

Glaucoma Surgery (MIGS)

Neal Tolchin, MD

Minimally Invasive Glaucoma Surgery (MIGS)

Are they worth it?

Glaucoma is the second leading cause of blindness world wide

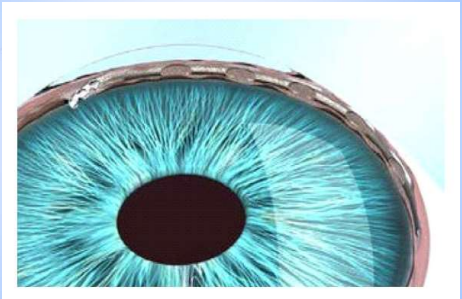
In the U.S., there are an estimated 3.7 million cases of glaucoma, and which will reach over 4 million cases in 2 years.

Standard treatment options for Glaucoma

- 1) Ocular Medications
- 2) Laser Trabeculoplasty
- 3) Surgery

Visual field loss of all the above include:

- Cost
- Long-term corneal surface damage
- Non-compliance (90% after 6 month?)
- Durability of response to drops and to laser trabeculoplastics
- Surgical risks with conventional trabeculectomy and valve placement procedures
- Visual field loss progression despite medical therapy



MIG (Minimally Invasive Glaucoma Surgery)

- An alternative option to traditional treatment
- Less risks than trabeculectomy and valve placement procedures
- MIGs surgery with cataract surgery lower intraocular pressure better than cataract alone.
- As many as 20% of cataract patients might have glaucoma comorbidity.

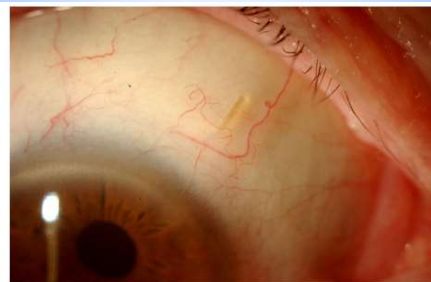


Figure 6 Lower-lying filtering bleb in XEN45 gel implant at 6 months.

MIGs Goal

Intervene earlier in the disease and lower IOP to reduce morbidity of glaucoma progression through a procedure

- AB Interno
- Minimally traumatic
- Safe and effective
- Rapid recovery
- Reduce medication burden
- Will reduce the need for more aggressive surgical options while these options

MIG Procedures

There are MANY different choices, and even different surgical options within certain categories.

Endoscopic Cyclophotocoagulation (ECP)

- Destroys ciliary body epithellum to lower IOP (decreasing aqueous production)
- Can be a stand-alone procedure

iStent and iStent Inject

- Patient trabecular micro-bypass stent (s)
- Only used in conjunction with cataract surgery



The Opportunity

- iStent inject® can help you effectively and comprehensively treat patients with cataracts and glaucoma
- The patient population with cataracts and glaucoma is huge
- iStent inject is clinically proven to significantly reduce a patient's intraocular pressure and may reduce their reliance on medication




iStent inject

Glaucoma Prevalence and Patient Need

Glaucoma Can Be Devastating

- Glaucoma is the second leading cause of blindness worldwide
- In the US, there are an estimated 3.7M cases of OAG, growing to more than 4M cases by 2020, with a significant number of patients going blind every year¹



1. 2017 National Eye Institute Glaucoma Report, data on file.

Standard Treatment Options for Glaucoma

Standard Treatment Options

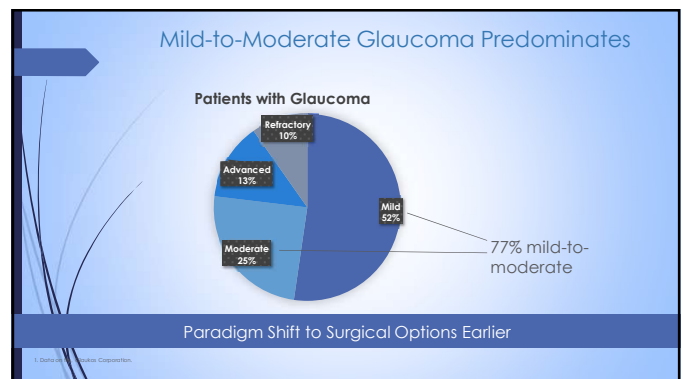
- Glaucoma Medications
- Laser Trabeculoplasty
- Invasive Surgery
 - Trabeculectomy / Shunt

iStent inject offers cataract patients with glaucoma a new option that can relieve eye pressure and may reduce reliance on medication

Challenges

- Long-term exposure to glaucoma medication can cause corneal surface damage
- Non-compliance to medication
 - More than 90% of patients are non-adherent, and nearly 50% stop taking their medications before 6 months¹
- Less durability in laser treatments
- Risks associated with invasive surgery
- Cost burden to patients & system

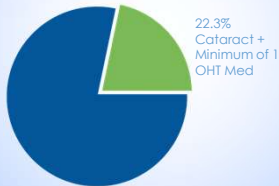
1. Standard of Care: Persistence and adherence with topical glaucoma therapy. Am J Ophthalmol. 2005;140:595-596.



