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Dida Kazakova
Sigrid Roters
Corinne C. Schnyder
Farid Achache
Christian Jonescu-Cuypers
André Mermoud
Günter Krieglstein

Ultrasound biomicroscopy images: long-term results after deep sclerectomy with collagen implant

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D. Kazakova (✉) · C.C. Schnyder
F. Achache · A. Mermoud
Glaucoma Department, University Eye Hospital Jules Gonin,
University of Lausanne, Switzerland
e-mail: dida_kazakova@hotmail.com
Tel.: +49-221-4784326
Fax: +49-221-4783101

D. Kazakova · S. Roters
C. Jonescu-Cuypers · G. Krieglstein
Center of Ophthalmology,
University of Cologne,
Joseph Stelzmann Strasse 9,
50921 Cologne, Germany

Abstract Purpose The aim of this study was to understand the long-term outflow pathway mechanisms after deep sclerectomy – when collagen implant is resorbed – using ultrasound biomicroscopy (UBM). *Methods:* Forty-three eyes of 32 patients with medically uncontrolled open-angle glaucoma at least 1 year after deep sclerectomy were studied in an observational, non-randomised, consecutive case series. Postoperatively 15 eyes (35.7%) had goniopuncture with the Nd:YAG laser. Four eyes (9.5%) had postoperative subconjunctival injections of mitomycin C and two eyes (4.7%) had an injection of 5-fluorouracil, because of intraocular pressure (IOP) increase. Complete examination and UBM of the filtering site were performed 1–6 years after surgery. The following parameters were assessed: (1) Presence of a subconjunctival filtering bleb; (2) presence and volume of an intrascleral cavity; (3) presence of a suprachoroidal hypoechoic area. *Results:* Intraocular pressure decreased significantly from 28.1±2.5 mmHg preoperatively to 12.4±3.8 (range 7–25) mmHg at the time of UBM (at least 1 year after surgery). Forty eyes showed clinically a diffuse filtering bleb. UBM demonstrated a subconjunctival space in all eyes. In 39 eyes (92.8%) an intrascleral cavity was observed. The mean volume of this cavity was 1.8 (range 0.11–6.53) mm^3. In 19 eyes (45.2%) we observed a hypoechoic area in the suprachoroidal space. *Conclusion:* UBM examination demonstrated several aqueous humour drainage pathways. A low-reflective diffuse subconjunctival space meant persistent filtration in all eyes. More than 1 year after surgery 92.8% of eyes had a remaining intrascleral cavity. In almost half of the patients an additional suprachoroidal outflow was observed, significantly correlated with a lower IOP.

Introduction

Non-perforating glaucoma surgery preserves the integrity of the trabecular meshwork and lowers the intraocular pressure (IOP) without penetrating the anterior chamber. The deep sclerectomy was first described by Kozlov et al. in 1989 [14]. In this technique a deep sclerectomy under a scleral flap is performed. Schlemm's canal is opened, and Descemet's membrane and trabecula are left in situ to provide flow resistance. In contrast to the trabeculectomy procedure the principle of this non-penetration surgery is to create filtration through a natural trabeculo-descemetic membrane, which reduces the IOP and minimises the risk of overfiltration and early postoperative hypotony [3, 5, 6, 7].

High-frequency ultrasound biomicroscopy (UBM) allows detailed anatomical assessment of the anterior segment of the eye in vivo close to histological prepara-

tions [22, 23]. It can detect even small amounts of fluid between the layers and has proven to be useful in the examination of filtering blebs and intrascleral aqueous drainage [1, 5, 6, 12, 13, 27].

In order to determine the IOP-lowering mechanisms of this technique, we performed a consecutive UBM observation of the sclerectomy site in patients with at least 1 year of postoperative follow-up when complete resorption of the collagen implant was observed [6].

Materials and methods

Patients

From March 2000 to July 2000 we examined 42 eyes of 32 patients with open-angle glaucoma – uncontrolled by conservative treatment – who had undergone deep sclerectomy with collagen implant in the time from 1994 to 1999. All patients were recruited from the Jules Gonin Hospital (Lausanne, Switzerland). Surgery was performed by one surgeon (A. M.) [17]. Exclusion criteria for the study were dysgenetic or secondary glaucoma or any type of angle-closure glaucoma, previous argon laser trabeculoplasty and ocular surgery 12 months prior to enrolment in the study. Complete eye examinations, including best-corrected visual acuity, slit-lamp examination, applanation tonometry with the Goldmann tonometer and fundus examination, were performed. We also performed a UBM examination of the sclerectomy site more than 1 year after surgery.

