MIGS:
What Is It and What Outflow Pathways Does It Target?

Deborah Ristvedt, DO

Audience Question #8

What percentage of your glaucoma patients would you estimate are candidates for a MIGS procedure?

a) 0%
b) 1-5%
c) 6-10%
d) 11-15%
e) 16-20%
f) 21-40%
g) More than 40%

Audience Question #9

How confident are you in your understanding of short-term complication rates and long-term tissue removal risks of various glaucoma surgical procedures?

a) Very confident
b) Confident
c) Neutral
d) Not so confident
e) Not confident at all

Audience Question #10

A 69-year-old female underwent a trabecular meshwork stent combined with phaco one year ago. Pressure has remained roughly unchanged. What is the most likely cause of the resistance?

a) Trabecular Meshwork
b) Narrow Angle
c) Ciliary Body
d) Collector Channels

Defining MIGS

MIGS IS:

IOP-lowering surgery with the following characteristics:

1. Minimally traumatic
2. Conjunctiva-sparing
3. High safety profile
4. Rapid recovery
5. Can be combined with cataract extraction or standalone
6. Provides more modest IOP lowering than trabeculectomy

Defining MIGS

MIGS ARE NOT:

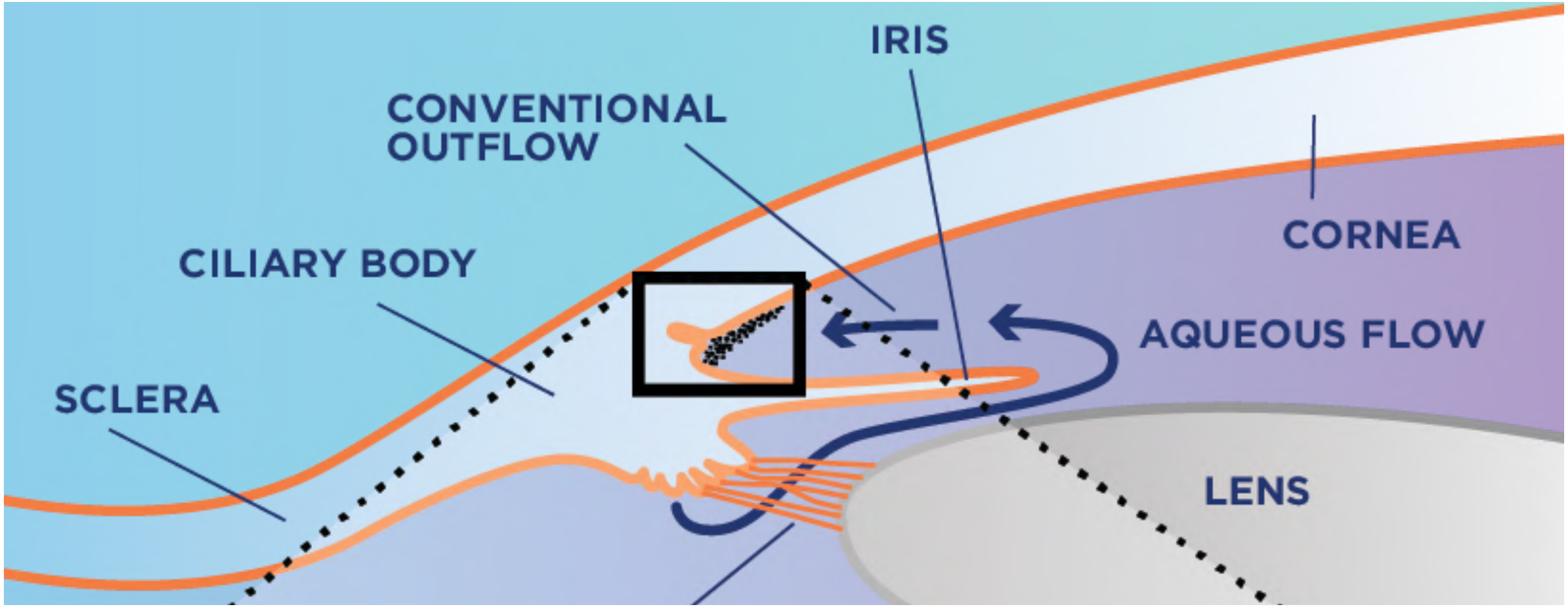
- Necessarily (include or require) a stent
- Only limited to the time of cataract surgery
  - Can be performed as a stand-alone procedure
- Only reserved for severe disease
  - May be beneficial for those appropriate patients with milder disease

Why MIGS?

To effectively lower IOP with a minimally-invasive procedure

Advantages:

- Micro-incisional
- Minimal tissue manipulation
- Higher safety profile
- Rapid visual recovery
- Efficacious

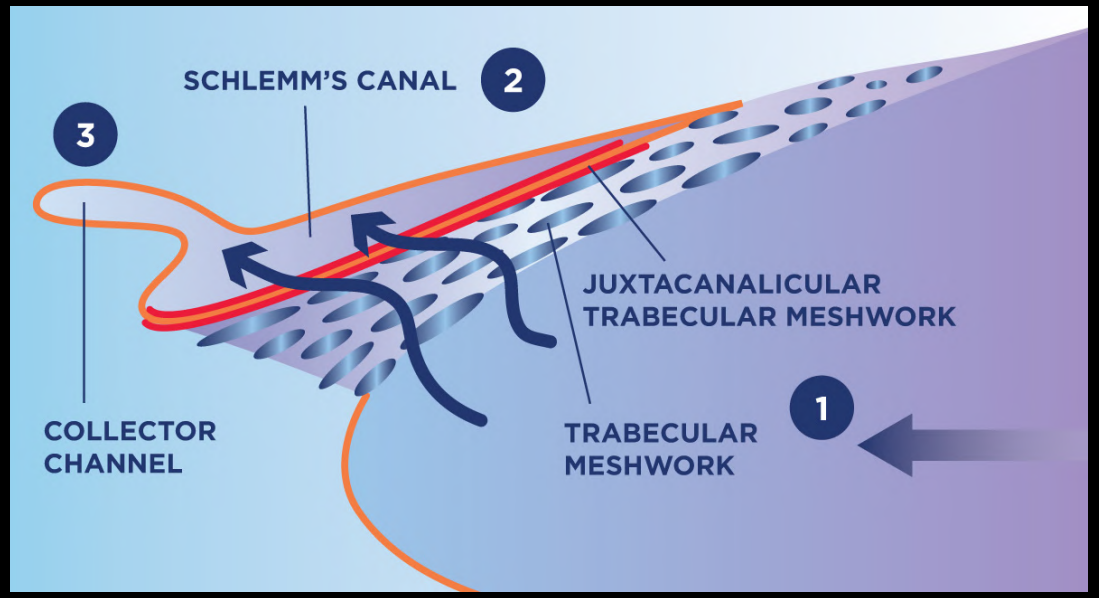


The Conventional Outflow Pathway

80% of outflow is conventional[1,2]

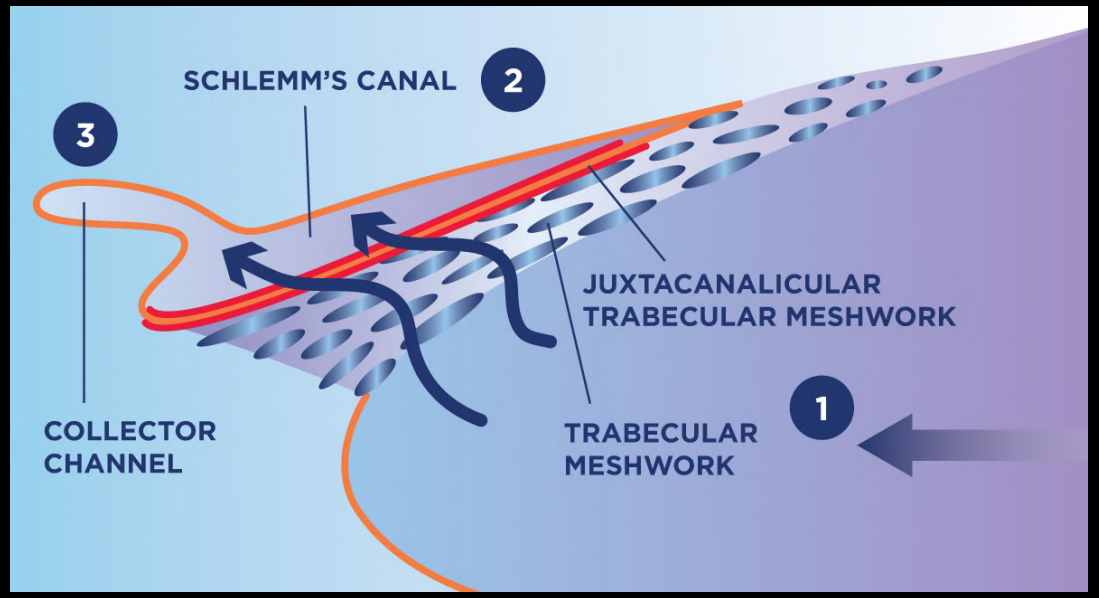
1. Cracknell KPB, Grierson I, Academic Press, Oxford, 2010, Pages 316-22. 2. Goel M, et al. Ophthalmol J. 2010;4:52–59.