Concomitant Cataract & Glaucoma Patients – US

- Significant treatment opportunity with more than 1 in 5 eyes with cataracts on OHT medication

3.9M US Cataract Procedures



Market Research, Inc. Third Medicare Administrative Claims Data (Center 95, SAT) 8/07-2015

iStent
inject

MIGS & iStent inject OVERVIEW

The Goal of Micro-Invasive Glaucoma Surgery

- MIGS Definition
 - Ab interno
 - Minimally traumatic, tissue sparing
 - Proven efficacy
 - Extremely high safety profile
 - Rapid recovery



Glaukos Technology Proven Safe and Effective Worldwide

10+

Years of experience bypassing trabecular meshwork

500K+

Eyes implanted

101

Articles published in peer-reviewed journals



iStent®
CE Mark 2004
FDA Approval 2012



iStent inject®
CE Mark 2010
FDA Approval June 2018

Both Utilize the Conventional Outflow Pathway

The iStent inject Trabecular Micro-bypass

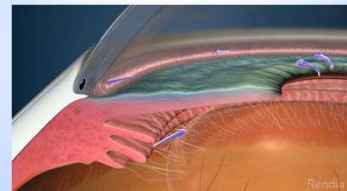
For patients with cataracts and glaucoma, iStent inject is:

- FDA approved therapy for the treatment of elevated IOP in adult patients with mild-to-moderate primary open-angle glaucoma in conjunction with cataract surgery
 - The first available *ab interno*, micro-bypass system designed to restore natural physiological outflow **through two openings** through the trabecular meshwork
- Excellent safety profile similar to that of cataract alone



Restore the Pathway for Natural Outflow

iStent inject creates two patent bypass pathways through the trabecular meshwork, resulting in multi-directional flow through Schlemm's canal



AQUEOUS HUMOR OUTFLOW

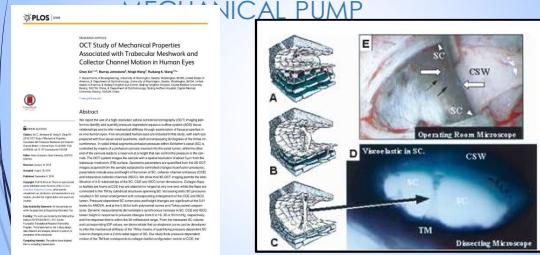
Conventional Outflow

- The aqueous humor leaves the eye at the anterior chamber angle through trabecular meshwork, the Schlemm's canal, intrascleral channels, and episcleral and conjunctival veins.
- Trabecular outflow accounts for 70-95% of the aqueous outflow.**

Unconventional Outflow

- The aqueous humor exits through the root of the iris, between the ciliary muscle bundles, then through the suprachoroidal-scleral tissues.
- 5-30% by uveoscleral outflow.**

AQUEOUS OUTFLOW AS A MECHANICAL PUMP



Murray A. Johnstone, MD

PULSE-DEPENDENT COLLECTOR



TRABECULAR MESHWORK PULSE-INDUCED MOTION VIDEO

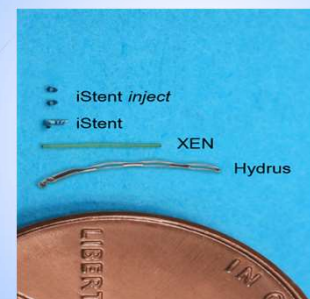


AQUEOUS ANGIOGRAPHY VIDEO

Aqueous Angiography Before and After Stenting

Alex Huang, MD, PhD

MIGS Technologies



iStent inject Advantages

- Creates two patent bypasses through the trabecular meshwork to restore natural outflow
- Significantly and effectively reduces IOP^{1,2}
- Optimizes aqueous outflow through the natural physiologic pathway
- Can reduce or eliminate the need for glaucoma medications (at discretion of eye care professional)
- Excellent overall safety profile similar to cataract surgery alone¹



1. iStent inject™ Trabecular Micro-Bypass System: Overview for Use, Part # 45-0176.
2. iStent inject™ II: Personal Experience with Second-Generation Trabecular Micro-Bypass Stents in Combination with Cataract Surgery in Patients with Glaucoma. 3. iStent inject™ ASUR, 2016 Presentation.

