Glaucoma Surgical Treatments

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Disclosures

- Murray Fingeret
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- Justin Schweitzer
  - Allergan, Glaukos, Bausch and Lomb, Bio-Tissue, Alcon, TearScience, Reichert
- Joseph Sowka
Glaucoma Surgical Treatments

• What are the indications for glaucoma surgery? (Murray)
• Selective Laser Trabeculoplasty – Is it best suited as a primary or secondary treatment option? (Murray)
• The Trabeculectomy – Has it become a relic? (Joe)
• MIGS – The iStent what is its role? Has it become a relic with the introduction of new MIGS devices? (Justin)
• MIGS - The Cypass and Xen gel implant – What are they and how do they differ from the iStent? (Justin)
• Bimatoprost SR – Are injections into the anterior chamber a viable therapeutic option? (Joe)
What are the indications for glaucoma surgery?
When is surgery indicated?

• Poor IOP control
  • After exhausting medical therapy, IOP is above target pressure
• Glaucomatous damage getting worse
• Poor compliance
  • Due to a host of reasons including cannot afford medication, cannot remember to take them
• Inability to instill eyedrops
  • Ie Parkinson's disease
• Medication side effects
• These may also be the reasons to consider a drug delivery device when available
  • Ring, punctal plug, contact lens, injection
When is surgery indicated?

• Indications for doing SLT are different than Filtration surgery which are different from implanting a MIGS device
• Insurance coverage must be considered
• Much quicker to do SLT or MIGS (if cataract present) than the trabeculectomy
• SLT and MIGS are often considered as a medication in regards to indications and complications
Surgery

• Laser trabeculoplasty
  • Selective
• MIGS
  • Istent
  • Cypass
  • Xen gel implant
• Filtering Procedures
• Filtering procedures with anti-fibroblastic agents
• Express implant
• Canaloplasty
• Implants
  • Molteno, Ahmed Glaucoma Valve, Baerveldt Glaucoma Implant
• Cyclophotocoagulation procedures
  • Endocyclophotocoagulation
Selective Laser Trabeculoplasty
Is it best suited as a primary or secondary treatment option?
Selective Laser Trabeculoplasty (SLT)

• Q-switched, frequency doubled Nd:Yag 532 nm laser
• Targets pigmented cells in trabecular meshwork
  • little damage to non-pigmented cells
  • less destructive procedure
• 400 μm spot size w 50 spots to 180° of TM
  • as compared to 50 μm spot size for ALT
  • spans entire height of TM
  • selectively targets pigmented cells wo causing structural or coagulation damage
  • eliminates scarring
• Reduced energy levels- 0.6 - 1.2 mJ
The Differences between ALT & SLT Treatments

Courtesy M. Latina, M.D.
Laser Spot Size Differences of ALT and SLT

- ALT (green area)
  - Requires focus on TM

- SLT (red area)
  - Covers TM
  - Does not require same sensitive focus as ALT

- Larger beam diameter
  - reduces need for focus
  - evenly distributes laser energy
Selective Laser Trabeculoplasty (SLT)

- **Advantage**
  - Little destruction to TM supports biologic theory
    - No coagulation effects
  - Reduced incidence of IOP spikes and complications
- **Relies on selective photothermolysis**
  - Targets melanin granules within cell
    - Cell death occurs
  - Less need for pigmented tissue
- **20-22% IOP reduction**
- **Works over 24 hour period**
- **Reduced structural damage to TM**
- **IOP reduced at 1 week**
Selective Laser Trabeculoplasty (SLT)

• Patient type
  • Effective as adjunctive or replacement tx
  • Also may be used as primary therapy
  • Being used early in stepped medical therapy
    • Do not wait until patient exhausted all medical options

• Contraindications
  • Secondary glaucomas
    • Traumatic angle recession
    • Inflammatory
    • Neovascular
# SLT Results

<table>
<thead>
<tr>
<th>Author/Yr</th>
<th>Eyes</th>
<th>Response</th>
<th>IOP Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latina, 1998</td>
<td>53</td>
<td>70%</td>
<td>23.5%</td>
</tr>
<tr>
<td>Gracner, 2001</td>
<td>50</td>
<td>88%</td>
<td>21.6%</td>
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<tr>
<td>Melamed, 2003</td>
<td>45</td>
<td>96%</td>
<td>30%</td>
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<tr>
<td>Cvenkel, 2004</td>
<td>44</td>
<td>62%</td>
<td>17.1%</td>
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<tr>
<td>McIlraith, 2006</td>
<td>74</td>
<td>83%</td>
<td>31.0%</td>
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</table>
Should SLT be used as Primary Therapy?

