

# Ab Interno Trabeculectomy: Development of a Novel Device (Trabectome™) and Surgery for Open-Angle Glaucoma

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**Purpose:** To design an instrument to selectively remove trabecular meshwork and Schlemm's canal inner wall (SCIW), and demonstrate its effectiveness by histologic analysis of treated cadaveric human tissue.

**Methods:** The design parameters of the instrument were the ability to permanently remove a segment of trabecular meshwork and Schlemm's canal inner wall without causing damage to surrounding tissue, and to allow use with standard anterior segment surgical techniques and equipment via an ab interno approach. Treatment was applied to 20 segments of human corneoscleral rims. The treated areas were examined using a confocal microscope and compared with matching areas in untreated controls and simulated goniotomy.

**Results:** The resultant instrument system surgically removes the trabecular meshwork and Schlemm's canal inner wall from an anterior chamber approach. It consists of a disposable surgical handpiece with irrigation, aspiration, and electrocautery to focally ablate the target tissues. The attached console includes a high-frequency (550 KHz) electro-surgical generator and irrigation/aspiration controlled by a foot pedal. Histologic examination of specimens treated with the Trabectome™ displayed disruption of the trabecular meshwork and Schlemm's canal inner wall without damage to surrounding structures. The specimens treated by simulated goniotomy displayed significant damage to the outer wall of Schlemm's canal and the surrounding sclera. The controls showed no disruption or damage to any tissues.

**Conclusions:** The Trabectome™ system is designed for performing trabeculectomy via an ab interno approach. It successfully removed

sections of trabecular meshwork and Schlemm's canal inner wall with less injury to the adjacent tissue compared with goniotomy knife in vitro. Theoretically, this procedure should provide direct access of aqueous humor to Schlemm's canal.

**Key Words:** ab interno, glaucoma, gonio surgery, trabectome, trabeculectomy

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Surgical therapy for open-angle glaucoma can be divided into procedures directed at decreasing aqueous inflow or increasing outflow. The latter is more common, and can be further divided into external filtering procedures (such as trabeculectomy), and outflow surgeries that attempt to increase physiologic aqueous outflow through the angle pathway. Direct modification of the outflow pathway surgically is justified by the hypothesis that the majority of outflow obstruction in primary open-angle glaucoma (POAG) lies in the juxtacanalicular trabecular meshwork (TM) or inner wall of Schlemm's canal (SC).<sup>1,2</sup> Examples of this approach are goniotomy, trabeculotomy, and other mechanical disruptions of the trabecular meshwork, such as trabeculopuncture,<sup>3</sup> gonio-photoablation, laser trabecular ablation, trabecular aspiration,<sup>4,5</sup> and goniosurretagement.<sup>6</sup>

Goniotomy and trabeculotomy have attained success rates of 65% and greater in congenital glaucomas.<sup>7–9</sup> However, despite an initial favorable response in the treatment of open-angle glaucoma, utilizing goniotomy or trabeculotomy long-term review of surgical results showed only limited success in adults.<sup>10,11</sup> In retrospect, these procedures may have failed due to cellular repair and fibrosis mechanisms and a process of “filling in” of the clefts created surgically.

Goniosurretagement, also performed via gonioscopic lenses, is designed to mechanically disrupt and remove segments of trabecular meshwork using a spoon-like instrument. The ‘gonioscraper’ consists of a small handle and a slightly convex-shaped arm for intraocular use and resembles a cyclodialysis spatula. The tip of the instrument is shaped as a tiny bowl 300 μm diameter and with its edges sharpened. Analysis of this procedure indicates that, in addition to a complete disruption of the trabecular meshwork and internal wall of Schlemm's canal, it may also cause damage to intracanalicular septae and splitting along the posterior wall of Schlemm's canal.

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Although gonioscurettage showed success in 6 patients, no additional data has been published about this procedure.<sup>6</sup>

In the trabeculopuncture or goniotomy procedures, a Q-switched Neodymium (Nd-YAG) laser is used to create full-thickness holes in the trabecular meshwork.<sup>12</sup> Over time, the relatively small holes created close and the procedure fails. A similar procedure, gonioablation, involves the use of an excimer laser to ablate the trabecular meshwork. This demonstrated limited success in clinical trials, again presumably due to filling-in of surgically created defects.