3 Points of Resistance Affecting the Conventional Outflow Pathway[1-3]



1. **TRABECULAR MESHWORK (TM)**
   could be a source of resistance to outflow, increasing IOP
2. **SCHLEMM'S CANAL (SC)**
   can cause resistance if atrophied or collapsed
3. **COLLECTOR CHANNELS (CC)**
   can cause resistance if atrophied or blocked

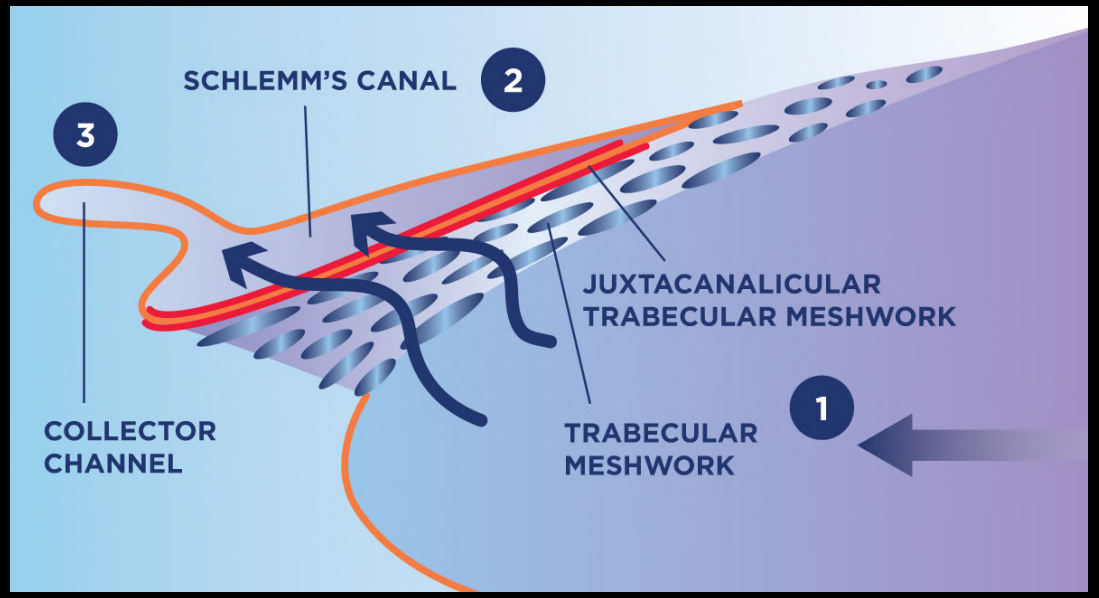
3 Points of Resistance Affecting the Conventional Outflow Pathway[1-3]



- **BETWEEN 50%-75%** may be in the trabecular meshwork[1]
- **UP TO 50%** of resistance may be in Schlemm's canal and distal collector channels[2]

1. *Grant WM. Arch Ophthalmol ol 1963: 69:783-801.*
2. *Rosenquist R et al. Curr Eye Res 1989; 8:1233-1240.*

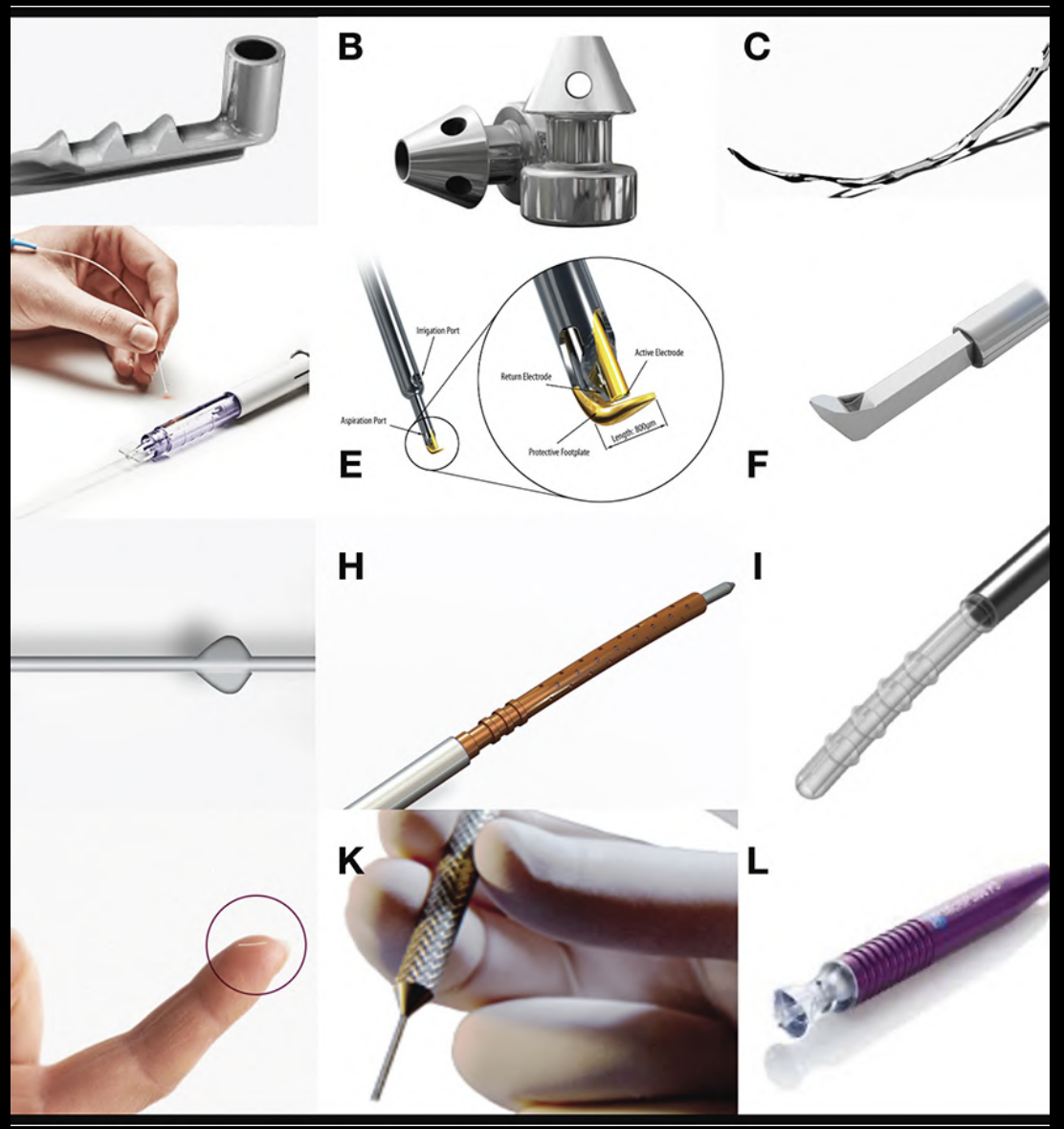
Enhance outflow across the trabecular meshwork and through Schlemm's canal



- Bypass or remove the juxtacanalicular trabecular meshwork to lower IOP through increased outflow.
  - Bypass can be achieved by placing a trabecular meshwork bypass stent which allows aqueous to flow directly through the stent from the anterior chamber into Schlemm's canal
  - Another approach to bypass the resistance of the trabecular meshwork is goniotomy or trabeculotomy which involves surgical incision and/or excision of this tissue and allows for improved aqueous outflow into Schlemm's canal
- Dilation of Schlemm's canal through cannulation and expansion with viscoelastic is yet another approach to improve outflow through the normal physiologic aqueous outflow system

