Minimally invasive glaucoma surgery

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ABSTRACT

Glaucoma is a progressive optic neuropathy. In 2040, it is estimated that more than 110 million people will have glaucoma. For this reason, there have been severe changes in the management of glaucoma in recent years. Although trabeculectomy is the gold standard in surgical treatment, many surgical methods have been defined as minimally invasive glaucoma surgery (MIGS).[1] Most of these are surgical approaches with implants, but there are also MIGS techniques without implants. Compared to conventional filtration surgery, MIGS promises a faster recovery and fewer severe complications.[2] It can be performed in combination with cataract surgery.[3] This review will review the current literature on MIGS, and surgeries with and without implants will be discussed.

Keywords: Minimally invasive glaucoma surgery, MIGS, GATT, implants.

INRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide.[4] To prevent the progression of glaucoma, it is imperative to reduce high intraocular pressure (IOP), which is a modifiable risk factor. Reducing IOP is the only way to prevent the progression of optic nerve damage and visual field defects.[5] Two main surgical approaches to reducing intraocular pressure are increasing outflow and decreasing aqueous humor production. In 1968, Cairns developed the trabeculectomy method in chronic open-angle glaucoma (OAG) by stating that the outflow resistance is mainly the trabecular meshwork in the inner wall of Schlemm's canal.[6] Currently, trabeculectomy remains the gold standard glaucoma surgery for IOP reduction, but it has limitations. There have been many innovations and changes in glaucoma surgery in recent years due to complications such as hypotony, endophthalmitis, choroidal effusion, suprachoroidal hemorrhage, cataracts, and corneal decompensation.[7] A group of surgical methods called minimally invasive glaucoma surgery (MIGS) has emerged. MIGS usually has features such as minimal tissue trauma with little intervention to the conjunctiva and sclera, rapid healing, and a good safety profile.[2] These surgeries are performed with an ab-interno or ab-externo approach.[2] These surgeries utilize physiological flow pathways and do not require a fistula for outflow. MIGS is divided into three groups according to the site of implantation or procedure: 1) MIGS that increases trabecular outflow by manipulating the trabecular meshwork and Schlemm's canal 2) Suprachoroidal MIGS that increases uveal scleral outflow via suprachoroidal shunt 3) Subconjunctival MIGS.[8] The methods utilizing implants in practice today are Gold micro-shunt (GMS, SOLX, Boston, Massachusetts, USA), iStent (Glaukos Corporation, Laguna Hills, CA, USA), Cypass (Transcend Medical, Menlo Park, CA, USA), iStent Supra (Glaukos Corporation, Laguna Hills, CA, USA), Xen GEL Stent (AbbVie Inc. North Chicago, Illinois, USA)(Aquesys, CA, USA), Hydrus (Ivantis Inc., Irvine, CA, USA), iStent inject, iStent Infinite, MINIject (iSTAR Medical, Wavre, Belgium), PreserFlo MicroShunt (Glaukos, Miami, USA), Ex-Press implant (Alcon Laboratories, Fort Worth, TX, USA). Surgeries without implants include ab-externo canaloplasty and Ab interno canaloplasty (ABic)(Ellex, Fremont, CA, USA), Omni/Visco 360 (Sight Sciences, Menlo Park, CA, USA), Streamline (New World Medical, Rancho Cucamonga, CA), Omni/Trab 360 system (Sight Sciences, Menlo Park, CA, USA), the Trabectome system (NeoMedix, Tustin, CA, USA), ab-externo trabeculotomy, Gonioscopy-

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assisted transluminal trabeculotomy (GATT), High-Frequency Deep Sclerotomy (HFDS) (Oertli Instrumente AG, Switzerland), Excimer laser trabeculostomy (ELT) (Glautec AG, Nürnberg, Germany), Kahook dual blade goniotomy (New World Medical, Rancho Cucamonga, CA, USA), endoscopic cyclophotocoagulation (Endo Optiks, Little Silver, NJ, USA). In this review, MIGS with and without implants will be discussed. Table 1 classifies the devices and methods used in MIGS.

A. MIGS without implants

1. Canaloplasty

Ab-externo Canaloplasty

Ab-externo canaloplasty surgery is one of the earlier methods compared to other current techniques. Canaloplasty is a modified viscocanalostomy method. In canaloplasty, the superficial and deep scleral flaps are created, and Schlemm's canal (SC) is found, after which the canal is catheterized 360 degrees. In 1995, Beck and Lynch reported on a technique in which there was a 360° incision of the trabecular meshwork (360°) using a 6-0 polypropylene (Prolene, Ethicon Endo-Surgery, Blue Ash, OH, USA) suture to treat congenital glaucoma.[9] Later, the catheter used for catheterization (iTrack 250; iScience Interventional) has an illumination system that allows the catheterization of the SC to be monitored. After 360-degree catheterization of SC, a 10/0 polypropylene suture is tied to the distal end of the catheter, and the catheter is retracted. The deep flap is excised, and the superficial scleral flap is sutured. This application causes both dilatation in the SC and damage to the inner wall of the SC and the surrounding trabecular area, leading to a decrease in IOP.[10] There are many studies on canaloplasty in the literature. In a prospective study by Grieshaber et al., the IOP value of black African patients with primary open-angle glaucoma (POAG) before canaloplasty was 45.0 +/- 12.1 mmHg. One week after surgery, IOP was 15.2 mmHg. These values remained stable throughout the three-year follow-up period of the study. There was also an additional three mmHg reduction in mean IOP in 49 eyes approximately two years after surgery. Operative success 36 months after canaloplasty defined by three IOP levels (≤21, ≤18, and ≤16 mmHg) was 81%, 67.8%, and 47.2%, respectively.[11] The most common intraoperative or postoperative complication was transient microhyphema. Two (3.3%) patients developed adherent Descemet's membrane detachment after two weeks. Greishaber et al. compared the size of the thread inserted into SC during canaloplasty.[12] 10/0 prolene suture was more successful than 6/0 prolene suture. The most common postoperative complication observed in this study was microhyphema. On the other hand, Bull et al. prospectively compared canaloplasty and phaco-canaloplasty patients.[13] In the first group, preoperative IOP and number of drugs (NOD) were 23.0±4.3 mmHg and 1.9±0.7 respectively, at the end of the three-year follow-up IOP and NOD decreased to 15.1±3.1 mmHg and 0.9±0.9 respectively. In the combined group, preoperative values were 24.3±6.0 mmHg and 1.5±1.2, and postoperative values were 13.8±3.2 mmHg and 0.5±0.7. Matlach et al. compared canaloplasty with trabeculectomy. This study showed the beneficial effect of canaloplasty on IOP reduction. The mean IOP reduction was 9.3 ± 5.7 mmHg and 10.8 ± 6.9 mmHg in the canaloplasty and trabeculectomy, respectively. Postoperative follow-up showed that canaloplasty is a safer procedure than trabeculectomy, with a lower incidence of postoperative complications regarding hypotony, choroidal detachment, and IOP elevation.[14] Rękas et al. compared phaco-canaloplasty results to phaco-non penetrating deep

Table 1: *MIGS Procedures.*

Canaloplasty	Trabeculotomy / Trabeculectomy	Cycloablative Therapy	Stents
Ab-externo Ab-interno - ABiC - OMNI/ Visco360 - Streamline	Trabectome Ab-externo trabeculotomy Gonioscopy-assisted transluminal trabeculotomy OMNI/TRAB 360 Excimer Laser Trabeculotomy-Trabeculectomy High-Frequency Deep Sclerotomy (HFDS) Kahook Dual Blade (KDB)	Endoscopic cyclophotocoagulation	Gold Micro-Shunt Trabecular Micro-bypass - iStent - iStent Inject - iStent Infinite - iStent Supra Hydrus Microstent Cypass MINIject XEN Gel Stent Preserflo Microshunt Ex-Press Implant

sclerectomy. There was a 34% decrease in IOP in the phaco-canaloplasty group and a 25% decrease in the other group.[15] In another retrospective study, 67 patients who underwent canaloplasty with pseudoexfoliative glaucoma (PXG) with at least two years of follow-up were evaluated.[16] The mean preoperative IOP was 31.2 ± 8.7 mm/Hg and the mean IOP at 2-year follow-up was 17.2 ± 6.7 mmHg, a mean reduction of 44.9% from baseline. After two years, the total NOD used preoperatively reduced from 3.5 ± 0.8 to 1.2 ± 1.4. Hyphema (30%), Descemet's membrane detachment (4.9%), and acute IOP elevation (61%) were observed. Long-term results of canaloplasty in PXG patients seem to be good. However, canaloplasty may not be appropriate, especially in patients with severe functional damage due to sudden IOP elevation. In another study, 25 patients with pigmentary glaucoma who underwent canaloplasty were followed up for 11 years postoperatively.[17] The mean preoperative IOP was 31.8 ± 10.9 mmHg, and a mean of 3.3 medications were used. After 1, 2, 3, and 4 years, the mean IOP was 15.9, 14.4, 14.1 and 15.7 mmHg, respectively. Follow-up showed that pigment granules were reabsorbed from the trabecular meshwork. This may explain the relatively high surgical success. The procedure is contraindicated in eyes with angle recession, neovascular glaucoma, chronic angle closure, and narrow-angle glaucoma and in patients with previous ocular surgery that would prevent 360° catheterization of Schlemm's canal.[18] In cases of failed canaloplasty, 360° suture trabeculotomy can be performed before trabeculectomy.[19]