Trabecular aspiration removes debris and pigment from the chamber angle with 100 mm Hg to 200 mm Hg suction using a specially designed irrigation-aspiration device to fit the chamber angle. This has not been successful over the long term according to the most recent publications.<sup>4,5</sup>

Non-penetrating deep sclerectomy (NPDS) has emerged as an alternative to standard filtration surgery and includes viscocanalostomy (VC) and deep sclerectomy with/without the collagen implant (DSCI). The purported mechanism of action of VC is to open Schlemm's canal by viscoelastic injection facilitating aqueous egress after it filters through an intact Descemet's membrane.<sup>13,14</sup> There should be no external filtration after viscocanalostomy. DSCI was developed with the same mechanism in mind, but may work as a filtering surgery similar to trabeculectomy. The collagen implant is used to maintain a deep scleral bed for aqueous to access either to Schlemm's canal or an external conjunctival filtering bleb. Filtration occurs either through a Descemet's window, or directly from the anterior chamber after laser perforation of Descemet's membrane postoperatively, required in approximately 40% of cases. In both VC and DSCI the outer wall and often inner wall of Schlemm's canal are stripped from the exposed area, but the trabecular meshwork is left intact.

In this article, we describe the development and results of in vitro application of ab interno trabeculectomy, utilizing a new technology, the Trabectome™. In theory, this new procedure should enhance aqueous outflow through normal outflow channels including Schlemm's canal and aqueous veins, without reliance on external filtration.

## METHODS

### Device and Procedure

The primary design goal was to develop an instrument to permanently ablate a strip of TM and SCIW so that the excised tissues will not re-approximate and close from fibrosis. Also, the device must create a very selective ablation so as to not damage surrounding structures, and must be able to gain access into the TM and SC complex reliably and maintain this position during ablation. Lastly, the procedure must take place under controlled conditions with constant anterior chamber maintenance and allow detailed viewing of the angle throughout the surgery.

### Histopathologic Analysis

Our in vitro studies were carried out on fresh donor human corneoscleral rims. The rims were obtained after the central corneal button was removed for penetrating keratoplasty and were maintained in holding media (Optisol, Bausch

& Lomb Surgical, San Dimas, CA). Each complete rim was divided into 3 segments, which were used for (1) control; (2) Maumenee goniotomy knife (Bausch & Lomb Surgical, Rochester, New York, USA) incision; or (3) Trabectome™ application. Various power settings ranging from 0.3W to 5.0W were used to assess the effects of the ablation on the surrounding tissue. All surgical maneuvers were performed under balanced salt solution with direct visualization through an operating microscope. During all procedures, the corneoscleral tissue was fixated by suction in an inverted position onto a device built for this purpose.

After the experimental manipulations, the specimens were fixed in 10% neutral buffered formalin and prepared for paraffin sectioning. Hematoxylin and eosin (H&E), periodic acid-Schiff, and trichrome stained sections were examined under a light microscope. A Zeiss LSM510 confocal microscope (Carl Zeiss, Inc., Oberkochen, Baden-Wuerttemberg, Germany) was used on H&E-stained sections to precisely measure the structures of the angle.

One specimen was serially sectioned to produce 48 consecutive 5-µm sections to determine the variability in measurement of the angle structures caused by processing artifact. The sections were stained with H&E, and the space between the severed ends of the TM was measured with the confocal microscope.

## RESULTS

### Device and Procedure

The Trabectome™ system consists of a disposable hand-piece connected to a console with irrigation and aspiration as well as an electrocautery generator. The handpiece tip is a 19.5-gauge instrument that will fit through a 1.6-mm corneal incision. The tip of the handpiece incorporates a specially designed insulated footplate (Fig. 1), and is pointed for ease of

