

TREATMENT AND MANAGEMENT OF GLAUCOMA

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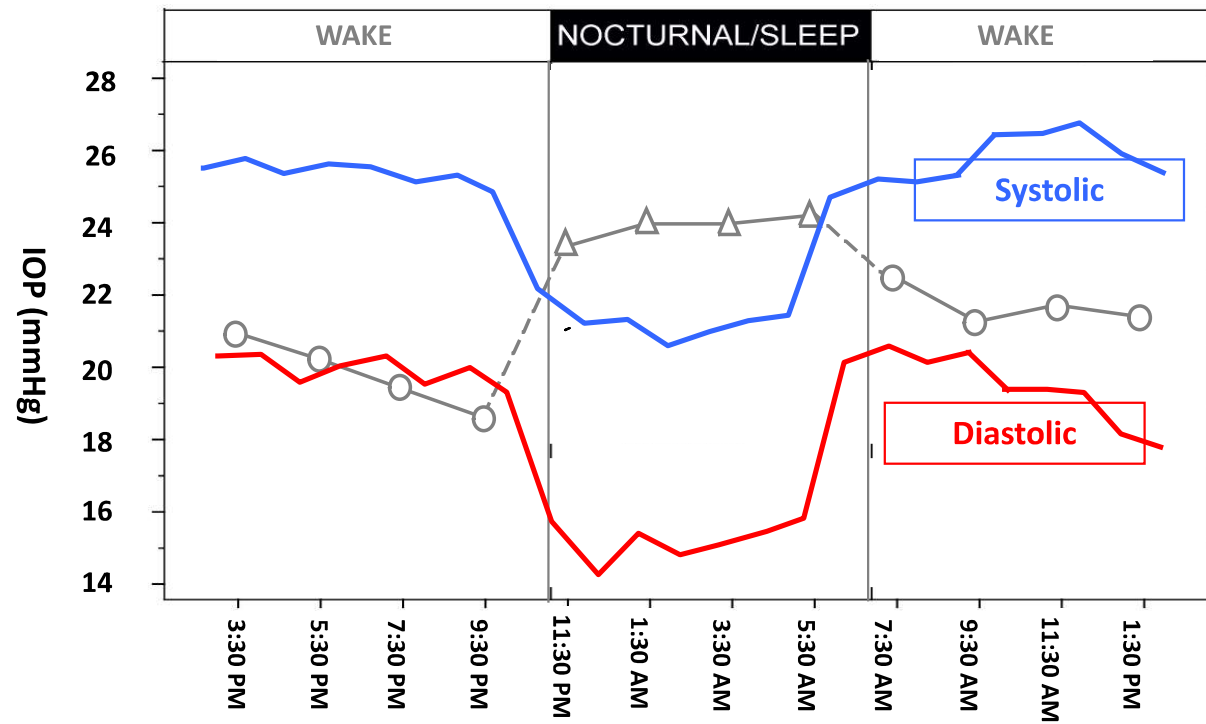
Challenges of Glaucoma

- 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

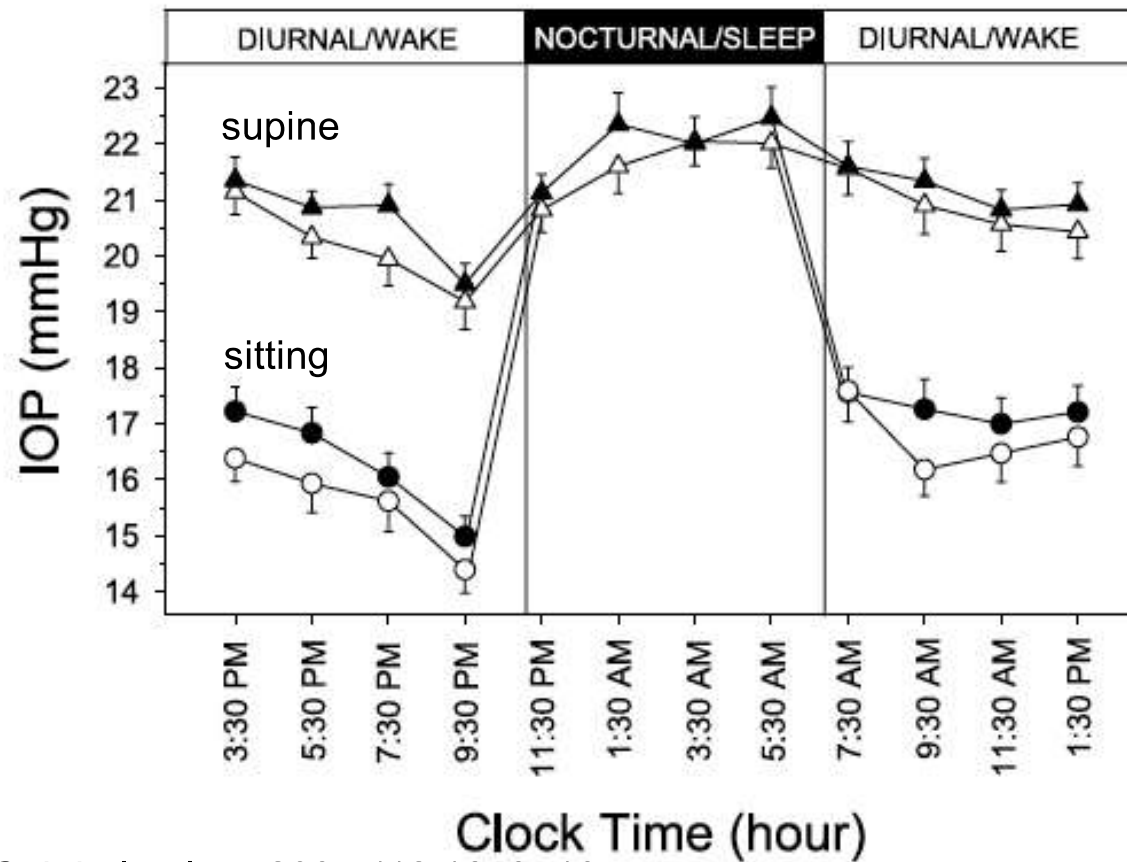
Strong Risk Factors for POAG onset:

Risk Factor	
Age	<ul style="list-style-type: none">Increasing risk with increasing age3.5x higher prevalence in individuals over 70 (Baltimore Eye Study)
Race	<ul style="list-style-type: none">African Americans 3-4x more likely than CaucasiansHispanics have higher percentage
Family History	<ul style="list-style-type: none">First degree relative 4-8 x more likely to develop glaucoma
Increased IOP	<ul style="list-style-type: none">Strongest associationModifiable risk factor
Central Corneal Thickness	<ul style="list-style-type: none">Thinner corneal thickness associated with increased risk of developing glaucoma (Ocular Hypertension Study)
Increased cup/disc ratio	<ul style="list-style-type: none">>0.6

Habitual IOP and Pulse Pressure



Diurnal Fluctuations



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

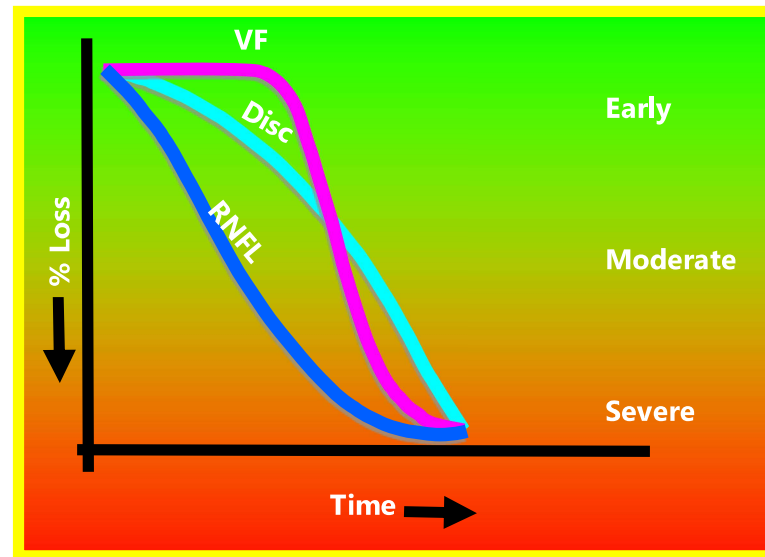
Clinical Features of POAG

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



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



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

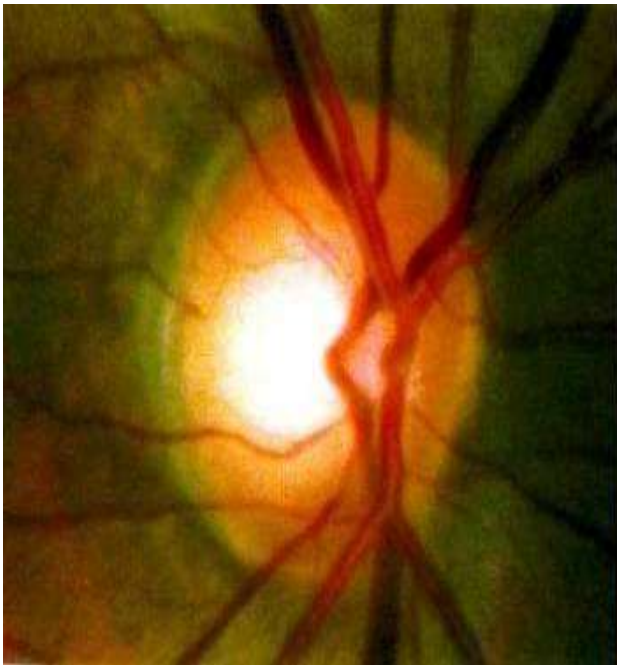
Anterior chamber angles
open OU

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



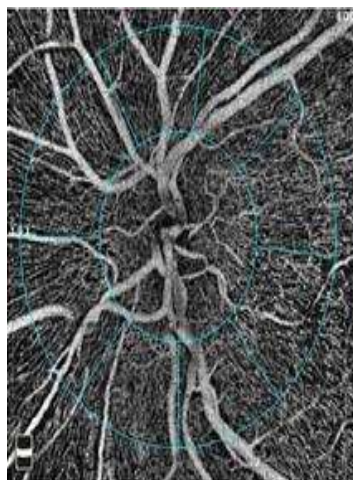
The Future of Glaucoma Diagnosis and Management???

