

Open Angle Glaucoma in the Primary Care Practice

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Financial Disclosures

None

Glaucoma at a Glance

- Definition of glaucoma has evolved...
- Progressive, irreversible optic neuropathy caused by retinal ganglion cell and nerve fiber loss which together lead to visual field loss and, ultimately, blindness
- Affects 70 million people worldwide and about **3 million in the US** - growing quickly as demographics change.
- The leading cause of irreversible blindness
- 70% of glaucoma is OAG (up to 50% of that is NTG)

Proposed Mechanisms for the Pathophysiology of OAG:

- **Biomechanical** - elevated IOP* causes laminar bowing which crushes axons passing through its fenestrations and impedes perfusion
- **Vascular** - vascular dysregulation and poor oxygenation due to reduced perfusion creates ischemia; believed to be non-pressure dependent (NTG)
- **Genetic** - genetically predisposed individuals have accelerated apoptosis (a form of programmed cell death) of ganglion cell axons

Phil's Four Step Process of Diagnosing Glaucoma

1. Assess the Risk
2. Assess the Disc
3. Assess the Structure
4. Assess the Function

1. Assessing the Risk

Non-Ocular Risk Factors

- **Fam Hx – 10X** (parent, sibling, child)
- **Age – 6X** (60 vs 40)
- **Race – 5X** (Hispanic/AA)
- **HTN – 1.5X**
- **DM – 1.5X**
- **Migraine, Raynaud's 1.25X**
- **Obstructive Sleep Apnea**
- **Hypotension***

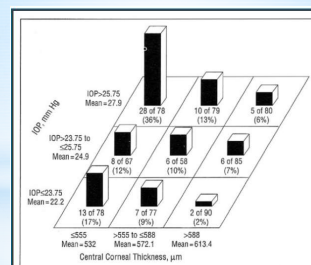
Assessing the Risk

Ocular Risk Factors

- IOP
- Central Corneal Thickness (CCT)
- Corneal Hysteresis (CH)
- Ocular Perfusion Pressure (OPP)

Ocular Risk Factors

- IOP
- Central Corneal Thickness (CCT)



Ocular Risk Factors

- CCT – IOP interplay
 - ❖ Mean CCT of 532 is **6X the risk** of CCT of 613
But normal CCT ranges from 450 μm to 650 μm
 - ❖ CCT of 500 μm with an IOP of 20 has **over 2X the risk** CCT of 600 μm with an IOP of 30!

Ocular Risk Factors

- IOP
- CCT
- Corneal Hysteresis (CH)
 - ❖ Uses a fixed air jet to measure the pressure required to flatten and reform the cornea
 - ❖ Attempts to measure the cornea's ability to absorb IOP – like a shock absorber – and estimates the IOP the eye is experiencing.
 - ❖ CH is often asymmetric (unlike CCT) - this may help explain the asymmetric nature of glaucoma and allow us to treat each eye as a unique entity.

Corneal Hysteresis (con'd)

- ❖ Is 1-2 mmHg lower in glaucoma patients
 - < 10 mmHg in glaucoma patients
 - > 10 mmHg in normal patients
- ❖ Is more strongly associated with structural and functional changes in glaucoma compared to CCT
- ❖ Has been shown to predict glaucoma progression better than CCT
- ❖ Has been shown to predict response to glaucoma therapy more strongly than CCT...

Ocular Risk Factors

- IOP
- CCT
- CH
- Ocular Perfusion Pressure
 - An interplay between systemic BP and IOP
 - Essentially systemic BP less IOP
 - A diastolic OPP of less than 50 mmHg is considered to increase the risk and progression of glaucoma
 - Thought to be the mechanism in NTG

Ocular Risk Factors

- IOP
- Central Corneal Thickness (CCT)
- Corneal Hysteresis (CH)
- Ocular Perfusion Pressure (OPP)
- **Myopia**
 - Low myopia (1-3 Diopters) – 2X
 - Moderate myopia (3-5 Diopters) – 3X
 - High myopia (6+ Diopters) – 6X

1. Assess the Risk
2. Assess the Disc

Assessing the Disc

- **Size** : CD ratio
 - Large - must account for DD
 - Vertical elongation
- **Depth** : Laminar dots/depth
- **Focal notching** - typically will be superior or inferior and more often temporal
- **ISNT rule** - Inf and Sup should be 1.5-2X temp
- **Vessel baring, bayoneting, nasalization**
- **Drance heme**
- **Beta zone atrophy**
- **NFL wedge defect**
 - Follows contour of NFL (arcuate)
 - Allows for greater visibility of choroidal vasculature