• Advantages to primary use
  • Cost
  • Adherence
  • IOP lowering effect wears off and questionable if repeatable
  • Lasts in 50% approximately 5 years
  • Few side effects and relatively safe
  • Works over 24 hour period

• Disadvantages to primary use
  • Only reduces IOP 20%

• Advantages to secondary use
  • Additive to all other medications
  • Can be utilized if first line therapy unsuccessful or needs additional reduction

• Explain options to patient and let them have voice in where therapy fits
Is it Repeatable?
Trabeculectomy – Has it become a relic?
Trabeculectomy – Has it become a relic?

- What filter (trabeculectomy) surgery is
  - Fistulization between AC and subconjunctival space

- Indications
  - Moderate/advanced disease, very high initial IOP, progressing disease, need for low and stable IOP
    - (CIGTS primary procedure?)

- Risks and complications
  - Several

- Is it being done less with MIGS now available?
  - Yes, but not for the reasons that you think
Trabeculectomy

- Trabeculectomy (1968)
  +/- anti-metabolite
- Bleb forming procedure
- Long established procedure with vast experience
Antifibrotic Agents

- Inhibit fibroblast proliferation

- **5FU**
  - Intraoperative: 50 mg/ml for 5 min
  - Postoperative: 5 mg subconj

- **MMC**
  - 100 times more potent than 5FU
  - Intraoperative: 0.2-0.5 mg/ml for 2-5 min
Antifibrotic Agents

- Inhibit fibroblast proliferation
  - MMC; 5-FU

- Indications
  - Neovascular glaucoma
  - Uveitic glaucoma
  - Previous ocular surgery (e.g. CE, failed filter)
  - African American race
  - Young age
    - Good healing
  - Need for a very low IOP
    - Very advanced disease
Outcomes: Trabeculectomy

Success After 20 Years:
- 57% = complete success
- 88% = qualified success (w/ meds)

Complications:
- Cataract: 55%
- Loss of ≥3 lines of acuity: 21%
- Bleb-related problems: 10%
- Infection: 4%

Jampel HD. Ophthalmol 2012
Gedde SJ. Arch Ophthal 2012
Is trabeculectomy a Panacea?

- Trabeculectomy will give low IOP
  - Single digits
- Long history of success
- Technically straightforward process
- Eye never looks/ feels the same
- Potential complications
Early Complications

- Failure to control IOP- scarring
  - Malignant glaucoma
  - Hyphema
  - Hypotony resulting maculopathy, suprachoroidal hemorrhage, choroidal effusion, or shallow anterior chamber
- Wound leak, may require additional sutures
- Endophthalmitis or blebitis
- Loss of vision
  - “wipe-out”
    - Hypotony maculopathy, choroidal effusion and detachment, pressure spike, idiopathic
Late Complications

- Cataract
  - Trabs cause cataracts
- Ptosis
- Bleb leak, due to breakdown of conjunctiva over the bleb, can cause hypotony
- Endophthalmitis and Blebitis - risk increases with bleb leak
Trabeculectomy

- Historically performed by general ophthalmologists
- As ophthalmology has evolved, most general ophthalmologists have abandoned trabs to glaucoma specialists
- Established glaucoma specialists have now learned tubes and seatons (drainage implants)
- Newer glaucoma specialists are increasingly learning drainage implants
- So, yes traditional trabeculectomy is becoming a relic compared to drainage devices (not MIGS)
Drainage devices/ Tube Shunts

