Keeping Current With Glaucoma Surgery

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Financial Disclosures

- Alcon (Speaker)
- Allergan (Speaker/Consultant)
- Glaukos (Research)
Human Cost of Glaucoma

Glaucoma is the second leading cause of blindness worldwide. Global estimates of glaucoma cases exceeded 60M in 2010 and are estimated to grow to 78M by 2020. Bilateral blindness is occurring at an alarming 7.5% of OAG cases globally, growing from 4.4M to 6M patients between 2010 and 2020. In the US, there are an estimated 2.2M cases of OAG, growing to >3M cases by 2020, with >88,000 of these patients going blind.

Problems with Glaucoma Meds

- Cost
- Compliance
- Quality of life
- Side effects:
  - Death from beta-blockers
  - Fatal aplastic anemia (CAIs)
  - Severe allergic reactions
  - Retinal detachment (pilocarpine)
  - Irritation, redness, etc.
- Future surgery success rate may be lower
Glaucoma: Surgical Disease

CIGTS:

- Glaucomatous optic disc progression is *higher* in patients on medical treatment than surgical patients

Glaucoma: Surgical Disease

Surgical options

- Laser trabeculoplasty
- Laser cyclophotocoagulation
- Trabeculectomy (+/- ExPress)
- Tube shunts
  - Ahmed, Baerveldt, Molten
- Safer, less invasive surgeries:
  - MIGS
Glaucoma: Surgical Disease

Trabeculectomy

• Advantages
  - Still the gold standard surgery
  - No device needed - available, cost-effective
  - Can achieve low IOPs

• Disadvantages
  - Complications in up to 40%
  - Failure in up to 50% at 5 years
  - Cataract in 50% at 5 years

TVT study: complications

- Early postoperative complications:
  - 21% (tube) and 37% (trab)

- Late postoperative complications (up to 5 years after surgery):
  - 34% (tube) and 36% (trab)

- Cataract surgery:
  - 54% of phakic tube eyes and 43% of phakic trab eyes

- Reoperation for surgical complications:
  - 22% (tube) and 18% (trab)
Bleb Leak

- Test with high concentration fluorescein
- Cascading darker/clear fluid with fluorescent edges is a leak
Endophthalmitis
Tube Erosion
Ideal Glaucoma Surgery?

- As effective as trabeculectomy but safe
- Reproducible/Predictable
- No bleb
- Easy to perform
- Less post-operative effort
- Cost-effective
Reduction in Intraocular Pressure after Cataract Extraction: The Ocular Hypertension Treatment Study

Steven L. Mansberger, MD, MPH, Mae O. Gordon, PhD, Henry Jampel, MD, MHS, Anjali Bhorade, MD, James D. Brandt, MD, Brad Wilson, PhD, Michael A. Kass, MD, for the Ocular Hypertension Treatment Study Group*

Cataract surgery vs. controls from OHTS:
16.5% reduction in IOP sustained for 36 months

Concomitant Cataract & Glaucoma (US)

1 in 5 Cataract Eyes on OHT Medication
MIGS
Minimally Invasive Glaucoma Surgery
Minimally Invasive Glaucoma Surgery (MIGS)

- Ab interno microincisinal approach
- Minimally traumatic to the target tissue
- Safe and (at least modest) IOP reduction
- Rapid recovery with minimal impact on the patient’s quality of life (like cataract surgery)
- Typically indicated for mild to moderate POAG
Minimally Invasive Glaucoma Surgery (MIGS) ~ angle surgery

- Schwalbe’s line
- Trabecular meshwork
- Scleral spur
- Ciliary body band
Overview of MIGS

- Xen implant
- InnFocus

MIGS
Outflow Targets

Schlemm’s Canal (Conventional outflow)

iStent

Hydrus

Trabectome

Scleral/Subconjunctival

Suprachoroidal Space (Non-conventional outflow)

Cypass

iStent Supra

Ike K Ahmed MD
MIGS: Conventional Outflow

iStent approved in 2012

- Xen implant
- InnFocus
iStent Trabecular Micro-Bypass Stent

- 1 mm x 0.33 mm
- Snorkel: 120 µm lumen
- Weight: 60 µg
- Surgical grade nonferromagnetic titanium
- Heparin-coated to promote self-priming and facilitate outflow

iStent® is FDA approved in the U.S., C.E. marked in the E.U., and has Medical Device Approval in Canada