Surgery

All patients underwent deep sclerectomy with collagen implant under retrobulbar anaesthesia with bupivacaine 0.75%, lidocaine 4% and hyaluridase 50 IU. A traction suture was placed on the superior rectus muscle for adequate exposure of the deep sclerectomy site, and the conjunctiva and Tenon's capsule were opened in the upper fornix. Careful haemostasis of the exposed sclera using wet-field cautery was performed. A scleral flap measuring 5 mm by 5 mm was created using a diamond knife. The scleral flap had a thickness of approximately 30–40% of the total scleral thickness. A limbus-based triangle of deep sclera with sides measuring 4 mm was removed including corneal stroma down to the Descemet's membrane. At that stage of the procedure, aqueous humour was percolating through the thin trabeculo-descemetic membrane. A collagen implant was placed radially in the centre of the deep sclerectomy site and was secured with a single 10/0 nylon suture. The superficial scleral flap was then closed with two 10/0 nylon sutures. Tenon's capsule and the conjunctiva were closed with running 8/0 Vicryl sutures.

Postoperatively, the patients were treated topically with corticosteroids and an antibiotic for 1 month followed by non-steroidal anti-inflammatory drugs for up to 3 months.

Collagen implant

The collagen device prevents reattachment of the scleral flap to the deeper sclera. We used a cylindrical collagen implant (Aquaflow; Staar Surgical, Nidau, Switzerland) that is processed by lyophilised highly purified porcine scleral collagen, which is gamma sterilised and processed to be biologically inert so that there is no systemic reaction. Microbiological analyses on 30 g of raw collagen should not show the presence of bacteria, virus, mycological organisms or parasites. This cross-linked, collagen-based bio-compatible material measures about 40×0.5 mm in its dry state. The idea of collagen implant is to occupy the surgically created intrascleral bleb under the superficial flap during the early postoperative period when the healing process is at its peak.

Ultrasound biomicroscopy

The Humphrey UBM 840 system (Humphrey Instruments, Carl Zeiss Group, Jena, Germany) was used to provide high-frequency (50 MHz), high-resolution (50 μm) ultrasonic scan images. Each patient received topically administered oxybuprocaine before a special eye cup (Carl Zeiss) was placed within the palpebral fissure and filled with a coupling medium (methylcellulose 2%). Radial and limbus-parallel scanning was performed at the limbus in the region of the deep sclerectomy. All examinations were performed by one examiner (D. K.) to avoid interobserver variability [26].

The following factors were assessed:

1. Presence of a subconjunctival filtering bleb. We classified the filtering bleb into four categories according to the classification of Yamamoto et al. [27]: L type (low reflexive), H type (high reflexive), E type (encapsulated) and F type (flattened)
2. Presence and volume of an intrascleral cavity. Exact measurements of the length, height and width of the intrascleral "lake" at its maximal dimension were performed
3. Presence of a hyporeflexive suprachoroidal space

Results

We examined 20 males and 12 females with a mean age of 67.8 years (range 45–88 years). Thirty-one patients were white and one black. Thirty-two eyes had primary open-angle glaucoma, seven eyes had pseudoexfoliation glaucoma and three eyes had pigmentary glaucoma.

Mean IOP decreased significantly from a preoperative value of 28.1±2.5 (SD) mmHg (range 26–32 mmHg) to 12.4±3.8 mmHg (range 7–25 mmHg) postoperatively.

Some eyes had an early postoperative increase of IOP to more than 21 mmHg and additional procedures were performed: Fifteen eyes (35.7%) had goniopuncture with Nd:YAG laser at the site of surgery when filtration through the trabeculo-descemetic membrane was considered to be insufficient with increased IOP. Five eyes (11.9%) had postoperative subconjunctival injections of mitomycin C, and two eyes (4.7%) were given a subconjunctival injection of 5-fluorouracil (5-FU), if the deep sclerectomy was the second (or more) antiglaucomatous surgery procedure.