Optic Nerve Features in Glaucoma

Break it down: **CRVO**

Vertical Disc Diameter and Expected CD Ratio

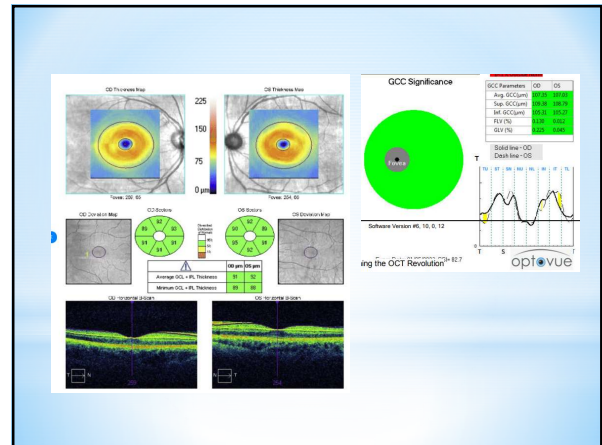
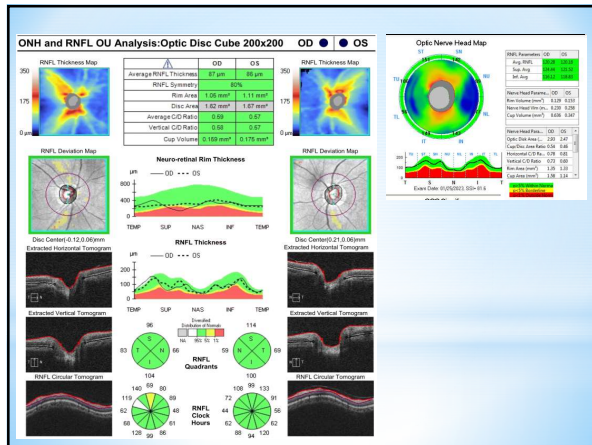
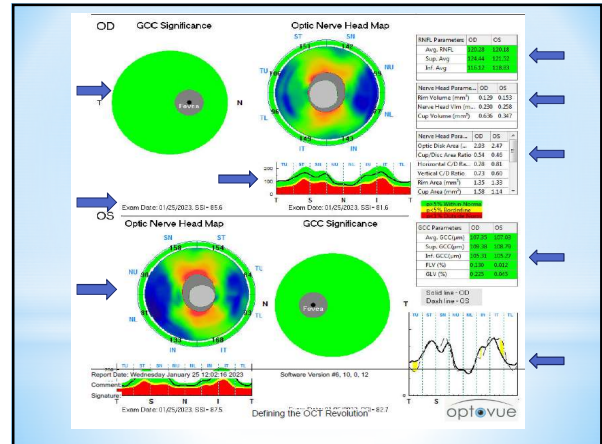
Disc Mean Upper Diameter	C/D	Limit
Small 1.0mm to 1.3mm	0.35	0.55
Medium 1.4mm to 1.7mm	0.45	0.65
Large 1.8mm to 2.0mm	0.55	0.75

Average VDD is largest in AAs and Hispanics

1. Assess the Risk
2. Assess the Disc

3. Assess the Structure: OCT Imaging in Glaucoma

- ❖ Peripapillary NFL thickness
- ❖ Ganglion Cell Complex thickness
 - First detectable sign of glaucomatous damage
 - FLV believed to be the earliest indicator
 - Less variable than RNFL thickness



Normal Peripapillary NFL thickness?

- ❖ Follows ISNT rule: 125/120/75/70
- ❖ Wide range of normal (0.75 – 1.5 million fibers)
- ❖ Means green isn't always normal – must use your head!

Making Sense of OCTs

- Look for ipsilateral and contralateral asymmetry
 - Special attention on ST and IT rims
- Should be consistent with disc assessment
- Must consider non-glaucomatous causes: vein occlusions, ischemia, AION, papilledema, optic disc drusen or pit, anomalous discs, macular disease, high myopia

Hodapp-Parrish-Anderson (HPA) Criteria for Establishing a Glaucomatous Defect

On two consecutive fields must have:

1. **GHT** outside normal limits; OR
2. **PSD** of P<5%; OR
3. **Cluster of 3 non-edge***, typical glaucoma points all of which are depressed on the PSD plot at P<5%, and one of which is P<1%

HPA Criteria for Early, Moderate and Severe Field Loss

Minimum criteria for diagnosing acquired glaucomatous damage
 A Glaucoma Hemifield Test outside normal limits on at least two fields; OR
 A cluster of three or more non-edge points in a location typical for glaucoma, all of which are depressed on the pattern deviation plot at a p<5% level and one of which is depressed at a p<1% level on two consecutive fields; OR
 A corrected pattern standard deviation that occurs in less than 5% of normal fields on two consecutive fields

