GLAUCOMA MANAGEMENT

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Challenges of Glaucoma

- Risk factors are not widely known among patients
  - Many do not know it runs in families or is more common in African and Hispanic ancestry
- The structural changes in early glaucoma can be difficult to distinguish
  - Wide variation of optic disc size in both normal and glaucoma patients
- Patients can't tell that they have it
  - Most do not notice loss of function until they are nearly blind

Clinical Features of POAG

- Age > 60 (range 50 – 90 years)
- Bilateral but usually **asymmetric**
- Chronic and progressive
- Open angle with no abnormalities
- Asymptomatic
  - Significant visual field loss occurs before symptoms are noted
  - Central VA not affected until later in the disease
  - Painless

Clinical Diagnosis

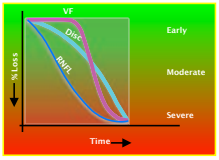
- Appearance of disc or appearance of RNFL
- Presence of characteristic abnormalities in visual field
- Adult onset
- Open angle on GONIOSCOPY
- Absence of secondary causes

Diagnosis and Progression of Primary Open Angle Glaucoma

- Assessment of Risk Factors
- Assessment of IOP
  - Tonometry, Pachymetry
- Assessment of the Anterior Segment
  - Slit-lamp, Gonioscopy, OCT
- Assessment of Structure: Retinal Nerve Fiber Layer and Optic Nerve
  - Ophthalmoscopy, Imaging (OCT/HRT)
- Assessment of Function: Visual Fields

It is Important to Understand the Structural / Functional Relationship in Glaucoma as the Disease Progresses

- Visual Field changes occur late in the disease
- The Optic disc often changes before visual fields
- The RNFL usually changes before both the visual fields and optic disc



Strong Risk Factors for POAG onset:

Risk Factor	
Age	• Increasing risk with increasing age • 3.5x higher prevalence in individuals over 70 (Baltimore Eye Study)
Race	• African Americans **3-4x more likely** than Caucasians • Hispanics have higher percentage
Family History	• First degree relative **4-8 x more likely** to develop glaucoma
Increased IOP	• Strongest association • **Modifiable risk factor**
Central Corneal Thickness	• Thinner corneal thickness associated with increased risk of developing glaucoma (Ocular Hypertension Study)
Increased cup/disc ratio	• **>0.6**

Key Points: POAG Features and Risk Factors

- POAG is an asymmetric, bilateral, progressive and chronic disease of the optic nerve occurring in individuals over 50 years of age
- POAG is a diagnosis of exclusion
- POAG has many risk factors
  - Notable risk factors: age, family history, race, CCT, IOP, Diabetes
- Assessment of risk factors is an important component of POAG diagnosis

Clinical Exam of the Optic Nerve Head Utility and Limitations

- Disc exam at the first visit – normal or abnormal?
  - Disc exams are subjective, or at best semi-quantitative
  - The wide variety of disc appearances requires long experience and expert judgment to separate normal from abnormal
  - Disc diameter must be taken into account
- Disc exam to assess change
  - Unless stereoscopic photographs are taken and compared over time, the ability of a clinician to judge change is very limited (chronology is important!)

Case

72 year old glaucoma suspect

Cup-to-disc ratio asymmetry

Highest untreated IOP 24 mm Hg OU

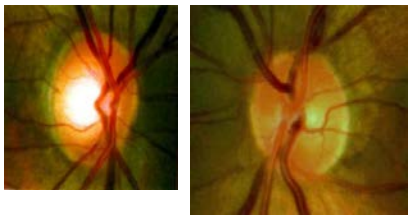
Anterior chamber angles open OU

Clear visual fields

- Central corneal thickness
  - 533 microns OD
  - 545 microns OS
- No prior ocular history or surgery
- No family history of glaucoma
- Good general health except for elevated cholesterol

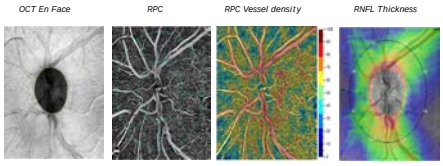
Case: Optic Nerves

OD OS



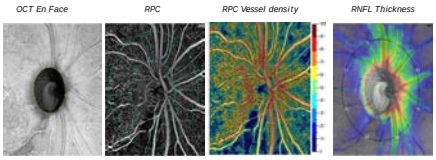
The Future of Glaucoma Diagnosis and Management???

Normal Eye



Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Moderate Glaucoma



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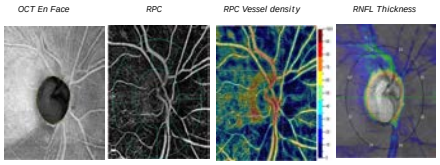
Advanced Glaucoma



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Glaucoma

- Goal of managing glaucoma = minimize the risk of visual disability or diminished quality of life due to the progression of nerve damage.
- Only understood and proven method of treatment is lowering the IOP.

Treatment and Management: Glaucoma

- **Initiation of therapy**: prostaglandin analogues (PGA) are recommended as first choice agents for most eyes with glaucoma.
- IOP reduction with initial monotherapy should be at least 20% from baseline.
  - ***Comment:*** IOP reduction of less than 10% should be considered as nonresponse.
  - ***Comment:*** Switching drugs within the PGA class may, upon occasion, provide greater IOP lowering.

Treatment and Management: Glaucoma

- Adjunctive therapy is indicated when existing therapy fails to reach the target IOP.
  - ***Comment:*** Adjunctive therapy should be limited to one drug from each class.
  - ***Comment:*** The efficacy of a drug when used as monotherapy is usually less when used as an adjunctive agent.

Treatment and Management: Glaucoma

- Surgery is indicated when:
  - medical therapy fails to adequately lower the intraocular pressure or prevent progression,
  - the risk of progression remains too high despite the use of medical therapy,
  - or is not possible due to allergy, intolerance, poor adherence or lack of availability.

Treatment Issues

- On average, most studies of glaucoma patients estimate that about 70% of doses are taken. This may vary depending on duration of treatment, number of medications taken and severity of the disease.
- Patient self-report of adherence is often overestimated.

Comment: Physicians do not accurately predict which patients are poorly compliant.

Patient Adherence

- Adherence = willingness to "stick to" a treatment that has been agreed upon with their clinician.
- Glaucoma Adherence and Persistence Study (GAPS)
  - Retrospective analysis of pharmacy/medical claims of 13,956 patients.
  - Calculated adherence based on medication possession ratio which is the days of supply /number of days between Rx filling.
  - 89% reported using medications everyday, but ratio indicated only enough medication for use 64% of the time.
  - Only 10% of subjects filled Rx continuous for 12 months, with 55% stopping/restarting at least one time.