- **AC tube**
  - Shunts aqueous from AC to plate
  - Maintains patency of fistula

- **Episcleral plate (explant)**
  - Located in equatorial region of globe
  - Forms a nonadherent capsule
Drainage Devices

- Ahmed valve; Baerveldt implant
- Good when previous trab failed or is expected to fail
- Now becoming popular as a primary procedure

TVT Study
- Trab with MMC and tube shunt can give sustained low teen IOP
- Tube shunt has greater success than trab with MMC in eyes with prior cataract and/or glaucoma surgery
- Similar safety profiles- tubes becoming popular
Drainage devices

- **Indications**
  - Neovascular glaucoma
  - Uveitic glaucoma
  - Previous ocular surgery (e.g. CE, failed filter)
  - Perilimbal conjunctival scarring
  - ICE syndrome
  - Congenital glaucoma refractory to angle surgery
Glaucoma surgical procedures

Glaucoma not well controlled

Moderate/advanced disease,
High baseline IOP,
Secondary glaucomas
Low target IOP

Trabeculectomy

Tube Implant

Mild disease,
Concurrent cataract,
desire to reduce med load

MIGS
is trabeculectomy being done less with MIGS now available? Yes and No

- **MIGS ≠ Trabeculectomy**
  - Easier with fewer complications
  - Lesser IOP reduction
  - Inducement for a lesser procedure to be done?
    - Delays more needed procedure?

- Trabeculectomy may be giving way to tubes
- Trabeculectomy will be around for a while longer
Minimally Invasive Glaucoma Surgery (MIGS)
The iStent - what is its role?
Have you MIGS devices reduced its value?
Safety First

iStent

8% postop corneal edema
3% elevated IOP

Safety profile similar to CEx

Unmatched safety profile compared to newly approved devices?
CyPass and Xen Gel Implant
CyPass Micro-Stent

- Guidewire Tube Diameter: 630 μm
- 3 Retention Rings
- 64 Fenestrations
- Outer Diameter: 510 μm
- Inner Diameter: 310 μm
- Length: 6.35 mm
COMPASS Study

374 Subjects CyPass + Cataract Surgery

72.5% stent + cataract achieved a > 20% reduction in unmedicated diurnal IOP at 2 years vs 58% in cataract alone

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>12 Months</th>
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<tbody>
<tr>
<td>IOP</td>
<td>24.4 mmHg</td>
<td>17 mmHg</td>
</tr>
<tr>
<td>Hypotony</td>
<td></td>
<td>2.9% @ 30 days</td>
</tr>
<tr>
<td>Overall safety profile was similar to CEx</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications</td>
<td>1.4</td>
<td>0.2</td>
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</table>
DUETTE Study

65 Eyes with medicated IOP greater than 21 at baseline

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP</td>
<td>24.5 +/- 2.8</td>
<td>16.4 +/- 5.5</td>
</tr>
<tr>
<td>Medications</td>
<td>2.2 +/- 1.1</td>
<td>1.4 +/- 1.3</td>
</tr>
</tbody>
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Most common adverse events: IOP > 30 beyond 1 month (11%), transient hyphema (6%) and cataract progression (12%)
Xen
Xen 45 Gel Stent: US Pivotal Clinical Trial

<table>
<thead>
<tr>
<th>Visits – IOP and Medications</th>
<th>Mean</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>Medicated IOP</td>
<td>25.1 (3.7)</td>
</tr>
<tr>
<td>Glaucoma Meds</td>
<td>3.5 (1.0)</td>
</tr>
<tr>
<td>12 Month</td>
<td></td>
</tr>
<tr>
<td>IOP</td>
<td>15.9 (5.2)</td>
</tr>
<tr>
<td>Glaucoma Meds</td>
<td>1.7 (1.5)</td>
</tr>
</tbody>
</table>

76.3% of patients reported a mean diurnal IOP reduction of > 20% from medicated baseline at 12 months.
Postoperative Adverse Events

Hypotony 16 (24.6%)
(IOP < 6 mmHg at any time)

