Evolution of MIGS

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What is MIGS (microinvasive glaucoma surgery)

- **Enhance preexisting pathways for aqueous outflow avoiding major alterations in normal anatomy**
- **ab interno approach, typically**
  - clear cornea incision with direct visualization of tissue target and avoids use of the conjunctiva
- **IOP lowering is often less then traditional filtering surgery but should be at least 20%**
- **The carry less risk of significant complications**
- **Rapid recovery**

Brief Timeline

- 1999: Glaukos produced first MIGS device- iStent prototype
- 2001: First human implant of the iStent
- 2005: FDA granted an IDE for US clinical trials
- 2012: FDA approval of iStent and first MIGS device approved in the US
- This was then followed by cypass in 2015 and Xen in 2016
- The term ”MIGS” was coined by Ike Ahmed

MIGS Target

Trabecular meshwork bypass via stent
- iStent
- Hydrus

Trabecular meshwork bypass by tissue excision
- Kahook Dual Blade
- Trabectome
- Gonioscopy assisted transluminal trabeculotomy (GATT)
- OMNI

Enhancing aqueous outflow through Schlemm's canal
- OMNI
- iTract canaloplasty
- Streamline

MIGS Target

Enhancing aqueous outflow through the suprachoridal space
- Cypass

Shunting aqueous outflow into the subconjunctival space
- Xen Gel Stent
- PreserFlo Microshunt

Reducing aqueous production by ciliary body ablation
- Endocyclophotocoagulation (ECP)
- Cyclophotocoagulation with G6 probe

Trabecular meshwork Bypass via Stent

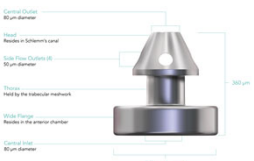
iStent

- Three versions
  - iStent (first generation)
    - L-Shaped
  - iStent inject (FDA approved 2016)
    - 2nd version called iStent W
  - iStent infinte (FDA approved 8/2/22)
    - FDA approved as standalone in refractory glaucoma
  - Typically best for patients mild- moderate glaucoma

iStent First generation

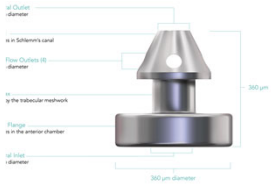
- 1 mm- made of heparin coated titanium
- Central lumen 120 microns
- Preloaded- one iStent
- Pivotal Study
  - Phaco (129) vs phaco/iStent (111)
  - Prospective, randomized trial
  - End point was IOP ≤21 at 12 months
  - 72% of istent/phaco vs 50% phaco only reached end point
  - 66% of istent/phaco vs 48% phaco only had IOP reduction of ≥20%
  - 68% of patients who received iStent at time of cataract surgery were medication free at 12 months

iStent infinte (W) generation



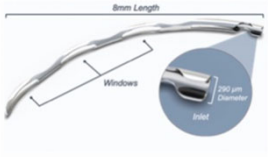
- 360 micron stent made of heparin coated titanium- pre loaded with two iStents
- Central lumen 80 microns
- iStent W is 360 microns vs 230
- Implanted 2-3 clock hours apart
- Pivotal Study:
  - Prospective, single- masked, multi center
  - 505 eys total- 387 were phaco/istent
  - 75.8% had ≥20% reduction in IOP vs 61.9% in phaco alone
  - Mean IOP drop 7±4 mmHg vs 5.4±3.7 mmHg
  - 84% were med free at 23 montsh vs 67% in phaco only group

iStent Infinte



- iStent W expect now 3
- First FDA standalone
- Approved for refractory glaucoma
- Pivotal Study
  - Uncontrolled glaucoma with previous surgery or on maximum tolerated medical therapy
  - 76.1% had ≥20% reduction without use of additional medication or secondary surgical procedures;
  - 53% had ≥30%
  - 21.2% had ≥40%

Hydrus



- 8 mm stent made of nitinol
- Spans 90 degrees of angle
  - Traverse the TM
  - Dilates the Schlemm canal
- Pivotal Study (Horizon Study)
  - 77.3% had ≥20% reduction in IOP vs 57.8% in phaco alone
  - IOP drop in hydrus/phaco vs phaco only 7.6±4.1 mmHg vs 5.3±3.9 mmHG
  - Drop amount 1.7±0.9 to 0.3±0.8 drops in hydrus/phaco vs 0.7±0.9 in phaco only