Normal Eye

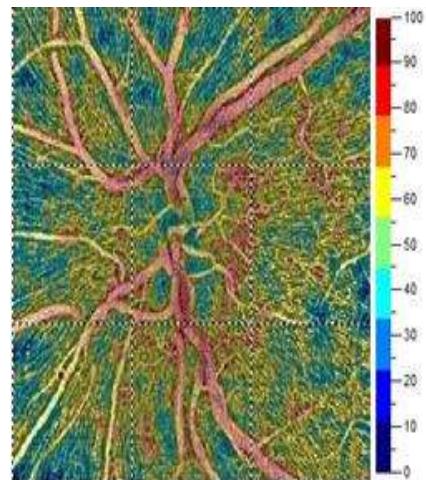
OCT En Face



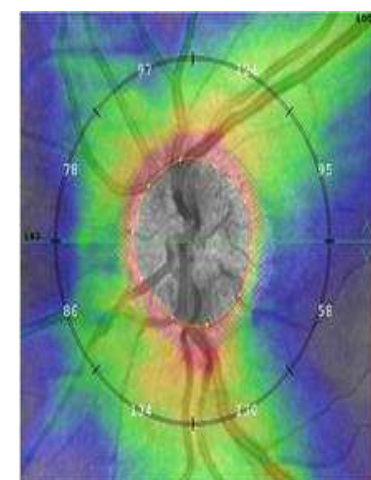
RPC



RPC Vessel density



RNFL Thickness



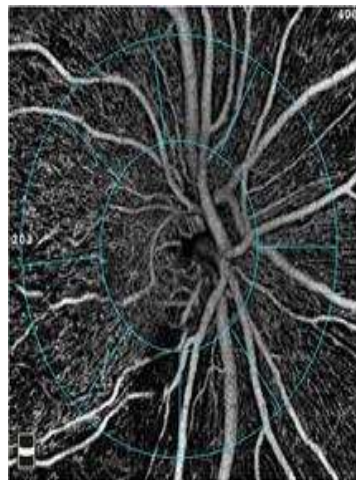
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Moderate Glaucoma

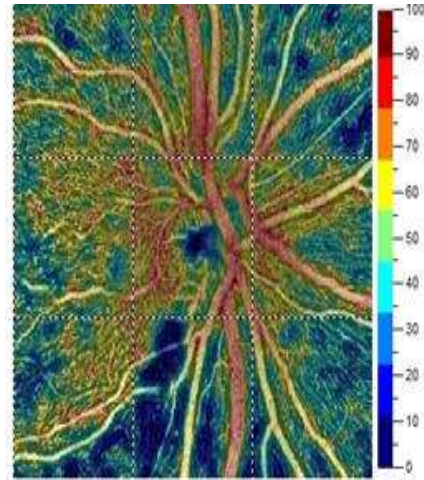
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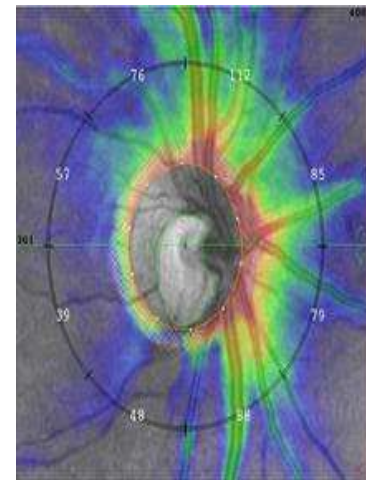
RPC



RPC Vessel density



RNFL Thickness



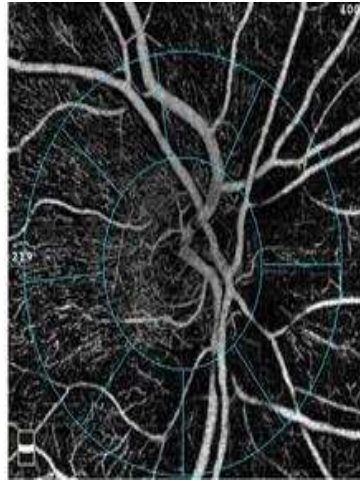
Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Advanced Glaucoma

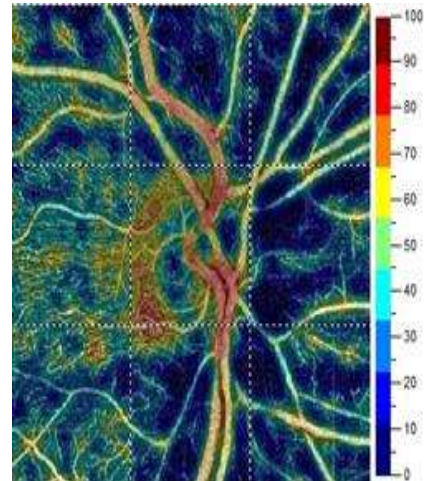
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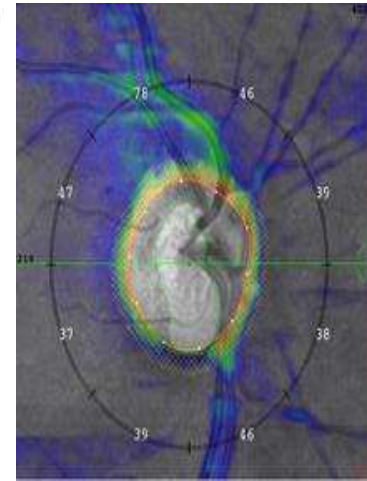
RPC



RPC Vessel density



RNFL Thickness

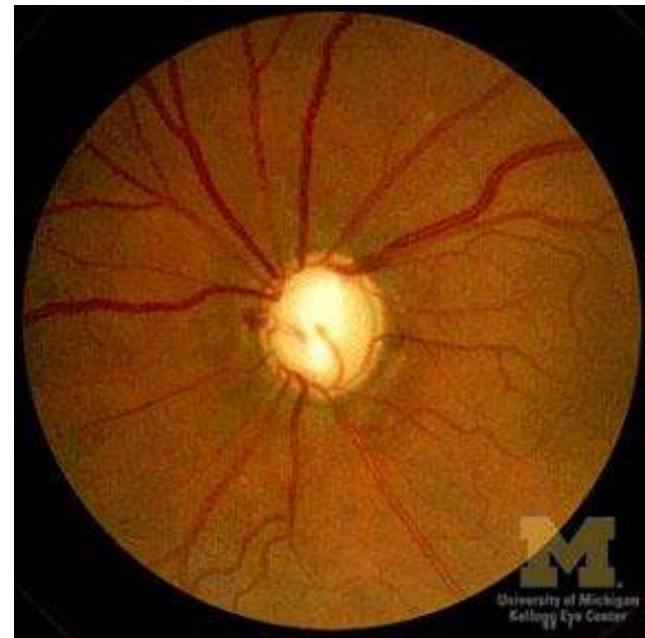


Images and data courtesy of Robert Weinreb, MD and Linda Zangwill, PhD, UC San Diego

Glaucoma Management

Glaucoma Management

- 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. ^[L]_{SEP}
 - **Comment**: IOP reduction of less than 10% should be considered as nonresponse. ^[L]_{SEP}
 - **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. ^[L]_[SEP]
- **Comment:** Adjunctive therapy should be limited to one drug from each class. ^[L]_[SEP]
- **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. [LSEP]
- Comment: Physicians do not accurately predict which patients are poorly compliant. [LSEP]

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.