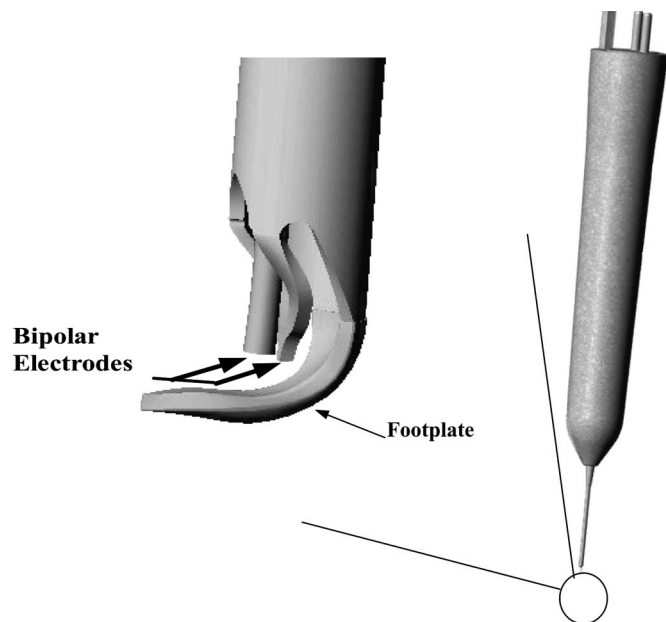


FIGURE 1. Trabectome™ handpiece tip.

insertion through the trabecular meshwork into Schlemm's canal. The size and shape of the tip of the handpiece were developed through testing in human donor corneal-scleral rims, and allow the footplate to guide the tip inside SC during ablation. The footplate provides a key function in lifting the TM and putting it on a slight stretch, positioning the tissue for maximal discharge effect from above while protecting underlying tissues. It is insulated with a multi-layered polymer coating that protects the outer wall of SC from thermal and electrical injury. This proprietary polymer exhibits an exceptional combination of thermal stability ( $>500^{\circ}\text{C}$ ), mechanical strength, biocompatibility, and chemical resistance under laboratory testing. Thin coats of the material are applied in multiple layers to the footplate and then thermally cured into a smooth, rigid, intractable polymeric film. In experimental studies on eye bank eyes, a temperature sensor was inserted between the footplate and Schlemm's canal, and indicated an increase of only  $1.2^{\circ}\text{C}$  while the handpiece is activated. The aspiration port is in close proximity (approximately 0.3 mm) to the cautery electrode, and removes debris generated during ablation. The irrigation is 3 mm from the surgical site and serves the dual purpose of keeping the eye pressurized and further dissipating heat energy.

The console includes an irrigation and aspiration (I/A) unit and high-frequency electrocautery generator (Fig. 2). The generator is a modified 800 EU unit from Aaron/Bovie (St. Petersburg, FL), and operates at a frequency of 550 kHz with adjustable power settings in 0.1 watt increments up to 10 watts. The standard power setting is 0.7 watts. The manufacturer's recommendation is not to exceed 1.5W of power during the procedure. The target tissue is disrupted and disintegrated by applying heat energy in bursts with a high peak power and low duty cycle. This means that the high energy bursts are bunched into small increments with comparably long time intervals in between. This accomplishes a disruptive and disintegrative, rather than a "cooking" effect such as that seen in cautery of blood vessels. The I/A has a pinch valve for on and off control of irrigation flow from a hanging bottle of balanced salt solution. The height of the bottle is adjusted manually with a standard height of 80 cm. The aspiration pump is peristaltic and allows for incrementally adjustable flow rates up to 10 mL/min, assuming a standard flow rate of 3 mL/min. Surgeon control is integrated through a foot pedal to activate irrigation, aspiration, and electrocautery power in a stepwise fashion similar to that used in phacoemulsification.

In an intact or living eye, a near limbal 1.6-mm temporal corneal incision is made parallel to the iris and viscoelastic is injected to inflate and stabilize the anterior chamber. The Trabectome™ handpiece is advanced nasally across the anterior chamber with the infusion on. A surgical gonioscopy lens is used to visualize the target trabecular meshwork nasally as the instrument tip is advanced across the anterior chamber. The tip of the footplate is inserted through the trabecular meshwork into Schlemm's canal. A foot switch activates the aspiration and electro-surgical elements that ablates and removes the strip of trabecular meshwork and inner wall of Schlemm's canal (Fig. 3) as the surgeon slowly advances the instrument along the meshwork in either a clockwise or counter-clockwise direction using the insertion site as a fulcrum. In