Ab-interno canaloplasty

In recent years, the iTrack microcatheter, OMNI system/ VISCO360, and Streamline surgical systems have been used for Ab-interno canaloplasty.

iTrack system: The catheter is inserted into the anterior chamber filled with viscoelastic material through the side port using the previously made goniotomy incision and is advanced to the angle with a tangential force with microforceps. The device's position in the SC is followed by a beacon light at the tip. After advancing for 360°, viscoelastic material is injected through the catheter at certain intervals, and the catheter is withdrawn. The aim here is to dilate the SC and collector canals (Figure 1).[20,21]

OMNI/ VISCO360: Used for canaloplasty and trabeculotomy. It affects the conventional flow pathway like trabecular implants, but unlike implants, it targets trabecular meshwork (TM), SC, and collector canals. SC dilatation and TM tissue excision can be performed 360 degrees with the help of a microcatheter through a single corneal incision.[22]

OMNI device is predicated on Visco360. This system aims to dilate the SC and collector vessels 360 degrees with viscoelastic materials using a polymer microcatheter inserted into the anterior chamber through a precise corneal incision. It can also be used in pathologies such as synechiolysis, intraocular lens capsular dissection, or cyclodialysis, which may require low amounts of viscoelastic in the anterior chamber (Figure 2).[23,24]

Streamline: The device has a pointed steel inner structure and a polymer outer structure. The SC is accessed through the anterior chamber, and viscodilation (7 µl) is performed, but trabeculotomy is not performed. Goniotomy is possible. Although Streamline decreases intraocular pressure significantly, long-term studies and comparisons with other MIGS methods are required.[25]

In general, ab-interno canaloplasty is comparable to ab-externo canaloplasty. Gallorda et al. reported that the IOP value was 17 mmHg or less in 95.5% of eyes, and only one topical medication was required in 68.2% of eyes at 36 months follow-up after AbiC.[26] With AbiC

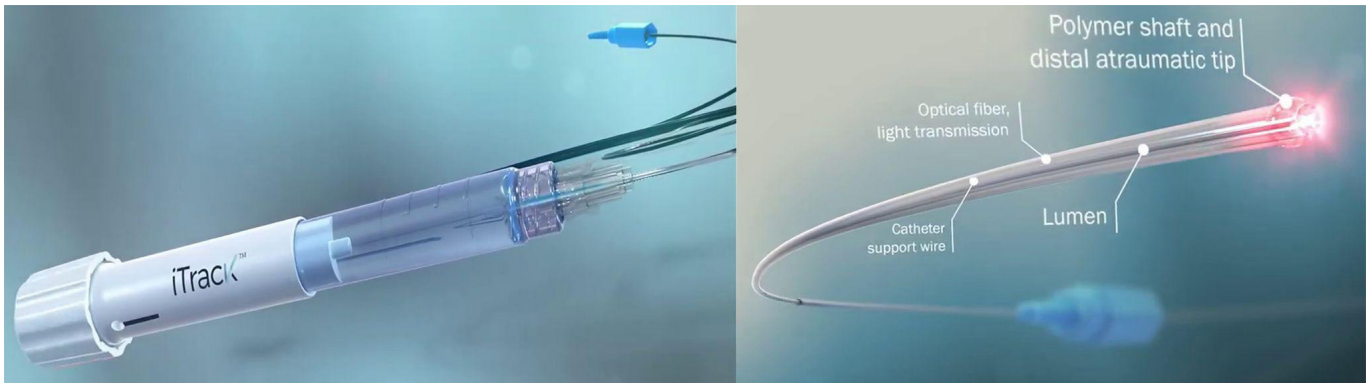

Figure 1: *ABiC injector and iTrack catheter system (https://glaucoma-itrack.com/physicians/).*

Figure 2: *OMNI system. (https://omnisurgical.com/wp-content/uploads/2023/08/OMNI-Flashcard-OM-2568-US-v2.pdf).*

surgery, approximately 30-40% reduction in IOP value was found with less than two medications at the end of 1 year.[27] Gallorda et al. compared ab-externo and ab-interno canaloplasty. No difference was observed in terms of IOP value and NOD.[28] In another study published in 2024, 27 eyes that underwent AbiC using iTrack were followed up for six years. While the mean preoperative IOP was 19.9±5.2 mm Hg and NOD was 1.9±1, it was 14.6±3.3 and 0.9±0.9 at the end of the 6-year follow-up period. iTrack ab-interno canaloplasty significantly reduced IOP and NOD in patients with POAG up to 6 years after the procedure. There was no statistical difference between POAG and pseudoexfoliative eyes after canaloplasty and phaco-canaloplasty surgery. No severe complications were recorded.[29] Toneatto et al. performed canaloplasty with the OMNI system in patients with POAG. The mean preoperative IOP decreased from 23.0 ± 5.7 mmHg to 15.6 ± 3.6 mmHg and NOD was reduced from 3.0 ± 1.1 to 2.0 ± 1.4 at the end of 12 months follow-up.[30] Hughes and Traynor also found that the results of canaloplasty performed with OMNI/VISCO360 were similar to those of the previous studies.[31] In another study, canaloplasty and phaco-canaloplasty were evaluated. Preoperative mean IOP was 21.1 ± 8.8 mm Hg and mean NOD was 2.0 ± 0.9, postoperative mean IOP and NOD were 15.3 ± 3.0 mm Hg and 0.9 ± 0.2, respectively.[32] It has been reported that canaloplasty performed with OMNI/VISCO360 alone or combined with phaco is effective and can be used safely.[32] The retrospective ROMEO study evaluated the efficacy of canaloplasty and trabeculotomy with an OMNI device in pseudophakic patients with POAG. A significant reduction was found in terms of IOP and NOD values.[33] In eyes with progressive POAG despite drug treatment, a 20% or more reduction in IOP has been shown to reduce the risk of further progression of glaucoma.[33] Significantly, Terveen et al. performed trabeculectomy and canaloplasty with the OMNI surgical system in POAG patients who had previously undergone trabecular micro bypass stent implantation. They found a significant decrease in IOP and NOD after surgery and showed that a second MIGS could be performed after MIGS.[34] We know that IOP fluctuation and peak IOP are risk factors for glaucoma. GEMINI study showed that patients who underwent canaloplasty and trabeculotomy with an OMNI device have significant decrease in IOP fluctuation and peak IOP values at the end of the 12-month follow-up.[35] Hyphema larger than 1 mm (4.2%), posterior capsule opacification (10.4%), cystoid macular edema (6.3%), and corneal edema (4.2%) were found after surgery.[36] The type of approach (viscodilatation only/viscodilatation+trabeculotomy) and concomitant cataract extraction significantly affect the complication rate.[37] In a 6-month study with the Streamline device, a 37% decrease in IOP and a 50% decrease in medication use were found after surgery.[38] In another study performed with cataract surgery, an IOP reduction of 20% or more was found in 80% of eyes at the end of a 12-month follow-up.[38] It has been shown that ab-interno canaloplasty can be applied together with cataract surgery and is effective in IOP reduction.[39]

2. Trabeculotomy/Trabeculectomy

Trabectome

Trabectome is one of the first MIGS procedures, which received FDA approval in 2004.[40] Trabectome has an electrocautery system that destroys the trabecular meshwork and the inner wall of the SC using a 19.5 gauge handpiece. The tip of the handpiece is pointed for ease of entry into the SC. It is insulated with a multilayer polymer coating that protects the outer wall of the SC from thermal and electrical injury.[41] It also has an aspiration-irrigation system.[40] The debris caused by cauterization is aspirated with irrigation support. Surgery is performed with a goniolens. The patient is given a head position, and the trabecular area is ablated 90-120 degrees at the