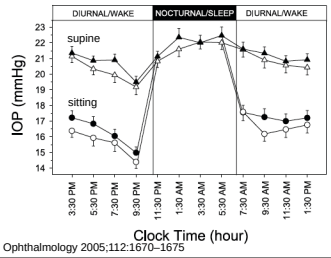
IOP Control

OHTS AND CORNEAL THICKNESS (CCT)
Shows risk of progressing to POAG

IOP (mmHg)	CCT < 555 um	CCT 555-588 um	CCT >588 um
>26	**36%**	13%	6%
24-26	**12%**	10%	7%
<24	**17%**	9%	2%

Gordon, M. O., et al. (2002) The ocular hypertension treatment study: baseline factors that predict the onset of primary open-angle glaucoma, Arch Ophthalmol, 120, 714-20.

Diurnal Fluctuations



Liu et al. Ophthalmology 2005;112:1670–1675

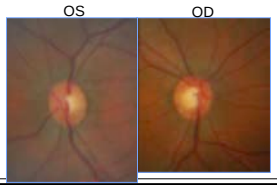
Setting Target Pressures

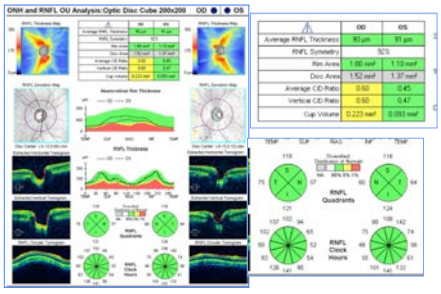
1. Establish baseline IOP (minimum 3 readings)
2. Classify amount of damage
   (i.e. mild, moderate, severe)
3. Use the highest IOP reading and set target
   - 20-30% lower for mild
   - 30-40% lower for moderate
   - 40-50% lower for severe damage
4. **Consider lowering IOP an additional 10% if:**
   - **Patient is <50 years of age**
   - **African North American decent**
   - **Sibling has advanced glaucoma**

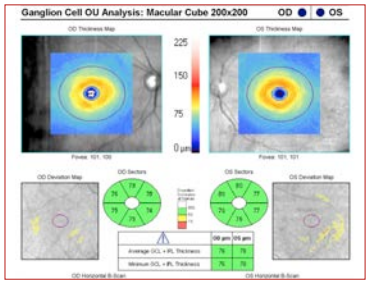
A.B. Litwak. The Glaucoma Handbook, 2001

Arturo: 50 y/o Russian Male

- RK 1991 -> 20/20 with hyperopic correction: +5.50 -1.50X090
- TA: 32/18
- Pach
  - 544 µ
  - 558 µ
- Gonio –CBB
- - PMHx
- - meds

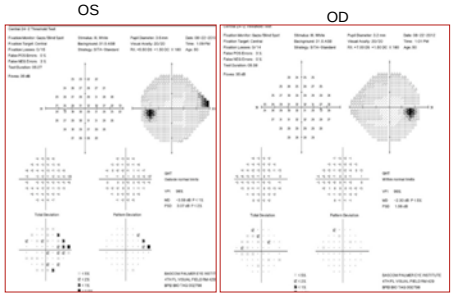






1 Mo Later

- TA: 24,25 RE; 18 LE
  - (Initial IOP 32/18)
- How do you account for the difference?
- Illustrates the importance of establishing a baseline

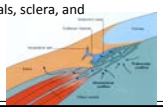


Topical Hypotensive Medications

- 5 Categories:
  - Prostaglandins
  - Adrenergic Antagonists (β-Blockers)
  - Adrenergic Agonists (α_2- agonists)
  - Carbonic Anhydrase Inhibitors
  - Cholinergic Agonists (Miotics)

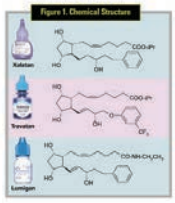
Prostaglandins

- First Line Treatment for almost all patients with ocular hypertension and open-angle glaucoma.
- Mechanism of Action: Increase uveoscleral outflow
  - The term *uveoscleral outflow* refers to the drainage of ocular aqueous humor other than through the trabecular meshwork
  - aqueous humor seeps through, around, and between tissues, including the supraciliary space, ciliary muscle, suprachoroidal space, choroidal vessels, emissarial canals, sclera, and lymphatic vessels.



Prostaglandin Analogues

- Medications Currently Available:
  - Latanoprost (Xalatan) by Pfizer
    - Only generic option!
  - Travatan Z (Travoprost) by Alcon
  - Lumigan (Bimatoprost) by Allergan
  - Zioptan (tafluprost) by Merck
- All are approved for once daily dosing.
  - Less satisfactory control of IOP is seen if dosage is increased.
  - Recommended QHS, but should be based on patient compliance.



Prostaglandin Analogues

- No evidence of drug tolerance has been seen.
  - Great for long term treatment.
- Good IOP control over 24 hour period.
- IOP reduction does not begin for at least 2 hours and will peak between 8-12 hours.
  - Not good for acute pressure spikes.

Side Effects of Prostaglandins

- Darkening of Iris Color
  - Occurs in 5-20% of patients in as early as 4 weeks.
  - Findings will not reverse after d/c medication.
  - Also increases eyelid pigmentation
- Hypertrichosis
  - Increased number, length, thickness, curvature, and darkening of the eyelashes.
- Conjunctival hyperemia
- Prostaglandin Associated Periorbitopathy:
  - Eyelid and orbital changes secondary to the use of Prostaglandin eye drops.

Contraindications

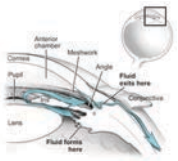
- Relative contraindications for patients with:
  - History of Uveitis
  - History of Herpes Simplex Virus
  - Prior incisional ocular surgery
- Use caution in patients after cataract surgery who have risk factors for CME:
  - Diabetes Mellitus
  - History of CME Diagnosis
  - Vitreous loss during cataract surgery
  - History of macular edema from retinal vein occlusion
  - Epiretinal membrane

Beta Blockers

Adrenergic Antagonists (Beta Blockers)

- First appeared during the 1970s and quickly became one of the mainstays of treatment for POAG.
- 5 Main Agents Currently on the US Market:
  - timolol
  - levobunolol
  - metipranolol
  - carteolol
  - betaxolol

Beta Blockers



- Mechanism of Action: **Decrease Aqueous Production**
  - This occurs by direct action of the drug on the ciliary processes to decrease secretion and local capillary perfusion (ultrafiltration).
  - Might be related to the inhibition of catecholamine-stimulated synthesis of cyclic adenosine monophosphate (AMP).