Classification of defects

Early defect:

- MD less than -6 dB
- Less than 25% of the points (18) are depressed below the 5% level and less than 10 points are depressed below the 1% level on the pattern deviation plot
- All point in the central 5° must have a sensitivity of at least 15 dB

Moderate defect:

- MD less than -12 dB
- Less than 50% of the points (37) are depressed below the 5% level and less than 20 points are depressed below the 1% level on the pattern deviation plot,
- No points in the central 5° can have a sensitivity of 0 dB
- Only one hemifield may have a point with sensitivity of <15 dB within 5° of fixation

Severe defect (any of the following results):

- MD greater than -12 dB
- More than 50% of the points (37) are depressed below the 5% level or more than 20 points are depressed below the 1% level on the pattern deviation plot
- At least one point in the central 5° has a sensitivity of 0 dB
- Points within the central 5° with sensitivity <15 dB in both hemifields

AAO Glaucoma Stage Definitions

- Mild** - Optic nerve abnormalities consistent with glaucoma but:
NO VF ABNORMALITIES on any test
- Moderate** - Optic nerve abnormalities consistent with glaucoma and:
VF ABNORMALITIES:
 IN ONLY 1 HEMIFIELD and
 OUTSIDE CENTRAL 5 DEGREES
- Severe** - Optic nerve abnormalities consistent with glaucoma and:
VF ABNORMALITIES:
 Involving BOTH HEMIFIELDS or
 INSIDE CENTRAL 5 degrees

AAO Moderate Glaucoma

AAO Severe Glaucoma

Table 4 Modified glaucoma staging system

Stage	Criteria
Stage 0 (no defect stage)	Does not meet the three criteria for minimal glaucomatous abnormality: pattern deviation probability plots with <5 % more than three of which are contiguous and one of which is <1 %; corrected pattern standard deviation or pattern standard deviation significant at p < 0.05; or glaucoma hemifield test outside normal limits
Stage 1 (early)	82 % <= VFI
Stage 2 (moderate)	63 % <= VFI <= 81 %
Stage 3 (advanced)	43 % <= VFI <= 62 %
Stage 4 (severe)	23 % <= VFI <= 42 %
Stage 5 (end)	VFI <= 22 %

VFI visual field index

- ### Visual Fields Summary Points
- ❖ Understand what is a reliable field
 - Gaze tracking
 - Patterned defect
 - Normal reliability indices
 - ❖ Understand and recognize typical glaucomatous field defects
 - Nasal step, arcuate loss, central loss
 - ❖ Choose a staging system you're comfortable with
 - ❖ Know how to recognize and measure progression
 - Increased MD, decreased VFI - GPA
 - ❖ Know when progression prompts additional IOP reduction
 - Extrapolation line to VFI goal precedes life expectancy
 - ❖ Know how to estimate additional IOP lowering necessary
 - Extrapolation of required IOP reduction from GPA slope*

Determining IOP target based on GPA

1. Get GPA and consider life expectancy
2. Extrapolate acceptable reduced progression rate*
3. Determine new target IOP from IOP Progression table*
4. Address whether medical or surgical approach best

Key Points in Diagnosis and Data:

- o Use your head and proceed in an organized way:
 - Risk, Disc, Structure, Function
- o Asymmetry is a key feature of glaucoma
- o Respect the power of prediction - software lacks this important dimension of clinical assessment.
- o Software assessment of "WNL" doesn't have all the info we have.
- o Be careful not to overestimate the significance of one field
- o Low reliability isn't always unreliable
- o Green is not always good, red is not always bad
- o Abnormal is not always glaucoma

71 YO WF - Sandra

- Using Trav Z HS OU and wants to know if she really needs to take drops

Oc Hx: "glaucoma"
 Gen Hx - HLD;
 Fam Oc Hx: negative

Rx: -6.00

	GAT	CH	CCT	Gonio
OD	20	10.5	600	nml
OS	22	11.0	625	nml

	On Travatan Z HS OU		Untreated	
	GAT	CH	GAT	CH
OD	20	11.4	33	10.0
OS	22	11.4	34	10.3

- Treat, observe or refer?
- What's the basis for your decision?

Jessica - 32 YO HF
 Oc Hx - normal; -2.00 Myope
 Gen Hx - normal
 Fam Oc Hx - normal

	GAT	CH	CCT	Gonio
OD	32	11.9	617	Nml
OS	40	11.9	625	Nml

- Treat, observe or refer?
- What's the basis for your decision?