May Help Meet the Needs of Your Practice

Prevalent Patient Profile

- Adults with mild-to-moderate POAG
- Undergoing cataract surgery

Complete Procedure

- Two multi-directional stents designed to restore natural outflow
- Address cataract and glaucoma together
- Possible medication reduction could yield OSD symptom improvement

Patient Retention

- Clinically proven IOP reduction may help prevent glaucoma progression and may decrease the patient's need for more invasive surgery

Predictable Co-Management

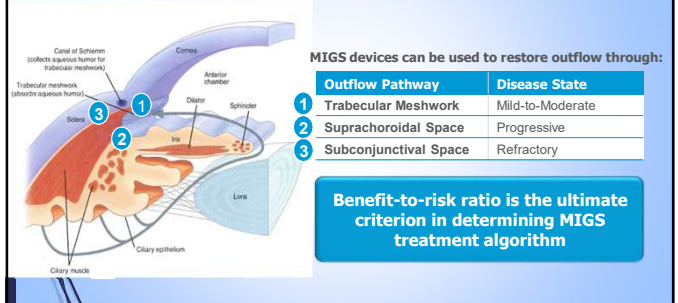
- Fits elegantly alongside cataract co-management
- iStent inject has an excellent overall safety profile similar to cataract surgery alone

Potential to Simplify the Management of Your Patient's Glaucoma

iStent
inject™

MIGS Treatment Algorithm

Areas of Aqueous Outflow



Considerations for Treating Mild-to-Moderate OAG

Safety

- ✓ First do no harm
- ✓ Minimal intraoperative, short- and long-term postoperative sequelae

Efficacy

- ✓ Ideal post-treatment target pressures of ≤ 15 mm Hg with ≤ 1 medication
- ✓ $\geq 20\%$ IOP reduction from preoperative baseline¹

Predictability/Patency

- ✓ Consistent, sustained IOP reduction over multiple years

Practice Efficiency

- ✓ Enhances practice offering
- ✓ Minimal disruption related to post-surgical sequelae, visual rehabilitation or administrative burdens

MIGS: Mild-to-Moderate Disease Interventions

Trabecular Bypass First

- Designed to restore and maintain natural physiological outflow
 - Up to 75% of resistance to outflow¹
- Overall safety profile consistent with cataract surgery alone
 - Episcleral venous back pressure of 8-11 mm Hg
- Maintaining the natural pathway avoids atrophy of Schlemm's canal¹
- Foundational therapy ➡ preferred safety-to-benefit option for mild-to-moderate intervention




Who is an iStent *inject* Candidate?

- Patients undergoing cataract surgery with mild-to-moderate primary open-angle glaucoma
- Cataract surgery patients who could benefit from better control of their IOP, which may allow for their medications to be reduced
- Patients wanting to decrease risk of IOP fluctuations associated with medication compliance or who are non-adherent to prescribed regimens
- Patients looking to avoid the risks of more invasive procedures
- Patients challenged in paying for medications or who cannot tolerate medications or have experienced negative side effects of glaucoma

Glaucoma Patients & Ocular Surface

Glaucoma Patients:


- Elderly (decreased tear secretion)
- On medications for life
- Frequently on multiple topical ophthalmic medications¹
- Abnormal tear film breakup time is associated with increasing number of eye drops and drops with and without BAK²
- May undergo filtering surgery (impact on healing)



Medeiros SA, Shor Y, Li J, Phillips P, Wall JC, Stanley TJ. Current management of glaucoma and the need for complete therapy. Am J Ophthalmol. 2008;146(suppl 1):S20-S27.
Wong W, Chang RW, Schwartz A, et al. Ocular Surface Disease in Glaucoma: Effect of Preoperative and Postoperative Systemic and Topical Steroids. 2012;15(1):e222-225.

Glaucoma Medications & Ocular Surface Disease (OSD)

Nearly 60% of Medically Treated Glaucoma Patients Report OSD Symptoms¹


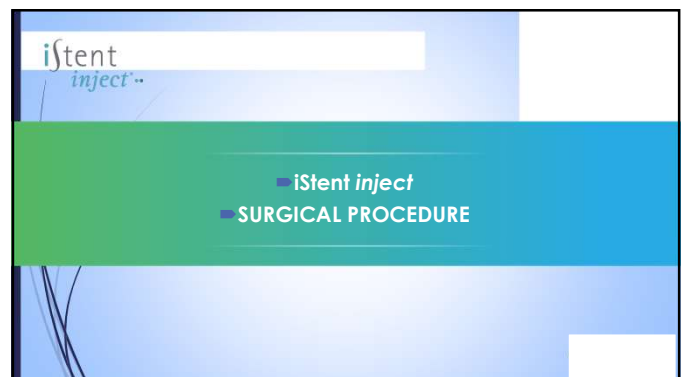


Reduction in topical glaucoma medications, which typically contain the preservative benzalkonium chloride (BAK), can help maintain the quality of tear film and potentially improve refractive outcomes.²

Levy S, Medeiros SA, Smith SE. Occurrence of Ocular Surface Disease in Glaucoma Patients. J Glaucoma. 2009;18(5):350-355.
Medeiros SA, Chang RW, Chang RW, et al. Ocular Surface Disease in Glaucoma: Effect of Preoperative and Postoperative Systemic and Topical Steroids. 2012;15(1):e222-225.