Characteristics of All Beta Blockers

- Exhibit IOP lowering effect of ~ 15-25%
  - Selective Beta Blockers ~15-20%
  - Non-Selective Beta Blockers ~ 20-25%
- IOP does not show significant reduction during the night.
  - Aqueous production is already at minimal levels.
  - Best time of use is in the morning.
- Onset of hypotensive effect is within 1 hour of instillation and peaks at ~ 3 hours.
  - Beneficial in cases of acute angle closure and IOP spikes.

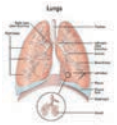
Characteristics of Beta Blockers

- Long term "drift" has been seen in all beta blockers.
  - Less than ½ of eyes initially treated with these medications will be on the original medication 5 years later.
- Patients will see a drastic drop in IOP right when the medication is initiated, but this will rise slightly and plateau within a few days to weeks.
- Monocular treatment will cause reduction in the IOP of the other eye as well, likely the result of systemic absorption.
- Exerts clinical effects for up to 2 weeks after treatment has been discontinued.

Cardiovascular Risks

- Bradycardia
  - Mean resting heart rate may decrease by 3-10 beats/minute.
- Systemic Hypotension
- Congestive Heart Failure
- Palpitations
- Fatalities have occurred
- Timolol has been shown to alter the plasma lipid profile in patients having an adverse effect on HDLs.

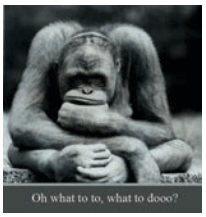
Pulmonary Side Effects



- Bronchospasm
- Wheezing
- Dyspnea
- Exacerbation of Asthma
- Average decrease of 25% in forced expiratory volume for COPD patients.

- Not seen as frequently with selective betaxolol, but can still occur and use is not recommended by pulmonary doctors.

CNS Side Effects



- History of Association with:
  - Depression
  - Confusion
  - Headaches
  - Insomnia
  - Sexual dysfunction
  - Lethargy
  - Weakness and Fatigue

- Onset of these symptoms varies from days to month after starting the medication and will only be transient.

Contraindications

- **Bronchial Asthma** (current problems or history of)
- Severe COPD
- Bradycardia
- Severe Heart Block
- Cardiac Failure
- Consider with caution for all patients with heart/lung problems of any sort.
- May mask the signs of hypoglycemia in diabetics.
- Children and Infants due to systemic profiles.
- Pregnancy Class C Drug.

Beta Blockers

- Despite the systemic risk factors, beta blockers are an excellent medication choice in patients without the contraindications.

- Excellent medication combined with prostaglandins due to the dosing schedule and different mechanisms of action.

Alpha Agonists

- Treatment dates back to the 1920s when epinephrine was topically applied to reduce IOP.

- Nonselective alpha agonists have a very high potential for side effects, thus they are very very rarely used.
  - Dipivefrin is still available and used as last effort when nothing else is an option.

Mechanism of Alpha Agonists

- Decrease Aqueous Production
  - Occurs within minutes of instillation.
  - This occurs mainly due to vasoconstriction reducing ultrafiltration of the plasma into the stroma of the ciliary processes.
- Increased Uveoscleral Outflow
  - This may take weeks to months to completely occur..

Adrenergic Agonists (α_2 Agonists)

- Modern day alpha agonists are selective in nature.
  - Activation of the presynaptic α_2 receptors inhibits neurotransmitter release resulting in decreased amounts of norepinephrine available for ciliary epithelium β receptors.
  - Also postsynaptic α_2 receptors reduce intracellular cyclic adenosine monophosphate.
- Agents include:
  - Brimonidine
  - Apraclonidine

Iopidine Ocular Side Effects

- Tachyphylaxis
  - Results in diminished hypotensive effect (frequently lasts 3 months or less).
- Conjunctival Blanching occurs in ~ 85% of patients with rebound hyperemia.
- Itching and Conjunctival Inflammation
  - Ocular intolerance develops quickly with long term use.
- Dilation of a Horner's Pupil

Iopidine Systemic Side Effects:

- Dry mouth and nose is the most common
- CNS Symptoms of fatigue and lethargy
- Can also see minimal effects on resting heart rate, arterial blood pressure, and respiration.

Brimonidine

- Very selective α2 agonist (30X more than Iopidine).
- Produces a dose dependent reduction in IOP by dual mechanism, but also thought to exert a neuroprotective effect that spares retinal ganglion cells (not well supported or understood).
- 20 – 25% IOP Reduction (Peak effect ~ to that of 0.5% timolol BID).

Brimonidine (Alphagan or Alphagan P)

- Approved for TID dosing as monotherapy and BID if used in combination with other hypotensive agents.
  - Studies show will work adjunctively with Prostaglandins, Beta Blockers, and Carbonic Anhydrase Inhibitors.

Ocular Side Effects

- Most frequent ocular side effects are:
  - Hyperemia
  - Burning
  - Stinging
  - Blurred Vision
  - Foreign Body Sensation

Ocular Side Effects

- Pupil miosis occurs 30-60 minutes after instillation.
  - Greater under scotopic than photopic conditions.
  - Duration ~ 6 hours.
- This is clinically useful in the treatment of night vision symptoms associated with refractive or cataract surgery.
  - Avoid repeated doses due to risks of reactions.

Brimonidine Systemic Side Effects

- Systemic Side Effects Include:
  - Dry mouth in 16-30% of patients using 0.2% concentration.
  - Decreases in BP and heart rate (very unlikely).
  - Fatigue and Lethargy.
  - Pregnancy Category B.

Alpha 2 Agonists

- Contraindications:
  - Use of Monoamine Oxidase Inhibitors
- Use Caution In:
  - Patients with severe cardiopulmonary disease
- Not recommended for children younger than 2.

Carbonic Anhydrase Inhibitors

CAI's in the Eye

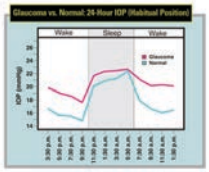
- Inhibiting carbonic anhydrase decreases the amount of bicarbonate and sodium that are moved into the posterior chamber, thus less aqueous is produced.
- Oral Medications:
  - Acetazolamide
  - Methazolamide
- Topical Medications:
  - Dorzolamide
  - Brinzolamide

Optometric Clinical Uses:

- Approved for use in a variety of glaucomas, including open angle, secondary glaucomas, and angle closure.
  - Often reserved for short-term IOP reduction due to the associated risks.
  - Produces ~30% inhibition of aqueous formation.
- Can be successfully used with all other hypotensive medications.
  - Despite similar mechanisms, combined therapy with beta blockers results in a nearly additive effect on aqueous outflow.
- CAI's can reduce the aqueous flow rate even during sleep (unlike beta blockers).
  - Acetazolamide reduced an additional 24% below the already limited nocturnal rate.

