Current Concepts in Glaucoma

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Is Glaucoma a Bad Disease?

Goals of Glaucoma Therapy

- Maximize the Patient’s Quality of Life
- Patient Maintains Functional Vision to Meet the Requirements of Daily Activities
- Glaucoma Patients Do Not Become Symptomatic Until Late in their Disease Process
- Does Not Have to be a Zero Tolerance Policy to Visual Field Loss
  - We Don’t Stop Glaucoma Progression with Treatment, But We Can Slow It Down
- Not Every Person with Glaucoma Goes Blind (Rule of 10)
- Difficult to Predict the Rate of Glaucoma Damage and How Long the Patient Has To Live
- Blinding or Killing A Patient to Achieve a Desired Target Pressure is Not Good Practice

When Should We Treat?

- 1. Does the patient have nerve damage?
  - If yes then in most cases – TREAT
  - If no, then access risk factors to determine the benefits of treatment vs observation
    - Level of IOP
    - CCT
    - Age
    - Race
    - FOH

When to Treat Elevated IOP without Glaucoma Damage

- NO Glaucoma Damage
- Elevated IOP
- Refer to OHTS
  - Greatest risk for developing glaucoma
    - IOP 26 or above
    - In conjunction with thinner CCT <555um
- OHTS lowered IOP by approximately 20% (Target Pressure)
  - One or two meds

No Damage, But Elevated IOP
CCT and Ocular Hypertension

Treating When There is Damage

- Strong evidence (clinical trials) that lowering IOP slows down glaucoma progression
- Generally, we are going to treat patients that exhibit glaucoma damage
- Includes patients with elevated IOP (COAG) and non-elevated IOP (NTG)
- How to determine if damage is present
Glaucoma Discriminates
- Glaucoma Often Asymmetrically Damages Between Above and Below and Between the Two Eyes
- Look for Notches in the Neuro-Retinal Rim Tissue
- Occurs in 30% of Glaucoma Patients
- Inferior Temporal Pole Most Common Site of Notching
- Associated With a Corresponding VF Defect

ISNT Rule
- Inferior>Superior>Nasal>Temporal Rim Tissue
- Nasal Rim Tissue Varies Considerably Because of Blood Vessels
- Glaucoma Does Not Selectively Damage Nasal Rim Tissue

Modified ISNT Rule
- Ignore the Nasal Rim Tissue
- Expected Ratios: 1.5-2.0x Inferior: 1.5-2.0x Superior: 1.0 Temporal
- Glaucoma Should Be Suspected When the Amount of Inferior or Superior Neuro-Retinal Rim Tissue Is Equal to or Less than the Temporal Rim Tissue

Disc Size Affects the ISNT Rule
- For Small Size Nerves: >2.0x Inferior: >2.0x Superior: 1.0x Temporal
- For Medium Size Nerves: 2.0x Inferior: 2.0x Superior: 1.0x Temporal
- For Large Size Nerves: 1.5x Inferior: 1.5x Superior: 1.0x Temporal

Does Size Really Matter?
- Is there a C/D ratio that defines glaucoma?
- Do You Think This Nerve Has Glaucoma?

A Big Cup Does Not Necessarily Mean Glaucoma
- There is No Demarcation Line Separating a Physiological Cup From a Glaucomatous Cup
- Physiological Cup Size Is Directly Related to Overall Disc Size
- Large Discs Will Have Large Physiologic Cups
- Small Discs Will Have Small Physiologic Cups
- Physiologic Disc and Cup Size Is Genetically Determined
- Physiologic Cup of .7 Or Greater Occurs in 2% of Normals
- A Small Disc With a Medium Size Cup Should Be As Suspicious As a Large Cup in a Medium Size Disc

How to Evaluate Disc Size
- Use a 60 D Lens at the Slit Lamp
- Make a Thin Vertical Beam
- Adjust Beam Height
- Read Disc Diameter off Scale on Slit Lamp
- Vertical Disc Diameter > 2.2 mm Is a Large Disc
- Vertical Disc Diameter < 1.8 mm Is a Small Disc

**Expected Physiologic Cup Size**
**Based on Measured Vertical Disc Diameter**
**Using a 60 Diopter Lens At The Slit Lamp**

