Micro-Invasive Glaucoma Surgery (MIGS): A look at Subconjunctival and Suprachoroidal Outflow

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Disclosure: Consultant for Alcon, Allergan
Overview of Current MIGS Procedures Commercialized and in Development

- Commercialized
  - Kahook Blade
  - Trabectome
    - Schlemm’s canal
  - iStent
    - Schlemm’s canal

- Investigational/Just approved
  - Hydrus
    - Schlemm’s canal
  - Cypass
  - iStent supra
    - Suprachoroidal space
  - SOLX
  - Xen gel stent
    - Subconjunctival space
  - Inn Focus
Surgery
Subconjunctival/Suprachoroidal

- Lower risks compared to Trabeculectomy
- May use as an earlier intervention
- Able to be performed by most surgeons
- Minimal additional equipment required
- Will be more expensive
- Use some in mild glaucoma, some in advanced glaucoma
The Eye’s Conventional Outflow System

In POAG: is TM the site of resistance?

- **yes**: demonstrated by Grant in 1963

- **trabeculotomy**:
  - normal eye: eliminates 50% of R
  - note: sclera has 50% of normal R:
    - IOP will not drop to 0 mmHg
Kahook Blade Animation
Kahook Blade
The Xen gel stent from Allergan is a flexible implant that shunts fluid from the anterior chamber to the subconjunctival space.

The Xen stent is implanted ab interno from across the eye through a clear cornea incision, in about 15 to 20 minutes.

It is made of porcine gelatin that’s crosslinked with gluteraldehyde.

The cylindrical, 6-mm long implant comes with three different-size lumens: 45 µm; 63 µm; and 140 µm.
- You get immediate intraocular pressure reduction and needs relatively little postoperative management.

- The small luminal diameter of this shunt seems to provide enough resistance to aqueous flow that postoperative hypotony is minimized.

- This procedure can be combined with a subconjunctival injection of mitomycin-C to enhance long-term intraocular pressure control.
The Hagen-Poiseuille equation

- AH production occurs at a rate of 2 to 3 μL/min.
- In order to prevent hypotony, a device would need to create approximately 5 mm Hg of steady-state pressure at this rate.
- This pressure can be thought of as the pressure difference between the two ends of a tube.
- The dimensions of a tube required to prevent hypotony was calculated.
- The length of the tube was set to 6 mm in order to conform to previous injector systems.
- Clinically, this length was also ideal to prevent device erosion and ensure that AH is directed posteriorly away from the limbus. At that length, a lumen of 45 μm would provide a steady-state pressure of approximately 6 to 8 mm Hg at 2 to 2.5 μL/min as calculated by the Hagen-Poiseuille equation.
The Hagen-Poiseuille equation was used to calculate the required dimensions of a tube that would prevent hypotony at average AH production.

\[ \Delta P = \frac{(8\mu LQ)}{(\pi r^4)} \]

- \( \Delta P \) – Pressure loss along the lumen of the tube
- \( \mu \) – dynamic viscosity
- \( L \) – Length of the tube
- \( Q \) – volumetric flow rate
- \( r \) – radius
Xen Gel Stent in Conjunctiva
Xen Gel Stent

- 118 subjects that have received the implants.
- The mean preoperative IOP was 23 mmHg with an average of 3 medications.
- At the 12 and 18 month postoperative follow ups, the mean IOP had decreased to 15.4 ± 4.5 mmHg and then 14.5 ± 3.1 mmHg, respectively.
- At 24 months it was 14.3 ± 5.1 mmHg. At all time points, the average number of medications was one and 33% of patients were using no medications at 24 months.
1) Dissect a fornix-based subconjunctival pouch deep to the equator and 90° to 120° wide. Ensure sclera is white and blood-free.

2) Insert 3 lasik shields soaked in 0.4 mg/mL Mitomycin C, into pouch, contacting all surfaces. Leave for 3 minutes, remove sponges and rinse well with BSS.

3) Mark a spot 3 mm from the limbus using the supplied pen and marker ruler. 4) Cut a shallow pocket with the angled knife just below the surface of the sclera that is 1mm wide and 1mm deep.

5) Form a needle tract by advancing a 25G needle through the pocket and under the limbus exiting at the angle.

6) Hold MicroShunt near beveled tip and advance tube through the pocket and needle tract into the anterior chamber. 7) Wedge fins firmly into pocket.

8) Check MicroShunt for flow through lumen. 9) Tuck tail under Tenons. 10) Suture conjunctiva closed with 10-0 Nylon suture.
A study of 23 eyes with Microshunt insertion, some with and some without cataract surgery, showed that over 80% of the patients had had an IOP ≤14 mmHg at 3 years.

At 3 years, the number of medications had fallen from 2.6 ± 0.9 to 0.8 ± 1.2 in the eyes with Microshunt alone, and from 2.0 ± 0.9 to 0.4 ± 0.1 in the eyes that underwent a combined procedure.

