Chapter 2

Minimally Invasive Glaucoma Surgeries

Rita D Page and Sandra J Johnson*

Department of Ophthalmology, University of Virginia Medical Center, USA

*Corresponding Author: Sandra J Johnson, Department of Ophthalmology, University of Virginia Medical Center, Charlottesville, Virginia, USA, Email: smjeyes@gmail.com

First Published May 25, 2016

Copyright: © 2016 Sandra J Johnson

This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source.

Introduction

Glaucoma and cataracts are common co-morbidities in the aging population. Recently there has been an increased interest in minimally invasive glaucoma surgery, also known as micro-invasive glaucoma surgery (MIGS). These surgeries use clear corneal incisions and can be combined with cataract surgery to treat glaucoma and cataracts simultaneously [1]. As the approach through a clear corneal incision is familiar to most ophthalmologists, general ophthalmologists can be trained to do these surgeries and incorporate them into their practice.

Cataract surgery alone results in lowering of intraocular pressure (IOP) in patients who also have glaucoma. Most prospective and retrospective studies show an average IOP reduction from cataract surgery of approximately 2 mm Hg [2]. This is because a large cataract may compress the ciliary body and narrow the trabecular plates and walls of Schlemm's canal. Therefore, when the cataract is replaced with a thinner IOL, it may result in a modestly lower IOP [3]. The magnitude of the effect depends on the type of glaucoma a patient has. The effect of phacoemulsification is small with primary open angle glaucoma (POAG) (13% IOP reduction, 12% medication reduction), is moderate for pseudo-exfoliative glaucoma (PXG) (20% IOP reduction, 35% medication reduction) and marked in primary angle closure glaucoma (PACG) (30% IOP reduction, 58% medication reduction) [4].
However, combining MIGS with phacoemulsification has the potential to reduce IOP and glaucoma medications even more. For instance, Samuelson et al [3] found a greater IOP reduction on fewer medications when comparing a group of mild-moderate open-angle glaucoma patients who underwent cataract surgery only to a group who underwent cataract surgery combined with a MIGS procedure called iStent (Glaukos, Laguna Hills, CA, USA). The overall safety profile was similar between the two groups [3].

MIGS have gained popularity in recent years as an alternative glaucoma treatment because they lower IOP and decrease the burden of glaucoma drops while avoiding complications that occur with traditional glaucoma surgeries [5]. Patients on topical pressure reducing agents have difficulty with compliance due to complex dosing regimens, difficulty administering drops, poor self-efficacy, and financial considerations [6,7]. Chronic use of glaucoma eye drops can also result in corneal damage and inflammation [8].

While the two most common glaucoma surgeries, trabeculectomy with antimetabolites and glaucoma drainage devices are effective at lowering IOP, they have significant side effect profiles and high failure rates. The Tube Versus Trabeculectomy (TVT) study, which evaluated these two surgical approaches, found serious complications including infection, hypotony, inflammation, hyphema, suprachoroidal hemorrhage, tube obstruction, and bleb-related complications that resulted in the need for reoperation in about one in six patients and significant vision loss in about one in seven patients after 5 years of follow up. After 5 years of follow up, 46.9% of trabeculectomy with adjunct high dose mitomycin C and 29.8% of tube group had failure defined as IOP >21mmHg or not reduced by 20%, IOP <5mmHg, additional glaucoma surgery, or loss of light perception vision [9].

According to Saheb et al, [5] MIGS are defined by five characteristics: 1) ab interno microincision, 2) minimal trauma, 3) efficacy, 4) high safety profile, 5) rapid recovery. MIGS surgeries are performed through a clear corneal incision. The approach is familiar to general ophthalmologists and is easily combined with cataract surgery. The anatomic landmarks may need to be visualized with gonioscopy and then a device or incision placed within the angle. This micro-incision approach causes little trauma to the tissues involved and attempts to not disrupt normal anatomy. The devices that are placed are made of biocompatible material and enhance existing physiologic outflow. Because there is less postoperative inflammation, there is more rapid recovery. The conjunctiva is spared, allowing for future filtration surgery if needed. The approach has a high safety profile as it avoids scarring, hypotony, the need for post-operative procedures, and the devastating complications that occur with traditional glaucoma surgeries [5].
MIGS have shown promise in lowering IOP and reducing glaucoma medications; however, the efficacy of current MIGS is modest compared to trabeculectomy and glaucoma drainage devices. Therefore, in the glaucoma treatment algorithm, MIGS fit in between topical medications and more invasive surgeries. They are ideal for a patient with mild-moderate glaucoma who do not have advanced disease or require very low unmedicated IOP [5].