Part 2: Treatment Considerations for OAG

In this section we will consider:

- Which landmark studies help guide us?
- How will we initiate treatment?
 - Medical - which agent(s)?
 - Surgical
- What is our target IOP?
- Ongoing treatment approaches
- When to refer for surgical management

Drugs that decrease Production

- **Timolol (Betimol)** - non-selective beta blocker
 - Efficacy - 25%
 - QD or BID, 0.25% or 0.50%
 - SEs/CI's - asthma, COPD, hypotension, fatigue, decreased libido, depression, bradycardia, CHF, athletes
 - NTG?
- **Brimonidine (Alphagan P)** - adrenergic agonist
 - Efficacy 20+%; BID or TID (all FDC are BID)
 - Unique - Also increases outflow via uveoscleral route
 - SEs Allergy, itching, dryness, hyperemia, fatigue
 - Contraindicated with MAOIs (antidepressants)
 - Isocarboxazid (Marplan)
 - Phenelzine (Nardil)
 - Selegiline (Emsam)
 - Tranylcypromine (Parnate)
- **Dorzolamide (Trusopt)** - CAI
 - Efficacy - 20% used TID
 - SEs include bad taste; fatigue; ?sulfa allergy, tinnitus?
 - Contraindicated with corneal edema risk (Fuch's)

Drugs that increase Outflow

- **PGA's**
 - Efficacy - 30% (primarily uveoscleral - some TM)
 - Only class to reduce PM IOP significantly
 - SEs - hyperemia, darkening of iris (hazel), periorbital darkening, lid ptosis/inf exposure, enophthalmus
- **Vyzulta** - latanoprost bunod - converts to latanoprost and butanediol(NO donating) intraocularly;
 - Efficacy - 35% Increases both TM and uveoscleral outflow
 - SEs - hyperemia
- **Rhopressa - Netarsudil** - rhokinase inhibitor
 - Efficacy similar to timolol through combination of increased TM outflow and decrease EVP/reduction of production. Question of neuroprotective component
 - SEs - significant hyperemia (53%), corneal verticillata and petechial conj hemes (20%)
- **Rocklatan** - latanoprost +netarsudil
 - Efficacy 30+% - More effective than latanoprost or Netarsudil - especially at **lower target pressures**
 - SEs - 60% hyperemia, corneal verticillata

Case 1: Bob - Con'd
 60 YO WM presents for 2nd opinion re: "glaucoma"
 General history -HTN, HLD
 Family ocular history - "My dad has glaucoma and macular degeneration"
 Rx + 1.00

	GAT	CH	CCT	Gonio
OD	28	9.8	592	nml
OS	32	8.4	555	nml

Month	Treatment		IOP		
	OD	OS	OD	OS	
2013	May	X	X	25	27
	August	X	X	24	27
	November	X	X	26	28
2014	May	X	X	26	27
	November	X	X	28	32

- Who would decide to treat at this point?
- OD or OS or both?
- How...medical or surgical?
- What would your target pressure be?

OHTS - Ocular Hypertension Treatment Study

5 year Data

- Lowering IOP 20% in those with OcHTN reduced the risk of developing glaucoma more than 50% (from 9.5% to 4.4%)

20 Year Data

- Incidence of POAG was
 - 49% among untreated patients
 - 42% among treated patients
 - 55% AAs vs 42% other races
 - Incidence by risk: low-32%, medium-48% high risk-60%
- Incidence of VF loss was 25%

LIGHT - Laser in Glaucoma and OcHTN Trial

- Compared SLT vs meds for initial treatment and found them comparable
- Repeat SLT nearly as effective

CIGTS - Collaborative Initial Glaucoma Treatment Study

Compared bleb vs meds for initial tx

- Patients with mild glaucoma did equally well, while patients who presented with advanced disease did better with surgery
- AAs and diabetics did worse with surgery
- Significant risks of cataract formation (requiring surgery) and endophthalmitis

Finally, back to Bob...

	GAT	CH	CCT	Gonio
OD	28	9.8	592	nml
OS	32	8.4	555	nml

Month	Treatment		IOP		
	OD	OS	OD	OS	
2013	May	X	X	25	27
	August	X	X	24	27
	November	X	X	26	28
2014	May	X	X	26	27
	November	X	X	28	32

Assuming you've decided to treat, how would you proceed?