A visible filtering bleb persisting one year or more after surgery was shown in 40 eyes. These blebs were clinically diffuse and shallow (Figs. 1, 3). In all successful eyes UBM showed subconjunctival filtration with a non-perforated thin trabeculo-descemetic membrane. Because of bleb fibrosis due to surgical failure, in seven eyes we injected antifibrotic agents (mitomycin C or 5-FU). Two eyes did not have clinical signs of a subconjunctival drainage. Nevertheless, these two cases did have subconjunctival filtration (visible on the UBM ex-

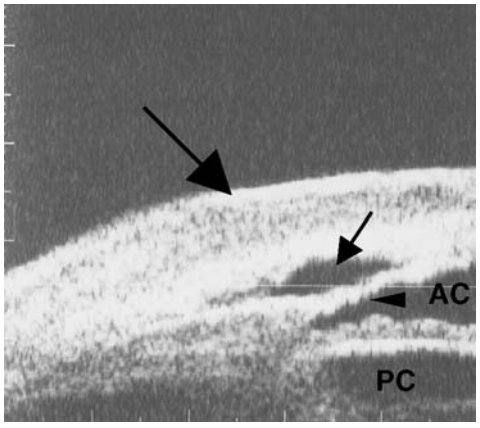

Fig. 1 UBM (radial section): A shallow and diffuse filtering bleb (*white arrow*) after deep sclerectomy with collagen implant, more than 1 year after surgery. The trabeculo-descemetic membrane is intact (*white arrowhead*) and separates the hyporeflexive intrascleral cavity (*black arrow*) from the anterior chamber (*AC*). *PC* Posterior chamber

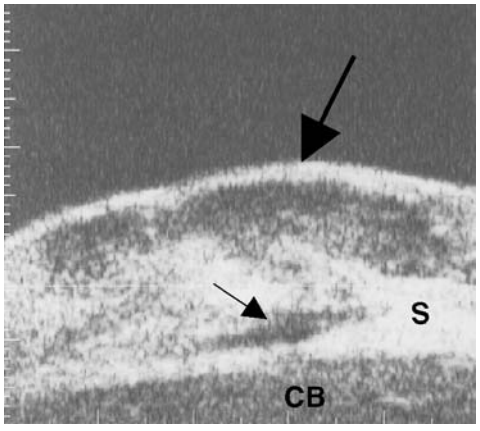

Fig. 2 UBM of the aqueous drainage in a subconjunctival space (*white arrow*) after sclerectomy with collagen implant and postoperative subconjunctival injection of mitomycin C. The *black arrow* indicates the intrascleral cavity; note the hyporeflexive connection to the subconjunctival space. *S* Sclera, *CB* ciliary body

aminations as a hyporeflexive subconjunctival layer) (Fig. 2). UBM further revealed an intrascleral cavity/tunnel (Fig. 3) in 39 eyes (92.8%). The volume of this hypoechoic area ranged from 0.11 mm^3 to 6.53 mm^3 (mean 1.8 mm^3). The intrascleral cavity volume was independent of IOP, the postoperative period, former surgery and any additional procedures. In 19 eyes we observed a hyporeflexive suprachoroidal space (Fig. 4). The mean IOP was significantly lower in eyes with suprachoroidal filtration (12.5±4.2 mmHg) than in those without suprachoroidal filtration (15.5±3.5 mmHg).

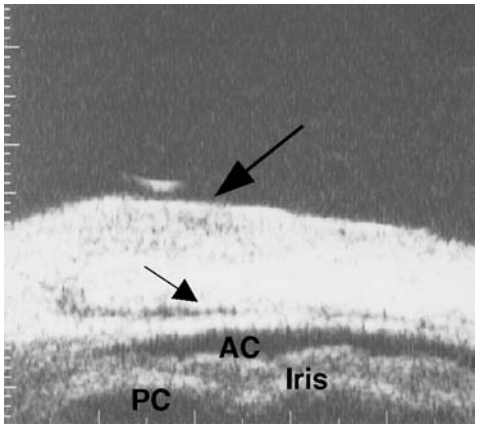

Fig. 3 UBM (transverse section). A small hyporeflexive subconjunctival space (*white arrow*) indicating a filtering bleb that was clinically not visible. The *black arrow* indicates the intrascleral cavity

