QUESTION: Why are we looking for alternatives to current glaucoma treatment?

Look at current surgical glaucoma treatments and their drawbacks

Overview of MIGS procedures

Xen Gel Stent focused review

WHY ARE WE LOOKING FOR NEW INNOVATIONS IN GLAUCOMA SURGERY?
Where does MIGS fit in the treatment paradigm for glaucoma?

MIGS may have a role in earlier treatment of glaucoma:

- **MEDICATIONS**
  - Poor IOP-lowering response
  - Allergy to medication
  - Inability or poor compliance with administration
  - Unaffordable
- **LASER**
  - Poor response to treatment
  - Angle not acceptable for treatment

**GLAUCOMA MEDICATIONS AND LASER**
TRABECULECTOMY AND TUBE SHUNTS

- Complication rates are relatively high
  - 50% transient perioperative complications
  - Anti-metabolites increase complications
  - Multiple possible complications
  - Short-term
  - Long-term

- Efﬁcacies or success rates are lower than what patients expect
  - One study: 36% failed to show desired result
  - 50%-93% success rate depending on type of glaucoma
  - 50% success rate without anti-metabolites

Complications of Trabeculectomy

- Intraoperative
  - Conjunctival button-holes
  - Scleral flap dehiscence
  - Intraoperative bleeding

- Postoperative
  - Early hypotony due to over-filtration
  - Aqueous misdirection
  - Bleb dysesthesia
  - Early or late bleb leak
  - Bleb failure
  - Bleb-related infection/endophthalmitis

Complications of Trabeculectomy
TRABECULECTOMY COMPLICATIONS

OVERFILTRATION

WOUND LEAK

BLEBITIS
COMPPLICATIONS OF TUBE SHUNTS

- Early hypotony
- Tube occlusion
- Elevated IOP
- Shunt exposure/extrusion
- Corneal decompensation
- Iris touch/inflammation
- Endophthalmitis

THE SAFETY OF MIGS IS WELL DOCUMENTED

- Improving efficacy is the goal
  - MIGS
  - Strategically plan and target areas of outflow
  - Looking for areas of lower resistance
    - Schlemm’s canal may not be continuously open
    - Stents may be placed away from collector channels
    - Collector channels may have their own resistance
    - Suprachoroidal and subconjunctival space have low resistance

MINIMALLY INVASIVE GLAUCOMA SURGERY (MIGS)
BEING MINIMALLY INVASIVE, IF THE MIGS PROCEDURE FAILS, THE TISSUE HAS BEEN PRESERVED, SO THAT MORE INVASIVE SURGERY CAN STILL BE DONE (TRABECULECTOMY OR TUBE SHUNT)

MIGS

3 MIGS OUTFLOW TARGETS:
- SCHLEMM'S CANAL
- SUPRACHOROIDAL SPACE
- SUBCONJUNCTIVAL SPACE

MIGS

ISTENT BY GLAUKOS
ISTENT INJECT BY GLAUKOS
HYDRUS BY IVANTIS

SCHLEMM'S CANAL STENTS AND SURGICAL PROCEDURES
SUPRACHOROIDAL SPACE STENTS

- CYPASS by Transcend
- iSTENT SUPRA by Glaukos

AQUEOUS OUTFLOW

AqueSys XEN 45 Gel Stent

SUBCONJUNCTIVAL STENT

AQUEOUS OUTFLOW
AQUEOUS OUTFLOW

Conventional = Trabecular meshwork/Schlemm's canal/Aqueous veins/Episcleral veins
- Pressure dependent
- 85-95% of drainage
- Adrenergic agonists and miotics increase
- Prostaglandins increase pulse wave

IS THE DISTAL OUTFLOW SYSTEM REGULATED, AND DOES IT HAVE ITS OWN RESISTANCE?

WHY DOESN'T TRABECTOME SURGERY DROP THE IOP TO EPISCERAL VENOUS PRESSURE?

CONVENTIONAL OUTFLOW

POSSIBLE REASONS WHY TRABECTOME DOES NOT LOWER IOP TO EPISCERAL VENOUS PRESSURE:
- Autoregulation - TM not present to open hinged scleral flaps in collector channels
- Extrinsic regulation - neural or endocrine signal to increase resistance in untreated angle structures

OUTFLOW REGULATION
Does the conventional outflow system have autoregulation and extrinsic regulation like the rest of our vascular system?

Aqueous outflow

Understanding the complexity of the conventional outflow system may help us in treatment. Unfortunately, this same complexity may preclude any straightforward or simple treatment in this pathway. Several treatments at different sites may be required.