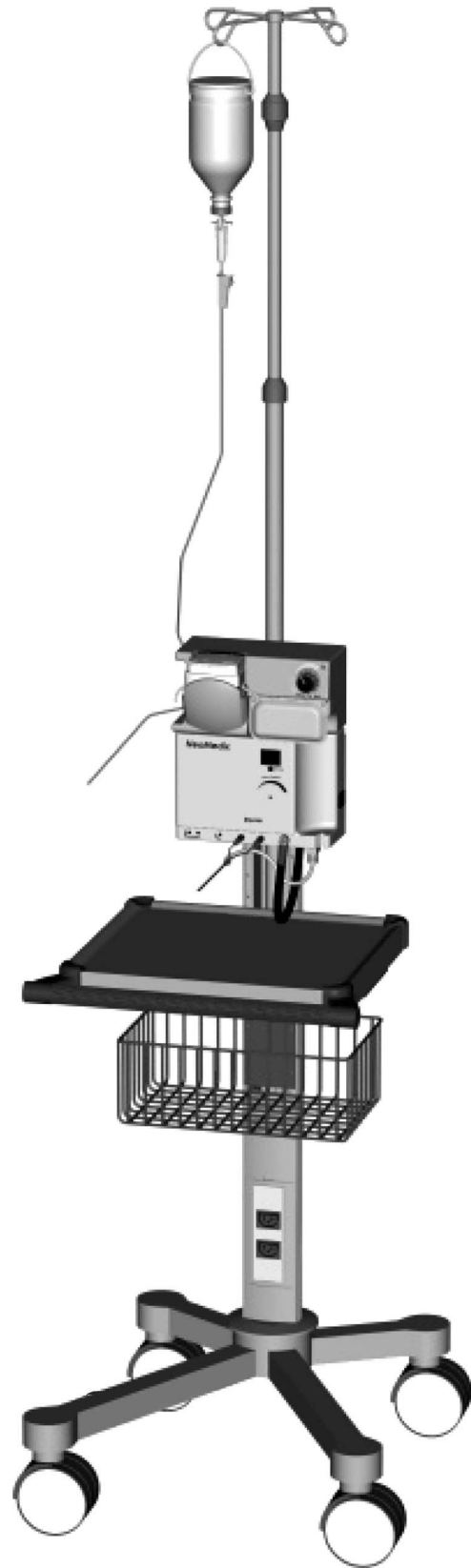
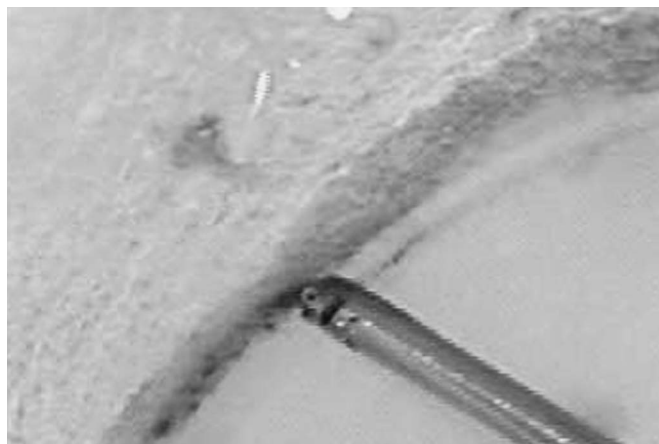


FIGURE 2. Trabectome™ Console System, mounted on a surgical cart.



**FIGURE 3.** The Trabectome™ device being applied to a section of a corneoscleral rim tissue. Intact darkly pigmented trabecular meshwork (TM) is seen in front (left) of the instrument as it is passed in a counterclockwise direction. The exposed Schlemm’s Canal (SC) appears as a white band behind (right) the instrument after the TM has been ablated.

typical cases, a 15° to 30° arc of tissue is removed in each direction, with a total arc of approximately 40° ablated.

### Histopathologic Analysis

Measurements of control tissue and experimental samples at different power levels are summarized in Table 1. The control tissue (Fig. 4A) shows well-preserved angle structures including peripheral cornea, Descemet’s membrane, Schwalbe’s line, TM, SC, sclera, and scleral spur. A small remnant of the ciliary muscle is seen in many of the specimens. There is no separation in the TM (0.0 μm), nor damage to the TM or SC in the controls.