There are four mechanisms with MIGS with four different anatomic targets: 1) Schlemm’s canal and the trabecular meshwork, 2) the supracilliary space, 3) the subconjunctival space, 4) the ciliary processes. The first category bypasses or ablates the trabecular meshwork to improve trabecular outflow. The second connects the anterior chamber to the suprachoroid to create an alternative drainage route. The third creates an alternative outflow pathway to the subconjunctival space. The final category decreases the production of aqueous humor by ablating the ciliary processes [1,5]. All mechanisms result in lowering the intraocular pressure (Table 1).

<table>
<thead>
<tr>
<th>Anatomic Target</th>
<th>Mechanism</th>
<th>MIGs procedure</th>
</tr>
</thead>
</table>
| Schlemm’s Canal and Trabecular Meshwork (TM) | Bypass or ablate the TM to improve trabecular outflow | iStent, Hydrus, Trabecu
tome |
| Supracilliary Space | Connect the anterior chamber to the suprachoroid to create an alternative drainage route | CyPass |
| Subconjunctival Space | Create an alternative outflow pathway to the subconjunctival space | Xen |
| Ciliary Processes | Decrease production of aqueous humor by ablating the ciliary process | Endoscopic Cyclophotoocoagulation (ECP) |

Table 1: MIGS sorted by anatomic target and mechanism.

In this chapter, we will discuss cataract extraction (CE) and intraocular lens implantation in combination with the following MIGS procedures:

- Endoscopic Cyclophotocoagulation (ECP)
  - Micro-Endoscope Ciliary Process Ablation
  - EndoOptiks, New Jersey, USA
- iStent and iStent Inject
  - Trabecular Micro-Bypass Stent
  - Glaukos Corporation, Laguna Hills, California, USA
- Hydrus
  - Schlemm Canal Scaffold
  - Ivantis Inc., Irvine, California, USA
• CyPass
  • Ab Interno Suprachoroidal Microstent
  • Transcend Medical, Menlo Park, California, USA

• Trabectome
  • Ab Interno Trabeculectomy with Electrocautery
  • Neomedix Inc., Tustin, California, USA

• Xen
  • Ab Interno Trabeculectomy Procedure
  • Aquesys, Orange County, California, USA

A discussion on each MIGS procedure will follow, including methodology, instrumentation, complications, and outcomes data.

Micro-Endoscope Ciliary Process Ablation: Endoscopic Cyclophotocoagulation

Methodology

Endoscopic cyclophotocoagulation (ECP) was introduced in 1992. It involves direct application of diode laser energy to ciliary processes through direct visualization, therefore causing less pain, inflammation, hypotony, and visual loss than transcleral cycloablation [10]. Ablating ciliary processes decreases production of aqueous humor, which reduces IOP [11].

Instrumentation

In the ECP procedure, a 810 diode laser is used to cycloablate the ciliary processes (Figure 1). This surgery can be performed through one clear cornea incision to treat 240 to 300 degrees. To treat up to 360 degrees of ciliary process, two incisions can be used [11].

Figure 1: The endo probe ablating the ciliary processes. Photo courtesy of Beaver Visitec, Little Silver, NJ, USA.

Complications

Traditionally, cycloablation was reserved for end-stage glaucoma that was refractory to other therapies, due to a high rate of complications including inflammation and phthisis [12]. The trans-scleral approach to cyclophotoco-
agulation could not titrate the power applied and required high power to reach the targeted tissue. However, ECP directly ablates the ciliary processes and is easier to titrate, so it has a lower rate of complications [11]. Therefore, indications for ECP have expanded to include patients with better visual prognosis [12]. Common complications of ECP include inflammation and hyphema. Short-term hypotony has also been described, although this was rare [11]. When ECP is combined with phacoemulsification, complication rates and visual acuity outcomes are similar to those of phacoemulsification alone [12].

**Discussion of Data on Outcomes**

Morales et al, [13] investigated the success of ECP when combined with cataract extraction (CE) in patients with advanced glaucoma in a retrospective study of 104 eyes. They defined absolute success as IOP ≤15 mm Hg without medication and qualified success as IOP ≤ 15 mm Hg with medications. At 1 year of follow up, they found that mean IOP decreased from 17 to 14.7 mm Hg; however, absolute success was found in only 11.9% of patients. Qualified success was demonstrated in 72.3% of eyes. Different types of glaucoma had varying success rates. POAG had a higher absolute and qualified success rate than PACG and PXG. Although absolute success rate was low, ECP did decrease the burden of glaucoma medications. While 75% of patients required more than three medications for IOP control before surgery, only 46% required this many medications after ECP [13].