nasal angle.[42] Trabectome system selectively removes the trabecular meshwork. It may even encourage some retraction of the incision edges with the heat effect.[41] This creates an opening to the anterior chamber through SC and collecting ducts. It is indicated in patients with open-angle glaucoma. Trabectome is contraindicated in neovascular glaucoma, increased episcleral venous pressure, active uveitis, and angle dysgenesis. Without external filtration, the Trabectome system has reduced early and late postoperative risks associated with excessive filtration or wound leaks seen with trabeculectomy and glaucoma drainage devices, including hypotony, flat anterior chambers, choroidal effusions or hemorrhage, cataract, and diffuse synechiae.[43,44] In the first study on the Trabectome, 101 patients with open-angle glaucoma were followed for 30 months after the procedure. While the mean preoperative intraocular pressure (IOP) was 27.6 ± 7.2 mm Hg, the mean IOP at 30 months postoperatively was 16.3 ± 3.3 mm Hg (n=11). IOP reduction during follow-up was 40%. Overall success (IOP≤ 21 mm Hg with or without medication and without further surgery) was 84%.[45] A review published in 2021 concluded that there is no high-quality evidence for the outcome of Trabectome surgery for open-angle glaucoma and that more studies are needed.[46] In a 2008 prospective study, trabeculectomy with Trabectome was performed in 304 consecutive eyes with glaucoma undergoing cataract surgery. Mean IOP was 20.0 mmHg 6.3 (SD) preoperatively, 14.8 ± 3.5 mmHg at six months and 15.5 ± 2.9 mmHg at one year. The use of glaucoma medications decreased by one year. Blood reflux was present in 78.4% of patients and resolved within a few days. This study supported the use of the Trabectome in combination with cataract surgery to lower IOP.[47] Comparative studies have also shown the efficacy of the Trabectome as a standalone procedure compared to phaco/Trabectome. Both Trabectome and phaco/Trabectome led to reductions in IOP and glaucoma medications over one year. However, only the Trabectome group showed statistically significant reductions in IOP and medications (P<0.01). Surprisingly, a retrospective analysis of 1340 eyes found an IOP reduction of 1.29±0.39 mm Hg at 12-month follow-up in subjects who underwent phaco/Trabectome.[48] Conversely, a different retrospective analysis showed that the Trabectome and phaco/Trabectome groups had a similar pattern of IOP and NOD reduction from baseline over one year.[49] In another study with a 5-year follow-up, phaco/Trabectome resulted in an IOP reduction of ≥20% in 67.5% of eyes.[50] Overall, the Trabectome appears to perform similarly to the phaco/Trabectome, and surprisingly, the latter may be less effective than a standalone procedure. No speculation has been made regarding plausible reasons for these results.[49-51] The Trabectome is also effective in pseudo exfoliation glaucoma(PXG) and steroid-induced glaucoma, with more significant IOP reduction observed in PXG and steroid-induced glaucoma compared to POAG.[47,49] It has been effective in severe glaucoma even after failed trabeculectomy or tube shunt implantation.[48,51] Jea et al. compared the results of 115 patients who underwent the Trabectome surgery and 102 patients who underwent trabeculectomy surgery with MMC.[52] At the end of follow-up, IOP decreased from 28.1 ± 8.6 mmHg to 15.9 ± 4.5 mmHg (43.5% decrease) in the Trabectome group and from 26.3 ± 10.9 mmHg to 10.2 ± 4.1 mmHg (61.3% decrease) in the trabeculectomy with MMC group. The Trabectome surgery resulted in a less decrease in IOP compared to trabeculectomy surgery. However, the Trabectome seems advantageous because of the absence of blebs and lower rates of vision-reducing complications.[52] Hyphema is the most common complication after the Trabectome. However, it resolves spontaneously within days. In addition to hyphema, peripheral anterior synechiae, transient high IOP, cyclodialysis, transient hypotony, iris damage, cystoid macular edema, and cataract may be observed.[53]

Ab-externo trabeculotomy

Developments in trabeculotomy surgery have been increasing in recent years. It is used safely in pediatric and adult glaucoma. Circumferential suture techniques and flexible microcatheters have been developed for SC cannulation. Among these techniques, 360-degree suture trabeculectomy (ST) provides a circumferential incision in the inner wall of the SC and the juxtacanalicular trabeculae to decrease the resistance between the SC and the anterior chamber and to increase aqueous humor outflow.[54] Chin et al. first evaluated the efficacy of 360-degree ST in adults with primary open-angle glaucoma (POAG) and secondary open-angle glaucoma (SOAG). The success rate was 84% and 89% in POAG and SOAG cases, respectively. Their study found that ab-externo 360-degree ST was more effective than metal trabeculotomy.[55] Hepşen et al. analyzed the results of ab-externo 360-degree ST in patients with pseudoexfoliation glaucoma at 6 and 12 months and the complete and qualified success rates were 77% and 100% at six months and 68.4% and 94.7% at 12 months, respectively.[56,57] At 12 months, IOP decreased by 58.9% (10.9 mm Hg), and NOD decreased from 3.15 to 0.30 at 12 months.[57] Hyphema, transient IOP elevations,

and peripheral anterior synechiae were observed as complications, but hypotony and vision-threatening surgical complications were not encountered in any case. Hemorrhage may develop in the angle during the procedure. Therefore, some viscoelastic material can be left in the anterior chamber as a buffer. Sato et al. examined the results of ab-externo 360-degree ST when combined with deep sclerectomy and cataract surgery in patients with POAG.[58] Yalınbaş et al. found a similar success rate with their study.[54] Aktas et al. retrospectively compared the results of ab-externo ST and trabeculectomy with MMC in adults.[42] Complete and partial surgical success rates in both groups were found to be 80%-100% and 82%-100%, respectively, and no statistically significant difference was found. In the MMC trabeculectomy group, hypotony was observed in 2 cases (8%) and cystic bleb in 1 (4%). In contrast, these complications were not observed in the ST group, but the most common complication was hyphema in 17 cases (73%), which resolved spontaneously and disappeared within 7-10 days. The occurrence of hyphema in this surgery is accepted as a postoperative indicator of the effectiveness of the surgery.[42] It is a good prognostic sign when reflux from episcleral veins is considered.[42] Wang et al. compared ab-externo trabeculotomy and canaloplasty in patients with previous incisional glaucoma surgery. At the end of 1-year follow-up, they found that both surgical outcomes were successful, but hyphema was more common in the trabeculotomy group.[59] Habash et al. retrospectively evaluated eyes with primer angle closed glaucoma (PACG) who underwent microcatheter-assisted ab-externo trabeculotomy as a secondary procedure after failed primary surgery. Preoperative IOP was 31.8 ± 6.6 mmHg, NOD was 3.9 ± 0.5, and postoperative IOP was 15.6 ± 3.7 mmHg. NOD was 1.1 ± 1.6.[60] El Sayed and Gawdat reported lower IOP and less need for glaucoma medication following this procedure compared to conventional rigid probe trabeculotomy.[61] Furthermore, Shi et al. demonstrated that IOP and NOD were significantly reduced in patients with PCG who underwent microcatheter-assisted trabeculotomy after failed angle operations.[62] In conclusion, studies show that microcatheter-assisted trabeculotomy is also effective and safe to use as a secondary procedure in patients with PCG after failed glaucoma surgery.

Gonioscopy-assisted transluminal trabeculotomy

We know that ab-external trabeculotomy has been used successfully in congenital and adult glaucoma patients in recent years. The disadvantage of ab-external trabeculotomy is the opening of the conjunctiva and scleral flap dissection. These steps may affect the success of subsequent trabeculectomy surgery. The introduction of flexible catheters has enabled the development of new minimally invasive surgical techniques in glaucoma. Grover et al. 2014 described GATT surgery.[63-65] GATT surgical technique: The temporal quadrant is crossed. The head is tilted in the opposite direction, and an angle view is obtained. A transparent corneal 23-gauge paracentesis incision is made, and the anterior chamber is filled with viscoelastic material. Subsequently, a goniotomy is performed in the nasal angle region with an MVR blade. The distal end of the microcatheter is placed in the goniotomy area and pushed to advance in the SC. The 360-degree rotation of the catheter can be monitored with the help of light. After 360-degree rotation is achieved, the distal tip is grasped with the help of forceps and its exit from the temporal incision is seen. Then, a 360-degree trabeculotomy is performed by applying traction to the catheter with the help of forceps (Figure 3). Some amount is left in the anterior chamber to buffer the hemorrhage in terms of viscoelastic.

Grover et al. reported a IOP reduction of 30% and 52.7% in their first study in POAG and secondary glaucoma

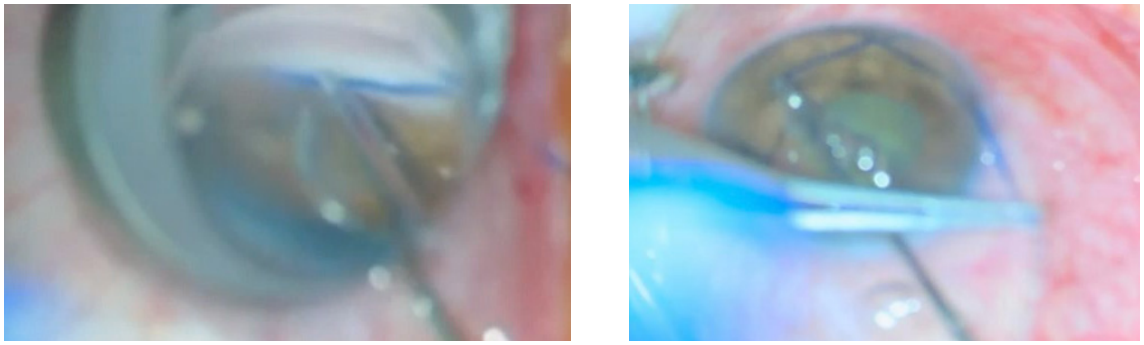

Figure 3: *Goniotomy assisted transluminal trebaculotomy with prolene suture (Courtesy of Dr. C. Deniz Genc).*

patients, respectively. The most common complication was hyphema (30%), which resolved spontaneously in 1 week.[63] Afterwards, they evaluated the results of GATT in patients with primary congenital glaucoma and juvenile glaucoma. Preoperative IOP was 27.3 mmHg, and postoperative IOP was 14.8 mmHg.[64] The results of the study suggested that it may be an alternative to ab-external trabeculotomy.