One specimen treated with simulated goniotomy shows full-thickness disruption of the TM into SC; however, the anterior and posterior segments of TM are overlapping with no separation in the TM (Fig. 4B). The other specimen shows an incision extending 110.71 μm into the sclera, deep to SC (Fig. 4C).

Four specimens were treated with a power setting of 0.3W and the average gap in the divided TM is 79.55 μm (0–156.22 μm). This includes one specimen with an intact TM where SC was apparently not cannulated by the instrument’s footplate. Elimination of this specimen from the analysis results in an average 106.1 μm (49.0–156.22 μm) separation in the divided TM of the remaining 3 specimens.

Six specimens were treated with a 0.5W power setting. The average separation between the divided portions of the TM is 106.8 μm (0–331.57 μm). One specimen, specimen 10, shows damage to the superficial TM, which is widely separated although the deep TM appeared to be intact. This suggests that the footplate of the device may have scraped along the surface rather than passing completely through the TM into SC. Because of the irregular nature of the trabecular beams, it is possible that the deep TM is in fact disrupted with

**TABLE 1.** Results of Histologic Examination of Various Methods of Trabecular Meshwork Disruption

Specimen	Age/ Gender	Technique or Power Setting (W)	Separation in the Trabecular Meshwork (μm)	Coagulation*
1	67/M	Control	0	
2	10//M	Control	0	
3	42/F	Goniotomy	100.2	
4	42/F	Goniotomy	0	
5	67/M	0.3	49.3	+
6	10//M	0.3	0	
7	23/M	0.3	112.66	++
8	10//M	0.3	156.22	++
9	50/F	0.5	29.51	++
10	22/F	0.5	0	
11	23/M	0.5	182.29	
12	67/M	0.5	48.21	++
13	50/F	0.5	331.57	++
14	22/F	0.5	49.5	+
15	17/M	0.7	198.67	
16	53/M	0.7	0	
17	50/F	0.7	181.6	+
18	42/F	0.9	254.85	
19	22/F	1.0	0	
20	15/M	1.5	185.09	
21	53/M	2.5	110.05	
22	53/M	4.0	74.28	++
23	17/M	4.5	208.6	++
24	65/M	5.0	176.59	

\*Coagulation was subjectively graded between 1+ and 4+.

+Trace amounts of coagulation indicated by the change in staining characteristic of the tissue—becoming more eosinophilic. The affected area is not large enough to indicate tortuosity of the trabecular beams.

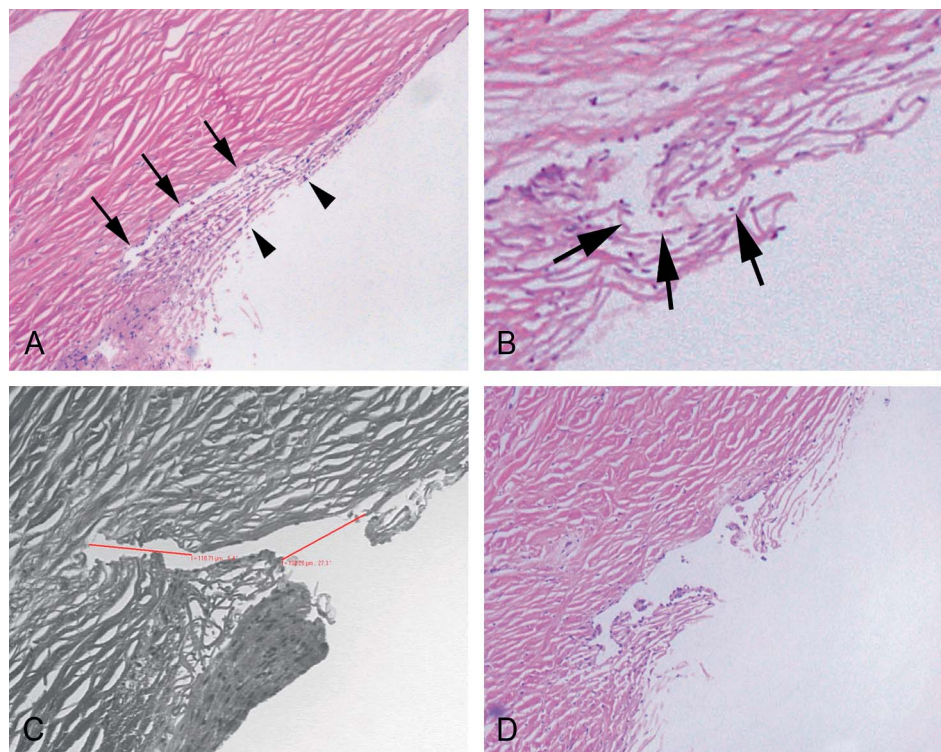
++Small clearly definable areas of coagulation indicated by thickening of the trabecular beams, an increase in tortuosity, retraction, and the above eosinophilic shift.