Francis et al, [12] studied outcomes in ECP combined with CE versus CE alone. In their prospective nonrandomized matched-control study of 160 medically-controlled POAG eyes with visually significant cataracts, they found that combined ECP and CE resulted in greater reduction of IOP and glaucoma medications than CE alone. This finding was statistically significant. Patients who underwent combined ECP and CE experienced a mean IOP decrease from 18.1 ± 3.0 to 16.0 ± 3.3 mm Hg at 2 years, while their glaucoma medications decreased from 1.5 ± 0.8 to 0.4 ± 0.7 drops [12].

In a retrospective consecutive case review of combined ECP and CE by Kahook et al, [11], one site versus two site ECP was compared. These investigators found that two site ECP resulted in greater IOP lowering and less dependence on glaucoma medications than one site ECP. Most of the patients in the study had POAG, but they also included neovascular glaucoma (NVG), traumatic glaucoma, closed angle glaucoma, and normal tension glaucoma [11].

**Trabecular Micro-Bypass Stent: iStent and iStent Inject**

**Methodology**

The iStent is approved in the United States for mild-to-moderate POAG being treated with glaucoma medications [14]. The iStent is a tiny device that is implanted
through the trabecular meshwork into Schlemm’s canal with a pre-loaded inserter (Figure 2 and Figure 3). One or multiple stents can be placed [5]. This device allows the aqueous humor to bypass the juxtacanicular trabecular meshwork, which is the area of highest outflow resistance in POAG [14]. Retention arches keep the stent in place, and the half cylinder model prevents obstruction from fibrosis over the tip [15]. The iStent Inject is the second generation device that is certified only in Europe. It is a smaller device that directly implants through the trabecular meshwork into Schlemm’s canal. It has the advantage of easier surgical technique, as there is no sideways sliding of the stent required for positioning. In addition, two devices can be implanted with a single inserter without having to reenter the eye [15].

Figure 2: Insertion of the iStent under gonioscopy (Photo used with permission of Glaukos Corporation, Laguna Hills, California, USA).

Figure 3: Slit lamp view of the inserted iStent (Photo used with permission of Glaukos Corporation, Laguna Hills, California, USA).
Instrumentation

The iStent is snorkel-shaped device that is made of heparin-coated titanium (Figure 4) [5]. It is 1mm in length by 0.3mm in height, making it the smallest US Food and Drug Administration approved implantable device (Figure 5) [15]. The iStent inject is the 2nd generation model that is certified in Europe. It is also made of heparin-coated titanium but it is bullet-shaped [5]. It is smaller than the first generation device at only 360 microns in length [15].

![Figure 4: The snorkel-shaped iStent device (Photo used with permission of Glaukos Corporation, Laguna Hills, California, USA).]

Complications

Complications include stent obstruction and malposition, though they are rare (<5%) and not associated with chronic ocular morbidity [2,14,16]. In the iStent Study Group, the pivotal randomized-controlled multicenter clinical trial, most complications occurred in the early postoperative period and were associated with cataract surgery. Other complications that occurred in the 2 years of follow up included posterior capsule opacification (6%), elevated IOP (4.3%), stent obstruction (4.3%), blur-
ry vision (3.4%), and stent malposition (2.6%). Notably, there was no difference between the iStent group and the control group in complications, and there was no inflammatory response from implantation of the stent [3,16].

Discussion and Available Data on Outcomes

An early randomized double-masked clinical trial conducted by Fea et al, [2] compared 12 patients with combined iStent and CE with 24 controls who underwent CE alone. They found a statistically significant greater IOP reduction in the combined group versus the control group (17.9 ± 2.6 mm Hg to 14.8 ± 1.2 mm Hg at 15 months versus 17.3 ± 3.0 mm Hg to 15.7 ± 1.1 mm Hg). After washout of glaucoma medications 16 months after surgery, mean IOP in the combined group was 16.6 ± 3.1 mm Hg, which was significantly lower than the mean of 19.2 ± 3.5 mm Hg in the control group [2].

One of the largest studies of the iStent was a multicenter, prospective, randomized, controlled trial performed by the iStent Study Group. It included 240 eyes with cataract and POAG, PXG or pigment dispersion glaucoma (PDG). They were randomized to CE alone (control group) or CE and iStent combined (treatment group). At two years of follow up, they found that 61% of the eyes in the treatment group and 50% of the eyes in the control group achieved the primary efficacy endpoint of an IOP of ≤ 21 mm Hg without medication. This difference was statistically significant. Glaucoma medication use was lower in the iStent group at 12 and 24 months, but only statistically significant at 12 months of follow up [3,16].