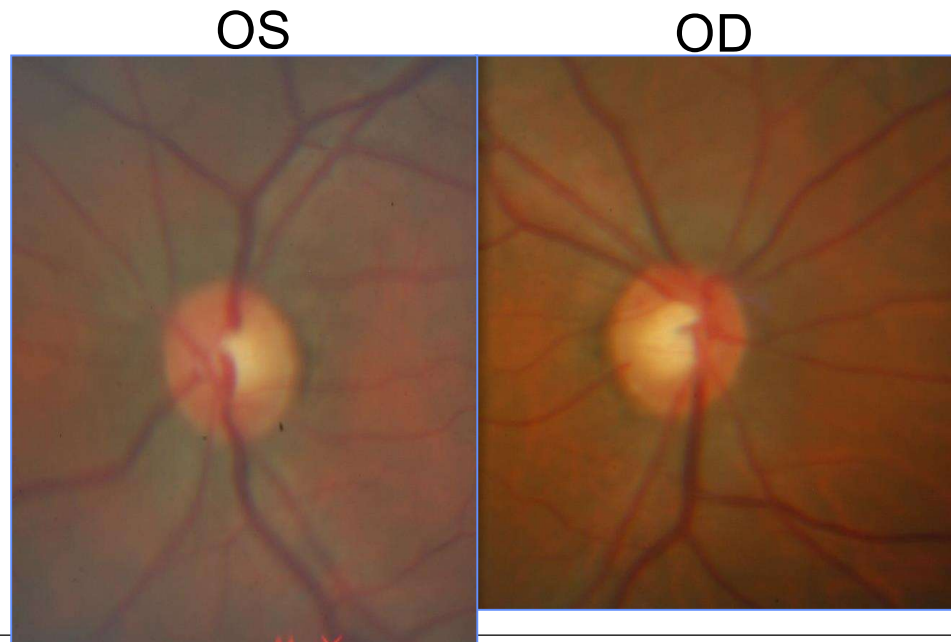
IOP Control

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**

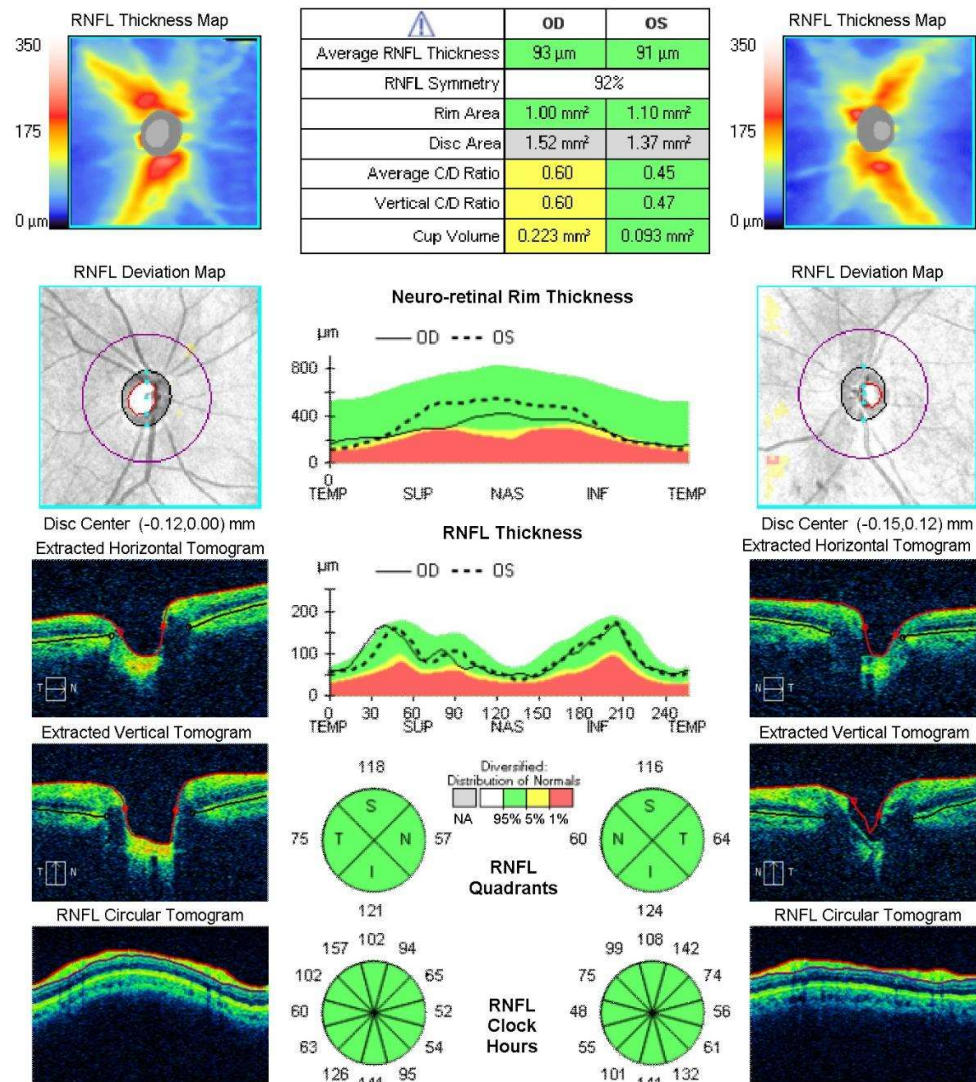
Arturo: 50 y/o Russian Male

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

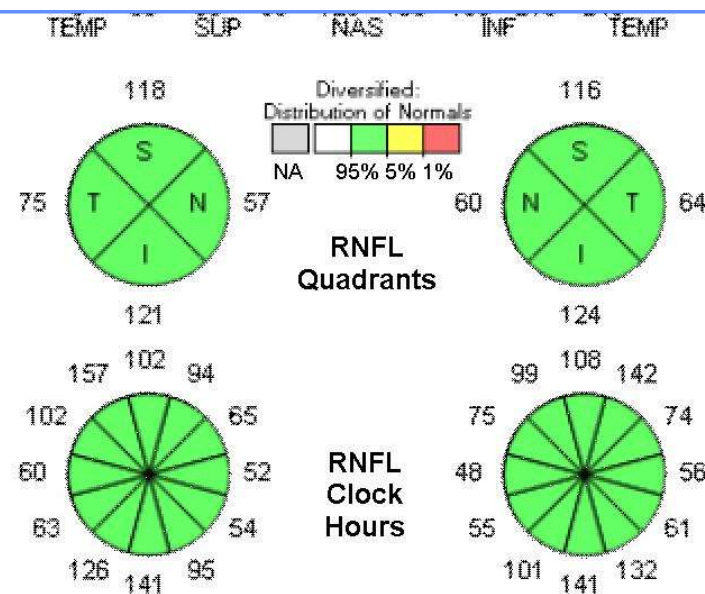


ONH and RNFL OU Analysis:Optic Disc Cube 200x200

OD ● ● OS



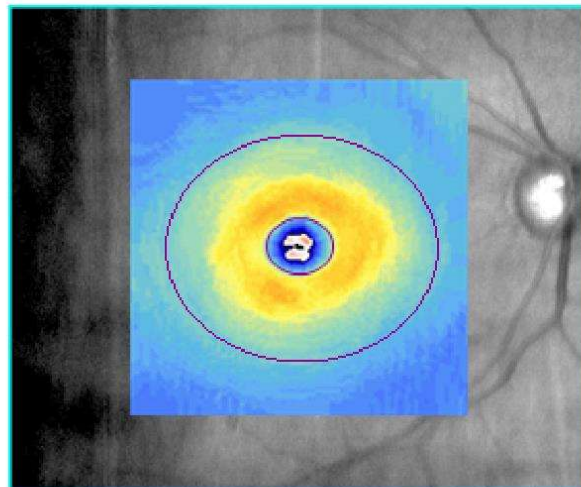
	OD	OS
Average RNFL Thickness	93 μm	91 μm
RNFL Symmetry	92%	
Rim Area	1.00 mm^2	1.10 mm^2
Disc Area	1.52 mm^2	1.37 mm^2
Average C/D Ratio	0.60	0.45
Vertical C/D Ratio	0.60	0.47
Cup Volume	0.223 mm^3	0.093 mm^3



Ganglion Cell OU Analysis: Macular Cube 200x200

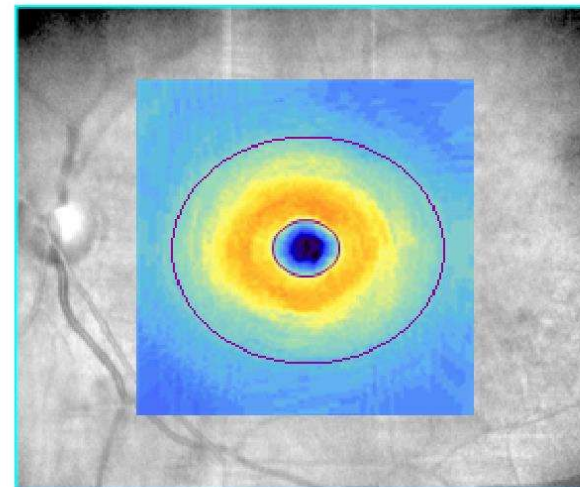
OD ● ● OS

OD Thickness Map



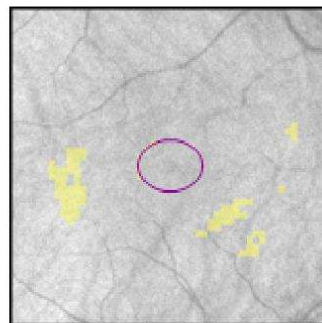
Fovea: 101, 100

OS Thickness Map

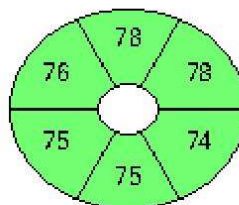


Fovea: 101, 101

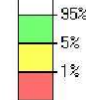
OD Deviation Map



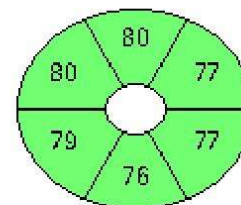
OD Sectors



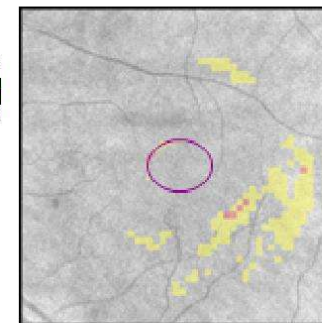
Diversified:
Distribution
of Normals



OS Sectors



OS Deviation Map



	OD μm	OS μm
Average GCL + IPL Thickness	76	78
Minimum GCL + IPL Thickness	76	78

OD Horizontal B-Scan

OS Horizontal B-Scan

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

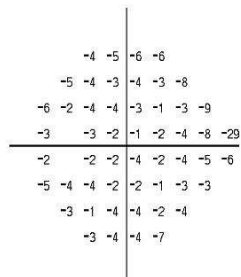
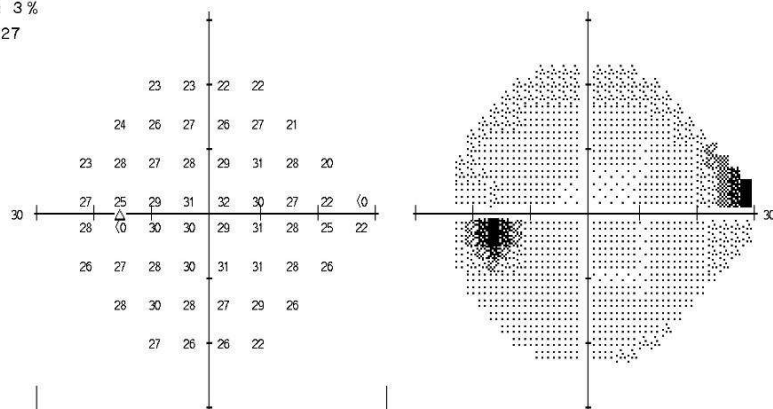
Central 24-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot
 Fixation Target: Central
 Fixation Losses: 0/15
 False POS Errors: 0 %
 False NEG Errors: 3 %
 Test Duration: 05:27