Why does efficacy at night matter so much?

- IOP is at its lowest point right before sleeping usually and the highest point right after waking.
- Aqueous has a dramatic decrease in production at night.
- Blood pressure also drops during sleep.



Systemic Side Effects

- Maximal doses produce intolerable effects in 30-80%, but side effects occur in some variety in nearly 100% of the individuals on Acetazolamide.
  - Sustained-release show better tolerance for prolonged use.
- Most Common Adverse Reactions:
  - Numbness and tingling of fingers, toes, and perioral region
  - Metallic Taste
  - Symptom complex of malaise, fatigue, weight loss, anorexia, depression, and decreased libido
  - GI Upset

Contraindications:

- **Known Hypersensitivity to Sulfonamides**
  - Little evidence to suggest overlapping sensitivity to CAI's and antimicrobial sulfas.
- Renal Disease
- Predisposition for Kidney Stones
- Clinically Significant Liver Disease
  - Increasing urine alkalinization causes increased levels of ammonia which can lead to liver toxicity.
- Severe COPD
- Caution in patients with sickle cell hemoglobinopathies
- Pregnancy (Category C Medication)

Comparing Rates of Adverse Reaction After Topical Antiglaucoma Medication Use by Self-Reported Allergy History

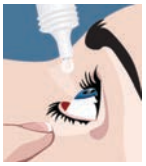
Sulfa Allergy	CAI	PGA	Alpha 2	B Blocker
Prior Sulfa vs other allergy	No difference	No difference	Significantly higher in Sulfa group	No difference
Prior allergy vs no allergy	Significantly higher in Sulfa	Significantly higher in Sulfa	Significantly higher in Sulfa	Significantly higher in Sulfa
Other allergy vs no allergy	Significantly higher in allergy	Significantly higher in allergy	No difference	No difference

Evaluation of Adverse Events in Self-Reported Sulfa-Allergic Patients Using Topical Carbonic Anhydrase Inhibitors. JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS Volume 29, Number 5, 2013
A retrospective case-controlled cohort study via chart review performed on 1,287 patients with a diagnosis of glaucoma.

Self-Reported Sulfa-Allergic Patients

- had the highest rate of local adverse reactions to alpha2-adrenergic agonists
- lowest rate of local adverse reactions to topical beta-adrenergic blockers
- patients who reported allergies to any kind of medication were more likely to develop an adverse reaction to topical anti-glaucoma medications than patients who reported no allergies to medications

Topical Carbonic Anhydrase Inhibitors



- Reduce IOP by 15-20%.
- Alter aqueous composition by lowering the pH, decreasing bicarbonate levels, and increasing levels of ascorbate in the posterior chamber.
- No additive effect of IOP reduction is achieved by combining topical and oral CAI's.

Side Effects of Topical CAI's

- Additional Ocular SE's:
  - Local irritation
  - Burning upon instillation
  - Blurry Vision
  - Hypersensitivity reactions
- Approximately 25% of patients will report bitter taste.
- Additional systemic SE's are very rare, although CNS effects, paresthesias, kidney stones, and fatigue have been reported.
  - Increased risk if prescribed in addition to oral CAI's.

Fixed Combinations

Combination Medications

- Combination medications should be used with caution – adding two medications at once is not recommended.
- Available medications:
  - Cosopt (timolol/dorzolamide)
  - Combigan (timolol/brimonidine)
  - Simbrinza (brinzolamide/brimonidine)
  - Xalacom (timolol/latanoprost)
  - DuoTrav PQ (timolol/travaprost)
  - Azarga (timolol/brinzolamide)

Cosopt

- Combination of timolol 0.5% and dorzolamide 2%.
- Available in PF single vials.
- Approved for BID dosing.
- IOP Reduction of medications in clinical study:
  - Cosopt BID: 27.4%
  - Dorzolamide TID: 15.5%
  - Timolol 0.5% BID: 22.2%
- Reduction has been reported to be comparable to Prostaglandins.

Side Effects of Cosopt

- Most common is burning and stinging.
- Side effects similar to dorzolamide and timolol, although less beta blockage effects are seen with Cosopt.

Combigan

- Combination of timolol 0.5% and brimonidine 0.2%.
  - Manufactured by Allergan.
  - Approved for BID dosing.
- IOP lowering is ~ 1 – 3 mmHg more than each medication administered alone, and slightly less than coadministration of the individual medications (timolol BID and brimonidine TID).
- Side effect profile is better than brimonidine 0.2% dosed separately.

Simbrinza

- Released April 2013 by Alcon Pharmaceuticals.
- Combination of Brinzolamide 1% and Brimonidine 0.2%.
- Approved for BID dosing.

Azarga®

- Brinzolamide hydrochloride 1% and timolol maleate 0.5% (5 mL)
- Instill 1 drop in affected eye(s) twice daily.

Xalacom® and DuoTrav PQ®

- Xalacom:
- Latanoprost (0.005%) and timolol maleate 0.5%
- Dosing is once a day in the morning

- DuoTrav PQ:
- Travoprost 0.004% and timolol 0.5%: (2.5 mL, 5 mL)
- Preserved with PolyQuad
- Instill 1 drop into affected eye(s) once daily in the morning or evening

Fixed Combinations

- In a 2012 review, fixed combinations of PG/BB were more effective than their component medications used separately and had less side effects than the individual PG.
- The fixed combinations were less effective than the two components used separately
- Most patients with POAG will require more than one medication for treatment and a fixed combination can potentially increase compliance and decrease potential side effects of multiple medications.