Grover et al. followed 198 patients who underwent GATT for 24 months. They found a decrease of 9.2 mmHg in IOP and 1.43 in NOD in POAG cases after follow-up.[66] An 8-year-old patient who used steroids for vernal keratoconjunctivitis and developed steroid-induced glaucoma underwent GATT surgery. While the preoperative IOP was 38, the 2nd year postoperative IOP value was 12.[67] Angle surgery in children protects the patient from complications of filtering surgery.

Smith et al. followed 32 patients with corneal transplantation for 24 months. Preoperative IOP was 30.9±11.5, and NOD was 4.2±1.0, while postoperative IOP was 13.9±4.7 mm Hg and NOD was 0.6±1.0. At the end of 24 months, 79.7% were successful. Only 2.6% of patients needed re-transplantation after GATT.[68] In contrast, 2-year corneal graft failure has been reported to be 40% after trabeculectomy and 35% to 74% after glaucoma drainage device.[69]

Eyes with a visual field mean deviation (MD) worse than -15 have been reported to have a higher risk of surgical failure following GATT, and it has been suggested that this may be attributed to atrophy of the collecting ducts in eyes with advanced glaucoma.[66] PXG is the most common form of secondary glaucoma worldwide with a worse prognosis than POAG.[70] Medical or laser therapy has been recommended as first-line treatment, but surgical treatment is usually required.[71] Sharkawi and colleagues prospectively reported the surgical outcomes of GATT in 103 eyes with pseudoexfoliation glaucoma; 50 eyes underwent phaco-GATT, while 53 pseudophakic eyes underwent GATT. While the mean preoperative IOP was 27.1 mmHg and best corrected visual acuity (BCVA) was 2.9 ± 1.1, the mean postoperative 24-month IOP was 13.0 mmHg and BCVA was 1.0 ± 1.1. No statistically significant difference was observed between the groups.[72] They also found that GATT lowered IOP more effectively than POAG in patients with secondary POAG (especially PXG).[73]

The incidence of glaucoma after uncomplicated pars plana vitrectomy (PPV) varies between 15-20%.[74] The etiology may be due to an increase in molecular oxygen in the anterior chamber angle of patients after vitrectomy, which induces oxidative stress and changes in the TM, ultimately leading to an increase in IOP.[75] Emulsified silicone in the anterior chamber also causes destruction of the TM and subsequent elevation of IOP.[74]

In a retrospective study by Quan and colleagues of 8 eyes with glaucoma after PPV and GATT, the mean preoperative IOP was 32.7 ± 5.1 mmHg and 13.6 ± 1.8 mmHg postoperatively, with a mean reduction of 50% at the last follow-up.[76] The mean preoperative NOD was 4.8 ± 0.9, and postoperative NOD was 1.6 ± 1.4. In these cases, GATT has the advantage of being a conjunctival sparing procedure in patients with extensive conjunctival scar layer but this study is limited to short-term follow-up.

Aktaş et al. retrospectively analyzed 15 eyes of 15 patients with silicone-induced glaucoma who underwent GATT after silicone oil removal. The mean IOP was 31.0 ± 4.1 mmHg preoperatively and decreased to 15.6 ± 4.6 mmHg at the end of 37.5 months of follow-up. IOP was ≤21 mmHg with medication in 93.3% of patients, while IOP ≥6 and ≤21 mmHg without medication was reported in 26% of patients.[77] The long-term efficacy of the procedure is unknown because emulsified silicone oil droplets cannot be completely removed from the eye, and these particles may obstruct the distal collecting ducts after GATT surgery.[77]

Based on the EAGLE study, lens extraction was recommended as the first-line treatment for chronic angle-closure glaucoma (CACG).[78] However, lens extraction alone was insufficient to control IOP in a subgroup of patients. Fontana and colleagues retrospectively analyzed the results of GATT in 15 pseudophakic eyes with CACG. They first performed sectoral goniosynechialysis and then ab-interno trabeculotomy. The mean IOP was 30.27 ± 4.20 mmHg preoperatively and 15.20 ± 2.08 mmHg one year postoperatively ($p< 0.001$). Mean IOP decreased by 49%.[79]

Chira-advise et al. retrospectively analyzed 39 eyes, including 37 with CACG, one with acute ACG attack, and one with plateau iris syndrome.[80] The mean IOP was 21.8 ± 5.4 mmHg preoperatively, 15.1 ± 3.8 mmHg at one month, 14.4 ± 1.2 mmHg at three months, 14.8 ± 2.1 mmHg at six months and 14.5 ± 0.8 mmHg at one year postoperatively. While the mean preoperative NOD was 3.5 ± 1.4, it was 1.5 ± 1.4 at one month, 0.9 ± 0.9 at three months, 1.4 ± 1.4 at six months, and 1.5 ± 0.5 at one year and decreased significantly.[80]

Qiao and colleagues retrospectively evaluated Kahook dual-blade (KDB) assisted ab-interno trabeculectomy (or excisional goniotomy) versus GATT surgery in patients with JOAG.[81] It reported promising results for GATT. Thirty-six eyes underwent GATT, while 13 eyes underwent KDB. The preoperative NOD was 3.71 ± 0.46 and 3.08 ± 0.86, and the preoperative mean IOP was 30.48 ± 12.9 mmHg and 26.08 ± 13.1 mmHg (p=0.164) in the GATT and KDB groups, respectively. At three months postoperatively, the mean IOP was 15.48 ± 5.93 mmHg in patients who underwent GATT and 20.0 ± 10.8 mmHg in patients who underwent KDB. At six months, the cumulative partial and complete success rate was 65.6% and 44.7% in the GATT group and 30.8% and 15.4% in the KDB group. This may be explained by the more extensive angle treatment in GATT than in KDB. Patients with shorter preoperative axial length had longer survival.[81]

Olgun et al. retrospectively compared 114 eyes with XEN implantation and 107 with GATT in patients with OAG.[82] They found that surgical success rates without medication were 34.2% and 50.5% in the XEN and GATT groups, respectively (p=0.039). The mean postoperative IOP reduction was more significant in the XEN group (57.9%) than in the GATT group (37.1%) (p<0.001). However, postoperative medication dependence was more significant in the XEN group (1.8±1.8) than in the GATT group (1.2±0.49) (p=0.009).[82]

Fontana et al. compared mitomycin C-enhanced trabeculectomy with GATT surgery and found that IOP reduction was more significant in the trabeculectomy group.[83] The mean IOP before surgery was 30.04 ± 7.5 in the trabeculectomy group and 27.59 ± 4.70 in the GATT group (p=0.072). At 18 months, the mean IOP after mitomycin C-enhanced trabeculectomy and GATT was 12.48 ± 4.58 mmHg and 15.26 ± 3.47 mmHg, respectively. Partial and complete surgical success were 59% and 27% after mitomycin C-enhanced trabeculectomy and 46% and 31% after GATT (p=0.353), with a higher reintervention rate in the GATT group. The most common complication was hypotony after trabeculectomy and hyphema after GATT.[83]

In conclusion, studies on GATT show positive results. Many studies have found that the IOP drop was greater than 30%, and the final IOP value was close to the teens. However, more studies are needed to examine the procedure's efficacy to halt glaucoma progression in advanced cases and conditions requiring very low IOP, such as normotensive glaucoma. It has also been reported that patients older than 60 years have a higher failure rate.[84] More studies are needed to evaluate the long-term outcomes of GATT and compare it with other minimally invasive glaucoma surgeries.

GATT is safe and effective in primary and secondary open-angle congenital/juvenile glaucoma patients. Contraindications include anticoagulant use, bleeding diathesis, unstable IOL, inability to see angle structures, especially the trabecular meshwork, closed angle, or severe endothelial insufficiency. Relative contraindications are previous corneal transplant surgery or inability to elevate the head 30 degrees in the first postoperative week.

OMNI/TRAB 360

TRAB360 was launched in 2015. The disposable handpiece contains a reservoir for viscoelastic material, a catheter with a rounded tip, and a wheel system that moves the catheter back and forth. The latest implementation of Trab360 is the OMNI device. The catheter is inserted through a transparent corneal incision in the temporal quadrant and advanced into the anterior chamber. When the angle is reached, the sharp tip of the cannula is inserted into the TM under gonioscopic visualization to enter Schlemm's canal. The catheter is advanced 180 degrees into the canal by turning the wheel system on the handpiece. As the cannula is withdrawn, the anterior wall of the canal is ruptured to merge with the anterior chamber. The 180-degree ab-interno trabeculotomy is repeated by turning the cannula in the other direction, and the remaining 180-degree trabeculotomy is completed. The procedure can be performed alone or in combination with cataract surgery.