the opposite sides very closely apposed. Eliminating this specimen from the data analysis increases the average separation to 128.2 μm (29.51–331.57 μm). The largest separation in the TM of all the specimens studied was in specimen 13, which was treated with the TAIT system at 0.5W.

In the group treated with 0.7W power the mean separation in the TM is 126.8 μm (0–198.67 μm). This includes one sample (specimen 16) that appears to have TM disruption; however, the cut ends have reapproximated leaving no space between them. To assess variability in measuring techniques caused by processing artifact, the 48 consecutive serial sections of a specimen treated at 4.0W were analyzed and showed a mean space between the severed ends of the TM of 57.1 μm (26.98–123.88 μm) with a standard deviation of 20.1 μm.

At powers greater than 0.7W all samples but one sample (specimen 19, 1.0W power setting) show disruption of the trabecular meshwork with separation of the severed ends ranging from 74.28 μm to 254.8 μm. Specimen 19 shows disruption of the TM with reapproximation of the severed ends. Only one sample was available at each power setting of 0.9W, 1.0W, 1.5W, 2.5W, 4.0W, 4.5W, and 5.0W (Fig. 4D).

**FIGURE 4.** (A) Control specimen. Intact trabecular beams of the TM (arrowheads) are seen overlying Schlemm's canal (arrows). The peripheral cornea, TM, SC, and surrounding sclera are well preserved (H&E  $\times 40$ ). (B) Simulated goniotomy specimen with overlapping segments of the TM shows a clear space (arrows) between the anterior and posterior flaps of the severed TM; however, the two severed ends have returned to close approximation with one another (H&E  $\times 100$ ). (C) Simulated goniotomy specimen under the confocal microscope shows a 110.73- $\mu\text{m}$  incision into the sclera deep to SC. The confocal microscope was used to precisely measure the structures of the angle as marked by the red lines (H&E  $\times 50$ ). (D) Specimen treated with 2.5W showing removal of a large section of the TM (H&E  $\times 40$ ).



No evidence of thermal damage is seen deep to the TM or the surrounding tissues in any of the experimental specimens. Ten of the specimens display coagulation of the TM at the margin of the disruption caused by the Trabectome<sup>TM</sup> device. The anterior TM is affected more commonly than the posterior TM. The affected trabecular beams show a homogeneous eosinophilic staining with thickening and increased folding (Fig. 4D).

## DISCUSSION

The obstruction of aqueous outflow in primary open-angle glaucoma is thought to reside in the trabecular meshwork, or possibly inner wall of Schlemm's canal. Standard glaucoma filtration surgery acts as a bypass to this area, creating a direct opening from the anterior chamber to the subconjunctival space. Because of complications associated with external filtering surgery, especially with the use of antifibrotics, attempts have been made to directly enhance trabecular outflow and restore physiologic mechanisms of aqueous drainage via Schlemm's canal.

Barkan developed the earliest technique to increase outflow through SC by incising the trabecular meshwork and exposing SC to the anterior chamber directly.<sup>15</sup> Although very successful in cases of congenital or infantile glaucoma, results in adults with POAG have been disappointing. The presumed higher elasticity of the trabecular tissues in infants may allow the cut ends of the TM to retract, thus preventing them from re-approximating and closing from fibrosis.<sup>16</sup> Adult angle tissue has thicker trabecular beams with less elastic tissue morphologically perhaps explaining why the severed ends of the TM after goniotomy in adults are more likely to fold back into their

original position and scar together.<sup>17–20</sup> Complete excision or ablation of the TM would, in theory, decrease the likelihood of re-approximation and thereby reduce this mechanism for failure. The trabectomy ab interno system selectively removes the trabecular meshwork and may even promote some retraction of the incision edges by heat effect.