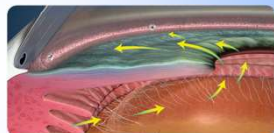
Diagnostic Testing for the iStent *inject* Procedure

- Manifest refraction and brightness acuity testing
- Careful slit lamp examination
 - Document existence of any secondary glaucomas such as pseudoexfoliation syndrome and pigment dispersion syndrome
- Glaucoma workup
 - Visual field
 - Optic nerve head OCT
 - Pachymetry
 - IOP
 - Gonioscopy – evaluating for synechia, iris processes, narrow anatomical angles, angle recession or any other abnormalities of the angle structure that may interfere with placement of iStent *inject*
 - Dilated fundus examination – rule out moderate/severe retinal pathology
 - Optic nerve head evaluation

iStent *inject* Surgical Procedure

- Placed in the eye during cataract surgery
- The procedure is straightforward, astigmatically-neutral, and minimally traumatic to the eye
- iStent *inject* has an overall safety profile similar to cataract surgery
- Reduces the risk of hypotony by utilizing the natural episcleral venous pressure^{1,2}



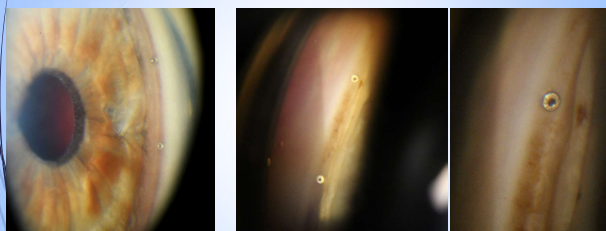
1. Rosenblatt, R., et al. Outflow resistance of emulsified human eyes of two different perfusion pressures and different extents of trabeculotomy. *Cornea* 1999;18:123-30.

