blebs, the nature of remodeling, and improved localization of sites of failure (ostium, sclera, episclera and bleb perimeter) need further investigation.

Management of failing filtration blebs is often unrewarding, despite the empirical use of digital compression, suture lysis, bleb needling, surgical revision, and antifibrotic agents. Correlation of *in vivo* characteristics of bleb structure with functional status and the ability to determine clinically the site of obstruction in failing or failed blebs should help to predict the future status of the bleb and lead to interventive procedures for those blebs that appear to be in early stages of functional decline.

High-frequency anterior segment ultrasound biomicroscopy (UBM; Zeiss-Humphrey, San Leandro, CA, USA) is capable of imaging *in vivo* anterior segment structures at resolutions approaching 50 μm[17-19] It has been used to examine normal and glaucomatous eyes and is proving useful in the elucidation of anatomic mechanisms underlying various types of pathology of the anterior segment.[20-25] We examined a variety of successful and failed blebs to evaluate the morphologic features revealed by UBM.

Materials and methods

The equipment and techniques of ultrasound biomicroscopy as developed by Pavlin *et al*[17,18] have been previously described. In general, higher-frequency transducers produce increased resolution of more superficial structures, while lower-frequency ones are used when increased depth of penetration is necessary. With our unit, scanning is performed using a 50-MHz transducer, giving tissue penetration of 4 mm with resolution of approximately 50 μm. The scanner produces a 5 x 5-mm field with 256 image lines at a scan rate of 8 frames per second. The probe is suspended from an articulated arm to diminish motion artifacts.

Eyes that had undergone filtration surgery were enrolled. We defined 4 types of blebs on the basis of clinical appearance on slit-lamp examination. We defined type 1 blebs as those that were cystic, ischemic blebs with thin walls and multiple fluid-filled spaces separated by septa. Type 2 blebs were diffusely elevated, more opacified, pale, and deeper in the epibulbar tissues. Type 3 blebs were flat, failed blebs with subconjunctival scarring. Type 4 blebs were those that were encapsulated (Tenon cyst) and in which the intraocular pressure (IOP) normalized after needling. Slit-lamp photographs were obtained on the same day as the UBM imaging.

UBM was performed under topical anesthesia using an eye cup and saline solution as the coupling medium.[26] All scanning was performed with the patient in the supine position under standardized room lighting conditions. Multiple cross-sectional images were taken of the anterior segment and the bleb, from the limbus to its posterior extent. The internal ostium and scleral flap were imaged. The image that displayed maximal bleb elevation was used for measurements. Bleb height and wall thickness were measured using calipers provided in the system software.

Results

Twenty-three blebs of 21 patients were scanned in a nonmasked fashion. There were 15 white and 6 black patients. Sixteen eyes had primary open-angle glaucoma, 4 had exfoliative glaucoma, 2 had uveitic glaucoma, and 1 had chronic angle-closure glaucoma. All eyes had received postoperative 5-fluorouracil injections. There were 7 fornix-based and 16 limbus-based conjunctival flaps.

Five blebs were considered to be type 1 (**Figures 1A** and **1B**), 10 were type 2 (**Figures 2A** and **2B**), 6 were type 3 (**Figures 3A** and **3B**), and 2 were type 4 (**Figures 4A** and **4B**). The results of the UBM measurements are shown in the **Table 1**.

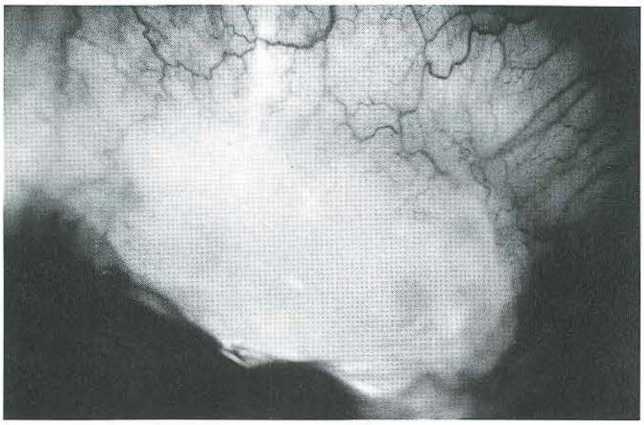

Figure 1A. Clinical photograph of a typical type 1 bleb, showing raised, ischemic, cystic loculations present 8 months after limbus-based trabeculectomy with 5-fluorouracil injections. The IOP was 8 mm Hg.