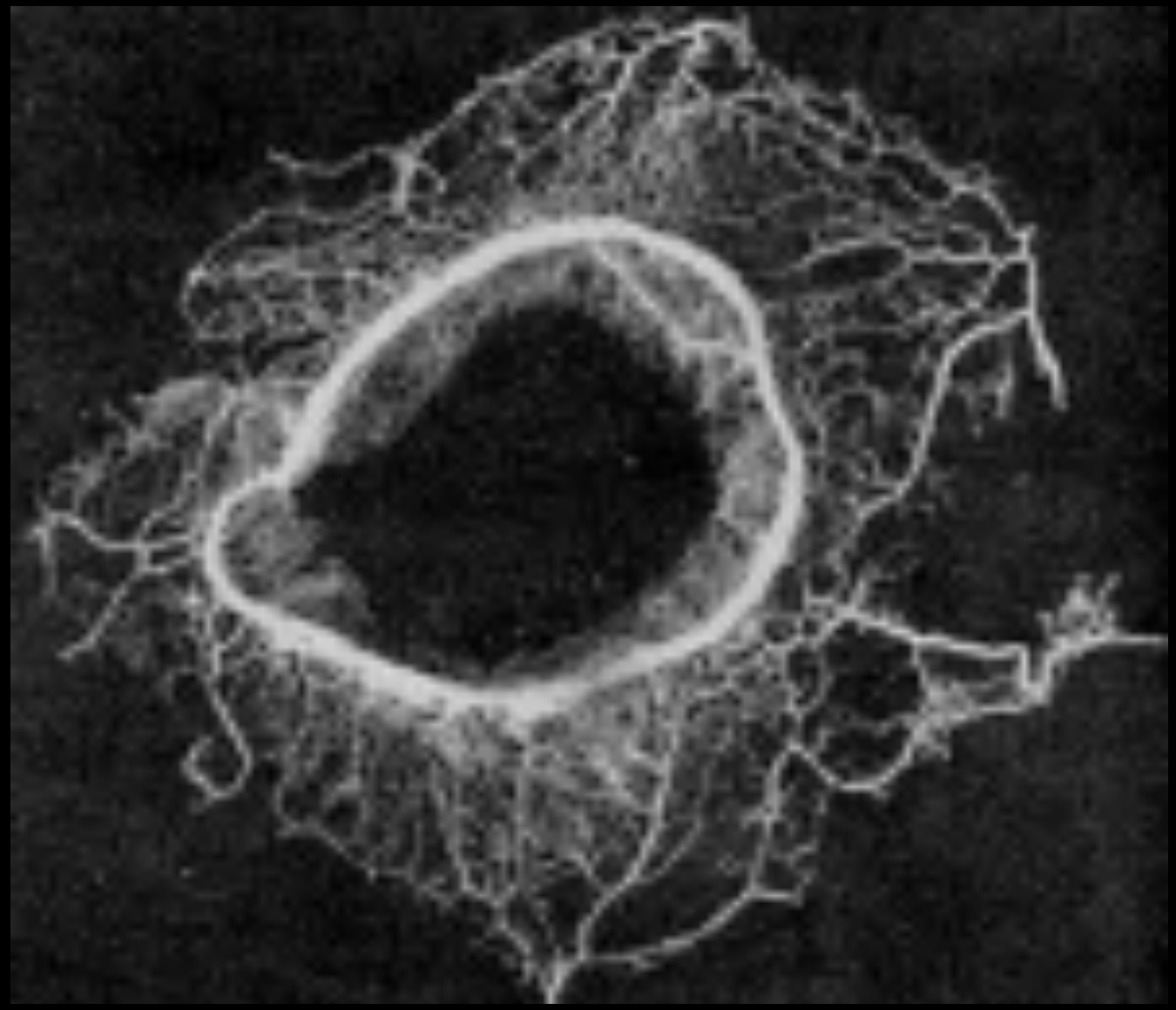
Canal-based

- Bypassing:
  - iStent
  - Hydrus
- Dilating:
  - Viscocanaloplasty (OMNI)
  - AbIC
- Ablative/TM Removal
  - Trabeculotomy (OMNI)
  - GATT
  - Trabectome



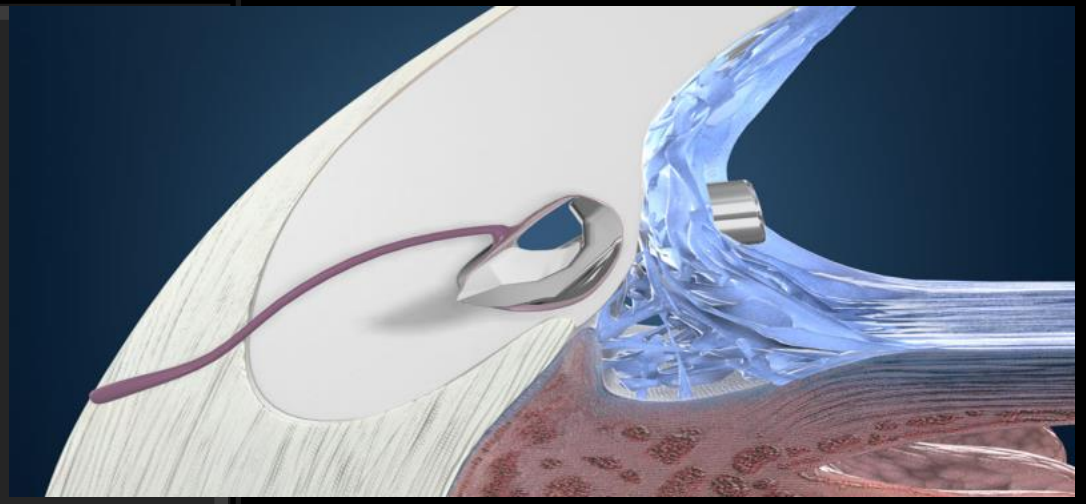
Aqueous Flow/Canal Based

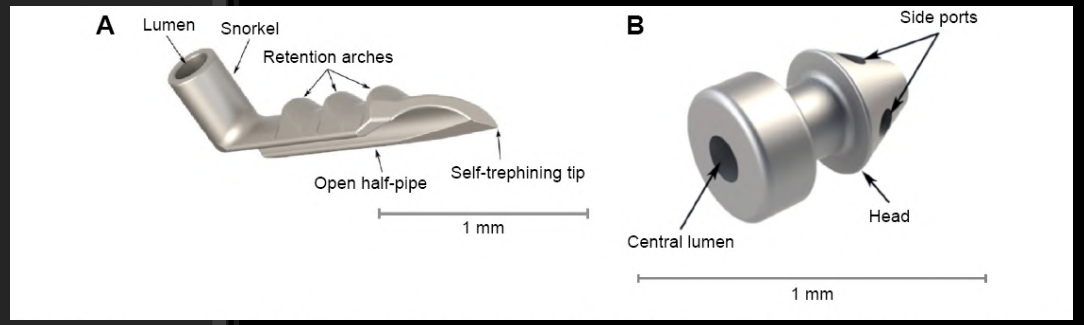
Designed to target natural outflow



iStent: Trabecular bypass

- Designed to restore continuous physiologic outflow
- Creates a patent bypass through the trabecular meshwork to Schlemm's canal
- Performed with cataract surgery
- Best for mild-moderate OAG
- iSTENT, iSTENT inject, iSTENT inject W





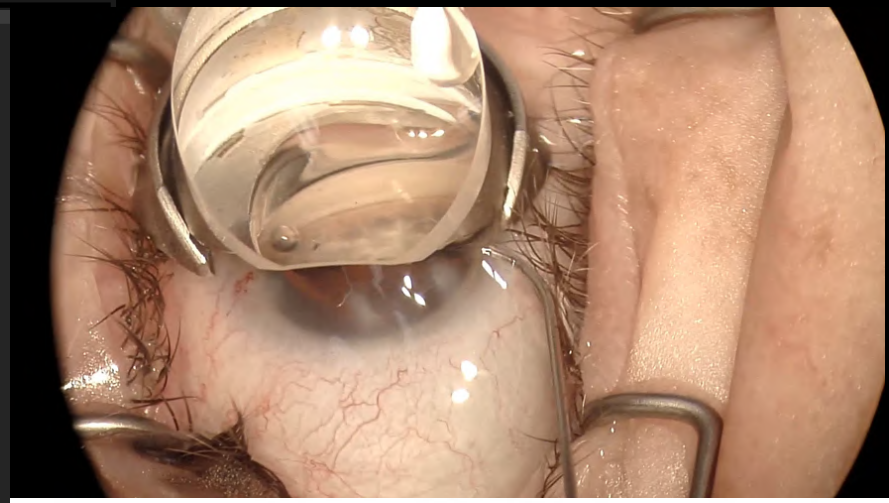
iStent inject with cataract surgery

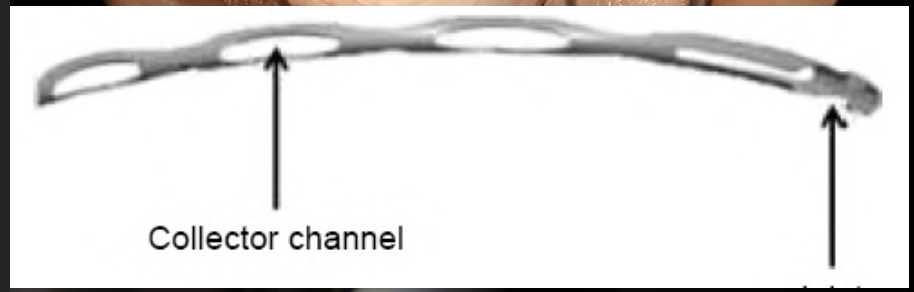
	iStent Inject	Control (cataract)
Baseline IOP	24.8 mmHg	24.5 mmHg
>20% reduction	75.8%	61.9%
Mean IOP reduc.	7.0 mmHg	5.4 mmHg
Med. free	84%	67%
IOP increase requiring management with oral or intravenous medications or with surgical intervention at month ≥1	1 (0.3%)	3 (2.5%)

Samuelson et al. Ophthalmology. 2019

Hydrus

- 8mm flexible microstent
- Made of nitinol
- 3 open windows face anterior chamber
- Performed with cataract surgery





Horizon Trial

Stent + Cataract (n=369)

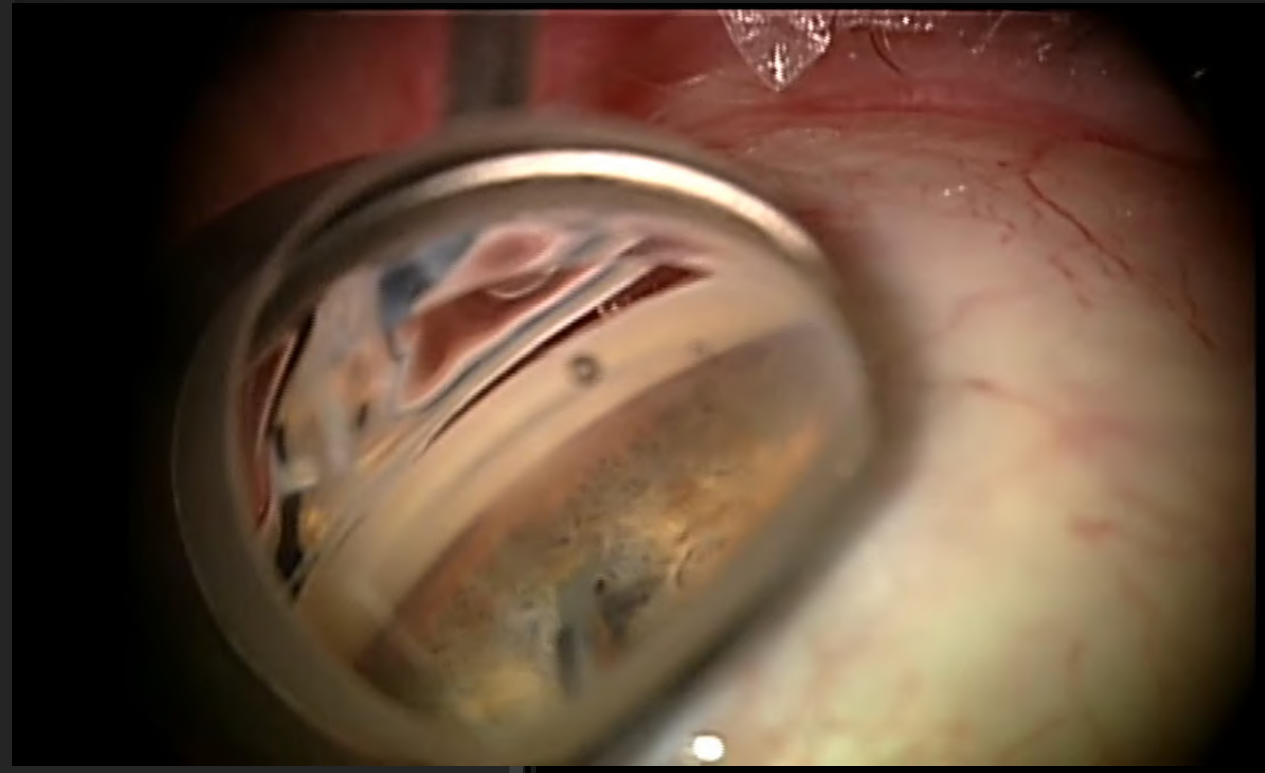
- Baseline IOP after washout
  - 25.5 (+/- 3.0)
- 24 months IOP after washout
  - 17.4 (+/-3.7)