Latest Additions to Ocular Hypotensive Drops

Vyzulta

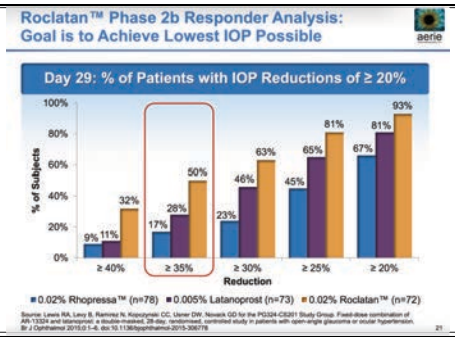
- Latanoprostene bunod 0.024% ophthalmic solution
  - Nitric oxide donating prostaglandin
- Mechanism:
  - Increases uveoscleral outflow + increases TM outflow
  - NO relaxes the TM, enhancing the outflow of aqueous
- VOYAGER Study:
  - All studied concentrations compared to Xalatan
  - Greater IOP reduction
  - Superior diurnal reductions in IOP
  - Slightly higher adverse effects (usually mild)
    - Most common side effect - hyperemia
- Bausch & Lomb

Rhopressa

- Netarsudil ophthalmic solution 0.02%
  - Rho Kinase inhibitor (ROCK inhibitor)/NET inhibitor
- Triple IOP lowering action
  1. Increases TM outflow
  2. Decreases aqueous production
  3. Lowers episcleral venous pressure (EVP)
- Dosing - QD
- Clinical Trials – Rocket 1, 2, 3, and 4
  - 5.5 mmHg IOP lowering
- Adverse effects:
  - No systemic effects
  - Conjunctival hyperemia - 48%
  - Corneal verticillata, conjunctival hemorrhage, blurred vision, erythema of eyelid
    - 3-5%
- Aerie Pharmaceuticals

Roclatan

- Netarsudil/latanoprost ophthalmic solution 0.02%/0.005%
  - Rho Kinase inhibitor (ROCK inhibitor)/NET inhibitor/prostaglandin analogue
- Quadruple IOP lowering action
  1. Increases TM outflow
  2. Decreases aqueous production
  3. Lowers episcleral venous pressure (EVP)
  4. Increases uveoscleral outflow
- Dosing – QD
- Clinical Trials – Mercury 1, 2, and 3
  - Superior to each of its components by up to 3 mmHg
- Aerie Pharmaceuticals



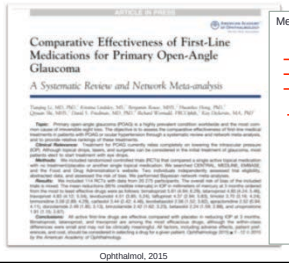
Prostaglandin Analogs

- Latanoprost 0.005%
  - Xalatan (0.02% BAK)
  - Generic (0.02% BAK)
- Travaprost 0.004%
  - Travatan Z (SofZia)
  - Generic (0.015% BAK)
- Bimatoprost
  - Lumigan 0.01% (0.02% BAK)
  - Generic 0.03% (0.005% BAK)
- Tafluprost 0.0015%
  - Zioptan (unpreserved)
- Latanoprostene bunod 0.024%
  - Vyzulta (0.02% BAK)

Which prostaglandin analog do you choose first?

1. **Efficacy**
2. **Cost**
3. **Generic vs. Branded**
4. **Adverse Effects**
5. **Contraindications**
6. **Tolerability**

Efficacy as First-Line Agents


Comparative Effectiveness of First-Line Medications for Primary Open-Angle Glaucoma

A Systematic Review and Network Meta-analysis

Ophthalmol, 2015

Mean IOP Reduction in mm Hg
at 3 months

→ Bimatoprost 5.61
→ Latanoprost 4.85
→ Travoprost 4.83
Levobunolol 4.51
→ Tafluprost 4.37
Timolol 3.70
Brimonidine 3.59
Carteolol 3.44
Levobetaxolol 2.56
Aproclonidine 2.52
Dorzolamide 2.49
Brinzolamide 2.42
Betaxolol 2.24
Unoprostone 1.91

Topical Glaucoma Drops

First Line

- Xalatan (Latanoprost 0.005%)
  - Generic available
- Travatan-Z (Travoprost (0.004%)
  - Generic available
- Lumigan (bimatoprost (0.03%)
  - Generic available
- Vyzulta (Latanoprostene bunod 0.024%)
- Roclatan (Latanoprost 0.005%/ Netarsudil 0.02%)
- Selective Laser Trabeculoplasty (SLT)

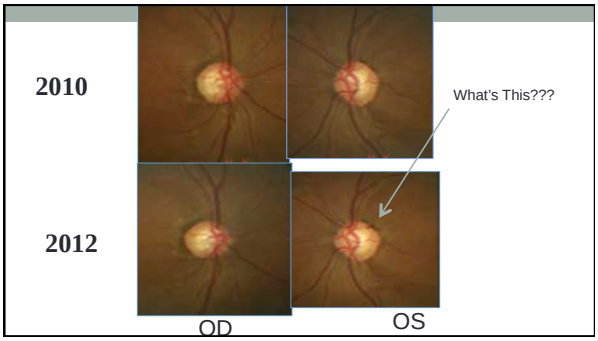
Second Line/Additional Therapy

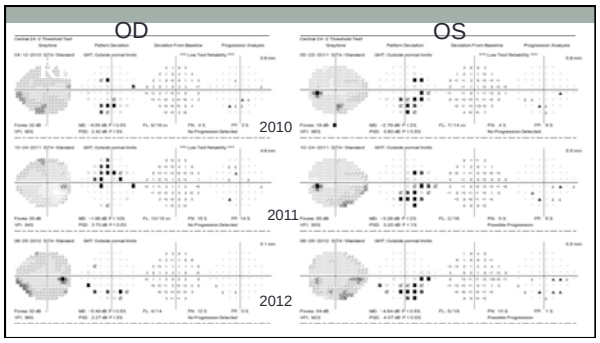
- Beta-blockers
- Alphagan P (Brimonidine 0.1% or 0.15%)
- Generic brimonidine 0.15% or 0.2%
- Rhopressa (Netarsudil 0.02%)
- Trusopt (dorzolamide 2%)
- Azopt (brinzolamide 1%)
- Combigan (timolol/brimonidine)
- Cosopt (timolol/dorzolamide)
- Simbrinza (brimonidine/brinzolamide)