Sarkisian et al. evaluated the 12-month results of 81 patients. While preoperative IOP was 30.2±6.7 mmHg and NOD was 1.7± 1.3, postoperative IOP was 16.1±6.0 mmHg and NOD was 1.1± 1.0. It was reported that 73% of the patients (19 patients) had drug-free follow-up, and the most common complication was hyphema, which regressed spontaneously within one week.[85]

Raymond et al. treated patients with juvenile glaucoma with Trab360 in their study. Patients were followed up for 16.2 months. While preoperative mean IOP was 30.9 mm Hg and NOD was 2.6, postoperative mean IOP was 20.3 mm Hg and NOD was 1.6. A statistically significant decrease in IOP and NOD was observed.[86]

Hirabayashi et al. retrospectively evaluated the 6-month follow-up of patients who underwent cataract surgery with

TRAB360 trabeculotomy, GATT and KDB (Kahook dual blade) excisional goniotomy.[87] Seventy-four eyes of 61 patients who underwent KDB excisional goniotomy and 27 eyes of 25 patients who underwent 360° trabeculotomy (19 eyes of 17 patients who underwent Trab360 and eight eyes of eight patients who underwent GATT) were included in the study. Surgical success was achieved in 81.7% of the KDB eyes and 84.6% of the 360° trabeculotomy eyes. More eyes with KDB excisional goniotomy achieved the target IOP at six months compared to 360° trabeculotomy. Additional IOP-lowering procedures were performed in 9.5% of KDB eyes and 22.2% of Trab360/GATT eyes. It was interpreted that a whole 360° TM procedure may not be necessary to achieve maximum efficacy from this class of micro-invasive glaucoma procedures.[87]

Excimer Laser Trabeculotomy-Trabeculectomy

Excimer laser trabeculectomy or trabeculectomy (ELT) uses a xenon chloride excimer laser with a wavelength of 308 nm to create micro perforations (8-10) over an area of 90 ° in the trabecular meshwork and inner wall of the SC. No thermal damage occurs during the procedure; thus, the tissue healing reaction is minimal. With the photoablation process, flow is expected to increase, and IOP is expected to decrease. Blood reflux and bubble formation during the procedure indicate a successful procedure.

The indications for ELT are POAG and ocular hypertension, narrow-angle and angle closure, NVG and corneal opacities that prevent the visualization of angle structures cannot be performed.[1]

Babighian et al. followed 21 patients who underwent ELT for two years. The mean IOP was 24.8±2.0 mmHg before treatment and 16.9±2.12 mmHg at the end of follow-up. While the rate of IOP reduction was 31.8%, eight patients (38.1%) needed additional medication, and treatment was unsuccessful in 2 patients (9.5%).[88] In another study by the same authors, the results of ELT were compared with those of selective laser trabeculoplasty (SLT). In the ELT and SLT groups, IOP was 25.0±1.9 mm Hg and 23.9±0.9 mm Hg before the procedure, while it was 17.6±2.2 mm Hg and 19.1±1.8 mm Hg after the procedure, respectively. The complete success rate was 53.3% and 40% in the ELT and SLT groups, respectively. While statistically significant IOP reduction was obtained in both groups, no significant difference was found in success rates.[89]

Töteberg-Harms et al. analyzed the one-year results of 28 patients with different types of glaucoma after phaco+ELT.[90] A decrease of 8.79 mmHg (34.7%) in IOP and 0.79 (62.7%) in the NOD were recorded. Short application time and absence of a conjunctival approach were reported as advantages of ELT. In another study, the success of phaco+ELT and the continuity of IOP decrease in a 1-year follow-up were also reported.[91]

High-Frequency Deep Sclerotomy (HFDS)

It shares the same philosophy as other MIGSs, aiming to bypass the resistance in the trabecular meshwork and create channels to connect directly with Schlemm's canal. Episcleral and conjunctival tissues are protected from damage. Indications include patients with mild to moderate glaucoma, monocular but large diurnal fluctuations, axial myopic and vitrectomized patients at risk of pigment dispersion syndrome (PDS), PSX, choroidal effusion or hemorrhage, young patients at risk of postoperative hypotony.

The handpiece is isolated from a high-frequency diathermy probe (abee® Glaucoma Tip, Oertli Instrumente AG, Switzerland), inner platinum, and outer coaxial electrodes. The tip is 1 mm long, 0.3 mm high and 0.6 mm wide. It is inclined 15 degrees posteriorly. The external diameter is 0.9 mm. At 500 kHz, 130 °C heat is generated at the tip.

Entering the anterior chamber through the upper temporal incision, a deep sclerotomy is created by inserting a 1 mm tip into the trabecular meshwork under gonioscopic visualization. This procedure is repeated 6 times in one quadrant. The procedure is completed by removing the viscoelastic from the anterior chamber. Although the target area is the trabecular meshwork, the sclerotomy increases the trabecular flow and aqueous passage to the suprachoroidal area.

Abushanab et al. followed 43 patients with COAG for nine months after HFDS procedure. The mean IOP was 31.4 mmHg before the procedure and 19.06 mmHg after the procedure. It was revealed that the success rate was 90.7%.[92] Kontic et al. followed 23 patients with COAG for one year after HFDS. It was found that the mean IOP value decreased by 8.6 mm Hg (33.6%) after one year.[93] In another study, 205 patients who underwent HFDS with cataract surgery were followed up for 48 months. While the mean preoperative IOP was 24.5 ± 4.3 mm Hg and NOD was 2.6 ± 1.0, the mean IOP was 15.0 ± 1.7 mm Hg and NOD was 0.48 ± 0.97 after 48 months.[94] Compared to trabeculectomy and perforating and non-perforating deep sclerectomy, the HFDS ab-interno method appears to have

a low postoperative complication rate and a stable low IOP level. HFDS is a safe and minimally invasive method for glaucoma surgery with good long-term outcomes.[94]

Kahook Dual Blade (KDB)

The Kahook Dual Blade is a customized trabeculotomy blade with a right angle, an anterior tip, two cutting edges, and a hollowed middle part (Figure 4).[95] The target tissue is the trabecular meshwork; with an ab-interno approach, a window is first opened in the trabecular meshwork, and then the trabecular meshwork is shaved and removed as a strip with the help of a micropipette. The unique design of the KDB causes minimal collateral damage to the surrounding tissues, contributing to faster healing times and fewer complications. Clinical studies have shown that KDB effectively reduces IOP and maintains this reduction over time.[96,97]

Figure 4: *Kahook Dual Blade Knife. (https://www.newworldmedical.com/kdb-glide).*

Seventy-one eyes with mild glaucoma who underwent cataract surgery and single-use double-blade goniotomy were followed up for six months. The mean preoperative IOP and NOD were 17.4 mmHg and 1.6 ± 1.3, respectively, and 12.8 mmHg and 0.9 ± 1.0 postoperatively.[98] In another prospective study, 48 patients who underwent goniosynechialysis with phaco+KDB were followed up for two years. A 23.4-39% decrease in IOP value was found at the end of the follow-up.

Salinas et al. found an IOP reduction of 24% in KDB, 36.6% in NOD, and at least 20% IOP reduction in 60% eyes of patients with severe and refractory glaucoma who underwent goniotomy with KDB.[99] Glaucoma developing in an infant who underwent lensectomy and anterior vitrectomy due to a congenital cataract was treated with ab-interno trabeculectomy in both eyes using a double-edged blade. At seven to ten weeks, IOP decreased from 35 to 17 mm Hg in the right eye and from 52 to 18 mm Hg in the left with no complications. The authors reported the efficacy and safety of Kahook's double-edged blade in pediatric glaucoma with a case report.[100]

A retrospective study of KDB (n=90) and trabectome (n=125) during cataract surgery was reported. The authors reported an IOP reduction of 11.2% (p=0.002) in the KDB group and 19.1% (p<0.001) in the Trabectome group with no significant difference between the groups at 12 months follow-up. Hyphema was the most common complication, with an incidence of 3% in the KDB group and 14% in the Trabectome group. They concluded it was safe during cataract surgery and reduced IOP for up to 12 months.[101] This study is limited by its retrospective design, lack of a control group, short-term follow-up, and inclusion of more than one type of glaucoma.

In a study by Omoto et al., patients who underwent goniotomy with micro-hook and KDB with cataract surgery were followed up for six months.[102] The results were reported to be similar in both groups. In another study, the same author followed the patients who used a spatula and dual blade micro-hook for 12 months. The results were similar in this study.[103] Stephen et al. performed goniotomy with PHACO+KDB in patients who had previously undergone selective laser trabeculoplasty (SLT). While the success rate was 46.2% with SLT, it was found to be 63.6% after goniotomy with PHACO+KDB. In the study, it was thought that the success rate of subsequent surgery would increase in patients who had successful SLT, and this was thought to be because SLT treatment increased the permeability of the distal Schlemm canal endothelial cells.[104]

In a retrospective study, 77 patients who underwent phaco-trabeculectomy were compared with 40 patients who underwent PHACO-KDB and goniotomy. IOP reduction rate was found to be 28.4% and 27.8%, respectively. No significant difference was observed between the surgeries.[105]

Another study compared 75 patients who underwent goniotomy with Xen Gel Microstent implantation and KDB. IOP reduction was 32.7% in the XEN implanted group and 40.4% in the KDB group. More additional intervention was required in the Xen-implanted group.[106] Studies have shown the effectiveness of KDB goniotomy.