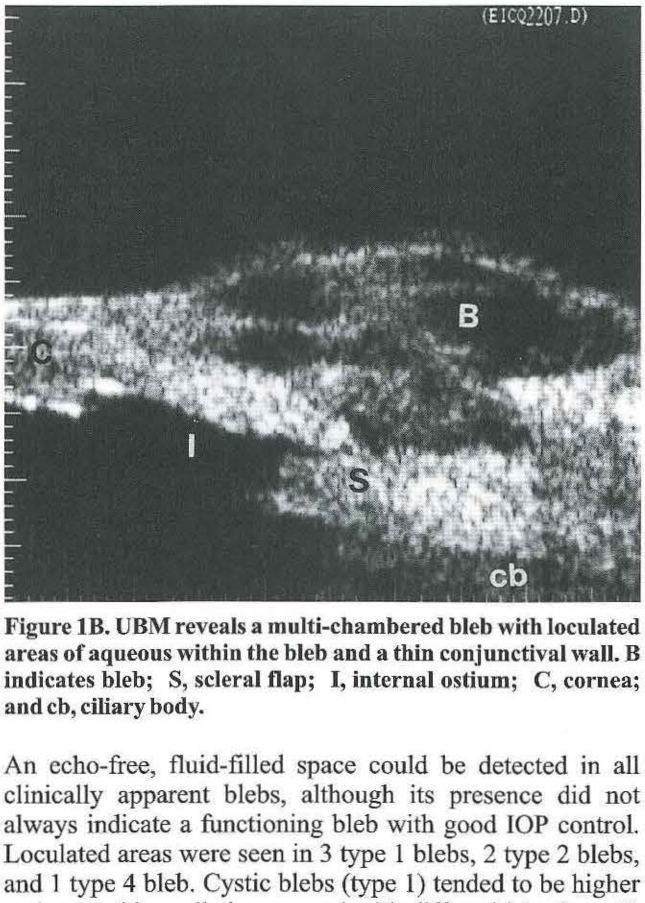

Figure 1B. UBM reveals a multi-chambered bleb with loculated areas of aqueous within the bleb and a thin conjunctival wall. B indicates bleb; S, scleral flap; I, internal ostium; C, cornea; and cb, ciliary body.

An echo-free, fluid-filled space could be detected in all clinically apparent blebs, although its presence did not always indicate a functioning bleb with good IOP control. Loculated areas were seen in 3 type 1 blebs, 2 type 2 blebs, and 1 type 4 bleb. Cystic blebs (type 1) tended to be higher and more thin-walled compared with diffuse blebs (type 2) (**Table 1**). Eyes with flat blebs had no evidence of subconjunctival filtration and demonstrated blockage to flow at the level of the episclera. The conjunctiva was thicker when compared with types 1 and 2 (**Table 1**). Although there were differences in the thickness of the overlying conjunctiva, bleb walls were relatively uniform in echo density. A patent internal ostium and the scleral flap could be imaged in all eyes.

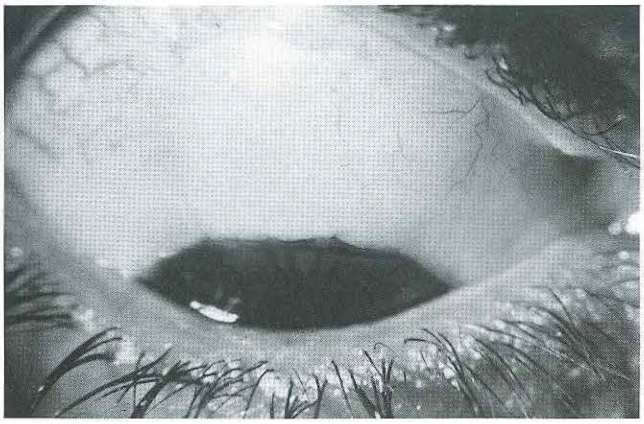

Figure 2A. Clinical photograph of a typical type 2 bleb, showing diffuse subconjunctival flow and ischemia 5 months after limbus-based trabeculectomy with 5-fluorouracil injections. The IOP was 13 mm Hg.