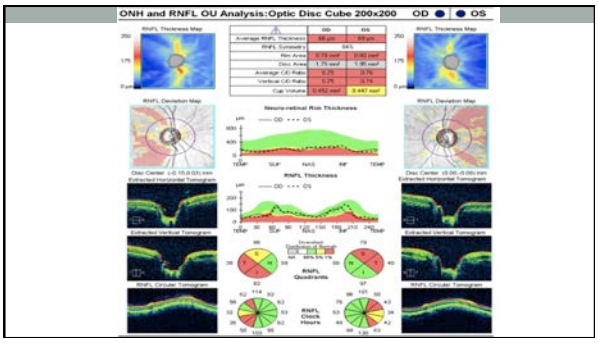
Case Courtesy of Dr. Mark Dunbar

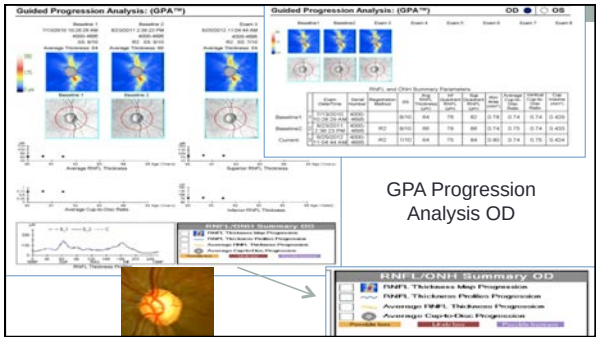
Vesta: 61 y/o Hatian Female

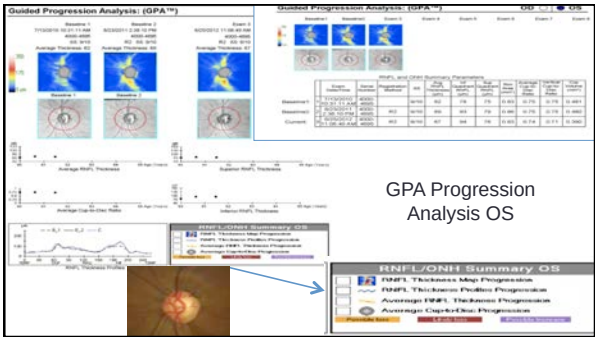
- GL suspect 2001 – suspicious ON's
- NTG since 2006
- Meds: Alphagan P bid OU, latanoprost qhs OU
- Medical Hx: HTN, HIV (+) for > 15 yrs
- VA: 6/6 (20/20)
- TA for the past 3 or 4 yrs: 9-13 mmHg OU
  - Last 2 visits 9 mmHg – today 13
  - Pachs: 450 microns











Case Courtesy Dr. Mark Dunbar

Vesta: 61 y/o Hatian Female

- NTG OU with thin corneas
- OS:
  - Optic Nerve and HVF show trend towards progression….
- OCT shows no change

Case Courtesy of Dr. Mark Dunbar

Vesta: 61 y/o Hatian Female

- How do you manage this patient?
  - Currently on latanoprost and alphagan OU
- This is what was done….
  - Stopped Alphagan P
  - Switch to Combigan bid OU
  - Continue with latanoprost qhs OU
  - RTC 1 mo

Case

- 50 YR WM
- POHx: had cataract surgery in his left eye at age 25 secondary to trauma to the eye,
  - Has a mid-dilated pupil post trauma
- PMHx: no known health problems and no medications
- VA: 6/6 (20/20) OD, OS

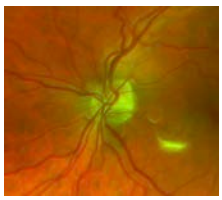
Health Assessment

- SLE:
  - OD unremarkable
  - OS: mid-dilated pupil with sluggish response to light
    - PCIOL well centered and no haze
- IOP: OD 12 and OS 26 mm Hg (TAG)
  - NCT OS (31 and 23)
  - Second visit: OD: 13 and OS: 27

Health Assessment

- Gonioscopy:
  - OD: unremarkable
  - OS: see photo

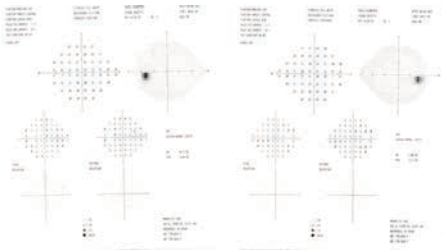
Optic Nerves



OS

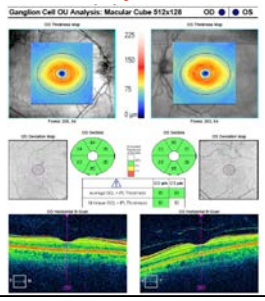
OD

Visual Fields

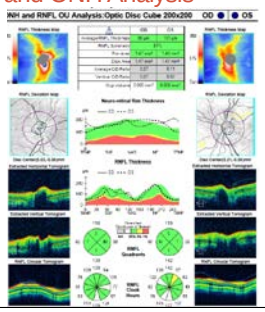


OS OD

Ganglion Cell Analysis



RNFL and ONH Analysis



Patient Update

- Patient was seen a year later
- Latanoprost qhs (remembers 5 days out of week)
- IOP's: OD: 14 and OS: 13 mm Hg
- No change in OCT

Selective Laser Trabeculoplasty (SLT)

- Newer form of laser therapy for patients with glaucoma
- Presented as an alternative to filtering surgery for patients whose open angle glaucoma was not controlled by meds
- Exact mechanism of effect is unknown but:
  - Biologic effects with increased inflammatory cells with "clean up" the TM
    - Laser energy causes chemical mediators to attracts macrophages and phagocytes to come and clean up the debris in the TM

Fundamentals of Optometric Laser Surgery
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NORTHEASTERN STATE UNIVERSITY

SLT Indications

- After maximum medications?
- When adding second/third drop?
- First line?

Selective Laser Trabeculoplasty Versus Medical Therapy as Initial Treatment of Glaucoma: A Prospective, Randomized Trial

L. Jay Katz, MD, William C. Steinmann, MD,† Azad Kabir, MD,‡ Jeanne Molineaux, COA,* Sheryl S. Wizov, COA,* and George Marcellino, PhD§ the SLT Med Study Group*

J Glaucoma • Volume 21, Number 7, September 2012

- SLT Med Study (2012)
  - Dr. Katz @ Wills Eye in Philadelphia
    - J Glaucoma 2012;21:460-468
  - SLT (100 applications over 360 degrees of TM) vs. prostaglandin analog
  - Primary outcome -> IOP
  - Secondary outcome -> # of treatment steps

SLT Med Study Treatment Arms

SLT vs. Prostaglandins

- SLT Med Study (2012)

Results:

1. IOP reduction:
   - SLT – 25.7% IOP reduction
     - IOP reduced from 24.5 to 18.2 (6.3 mmHg reduction)
   - Prostaglandin – 28.3% IOP reduction
     - IOP reduced from 24.7 to 17.7 (7.0 mmHg reduction)
2. # of treatment steps:
   - SLT group - 11% of eyes required additional SLT
   - Prostaglandin group -> 27% of eyes required additional medication

SLT Med Study

Conclusions: IOP reduction was similar in both arms after 9 to 12-months follow-up. More treatment steps were necessary to maintain target IOP in the medication group, although there was not a statistically significant difference between groups. These results support the option of SLT as a safe and effective initial therapy in open-angle glaucoma or ocular hypertension.