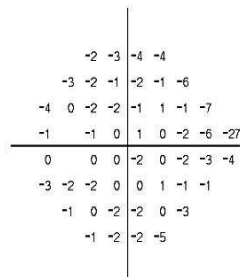
Stimulus: III, White
 Background: 31.5 ASB
 Strategy: SITA-Standard

Pupil Diameter: 3.6 mm
 Visual Acuity: 20/20
 RX: +5.50 DS +1.50 DC X 180
 Date: 08-22-2012
 Time: 1:09 PM
 Age: 50

Fovea: 35 dB



Total Deviation



Pattern Deviation

GHT
 Outside normal limits

VFI 98%

MD -3.58 dB P < 1%

PSD 3.07 dB P < 2%

⋯ < 5%
 ⋯ < 2%
 ⋯ < 1%
 ■ < 0.5%

BASCOM PALMER EYE INSTIT
 4TH FL VISUAL FIELD RM 429
 BPEI BIO TAG 002798

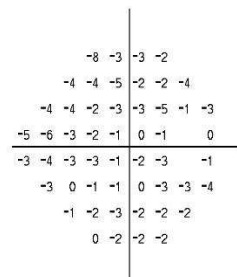
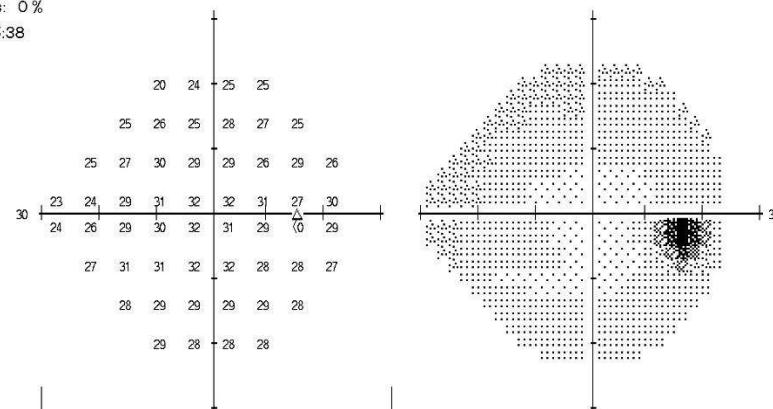
Central 24-2 Threshold Test

Fixation Monitor: Gaze/Blind Spot
 Fixation Target: Central
 Fixation Losses: 0/14
 False POS Errors: 3 %
 False NEG Errors: 0 %
 Test Duration: 05:38

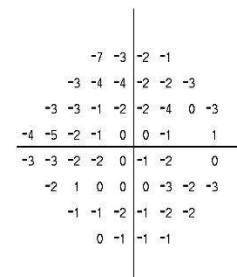
Stimulus: III, White
 Background: 31.5 ASB
 Strategy: SITA-Standard

Pupil Diameter: 3.2 mm
 Visual Acuity: 20/20
 RX: +7.00 DS +1.50 DC X 180
 Date: 08-22-2012
 Time: 1:01 PM
 Age: 50

Fovea: 35 dB



Total Deviation



Pattern Deviation

GHT
 Within normal limits

VFI 99%

MD -2.30 dB P < 5%

PSD 1.56 dB

⋯ < 5%
 ⋯ < 2%
 ⋯ < 1%

BASCOM PALMER EYE INSTITUTE
 4TH FL VISUAL FIELD RM 429
 BPEI BIO TAG 002798

Topical Hypotensive Medications

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



Topical Glaucoma Drops

First Line

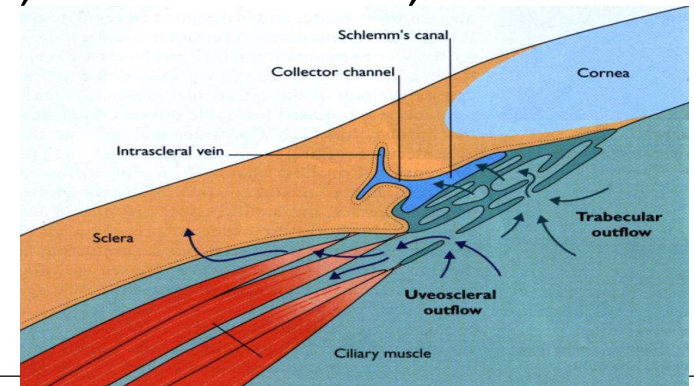
- Xalatan (Latanoprost 0.005%)
 - Generic available
- Travatan-Z (Travoprost (0.004%)
 - Generic available
- Lumigan (bimatoprost (0.03%)
 - Generic available
- Vyzulta (Latanoprostene bunod 0.024%)
- Roclatan (Latanoprost 0.005%/Netarsudil 0.02%)
- Selective Laser Trabeculoplasty (SLT)

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)

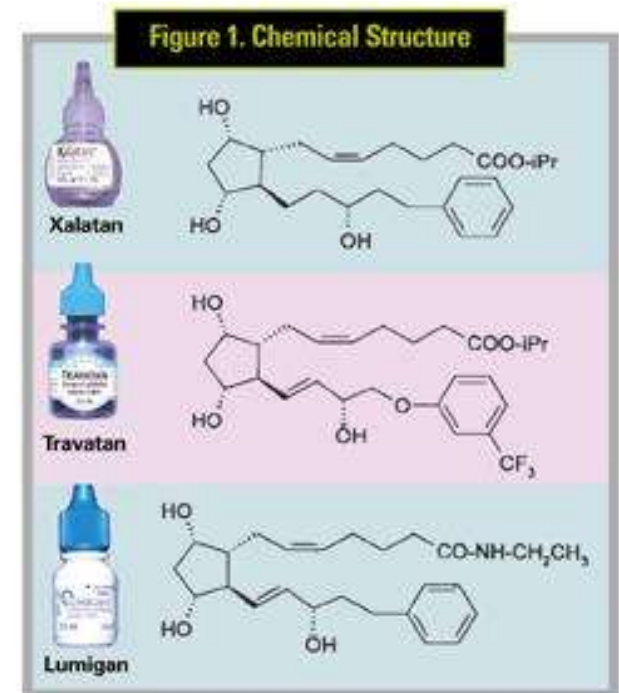
Prostaglandins

- 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

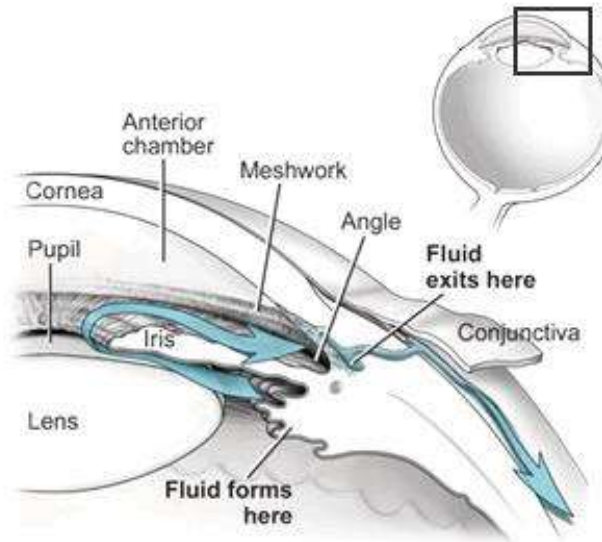
- Relative contraindications for patients with:
 - History of Uveitis
 - History of Herpes Simplex Virus
 - Prior incisional ocular surgery
- Use caution in patients after cataract surgery who have risk factors for CME:
 - Diabetes Mellitus
 - History of CME Diagnosis
 - Vitreous loss during cataract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

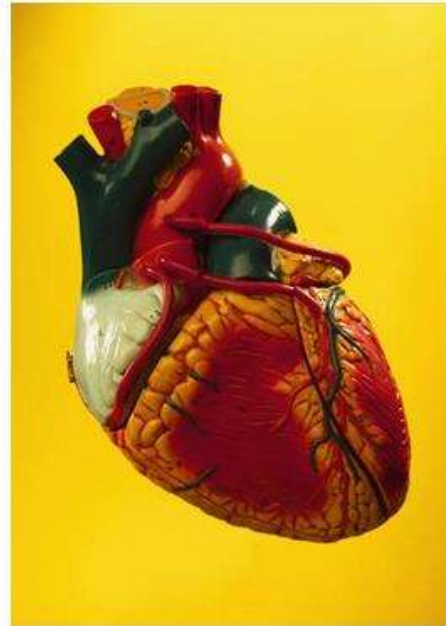
- Exhibit IOP lowering effect of ~ 15-25%
 - Selective Beta Blockers ~15-20%
 - Non-Selective Beta Blockers ~ 20-25%
- IOP does not show significant reduction during the night.
 - Aqueous production is already at minimal levels.
 - Best time of use is in the morning.
- Onset of hypotensive effect is 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.

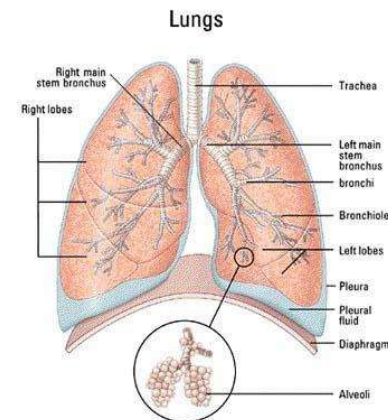
Cardiovascular Risks

- 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.