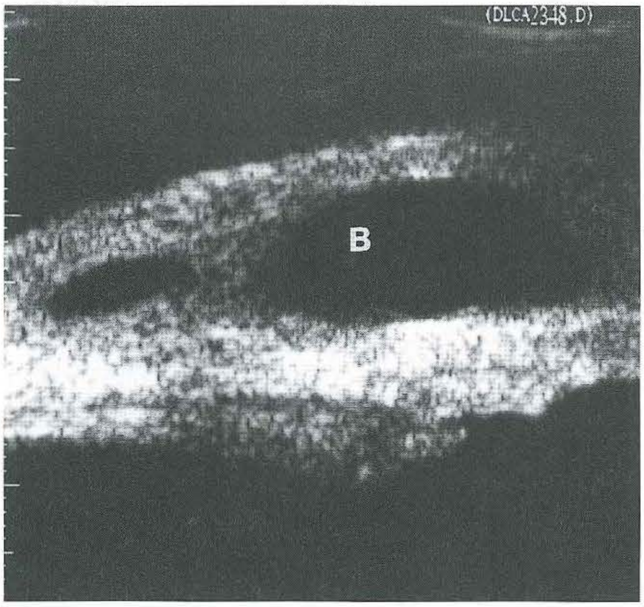

Figure 2B. UBM reveals a multi-chambered bleb that is also loculated, but with a thicker conjunctival wall than the one shown in Figure 1B. There was no visible communication between the 2 areas in any of the UBM images. B indicates bleb.

Discussion

The detailed appearance of filtration blebs has not been extensively studied. Blebs can be categorized according to morphology (cystic and elevated or diffuse and shallow),[14,27,28] function (underfiltering or overfiltering),[10] and degree of conjunctival inflammation.[15] Diffuse, noncystic, thicker blebs are more common after trabeculectomy,[3] while more localized, cystic, thinner blebs are more common following full-thickness surgery[4,6] and the use of adjunctive antimetabolites.[4,6-8,29] Failed blebs are flat and often vascularized.[13,14] Encapsulated blebs appear as elevated, localized, thick-walled cysts and may have prominent surface vessels.[11,12,30,31] Although the spectrum of bleb appearance varies widely, successful filtration is characterized by several common features: elevation of the conjunctiva off the surface of the episclera, relative pallor or ischemia of the overlying conjunctiva, and conjunctival microcystic edema.[14,27,32]

The anatomy of the aqueous outflow pathway in clinically successful blebs could be visualized. Functional cystic and diffuse blebs had differences in UBM morphology, which correlated with clinical appearances. The bleb walls were thinner in cystic blebs than in diffuse blebs. In all eyes with successful filtration, an echo-free area was present in the subconjunctival space.

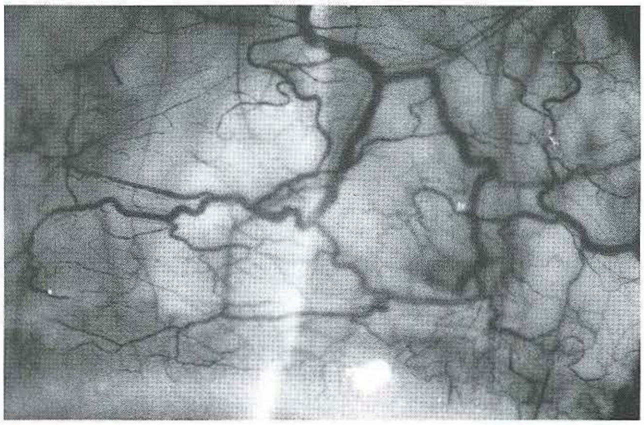

Figure 3A. Clinical photograph of a typical type 3 bleb, showing flattened conjunctiva with prominent overlying vessels 6 months after fornix-based trabeculectomy with 5-fluorouracil. No bleb is evident. The IOP was 23 mmHg on maximally tolerated antiglaucoma medications. The overlying conjunctiva was flat and vascularized.