Cataract Only (n=187)

- Baseline IOP after washout
  - 25.4 (+/- 2.9)
- 24 months IOP after washout
  - 19.2 (+/-3.8)

Kahook dual blade

- Unroofing of TM
- 3 clock hours
- Exposes collector channels
- Stand-alone or combined with cataract surgery

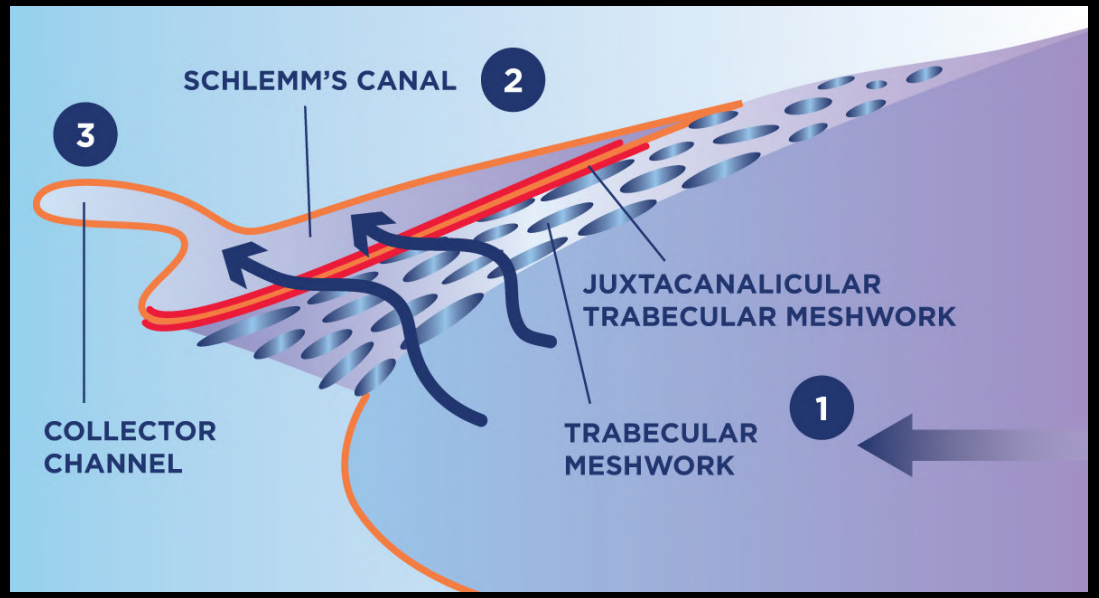


Stand-alone KDB in mild to severe POAG

- 42 eyes
- Mean med use 2.6
- Mean IOP 21.6 at baseline
  - 16.5mmHg at 12 months

ElMallah MK, Berdahl JP, Williamson BK, Dorairaj SK, Kahook MY, Gallardo MJ, Mahootchi A, Smith SN, Rappaport LA, Diaz-Robles D, Lazcano-Gomez GS. Twelve-Month Outcomes of Stand-Alone Excisional Goniotomy in Mild to Severe Glaucoma. Clin Ophthalmol. 2020 Jul 3;14:1891-1897. doi: 10.2147/OPTH.S256423. PMID: 32694910; PMCID: PMC7340474.

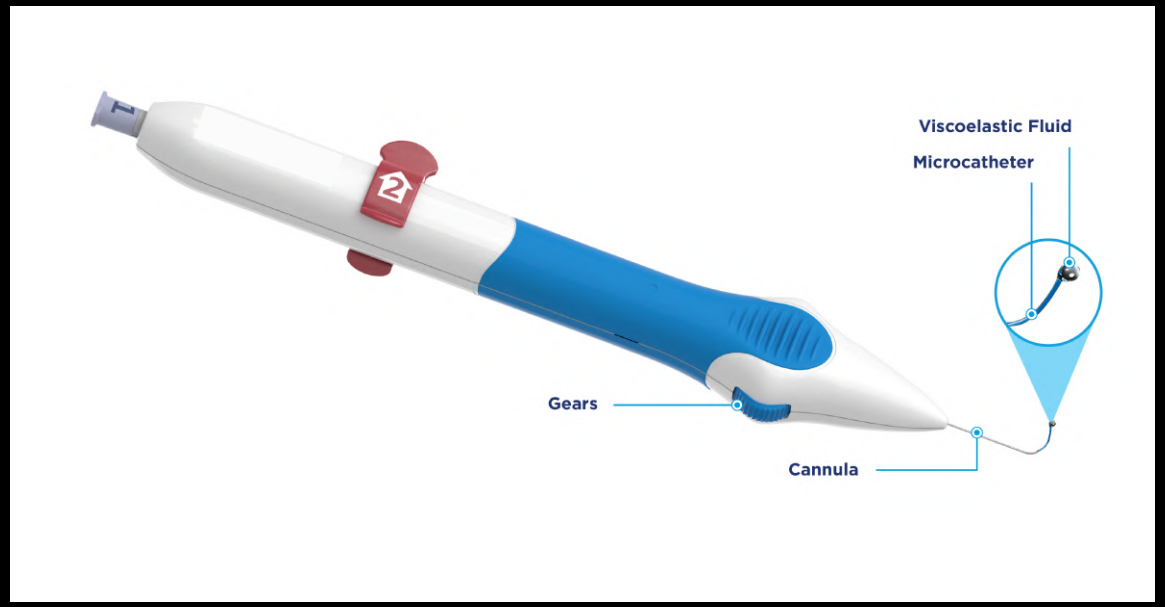
Combination of these approaches to achieve both viscodilation and trabeculotomy in one procedure

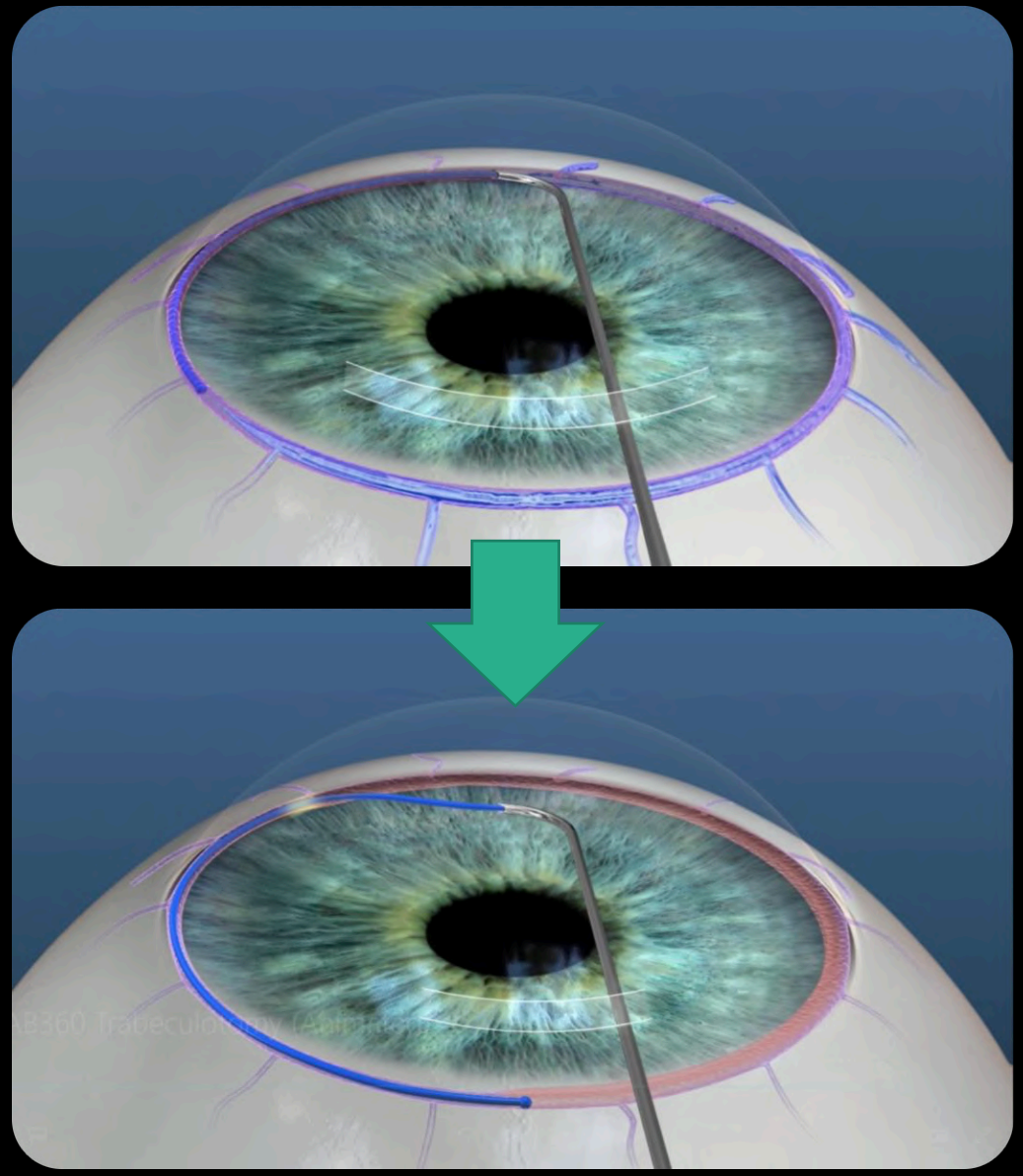


Targeting three points of resistance in the conventional outflow pathway:

1. Trabecular meshwork
2. Schlemm's canal
3. Collector channels

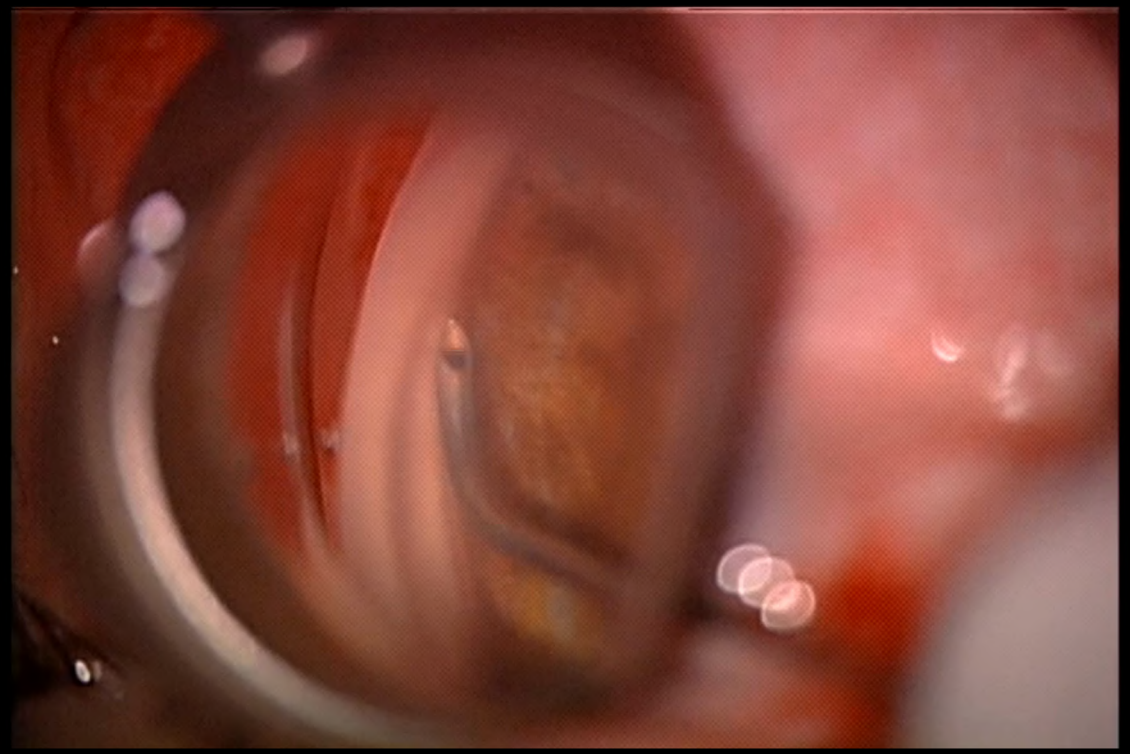
OMNI





OMNI 360/180

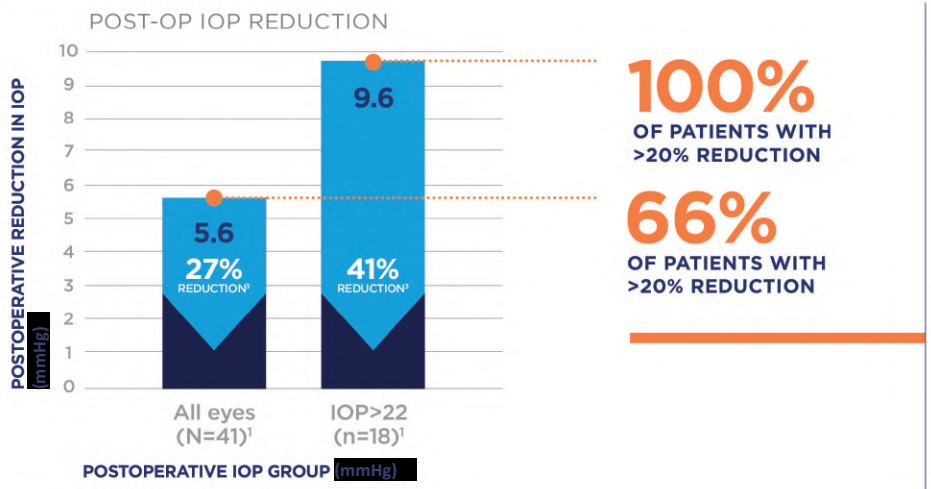
- Treats all 3 points of resistance
- Stand-alone or combined with CE
- Versatility (OHT, High risk POAG suspect, Mild to Severe POAG)
- Titratability (Viscocanaloplasty vs. Vicso/Trabeculomtomy)



Trabeculotomy Combined with Viscodilation of Schlemm's Canal for Reducing IOP in Mild to Moderate and More Advanced Open Angle Glaucoma (Brown et al. 8-month Results)

41 EYES: COMBINED WITH CATARACT SURGERY

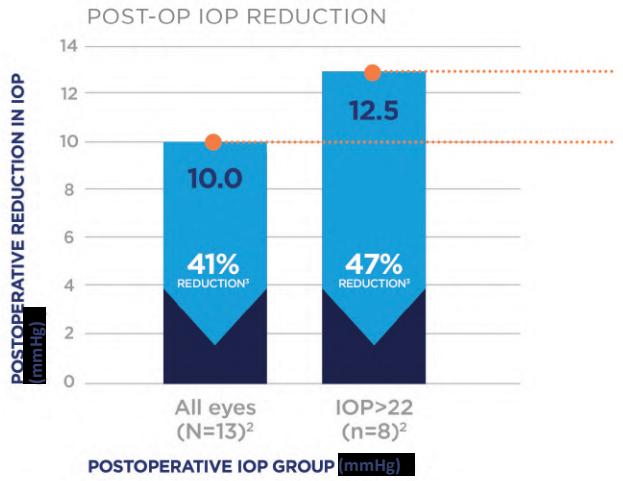
RESULTS:



100%
OF PATIENTS WITH >20% REDUCTION

66%
OF PATIENTS WITH >20% REDUCTION

13 EYES: STANDALONE PROCEDURE IN PSEUDOPHAKIC EYES



100%
OF PATIENTS WITH >20% REDUCTION

COMPLICATIONS:

- No complications related to cataract surgery
- Hyphema minimal in 2 eyes (4%) - Cleared by 1 week
- No eyes have undergone secondary glaucoma surgery

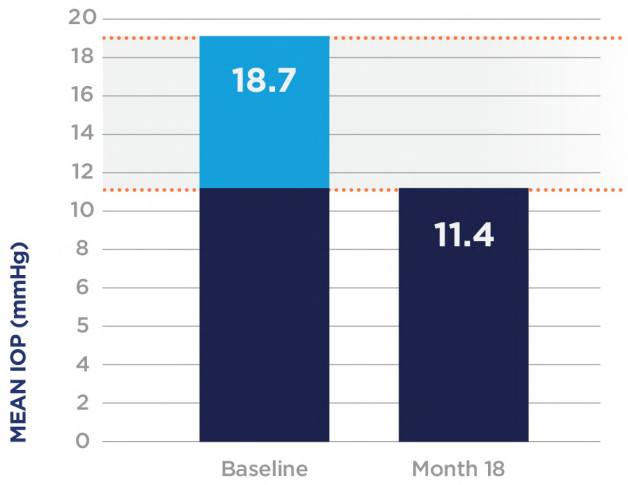
CONCLUSION:

- Phaco + OMNI safely lowers IOP. Magnitude of IOP reduction highly correlated with preop IOP
- Patients with highest preop IOP = greatest postop IOP reduction.
- OMNI stand-alone lowers IOP 41%

1. *Brown R, et al. Journal of Cataract and Refractive Surgery. 46(4):644-645, April 2020.*
2. *Brown R, et al. ASCRS presentation, May 2019 (submitted to JCRS)*