Value of a Monocular Trial

Untreated IOPs

OD	21	18	24
OS	25	23	28

Treated OU Possible Results and Conclusions:

OD	21	There is no valid conclusion regarding efficacy! This could represent success or failure.
OS	25	
OD	18	There is no valid conclusion regarding efficacy! This could represent success or failure.
OS	23	
OD	16	Efficacy likely demonstrated but by an unknown amount
OS	20	

Value of a Monocular Trial

Untreated IOPs

OD	21	18	24
OS	25	23	28

Treated OS only Possible Results and Conclusions:

OD 21 Conclusion that there was no efficacy is valid as inter-eye IOP differential is unchanged from pretreatment IOPs.

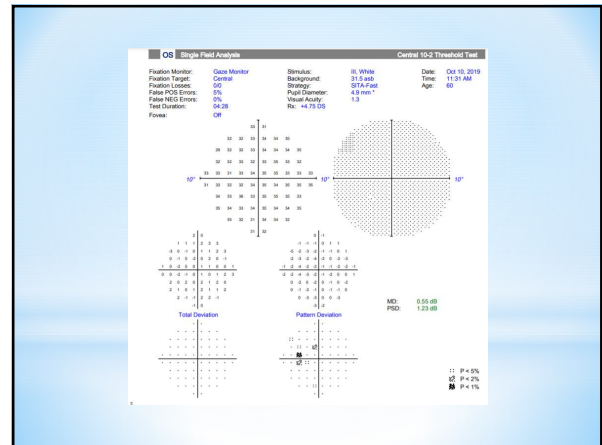
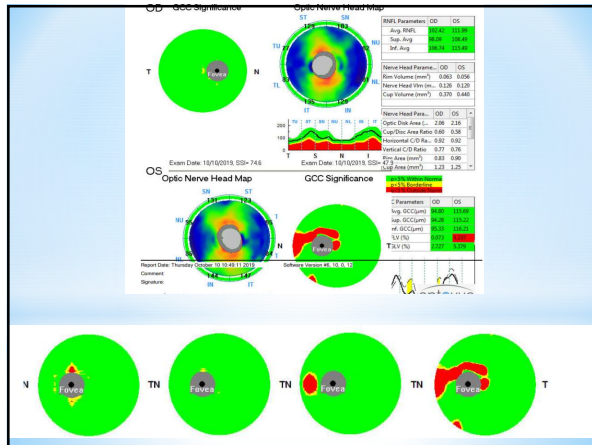
OS 25 Again, the logical conclusion is that there was no efficacy as IOP differential is unchanged from untreated baseline.

OD 18 Logical conclusion is twofold: Since the IOP lower than expected there was efficacy; and secondly, the efficacy was -26%

OD	18
OS	23

OD	18
OS	17

		Treatment		IOP	
		OD	OS	OD	OS
2013	Month				
	May	X	X	25	27
	August	X	X	24	27
2014	Month				
	May	X	X	26	29
	November	X	X	28	32
	December	X	Lumigan	24	20



Based on OCT and field I elected to add timolol* OS...

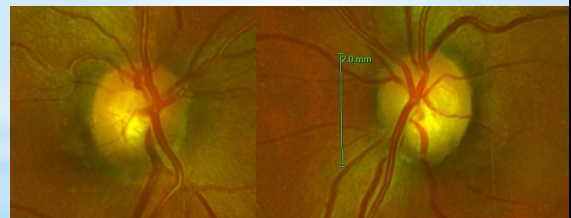
2019	Dec	Lat	L + T	24	18
2020	April	Lat	L + T	22	17
	October	Lat	L + T	24	19

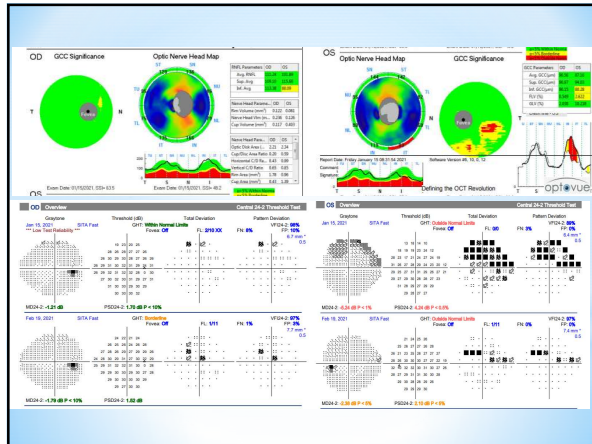
So where are we? $18/27 = 0.67$ which is a 33% drop - Is that good enough? Time, CH, OCT and VFs will tell

Thoughts for next step medical step if pressures rise or if there's progression?