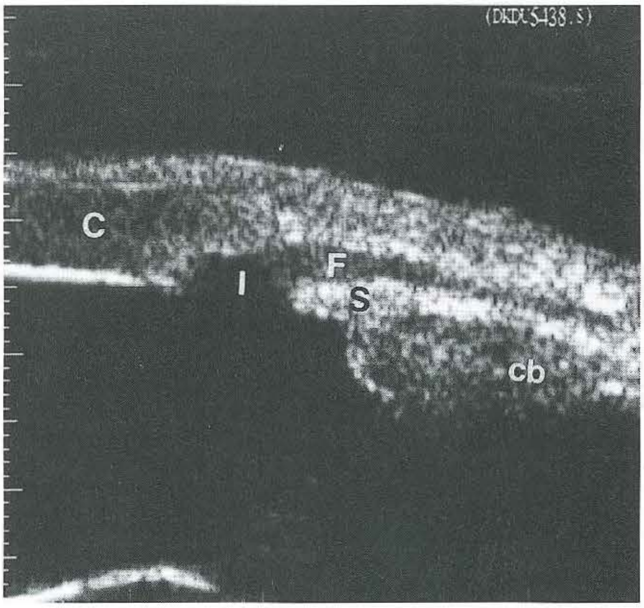

Figure 3B. UBM shows a patent internal ostium with a filtration track into the episcleral region, with no subconjunctival reservoir. S indicates sclera; I, internal ostium; F, filtration track; C, cornea; cb, ciliary body.

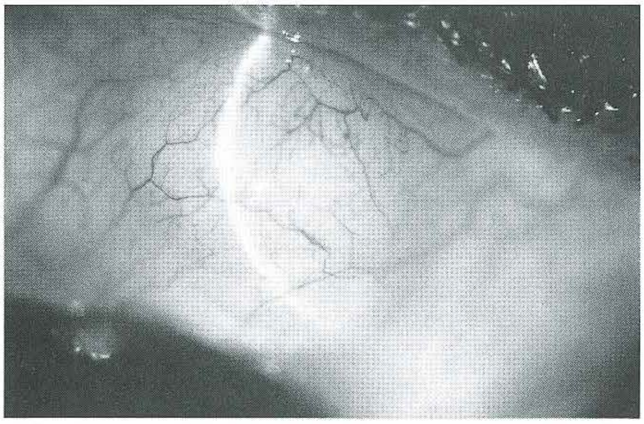

Figure 4A. Clinical photograph of a typical type 4 bleb, showing a raised but encapsulated bleb. The IOP was 23 mm Hg after the administration of a topical beta-blocker.

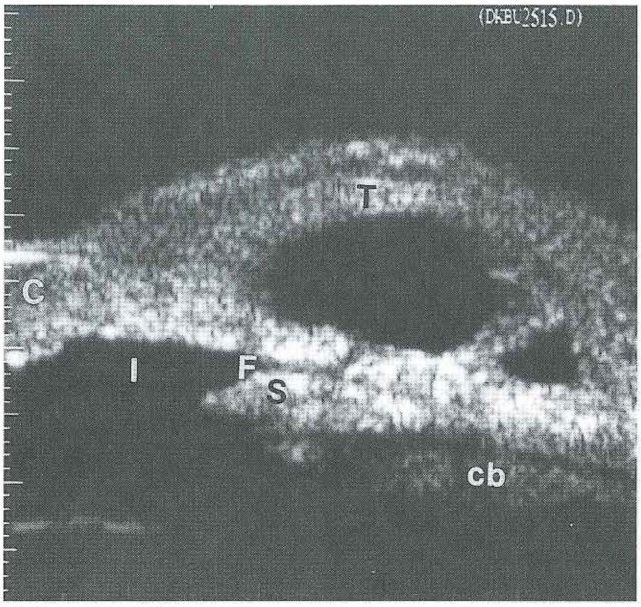

Figure 4B. UBM showed the cyst wall to be bilayered, possibly representing an area of subconjunctival flow. The scleral flap is approximately half thickness. T indicates Tenon cyst wall; S, scleral flap; I, internal ostium; F, filtration track; C, cornea; and cb, ciliary body.