SLT as Primary Therapy

- IOP decreased by 30% (7.7 mmHg), from 25.5 to 17.9 mmHg over the f/u period
- Forty eyes (89%) had a decrease of 5 mmHg or more

"Selective laser trabeculoplasty is effective and safe as a primary treatment for patients with ocular hypertension and open-angle glaucoma."

Arch Ophthalmol. 2003;121: 957-960

SLT as first line?

- American Academy of Ophthalmology Preferred Practice Patterns
  - "Laser trabeculoplasty can be considered as initial therapy in selected patients."

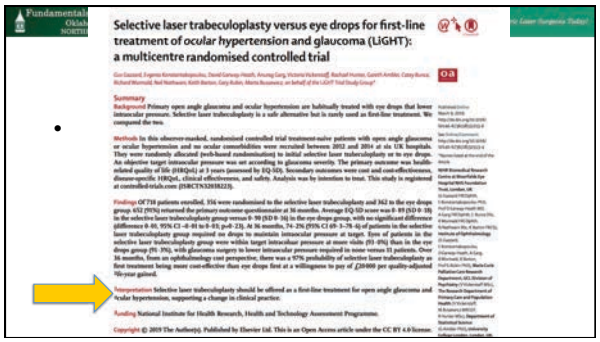
SLT as first line?

- UpToDate
  - "Once the decision has been made to treat a patient with open-angle glaucoma, we recommend pharmacologic or laser therapy as first line treatment."
  - Grade 1B evidence

UpToDate
PROVIDING ANSWERS TO CLINICAL QUESTIONS

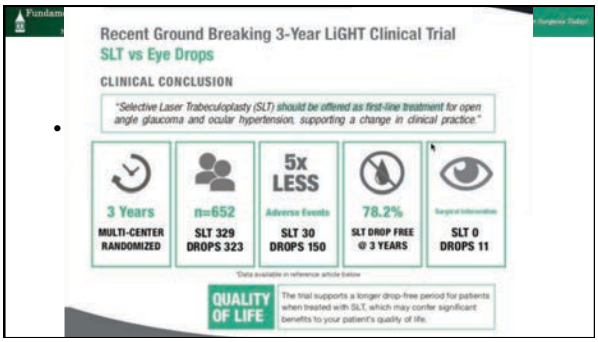
SLT as first line?

- 2015 Meta-Analysis (Oi Man Wong et. al)
  - "Robust evidence that SLT may be...offered as a primary treatment to patients with OAG."



Selective laser trabeculoplasty versus eye drops for first-line treatment of *ocular hypertension* and glaucoma (LiGHT): a multicentre randomised controlled trial

Oa



LTP Indications

- POAG
- Normo-tensive glaucoma
- Pigmentary dispersion glaucoma
- Pseudoexfoliative glaucoma
- Ocular hypertension

LTP Contraindications

- Advanced POAG
- Narrow Angle Glaucoma
- Angle Closure (Emergency IOP decrease)
- Inflammatory Glaucoma
- Angle Recession Glaucoma
- Neovascular Glaucoma
- Congenital Glaucoma
- Prior LTP that failed
- Under 40 years of age
- Hazy media

SLT Pre-op Exam

- Gonioscopy
  - Rule out angle recession & PAS
- Slit Lamp Exam
  - Rule out NVG & inflammatory glaucoma
- Educate Pt
- Informed Consent Signed
- Take Vitals
  - BP, pulse

Selective Laser Trabeculoplasty (SLT)

- SLT complications/risks
  1. IOP spike/elevation
     - Most often transient
     - High risk pt – may consider Diamox
  2. Inflammation
     - Anti-inflammatory
     - Use appropriate laser energy
  3. Stromal haze/edema/decreased endothelial cell count
     - Rare – usually responds to a topical steroid
  4. Peripheral Anterior Synechie (PAS)
     - Less likely due to less/no scar tissue formation
     - May increase IOP long-term
  5. Angle bleeds
     - hold pressure with laser lens
     - will stop 1 minute or less usually

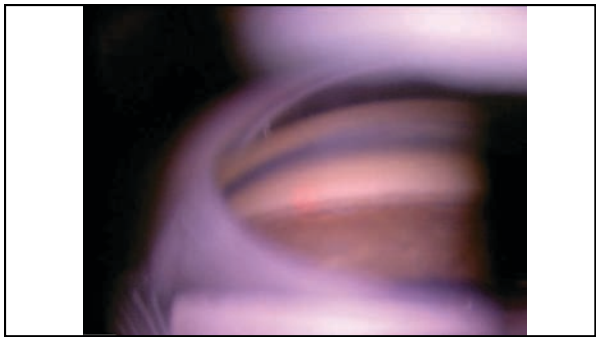
Latina SLT Gonio Lens

The Latina SLT Gonio Laser Lens was designed specifically for Selective Laser Trabeculoplasty. 1.0x magnification maintains laser spot size and 1 to 1 laser energy delivery. Tilted anterior lens surface corrects astigmatism to maintain circular laser beam profile and give sharp images for examination. Suitable for standard laser trabeculoplasty.

Rapid SLT Gonio Lens

SLT Procedure

- How many degrees to treat?
  - 180 vs. 360
  - Our current protocol is to treat 360 degrees in one eye unless the patient has PDS, PDG, or significant pigment in the TM (then 180 degrees is done)
  - 2nd eye is also treated 360 degrees 6-8 weeks after that so the effect of the first treated eye can be seen



Trabeculoplasty efficacy

- Expected IOP reduction: 20-30%
- 80-90% effective at one year
- 30-50% effective at five years

Predicting SLT Success

- SLT is not 100% effective
  - Modest response in some
- What if we could predict nonresponders?