2. Rosenblatt, R., et al. Trabecular Micro-Regulation System: Directions for Use, Part 4. 4/20/06.

iStent *inject* Surgical Procedure



iStent *inject* Post-Op Images



Courtesy of Dr. Marc Taleberg

2-year post-op
Courtesy of Dr. George Reiss

iStent
inject

COMPELLING CLINICAL RESULTS

KEY GLOBAL DATA POINTS

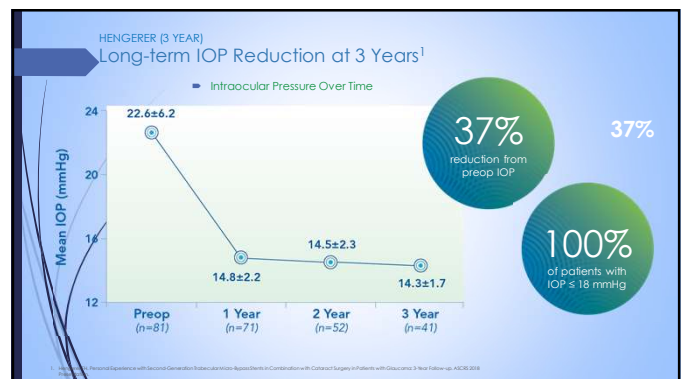
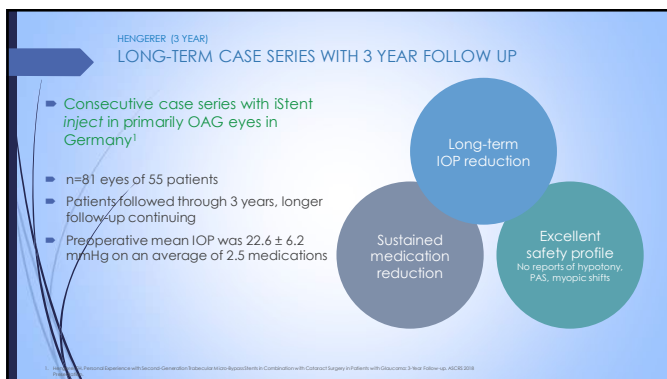
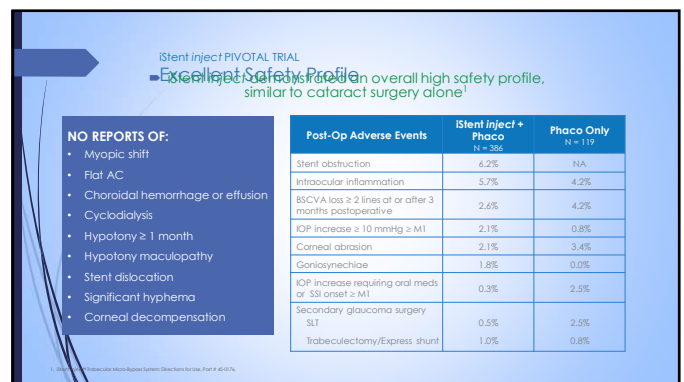
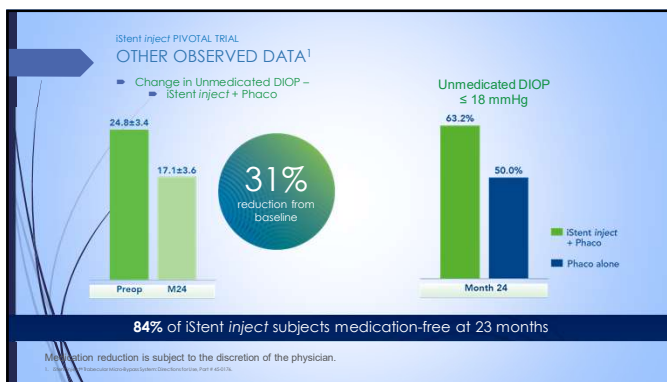
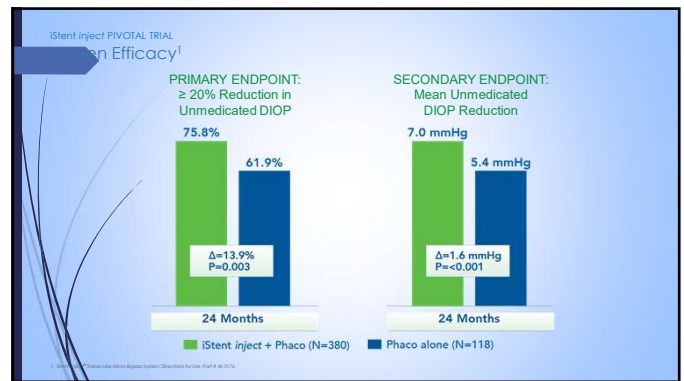
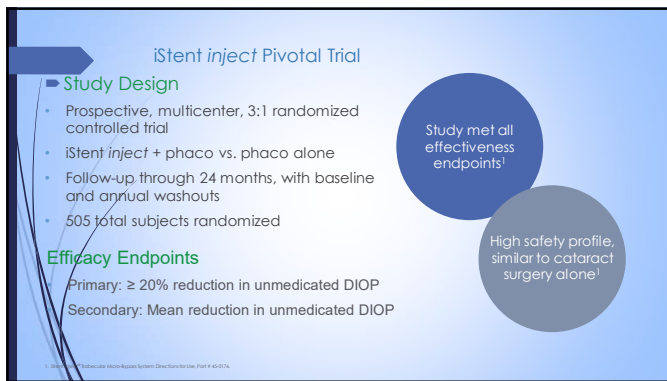
- Pivotal Trial Data- US
 - The study met all effectiveness endpoints
 - At 24 months, the mean reduction in unmedicated DIOP was 7.0 mmHg
 - At 24 months, 75.8% met the primary endpoint of $\geq 20\%$ reduction of unmedicated DIOP from baseline
 - 84%** of iStent *inject* subjects that were responders were medication-free at 23 months
 - High safety profile, similar to cataract surgery alone
- Hengerer 3 yr data- Germany
 - At 3 yrs, 100% of patients with IOP ≤ 18 mmHg
 - This demonstrates treatment still safe and effective at 3 yrs