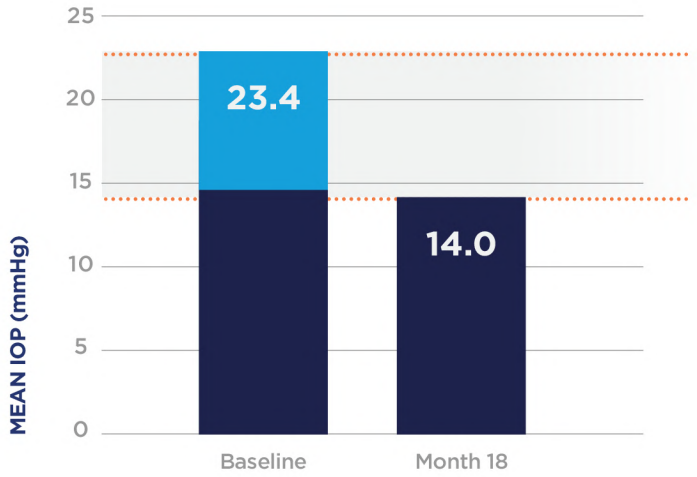
OMNI Surgical System in open-angle glaucoma treatment: an 18-month follow-up[1]

OMNI W/ CATARACT SURGERY (N=10)



39%
REDUCTION IN MEAN IOP

OMNI STANDALONE PROCEDURE (N=14)



40%
REDUCTION IN MEAN IOP

COMPLICATIONS:

- IOP-spikes (9 eyes)
- Hyphema (6 eyes)
- Fibrin in the anterior chamber (5 cases) that resolved in the first week after surgery

CONCLUSION:

- OMNI® Surgical System is a promising approach for the treatment of non-advanced OAG
- The procedure achieves reduction of the IOP and the number of glaucoma medications
- It also demonstrates good safety profile
- Further studies are needed

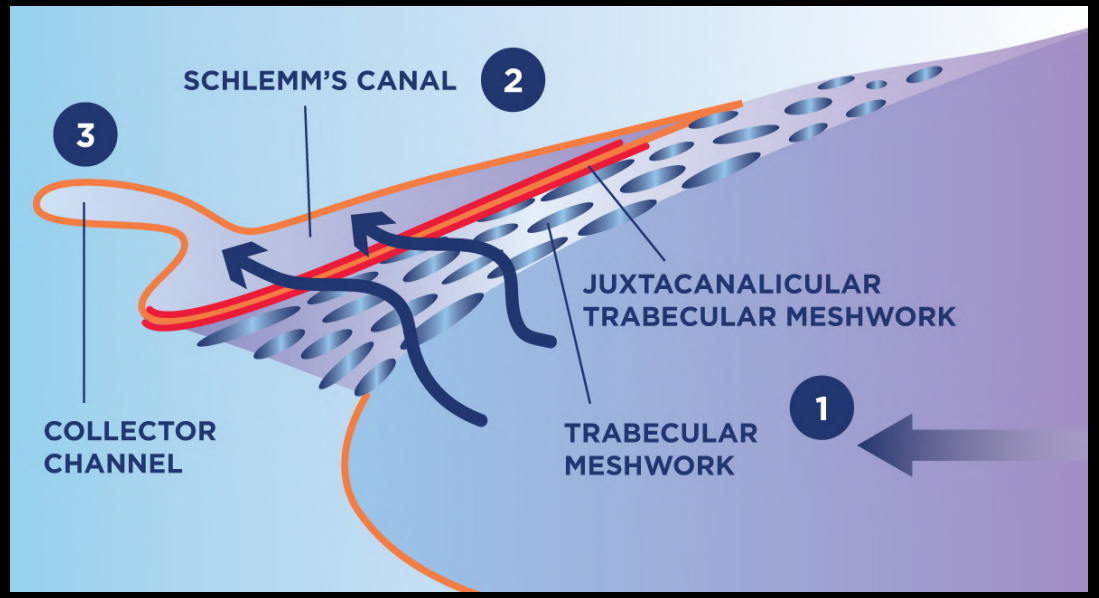
1. *Grabska-Liberek I, et. al. ESCRS 2019, Presented Poster Session: Glaucoma II (https://www.escrs.org/paris2019/programme/poster-village-details.asp?id=33863&day=0).*

OMNI Standalone: Dr. Ristvedt

36% mean IOP reduction at 3 months

63% mean medication reduction at 3 months

Increase outflow via alternate pathways

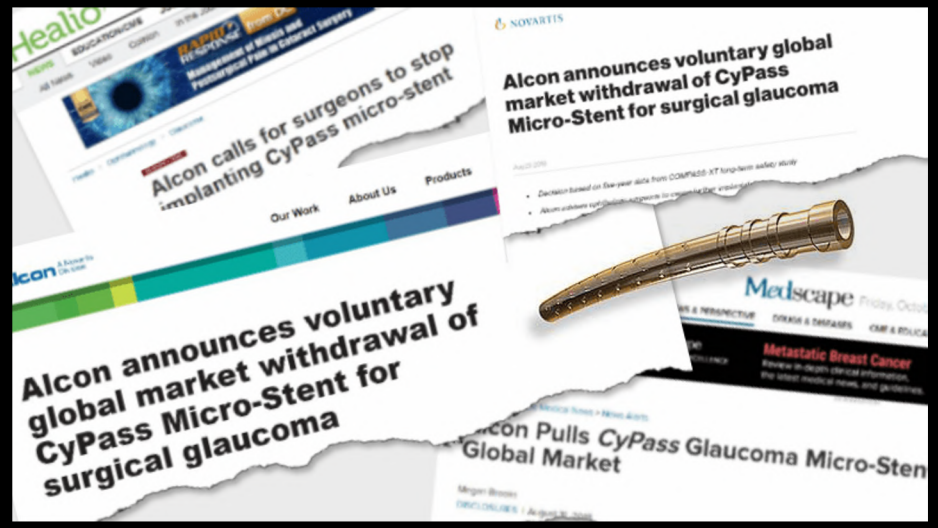


- Accessing the suprachoroidal space with microstent placement
- If traditional outflow pathways are unlikely to be improved, aqueous can be shunted into the subconjunctival space through an ab interno, small incision approach

Suprachoroidal space

Cypass

- Watch for corneal edema and ECC loss
- Cut if too long
- Observation if ECC looks good

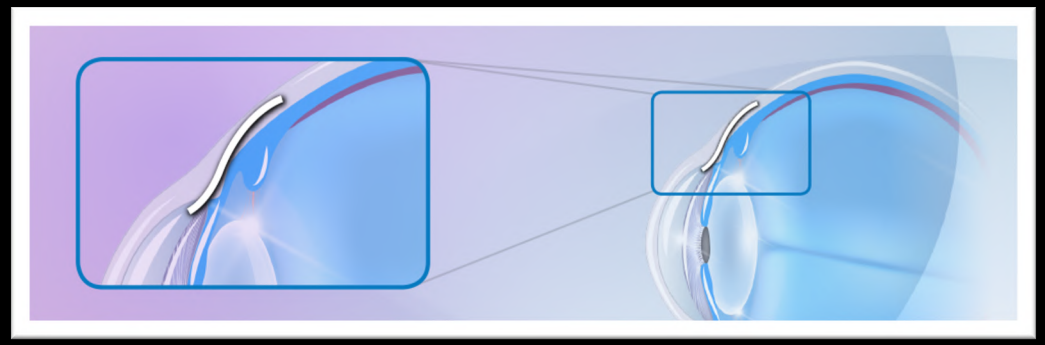


iStent supra

- Awaiting FDA approval

Subconjunctival space

- Xen gel stent



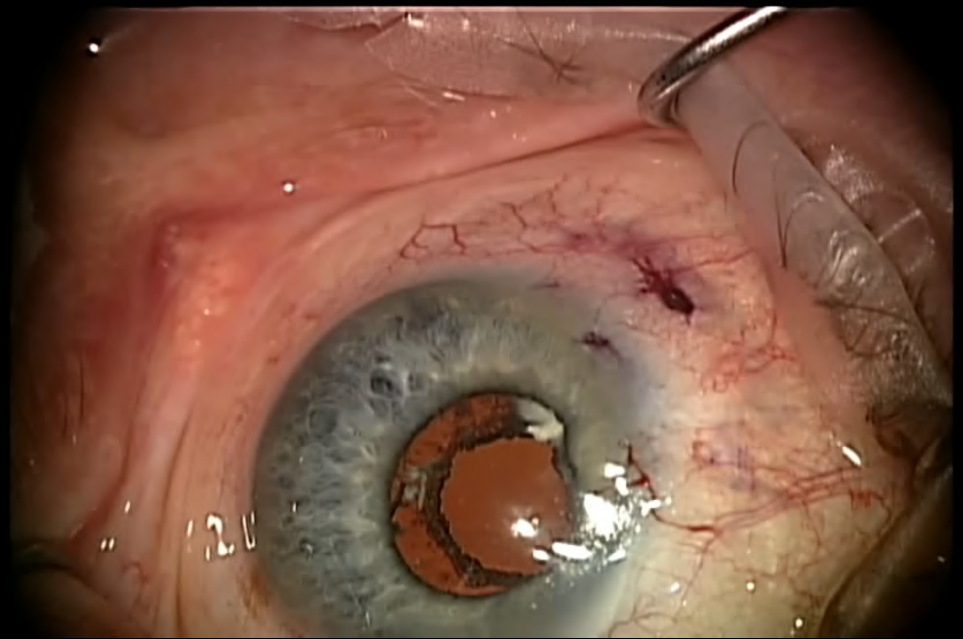
- Preserflo microshunt

- Indication: Refractory glaucoma, on MTMT
- Bypasses angle
- Opportunity to intervene earlier
- Lower risk than trabeculectomy
- Complete success (IOP between 6 and 18 mm Hg with or without medication) comparable to trabeculectomy