3. Cycloablative Therapy

Endoscopic cyclophotocoagulation (ECP) was developed by Martin Uram in 1992 to minimize the complications of

transscleral cyclophotocoagulation.[107] The ECP laser unit consists of a xenon light source, a helium-neon laser aiming beam, a video camera with a 110°-160° field of view, and a semiconductor diode laser probe. The probe is available in straight and curved versions. After injecting viscoelastic material into the ciliary sulcus to widen the space between the iris and the lens, the endoscope is usually inserted through a corneal incision along the anterior chamber and directed posteriorly to view the ciliary body. Starting at approximately 200 mW, depending on the surgeon's preference, the laser energy is titrated until it whitens and shrinks the ciliary body.

The ab-interno approach allows targeted treatment of the ciliary body epithelium in particular, with less unnecessary damage to other parts of the ciliary body, such as the ciliary muscle, ciliary body stroma, and pars plana.[108] Another advantage is the ability to determine the lowest laser energy required. It is thought that laser energy absorbed by the melanin in the pigmented epithelium of the ciliary body causes thermal damage to the non-pigmented epithelium of the ciliary body where aqueous humor production occurs.[108]

Uram followed ten patients with neovascular glaucoma for 8.8 months after ECP. He found a 65% decrease in IOP value.[107] In a retrospective study, 68 eyes with refractory glaucoma were followed up for 12.9 months after ECP. The mean IOP reduction was 35%, and NOD decreased from 3 to 2. Complications included fibrin exudation (24%), hyphema (12%), cystoid macular edema (10%), choroidal detachment (4%) and malignant glaucoma (1%). Hypotony and phthisis bulbi were not observed.[109]

Lima et al. compared ECP with Ahmed glaucoma valve (AGV) tube. They included patients with at least one failed trabeculectomy. The success rate was 71% with AGV and 74% with ECP.[110] In a prospective study of 45 eyes with refractory glaucoma treated with ECP, a 52% reduction in IOP, significantly fewer glaucoma medications, and a significant increase in BCVA were found at postoperative month 21.[111] In 2011, 25 patients who had previously undergone AGV tube placement were prospectively evaluated. After ECP, IOP decreased from 24.0 to 15.4 mm Hg (30.8%), and the mean NOD decreased from 3.2 to 1.5.[112]

In patients with POAG, the benefit of IOP reduction from cataract extraction has been shown to be variable and small (2-4 mm Hg), with a diminishing effect after 18-24 months.[113] ECP has been shown to be applicable not only in the treatment of refractory glaucoma but also in the treatment of mild to moderate glaucoma when combined with phacoemulsification.[114]

In 2001, 36 eyes with refractory pediatric glaucoma underwent ECP. After ECP, IOP decreased from 35.1 to 23.6 mm Hg (30% reduction). Complications included retinal detachment in 2 patients, hypotony in 1 patient, and progression from hand movement to no light perception in 1 patient. All complications occurred in aphakic patients, suggesting that ECP may not be a good idea for aphakic eyes.[115]

Noecker presented the most extensive study on the complications of ECP at the American Society of Cataract and Refractive Surgery meeting. In an analysis of 5824 eyes undergoing ECP with a mean follow-up of 5.2 years, the following complications occurred: cataracts (24.5% of phakic eyes), postoperative IOP elevations (14.5%), intraocular hemorrhage (3.8%), CME with visual loss (1.0%), serous choroidal effusion (0.4%), retinal detachment (0.3%), hypotony/phthisis (0.1%) and massive choroidal hemorrhage (0.1%). Only 1% of patients experienced visual loss of more than two lines.[116]

B. MIGS with implants

1. Gold Micro-Shunt

The 5.2 mm long and 3.2 mm wide Gold micro shunt is a valveless mini shunt made of 24-karat gold. It is placed in the suprachoroidal area with one end in the anterior chamber after a 4 mm long full-thickness scleral dissection after opening the conjunctiva through an ab-externo approach.[87] Melamed et al. followed 38 patients who underwent implantation for 12 months. While the mean preoperative IOP was 27.6±4.7 mmHg, the mean postoperative IOP was 18.2±4.6 mmHg. The mean NOD was 2.0±0.8 preoperatively and 1.5±1.0 postoperatively.[117]

Agnifili et al. found the presence of fibrosis and encapsulation in the mini shunt in their histopathologic examinations in 5 eyes with POAG and failed shunt surgery.[118] In another study, connective tissue accumulation around the shunt was observed in failed cases. It should be concluded that micro implant occlusion is caused by connective tissue proliferation and is the cause of surgical failure. This process may also result from chronic inflammation in the suprachoroidal space.[119]

2. Trabecular Micro-bypass (iStent)

Table 2 summarizes different types of iStent devices.

Table 2: *iStent types and specifications.*

Type	Lumen	Material	Miscellaneous
iStent	120 micron	titanium	heparin coated asymmetrical design 1 stent per injector
iStent inject	80 micron	titanium	heparin coated symmetrical design 2 stents per injector
iStent infinite	80 micron	titanium	heparin coated symmetrical design 3 stents per injector
iStent supra	165 micron	polyethersulfone and titanium	designed for suprachoroidal space

a. iStent

The iStent is a 1 mm long, L-shaped, titanium stent that is implanted ab internally into Schlemm's canal through a corneal incision using a preloaded syringe with goniolens.[120] It bypasses the trabecular meshwork and provides a permanent aqueous flow between the anterior chamber and the SC. iStent was approved in the US in 2012 for use in combination with cataract surgery in patients with ocular hypertension or mild-to-moderate glaucoma.

Vold et al. reported a prospective randomized study comparing primary treatment with two trabecular micro-bypass stents with topical prostaglandin therapy in 101 phakic eyes with newly diagnosed POAG.[121] Mean IOP was 25.1 ± 2.5 mmHg before stent implantation and 25.1 ± 4.6 mmHg in drug-treated eyes. At three years, the mean IOP was 14.6 mmHg in stent-treated eyes and 15.3 mmHg in drug-treated eyes.[121]

Donnenfeld et al. followed phakic or pseudophakic patients with medically uncontrolled POAG for 36 months after two iStent implantations. At the end of 36 months, a 37% reduction in mean IOP was found.[122] As the number of implants implanted increased, a further decrease in IOP was found, but the number of implants to be implanted should be determined according to the target pressure.[123] Malvankar-Mehta et al. published a meta-analysis that included only iStent-implanted patients. At the end of the 18-month follow-up, a 22% decrease in mean IOP value was observed in patients with single iStent implantation, while a 30% decrease was found in patients with two iStents and a 41% decrease in patients with three iStents at 6-month follow-up.[124]

Samuelson et al. performed phaco alone or phaco+iStent in 240 eyes with early or intermediate POAG and followed up for one year.[125] While IOP decreases were similar at the end of the follow-up period, IOP levels below 21 mmHg without medication were achieved in fewer eyes in the combined surgery group than in the phaco group (50% vs. 72%). In the 2-year follow-up of the same study group, it was reported that IOP remained stable in the combined group (17.0±2.8 mmHg in the 1st year, 17.1±2.9 mmHg in the 2nd year), whereas an upward trend was reported in the phaco alone group (17.0±3.1 mmHg in the 1st year, 17.8±3.3 mmHg in the 2nd year).[126]

The safety profile of trabecular micro-bypass is high. The most commonly reported complications include mild hyphema, transient IOP elevation, corneal edema, stent occlusion, anterior chamber collapse, failure to implant the stent, vitreous incarceration, stent mispositioning, and the need for secondary surgery. Obstruction of the stent lumen by a blood clot or iris may resolve spontaneously or after iridoplasty.[87]

b. iStent Inject

In response to the success of the iStent, iStent Inject was approved by the FDA in 2018. It is made of heparin-coated titanium. The lumen opening is 80 microns. This device has a preloaded injector system that allows the implantation of two stents, further enhancing IOP reduction (Figure 5).[127,128]

iStent Inject is a new design for trabecular flow augmentation and is 360µ long with sections in the anterior chamber, trabecular meshwork, and SC. iStent Inject can be used alone or in combination with cataract surgery. Several studies have shown that iStent Inject is generally preferred in terms of safety and efficacy, especially regarding the benefits of the double stent approach.[127,129]

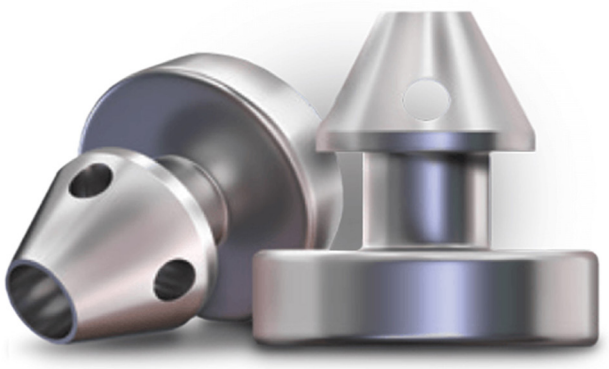

Figure 5: *iStent Inject (https://www.glaukos.com/glaucoma/products/istent-inject-w)*

In a study, phaco and phaco+iSTent injected patients were followed up for two years. At the end of the follow-up, mean IOP was found to be 1.6 mmHg lower in the combined group. There was also a significant decrease in the IS used.[130] In another study, phaco+iStent was compared with phaco+iStent Inject. More IOP reduction was detected in the injected group.[131] Studies have shown that iStent injecting is more effective than iStent injection.[132,133]

Fea et al. compared the efficacy of 2 iStent inject implantations (group 2) against two antiglaucoma medications (group 1). The mean IOP reduction was 7.2±2.2 mmHg in the first group and 8.1±2.6 mmHg in the second group. It was concluded that the implant was at least as effective and safe as drug use.[134]

Gonnerman et al. evaluated patients who underwent phaco+iStent injection in one eye and phaco+trabectome in the other eye. The study found no significant difference between the two procedures regarding the IOP-lowering effect for one year.[135] Only six weeks after surgery, the amount of topical medication was significantly higher in the trabectome group than in the iStent group. The mechanism of trabectome surgery causes trauma to the trabecular meshwork and leads to scar formation.[136] A potential advantage of iStent injection may be minor damage to the trabecular meshwork compared to the trabectome procedure.