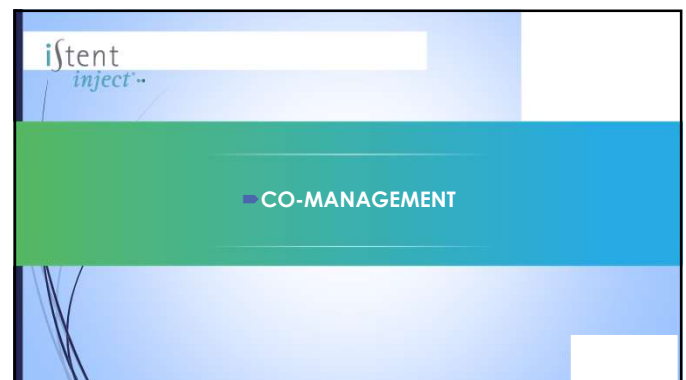
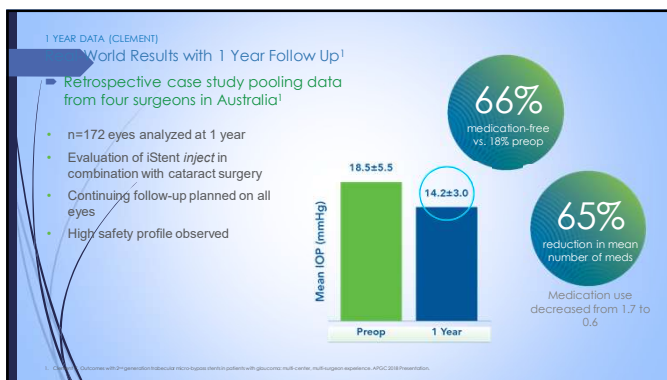
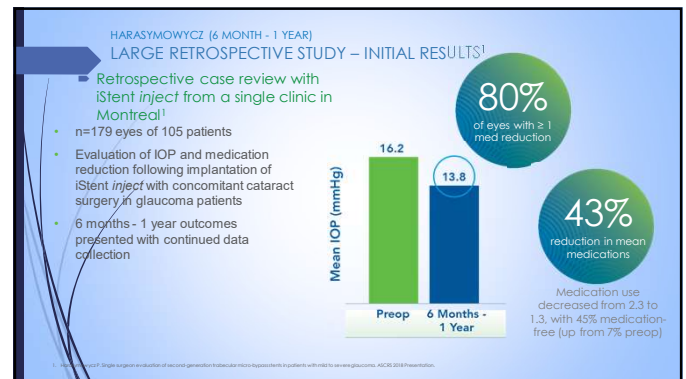
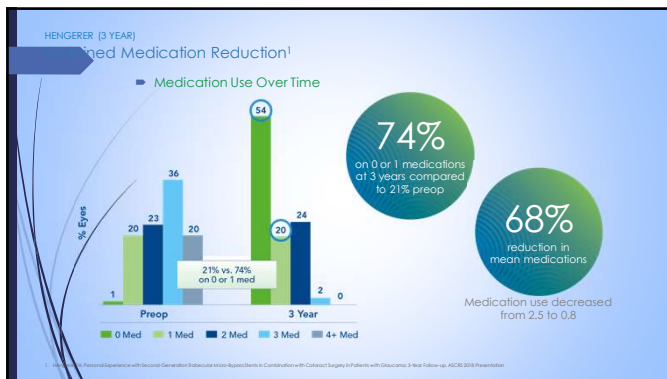
>40K iStent *inject* implants · 17 clinical publications on iStent *inject*

KEY GLOBAL DATA POINTS

- Harasymowycz 1 yr data- Canada
 - Medication use decreased from 2.3 to 1.2, with 45% medication-free (up from 7% preop)
 - 80% of eyes with ≥ 1 med reduction
 - 43% reduction in mean number of medications
- Clement 1 yr data- Australia
 - 66% are medication free at 1 year
 - Medication use decreased from 1.7 to 0.6
 - 65% reduction in mean number of medications

>40K implants · 17 clinical publications on iStent *inject*





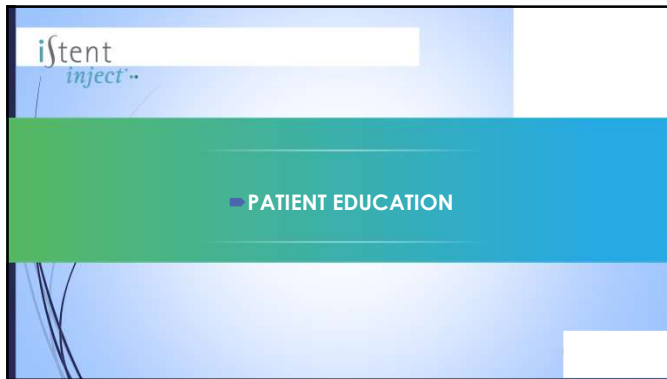
Co-Management Considerations

- Establish medical necessity for cataract and glaucoma surgery
- Accurately document all preoperative evaluations or diagnostic tests
- Obtain patient consent to co-management
 - Clearly explain and document patient logistics
 - Financial arrangement disclosures
 - Consent to share information between surgeon and postop care provider
 - Provisions if complications occur
 - Signatures (patient, surgeon, co-managing doctor)

Co-Management of Cataract Example


Surgeon's Care		Optometrist's Care	
0 May 1	10 May 12	90 July 30	
5/1	66984-54		
5/2-5/11	66984-55	5/12-7/30	66984-55

- 66984 has a global period of 90 days
- Postop care is 20% of global package
- Value of postop care apportioned
- In this example:
 - 10/90th of 20% to the surgeon
 - 80/90th of 20% to the optometrist




Express the Benefits of iStent *inject* to Your Patients

- You play an important role in the patient's decision about the iStent *inject*—they trust you and want your guidance.



