A REVIEW OF MINIMALLY-INVASIVE GLAUCOMA SURGERY (MIGS)

Felise May Barte, MD

CECOM Symposium 2019

I. Traditional glaucoma surgery

A. Trabeculectomy

B. Tube Shunt

C. Tube versus Trabeculectomy Study

Gedde SJ, Herndon LW, Brandt JD, Budenz DL, Feuer WJ, Schiffman JC, Tube Versus Trabeculectomy Study G. Postoperative complications in the Tube Versus Trabeculectomy (TVT) study during five years of follow-up. *Am J Ophthalmol*2012;153(5):804-814 e801

- Trabeculectomy and tube shunt surgeries are highly effective, but high risk of complications.

II. Micro-invasive glaucoma surgery (MIGS)

A. Background

1. Purpose: benefit from lower IOP but do not warrant the risk of traditional surgery.
2. Cardinal features:
   - Ab interno, micro-incisional approach
   - Minimal trauma/disruption to normal anatomy and physiology
   - Reliable IOP lowering
   - High safety profile
   - Rapid post-op recovery, with minimal need for follow-up
3. Indications- mild and moderate glaucoma
4. Mechanism of Action (MOA)
   1. Increasing trabecular outflow
      a. Meshwork bypass
         i. iStent Micro-Bypass
         ii. iStent Inject
         iii. Hydrus Microstent
      b. Trabeculotomy
         i. Gonioscopy-assisted transluminal trabeculotomy (GATT)
         ii. Trabectome
         iii. Kahook Dual Blade
         iv. TRAB 360 Trabeculotomy
      c. Canaloplasty
         i. Ab interno canaloplasty (ABiC)
         ii. VISCO 360
   2. Increasing uveoscleral outflow/suprachoroidal/supraciliary outflow
      a. CyPass Micro-Stent
      b. iStent Supra
   3. Increasing subconjunctival outflow
      a. XEN
      b. InnFocus MicroShunt
   4. Decreasing aqueous production.
      a. Endocyclophotocoagulation (ECP)
5. Most common complications: IOP spike, hyphema

B. **iStent** *(Glaukos Corporation)*

1. Heparin-coated, non-ferromagnetic titanium stent; 1.0 mm x 0.3 mm.
2. First FDA-approved (2012) trabecular microbypass
3. Ab interno insertion into Schlemm's canal
4. iStent Study Group conducted largest RCT- 240 subjects with mild to moderate glaucoma.

Craven ER, Katz LJ, Wells JM, Giamporcaro JE, iStent Study G. Cataract surgery with trabecular micro-bypass stent implantation in patients with mild-to-moderate open-angle glaucoma and cataract: two-year follow-up. *J Cataract Refract Surg* 2012;38(8):1339-1345

-At 2 years, primary endpoint, IOP ≤ 21 mmHg without glaucoma medications, remained significantly higher in the iStent with CE group (61% vs 50%, p = 0.036)

- NO significant difference found in secondary endpoint, (decrease in IOP of ≥ 20%), without glaucoma medications and number of glaucoma medications used
- Efficacy was modest but allowed prolonged reduction in IOP and medication burden
- No serious complications associated
- Most common complications: obstruction (4.3%), malposition (2.6%)

5. Multiple iStents

Belovay GW, Naqi A, Chan BJ, Rateb M, Ahmed, II. Using multiple trabecular micro-bypass stents in cataract patients to treat open-angle glaucoma. *J Cataract Refract Surg* 2012;38(11):1911-1917

- To evaluate the efficacy of multiple iStents (2 or 3) in conjunction with CE, a prospective study of 53 eyes with OAG
- Statistically significant: After 1 year, the overall mean IOP lower than baseline in each group (2 or 3).
- Decrease in mean glaucoma medication at 1 year by 74%. 31 study eyes (59%) were off all medications at 1 year.
- Multiple iStents can be safely implanted and result in effective IOP reduction on fewer glaucoma medications.

C. iStent Inject *(Glaukos Corporation)*

1. Smaller, (0.36 mm x 0.23 mm)
2. Each device pre-loaded with 2 stents- both inserted in one procedure
3. FDA approved in June 2018
4. Samuelson TW. Prospective, randomized, multicenter clinical investigation of the Glaukos iStent inject. Presented at: American Society of Cataract and Refractive Surgery annual meeting; April 13-17, 2018; Washington

- Statistically significant reduction in unmedicated diurnal IOP in patients

- Adverse Events: stent obstruction (6.2%), intraocular inflammation (5.7% for iStent inject vs. 4.2% for cataract surgery only), secondary surgical intervention (5.4% vs. 5.0%) and BCVA loss ≥ 2 lines ≥ 3 months (2.6% vs. 4.2%).