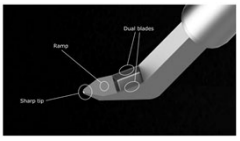
Compare Study

- Prospective Randomized trial comparing Hydrus and iStent 2nd generation
- Standalone treatment of OAG
- End point: IOP difference between groups and medications at 12 months
- Complete success: freedom from repeat glaucoma surgery, IOP ≤ 18 mmHg and no glaucoma medication
- 152 eyes from 152 patients (75 hydrus and 77 iStent)
  - Hydrus achieved an IOP ≤ 18 mmHg more often: 30.1% vs 9.3%
  - Hydrus group also eliminated more medication 1.6 meds vs 1.0
- Conclusion: hydrus resulted in a higher surgical success rate and fewer medications

Trabecular Meshwork Bypass by Tissue Excision

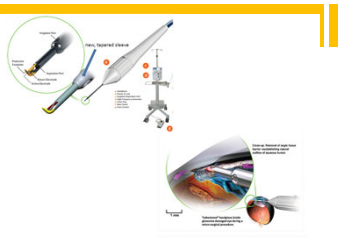
Kahook Dual Blade (Glide)

- 2 versions: Glide released October 2020
- Single use, disposable blade
- Glide: Rounded heel, tapered sides and smaller footplate
- Clinical study:
  - 52 eyes KBD with cataract
  - At 1 year mean IOP 16.8±0.6 mmHg to 12.4±0.3 mmHg
  - 57.7% had experienced a reduction ≥20% IOP reduction
  - Drops decreased from 1.6±0.2 to 0.8±0.1



Trabectome

- Single use hand piece attached to a generator
  - Bipolar 550 *kHz electrode*
- Designed to disrupt or remove the inner wall of Schlemm canal and TM, opening canal and downstream collector channels
- Tip provides irrigation and aspiration and electrocautery in sequence
  - dissipate heat, remove debris and maintain anterior chamber
- Clinical outcome
  - Similar results with stand alone vs combined with phaco
  - 80 eyes of 69 pts with standalone
  - IOP dropped from 26.6±8.1 mmHg to 17.4±3.4 mmHg at 6 months po
  - Drops decreased from 4.0±1.4 to 2.3±1.2



Gonioscopy- Assisted Transluminal Trabeculotomy (GATT)

- Ab interno trabeculotomy
- Can use either a 4-0 or 5-0 prolene suture or iTrack microcather
- Nasal goniotomy is performed then prolene suture or iTrack is advanced 360° in Schlemm's canal
  - If using a prolene suture, cautery is applied to suture tip to induce a mushroom head
- Proximal end is retracted while leading edge is grasped leading to shearing of TM 360
- Retrospective study of 198 eyes showed IOP reduction of 9 mmhg in POAG and 14 mmHg in secondary open angle at 2 years

OMNI

- Single use hand piece
- Can do canaloplasty or trabeculotomy
- Tip is used to pierce TM and suture within OMNI is advanced 180°- when dialed back, canaloplasty is performed. Re advances and pulled out, trabecultomy is performed
- Clinical study (with Trab360)
  - 81 eyes of 57 patients (all types of glaucoma)
  - stand alone
  - At 1 year, 41 eyes were available for analysis
  - The mean IOP reduction was 7.3±6.7 mmHg and 59% of eyes experienced a ≥20% reduction in IOP.
  - Drops decreased 1.7±1.3 from to 1.1±1.0

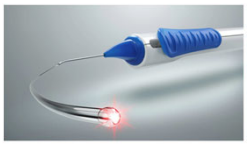
Enhancing Aqueous Outflow through Schlemm's Canal

OMNI (VISCO)

- 106 eyes of 71 patients
  - Group 1 IOP ≥18 mmHg
  - Group 2 IOP <18 mmHg
- Mild/Moderate glaucoma
- End point was IOP reduction and reduction in drops
- Group 1
  - 72 total (11 VISCO360 and 61 combo)
    - IOP reduced from 24.6±7.1 mmHg to 14.6±2.8 (average reduction 41%)
    - 87% achieved ≥20% reduction in IOP
    - Drops reduced from 2.1±1 to 0.2±0.6
      - 85% required no medication
- Group 2
  - 34 total (33 combo, 1 VISCO360)
    - IOP reduced from 14.9±1.8 mmHg to 13.6±2.3 mmHg
    - Drops reduced from 1.8±0.9 to 0.2±0.6
      - 88% required no medication

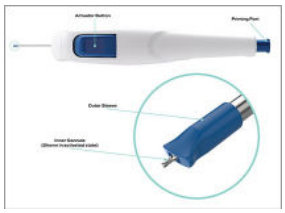
iTrack (Ab interno canaloplasty)