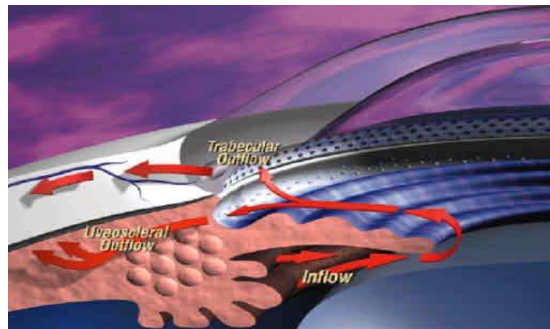
Beta Blockers

- 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

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 α_2 agonist (30X more than lolidine).
- 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

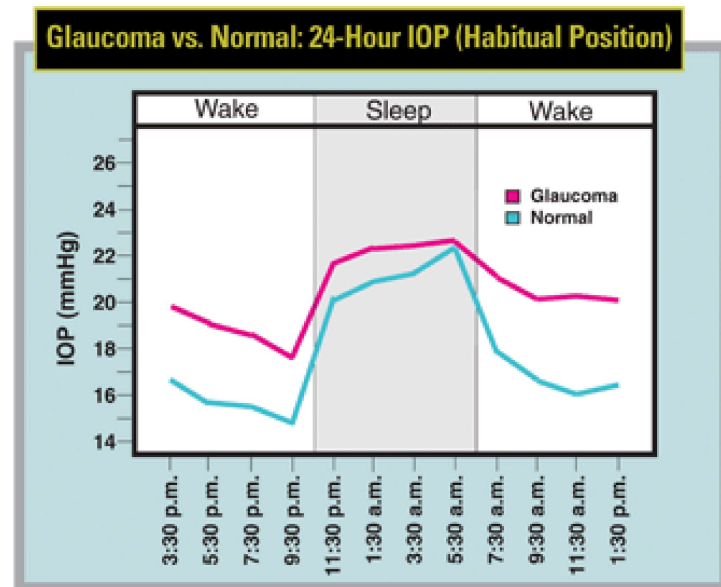
- Inhibiting carbonic anhydrase decreases the amount of bicarbonate and sodium that are moved into the posterior chamber, thus less aqueous is produced.
- Oral Medications:
 - Acetazolamide
 - Methazolamide
- Topical Medications:
 - Dorzolamide
 - Brinzolamide

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.
- 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.

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

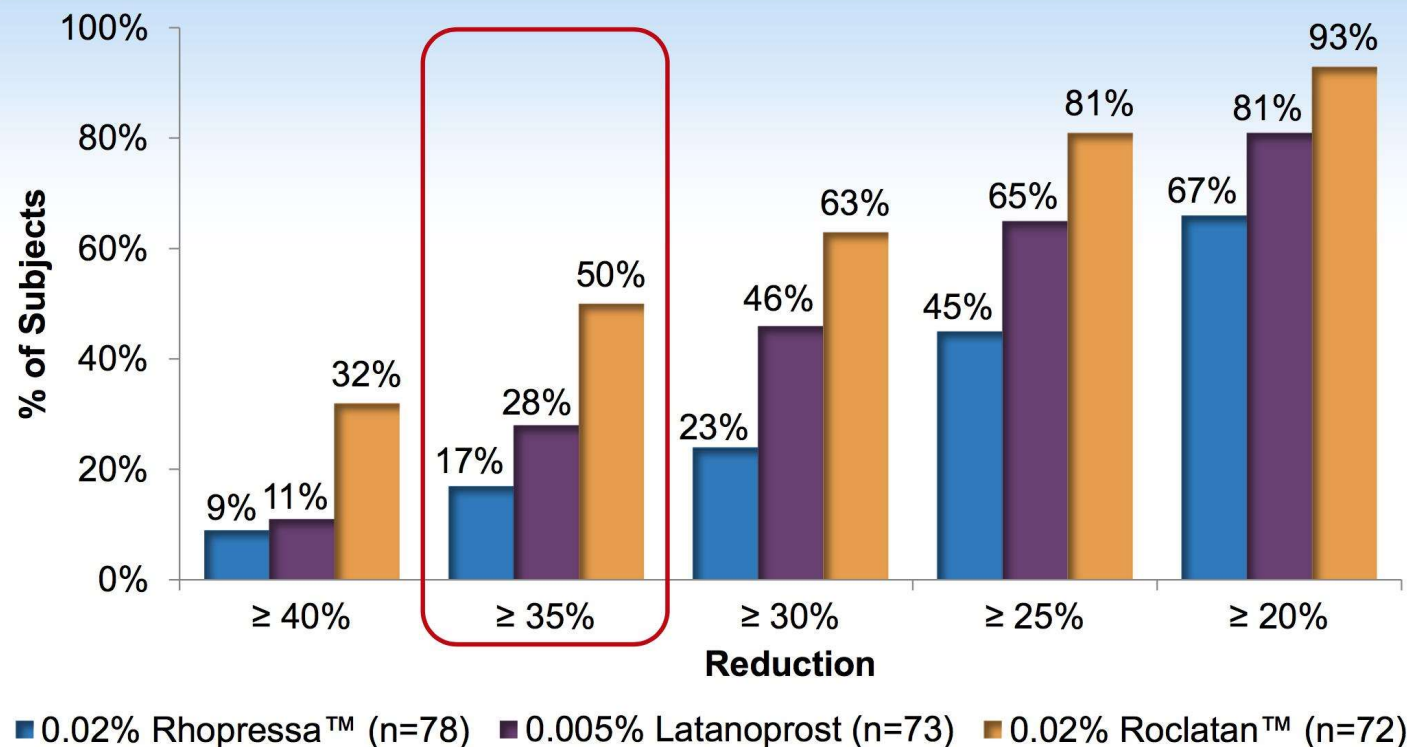
Roclatan

- 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

Roclatan™ Phase 2b Responder Analysis: Goal is to Achieve Lowest IOP Possible



Day 29: % of Patients with IOP Reductions of $\geq 20\%$

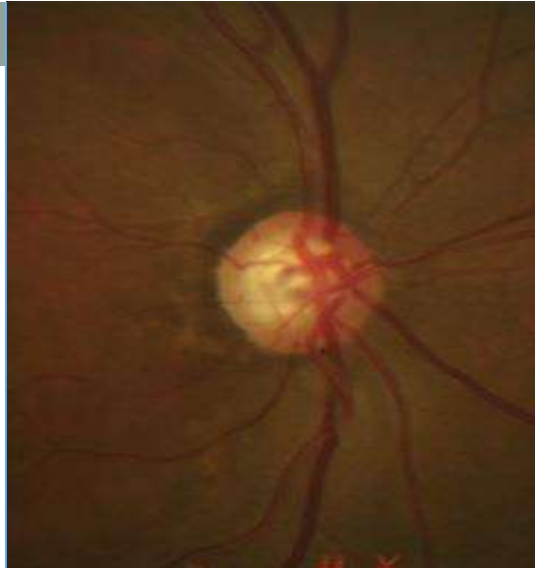


Source: Lewis RA, Levy B, Ramirez N, Kopczynski CC, Usner DW, Novack GD for the PG324-CS201 Study Group. Fixed-dose combination of AR-13324 and latanoprost: a double-masked, 28-day, randomised, controlled study in patients with open-angle glaucoma or ocular hypertension. Br J Ophthalmol 2015;0:1–6. doi:10.1136/bjophthalmol-2015-306778

Vesta: 61 y/o Haitian 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

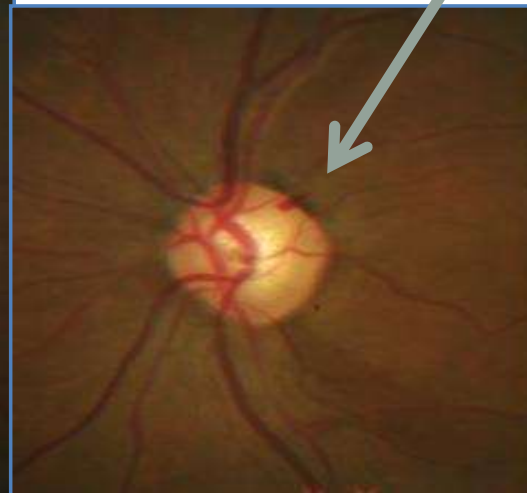
2010



What's This???