62 YO HF - Maria
 Oc Hx - normal
 Gen Hx - HTN, depression
 Fam Hx - normal
 Rx -3.00

	IOP	CH	CCT	Gonio
OD	21	8.0	533	nml
OS	26	8.5	527	nml





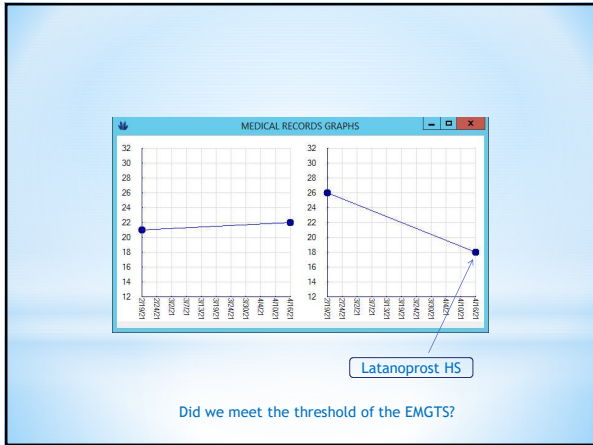
EMGT - Early Manifest Glaucoma Trial

Treated patients with early VF changes to achieve a 25% reduction in IOP

- Reduced risk of progression 50%
- Reduced the risk of progression 10% for each mmHg of IOP reduction
- Systolic OPP \leq 125 mmHg predicted progression

REDUCTION OF PERIMETRIC RATE OF PROGRESSION WITH IOP LOWERING		
Decrease in Intraocular Pressure	Assuming Linearity	Assuming Nonlinearity
1 mm	12%	12%
2 mm	24%	23%
3 mm	36%	32%
4 mm	48%	40%
5 mm	60%	47%
6 mm	72%	53%
7 mm	84%	59%
8 mm	96%	64%

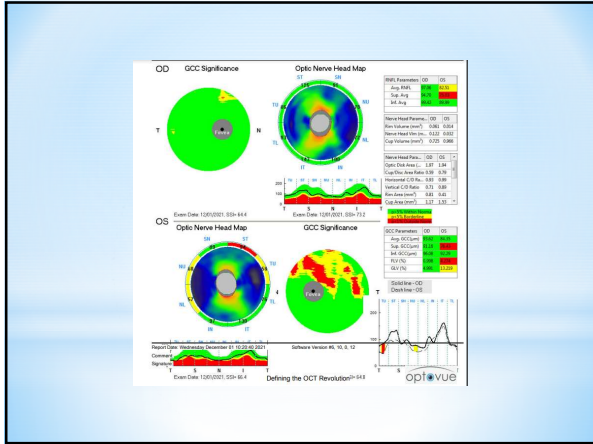
Table 9-1
This table assumes that the rate of perimetric progression (RoP) decreases 12% per mm of decrease in intraocular pressure, which is the median rate found in four large clinical trials.^{14,16,19,20} The middle column assumes a 12% reduction of the initial RoP for every mmHg of IOP lowering, while the right-hand column assumes that each incremental millimeter of pressure reduction reduces the remaining RoP by 12%.

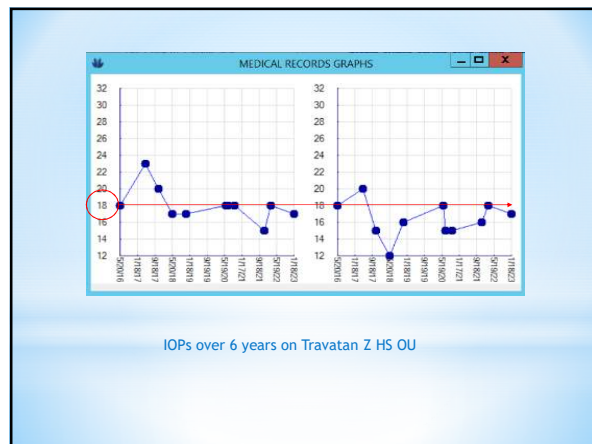
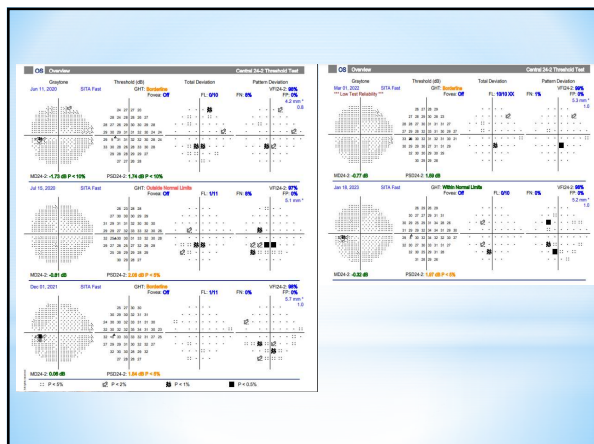


AJ "I forget my drops sometimes"
68 YO AAF
Gen Hx: T2DM(metformin), HTN(atenolol), brain aneurism, COPD, RA
Oc Hx: POAG Rx: plano
Fam Oc Hx: cataract

	Tmax	CH	CCT	Gonio
OD	24	11.1	565	Normal
OS	26	9.5	560	Normal

The figure shows two fundus photographs of the optic nerve head. The left image shows a normal optic nerve head with a vertical scale bar of 1.8 mm. The right image shows a slightly larger optic nerve head with a vertical scale bar of 2.0 mm.