Khan et al, [17] compared two different MIGS procedures in a retrospective interventional comparative case series. They examined the outcomes of combined CE with 2 iStents versus combined CE with trabectome. They included POAG, PXG, and PDG. At 12 months of follow up, they found a lower mean IOP and a lower median number of glaucoma medications in the stent group. However, both types of surgery significantly reduced IOP and medication use. They found that 39% in the stent group and 14% in the trabectome group achieved “success” at 12 months, which they defined as IOP <18, no glaucoma medications, and no reoperations. The stent group also had reduced incidence of postoperative hyphema compared with the trabectome group (4% vs. 23%) [17].

A review of 3 randomized controlled trials and 7 case series that tested the outcomes of single or multiple iStents with or without CE was conducted by Le et al [15]. They found that IOP reduction ranged from 16% to 33% and medication reduction ranged from 0.5 to 2.0 agents in these studies. They also reviewed the data available for the second generation iStent Inject. Only 2 case series were available, and both studies examined the effect of 2 stents. They discovered an IOP decrease of almost 40% and medication reduction of 1 agent [15].
Malvankar-Mehta et al, [18] also performed a systematic review and meta-analysis of the iStent literature to determine how much of the IOP lowering effect in combined procedures was due to the iStent versus CE alone. They included 37 studies with 2495 total eyes. They determined that IOP decreased by 4% from baseline with CE alone, 9% with 1 stent and CE, and 27% from 2 stents and CE. They concluded that compared to CE alone, iStent combined with CE caused significant IOP reduction with a standard mean difference of -0.46, 95% CI (-0.87, -0.06). For glaucoma medications, they found a mean reduction of 1.01 agents from CE alone, 1.33 after 1 stent, and 1.1 after 2 stents. Compared with CE alone, iStent showed significant decrease in glaucoma medications (standard mean difference of -0.65, 95% CI (-1.18, -0.12). However, they did note that there was significant heterogeneity in the data between the studies due to different populations, surgical techniques, peri-operative management, follow-up timing, facilities used, and rates of complications [18].

**Schlemm Canal Scaffold: Hydrus**

**Microstent**

**Methodology**

The Hydrus Microstent is a Schlemm canal scaffold that is implanted through a clear corneal incision under direct gonioscopic view. It is inserted through the trabecular meshwork using a manual inserter [5]. It decreases aqueous outflow resistance by two mechanisms. First, it bypasses the trabecular meshwork, which is the site of highest resistance. Second, it dilates and stents three clock-hours of Schlemm’s canal. Therefore, it works like a scaffold to allow aqueous to drain to multiple collector channels (Figure 6) [14].

**Figure 6:** Schematic of trabecome in surgical position inside eye. (Photo used with permission of Neomedix Inc., Tustin, California, USA).

**Instrumentation**

The Hydrus Microstent is a crescent-shaped implant that is made of nitinol, a metal alloy of nickel and titanium. It is open posteriorly and contains three windows along its 8mm length (Figure 7) [5].
Complications

Two studies have shown the biocompatibility of the Hydrus Microstent using animal eyes. In one study, 2 non-human primates were implanted with the Hydrus. After 90 days of implantation, the histology from these eyes were compared to that of 1 sham control. In another study, 8 rabbits each were implanted with the Hydrus in one eye. Then after 6 months, the histology of the implanted eye was compared to that of the unimplanted eye, or the sham eye. No significant acute or chronic inflammatory response, granulation response, or fibrosis in the outflow system or adjacent tissues was found [19].

Fea et al, [20] examined whether or not the Hydrus Microstent causes endothelial cell loss. Although cataract surgery itself can cause damage to the corneal endothelium, these investigators tested if the Hydrus would cause more damage, since it is implanted in the anterior chamber angle very close to the corneal endothelium. They included 25 eyes with cataracts and 37 eyes that had cataracts and POAG in the study. They divided the POAG group into group A, which underwent CE alone and group B which underwent CE and Hydrus implantation. They examined the endothelium before and 6 months after surgery. Before surgery, all groups had similar endothelial cell parameters, but after surgery, all groups lost endothelial cells, with Group 1 losing 9.1%, Group 2A 17.24%, and group 2B 11.71%. They concluded that the change in endothelial cells after Hydrus implantation was comparable to that of those who underwent CE alone [20].

In the HYDRUS II study, a multicenter, randomized, controlled trial, notable complications associated with Hydrus implantation were focal peripheral anterior synechiae (1-2mm in length). Otherwise the complication frequency was similar to that of CE alone. There was no difference in visual acuity between the Hydrus plus CE combined group and the CE alone group [21].