5. Contraindications: angle-closure glaucoma, traumatic, malignant, uveitic, or neovascular glaucoma, discernible congenital anomalies of the anterior chamber angle, retrobulbar tumor, thyroid eye disease, or Sturge-Weber Syndrome or any other type of condition that may cause elevated episcleral venous pressure.

D. Hydrus Microstent (*Ivantis, Inc*)

1. Improves aqueous outflow into multiple collector channel ostia by serving as an "intracanalicular scaffold" for Schlemm's canal and a bypass of the TM.

2. 8-mm ("3 clock hours") long, crescent-shaped scaffold composed of a nickel-titanium alloy (nitinol) with windows and spines. Comes preloaded in hand-held injector.

3. Samuelson TW, Chang DF, Marquis R, Flowers B, Lim KS, Ahmed IIK, Jampel HD, Aung T, Crandall AS, Singh K, HORIZON Investigators. A Schlemm canal microstent for intraocular pressure reduction in primary open-angle glaucoma and cataract: the HORIZON study. *Ophthalmology* 2018.

- Statistically significant - IOP was reduced by ≥20% in 77.3% of Hydrus + CE group. Mean number medications reduced from 1.7±0.9 at baseline to 0.3±0.8 at 24 months in study group. No serious ocular adverse events related to the microstent. No significant differences in safety parameters between the 2 groups.

4. Complications: peripeheral anterior synechiae

E. Gonioscopy-assisted transluminal trabeculotomy (GATT)

1. Illuminated microcatheter (iTrack; *Ellex*) or suture (typically 5-0 or 6-0 nylon or prolene) passed through a 1-2 clock hour goniotomy into Schlemm's canal then advanced for 360 degrees. Catheter or suture pulled centrally, applying force to lyse through the trabecular meshwork (TM) and creating a 360-degree trabeculotomy
2. Track microcatheter has a 200-micron diameter shaft with a lubricated coating, along with a lighted tip, which can be constantly or intermittently illuminated to monitor catheter location
3. Indications: medically-uncontrolled OAG and can be performed with or without CE
4. Grover DS, Godfrey DG, Smith O, Feuer WJ, Montes de Oca I, Fellman RL. Gonioscopy-assisted transluminal trabeculotomy, ab interno trabeculotomy: technique report and preliminary results. *Ophthalmology* 2014;121(4):855-861.

-IOP decreased by 40%

- 1.1 ± 1.8 fewer glaucoma medications.
- No statistically significant difference in IOP change related to lens status or whether concurrent CE was performed
- Primary complication: transient hyphema in 30%
- Additional glaucoma surgery needed in 9% (8/85)

5. Contraindications

Absolute: anticoagulation, bleeding diatheses, angle closure, obscured angle structures, severe endothelial compromise, intraocular lens instability, neovascular glaucoma, traumatic glaucoma

Relative: previous corneal transplant, inability to elevate patient's head 30° during the first postoperative week.

F. Trabectome *(NeoMedix Inc)*

1. FDA-approved (2004) device used to perform ab interno trabeculectomy
2. Combines electrocautery with irrigation and aspiration
3. 19.5 gauge handpiece with a bipolar 550 kHz electrode. Handpiece is disposable and requires separate irrigation and aspiration console with a high frequency generator. As electrocautery ablates trabecular meshwork up to 180 degrees, the natural drainage pathway is exposed. Simultaneously aspiration and irrigation are used to remove ablated tissue to allow aqueous outflow.
4. Indication: primary OAG patients with uncontrolled IOP on maximal medical therapy. Reported use in narrow angle glaucoma, pseudoexfoliation and patients with a history of a failed trabeculectomy
5. No random clinical trials have been conducted examining trabectome
6. Complications: transient hyphema, peripheral anterior synechiae, corneal injury, and transient IOP spike. Rate of serious vision-threatening complications was minimal (< 1%): hypotony, cyclodialysis cleft, choroidal hemorrhage, and endophthalmitis.

G. Kahook Dual Blade (*New World Medical*)
1. Single-use, tapered, stainless steel blade used to incise and remove nasal strip of TM. Through one incision, the TM may be removed for a total of up to 180 degrees
2. Unlike Trabectome, no need for additional machinery for electrocautery- no collateral thermal damage.
3. Dorairaj SK, Seibold LK, Radcliffe NM, Aref AA, Jimenez-Roman J, Lazcano-Gomez G, Sarlington JK, Mansouri K, Berdahl JP. 12-Month outcomes of goniotomy performed using the Kahook Dual Blade combined with cataract surgery in eyes with medically treated glaucoma. *Adv Ther.* 2018; 35 (9): 1460-1469.