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iStent: Indication

- Mild-moderate OAG
- In conjunction with cataract surgery
- Currently treated with ocular hypotensive medication
iStent: Mechanism

- Improves aqueous outflow thru the natural physiologic pathway
- Creates a bypass thru trabecular meshwork to Schlemm’s canal

iStent® is FDA approved in the U.S., C.E. marked in the E.U., and has Medical Device Approval in Canada

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iStent
At 12 months: 68% of iStent subjects with IOP ≤ 21 mm Hg without medication vs. 50% with cataract surgery alone (p=0.004)
Randomized Evaluation of the Trabecular Micro-Bypass Stent with Phacoemulsification in Patients with Glaucoma and Cataract

At 12 months:
- 15% of iStent vs.
- 35% cataract group on medication (p=0.001)
<table>
<thead>
<tr>
<th>Complication</th>
<th>iStent + Cataract Surgery N = 111</th>
<th>Cataract Surgery N = 122</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticipated early postoperative event</td>
<td>14(13%)</td>
<td>15(12%)</td>
</tr>
<tr>
<td>Stent obstruction by iris, vitreous, fibrous overgrowth, fibrin, blood, and so forth</td>
<td>4(4%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Posterior capsular opacification</td>
<td>3(3%)</td>
<td>8(7%)</td>
</tr>
<tr>
<td>Stent malposition</td>
<td>3(3%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Subconjunctival hemorrhage</td>
<td>2(2%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Elevated IOP, other</td>
<td>2(2%)</td>
<td>1(1%)</td>
</tr>
<tr>
<td>Epiretinal membrane</td>
<td>2(2%)</td>
<td>1(1%)</td>
</tr>
<tr>
<td>Iris atrophy</td>
<td>2(2%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Blurry vision or visual disturbance</td>
<td>1(1%)</td>
<td>6(5%)</td>
</tr>
<tr>
<td>Iritis</td>
<td>1(1%)</td>
<td>6(5%)</td>
</tr>
<tr>
<td>Dry eye</td>
<td>1(1%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Elevated IOP requiring treatment with oral or intravenous medications or with surgical intervention</td>
<td>1(1%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Macular edema</td>
<td>1(1%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>0(0%)</td>
<td>3(2%)</td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>0(0%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Mild pain</td>
<td>0(0%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Rebound inflammation from tapering steroids</td>
<td>0(0%)</td>
<td>2(2%)</td>
</tr>
</tbody>
</table>
iStent
because I can
GiggleMed.com

iStent
Lower IOP
Fewer medications
No bleb!!
iStent

- Personal experience:
  - ~250 cases since November 2013
  - No stent-related complications
## Cost Effectiveness

Projected cost savings at 6 years in $:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>1 drop</th>
<th>2 drops</th>
<th>3 drops</th>
</tr>
</thead>
<tbody>
<tr>
<td>iStent</td>
<td>-20.77</td>
<td>1272.55</td>
<td>2124.71</td>
</tr>
<tr>
<td>ECP</td>
<td>779.23</td>
<td>2072.55</td>
<td>2924.71</td>
</tr>
<tr>
<td>Trabectome</td>
<td>279.23</td>
<td>1572.55</td>
<td>2424.71</td>
</tr>
</tbody>
</table>

What's in the Pipeline?

iStent Inject (G2)

2 “iStent inject” vs latanoprost/timolol

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What's in the Pipeline?
Hydrus

Bigger/longer than iStent G1 (3 clock hrs)
What's in the Pipeline? Hydrus
MIGS - Suprachoroidal

- Xen implant
- InnFocus

Outflow Targets

- Schlemm’s Canal (Conventional outflow)
- Suprachoroidal Space (Non-conventional outflow)
- Cypass
- iStent
- Hydrus
- Trabectome
Suprachoroidal Outflow

- 50% of aqueous outflow in normal human eyes
- Similar to PGAs and cyclodialysis cleft
Suprachoroidal outflow:
- CyPass
- Xen implant
- InnFocus

MIGS Outflow Targets

- Schlemm's Canal (Conventional outflow)
- Suprachoroidal Space (Non-conventional outflow)
- Cypass
- iStent Supra
- Hydrus
- Trabectome

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Suprachoroidal Outflow: Cypass

- FDA approved in 2016 (CE mark in 2008)
- Awaiting insurance coverage
- Polyamide, 6.35 mm long
Suprachoroidal Outflow: Cypass: Efficacy