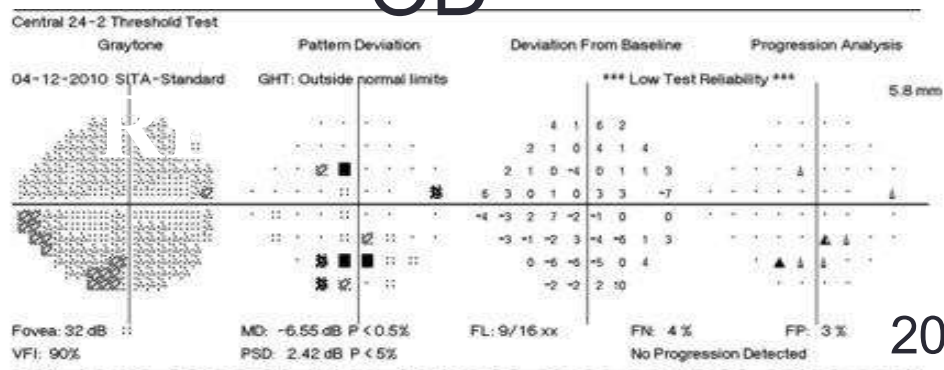
2012



OD

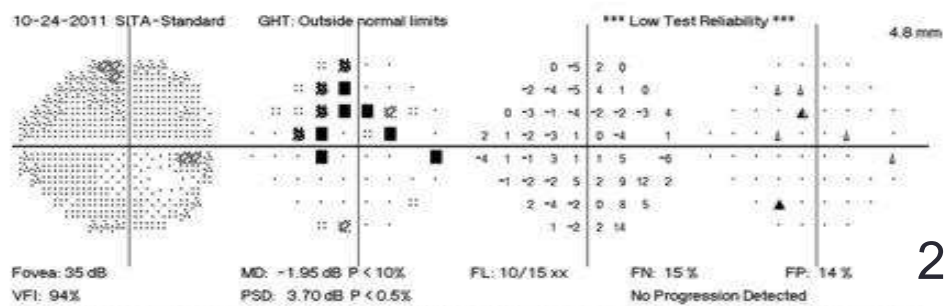
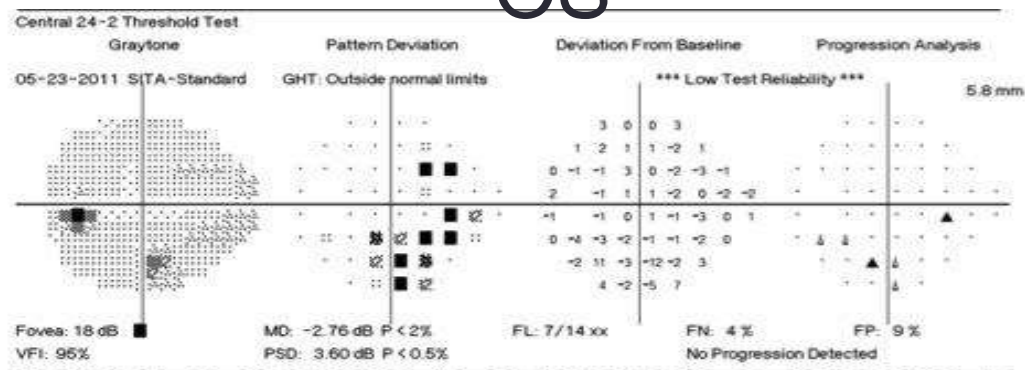
OS

OD

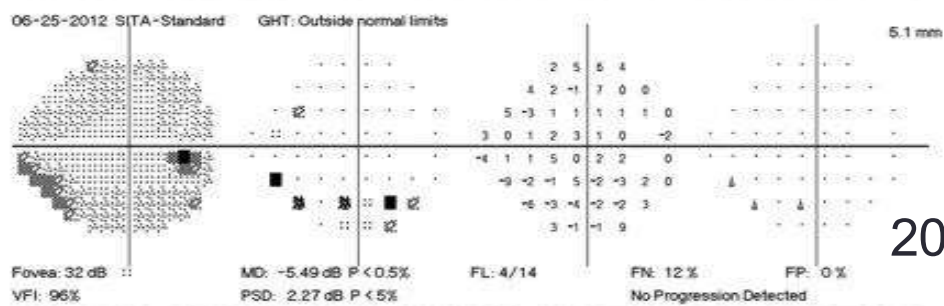
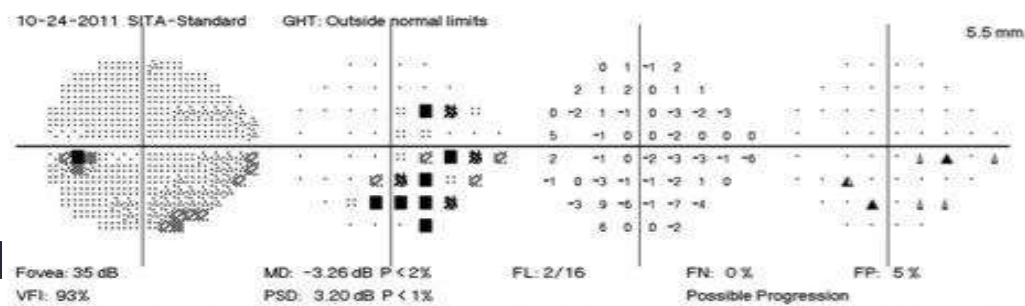


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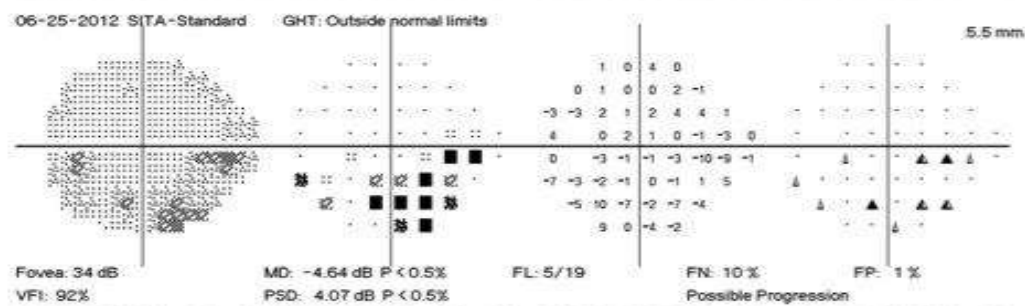
OS



2011

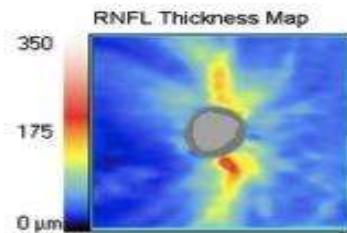


2012

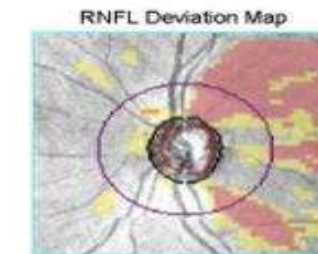
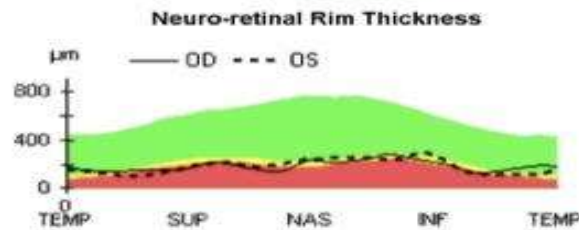
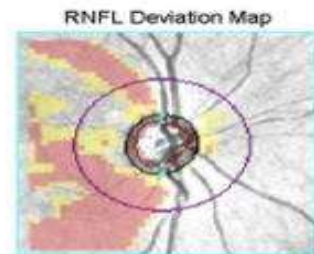
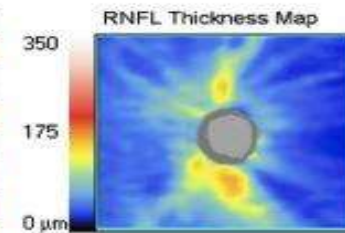


ONH and RNFL OU Analysis: Optic Disc Cube 200x200

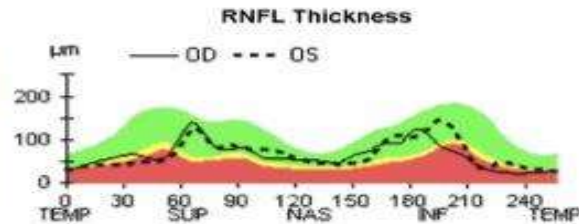
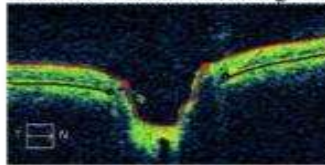
OD ● OS



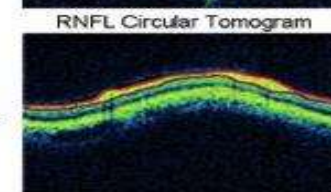
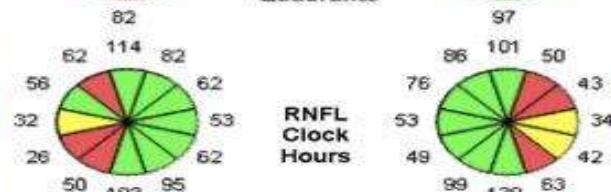
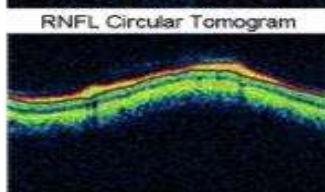
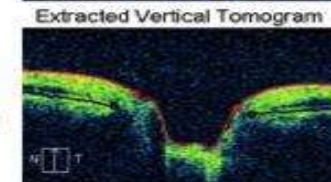
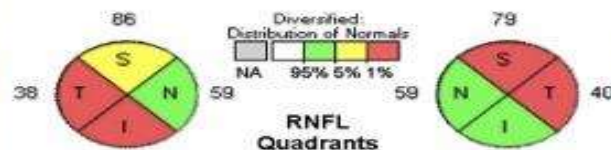
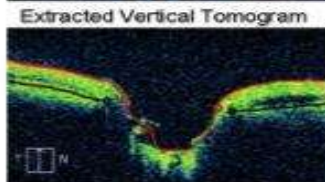
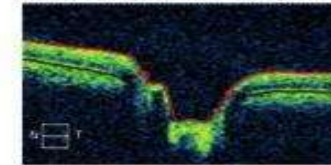
	OD	OS
Average RNFL Thickness	66 μm	69 μm
RNFL Symmetry	84%	
Rim Area	0.78 mm²	0.82 mm²
Disc Area	1.75 mm²	1.95 mm²
Average C/D Ratio	0.75	0.76
Vertical C/D Ratio	0.75	0.74
Cup Volume	0.452 mm³	0.447 mm³