<table>
<thead>
<tr>
<th>Vertical Height (mm)</th>
<th>-2std</th>
<th>-1std</th>
<th>Mean</th>
<th>+1std</th>
<th>+2std</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.6</td>
<td>1.8</td>
<td>2.0</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>Expected C/D ratio</strong></td>
<td><strong>0.0</strong></td>
<td><strong>0.2</strong></td>
<td><strong>0.4</strong></td>
<td><strong>0.6</strong></td>
<td><strong>0.8</strong></td>
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**NFL Anatomy**
**Patterns of Diffuse NFL Loss**
**Focal NFL Defects**
**Cirrus™ HD-OCT**

- Optic Disc scan
- Cube scan with 6mm x 6mm area
- 200x200 (200 A-scans per B-scan; 200 B-scans)

**The ganglion cell complex (ILM – IPL)**

**Should We Look Elsewhere for Glaucoma Damage other than the Optic Nerve?**
- The ganglion cell complex (ILM – IPL)
- Ganglion Cell Analysis
- Measures thickness for the sum of the ganglion cell layer and inner plexiform layer (GCL + IPL layers) using data from the Macular 200 x 200 or 512 x 128 cube scan patterns.

**Advantage of Ganglion Cell Analysis**
- More reproducible measurement than peripapillary RNFL
• Less physiological variation compared to peripapillary RNFL
• Less major blood vessels to create pseudo-thickness measurements
• Better symmetry between superior and inferior and between eyes than peripapillary RNFL
• Clinical Correlation is Paramount

Squeegee Sign
• Glaucoma initially damages the temporal side of the ganglion cell bodies in the macula
• Glaucoma asymmetrically damages between the superior and inferior ganglion cell bodies
• Squeegee Sign to the superior or inferior temporal ganglion cell bodies is the initial indication of glaucoma damage on the GCA.

Setting Target Pressures
• Good mental exercise to incorporate for all glaucoma and glaucoma suspect patients
• Avoids "cookbooking" glaucoma management
• Look at the individual characteristics of each patient
• Decide how aggressively or non-aggressively to treat
• Reinforces the concept that each glaucoma or glaucoma suspect patient is unique

Setting Target Pressures
• "Estimated IOP where the risk of future visual impairment is balanced against the side effects of treatment"
• Based on the Baseline IOP Readings (use the highest IOP reading)
• Based on the Amount of Optic Nerve Damage
• Based on the Rate of Glaucoma Progression

Other Factors to Consider
• Age of the Patient
• Race of the Patient
• FOH of Severe Visual Loss from Glaucoma
• Status of the Fellow Eye
• Compliance Factors

IOP
• Deemphasize that elevated IOP defines glaucoma
• Emphasize that elevated IOP is the most significant risk factor for developing glaucoma and the risk factor we can alter
• Higher the IOP the greater the risk
• Suggestion that the greater the diurnal variation of IOP, the greater the risk of developing glaucoma and progressing with glaucoma
IOP is not a static measurement

IOP Varies More Than You Think
- Average diurnal variation for a glaucoma patient is 6 mm HG
- Mark sure you get baseline IOP readings before you start a patient on treatment
- 3 readings is the minimum
- You can never rule out an IOP spike
  - Personally I believe the highest IOP reading is more important than the average IOP reading
  - Which patient concerns you more
    - Patient #1 IOP 24, 24, 24
    - Patient #2 IOP 24, 18, 32

Setting Target Pressures
- “Estimated IOP where the risk of future visual impairment is balanced against the side effects of treatment”
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Quantifying Glaucoma Damage
- Optic nerve assessment
- NFL assessment
- New technology assessment
  - HRT
  - GDx
  - OCT
- Visual Field assessment

Guidelines For IOP Target Values
- No Damage – OHTS recommended 20% Reduction Of Baseline IOP
- Mild Damage - 30% Reduction Of Baseline IOP
- Moderate Damage - 30-40% Reduction Of Baseline IOP
- Severe Damage - 40-50% Reduction Of Baseline IOP

What’s It Going to Take?
- 20-30% reduction - 1 or 2 meds
- 30-40% reduction – 2-3 meds +/- ALT/SLT
- 40-50% reduction – 3-4 meds +/- ALT/SLT +/- filter

Don’t Like Math – I generally set 3 target pressures:
1. Patient with high risk ocular hypertension – elevated pressure but no glaucoma damage. Treat with 1-2 meds max
2. Patients with definite glaucoma damage, but in the mild-moderate stage of damage
   Target pressure < 18 (consistent). Will use multiple meds and laser to achieve, but not filtering surgery
3. Patients with definite damage in the moderate to severe stage of damage
Target pressure < 15 (consistent). Will use multiple meds and laser to achieve and will consider filtering surgery in select cases early and will not delay filtering surgery in cases of progression on MMT.