• COMPASS (with CE/IOL vs CE/IOL alone)
  • N=505, 2 year f/u
  • 72.5% CyPass vs 58% Controls achieved ≥ 20% decrease in unmedicated IOP from baseline (p=0.0030)

• Other studies:
  • with CE/IOL (Hoeh et al 2013): 37% IOP reduction, 50% reduction in meds
  • alone (García-Feijoo et al 2015): 35% IOP reduction, 36% reduction in meds
Serious AEs:

- Hypotony maculopathy: 3 cases (0.8%)
- Maculopathy without hypotony: 2 cases (0.5%)
- Malposition: 7 cases (1.9%)
- Chronic anterior uveitis: 1 case (0.3%)
- Persistent corneal edema requiring corneal transplant: 1 case (0.3%) (baseline compromised cornea)
- Additional surgery 20 cases (5.3%)
Suprachoroidal Outflow: Cypass: Adverse Events

Most common

- Iritis 8.6%
- Loss of BCVA at least 10 letters 0.8%
- Visual field loss progression 6.7%
- Corneal edema 3.5%
- Later hypotony 2.9%
- Later IOP $\geq$10 mmHg over baseline 4.3%
Suprachoroidal Outflow: Cypass: Adverse Events

Intraoperative AEs:
• Hyphema obscuring surgeon’s view 2.7%
• Larger than expected cyclodialysis cleft 1.9%
• Inability to implant stent 0.5%
• Iridodialysis 0.3%

Most common clinical safety findings:
• Microhyphema 16%
• Focal PAS 13%
• Early hypotony 9%
• AC shallowing 6%
• Partial obstruction of the CyPass lumen 5%
• Pigment dispersion 5%
Suprachoroidal Outflow: iStent Supra

- Xen implant
- InnFocus
iStent Supra

Glaukos iStent Supra®
IOP Lowering MicroDevice
Ab Interno Implant. EU approved.
Now Awaiting FDA Approval.

new-glaucoma-treatments.com

• Phase III clinical trial in US
• Finished enrollment in 2016; 3 year follow-up
• MEA one of ~40 sites
• 4 stents implanted

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iStent Supra
MIGS - Sunconjunctival

- Xen implant
- InnFocus

Outflow Targets:
- Schlemm’s Canal (Conventional outflow)
- Suprachoroidal Space (Non-conventional outflow)
- Cypass
- iStent
- Hydrus
- Trabectome
- iStent Supra
XEN Gel Stent

- Subconjunctival, ab interno
- Flexible stent
- 45 micron lumen
XEN Gel Stent

- Results in a bleb
- Mitomycin-C used
- May need needling
XEN Gel Stent

Efficacy (from pivotal study, N=65)

- IOP 25.1 (+/-3.7) mmHg \rightarrow 15.9 (+/-5.2) mmHg (at 12 months postop)

- IOP-lowering meds 3.5 \rightarrow 1.7 (at 12 months)
XEN Gel Stent
Adverse Events

• BCVA loss > 2 lines (< 30 days 15.4%; > 30 days 10.8%; 12 months 6.2%)
• Hypotony (IOP < 6 mm Hg at any time) 24.6% — (no clinically significant consequences, no persistent hypotony, and no surgical intervention required)
• IOP increase > 10 mm Hg from baseline (21.5%)
• Needling procedure (32.3%)
What's in the Pipeline?

InnFocus Microshunt

• Subconjunctival
• Ab interno
• CE Mark in 2012
• FDA trial vs. trab
• Made of SIBS, the most biostable thermoplastic elastomeric material currently in existence
Summary of MIGS

- Xen implant
- InnFocus
Increasing Trabecular Outflow

- Schwalbe’s line
- Trabecular meshwork
- Scleral spur
- Ciliary body band
Increasing Trabecular Outflow

Remove or cut TM (inner wall of Schlemm’s)
- Trabectome
- Kahook dual blade
- GATT (gonioscopy assisted transluminal trabeculotomy)
- Trab360

Canaloplasty
- Visco360
- ABiC (Ab interno canaloplasty)

- All FDA approved and available
- All ab interno
- Can be done +/- cataract surgery

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Trabectome

- Approved since 2004
- Uses electrocautery to ablate and remove a strip of TM to re-establish access to the eye’s natural drainage pathway (Schlemm’s canal)
Review of 115 Trabectome pts vs. 102 trab-MMC pts