Outflow regulation and feedback loops

It is possible the best treatment IOP we can achieve through this pathway will be mid-teens, due to the regulatory feedback loops. To achieve lower pressures, we will probably need to bypass this pathway to the supra-choroidal or subconjunctival spaces.

Outflow regulation and feedback loops
MIGS

- SUBCONJUNCTIVAL STENT
- XEN GEL STENT
  - Stand alone procedure

AQUESYS XEN45 GEL STENT

AQUESYS XEN45 GEL STENT
DR. YOUNG’S RESULTS
- 11 eyes of 10 patients
- 5 right eyes, 6 left eyes
- Average pre op IOP: **23 mmHg (13-39)**
- Average pre op drops: **1.6**
- Average post op IOP (1 Month): **16.2 mmHg**
- Average post op IOP (3 Months): **13.9 mmHg**
- Average post op drops: **.3**

CONSIDERATIONS WITH XEN
- Learning curve
- Patient selection
  - Young patients
  - Thick Tenon’s capsule
  - Scar formers
- Desired level of placement in Tenon’s capsule
- Amount and location of intraoperative mitomycin

CONSIDERATIONS WITH XEN
- Surgical manipulation of curled stent
- Postoperative medications and duration
- Postoperative manipulation of stent
- Postoperative mitomycin and needling procedures
- Bleb management
- Massage
CONSIDERATIONS WITH XEN COMPARED WITH TRABECULECTOMY

- Xen procedure is not as traumatic, but trabs will have lower pressures
- Extensive dissection with trab allows for larger, more diffuse blebs
- Xen still requires close bleb management for at least 3 months after surgery

CONSIDERATIONS WITH XEN COMPARED TO TRABECULECTOMY

- Whereas with the achievable IOP with trabeculectomy and mitomycin is 10 or less, the achievable IOP with Xen is probably going to be higher, as in the low-teens

INDICATIONS FOR XEN

- Primary open angle glaucoma with less than adequate control
- After medication and selective laser trabeculoplasty options have been exhausted
- Allergies to, or intolerance for, or poor compliance with, medications
- Possible step before the more invasive trabeculectomy or tube shunt procedures
POSSIBLE EXPANDED USE OF XEN:
- Pigmentary or PXE glaucoma
- Steroid responders
- Prolonged post-op IOP elevation
- Inflammatory glaucoma (PAS)
- Neovascular glaucoma
- Lowering IOP before corneal transplant
- After failed trabeculectomy

CONCLUSIONS:
- We need a more safe and efficacious way to perform glaucoma surgery.
- Current surgeries have unacceptably high complication and failure rates.
- MIGS procedures offer safety, but as yet have not been shown to lower IOP sufficiently.
- MIGS using Schlemm’s canal as target have only a modest IOP-lowering effect, possibly due to resistance in the canal or collector system.

CONCLUSIONS
- Autoregulation and Extrinsic Regulation of aqueous production and outflow may be similar to other vascular loops in the body.
- Distal outflow resistance in the collector channels may play a more important role than previously realized.
CONCLUSIONS

- The complexity of the conventional outflow system may preclude an easy treatment algorithm.
- Mid-teens may be all we can achieve in treatment through this outflow pathway.
- Other low-resistance targets with less complexity may result in lower IOP.

MIGS

- Conclusions:
  - MIGS procedures using lower resistance targets may be the answer to lowering intraocular pressure.
    - Suprachoroidal space
    - Subconjunctival space
    - XEN GEL STENT
  - MIGS may have expanded use besides POAG.

XEN CONCLUSIONS

- Learning curve is fairly steep.
- Patient selection is important.
- Correct placement of stent is critical to success.
- Intraoperative and postoperative mitomycin are utilized.
Surgical and postoperative manipulation of stent may be required
Bleb management still required for at least 3 months after surgery
Less traumatic than trabeculectomy, but final pressures will be higher
Expect final pressures in low teens with Xen procedure

XEN CONCLUSIONS

XEN GEL STENT

OMAHA AND LINCOLN EYE AND LASER INSTITUTES
MARK R. YOUNG, M.D.
April 7, 2018
Amniotic Membrane Transplantation for Ocular Surface Disease
Reid Turner, MD
Omaha/Lincoln Eye and Laser Institute

Financial Disclosures
- I have no financial disclosures relevant to this talk

Objectives
- Review the discovery and development of amniotic membrane transplantation (AMT)
- Describe the differences between cryopreserved and dehydrated amniotic membrane
- Provide an overview of ocular surface disorders which may benefit from amniotic membrane transplantation
**AMNIOTIC MEMBRANE**
- Membrane derived from fetal tissue (embryonic ectoderm) that lines the inner surface of the placenta.