XEN gel stent approach

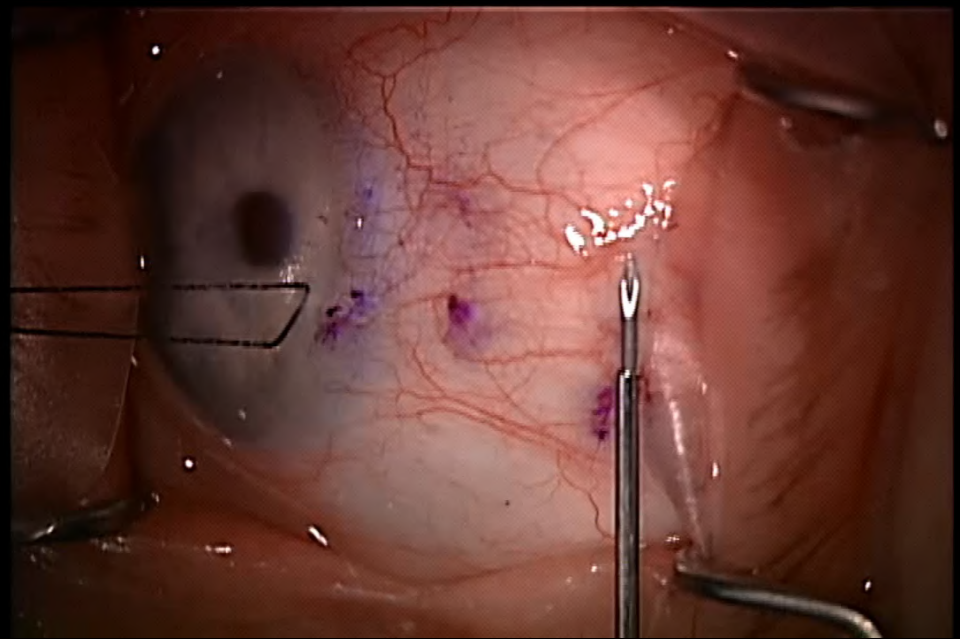
Ab Interno

- Incision through cornea
- Angle viewed with placement
- Confirm above tenons



Ab Externo

- No incisions
- Target placement under conjunctiva
- Blind entry

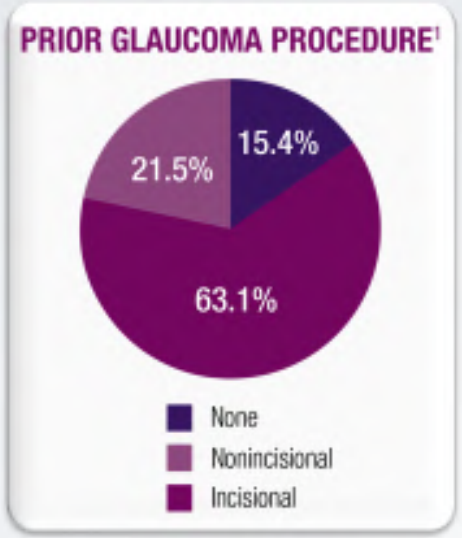


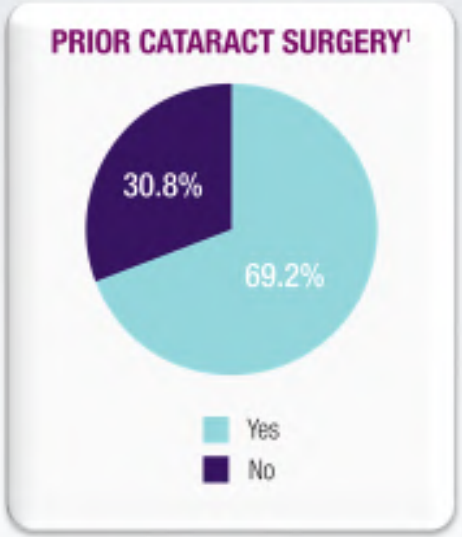
Significant IOP Efficacy in a Challenging Group of Patients

A Prospective, Multicenter, Single-arm, Open-label, US Clinical Trial of Refractory Glaucoma Patients[1]

All procedures were stand-alone XEN® Gel Stent, with no concurrent cataract procedures[1]

Select Baseline Characteristics 65 Patients With Refractory Glaucoma[1]	
Mean age	70 years old
Mean cup-to-disc ratio	0.8
Visual field mean deviation (MD) score	-15 dB
Mean medicated IOP at baseline	25.1 (± 3.7) mm Hg
Mean IOP-lowering medications at baseline	3.5 (± 1.0)





Study design[1,2]: Prospective, multicenter, single-arm, open-label study evaluated the safety and effectiveness of the XEN® Gel Stent in refractory glaucoma subjects (N = 65) where IOP was unresponsive to maximally tolerated medication, or previous filtering or cilioablative procedures failed. Mitomycin C was administered according to its label using sponges via conjunctival cut-down. Medication washout was not performed. All IOP-lowering medications were discontinued on the day of surgery.

1. XEN® Directions for Use; **2.** Data on file, Allergan, 2013; US Study Protocol P13-001.

Primary Endpoint and Effectiveness

Primary Endpoint: IOP Lowering at 12 Months Compared to Baseline for All Enrolled Patients[1,*]

76% **ACHIEVED ≥ 20%**
mean diurnal IOP reduction on the same or fewer medications vs baseline[†]

6.4 mm Hg **MEAN DIURNAL IOP**
reduction vs baseline[‡]

Of the 65 enrolled patients, 52 attended the 12-month exam, had no secondary surgical interventions (SSI), and no explants

- 9 had explant and/or SSI
- 2 died[††]
- 2 lost to follow-up[††]

Primary Effectiveness Analysis for Subjects who Completed the 12-Month Visit[1,*]

9.2 mm Hg REDUCTION
Mean IOP reduced from 25.1 mm Hg (medicated) at baseline to 15.9 mm Hg[§]

3.5 **MEAN IOP-LOWERING MEDICATIONS AT BASELINE REDUCED TO** **1.7**[**]

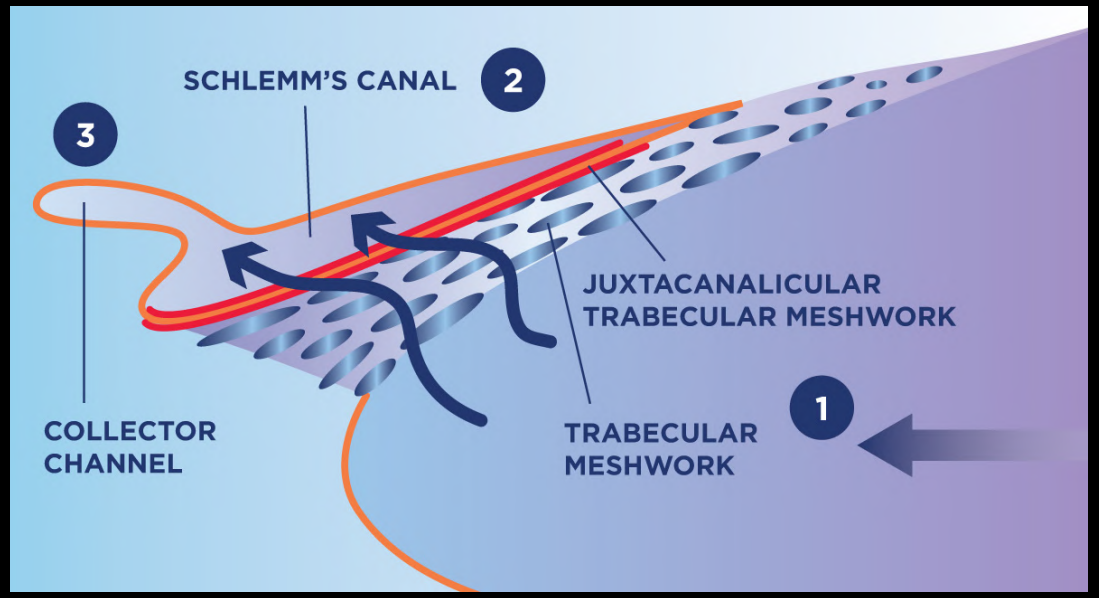
This analysis included only those subjects (n = 52) that:

- Attended the 12-month exam
- Still had the XEN® in place (no explant)
- Had no SSI

*Study eyes undergoing glaucoma-related SSI and/or removal of the XEN® Gel Stent prior to the 12-month evaluation were considered to be nonresponders. Seven subjects in the study underwent needling procedures with mitomycin C; 4 of these subjects were considered responders. †76.3% (95% confidence interval [CI] = 65.8%, 86.8%); using observed data and failures for subjects with glaucoma-related SSI and multiple imputations for missing data (N = 65). ‡-6.4 ± 1.1 (95% CI = -8.7, -4.2); using observed data and worst within-eye IOP for subjects with glaucoma-related SSI and multiple imputations for missing data (N = 65). §Baseline 25.1 (± 3.7) mm Hg; 12-month 15.9 (± 5.2) mm Hg. **Mean medications at baseline 3.5 ± 1.0; at 12 months 1.7 ± 1.5 (n = 52). ††Multiple imputations for missing data.