In the group as a whole, the mean IOP at 3 years was 10.7 ± 3.5 mmHg and the qualified success rate (IOP ≤14 mmHg and IOP reduction ≥20%) was 95%.

The most common complications were transient hypotony (13%) and transient choroidal effusion (8.7%), which all resolved spontaneously.

There were no leaks, infections, migrations, erosions, persistent corneal edema, or serious long-term adverse events.

The device is placed in the angle of the eye, with the proximal end extending into the anterior chamber, and the distal end residing in the supraciliary space.

This allows for outflow of aqueous from the anterior chamber into the supraciliary and suprachoroidal spaces.
Cypass Device

- It is a fenestrated microstent made of biocompatible polyimide material.
- The device is 6.35 mm long, with 300-μm and 510-μm internal and external diameters, respectively.
- During insertion, it is flexible and follows the scleral contour along the supraciliary space.
- A series of protruding retention rings at the proximal end ensure the device's positional stability in the angle and the supraciliary space.
Cypass Compass Trial: Inclusion Criteria

- 505 patients diagnosed with POAG. In the study, 374 patients were randomized to the CyPass Micro-Stent in combination with cataract surgery, and 131 patients were randomized to cataract surgery alone.

Inclusion Criteria for patients:

- (1) age ≥45 years;
- (2) diagnosed or confirmed POAG (Shaffer grade ≥3 in all quadrants of the study eye) within 90 days of screening;
- (3) screening medicated IOP ≤25 mmHg or unmedicated IOP between 21 and 33 mmHg;
- (4) baseline unmedicated diurnal IOP between 21 and 33 mmHg, and ≥3 mmHg higher than screening IOP;
- (5) age-related cataract with best-corrected visual acuity (BCVA), or acuity testing with a Brightness Acuity Meter, of 20/40 or worse that was eligible for phacoemulsification cataract surgery with IOL implantation.
Cypass Compass Trial: Criteria

- 83% of patients enrolled were white and 53% were women.
- Exclusion Criteria;
  - (1) if pt has >3 ocular hypotensive medications;
  - (2) significant risk associated with ocular hypotensive medication washout;
  - (3) previous corneal or glaucoma surgery (except laser trabeculoplasty);
  - (4) clinically significant ocular pathology other than cataract and glaucoma;
  - (5) diagnosis of acute angle closure or traumatic, congenital, malignant, uveitic, pseudoexfoliative, pigmentary, or neovascular glaucoma.
Cypass Compass Trial: Patients

- Patient followup:
- Patients were all scheduled for follow-up examinations at postoperative days 1 and 7 and months 1, 3, 6, 12, 18, and 24.
Cypass Compass Trial: Efficacy

- The study evaluated the percentage of patients with reduction of at least 20% in mean diurnal IOP from baseline and adverse events (AEs) for 24 months after implantation.
- Of the patients randomized to the stent, 72.5% achieved a significant lowering of their IOP, compared to 58% of patients who had cataract surgery alone.
Cypass Insertion Pearls

- Must use a goniolens for a direct view of the angle structures.
- Place acetylcholine (10mg/ml) after the phacoemulsification is completed.
- It is crucial that the patient’s head be turned approximately 45 degrees away from your temporal position.
- The microscope should also be tilted about 45 degrees.
- Hyperinflate the anterior chamber to allow the surgeon to enter from a steeper approach. This also helps to avoid areas of dialysis and helps to avoid the corneal endothelium and allows the device to be placed right into the supraciliary space.
- Aim just below the scleral spur.
- It is intuitive to place the guide wire in the vicinity of the iris root and simply push forward.
- This will direct the implant into the supraciliary space.
- When sliding the guide wire into the supraciliary space, ensure you are as radial as possible to the globe and have the device perpendicular to the iris plane.
- Ensure removal of visoelastic at the end of the case.
Cypass Surgery Dr. Misheev
Post Operative Medications

- A postoperative regimen of topical antibiotics (1 week), nonsteroidal anti-inflammatory drugs (3 weeks), and a steroid (tapered over 1 month).

- Reintroduction of topical hypotensive medication(s) was indicated if IOP was >21 mmHg at 2 consecutive visits within a 2-week period after the 1-month postoperative visit.

- Administering ocular hypotensive medication in subjects with IOP >18 and <21.0 mmHg was considered on a case-by-case basis.
RESULTS

Cypass reduces intraocular pressure (IOP) in glaucoma patients.