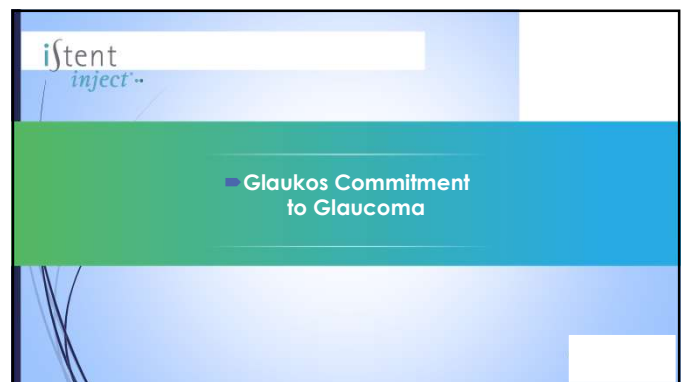
- iStent *inject* is implanted at the same time as cataract surgery with an excellent overall safety profile
- Proven in patients all around the world
- Proven to reduce IOP and may reduce glaucoma medication usage

iStent *inject* Patient Educational Materials



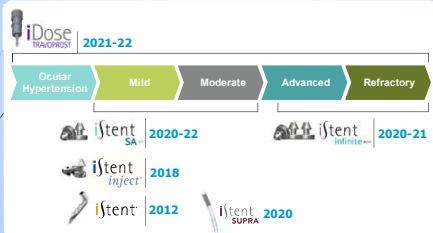
Screening Questionnaire Patient ID Reference Sheet Post-It Note Website Content Patient Poster

Patient Brochure Clinician Aid Find an iStent *inject* Physician on Glaukos.com Acrylic Display Educational DVD



The Future MIGS Treatment Algorithm

Addressing a wide range of glaucoma disease states and progression



iDose TRAJECTORY 2021-22

Ocular Hypertension Mild Moderate Advanced Refractory

iStent SA 2020-22 iStent *inject* 2018 iStent 2012 iStent SUPRA 2020

KEY GLOBAL DATA POINTS

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Hengerer 3 yr data- Germany

- At 3 yrs, 100% of patients with IOP ≤ 18 mmHg
- This demonstrates treatment still safe and effective at 3 yrs

>40K iStent *inject* implants · 17 clinical publications on iStent *inject*

CyPass

- Microstent into supraciliary space creating negative pressure
- Pulled off the market due to corneal concerns

CyPass® Micro-Stent: Intuitive Implantation Approach

The CyPass® Micro-Stent is minimally invasive, spares the conjunctiva, and avoids the formation of a filtering bleb.

The procedure is ab-interno, using the primary clear corneal incision made at the time of cataract surgery.

Proximal rings, clearly visible under a gonioscopy lens, provide guidance for proper insertion and depth.

CyPass® Micro-Stent: Enhanced Aqueous Outflow

- The supraciliary space has a negative pressure gradient that drives aqueous outflow and reduction of intraocular pressure¹
- The uveoscleral pathway bypasses Schlemm's canal and collector channels, which may be atrophic in glaucoma patients²
- The CyPass® Micro-Stent utilizes the same outflow pathway as first line prostaglandin analogues³

1. Sakai H, Iwatsubo T. Animal I. Optical coherence tomography of the supraciliary space after CyPass Micro-Stent implantation for the reduction of IOP in glaucoma. *OP-2* (Abstract). 2015;10:10-23.
2. Fattah M. Supraciliary uveoscleral outflow: correlation with the type and extent of cataract-based surgery. *ASG* 2011 abstract.
3. Voonak P, Tuck J, Glick B. et al. Effects of prostaglandins on the aqueous humor outflow pathway. *Surv Ophthalmol* 2002;47(suppl 1):S22-S24.