- At month 12, 57.7% of eyes had IOP reduction ≥ 20% from baseline, and 63.5% were on ≥ 1 fewer IOP-lowering medications. In subgroup analysis, 84.6% of eyes with lower mean baseline IOP were using ≥ 1 fewer medications at month 12, and 100% of eyes with higher mean baseline IOP had IOP reductions ≥ 20%.

4. Adverse events- pain/irritation, opacification of the posterior lens capsule, and IOP spike > 10 mmHg. hyphema.

H. TRAB 360 Trabeculotomy *(SightSciences)*
1. Disposable, non-powered device used to perform an ab interno 360° trabeculotomy
2. Device consists of cannula, from which a flexible nylon-like trabeculotome is advanced into Schlemm's canal for 180 degrees. After the trabeculotomy is created, the trabeculotome can be retracted and advanced into the remainder of Schlemm's canal in the opposite direction for up to a total of 360 degrees.
3. Indicated for open angle glaucoma when IOP is not optimized on medical management
4. Sarkisian SR, Allan EJ, Ding K, Dvorak J, Badawi DY. New Way for Ab Interno Trabeculotomy: Initial Results [poster]. ASCRS ASOA Symposium and Congress; 17-21 April 2015; San Diego, CA

Surgical success, defined as IOP between 6-21 mmHg, was achieved in 25 of 30 eyes (83%) with or without glaucoma medications at the final follow-up visit.

Glaucoma medication burden was also decreased from a mean of 1.1 ± 1.2 pre-op medications to a mean of 0.2 ± 0.5 medications at the final visit.

5. Complications: Transient hyphema, resolved by 1 week postoperatively in all cases.

I. Ab interno canaloplasty (ABic)
1. Increases aqueous outflow through cannulation of Schlemm's canal with an illuminated microcatheter (iTrack, Ellex), which is withdrawn as an ophthalmic viscosurgical device (Viscoat) injected to viscodilate Schlemm's canal and proximal collector channels. Viscodilation may also create microperforations within the TM to aid in aqueous outflow. As the viscoelastic is injected, blanching of episcleral vessels, which is indicative of a patent collecting system, serves as an indirect indicator of success.
2. Indications: mild to moderate OAG. Can be performed as a standalone procedure or with CE.
3. Better option for high risk monocular patients or for patients who are unable to stop anticoagulation- minimally disrupts the TM with lower rates of hyphema.
4. Contraindications: similar to those of GATT
6. Ellex iScience. Ab-Interno Canaloplasty: A Comprehensive Minimally Invasive Glaucoma Surgery That Keeps Its Promise: 12 month case series review, 2016. (Gallardo and Khaimi retrospective review)

Mean IOP decreased 30%, mean postop number glaucoma medications decreased 50%.

7. Complications: Descemet's detachment during injection of viscoelastic. Hyphema not reported.

J. CyPass Micro-Stent (*Alcon*)
1. FDA-approved (2016) suprachoroidal shunt used to increase uveoscleral outflow.
2. Flexible, fenestrated micro-stent sized 6.35 mm x 510 μm with a 300 μm lumen and composed of biocompatible, polyimide material. Comes preloaded with micro-stent on guide-wire conformed to the

shape of the sclera to facilitate dissection and insertion between the anterior chamber/sclera and suprachoroidal space.
3. Vold S, Ahmed, II, Craven ER, Mattox C, Stamper R, Packer M, Brown RH, Ianchulev T, CyPass Study G. Two-Year COMPASS Trial Results: Supraciliary Microstenting with Phacoemulsification in Patients with Open-Angle Glaucoma and Cataracts. *Ophthalmology* 2016;123(10):2103-2112.

Multicenter RCT. At 2 years, there was a statistically significant difference in: primary endpoint, a 20% reduction in diurnal, washed-out IOP compared to baseline, mean reduction in IOP in the Cypass Micro-stent + CE, mean glaucoma medications per patient and the proportion of patients who did not require medications after 2 years.

Adverse events: transient BCVA loss ≥ 2 lines (8.8%), visual field loss progression (6.7%), transient iritis (8.6%), transient corneal edema (3.5%), and transient hypotony (2.9%)
4. Complications: hypotony maculopathy, cyclodialysis cleft,
5. *Voluntarily withdrawn from the global market by Alcon on August 28, 2018*.
COMPASS-XT study- statistically significant increase in endothelial cell loss in the CyPass group after 5 years of follow up.

K. iStent Supra (*Glaukos Corporation*)
1. Suprachoroidal stent - designed to increase uveoscleral outflow
2. Heparin-coated, 4 mm tube with a 0.16 - 0.17 mm lumen, made of polyethersulfone (PES) with a titanium sleeve. Device has retention ridges to hold the device in place. Preloaded into injector device, which is used to direct the device between the anterior chamber/sclera and suprachoroidal space.
3. Can be combined with CE
4. Myers J, Katz J. Open Angle Glaucoma Treated with a Suprachoroidal Stent and Topical Travoprost. 23 rd Annual American Glaucoma Society Meeting. March 2013, San Fancisco, CA

All patients were treated postoperatively with Travoprost unless IOP was less than 6mmHg.

