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
- 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**
- Glaucoma is a disease of the ganglion cell axons
- Damage occurs at the level of the lamina cribrosa
- Selective damage to the superior and inferior poles of the optic nerve
- Relative preservation of the temporal and nasal poles

**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

**Compare Neuro-Retinal Rim Tissue Between Superior and Inferior**
- Vertical Extension of Cupping Supra or Infra Temporal
- Normal Ratio of Neuro Rim Tissue Is:
  - 2.0 Inferior: 1.5 Superior: 1.0 Temporal
- Glaucoma Should Be Suspected When the Amount of Temporal Neuro-Retinal Rim Tissue Is Greater Than or Equal to the Inferior or Superior Rim Tissue

**NFL Anatomy**

**Patterns of Diffuse NFL Loss**
- Focal NFL Defects

**Cirrus RNFL and ONH Analysis Elements**
- RNFL Peripapillary Thickness profile, OU compared to normative data

**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.
- RNFL distribution in the macula depends on individual anatomy, while the GCL+IPL appears regular and elliptical for most normals. Thus, deviations from normal are more easily appreciated in the thickness map by the practitioner, and arcuate defects seen in the deviation map may be less likely to be due to
anatomical variations.

**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

**Errors in Interpretation**
- Green always represents Non-Disease
- Red always represents Disease

**Red Disease Does Not Always Mean Glaucoma**
- Clinical Correlation is Key

**Does Green Always Mean Normal?**
- Symmetry is a Beautiful Thing!
- Lack of Symmetry Should Raise Suspicion!

**OCT Clinical Pearls**
- Normal data bases for optic nerve and RNFL are difficult to construct
- Blood vessels, astrocytes and glial cells can taint optic nerve and RNFL measurements
- If you simply evaluate the OCT printout in isolation, you will make interpretation errors
- Understand that GREEN does not always mean NORMAL and RED does not always mean ABNORMAL
- The doctor should always correlate the data from the OCT printout with clinical data before making management or treatment decisions in glaucoma.

**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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- Based on the Amount of Optic Nerve Damage
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Quantifying Glaucoma Damage
- Optic nerve assessment
- NFL assessment
- New technology assessment
  - HRT
  - GDx
  - OCT
Visual Field assessment

Visual Field Quantification (Mild, Moderate, Severe)

- Mean Deviation (MD)
- Number of Abnormal Points on the Pattern Deviation Plots
- Decibel Value of the Four Points Just Off Fixation

Mild Visual Field Defect

- The Mean Deviation Index (MD) Is Better Than -6 dB
- On the Pattern Deviation Plot, Fewer Than 18 of the Points Are Depressed Below the 5% Level and Fewer Than 10 Points Are Depressed Below the 1% Level
- No Point in the Central 5 Degrees Has a Sensitivity < 25 dB

Moderate Visual Field Defect

- The Mean Deviation Is Better Than -12 dB
- On the Pattern Deviation Plot, Fewer Than 36 of the Points Are Depressed Below the 5% Level and Fewer Than 20 Points Are Depressed Below the 1% Level
- No Point in the Central 5 Degrees Has a Sensitivity < 15 dB

Severe Visual Field Defect

- The Mean Deviation Is Worse Than -12 dB
- On the Pattern Deviation Plot, More Than 36 of the Points Are Depressed Below the 5% Level or More Than 20 Points Are Depressed Below the 1% Level
- Any Point in the Central 5 Degrees Has a Sensitivity <15
- There Are Points Within the Central 5 Degrees With Sensitivity <25 dB in Both Hemifields

Guidelines For IOP Target Values

- No Damage – OHTS recommended 20% Reduction Of Baseline IOP
- Mild Damage - 20-30% 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?

Diurnal IOP Range and Disease Progression
Latanoprost qd vs Dorzolamide tid
and Timolol bid Over 24 Hours

Prostaglandin Agonists

- Xalatan
- Travatan
- Lumigan

XLT Study
Hyperemia Grading Scale
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?**

**Beta-Blockers**

• 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

**Combination Glaucoma Medications**

• Cosopt – Timolol .5% and dorzolamide 2%
• Combigan – timolol .5% and brimonidine .2%
• Simbrinza – brimonidine .2% and brinzolamide 1%

**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

**Uniocular Trials**

**Standard of Care or Substandard?**

• Cross over effect of adrenergic agents
• Assumes that diurnal variation is constant between the two eyes
• Compare a series of IOP readings pre-medication and a series post-medication
• Make sure you have established the baseline diurnal variation

**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...
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

#### Hydrus II Microstent Study

- 100 glaucoma patient with mild to moderate disease randomized to cataract surgery with or without Hydrus II Microstent
- 11 months after surgery
- Treatment group had IOP 16.0 on .4 meds
- Control group had IOP 15.8 on .9 meds
- No major adverse effects reported

#### Glaukos iStent

- Ab internal micro titanium device
- Inserted through the trabecular meshwork into Schlemm canal during cataract surgery
• Approved in US in 2012

**Glaukos iStent**
- Samuelson et al Ophthalmology 2011;118:459-467
- 240 eyes randomized to cataract surgery vs cataract surgery with iStent
- 12 month follow up
- Mean IOP reduction in iStent was 8.4 mmHG vs 8.5 mmHG in the control group
- Mean reduction in eye medications 1.4 meds in iStent vs 1.0 meds in control group
- 66% of iStent eyes vs 48% of control group achieved an IOP reduction of 20% without medications
- 4% stents become obstructed with iris, vitreous, fibrous overgrowth
- 3% become malpositioned
- 1% need to be removed

**Glaukos iStent**
- Prospective randomized controlled multicenter clinical trial
- 240 eyes with mild to moderate glaucoma randomized to cataract surgery or cataract surgery + stent
- IOP reduction of 20% without meds 61% in the iStent group vs 54% control group
- At 24 months the IOP in the iStent group was 17.1 mm on .3 medications and in the control group 17.8 mm HG on .5 medications
- There was no difference in safety profile between the two groups

**Glaukos iStent**
- Long term results (Arriola-Villalobos, BrJOphthalmol 2012;96:645-649)* authors had no commercial or proprietary interests
- 19 patients
- Combined cataract surgery and iStent
- Minimum 3 year follow up (ave 54 months)
- IOP reduced from 19.4 to 16.3 mmHG (16% reduction)
- Meds reduced by .5 medication
- Not a randomized clinical trial so no control group to compare results
- 21% had malpositioned stent
- 11% had partially occluded stent with PAS

**Cost and Reimbursements**
- Cost of the iStent $1,000
- 2013 Medicare facility reimbursement $2,978
- Ambulatory surgery center reimbursement $1,671
- Average physician fee $850
- 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
Is Cataract Surgery the New Glaucoma Surgery?

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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

HRT: Progression Analysis Overview

Advanced Serial Analysis Printout

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 Summary Legend 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)
Updated Guided Progression Analysis (GPA™)
Optic Nerve Head information now included

- Average Cup-to-Disc Ratio plotted on graph with rate of change information.
- RNFL/ONH Summary includes item “Average Cup-to-Disc Progression”.
- Printout includes an optional second page with table of values, including Rim Area, Disc Area, Average & Vertical Cup-to-Disc Ratio and Cup Volume. Each cell of the table can be color coded if change is detected.
- Miscellaneous updates to the report design.
- Updated Guided Progression Analysis (GPA™)

Glaucoma Progression Analysis
(Nerve Head Map of stable eye)

Variability Issues with Standard Perimetry

GPA Overview

Glaucoma Progression Analysis

GPA Symbols