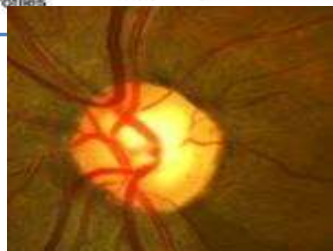
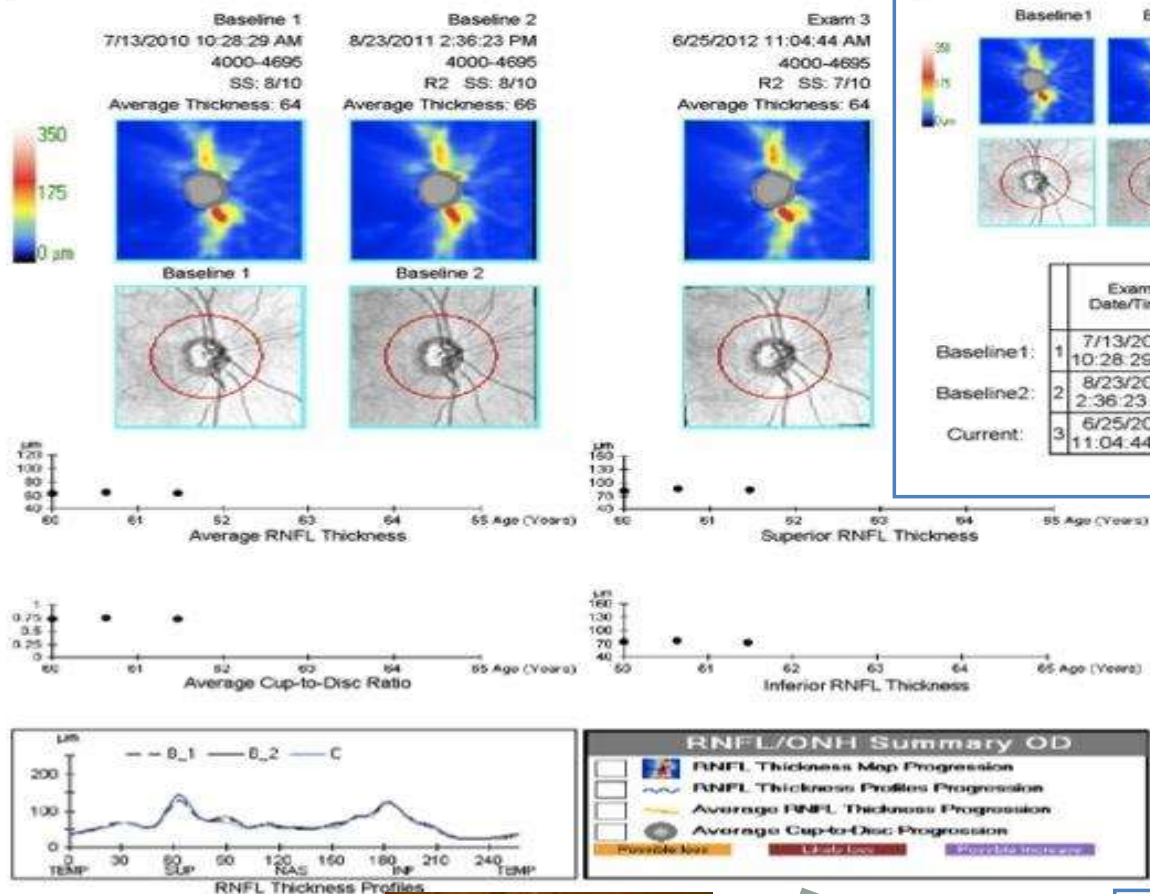
Disc Center (-0.15,0.03) mm
Extracted Horizontal Tomogram



Disc Center (0.00,-0.09) mm
Extracted Horizontal Tomogram

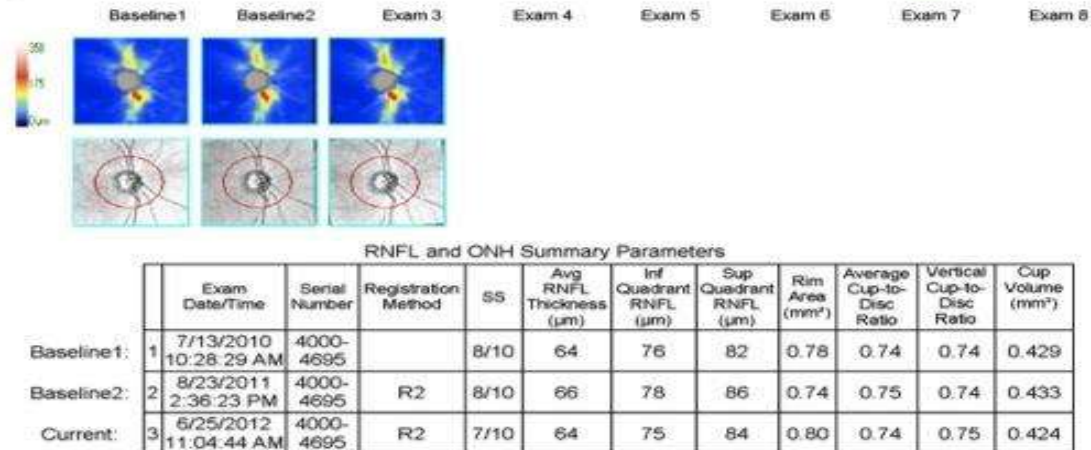


Guided Progression Analysis: (GPA™)



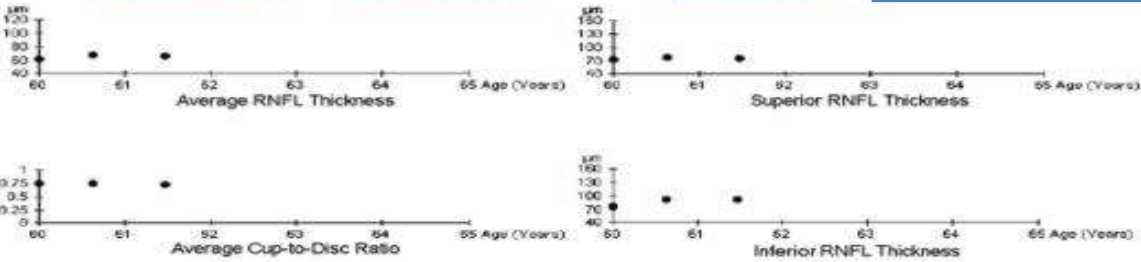
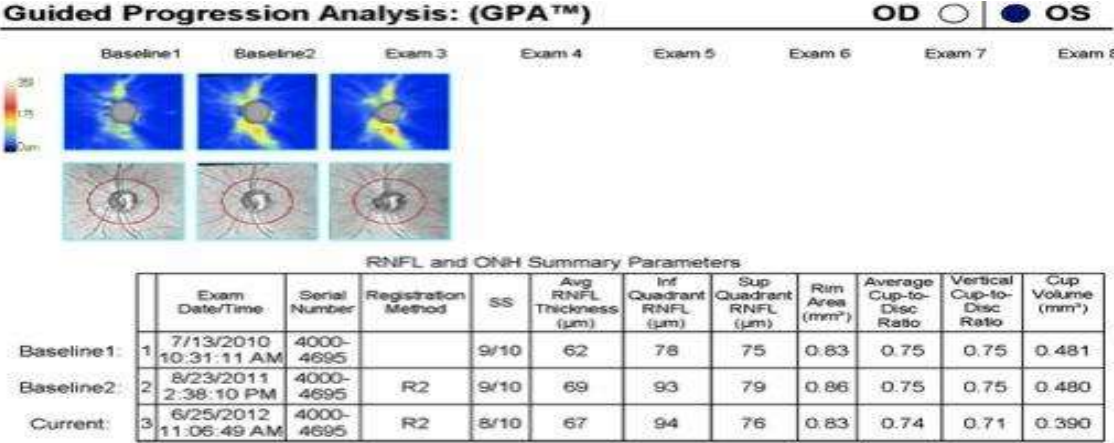
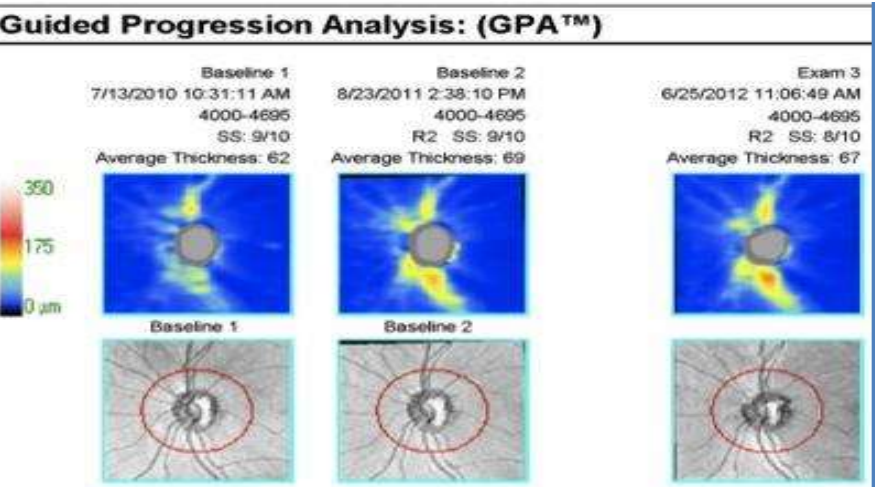
Guided Progression Analysis: (GPA™)

OD ● OS ○



GPA Progression
Analysis OD





GPA Progression Analysis OS



Vesta: 61 y/o Hatian Female

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

Vesta: 61 y/o Haitian 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
 - PCIOI 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