Discussion and Available Data on Outcomes

The HYDRUS II study investigated the effectiveness of the Hydrus microstent with a prospective, multicenter,
randomized, single-masked controlled clinical trial. One-hundred eyes were randomized into two groups: CE with Hydrus microstent versus CE alone. The investigators performed a washout of hypotensive medications at 12 and 24 months. They measured the “response to treatment” which they defined as 20% or more decrease in washout diurnal IOP at 12 and 24 months of follow up compared to baseline. They found that the Hydrus plus CE group had a statistically significant higher “response to treatment” at 24 months than CE alone (80% versus 46%). The washout diurnal IOP of the Hydrus plus CE group was significantly lower at 24 months than CE alone (16.9 ± 3.3 mm Hg versus 19.2 ± 4.7 mm Hg). Finally, the proportion of patients using no glaucoma medications was significantly higher in the Hydrus plus CE group (73% versus 38%). By comparing their 24 month results to that of the 24 month results of the randomized controlled trial that evaluated the outcomes of the iStent, Pfeiffer et al assert that the data suggests a more durable treatment effect using the Hydrus. However, these two devices have not been compared in a clinical trial directly [21].

**AB Interno Supraciliary Microstent: CyPass**

**Methodology**

The CyPass implant is inserted with gonioscopic view, ab interno into the supraciliary space with a manual inserter. Aqueous enters through its opening in the anterior chamber and passes into the supraciliary space through multiple fenestrations that are present along the length of the device (Figure 8) [5]. Its mechanism is similar to the manner by which prostaglandin analogue drops work; they both decrease IOP by increasing uveoscleral outflow [14].

**Figure 8:** Close up of the implant within the needle for injection. (Photo courtesy of Aquesys, CA, USA.)

**Instrumentation**

The CyPass implant is made with polyamide, which is both biocompatible and non biodegradable. It is 6.35mm long and has a single lumen of 300 µm [5]. Currently, the CyPass Micro-Stent is an investigational device only in the United States and has not been approved by the U.S. Food
and Dug Administration for widespread use. It has been approved in the European Union.

Complications

In a study of concomitant CyPass implantation and CE in 184 eyes with POAG and cataract, there were no sight-threatening intraoperative complications. They found no major surgical complications such as endophthalmitis or retinal or choroidal detachment. There were no cases of hypotony maculopathy, corneal edema that lasted more than 1 month, suprachoroidal hemorrhage, or iris atrophy. Common complications included transient early hypotony (13.8%) and transient IOP increase (10.5%) [22]. In another study that evaluated the safety of CyPass implantation in 65 patients with POAG, the most common adverse events included IOP increases >30 mm Hg beyond 1 month (11%), transient hyphema (6%), and cataract progression (12% of phakic eyes). They did not report transient early hypotony, but there were no cases of hypotony that persisted beyond 1 month or hypotony maculopathy. There were no serious intraoperative events or major adverse events in this series [23].

Discussion and Available Data on Outcomes

In an open-label interventional multicenter safety study, Hoeh et al investigated the outcomes of patients with coexisting POAG and cataract who underwent implantation with the Cypass micro-stent and CE. The investigators divided the 184 patients with Shaffer grade 3 and 4 POAG and cataracts who were enrolled in the study into two groups. Cohort 1 had uncontrolled (≥21 mm Hg) and cohort 2 had controlled (<21 mm Hg) medicated IOP at baseline. They found that cohort 1 had a 37% IOP reduction with more than a 50% reduction in glaucoma medications at 6 months of follow up. Cohort 2 had a 71.4% reduction in glaucoma medications at 6 months of follow up. However, almost half of the patients who were initially enrolled were lost to follow up by 6 months [22].

Garcia-Feijoo et al conducted a multicenter, single-arm interventional study to evaluate the safety and efficacy of the CyPass Micro-Stent. They enrolled 65 eyes and monitored adverse events, IOP changes, and need for IOP lowering medications for 12 months after CyPass implantation. They found that IOP decreased by 35% from a baseline of 24.5 ± 2.8 mm Hg to 16.4 ± 5.5 mm Hg at 12 months. The mean medication usage was also reduced from a baseline of 2.2 ± 1.1 to 1.4 ± 1.3 agents at 12 months. Both of these findings were statistically significant [23].

Finally, Hoeh et al published another study of 167 eyes with POAG and cataract who underwent combined CE and CyPass implantation. The follow up of this study was better, with a 30% attrition rate due to loss to follow up and premature exit of the study due to need for subsequent glaucoma surgery. Mean IOP was reduced by 14% from a baseline of 20.2 ± 6.0 mm Hg to 15.9 ± 3.1 mm Hg. Glaucoma medications were reduced by 49% in cohort 1 (medicated IOP ≥21 mm Hg at baseline) and by 75% in cohort 2 (medicated IOP <21 mm Hg at baseline).
However, reintroduction of IOP lowering medications was at the discretion of individual investigators allowing for bias. There was a lack of a control group as well, so the effect from the CE alone versus the CyPass is uncertain. A medication washout period was not included in the study, which could have allowed for better assessment of IOP lowering that is attributable to the CyPass alone. The investigators note that these limitations are being addressed in the COMPASS trial, a large, randomized, controlled trial of the CyPass Micro-Stent that is underway [24].