- 250 micro single use microcatheter with fiber optic light
- Schlemm's canal is cannulated 360 degrees and then vasodilation of the canal system and distal outflow system is performed upon withdrawal of the catheter.
- Can also do trabeculotomy like in GATT
- Clinical studies:
  - 75 eyes of 68 patients with POAG
    - 41 standalone
    - 34 with phaco
  - IOP drop: 20.4±4.7 mmHg to 13.3±1.9 mmHg at 12 months PO in both groups
  - 84.9% experiences an IOP reduction of ≥20% from baseline
  - Drops decreased from 2.8±0.9 drops to 1.1±1.1
  - At 1 year- 40% were off all drops



Streamline Surgical System

- Single use and disposable
- Stainless steel cutting inner cannula with a polymer outer sleeve
- Depression of the actuator button creates 150 uM diameter gonitomy while delivering approximately 7uL of OVD for dilation of Schlemm's canal and collector channels
- Clinical trials:
  - Prospective, non randomized trial
  - 37 eyes from 37 patients- all Hispanic
  - IOP dropped from 23.2±2.3 to 16.2±2.2 mmHg at 12 months
  - 80% had ≥20% reduction in IOP at 1 year
  - Drops decreased from 2.0 ± 0.8 to 0.8



Procedure	Time Point (Months)	Baseline IOP	Mean IOP Reduction (%)	% Achieving ≥20% IOP Reduction	Mean Medication Reduction (%)	% Medication-Free
STREAMLINE transluminal dilation of the canal of Schlemm (current study)	12	23.2 mmHg*	30.2%	80%	60.5%	51.4%
iStent (1st generation)[16]	12	25.4 mmHg*	33.1%*	66%*	NR	85%
2 iStents (1st generation)[17]	12	27.3 mmHg*	18.7%*	13.3%*	37.4%	24%
iStent inject (2nd generation)[18]	24	24.8 mmHg*	31%*	78.5%*	75%	86.7%
Hydrus[17]	12–24	26.3–27.5 mmHg*	29.8%–35.7*	39.7%–80*	60.4–75%	46.6–72.9%
Hydrus[19]	24	26.3 mmHg*	35.7%*	80%*	75%	72.9%
Visco360[20–22]	12–18	22.0–24.6 mmHg	22–41%	87%	32–89%	32–86%
iTrack device[23–30]	12–48	18.1–23.6 mmHg	26–40%	78.4%	39–97%	25–80%

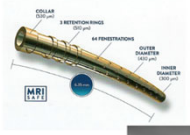
Note: *Unmedicated.

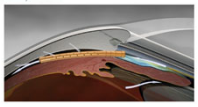
Abbreviation: IOP, intraocular pressure.

Enhancing Aqueous Outflow Through the Suprachoridal space

Cypass

- FDA recalled it from market in 2018 due to concern for endothelial cell lose found in COMPASS-XT trail
- Supraciliary device
- Stent was 6.35 mm long; inner diameter of 300 uM and outer 430 uM with 76 uM fenestrations along length of device
- It was a controlled cleft formation
- Proximal edge of stent had three retention rings

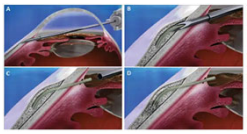




Shunting Aqueous Outflow into the Subconjunctival Space

Xen Gel Stent

- 6mm composed of procine-derived gelatin cross linked with glutaraldehyde
- Inner lumen is 45 uM in diameter and outer diameter is 150 uM
- Loaded on single use handpiece and injected with 27 gauge needle
- ab interno technique is the xen introduced via a clear cornea incision, injector pierces from Tm and scleara (visualization helped with a gonio lens) into subconjunctival space.
  - MMC injected before or after
- Pivotal Study:
  - 65 patients with refractory glaucoma
  - Trial cut down conj and pre soaked MMC on bare sclera then did ab interno implantation
  - IOP decreased avaerge of 9.1 mmGH
  - 75.5% of patient had ≥20% reduction in IOP.
  - Drops decreased from 3.5 drops at baseline to 1.