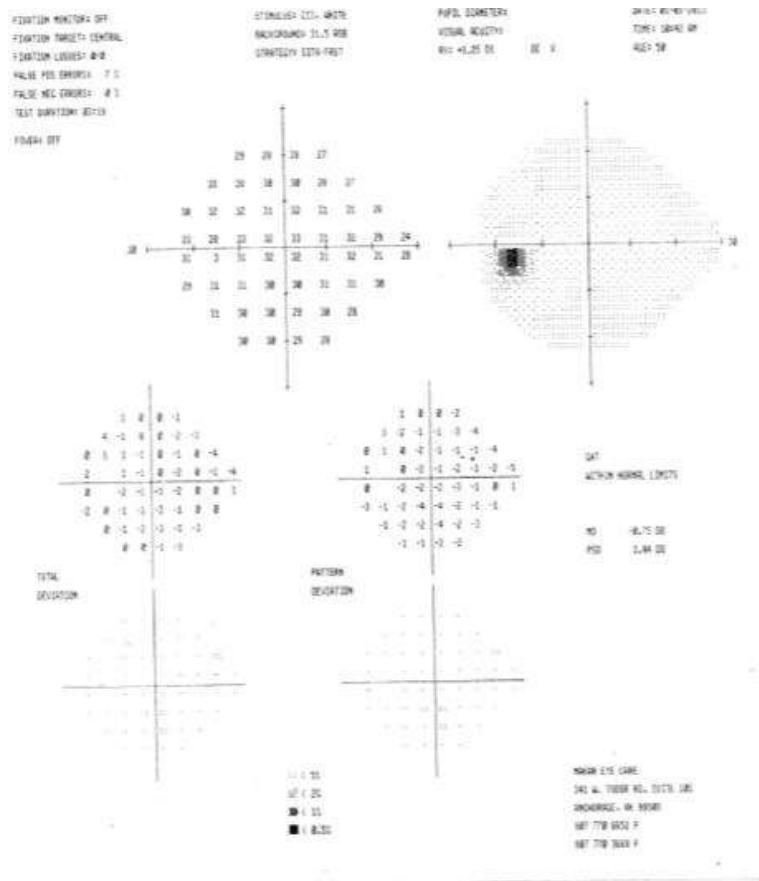


OS

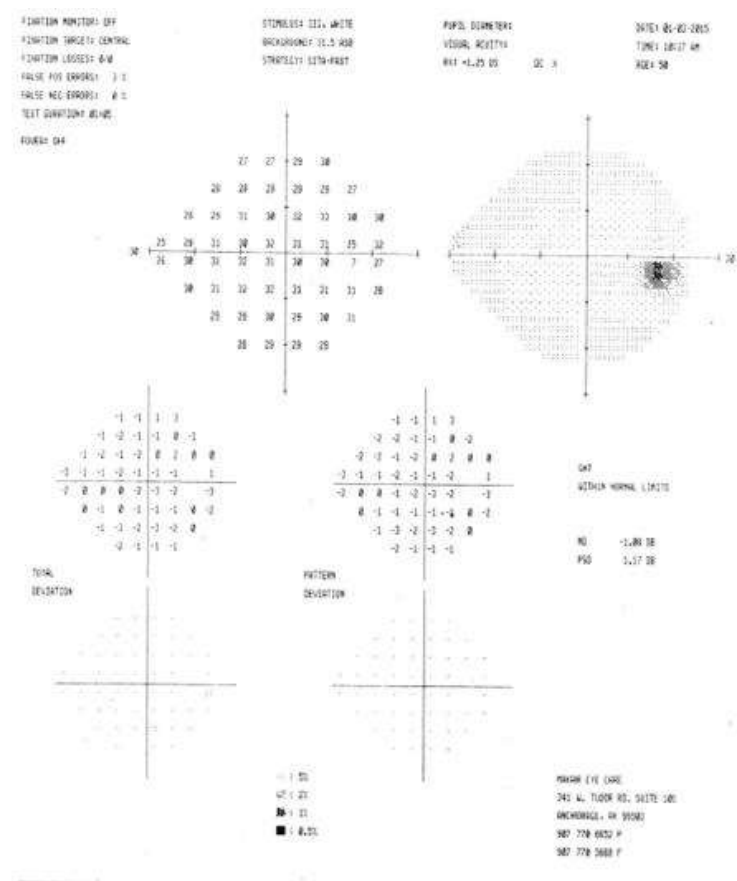


OD

Visual Fields

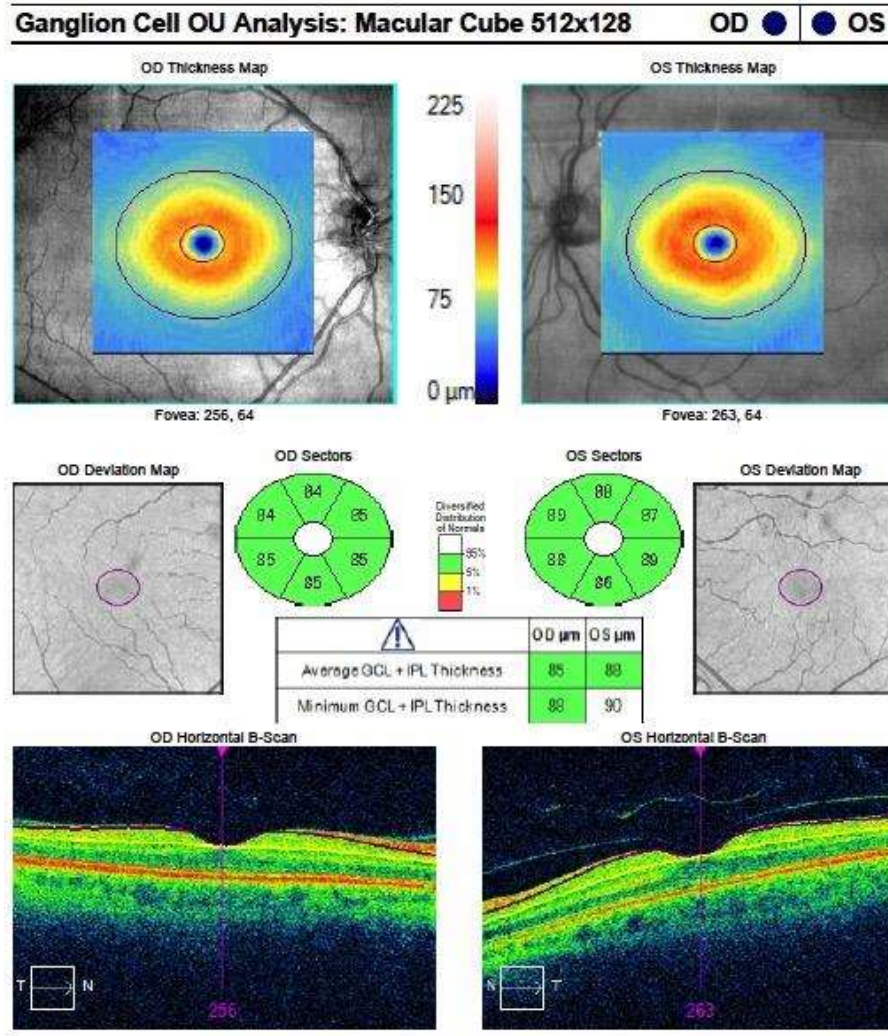


OS



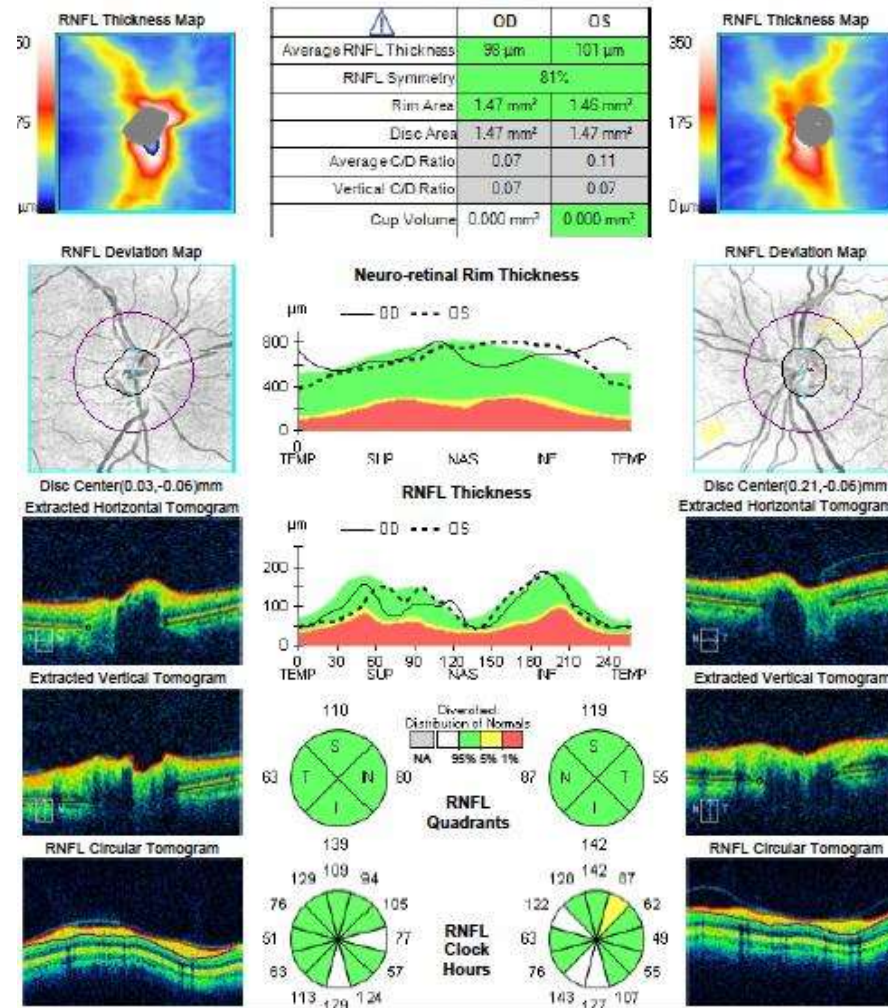
OD

Ganglion Cell Analysis



RNFL and ONH Analysis

ONH and RNFL OU Analysis: Optic Disc Cube 200x200 OD ● OS ●



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