**AB Interno Trabeculectomy with Electrocautery: Trabectome**

**Methodology**

The trabectome utilizes a high frequency electrocautery device to ablate the trabecular meshwork and inner wall of Schlemm’s canal (Figure 9). This removes the primary site of abnormal flow resistance in POAG, thus increasing aqueous humor outflow and decreasing intraocular pressure [25].

![Figure 9: XEN injector. (Photo courtesy of Aquesys, CA, USA).](image)

**Instrumentation**

The Trabectome was approved by the United States Food and Drug Administration in April 2004. It was first used in the United States in January 2006. This device is made up of a 19.5 gauge handpiece and insulated footplate (Figure 10) [25]. It is controlled with a foot pedal with stepwise activation of irrigation, aspiration, and cautery. The irrigation keeps the anterior chamber formed and dissipates heat. The aspiration is next to the cautery electrode [5].
Complications

Since the manufacturer of the trabectome required users to report the outcomes of their first 20 cases, the initial studies of this device include patients from multiple centers. However, reporting of only 1 year of follow up was required, so long-term data on complications is limited. The most common complications reported were postoperative hyphema on post-operative day one (73%) and IOP elevations of more than 10 mm Hg above baseline (22%) at a median of 24 days postoperatively [25]. The ab interno trabeculotomy approach causes a permanent opening in the blood-aqueous barrier, so spontaneous hyphemas can occur months or years after surgery [25].

Discussion and Available Data on Outcomes

Bussell et al, [26] conducted a prospective study to examine the effect of the trabectome in narrow angle glaucoma. Patients were divided into two groups by the degree of angle opening. Patients with Shaffer angle grade (SG) ≤ 2 were compared to those with SG ≥ 3 as well as to open angles. They compared the outcomes of these groups, including IOP, glaucoma medications, complications, secondary surgery, and “success” which was defined as IOP <21 and >20% reduction without further surgery. The investigators concluded that SG ≤ 2 was not associated with worse outcomes for trabectome or trabectome combined with CE. However, narrow anterior chamber angle is considered a relative contraindication for trabectome surgery.

In a retrospective interventional single-surgeon case series, Ahuja et al, [25] studied the outcomes of trabectome surgery. There were 88 cases of trabectome only surgeries and 158 cases of combined trabectome with CE included in the study. The outcomes measured included criteria A (IOP of ≤ 21 or ≥ 20% reduction in IOP) and criteria B (IOP of ≤ 18 mm Hg and ≥ 20% reduction in IOP). The study found a success rate of 62% for criteria A and a 22% success rate for criteria B at 24 months. Failure was defined as not meeting the above criteria or requiring subsequent surgery or increased glaucoma medications.

Figure 10: The design of the Kahook blade. (Photo courtesy of New World Medical, CA, USA).
POAG was associated with a three-fold increase rate of failure, and past argon laser trabeculoplasty was associated with a two-fold increase in likelihood of failure. However, PXG patients had a two-fold increased likelihood of success. Almost 30% of patients required a subsequent surgery on average 10 months post-trabectome. At 24 months post-operatively, the mean IOP was reduced by 29% with a mean IOP of 15.3 ± 4.6 mm Hg and glaucoma medications were reduced by 38% to 1.9 ± 1.3. The more stringent criteria (criteria B) showed a low success rate, so the authors concluded that trabectome surgery was appropriate for a patient who desires a lower risk surgery and who requires a more modest IOP reduction with a target IOP of 21 mmHg or above. The authors proposed that their study’s better follow up and retention rate might explain why they found a lower success rate for IOP reduction.

Argon laser trabeculoplasty (ALT) is known to cause scarring of the trabecular meshwork, Schlemm’s canal, and collector channels, making trabectome surgery less effective [27]. Therefore, Klamann et al, [28] investigated whether prior selective laser trabeculoplasty (SLT) causes trabectome surgery to be less effective with a retrospective comparative cohort outcome study with 6 months of follow up. In particular, they looked at patients who underwent combined trabectome and CE surgery after SLT treatment. They found that failed prior SLT treatment does not negatively impact outcomes for combined trabectome and CE surgery. SLT treatment was actually found to have a positive impact on combined trabectome and CE outcomes for patients with PEX and PG.

In a small case-matched retrospective study, Widder et al, [29] determined if CE combined with trabectome and trabecular aspiration had different outcomes than CE combine with trabecular aspiration. There were 30 patients in each group. The investigators found that the triple procedure was more effective in lowering IOP compared to the double procedure in PXG.