- Anterior chamber shallow with peripheral irido-corneal touch 1 (1.5%)
- Anterior chamber fill 1 (1.5%)

Bleb Needling 21 (32.3%)
Are injections into the anterior chamber a viable therapeutic option?
Options for drug delivery
Evolution of sustained delivery

1974
Ocusert®
(Pilocarpine) - for Glaucoma

1996
Vitrasert®
(Ganciclovir) - for CMV Retinitis

2005
Retisert®
(Fluocinolone) - for non infectious posterior uveitis

2009
Ozurdex®
(Dexamethasone) - for Macular Edema, Non Infect. Uveitis, Retinal Vein Occlusion, Diabetic Macular Edema (DME)

2011
Iluvien®
(Fluocinolone) - for DME
Allergan is currently performing phase 3 clinical trials on its bimatoprost sustained-release implant (bimatoprost SR), which is an intracameral depot implant injected into the anterior chamber.
Implant comprising a prostamide associated with a biodegradable polymer matrix that releases an amount of a prostamide
Phase 2 trials of the implant showed mean overall IOP reductions from baseline through week 16 after the first implantation of the bimatoprost sustained-release device:
- 7.2, 7.4, 8.1, and 9.5 mm Hg with the 6-, 10-, 15-, and 20-microgram doses compared with an 8.4 mm Hg decrease in the pooled fellow eyes treated with topical bimatoprost (0.03%).
bimatoprost SR

• The implant lowered IOP in 92% of patients at 4 months and 71% at 6 months.
  • Did not need additional rescue therapy

• There were no serious adverse ocular events
  • The most common adverse event was transient conjunctival hyperemia (median duration of 5 days), which developed within 2 days after the implant was injected.

• In 24 eyes that did require another treatment to control IOP, the overall mean IOP reduction from the baseline IOP was 8.0 mm Hg through 16 weeks after the repeat bimatoprost sustained-release treatment.
Travoprost SR

ENV515 Intracameral Extended-Release

Target Product Profile
- 24/7 control of IOP (25-30% decrease)
- 6 month duration of action
- Less hyperemia than drops
- Easy administration
- Fully biodegradable
- Excellent safety

Extended-release biodegradable travoprost formulation puts the treatment of the disease in the hands of the doctor, not the patient.
8 Months of IOP Reduction in Hypertensive Beagle Dogs

32% reduction in baseline IOP over 8 months from single dose of ENV515

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Travoprost SR

- ENV515- phase 2a open-label, 28-day dose-ranging study of 21 patients yielded 28% IOP lowering at day 25 in one group, which was comparable to once-daily Travatan Z

- Envisia is planning to advance to a 12-month study to evaluate the long-term IOP lowering of ENV515.
Envisia Therapeutics Pipeline

**ENV515 (glaucoma)**
- Pre-clinical
- Ph 2a
- Ph 2b
- Ph 3

**ENV905 (post cataract inflammation)**
- Research
- Pre-clinical
- Ph 2
- Ph 3

**Partnership (back of the eye)**
- Research
- Research Collaborations
- Product Development

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Not So Great Things About Sustained Delivery

- Injectable meds and implants— if med doesn’t work topically or has adverse effects, drop is stopped; can’t easily stop implantable devices.
- Implants can theoretically block parts of the angle
- Complications with invasive options
  - Endophthalmitis
- Decreased access to care?
Not So Great Things About Sustained Delivery

- Limitations - how many drugs can you load into the anterior chamber?
- Drugs may work better in pulsatile form and not so well in constant delivery
- PGAs less effective at BID dosing - receptor supersaturation and desensitization
  - Downtime between drops prevents desensitization
  - Some concentrations of bimatoprost SR were less effective than topical 0.03%
Not So Great Things About Sustained Delivery

- SR products seem less effective than drops
- Will insurance pay for it just to increase compliance?
Anti-VEGF model for amd

- Compared to clinical trials, VA outcomes are worse and there are fewer injections done in the real world. Patients lost to follow-up are doing poorly.
- Drop out rate 20%-30%
Will patients go for it?