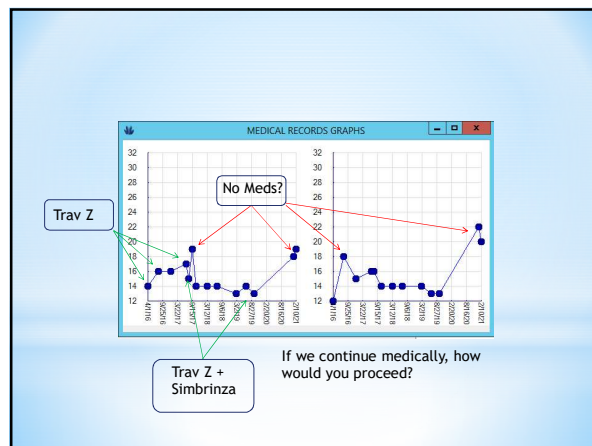
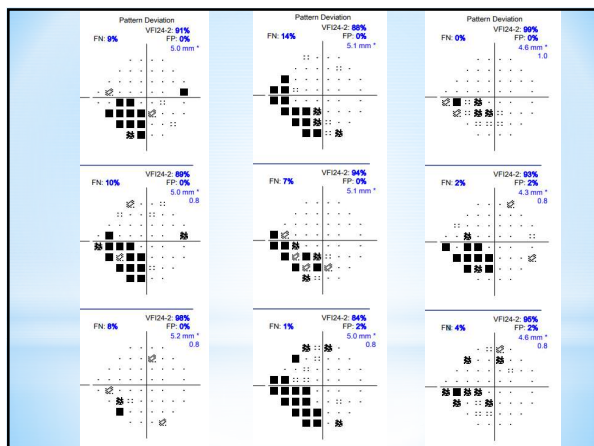
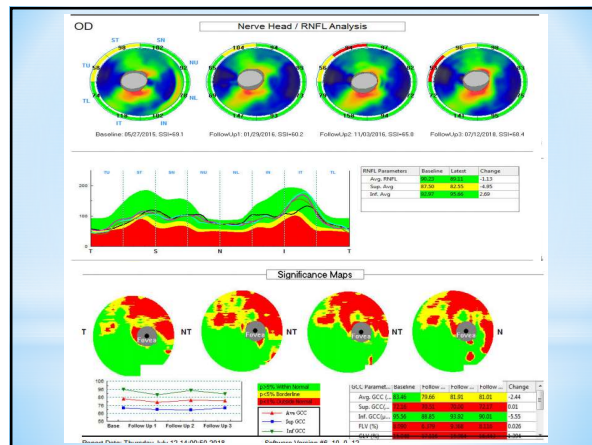


IOPs over 6 years on Travatan Z HS OU

66YO AA F Janice
 General health history -HTN, HLD, GERD
 Ocular history - normal
 Family ocular history - normal