**Glaucoma Drugs – Who’s on First?**

**Prostaglandin Agonists**

- Xalatan
- Travatan
- Lumigan

**XLT Study**

*Mean Hyperemia Score*

**Equivalent IOP-Lowering**

TRAVATAN® Z Solution and TRAVATAN® Solution

**Study Results**

- Across all 9 study visits, mean IOP reduction range:
  - 7.3 – 8.5 mm Hg travoprost 0.004%
  - 7.4 – 8.4 mm Hg travoprost 0.004%
- Statistical equivalence was also demonstrated for the comparison of mean IOP changes
- 6.4% of patients treated with travoprost BAK-free, and 9.0% treated with original travoprost experienced an adverse event due to hyperemia

**Lumigan .01%**

- Bimatoprost .01% compared to .03%
- Contains 4x the BAK
- Same IOP lowering
- Improved side effects

**When Should We Use Prostaglandins?**

- 1st Line POAG
- Pseudophakia with Glaucoma
- Uveitic Glaucoma
- Acute Angle Closure Glaucoma
- Chronic Narrow Angle Closure Glaucoma
- Pigmentary Glaucoma
- Pseudo-exfoliative Glaucoma
- Neovascular Glaucoma
- Traumatic/Angle Recession Glaucoma
- Normal Tension Glaucoma

**Beta Blockers**

**Bad Drugs or Bad Rap?**

- Most Cost Effective Glaucoma Medication
- Tolerated Very Well By The Majority of Patients
- Well Studied and Long Track Record (1979)
- Screen Patients for Potential Contraindications

**Can I Interest You in a Combo?**
Glaucoma Management

- Start with a prostaglandin
- Add Beta-blocker as second line
- Change beta-blocker to Cosopt (or Combigan)
- Add Alphagan (or topical CAI) as third drug
- OR consider ALT/SLT
- Filtering surgery
  - Only if the benefits outweigh the risks

Rhopressa
- Aerie pharmaceuticals Rho Kinase inhibitor and norepinephrine transporter
- IOP reduction mechanism is an increase in TM outflow, decrease in aqueous production and lowering episcleral venous pressure
- .02% concentration dosed once a day
- 4 mm average diurnal IOP reduction
- Non-inferior compared to timolol bid, but only for IOP <26
- No major systemic side effects
- Conjunctival hyperemia major ocular side effect (40-60%)
- Conjunctival hemorrhages, corneal deposits and blurry vision (5-15%)
- Discontinue rate 15%

Roclatan
- Combination of Rhopressa and Latanoprost
- Dosed once a day
- 34% IOP reduction
- 2 mm additional IOP reduction than latanoprost alone
- Hyperemia the major side effect

AMA0076
- Amakem Therapeutics Rho Kinase inhibitor
- Started human clinical trials
- Less conjunctival hyperemia

Lasers Wars – ALT vs SLT?

ALT
- ALT (argon laser trabeculoplasty) was initially utilized in patients who failed medical therapy
- The Glaucoma Laser Trial (GLT) established efficacy of ALT in lowering IOP as 1st line treatment in newly diagnosed primary open-angle glaucoma patients
- ALT should not be repeated to the same area of trabecular meshwork (thermal damage)

Selective Laser Trabeculoplasty
- Uses Q-switched Nd:YAG Laser
- 532 Nm Wavelength
- Short Pulse Duration (3 Nanoseconds)
- 400 um Spot Size
- 50 Spots Over 180 Degrees Of Tm 0.6-1.2 MJ
Selective Laser Trabeculoplasty
- Selectively Targets Pigmented Trabecular Cells Without Thermal Damage To Adjacent Cells (Biological Effect)
- Less “traumatic” than ALT
- May be able to repeat treatment with SLT