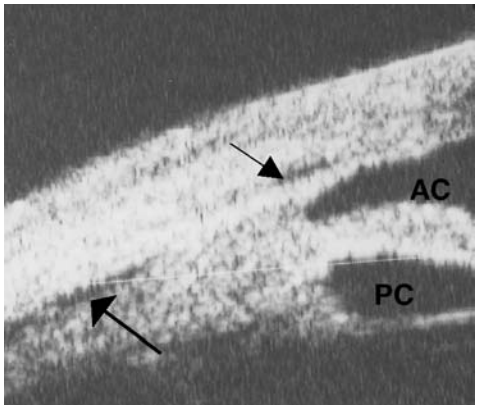

Fig. 4 UBM (radial section). Suprachoroidal hypoechoic space (*white arrow*) persisting more than 1 year after deep sclerectomy. The *black arrow* indicates the intrascleral cavity

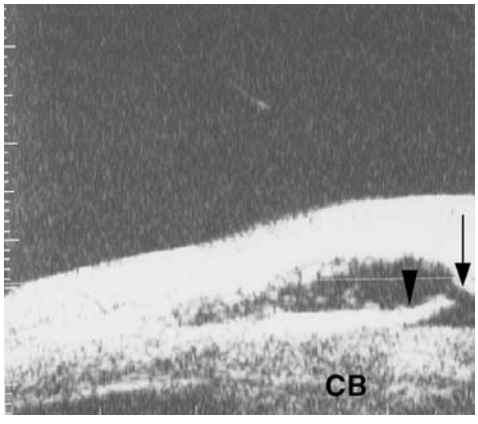

Fig. 5 UBM (radial section) of the intrascleral cavity that was opened with Nd:YAG laser goniopuncture (*black arrow*), interrupting the structure of the trabeculo-descemetic membrane (*white arrowhead*)

The mean IOP was 11.4±3.2 mmHg in eyes with deep sclerectomy and collagen implant (n=21), 12.5±2.5 mmHg in eyes with additional laser goniopuncture (n=15) (Fig. 5) was and 17.8±3.5 mmHg in eyes with additional mitomycin C or 5-FU.

Discussion

The use of UBM permits the detailed non-invasive observation of the inner ocular architecture after glaucoma surgery, whereas slit-lamp examination allows conjunctival (and sometimes superficial scleral) observation only. UBM revealed a small filtering bleb even in eyes where the slit lamp could not show it. Furthermore, high-resolution ultrasonography provides information about the intrascleral and choroidal conditions near the anterior chamber angle.

Ultrasound biomicroscopy has proved to be useful in studying filtering blebs after conventional trabeculectomy and has shown that blebs with low reflectivity and a visible route under the scleral flap correlate with a low IOP [1, 2, 12, 27].

Further UBM studies regarding deep sclerectomy with collagen implant aim to understand the aqueous humour outflow mechanisms of this non-perforating surgery [5, 6]. Only the trabeculo-descemetic membrane remains intact, and a very thin layer of the posterior part of the cornea divides the sclerectomy from the anterior chamber. The aqueous humour outflow bypasses the juxtacanalicular meshwork (inner wall of Schlemm's canal) and Descemet's membrane through the sclera. Mermoud and Vaudaux demonstrated with ocular ferritin perfusion after deep sclerectomy in porcine eyes the main outflow at the level of the anterior trabecula [18].

The removal of the inner scleral flap and the placement of the collagen implant facilitate the scleral passage to capillaries and veins within the subconjunctival tissue. Other outflow pathways such as intrascleral and episcleral canals, which are adjacent to collecting veins, facilitate the suprachoroidal drainage [25]. Using scatter diagrams for interpretation, we found the intrascleral lake size to be independent of the length of the postoperative period, IOP, former surgery and any additional procedures. Because of the different additional procedures (Nd:YAG laser, subconjunctival injections of mitomycin C or 5-FU) and different former operations, the groups for analysis became too small for statistical processing.

Despite the thin trabeculo-descemetics membrane the functional success of non-perforating glaucoma surgery in many patients may be limited by endothelial covering of the trabecular meshwork [9]. The resistance to aqueous outflow is still high, as shown by the high rate of surgical modifications (trabecular aspiration, trabecular stripping). The goniopuncture with Nd:YAG laser changes the non-penetrating procedure into a penetrating filtering procedure. Mermoud et al. [20] reported laser goniopuncture in 24–47% of their patients; the figure in this study was 35%. Hamard et al. [11] obtained satisfactory results by combining deep sclerectomy with application of 5-FU. In this study, in the case of a failed bleb – in 16.6% of the patients – we used a subconjunctival postoperative injection of mitomycin C and 5-FU. The deep sclerectomy with collagen implant reduced the IOP without additional procedures in 50% of the patients.