Previous measurements of bleb walls have been made *in vitro*.[32] The wall thickness correlated with the clinical description of functioning blebs.[13,14,33] In our UBM images, there were cystic areas within some of the blebs, predominantly in the type 1 blebs. This appears to be more prevalent amongst the cystic blebs, where septated and loculated areas within the blebs could be seen. Theoretically, this may represent remodeling and formation of connective tissue and elastic fibers, although the correlation of these alterations with bleb function is unclear.[32,34] There have been morphologic and histopathologic studies of the microcystic changes in the bleb wall and within the bleb.[13,32,33,35,36] Some have suggested that aqueous flow into the subconjunctival space separates the subconjunctival tissue to multiple small pockets. These small cystic structures give rise to relative transparent blebs containing multiloculated cysts.[13,14,33] The different amount of aqueous flow in the subconjunctival tissue in the early postoperative period has been hypothesized to be responsible for the appearance of a cystic or a diffuse bleb.[14]

The UBM appearance of filtering blebs following trabeculectomy with adjunctive mitomycin C was described by Yamamoto et al,[37] Sakuma, and Kitazawa, who created a bleb classification system based on UBM appearance. Blebs with low internal reflectivity tended to have better IOP and required fewer antiglaucoma medications. In addition, the route under the scleral flap could be clearly visualized in 81 of 82 eyes with good pressure control, compared with only 21 of 35 eyes with fair or poor control.[37] Although our classification system was based on clinical appearance rather than UBM appearance, the UBM features of functional, encapsulated, and failed blebs were similar between the 2 studies. For example, blebs with good IOP control in our series had thinner walls and lower internal reflectivity and encapsulated blebs were characterized by elevation and a thicker external wall.

Bleb encapsulation (Tenon cyst) develops in approximately 10% to 13% of eyes following trabeculectomy.[11,31,36] A histopathological study of Tenon cyst walls revealed fibroblastic proliferation of Tenon capsule that was acellular.[30] Risk factors for development of bleb encapsulation have been thought to include postoperative hypotony, flat anterior chamber, postoperative hyphema, age young than 35 years, and previous intraocular surgery.[11] UBM showed a discrete cystic encapsulation with an echolucent area between the conjunctiva and outer cyst wall possibly representing an area of subconjunctival aqueous flow.

In the vast majority of cases, external blockage is the cause of bleb failure.[9,32,34,38,39] In the 6 failed blebs imaged, the internal ostia were patent with a filtration space beneath the scleral flap (Figure 3B). There was no filtration track at the external entrance of the scleral flap, suggesting that the blockage of aqueous outflow appears to be at the level of the episclera.

Table 1. Bleb Height, Wall Thickness, and Intraocular (IOP)*.

Bleb Type	IOP, mmHg	Bleb Height, mm	Conjuntival wall Thickness, mm
1 : Cystic (n=5)	8.4 ± 2.1 (6-12)	1.7 ± 1.0 (0.63-3.00)	0.19 ± 0.12 (0.07-0.35)
2 : Diffuse (n=10)	13.6 ± 2.1 (9-17)	0.84 ± 0.37 (0.42-1.4)	0.34 ± 0.2 (0.14-1.0)
3 : Flat (n=6)	24.4 ± 4.8 (20-34)	0	0.47 ± 0.08 (0.34-0.59)+
4 : Encapsulated (n=2)	15.0 ± 1.0 (14-16)	1.60 ± 0.20 (1.40-1.80)	0.20 ± 0.02 (0.18-0.21)

+ In cases in which no bleb was present, the thickness of the conjunctiva overlying the apex of the scleral flap was measured.
*Values are given as the mean (± SD). Values in parentheses are the range.

The UBM images obtained are potentially clinically useful by helping to determine the cause of filtration failure, so that therapy may be appropriately directed. Blockage at the level of the conjunctiva-Tenon fascia-episcleral interface may respond to transconjunctival bleb needling, whereas blockage beneath the scleral flap may require more extensive surgical revision. Improved knowledge of the internal structure of filtration blebs should allow us to recognize earlier stages of bleb failure and characteristics of nonfunctional blebs with the idea of manipulating bleb structure to establish or improve function. We are currently investigating the possibility of local surgical revision under direct ultrasonographic guidance to resurrect failing filtration blebs in an attempt to avoid reoperation at a different site

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