Selective Laser Trabeculoplasty Clinical Results
- Mean IOP Reduction 6 mm Hg (25% Reduction) from pre-treatment baseline of 24 mm Hg
- 24% Showed Post-op IOP Spike Of 5 mm Hg Or Greater
- International studies show IOP reductions of 22%-28% with 36-49 weeks follow-up
- In a prospective, randomized clinical trial, SLT and ALT were shown to have a similar effect on IOP reduction
- 70% of patients [uncontrolled OAG on Max. Rx and prior failed laser trabeculoplasty (PFLT)] respond with > 3 mm Hg drop in IOP
- How often can you repeat SLT?

Is SLT Repeatable?
- SLT lowers IOP 20-30% depending if it primary vs secondary therapy
- SLT may start to lose effectiveness in some patients after 6 months
- If you repeat SLT, you can lower IOP to the level of the 1st SLT, but not lower
- If SLT does not work the 1st time it is unlikely to work with a repeat attempt
- 2nd SLT also loses effectiveness over time

Who Are Good SLT Candidates?
- Patients with poor compliance; good for flattening diurnal curve
- Can be considered first line treatment in POAG
- SLT targets pigmented cells- probably works better in patients with more pigment in TM
- Works well in pigmentary and pseudoexfoliation
- Patients with very heavy pigmentation have difficulty - absorption is so good that you have to turn power down due to discomfort
- Can use after successful ALT and may avoid the need for filtering surgery

Who are Poor SLT Candidates?
- Inflammatory or uveitic glaucoma
- Congenital glaucoma/ICE syndromes/NVG and angle recession
- Narrow angle glaucoma or patients in whom it is difficult to visualize TM
- 400 um spot size – this is large spot size; so need good/deep angle to fit this spot size
- Might try pilo prior to tx to see if can visualize more of angle

When Do We Filter?
- Filtering surgery has significantly greater potential complications than medications and laser
I rarely recommend filtering surgery to achieve an initial target pressure
Risk/Benefit Ratio
Patient shows documented progression despite maximal tolerated medical and laser therapy

**What are the benefits of filtering surgery**
- Achieve low target pressures
- Control IOP spikes
- Less reliance on patient’s taking their medications

**What are the drawbacks of filtering surgery**
- In skilled surgeon hands, it is still only 80% successful
- IOP is often higher in a failed filter than before the surgery
- Accelerate cataract formation
- More local foreign body sensation
- Risk of catastrophic complications

**MIGS - Express, Mini, and Stents**

**Is Cataract Surgery the New Glaucoma Surgery?**
- Cataract surgery lowers IOP 2-4 mmHG
- Clear cornea phaco lowers IOP greater than extracapsular cataract extraction
- Effect is long lasting
- 80% maintained 3 mmHG IOP lowering for 5 years

**Progression Rates Vary From Patient to Patient**

**Re-assessment of Target Pressures**
- Glaucoma progression is general slow
- Important to identify rapid progressors
- Patients are followed with various tests to judge progression
- Patient who progress at a certain target pressure need further IOP lowering
- Consider filtering surgery for patients who are rapid progressors

**Cirrus Guided Progression Analysis (GPA)**
- RNFL Thickness Change Maps demonstrate change in RNFL between exams. Up to 6 progression maps are compared to baseline. Areas of statistically significant change are color-coded yellow when first noted and then red when the change is sustained over consecutive visits.
  - TSNIT values from baseline and current exams are plotted.
  - Areas of statistically significant change are color-coded yellow when first noted and then red when the change is sustained over consecutive visits.
  - Average RNFL Thickness values are plotted for each exam.
  - Yellow marker denotes change from both baseline exams.
• Red marker denotes change sustained over consecutive visits.
• Rate and significance of change are shown in text

Cirrus GPA™ Analysis
• RNFL SummaryLegend summarizes GPA analyses and indicates with a check mark if there is possible or likely loss of RNFL
• RNFL Thickness Map Progression (best for focal change)
• RNFL Thickness Profiles Progression (best for broader focal change)
• Average RNFL Thickness Progression (best for diffuse change)