Predicting SLT Success

Development of a Prediction Rule to Estimate the Probability of Acceptable Intraocular Pressure Reduction After Selective Laser Trabeculoplasty in Open-angle Glaucoma and Ocular Hypertension

Alexander J. Mao, MD, OD, MPH, Xiao-jing Pan, MD,† Ian McIlraith, MD,* Maurice Strasfeld, MD,* George Colev, MD,* and Cindy Hunnik, MD**

- Looked at:
  - Pre-treatment IOP, current medications, phakic status, level of pigmentation, steroid use, age, gender

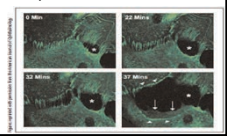
Pre-laser IOP (mmHg)	20	22	24	26	28	30	32	34	36	38	40	42	44	48	50
14	29	26	20	20	17	15	13	11	9	8	7	6	5	3	3
16	40	36	30	28	25	22	19	16	14	12	10	9	8	5	5
18	51	47	40	39	35	31	27	24	21	18	16	13	12	8	7
20	63	59	50	50	46	42	37	33	30	26	23	20	17	13	11
22	73	69	70	62	57	53	49	44	40	36	32	29	25	19	17
24	81	78	80	72	68	64	60	56	52	48	43	39	35	27	24
26	87	85	90	80	78	74	71	67	63	59	55	51	46	38	34
28	92	90	90	87	85	82	80	77	73	70	66	62	58	49	45
30	95	94	90	91	90	88	86	84	82	79	76	72	69	61	57
32	97	96	100	94	93	92	91	89	88	86	83	81	78	71	68
34	98	97	100	96	96	95	94	93	92	90	89	87	85	80	77
36	99	98	100	98	97	97	96	96	95	94	93	91	90	86	84
38	99	99	100	99	98	98	98	97	97	96	95	94	94	91	90
40	99	99	100	99	99	99	98	98	98	97	97	96	96	94	93

SLT and prostaglandins (PGA)

- SLT may function similarly to PGA
  - Low-grade inflammation
- 2007 study: In patients on drops, SLT had the least impact in eyes already treated with PGA

SLT and prostaglandins (PGA)

- Alvarado et. al
- Two parts to study
  - In vitro
    - PGA and trabeculoplasty have competitive mechanism of action
  - Clinical arm



Alvarado et. al Clinical Arm

24 patients

- Withdrew PGA for washout period, then did SLT
- Measured SLT response after 90 days

Alvarado et. al Clinical Arm

- Average IOP reduction
  - PGA: 25%
  - SLT: 30%
- PGA responders tended to be SLT responders (at equivalent levels)

Alvarado et. al Proposed Protocol

- If patient is on no glaucoma meds preoperatively
  - Test response with PGA
  - If successful, proceed with SLT
  - SLT functions like starting PGA
- If patient is already on PGA preoperatively
  - Discontinue PGA for 1 month
  - If IOP increases, expect SLT to work
  - SLT basically replaces PGA

Alvarado et. al Proposed Protocol

- If patient needs further IOP reduction following SLT, consider using non-PGA medication
- So overall how can we predict success?
  - Higher overall IOP pre-laser
  - If prostaglandin works, SLT works..... but maybe take them off of prostaglandin first

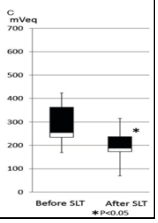
SLT and normal tension glaucoma (NTG)

- How much IOP reduction can we expect?
- Does improved diurnal control still apply?

Pre-laser IOP (mmHg)	20	22	24	26	28	30	32	34	36	38	40	42	44	46	50
14	29	26	20	20	17	15	13	11	9	8	7	6	5	3	3
16	40	36	30	28	25	22	19	16	14	12	10	9	8	5	5
18	51	47	40	39	35	31	27	24	21	18	16	13	12	8	7
20	63	59	50	50	46	42	37	33	30	26	23	20	17	13	11
22	73	69	70	62	57	53	49	44	40	36	32	29	25	19	17
24	81	78	80	72	68	64	60	56	52	48	43	39	35	27	24
26	87	85	80	80	78	74	71	67	63	59	55	51	46	38	34
28	92	90	90	87	85	82	80	77	73	70	66	62	58	49	45
30	95	94	90	91	90	88	86	84	82	79	76	72	69	61	57
32	97	96	100	94	93	92	91	89	88	86	83	81	78	71	68
34	98	97	100	96	96	95	94	93	92	90	89	87	85	80	77
36	99	98	100	98	97	97	96	96	95	94	93	91	90	86	84
38	99	99	100	99	98	98	98	97	97	96	95	94	94	91	90
40	99	99	100	99	99	99	98	98	98	97	97	96	96	94	93

SLT and normal tension glaucoma (NTG)

- 14-16% IOP reduction
  - –2015 meta-analysis of SLT studies
- Diurnal control benefits
  - –2014 study: SLT decreases nocturnal spikes in NTG patients



Selective Laser Trabeculoplasty (SLT)

- Long term outcome
  - – 80-90% effective at 1 year
  - – 40-50% effective at 5 years
  - – 20-30% effective at 10 years
- Tends to be very effective for 12-60 months
  - – Effect perhaps wanes after that

Selective Laser Trabeculoplasty (SLT)

- Retreatments
  - – Since no mechanical damage -> can we repeat SLT???

–yes

ALT & SLT Coding/Billing

- Code for ALT & SLT is the same
  - – 65855
- How much do we get paid?
  - – $212.99/eye
  - – If you do them on the same day
    - 100% of the first eye
    - 50% of the second eye
- Global Period is the same as well
  - – 10 global period
  - – Contrast that to YAG cap
    - 90 days

Projected Cost Comparison for POAG
Primary SLT vs. Medications

- Patients aged 65 years or more
- Source: Ontario Health Insurance Plan
- Medication Therapy Groups:
  - – Monotherapy
  - – Bi-drug Therapy
  - – Tri-drug Therapy
- Cost of SLT Analysis Scenerios
  - – SLT Effective for 2 years
  - – SLT Effective for 3 years
- Repeatability of SLT was assumed

Lee R, Hutnik CM: Can J Ophthalmol. 2006 Aug;41(4):449-56

Projected Cost Comparison for POAG Primary SLT vs. Medications

- 6 year cost comparison

a. SLT Effective for 2 years
- Monotherapy: $206.54
- Bi-therapy: $1,668.84
- Tri-drug therapy: $2,992.67

b. SLT Effective for 3 years
- Monotherapy: $580.52
- Bi-therapy: $2,042.82
- Tri-therapy: $3,366.65

Lee R, Hutnik CM: Can J Ophthalmol. 2006 Aug;41(4):449-56

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ALT & SLT Summary

- Positives
  - Work about 80-95% of the time
  - On average, takes the place of 1 medication
    - ALT & SLT average IOP reduction of 20-35%
      - ALT 20-25% reduction
      - SLT 28-35% reduction as primary therapy
      - SLT 21-25% reduction as secondary therapy
  - Doesn't interfere with other treatments or meds
  - Blunts nocturnal IOP spike
  - **Cost benefit?**
- Negatives
  - Effect tends to diminish over time
  - ALT has more side effects and fails more often as time goes by than SLT