Trabectome<sup>TM</sup> ab interno trabectomy with the system (TAIT) was developed to create an opening from the anterior chamber directly to Schlemm's canal by removing the trabecular meshwork and inner wall of SC. It is therefore a true outflow surgery and is not dependent on filtration to the subconjunctival space. Thus, it has the theoretical advantages over external filtering surgery of re-establishing normal aqueous drainage in eyes with diminished outflow facility. It should reduce the risks seen in trabectomy and glaucoma drainage devices in the early and late postoperative periods including hypotony due to overfiltration or wound leaks, flat anterior chambers, choroidal effusions or hemorrhage, cataract, and extensive synechiae formation.<sup>21,22</sup> Ab interno trabectomy, because it does not create an external filtration, will not exhibit conjunctival wound leaks. Because it is not a penetrating filter, it should not cause hypotony from overfiltration. Because it does not rely on an external filtering bleb or glaucoma drainage device, there should be minimal risk of conjunctival breakdown and subsequent bleb infection or endophthalmitis. Although experimental studies have not shown collateral damage to structures adjacent to Schlemm's canal, there is risk to the endothelium, Decemet's membrane, the iris, and lens as for all ab interno procedures.

In the present study, the control specimens showed no breaks in the TM or damage to SC or surrounding tissue that

could be attributed to processing artifact. Of the 20 specimens treated with the TAIT system, the mean separation between the severed ends of the TM was 117.4  $\mu\text{m}$ . Only 4 specimens showed no separation in the TM. The results in two of those, specimens 6 and 10, appear to be due to surgical technique, with the instrument foot plate failing to pass into SC. Thus, only 2 of 18 specimens showed disruption of the TM without separation of the anterior and posterior margins. In these 18 samples the mean separation was 130.5  $\mu\text{m}$ .

Two specimens underwent simulated goniotomy. One specimen showed disruption of the TM with no apparent loss of the TM tissue; the other had a large separation between the severed ends of the TM; however, this was accompanied by a large incision into the sclera deep to SC measuring 110.71  $\mu\text{m}$ . The depth of incision with the TAIT system appears to be more precisely controlled than with goniotomy. None of the specimens treated with the TAIT system displayed mechanical damage to the deep wall of SC or the surrounding sclera. Additionally, the coagulation was confined to the TM, and there was no histologic evidence of thermal damage to the posterior wall of SC, the surrounding sclera, or the cornea.

No difference was seen in the size of the openings in the TM, presence of coagulation of the TM, or damage to surrounding structures with respect to the ablation power settings within the range studied (0.3W–5.0W). However, the sample size at each power setting is small and the sample sizes vary; so a trend might emerge if more samples were treated.

Possible sources for error in this study include variations in the tissue caused by processing and contraction during the tissue dehydration by ethanol and xylene solutions. There was variation in the position of the flaps seen in the serial sections; thus, there was variation in the size of the opening, probably due to processing artifact and mounting of the sections. In the serially sectioned segment, we observed a 57.1- $\mu\text{m}$  mean separation in the tissue with a standard deviation of 20.1  $\mu\text{m}$  over 48 serial 5- $\mu\text{m}$  sections. Another possible source of error is the age of the donors. Several of the donors were young; there could be age-related changes to the TM that may affect the retraction of the tissue.<sup>20</sup> Because of the small number of samples and the different number of samples in each group no significant trend could be found with respect to the age of the donor rim.