1. XEN® Directions for Use.

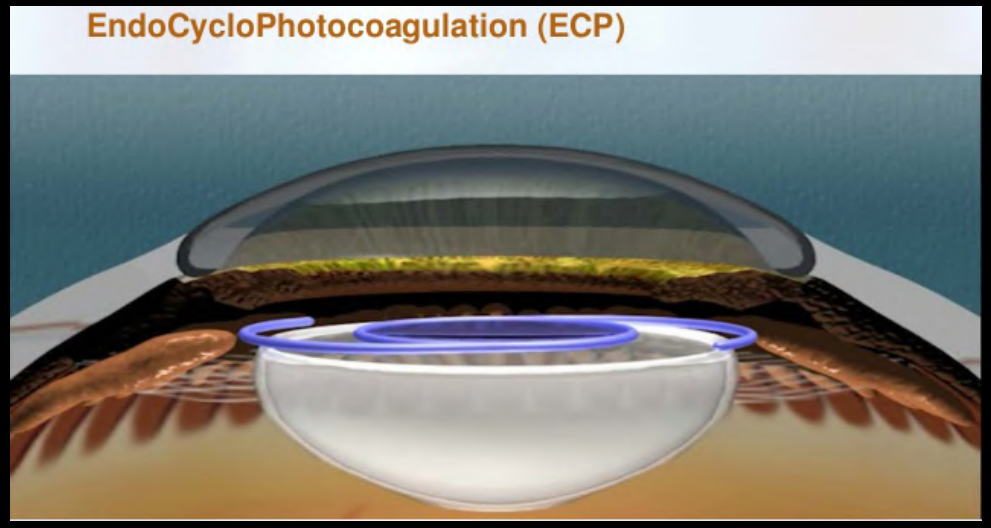
Decrease aqueous production by ablation of the ciliary body



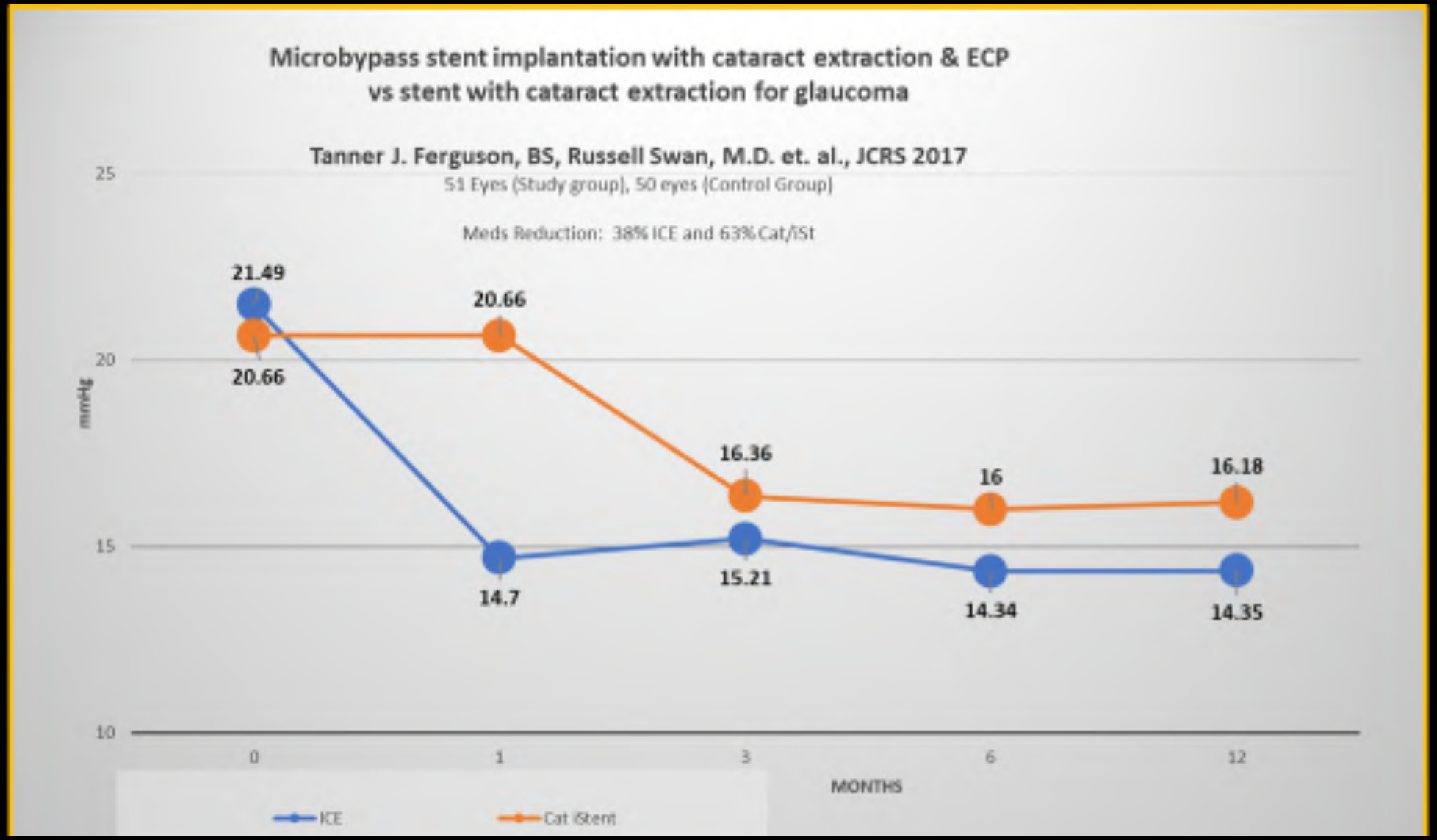
- Endocyclophotocoagulation in which an endoscopic laser probe is inserted through a clear corneal incision and used to directly visualize and ablate the ciliary body

Aqueous Suppression

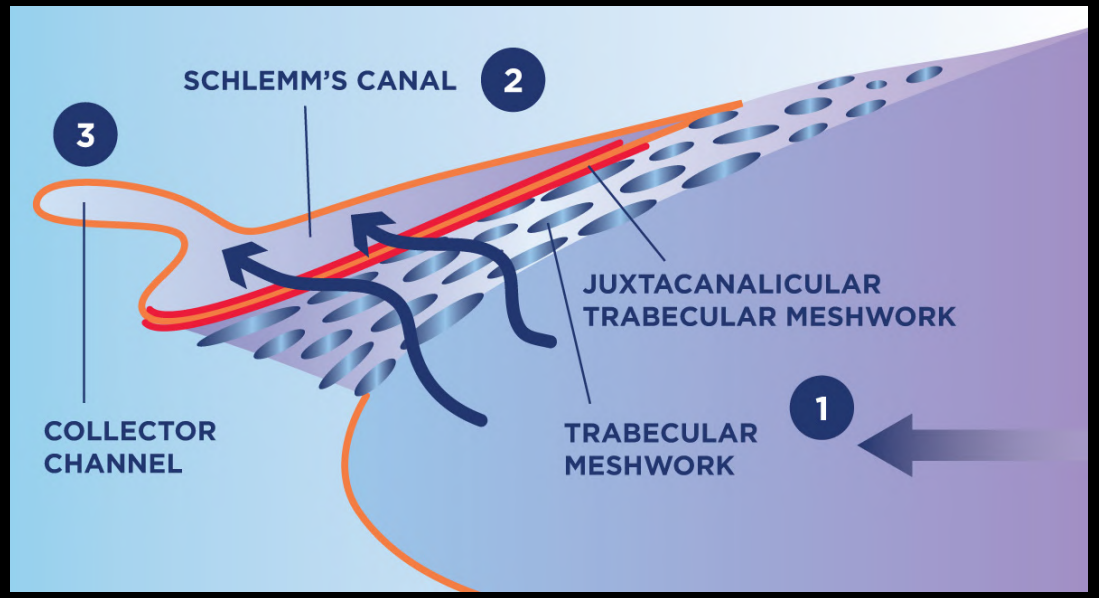
ECP
(Internal approach)



Micropulse
(Transcleral approach)


Microbypass stent implantation with cataract extraction & ECP
vs stent with cataract extraction for glaucoma
Tanner J. Ferguson, BS, Russell Swan, M.D. et. al., JCRS 2017
51 Eyes (Study group), 50 eyes (Control Group)
Meds Reduction: 38% ICE and 63% Cat/iSt
25
20
15
10
mmHg
21.49
20.66
20.66
16.36
16
16.18
14.7
15.21
14.34
14.35
0
1
3
6
12
MONTHS
ICE
Cat iStent

Summary and Conclusions



Outflow Pathways of MIGS:

1. Enhance outflow across the trabecular meshwork and through Schlemm's canal
2. Increase outflow bypassing the conventional outflow pathway
3. Decrease aqueous production by ablation of the ciliary body
4. Combination of these approaches (Mix and Match MIGS)

MIGS CONSIDERATION

- COMBO Cataract vs Standalone
- Severity of OAG/ VF staging
- Secondary glaucoma
- IOP target
- Refractory vs. stable
- Pt. Compliance with gtts
- Age
- Blood thinners
- Prior glaucoma procedures
- Prior eye procedures (retina, cataract)
- Ocular health/anatomy (Dry eye, Angle)
- Follow-up appointments and post-op care

Cataract Surgery + MIGS

OHT

- Canaloplasty

Mild to Mod

- iSTENT
- OMNI 360/180
- Hydrus
- KDB
- OMNI/ECP
- iSTENT/Canaloplasty

Severe

- OMNI 360/360
- OMNI/ECP
- GATT
- Xen gel stent

Deborah Ristvedt, DO Jan 2021

MIGS Standalone

Stable OAG with less drop dependence

- SLT
- Durysta
- OMNI
- KDB

OAG with progression

OMNI
OMNI/ECP
KDB/ECP
Xen gel stent

Deborah Ristvedt, DO Jan 2021

Audience Question #11

After what you learned today, how confident are you in your understanding of the short and long-term benefits of MIGS procedures?

a) Very confident
b) Confident
c) Neutral
d) Not so confident
e) Not confident at all