24 of 25 patients experienced >20% reduction in IOP compared to preoperative un-medicated IOP. 21 of 25 eyes experienced >20% reduction in IOP vs preoperative medicated IOP.

Adverse events: Hypotony-resolved by POM1. Choroidal detachment, resolved by POM3.

5. Further clinical trials are ongoing in the United States to evaluate the safety and efficacy

L. XEN (*Allergan*)
1. FDA-approved 2016

2. Subconjunctival stent - allows aqueous outflow from anterior chamber into the subconjunctival space

3. Device is a 6 mm tube composed of gelatin and glutaraldehyde. Preloaded within a 27-gauge needle on a disposable injector. The device is inserted into the anterior chamber, passed ab interno, and then tunneled through sclera to deploy the device within the subconjunctival space. After implantation, the device creates a filtering bleb. It may be performed with or without adjuvant antimetabolites (MMC).

4. Three sizes of the XEN gel stent based on lumen diameter. The XEN45 (45 μm lumen) is the only currently FDA-approved size

5. Indications: refractory glaucoma failing surgical treatment, primary OAG, pseudoexfoliative, or pigmentary glaucoma with open angles that have failed maximum medical therapy.

6. Galal A, Bilgic A, Eltanamly R, Osman A. XEN Glaucoma implant with mitomycin C 1-year follow up: result and complications. *J Ophthalmol* 2017; 2017: 5457246.

Prospective interventional study, 13 eyes with POAG underwent XEN implantation with subconjunctival MMC. 3 pseudophakic and 10 underwent simultaneous phacoemulsification and XEN. Complete success was defined as IOP reduction ≥20% from preoperative baseline at 1 year without any

glaucoma medications. Partial success as IOP reduction of ≥20% at 1 year with medications. 42% of eyes achieved complete success and 66% qualified success.

Complications: choroidal detachment, implant extrusion, and 2 eyes underwent trabeculectomy.

7. Bleb surgery. 30-40% patients require needling, bleb encapsulation
8. Other sizes of the XEN gel stents (63 μm and 140μm) have been studied in pilot trials

M. InnFocus MicroShunt (*InnFocus Inc/Santen*)

1. Allows aqueous drainage into the subconjunctival space using an ab externo approach.
2. Device is 8.5 mm x 0.350 mm with a 70 μm lumen and composed of SIBS [poly(styrene-block-isobutylene-block-styrene)] material which regulates aqueous flow. After making a small conjunctival peritomy, a needle is used to create a small scleral pocket, within which a smaller needle enters the anterior chamber. The device is then implanted and allows aqueous humor to drain from the anterior chamber into sub-Tenon's space to form a bleb. Mitomycin C is routinely placed in the area of the intended bleb.
3. Not yet FDA-approved, but is indicated for the treatment of mild, moderate, or severe OAG. May be performed with or without CE.
5. Palmberg PF. Two-center results of a SIBS-based micro shunt at 1 to 4 years. Presented at: American Glaucoma Society annual meeting; March 2-5, 2017; Coronado, Calif

79 eyes implanted with the device and MMC and followed over 4 years. 80% eyes achieved IOP of 14 mm Hg or less from a mean baseline of 24.8 mm Hg. Mean number of glaucoma medications, which at baseline was 2.3, was reduced 61% to 0.9 medications per patient, with 62% of patients taking no glaucoma medications. Adverse events: Hypotony (11.3%). resolved spontaneously. No cases of chronic hypotony or endophthalmitis.

6. Advantages: no need for suture lysis/release. Less complex surgery than tube or trab surgery.

N. Endocyclophotocoagulation (ECP) (Endo Optiks Inc)

1. Cyclodestruction of the ciliary body epithelium to reduce aqueous production
2. Probe is reusable device, which includes a laser source, camera, and light source. After probe introduced into anterior chamber, the probe directed towards the anterior ciliary processes to deliver precise continuous energy (810 nm wavelength). Through a single corneal incision, approximately 240 to 300 degrees of the ciliary processes can be treated.
3. Francis BA, Berke SJ, Dustin L, Noecker R. Endoscopic cyclophotocoagulation combined with phacoemulsification versus phacoemulsification alone in medically controlled glaucoma. *J Cataract Refract Surg* 2014;40(8):1313-1321

ECP with CE effective in decreasing IOP and medication burden, compared to CE alone in a group of 160 consecutive patients with medically-controlled OAG

Reported adverse events- hyphema, inflammation, and IOP spike

4. Good option for: iris plateau, angle closure, patient on anticoagulants, previous tube surgery.