Another study compared phaco+iStent injection (group 1) with phaco+iStent injection+endocyclophotocoagulation (group 2). At the end of 12 months, mean IOP decreased by 21% in group 1 and 35% in group 2. NOD decreased by 33% in group 1 and 45% in group 2. This study emphasized the additive effect of 2 different MIGC procedures.[137]

A retrospective review compared 70 patients who underwent iStent injection ± iStent (Multi-Stent group) with 40 patients who underwent trabeculectomy + mitomycin C (Trab group) for moderate to severe open angle glaucoma (OAG) and were followed for at least three months. They reported that an IOP reduction of ≥20% was 62.9% vs 30.0% in Multi-Stent and Trab eyes, respectively, with Multi stents achieving the best results (p = 0.001).[138]

c. iStent Infinite

iStent Infinite consists of 3 microscales wide flanged (iStent inject W) stents on a single preloaded injector. The stents are designed to be implanted ab-interno at three separate sites (each ~2 hours apart) along the nasal 4-hour quadrant of the trabecular meshwork to increase aqueous humor flow and reduce IOP, creating a bypass from the trabecular meshwork to the SC. It preserves the natural angle architecture by preventing disruption of the peristaltic function of Schlemm's canal.[139] Furthermore, each additional stent gradually increases the treatment effect.[140]

Sarkisyan et al. applied iStent Infinite to 72 patients with refractory glaucoma who had previously undergone glaucoma surgery and received implants. At the end of the 12-month follow-up, they found a 5.9% decrease in mean IOP value. The mean NOD was 3.10±0.89 at baseline and 2.70±1.03 at 12 months postoperatively. In addition to efficacy, the safety profile was also quite favorable.[141]

d. iStent Supra

iStent Supra contains heparin-coated polyethersulfone and titanium sleeves. It is implanted into the suprachoroidal space via an ab-interno approach. It is implanted just below the scleral spur, appropriately beveled into the suprachoroidal space. It was developed to support increased uveoscleral flow.

Myers et al. applied iStent+iStent Supra+postoperative travoprost to patients with refractory glaucoma who had previously undergone glaucoma surgery. They found a 37% reduction in IOP value after surgery. The most common complication was cataracts (16%).[142]

3. Hydrus Microstent

Hydrus is a highly elastic, biocompatible, 8 mm long, circular implant made of nitinol (nickel+titanium) alloy, suitable for the curvature of Schlemm's canal.[143] It was observed that aqueous outflow was increased by expanding Schlemm's canal with a micro stent placed into Schlemm's canal with an ab-interno approach.[144] In surgery, the nasal quadrant is often chosen for easy application with temporal

corneal incision. This is also the region with the highest rate of collecting ducts.[145] It can be used in patients with POAG and PXG. It is contraindicated in patients with neovascular glaucoma, angle closure glaucoma, uveitic, traumatic, steroid-induced, and lens-induced glaucoma. It should also not be used in patients undergoing tube implantation, laser trabeculoplasty, cyclodestructive procedures, or trabeculotomy.

In their study, Hays et al. implanted a Hydrus micro stent in one eye and two iStents in the other eye. The Hydrus micro stent increased outflow (73% versus 34%).[146] Johnstone et al. compared 8 mm and 15 mm Hydrus micro stents to determine the anatomical changes seen in the SC and collecting duct after implantation. Electron microscopic evaluations suggested that 15 mm micro stents caused more deformation in the outer wall of the SC and, therefore, may have the potential to cause more obstruction in the collecting duct ostium.[147]

In a prospective study, patients who underwent phaco+hydrus and phaco were followed up for five years. At the end of the follow-up, the mean IOP level was <18 mmHg in 49.5% of eyes in the combined group and 33.8% of eyes in the phaco group. 66% in the combined group and 46% in the phaco group did not use any medication after surgery. Postoperative incisional glaucoma surgery was required in 2.4% of eyes in the combined group and 6.2% of eyes in the phaco group.[148] When visual fields were evaluated, it was found that visual field loss remained stable in the combined group.[149] Fea et al. compared Hydrus with SLT. It was reported that there was less drug use in the Hydrus group.[150] Gandolfi et al. compared Hydrus with canaloplasty. They found similar and significant IOP reduction.[151] Complications of the Hydrus implant include subconjunctival hemorrhage, peripheral anterior synechiae, sudden IOP elevations, and hyphema.[152]

4. Cypass

Cypass is a supraciliary micro-stent that received FDA approval in 2016. It is a polyamide implant with a length of 6.35 mm and a thread diameter of 510 microns. Holes on its body allowed aqueous to pass into the suprachoroidal space. It is placed in the suprachoroidal space through a precise corneal incision with the help of goniolens by the ab-interno approach. It provides flow from the anterior chamber to the supraciliary space.[87] In their multicenter study, Hoeh et al. followed the groups of patients (n=184) with POAG who had glaucoma and cataracts and whose IOP was controlled with or without medication for an average of 6 months after phaco+Cypass application.[153] The mean preoperative IOP was 21.1±5.91 mmHg, and the mean NOD was 2.1±1.1. At the end of the follow-up period, a 37% decrease in IOP and a 71.4% decrease in the NOD were recorded. The most common complications were hypotony in the first month (13.8%), transient IOP elevation (10.5%), and anterior chamber inflammation (4.4%). Nine eyes required additional glaucoma surgery during follow-up, but micro stents were not removed in any case. In the other study, the authors followed 167 eyes with phaco combined with microstates for 12 months. The study evaluated patients with an IOP of 21 mmHg and above with medication (n=65) and patients with an IOP below this value (n=102). In the first group, IOP decreased by 35%, and the NOD decreased by 49%. The rate of decrease in the NOD in the second group was calculated as 75%.[154] Vold et al. compared patients who underwent phaco and phaco+Cypass. At the end of the 2-year follow-up, 7.4 mm Hg IOP reduction was found in the combined group and 5.4 mm Hg in the phaco group. No additional medication was needed in 85% of the combined group and 59% of the phaco group.[155]

5. MINIject

MINIject is a supraciliary implant designed for placement in the suprachoroidal space. It is 5 mm long and has a soft, flexible structure. It has a green colored ring positioned 0.25 mm from the tip of the device to aid implant placement. The center of the green-colored ring should be at the level of the scleral spur. Its biocompatible and porous structure reduces tissue reaction and fibrosis.

Denis et al. followed 25 patients with refractory POAG for six months post-implant. While the mean IOP was 23.2 ± 0.6 and NOD was 2.0 ± 1.1 before implant, the mean IOP was 14.2 ± 0.9, and NOD was 0.3 ± 0.7 at the end of the follow-up. There were no severe side effects at the end of the follow-up, and no additional surgery was required.[156] Three prospective, single-arm studies involving 66 patients showed consistent positive results at two years.[157] The MINIject implant targets the visceral pathway via an ab-interno approach, providing an opportunity to lower IOP using an efficient and safe outflow route.

6. XEN Gel Stent

Xen GEL Stent is a 6 mm long gel stent of collagen structure. It is implanted via an ab-interno approach with an injector system. It is designed with three different lumen diameters (45 µ, 63 µ, and 140 µ) to prevent hypotony in the clinical

situation. It is a preloaded device with a disposable 27G syringe designed to be implanted in the anterior chamber through an ab-interno approach.[158] Bleb formation occurs at the end of the procedure, and mitomycin C can be used to reduce fibrosis. The most common implantation site is the superonasal quadrant. The Xen gel implant may pass into the anterior chamber or through the conjunctiva, or the stent may disintegrate. Although the implantation time is short, the surgical technique has a learning period, and postoperative bleb-related problems cannot be ruled out. Xen gel stent has been used in open-angle glaucoma, uveitic glaucoma, iridocorneal endothelial syndrome, and pediatric glaucoma.[159-162] Postoperative needling is required in 43% of cases, and the subconjunctival segment may be cut inadvertently during needling.[159,163] Elevated IOP on the first postoperative day is the most crucial determinant for needling.[164]

During and after the implant, failure may occur due to improper positioning, bleeding, wound leakage, hypotony, and occlusion.[165-167] In the late period, implant migration resulting in falling into the anterior chamber and stent-iris contact, endothelial cell loss, erosion or exposure, bleb-related complications, permanent hypotony, suprachoroidal hemorrhage, and endophthalmitis may be observed.[160,165,168,169]

