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- Glaucoma Evolution
- Glaucoma Evaluation is Transforming
- In the past, detection & management relied on functional assessment
  - Visual fields (white-on-white)
    - Insensitive for detecting early POAG
    - High degree of variability
- Recently, structural change over time longitudinal studies have

validated the role of structural imaging

- Are structural defects with normal functional tests false positives or POAG?

- Glaucoma Evaluation is Transforming
- Glaucoma considered a NOCTURNAL disease
- IOP increases starting at bedtime and stay high all night
- Concept of “flattening the curve” of IOP
- New emphasis on sleep apnea link to POAG
  - Blood flow issues
  - Sleep lab studies
- Ocular blood flow

- Systemic medications worsen blood flow to head
- CMS temporary code for measuring ocular blood flow
- Angle Laser Surgery
- Wise – 1970
- Mechanism – not known but shrinkage of trabecular ring with widening of spaces and decreased resistance to outflow is probable
- Particularly effective (90% controlled after one year)
  - Pseudo-exfoliation (PXF)
  - Pigment dispersion syndrome (PDS)
  - POAG
- Slowly and constantly loses effect
  - 55% at 5 years

- 30% at 10 years
- Low complications with spike in IOP 30% (post-op)
- Surgical Glaucoma Therapy
- Argon Laser Trabeculoplasty (ALT, LTP)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Increases immune system by increasing monocytes & macrophages in TM
  - Causes appreciable damage to TM
  - 85 confluent applications to 180 degrees @0.06mJ
    - Blanching or bubble phase needed to assure proper treatment
  - Addresses greatest roadblock = compliance with medical therapy

- Usually performed over 180 degrees of TM
  - Can be repeated to the other 180 degrees later if needed
- Surgical Glaucoma Therapy
- Selective Laser Trabeculoplasty (SLT)
  - Q switched Nd:YAG selectively targets pigmented trabecular cells (increasing activity?)
  - Selective because it does not cause appreciable damage to TM
  - 50 confluent applications to 180 degrees @0.06mJ using 400u spot size (large) applied for 3 nano-seconds
    - No blanching or bubble phase needed
  - Results – 4.6mmHg decreased IOP at 8 months

- Addresses greatest roadblock = compliance with medical therapy
- Laser Surgery Before Medical Therapy?
- Glaucoma Laser Trial (GLT)
  - Multicenter/randomized study of safety and efficacy of laser first for newly diagnosed glaucoma
  - IOP better controlled at 2 years and 7 years
    - Less deterioration of cupping
    - Less deterioration of visual field
  - Limitations
    - Temporary effect
    - Better topical drugs with low side effects
- Laser Cycloablation
- Historic methods of ciliary body destruction

- Cyclocryopexy, etc
- Many complications including cataract, pain, phthisis
- Simple and in-office procedures
- Ab interno
- Ab externo
  - Non-contact or contact Nd:YAG
  - Non-contact or contact Nd:Diode
- Surgical Glaucoma Therapy
- Trabeculectomy alone
- Trabeculectomy with surgical adjuncts
  - 5 FU (lower risk eyes)
  - Mitomycin-C (MMC) – higher risk eyes
- Indications
  - Maximum tolerated medical therapy
  - Progression of disease
  - Unable to instill medications
  - Secondary glaucomas (Neovascular glaucoma)
- Consideration

- Age, HTN, DM, Anticoagulants, Preop IOP, previous vitrectomy
- Degree of visual impairment,
- Lens status
- Comorbidities
- Trabeculectomy Complications
- Shallow or flat chambers
- Choroidal detachments
- Hypotony maculopathy
- Hyphema
- Bleb leak
- Bleb infection
- Inadequate fistula and bleb failure
- cataracts
- Surgical Glaucoma Therapy
- Future directions
  - Newer antifibrinolytics
    - CAT-12, a monoclonal antibody to TGF-B2
  - Photodynamic therapy



- Novel drug delivery systems
  - Collagen implants, bioerodable polymers, liposomes & microspheres
- Glaucoma drainage implants instead of filtering surgery
  - Shunts aqueous from AC tube through an episcleral plate
- Ocular genetics
  - Discover genes, gene therapy, primary prevention of glaucoma may become a reality

## ■ Surgical Glaucoma Therapy

### ■ Future directions

- Glaucoma drainage implants instead of filtering surgery
  - Shunts aqueous from AC tube through an episcleral plate
- Miniature Tube Shunt
  - Ex-Press Mini Glaucoma Implant – Optonol LTD

- Biocompatible 24 karat gold implant
  - SOLX Gold Shunt – SOLX
- Device for surgical lowering of IOP (before trabeculectomy)
  - Trabectome – NeoMedix, INC
  
- Advantages of Surgical Therapy
- Potential for unlimited reduction of IOP
- Lower long term cost
- Little or no impact on QOL
- Independent from patient compliance
  
- Advantages of Medical Therapy
- Preferred for early stage of the disease

- Variety of drug options
  - Can be precisely titrated to individual needs
  - Easily reversed
  - Monocular trials are possible
  - Discontinuation of therapy is possible
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- Disadvantages of Medical Therapy
  - Lifelong potential side effects
  - Cost
  - Impact on QOL
  - Dependent on patient compliance for success
  - Loss of response to drugs over time

- Reasons to Opt for Medical Therapy
- Easily Reached Target IOP
- Documented progression is slow
- Severe loss of vision unlikely
- Marked surgical risk
- Effect of treatment on IOP likely can be maintained
- Candidate for Medical Rx – elderly, compliant, limited life expectancy, moderately elevated IOP
- Advantages of Surgical Therapy
- Potential for unlimited reduction of IOP
- Lower long term cost
- Little or no impact on QOL