Luebke et al, [30] investigated the visual acuity outcomes of trabectome surgery by conducting a retrospective observational study. They compared visual acuity outcomes of patients who underwent CE combined with trabectome (137 eyes) versus a control of 1704 eye that had cataract surgery alone. They found that visual outcomes were similar in both groups. They found a slightly higher rate of cystoid macular edema in the combined group (2.2% vs. 1.9%); however, the 2 cases improved with treatment and visual acuity improved.

### AB Interno Trabeculectomy

**Procedure: Xen Implant**

**Methodology**

The Xen implant utilizes the same mechanism as traditional glaucoma surgeries such as trabeculectomy and
tube surgeries, by allowing for outflow of aqueous from the anterior chamber into the subconjunctival space. However, it achieves this without dissecting the conjunctiva. It is designed to cause less hypotony than these traditional surgeries as well [31]. In the United States, it is an investigational device as it has not yet been approved by the US Food and Drug Administration.

**Instrumentation**

The Xen gel implant was designed to have the optimum sized lumen to avoid hypotony but to maximize outflow. It is 6mm long and the width varies by model. There are three models that are named by their diameters: XEN140, XEN63, XEN45, with diameters of 140um, 63um, and 45um respectively [32]. The Xen gel implant is a hydrophilic tube composed of porcine gelatin crosslinked with glutaraldehyde [32]. This material is soft, biocompatible, and non-inflammatory. It is injected through a clear corneal incision using a preloaded IOL-like injector.

**Discussion and Available Data on Outcomes and Complications**

As the Xen implant is still an investigational device in the United States and has not yet been approved by the US Food and Drug Administration, there is limited data on outcomes and complications.

Lewis et al, [32] conducted a review of the Xen implant that describes the data that is available on the Xen including data to support its flexibility, stability, biocompatibility, and viability. They describe its theoretical benefits over traditional glaucoma surgeries, including ab interno placement that is minimally invasive and conjunctival sparing as well as decreased adverse events including a decreased rate in hypotony. The Xen is made of a material that is soft and flexible when hydrated. Because the implant softens within 1-2 minutes of implantation, it is able to conform to surrounding tissue, which avoids migration or erosion [32]. For instance, the Xen 45 is about 100 times more flexible than the silicone tubing used in tube shunts, rendering it less likely to exert force on the tissue layers as it exits the anterior chamber and bends at 35 degrees under the sclera [32]. The material is also resistant to hydrolytic degradation. Ten year accelerated flow testing has shown no changes in lumen or wall thickness. Implantation of the device in dogs and nonhuman primates showed no foreign body reaction. Viability studies in human eyes showed that the lumen did not occlude [32].

A major complication of traditional glaucoma surgeries is hypotony, which can result in loss of vision. The Xen implant was designed to prevent hypotony. The ideal length and width for the device was calculated by the Hagen-Poiseuille equation to design an outflow tract that would prevent hypotony [31]. Sheybani et al [31] described the fluidics of the Xen implant and compared it to
the fluidics of two commonly used non-valved glaucoma devices, the Ex-Press implant and the Baerveldt, to determine if the Xen implant had any advantage in preventing hypotony. They used a syringe pump and pressure transducer at multiple flow rates and compared pressure differentials across the Xen implant, the Ex-Press implant and the 10mm silicone tubing from the Baerveldt. They found that the Xen micro-fistula was able to supply backpressure above the level that would cause hypotony without the use of a valve. The pressure differential for the Xen implant was 7.56mm Hg at physiologic flow rate. At the same flow rate, the Ex-Press implant and the 10mm of tubing from the Baerveldt had pressure differentials of 0.09mm Hg and 0.01mm Hg. This study concluded that fluid dynamics showed that the Xen implant could help prevent hypotony [31].

Gonioscopy Assisted Transluminal Trabeculotomy (GATT)

Methodology

This procedure utilizes a micro catheter or suture to perform trabeculotomy ab interna, which spares the conjunctiva [33,34]. The goal is to unroof the trabecular meshwork and inner wall of Schlemm’s canal to remove the primary site of abnormal flow resistance in POAG, thus increasing aqueous humor outflow and decreasing intraocular pressure. This procedure has been adapted from 360 degrees trabeculotomy using a suture in adults and a micro catheter as used in congenital glaucoma [35,36].