In a prospective study, Sheybani et al. followed 49 patients who underwent Xen gel implantation with MMC for 12 months. While the mean IOP before implantation was 23.1 ± 4.1 mmHg and the mean NOD was 3.0 ± 1.1 mmHg, there was a 20% IOP decrease in 89% of eyes at the end of the follow-up. During the follow-up, 40% of the patients did not need medication.[170]

Fea et al. followed 12 eyes with Xen implantation for one year. They evaluated bleb morphology before and after Xen implantation with anterior segment OCT (AS-OCT) and in vivo confocal microscopy.[171] An unmedicated IOP of 18 mmHg or less was considered a success. In the 1st year, qualified success (with medication) was reported in 10 eyes and complete success in 5 eyes. Mean IOP and NOD decreased by 31.62% and 82.88%, respectively. No biomicroscopic difference was observed in bleb morphology. Preoperative confocal microscopy images in the upper nasal conjunctival tissue showed optically transparent, round, or oval-shaped, non-clustered microcysts surrounded by a low reflective wall. In contrast, postoperative microcysts were clustered in different shapes and sizes and surrounded by a low reflective wall, and postoperative mean microcyst area and density increased significantly. It was emphasized that biomicroscopic examination methods were not sufficient for bleb follow-up and that additional instruments were needed in terms of postoperative fibrosis follow-up.[171]

77. PreserFlo (InnFocus) Microshunt

The PreserFlo MicroShunt previously known as InnFocus is an 8.5-mm long glaucoma filtration surgical device made of SIBS (polystyrene block-isobutylene-block styrene) with an outer diameter of 350 µm and a lumen of 70 µm, implanted through an ab-externo approach.[172,173] The proximal end of the device rests in the anterior chamber parallel to the iris. In contrast, the distal end sits under the conjunctiva and Tenon's capsule, approximately 6 mm beyond the limbus, allowing aqueous humor to pass through the lumen to create a posterior bleb after implantation. It causes minimal inflammation and scar development in the tissue.

The conjunctiva is dissected through the limbal approach; then, a 25 gauge needle is inserted into the anterior chamber through a 25 gauge needle opening under a half scleral thickness scleral pocket (1x1 mm). The aim is to ensure aqueous humor flow between the anterior chamber and the subconjunctival area. The surface protrusions of the implant prevent unwanted dislocation of the microchannel.[174] Surgery is easy to perform, and the operation time is short. However, MMC application is recommended to prevent fibrosis.

Riss et al. tested two MMC doses (0.4 mg/ml, 0.2 mg/ml) with different application methods in 87 eyes in which an InnFocus micro shunt was implanted.[175] In the study, MMC at a dose of 0.4 mg/ml was administered to 23 eyes intraoperatively (group 1), MMC at a dose of 0.2 mg/ml was administered to 31 eyes (group 2), and MMC at a dose of 0.4 mg/ml was administered to 33 eyes in the deep application (group 3). At the end of the one-year follow-up period, IOP decreased from 23.8±5.3 to 10.7±2.8 mmHg in group 1, from 27.9±6.7 to 13.3±3.3 mmHg in group 2, and from 25.4±7.9 to 15.7±4.6 mmHg in group 3. IOP reduction rates in the groups were 55%, 52%, and 38%, respectively. No severe complications were encountered after the operations.

In a retrospective study, Beckers et al. followed 91 patients with primary OAG who underwent InnFocus and Phaco+InnFocus for 12 months.[176] Preoperative IOP decreased from 24.3 mmHg with 2.4 drugs to 13.3 mmHg with 0.4 medications at the end of follow-up. Interestingly,

83% of patients were free of glaucoma medications postoperatively. Ten patients had a transient hypotony (<6mmHg) and some minor hyphema that resolved on its own after three months. Finally, the authors noted that "many cases" required needling or bleb modification to reduce IOP.[176]

In a retrospective study, Fea et al. evaluated the 12-month outcomes of 104 eyes with POAG (81 eyes) and PXG (23 eyes) implanted with PreserFlo MicroShunt.[177] Mean IOP decreased significantly in eyes with POAG (25.0 mmHg at baseline vs. 14.3 mmHg at 12 months) and PXG (25 mmHg at baseline vs. 13.5 mmHg at 12 months). At the end of follow-up, the mean IOP-lowering effect and postoperative side effects were similar in both groups.[177] Finally, although evidence suggests that individuals with PXG suffer from blood-aqueous barrier disruption after intraocular surgery, topical steroid therapy was not used longer or more intensively in the PXG subgroup in this study.[178,179] These results suggest that MicroShunt may induce a limited inflammatory response and offer a good safety profile in other types of open-angle glaucoma.[177]

In a study, patients who underwent MicroShunt and trabeculectomy were followed up for six months. Mean IOP was 10.8 mmHg in the Preserflo group and 10.3 mmHg in the trabeculectomy group. There was no statistically significant difference in IOP fluctuation between the groups. The trabeculectomy group had a statistically significantly higher postoperative intervention rate than the MicroShunt group, which may offset the higher costs of PreserFlo during surgery. None of the patients experienced any severe side effects.[180]

POAG patients in whom PreserFlo MicroShunt was implanted after a single failed trabeculectomy performed at least six months ago were followed up for one year.[181] At the end of the follow-up, the mean IOP decreased by 47.93%, and the mean NOD decreased from 3.29 to 0.46. Furthermore, only a few minor complications occurred in the postoperative period. Transient hypotony and choroidal effusion were the most common.

Wagner et al. compared patients implanted with Xen Gel Stent, PreserFlo MicroShunt, and trabeculectomy with MMC.[182] At the 6-month follow-up, complete success was 73.5 percent in the trabeculectomy group, 51.4 percent in the XEN group, and 74.2 percent in the PreserFlo group. The IOP reduction in the trabeculectomy group was 12.1 mmHg, significantly higher than the other two subgroups (5.8 mmHg higher than the XEN group and 4.8 mmHg higher than the PreserFlo group). In conclusion, all three methods were successful and showed comparable surgical success after six months.

PreserFlo can be used alone or in combination with phacoemulsification. It provides a significant decrease in the NOD and mean IOP level.[183,184]

8. Ex-Press Implant

The Ex-Press implant is a minimally valveless stainless invasive device designed to create subconjunctival drainage pathways for aqueous humor and effectively reduce IOP in patients with glaucoma.[185] Available since 2002, it is a less invasive alternative to trabeculectomy. It consists of a stainless steel tube with a length of 2.64 mm and an outer diameter of 400 microns.[185,186] There are two models for lumen size (P-50 and P-200). The smaller lumen of the P-50 is designed to provide a more controlled, slower aqueous humor outflow and reduce the risk of hypotony. The Ex-Press device is placed under a partial thickness scleral flap to allow aqueous humor to pass into the subconjunctival space. After corneal paracentesis, the device is inserted into the anterior chamber under a small partial-thickness scleral flap, creating a fistula that allows aqueous humor to bypass the trabecular meshwork. The scleral flap is then closed postoperatively with titratable sutures to control fluid flow and maintain optimal IOP.[185,186]

The Ex-Press device and transscleral cyclophotocoagulation are well equipped to control IOP in NVG eyes that do not respond adequately to panretinal laser photocoagulation and topical antiglaucoma medications. In addition, these applications can be considered the first effective interventional option to lower IOP instead of trabeculectomy surgery, which carries the danger of fibrosing and failed blebs.[187] Dahan et al. prospectively compared patients who underwent Ex-Press implantation and trabeculectomy. Significant IOP reduction was seen in both treatment groups. It was 44% for the Ex-Press implant group and 48% for the trabeculectomy group. However, eyes receiving Ex-Press implantation had a significantly higher probability of complete success.[188] Ex-Press glaucoma mini shunt implantation has been found to be effective in reducing postoperative inflammation of filtering surgery and achieving a high success rate.[188-190] One study found that PHACO-Ex-Press reduced the NOD (0.24 ± 0.56 vs. 1.02 ± 1.08) and had a higher complete success rate than phaco-trab (84.9% vs. 41.2%). However, there was no statistically significant difference in the qualified success rate between the two groups at 12 months

postoperatively. Therefore, for patients with concomitant POAG and cataracts, phacoemulsification with Ex-Press instead of trabeculectomy may provide better IOP control and less postoperative antiglaucoma medication. Number of corneal endothelial cells at 12-month visit.[191]

It has early postoperative advantages, such as reduced IOP fluctuation and corneal endothelial cell loss rates. Ex-Press implantation is also an effective treatment in advanced glaucoma cases where stable IOP reduction is required.[192]

CONCLUSION

MIGS has started a new era in glaucoma treatment and follow-up with less tissue trauma, rapid postoperative recovery, and increased patient satisfaction.[193] Currently, popular MIGS are less invasive than conventional glaucoma surgery. In addition, a more effective result can be achieved by combining MIGS with Phacoemulsification. In the early treatment of mild to moderate glaucoma, it aims to achieve success with fewer complications than conventional surgeries. MIGS offer an effective treatment with a lower impact on quality of life, making MIGS a more suitable option for many patients. Despite its advantages, MIGS has limited efficacy in severe cases of glaucoma, requires longer-term data, and has limitations, such as cost and accessibility issues. Proper training and patient selection are essential in MIGS techniques.

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