- Independent from patient compliance
  
- Disadvantages of Surgical Therapy
- Complications
  - Intra-operative
  - Post-operative
  - Long term
- Loss of IOP control over time
- Need for additional medications
- Low specificity of operations
- Reasons to Opt for Surgical Therapy
- Unable to reach Target IOP
- Documented progression despite control under medications

- Severe loss of vision & high IOP at presentation
- Proven intolerance to drops
- Unable to apply medications
- Candidate for Surgical Rx – young, compliant/non-compliant, high IOP, advanced damage at time of diagnosis
- Glaucoma Tube Implants
- Developed for patients with high risk of failure from standard surgery
- Design – silicone rubber tubing and ridged plastic or silicone rubber explant
  - Materials do not allow fibroblast to adhere to device

- Equatorial placement of explant
    - Anterior edge of explant is 8-10mm posterior to corneoscleral junction
  - Tube into anterior chamber by 2mm
  - Superior temporal position is preferred
  - Patching material required to adequately cover implant
    - Sclera, dura, pericardium
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- Glaucoma Tube Implants
  - Drain – allows flow of aqueous from anterior chamber through tube into implant
    - Passive diffusion into surrounding peri-ocular tissues
    - Uptake by lymphatic system and venous capillaries

## ■ Available Implants

- Non-valved
  - Molteno
  - Baerveldt
- Valved
  - Ahmed
  - Krupin
- Single plate and double plate designs

## ■ Glaucoma Tube Implants

## ■ Indications

- Failure of conventional therapies
  - Topical
  - Laser
  - Trabeculectomy with or without MMC
- Conjunctival diseases, pemphigoid, chemical injuries, severe dry eyes, trauma related glaucoma with scleral thinning, uveitic glaucoma, congenital glaucoma,



- Neovascular diseases – Neovascular glaucoma, diabetic retinopathy, retinal vascular occlusions.
- Glaucoma Tube Implants
- Special intra-operative and post-operative considerations
  - Temporary ligature of drain tube of non-valved implants
    - 2-4 weeks
    - Allows capsule to develop
    - Resistance to flow is established
    - Best completed with absorbable external suture or prolene suture placed into tube
      - Removed via small conjunctival incision in office
- Complications
  - Corneal endothelial issues in vicinity of tube, hypotony,

obstruction of tube with fibrin,  
vitreous, blood, epithelial ingrowth

## ■ Cataract Surgery in Glaucoma Patients

- Combined surgery indications
  - Glaucoma treatment failing with topicals
  - Significant disc changes and visual field damage
  - Transient elevations of IOP associated with surgery or topical steroids may cause further damage
  - Cataract surgeons should spare conjunctiva superiorly for future placement of filters or implants

- Benefit of definitive surgical solution to both problems with one operation

## ■ Nanosensor IOL

- Fraunhofer Institute in Germany
  - Microelectric Circuits and Systems IMS
- Implant sensor for continuous IOP monitoring
- Integrated a 2.5 by 2.6 millimeter sensor in an IOL
- The top and bottom of the sensor are electrodes
  - The top electrode is flexible, bottom of the sensor is rigid
  - When the intraocular pressure increases, the top electrode is pushed in, reducing the distance between the top and bottom of the sensor and thus increasing the capacitance

- Implant sends the pressure data to a reader that is fitted into the frame of a pair of spectacles
- An antenna in the spectacle frame supplies the sensor with the required energy via an electromagnetic field
- Currently undergoing clinical trials
- Could come available in two to three years time
- **Nanosensors IOP**
- MIT Technology Review
- A pressure sensor to measure glaucoma IOP
- Tiny microchip implanted subretinal
- The sensor is designed to measure IOP
  - wirelessly transmit the data to computer
- One of the major obstacles in creating this type of device is designing a tiny but highly functional chip that uses very little power

- Sensor runs on nanowatts rather than on microwatts
- The researchers began testing the implant in animals last December
- **Is Glaucoma a Medical or Surgical Disease?**
- Slowly developing disease with time course over decades
- POAG is 80% of all forms of glaucoma
- 80% of all glaucoma is in early stage
  - Responds well to medications
- Goal in therapy is to maintain adequate vision during expected lifetime of the patient
  - Affordable and minimally interfere with QOL
- Treatment of OHTN w/o additional risk factors may be unnecessary

- Treatment of very advanced disease may be ineffective
- Is Glaucoma a Medical or Surgical Disease?
- BOTH!
- Art of glaucoma treatment is individualizing care
  - No unique formula for all forms and stages of glaucoma
- Surgery solely aims at IOP reduction
- Surgery can be a first-line treatment
- Medical therapy aims at lowering IOP but will include neuroprotection of the environment and neuro-

regeneration of NFL with stem cells

- Neuroprotection in Glaucoma
- Tsai Curr Eye Res 2005
- EPO (erythropoetin) found to have protective effect on RGCs
  - Currently approved and well understood for anemias, post chemo-therapy, and renal diseases
- Others under study include brimonidine, memantine, BDNF
- Future will be neuroprotection to improve environment and neuroregeneration with stem cells
- Vitrectomy Causes Cataract & Glaucoma
- Chang,S AJO 2006

- Vitrectomy well known to result in cataract within 2 years
  - O<sub>2</sub> now discovered to be responsible
  - After cataract and vitrectomy angle oxygen changed from 12mmHg to 32mmHg
- Study found increased IOP in operated eye compared to fellow eyes
  - 68% of OAG developed in operated eye
  - Presence of natural lens at time of vitrectomy associated with 28 month delay in OAG
- Glaucoma Pipeline
- Extracellular Matrix metalloproteinases
- Oral neuroprotectants - Memantine (Nameida)
- Sustained release formulations
  - Punctal plugs
  - Weekly preparations



## ■ Home IOP monitors