Instrumentation

This procedure requires two paracentesis sized incisions to access the trabecular meshwork. The procedure is done before the cataract extraction. Some viscoelastic is placed to maintain the anterior chamber. A Swan-Jacobs goniolens to view the trabecular meshwork and a micro-surgical blade is used to create a small 2mm goniotomy site in which to introduce the catheter or suture. The illuminated micro catheter (Itrack; Ellex, Adelaide Australia) has a blinking tip that can be seen as it is threaded along Schlemm’s canal counter clockwise with microsurgical forceps. If a suture is used it is marked at its tip with a sterile pen and then blunted with cautery and the tip color can be visualized as the suture is threaded. The authors suggest using 4-0 or 5-0 clear nylon. Once the tip completes the 360 degrees the two ends of the catheter or suture are pulled and unroof the canal of Schlemm. If a full 360 degrees cannot be cannulated with either method then a cut down can be made into the TM to obtain the tip and perform some trabeculotomy and then the canal recannulated to complete the remaining part of the 360 degrees.

Discussion and Available Data on Outcomes

The authors recommend the patient be off blood thinners since bleeding is expected and blood has been noted in the anterior chamber up to one-month post operatively.
[33]. The authors have reported results of 21 eyes of 17 patients with up to 12 month follow up. Sixteen eyes with primary open angle glaucoma had the procedure combined with cataract surgery and had 9+-2.4 months of follow up with all 16 completing 6 months. The pre operative IOP was 23.9+-7.2 which was reduced to 16.9+-10.5 mm Hg with a reduction in medications from 2.9+-1.1.

An additional eleven patients with other open angle glaucomas were in the study. In this group there was follow up of 10.5+-2.1 months with one patient requiring further glaucoma surgery. The other 10 all had 6 month follow up with IOP reduced from pre op 26.6+-1.8 to 13.4+-3.6 mm Hg. The medications decreased from 2.9+-1.3 to 1.1+-1.2 [33]. There was no statistical difference between patients undergoing a cataract surgery versus the group that had the glaucoma procedure alone.

**Kahook Blade**

**Instrumentation**

This blade (Figure 10) has been studied versus goniotomy and the Trabectomein pre clinical trials [37]. It aims to create a better removal of the trabecular meshwork with less residual leaflets of tissue that could potentially lead to fibrosis of the cleft with time. It is in clinical trials at this time.

---

**Summary and Further Considerations**

Minimally invasive glaucoma surgeries (MIGS) are exciting innovations that expand the possibilities for treating glaucoma patients. While they have demonstrated only a modest reduction of IOP as compared to traditional glaucoma surgeries, they have a more favorable side effect profile. Therefore, they have been suggested to be optimal for the patient with mild to moderate glaucoma that desires a safer procedure to help control their glaucoma and decrease their glaucoma drop burden.

MIGS are performed through clear corneal incisions and are thus easily combined with cataract surgery. However, new skills are necessary for these new procedures. They require intra operative gonioscopy, manipulation of the microscope and the patient head, and a new, unfamiliar angle of approach for some surgeons [14]. The lacy and often non-pigmented trabecular meshwork can be difficult to visualize. Therefore, these surgeries not only demand excellent gonioscopy skills, but also, they require access to a surgical microscope with excellent optics, tilt capability, and illumination with high Kelvin color temperature [1]. Therefore, in order to incorporate MIGS into practice, additional training and specialized equipment may be needed.
There are numerous MIGS currently available, each with a slightly different approach. While the effectiveness of each MIGS has been studied, more studies are needed to compare the different MIGS head to head. Even for each device, there are a number of variables that could be better optimized, such as the number of inserted devices, the dimensions of the device, and the width of the trabecular meshwork or ciliary body that is ablated. Furthermore, the cost effectiveness of MIGS is another area that requires future research. It is unknown whether the initial cost in the OR of placing these devices is outweighed by the potential cost savings by decreasing medications and need for further surgeries. Moreover, the majority of the data available on MIGS are retrospective case studies. While there are a few randomized controlled trials, they are often industry sponsored with short follow up. It is difficult to directly compare the studies that are available as they often have different “success” or “failure” criteria. There is a need for more randomized controlled trials that are independent of industry funding and compare the different MIGS directly with longer follow up to fully understand the effectiveness of these new surgeries.

For the patient with mild-moderate glaucoma and concomitant visually significant cataract, a combined CE with MIGS procedure is an exciting new option. Data supports the efficacy and safety of many of these surgeries. While they have proven to be less efficacious at reducing IOP than traditional glaucoma surgeries, they have a better safety profile. More studies are necessary to compare MIGS procedures directly to guide the ophthalmologist in selecting the best MIGS to select for their patients.

References


5. Saheb H, Ahmed II. Micro-invasive glaucoma surgery: current perspectives and future direc-


17. Khan M, Saheb H, Neelakantan A, Fellman R, Vest Z. Efficacy and safety of combined cataract surgery with 2 trabecular microbypass stents ver-


28. Klamann MKJ, Gonnermann J, Maier AKB,


34. Grover DS, Fellman RL.