Two-Year COMPASS Trial Results: CyPass® Micro-Stent Achieved Primary & Secondary Endpoints

72.5% of eyes achieved a ≥20% reduction in unmedicated diurnal IOP at two years*

61.2% of eyes maintained an unmedicated diurnal IOP range between 6 and 18 mmHg at 24 months

Endpoint	CyPass Micro-Stent 1 (n=101)	Control surgery (n=101)
≥20% reduction in unmedicated diurnal IOP at 24M	72.5%	58.0%
Maintained unmedicated diurnal IOP range 6-18 mmHg at 24M	61.2%	43.5%

*Prospective, randomized, multicenter clinical trial in patients (n=202) with open-angle glaucoma undergoing vitreous and lens surgery undergoing to microstent (n=101) or phacemulsification (n=101). Primary outcome measure was unmedicated diurnal IOP reduction at 24 months versus control surgery alone at baseline. Secondary outcome measure was mean change in 24 month IOP from baseline and 24 month unmedicated mean IOP between 6 mmHg to 18 mmHg versus control surgery alone. Medication use at 24 months was also analyzed. The primary and secondary effectiveness analyses were performed using intent-to-treat (ITT) population.

Safety Findings Support Intended Use

- Safety based on 2-year follow-up with 95% of randomized patients completing study
- Comparable BCVA to cataract surgery
- Ocular SAEs had no long-term impairment
- Overall rate of ocular AEs balanced
- Significant ocular AEs infrequent
- CyPass® Micro-Stent – specific AEs managed with good outcomes
- ECL as expected after cataract surgery

Early Success

- First in the state to perform the procedure.
- Allowed select patients to purchase the device and inserted free of charge.
- As a stand alone procedure especially for some sick eyes and complicated patients it offered a unique solution
- Then we started rolling it out with our cataract patients with pre-existing glaucoma.
- Learned quickly that this was not an iStent substitute

Where did we go wrong?

- Significant complications including
 - Myopic shift
 - Chronic hypotony
 - Delayed supra choroidal hemorrhage
 - Intermittent postoperative IOP spikes
- Company was very responsive and concerned, but "You are the only one seeing these complications"
- Due to the increased endothelial cell loss found in the 5 year Compass Trial the product was voluntarily withdrawn from the market.

What now?

- We sent out a letter to all of our patients explaining that CyPass was withdrawn from the market and why.
- We have brought in every patient for a free exam to check the positioning of the CyPass and to answer any questions.
- We are looking for CyPass alternatives for our patients

OMNI Glaucoma Treatment System

- Combines Canaloplasty with Goniotomy
- Overcomes three points of resistance –The trabecular meshwork Schlemm's canal, and the collector channels
- Can be done as a stand-alone procedure in addition to being combined with cataract surgery.



OMNI™ Surgical System

Introduction to Sight Sciences

Speaker Deck
2019



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Transforming Ophthalmology and Optometry by
addressing the underlying causes of the world's most
prevalent eye diseases

OMNI Speaker Deck - 061078

MICRO-INVASIVE GLAUCOMA
SURGERY
(MIGS)

DRY EYE DISEASE



50 Global Patents for Surgical
Glaucoma



20 Global Patents for Dry Eye
Disease

2019



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FASTEST GROWING SEGMENT
in ophthalmic surgery

"Global market is projected to display a **robust growth** represented by a **Compound Annual Growth Rate (CAGR) of 47.10%** during 2017-2022, chiefly driven by several MIGS devices entering the market in next five years, rising number of glaucoma patients and rapidly aging population, high safety profile and reduced dependency on prescription eye drops."¹

Source: Global Vision Care and Ophthalmic Surgery - Global Markets, Research and Markets, 2017
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Primary target for surgical intervention

80% Conventional pathway contributes ~80% of outflow in a normal eye

1st 75% of surgeons still want to address the conventional outflow pathway first¹

Shield Episcleral venous back pressure serves as a backstop which may prevent hypotony post-operatively

Source: Global Vision Care and Ophthalmic Surgery - Global Markets, Research and Markets, 2017
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Conventional Outflow Pathway:

Three(3) potential points of resistance

1 **Trabecular Meshwork** could be a source of resistance to outflow, increasing IOP

2 Resistance can also be found in **Schlemm's Canal** which may be atrophied or collapsed

3 The **collector channels** can be a third source of resistance as they may be atrophied or blocked

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INDICATION

The OMNITM Surgical System is a manually operated device for delivery of small amounts of viscoelastic fluid, for example Healon[®] or HealonGV[®] from Abbott Medical Optics (AMO), Amvisc[®] from Bausch & Lomb, or PROVISC[®] from Alcon, during ophthalmic surgery. It is also indicated to cut trabecular meshwork tissue during trabeculotomy procedures.

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Combines two distinct implant-free procedures in one device

Transluminal viscoelastic delivery + Titratable trabeculotomy

OMNITM Surgical System

Targets three points of resistance in the conventional outflow pathway:

1. Trabecular Meshwork
2. Schlemm's Canal
3. Distal Collector Channels

Each of these procedures is sufficiently established to have its own Category 1 CPT code

Standalone procedure or in conjunction with cataract surgery

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Transluminal Viscoelastic Delivery

Trabeculotomy (ab interno)

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