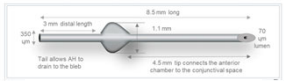


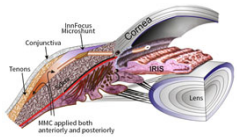
GPS Study: Xen vs Trab

- Prospective randomized, multicenter, noninferiority study
- Primary end points:
  - ≥ 20% IOP reduction from baseline at the 12-month visit without any of the following:
    - Increase in topical IOP-lowering medication
    - Clinical hypotony (IOP ≤ 6 mm Hg with vision reduction [≥ 2 lines] related to macular changes [macular folds], optic disc edema, and/or serous choroidal detachments)
    - Vision loss to counting fingers
    - Secondary surgical intervention (SSI)
- Secondary end points
  - mean IOP and medication count,
  - postoperative intervention rate
  - visual recovery
  - patient-reported outcomes (PROs)
- End results:
  - Xen was non inferior to trab: 62.1% vs 68.2% achieved primary end point
  - 62% were medication free in xen vs 71% in trab
  - Xen mean IOP was 14.4 mm Hg on 0.6 mean medications and trab mean IOP 11.8 mm Hg on 0.3 medications
  - Speedier visual recovery and less patient reported outcomes in xen

PreserFlo Microshunt

- Not FDA approved
- oly(styrene-block-isobutylene-block-styerene) or SIBS- biologically inert
- Length 8.5 mm, divided by a 1mm "fin" into distal (3 mm) and proximal (4.5 mm) segments. The external lumen is 350um and the internal lumen is 70um; a beveled tip at the proximal end.
- Clinical trial:
  - 2 year, prospective randomized trial
  - 395 microshunt vs 132 trabeculectomy
  - At 1 year, IOP decreased from 21.1+4.9 mmHg to 14.3+4.3 mmHg in MicroShunt versus 21.1+5.0 mmHg to 11.1 +4.3 mmHg in trab
  - Probability of success was higher in patients randomizes to trab- 72.7% vs 53.9%





Reducing Aqueous Production by Ciliary Body Ablation

Endocyclophotocoahulation (ECP)

- Endoscope probe attached to diode laser (810 nm) unit
  - Xenon light source
  - Helium-neon aiming beam
  - Fiber optic imaging
- Video monitor provides a view
- Laser setting is 0.2-0.25 watts→ continous
- Treatment is 200-360 degrees
- Treat until see ciliary body shrink and turn white
- Clinical study:
  - Non- randomized prospective study: 2 year f/u
  - ECP+CE vs CE in 160 patients with medically controlled glaucoma
  - Iop decreased from 18.1 ± 3.0 mmHg to 16.0 ± 3.3 mmHg in ECP/CE vs 18.1 ± 3.0 mmHg to 17.3 ± 3.2 mmHg in CE only
  - Drops: 1.5 ± 0.8 to 0.4 ± 0.7 vs 2.4 ± 1.0 to 2.0 ± 1.0

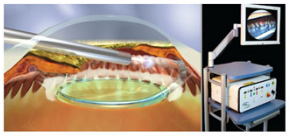


Figure 13. Endocyclophotocoagulation. ECP probe in ciliary sulcus space delivering energy to ciliary processes. Video screen of cryophotocoagulated ciliary processes after ECP procedure. Images used with permission.

Micropulse Transscleral Cyclophotocoagulation

- Destroys the pigmented CB epithelium to decrease aqueous humor production
- In past, CPC reserved for refractory cases
  - High risk of uveitis, vision lose, chronic hypotony, choroidal detachment and phthisis bulbi and rarely sympathetic ophthalmia
- Micropulse is alternative, safer version → instead of continuous energy, it delivers a series of repetitive short pulses of energy alternating with rest periods between pulses
  - Rest period allows for "cooling" which minimizes collateral tissue damage
- 810 nm diode laser probed placed perpendicular to eye surface along limbus ("bunny ear" on the limbus)
  - Duty cycle is 31.3% →on 0.5 ms/off 1.1 ms per cyle
  - 2000-2500mW
  - Total treatment ranges from 100-360 seconds
  - Avoid 3 and 9 o'clock position → long posterior ciliary nerves

iStent inject

[redacted]

Hydrus

[redacted]

OMNI/Hydrus

Old iTrack with GATT

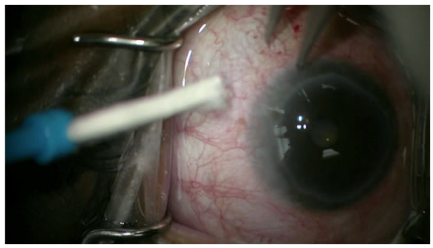
iTrack

Streamline

Trabectome

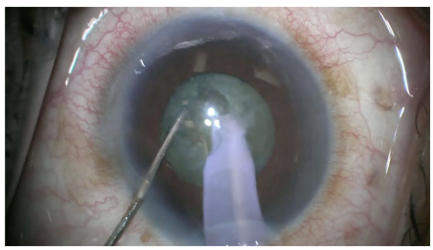
Xen Open Conjunctiva ab externo

Xen ab interno



PreserFlo Microshunt

KBD with ECP



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