A-Cypass increased the percentage of glaucoma patients who achieved a ≥20% decrease in unmedicated baseline IOP versus phacoemulsification alone.
**B-** Unmedicated mean IOP was reduced to a greater extent by Cypass versus phacoemulsification only.
C-Cypass increased the proportion of glaucoma subjects who achieved unmedicated IOPs between 6 and 18 mmHg.
A- mean topical glaucoma medication use decreased from 1.4±0.9 to 0.2±0.6 drugs in the stent group.
B-At the 2-year study end point, IOP control in controls required a 3-fold greater number of drugs than in stent recipients.
C-Two years after surgery, 85% of Cypass patients with glaucoma maintained target IOP without any hypotensive medications, whereas only 59% of phacoemulsification-only subjects were drug-free.
Ocular Adverse Events through 24 Months of Follow-up

- BCVA loss $\geq 10$ letters
  - 33 (8.8%) stent group
  - 20 (15.3%) control group

- Corneal abrasion
  - 7 (1.9%) stent group
  - 2 (1.5%) control group

- Corneal edema
  - 13 (3.5%) stent group
  - 2 (1.5%) control group
Ocular Adverse Events through 24 Months of Follow-up

- Conjunctivitis
  - 4 (1.0%) stent group
  - 3 (2.3%) control group

- Cyclodialysis cleft >2-mm circumference
  - 7 (1.9%) stent group
  - 0 (0.0%) control group

- Hyphema, transient intraoperative
  - 10 (2.7%) stent group
  - 0 (0.0%) control group
Ocular Adverse Events through 24 Months of Follow-up

- **Iritis**
  - 32 (8.6%) stent group
  - 5 (3.8%) control group

- **Hypotony (IOP <6 mmHg)**
  - 11 (2.9%) stent group
  - 0 (0%) control group

- **IOP ≥10 mmHg over baseline**
  - 16 (4.3%) stent group
  - 3 (2.3%) control group
Ocular Adverse Events through 24 Months of Follow-up

- Maculopathy, cystoid edema
  - 6 (1.3%) stent group
  - 1 (0.8%) control group
- Stent obstruction
  - 8 (2.1%) stent group
  - N/A control group
- Subconjunctival hemorrhage
  - 6 (1.6%) stent group
  - 1 (0.8%) control group
Ocular Adverse Events through 24 Months of Follow-up

- Secondary ocular surgical intervention
  - 20 (5.5%) stent group
  - 7 (5.3%) control group
- Visual field loss progression, confirmed
  - 25 (6.7%) stent group
  - 13 (9.9%) control group
iStent Supra (Glaukos Corporation, Laguna Hills, CA, USA) is a 4-mm tube made of polyethersulfone and titanium. The concept and mode of delivery is almost identical to the Cypass. There are currently no published studies on surgical outcomes, although preliminary results presented in scientific meetings have demonstrated promising results.
SOLX Gold Shunt
Gold Shunt

- GMS is a nonvalved flat-plate drainage device made of 24-karat medical-grade gold
- Designed to shunt aqueous from the anterior chamber to the suprachoroidal space
Interior View of sGMS+

- 5.6 mm Long
- 3.2 mm Wide at AC end
- 80 Microns thick
- 8.0 mg weight

- 2.4 mm Wide
sGMS+ positioned into AC using bent 27g needle
Comparison of IOP Lowering

Comparison of Pre and Post-Operative IOP

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<tr>
<th>Procedure</th>
<th>Pre-op IOP</th>
<th>Post-op IOP</th>
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<td>17.1</td>
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<tr>
<td>Combined Phaco/Hydrus</td>
<td>18.9</td>
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<td>CyPass</td>
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<td>XEN 45</td>
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<td>InnFocus</td>
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IOP (mmHg)
MIGS and the Cataract Surgeon

Why should adjunct MIGS technology appeal to cataract surgeons?

One important reason is the projected growth in the number of patients with both cataract and glaucoma over the next several decades.

It is already estimated that more than 20% of cataract patients have comorbid glaucoma.

MIGS represents an opportunity to improve glaucoma treatment by taking advantage of the intraocular surgical access already afforded by the cataract procedure.
MIGS and the Cataract Surgeon

- MIGS procedures avoid or reduce the risk of bleb complications that can occur with conventional glaucoma surgery.
- Some MIGS spare the conjunctiva and should not diminish the later prognosis for a successful trabeculectomy.
Economic Benefit

- In an economic analysis of iStent use in the Canadian medical system there is significant cost savings per patient were estimated over 6 years, when comparing two iStents versus mono-, bi-, and triple therapy, respectively.
- Two stents plus one medication still showed savings over two or three drops.
- In a CyPass study 83% of uncontrolled patients did not require trabeculectomy after CyPass insertion as a stand alone procedure.
- This is likely to be associated with significant savings in theatre time and follow-up appointments, and similar savings have been discussed with the use of subconjunctival space stents.
Newer glaucoma surgical options are available for mild and early glaucoma for patients undergoing cataract surgery.

The more advanced the glaucoma, the lower target IOP.

Safety, Efficacy, Convenience and Cost remain critical to the value of any therapy.

Consider earlier surgery in the hands of experienced surgeon for advanced disease and high pressure fluctuation.

Keep an open mind to the new and upcoming microinvasive surgical techniques that will revolutionize glaucoma surgery.
Thank you!