The deep sclerectomy can lead to permanent regulation of pressure without the risk of sudden decompression, thereby avoiding most of the possible serious complications of standard trabeculectomy [19, 24, 28]. However, it is a very delicate operation with a slow and difficult learning curve. Morphological studies have shown that the correct preparation of the deep scleral flap mainly succeeds, but variations are known [10]. Measurements with UBM of the residual trabeculo-descemetic membranes are difficult because of their size, approaching the limit of resolution of the ultrasound biomicroscope. In addition, microperforations of the underlying trabecula cannot be observed. Other factors, for example the suturing of the external flap or invisible microruptures of the trabecular meshwork, could be of importance for the early postoperative IOP.

In contrast, Dietlein et al. [10] described in a clinicopathologic examination that the morphology of the deep excised scleral flap showed no significant correlation to postoperative IOP. Even the unintentional microresection of the trabecular meshwork had no significant influence on later IOP.

Further UBM studies showed resorption of the collagen implant within 6–9 months after surgery, leaving a tunnel in the sclera [6]. This study regarded the different mechanisms of aqueous outflow pathways and lowering of IOP more than 1 year after surgery and after complete resorption of the collagen implant reported to take 6–9 months [5].

1. Subconjunctival bleb.- Following trabeculectomy, patients undergoing non-penetrating filtering operations have, in almost 100% of cases, a diffuse, sub-conjunctival bleb on the first day after surgery. Years after the operation, as assessed by UBM, all successful cases still show a low-profile, diffuse filtering bleb, indicating persistent filtration. This bleb is, however, usually smaller than the one seen after trabeculectomy and minimises the complications seen with large cystic blebs.
2. Intrascleral cavity. When deep sclerectomy is performed a certain volume of sclera is removed, ranging between 5 $mm^3$and 8 mm^3. If the superficial scleral flap does not collapse, this scleral volume may be transformed into an intrascleral filtering bleb. In order to keep this intrascleral volume different implants may be used, such as the collagen implant. Hyaluron-

ic acid or non-resorbable Hema implants are also used [15]. Using the UBM method, an intrascleral "lake" is observed in more than 90% of cases. The mean volume of the intrascleral flap is 1.8 mm^3. In the intrascleral "lake" the aqueous resorption may be different from that occurring in the subconjunctival bleb. The aqueous humour is probably resorbed by new aqueous drainage vessels, as demonstrated by Delarive et al. [8], whose study was performed in rabbits and showed the growth of new aqueous humour drainage vessels in the scleral space. Similar results were obtained by Nguyen et al. [21] using the same model and performing anterior segment fluorescein and indocyanine green angiography.

3. Subchoroidal space. Since the remaining layer of sclera over the ciliary body and peripheral choroid after deep sclerectomy is very thin, there may be a drainage of aqueous humour in the suprachoroidal space. Using UBM, it is possible to observe a fluid between the ciliary body and the remaining sclera in 45% of the patients studied years after the deep sclerectomy. Ultrasound biomicroscopy provides detailed information about the extension and width of suprachoroidal clefts, even when they are not visible in gonioscopy [13]. Aqueous humour in the choroidal space may reach the uveoscleral outflow and increase this outflow pathway [4]. It may also induce a chronic ciliary body detachment and reduce the aqueous production [16]. In this study there was a significant correlation with lower IOP, when a hyporeflexive suprachoroidal space could be demonstrated.
4. Schlemm's canal. When performing the deep sclerectomy dissection, Schlemm's canal is opened and unroofed. On either side of the deep sclerectomy the two ostia of Schlemm's canal may drain the aqueous humour into the episcleral veins. This mechanism may be more important after viscocanalostomy since Schlemm's canal is dilated with high-viscosity hyaluronic acid during the surgery [25]. It may also play a role when a Hema implant is used, since this implant has two arms inserted into two ostia of Schlemm's canal.

Ultrasound biomicroscopy is a useful method of assessing the anatomical results of eyes undergoing deep sclerectomy with collagen implant. It allowed us to understand the aqueous humour drainage mechanisms of this non-perforating surgery. The demonstrated combined outflow pathways might offer better IOP reduction. Further prospective non-randomised studies are needed to evaluate the advantages of non-penetrating and standard filtering procedures.

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