**AMNIOTIC MEMBRANE PROPERTIES**
- Non-immunogenic
- Almost no expression of HLA Class I or II antigen
- Anti-inflammatory
  - Supresses pro-inflammatory cytokine, IL1.
  - Produces TIMP (tissue inhibitors of MMP)
- Prevents Scarring
- Downregulates expression of TGF-beta in fibroblasts
- Basement membrane acts as a scaffold substrate for re-epithelialization
- Anti-infectious
  - Expression inhibits HA, HB, cystatin E, B-defensins, cysteine protease inhibitors, etc.

**OCULAR USE OF AMT**
- 1910: first used as part of skin transplantation by Dr. JW Davis at the suggestion of WL Thornton, 4th-year medical student at Johns Hopkins
- 1940: first used for conjunctival surface reconstruction (De Roth)
- 1946: first used for acute ocular burns (Sorley)
- 1995: reintroduced use (Kim and Toeng)
- Transplantation of preserved human amniotic membrane for surface reconstruction in severely damaged rabbit corneas, Cornea 1995
Preservation of Amniotic Membrane

- 2 most common methods = cryopreserved and freeze dried
- FDA recommends testing mother for HIV, Hepatitis B/C, Syphilis, Prion Disease
- Cleanse the tissue with antimicrobial mixture
- Bluntly dissect Amnion from Chorion and fix to microcellulose paper epithelial side up

Most Commonly Used AM

Cryopreserved

Freeze-Dried

Cryopreserved AM
Prokera

- Sheets of AM stored in sterile containers of glycerol and stored at 4°C
- Simple
- Allows storage for up to 5 years
**AmbioDisc (Freeze Dried)**

- AM is pasteurized
- Treated with 70% alcohol
- Freeze Dried to remove water
- Then sterilized to remove bacteria

**Prokera (Cryopreserved)**

<table>
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<tr>
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<th>Consistent Results</th>
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<td>Cost</td>
<td>$500-600</td>
<td>$600-700</td>
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<tr>
<td>Ease of Use</td>
<td>User friendly, but requires Lid Speculum and Forceps</td>
<td>Comparable to placing BCL</td>
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<tr>
<td>Patient Comfort</td>
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**Post Implantation Considerations**

- Lubrication is important to keep the AM from drying out
  - Prokera→Discontinue QID, Ats QID
  - AmbioDisc→Ats QID/Ats QID
- AM lasts 3-14 days depending on amount of inflammation and thickness of AM
  - AmbioDisc→1 check day, eg 7 and typically remove
  - Prokera/Slim=3-5 days
  - Prokera=6-2 Weeks
- Remove Carefully to Avoid Causin another Epithelial Defect!
- Use Konura/CL over the AmbioDisc and watch out for fluorescein/flocking.

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**Effectiveness**

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**Reimbursement**

- CPT 65788: Placement of amniotic membrane on the ocular surface; without sutures
- Medicare Allowable = $1,448
- Global Period = 0 Days
- Obtain Prior Authorization
- Inform Patient of Cost if high-deductible plan

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**AM for Ocular Surface Disorders**

- Severe, Resistant Dry Eye
- Recurrent Corneal Erosions
- Neurotrophic Ulcers
- Pterygium/Conjunctival Lesion Removal
- Chemical/Thermal Injuries
- Stevens Johnson Syndrome

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**AM for Dry Eye**

- Important to identify underlying cause and start appropriate therapy
- In resistant or extremely symptomatic patients, AM can significantly improve the corneal surface and symptoms
Recurrent Corneal Erosions
- 1st Line: lubrication, Muro-Ointment QHS, low potency topical steroid, BCL, Aflox
- 2nd Line: Superficial Keratectomy with BCL
- High Risk or Recurrent Cases: Superficial Keratectomy with AM

Neurotrophic Ulcer
- Severe Keratopathy or shallow ulcer → Prokera/Ambiodisc
- Significant ulceration of >30% stromal thickness → Layered AM via TissueGlue

Ptterygium Surgery
Immediately after AMT

Stevens Johnson Syndrome due to Bactrim

Take Home Points
- AMT can significantly improve a wide variety of ocular surface disease
- AmbioDisc and Prokera are both great products
- AMT may have a high out of pocket expense for the patient