By improving aqueous outflow through the TM and SC system, ab interno trabeculectomy delivers a way to enhance outflow without external filtration. With proper patient selection and careful surgical technique, it has promise as a relatively simple and rapid surgical method for improving aqueous outflow. A recently completed clinical series of the device has shown effective intraocular pressure lowering in the treatment of open-angle glaucoma.<sup>22</sup>

## REFERENCES

1. Rosenquist R, Epstein D, Melamed S, et al. Outflow resistance of enucleated human eyes at two different perfusion pressures and different extents of trabeculectomy. *Curr Eye Res.* 1989;8:1233–1240.
2. Grant WM. Experimental aqueous perfusion in enucleated human eyes. *Arch Ophthalmol.* 1963;69:783–801.
3. Gaasterland DE, Bonney CH 3d, Rodrigues MM, et al. Long-term effects of Q-switched ruby laser on monkey anterior chamber angle. *Invest Ophthalmol Vis Sci.* 1985;26:129–135.
4. Jacobi Philipp C, Dietlein Thomas S, Krieglstein Günter K. Comparative study of trabecular aspiration vs trabeculectomy in glaucoma triple procedure to treat pseudoexfoliation glaucoma. *Arch Ophthalmol.* 1999; 117:1311–1318.
5. Jacobi PC, Dietlin TS, Krieglstein GK. Effect of trabecular aspiration on intraocular pressure in pigment dispersion syndrome and pigmentary glaucoma. *Ophthalmology.* 2000;107:417–421.
6. Jacobi PC, Dietlin TS, Krieglstein GK. Technique of goniosurgery: a potential treatment for advanced open angle glaucoma. *Br J Ophthalmol.* 1997;81:302–307.
7. Dascotte JC, Asseman R, Francois P, et al. [Surgical treatment of congenital glaucoma. Long-term results.] *J Francais d Ophthalmologie.* 1991;14: 229–233.
8. Mendicino ME, Lynch MG, Drack A, et al. Long-term surgical and visual outcomes in primary congenital glaucoma: 360 degrees trabeculectomy versus goniotomy. *J AAPOS.* 2000;4:205–210.
9. Gramer E, Tausch M, Kraemer C. Time of diagnosis, reoperations and long-term results of goniotomy in the treatment of primary congenital glaucoma: a clinical study. *Int Ophthalmol.* 1996;20:117–123.
10. Herschler J, Davis EB. Modified goniotomy for inflammatory glaucoma. Histologic evidence for the mechanism of pressure reduction. *Arch Ophthalmol.* 1980;98:684–687.
11. Luntz MH, Livingston DG. Trabeculectomy ab externo and trabeculectomy in congenital and adult-onset glaucoma. *Am J Ophthalmol.* 1977;83: 174–179.
12. Hill Richard A, et al. Laser Trabecular Ablation (LTA). *Lasers Surg Med.* 1991;11:341–346.
13. Johnson DH, Johnson M. Glaucoma surgery and aqueous outflow: How does nonpenetrating glaucoma surgery work? *Arch Ophthalmol.* 2002; 120:67–70.
14. Johnson DH, Johnson M. How does nonpenetrating glaucoma surgery work? Aqueous outflow resistance and glaucoma surgery [comment]. *J Glaucoma.* 2001;10:55–67.
15. Barkan O. Technique of goniotomy. *Arch Ophthalmol.* 1938;19:217–221.
16. Horstmann HJ, Rohen JW, Sames K. Age-related changes in the composition of proteins in the trabecular meshwork of the human eye. *Mech Ageing Dev.* 1983;21:121–136.
17. McMenamin PG, Lee WR, Aitken DA. Age-related changes in the human outflow apparatus. *Ophthalmology.* 1986;93:194–209.
18. Hirano K, Kobayashi M, Kobayashi K, et al. Age-related changes of microfibrils in the cornea and trabecular meshwork of the human eye. *Jpn J Ophthalmol.* 1991;35:166–174.
19. Ito S, Nishikawa M, Tokura T, et al. [Histopathological study of trabecular meshwork after trabeculectomy in monkeys.] *Nippon Ganka Gakkai Zasshi.* 1994;98:811–819.
20. Mac I, Soltau JB. Glaucoma-filtering bleb infections. *Curr Opin Ophthalmol.* 2003;14:91–94.
21. Edmunds B, Thompson JR, Salmon JF, et al. The National Survey of Trabeculectomy. III. Early and late complications. *Eye.* 2002;16:297–303.
22. Minckler DS, Baerveldt G, Alfaro MR, Francis BA. Clinical results with Trabectome™ for treatment of open angle glaucoma. *Ophthalmology.* 2005;112:962–967.