Success rates (IOP<21 mmHg or >20% reduction) at 2 years:

22.4% for trabectome vs 76.1% for trab (P=0.001)
Ab Interno Trabeculectomy Versus Trabeculectomy for Open-Angle Glaucoma

Seung Youn Jea, MD, PhD,1 Brian A. Francis, MD, MS,2 Ghazal Vakili, MD,2 Theodoros Filippopoulos, MD,1 Douglas J. Rhee, MD1

Trabectome had 100% hyphema POD #1, plus 4.3% other complications, compared to 35.3% complication rate for trabeculectomy (P=.001)
Adverse events:

• Hyphema
• Descemet’s injury
• Ciliary body injury
• Zonule injury
Kahook Dual Blade

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Visco360

Reservoir and Infusion Pump (Inside the handle)

Retainer Pin

Control Wheel (For advancement and retraction)

Cannula

Microcatheter

Viscoelastic Fluid

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BONUS:
Cyclophotocoagulation
- Endoscopic
- Transscleral

Can be considered MIGS
CPC Indications

- Mild to moderate glaucoma (any type)
  or
- Refractory glaucoma (after multiple failed glaucoma surgeries)
Endoscopic Cyclophotocoagulation
ECP

- Selective ablation of aqueous producing ciliary processes
  - *ab interno* approach
  - Inhibits aqueous production
  - Performed globally for >12 years
Phaco-ECP: Combined ECP and Cataract Surgery

**Figure 1** Mean intraocular pressure (IOP) over time with 95% CIs.

**Figure 3** Medications over time.

Lindfield D, Ritchie RW, Griffith MF. BMJ Open 2012
ECP COLLABORATIVE STUDY GROUP

SAFETY STUDY: COMPLICATIONS

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP Spike</td>
<td>14.5%</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>3.8%</td>
</tr>
<tr>
<td>Serous Choroidal Effusion</td>
<td>0.36%</td>
</tr>
<tr>
<td>IOL Dislocation</td>
<td>0.36%</td>
</tr>
<tr>
<td>CME</td>
<td>1.03%</td>
</tr>
<tr>
<td>RD</td>
<td>0.27%</td>
</tr>
<tr>
<td>Massive Choroidal Hemorrhage</td>
<td>0.09%</td>
</tr>
<tr>
<td>Hypotony or Phthisis</td>
<td>0.12%</td>
</tr>
<tr>
<td>NLP Vision</td>
<td>0.12%</td>
</tr>
<tr>
<td>Cataract</td>
<td>24.5%</td>
</tr>
<tr>
<td>Acute Graft Rejection</td>
<td>5.3%</td>
</tr>
<tr>
<td>Chronic Graft Rejection</td>
<td>0</td>
</tr>
<tr>
<td>Chronic Inflammation</td>
<td>0</td>
</tr>
<tr>
<td>Flat AC</td>
<td>0</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0</td>
</tr>
<tr>
<td>Diplopia</td>
<td>0</td>
</tr>
<tr>
<td>Wound Leak</td>
<td>0</td>
</tr>
<tr>
<td>Bleb Complications</td>
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</tbody>
</table>

5824 PATIENTS

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Micropulse Trans-scleral CPC
Micropulse Trans-scleral CPC

- 33% IOP reduction at 18 months, N = 38 patients
- 61% med reduction (2.1 to 1.3)
- 73% success rate with 1.3 sessions

Micropulse Trans-scleral CPC

- 19 patients
- Follow-up 60 days
- Mean IOP dropped 37.9 preop -> 22.7 at last follow-up (40% decrease)
- Success rate 73.7% (=IOP 6-21 or IOP reduction by 20 % at the last follow-up visit)
- 3 pts underwent a 2nd treatment, increasing the overall success rate to 89.5%
- 4 pts gained 1 line of vision, 4 pts lost 1 line

Medication Delivery Methods

- Ocusert (1970s), Ozurdex, etc.
- Intracanalicular/Punctal plug
- Drug-eluting contact lens
- Intracameral (AC) injection ( +/- erodible)
- Subconjunctival implant ( +/- erodible)
Summary

- Appreciation for the risks and complications associated with traditional glaucoma surgery has ignited the MIGS revolution
- MIGS +/- cataract surgery, provides safe new options for IOP reduction
- Lots of options, data is forthcoming
- Trabeculectomy and tube shunt surgery for advanced glaucoma and more significant IOP reduction
Questions?
Thank you!

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