Rx - plano OU

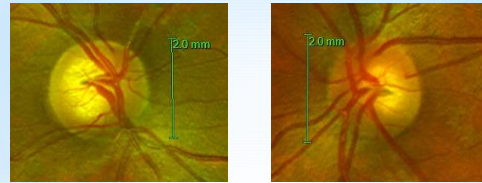
	GAT	CH	CCT
OD	22	10	560
OS	22	08	570



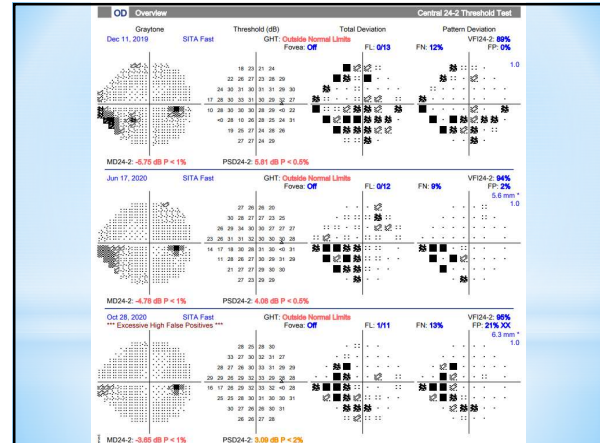
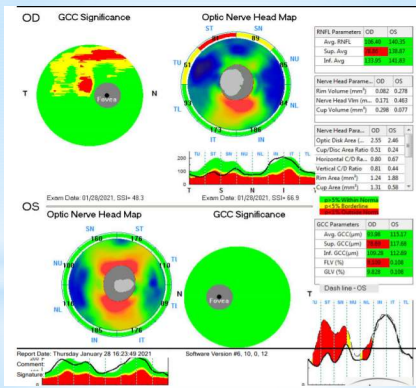
- 34 YO HF Low Rider
- General Health history - migraine
 - Ocular history - negative
 - Family ocular history - negative
 - -1.75 sph OU

	GAT	CH	CCT	Gonio
OD	20	9.2	530	nml
OS	18	10.3	534	nml

Assess the Disc - CRVO



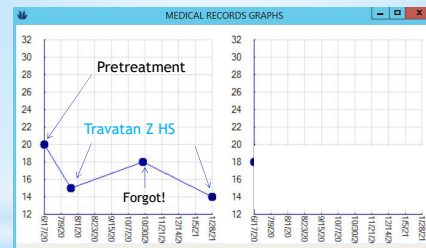
Assess the Structure



■ CNTGS - Collaborative Normal Tension Glaucoma Treatment Study

- Demonstrated a lower rate of progression with a 30% reduction of IOP
- Factors independent of IOP lead to progression
 - Women
 - Migraine
 - Disc(Drance)heme

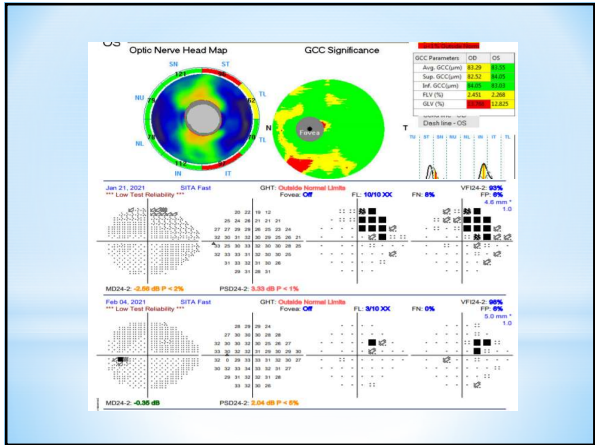
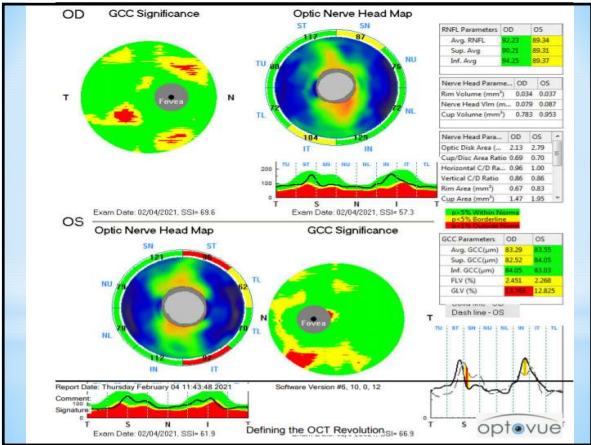
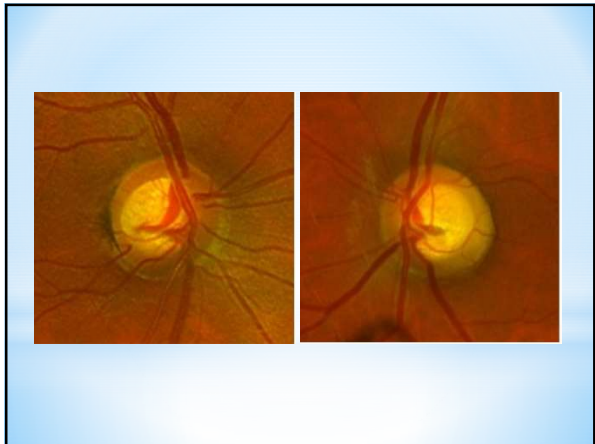
Given advanced nature of loss (centrality) RF and patient age I elected to begin a monocular trial OD and set a low target IOP.



	Baseline IOP-CH	Treated IOP-CH
OD	20 = 9.2	14 = 10.4
OS	18 = 10.3	NA

Mr. Big Man
 59YO WM in for routine exam
 Ocular history - glaucoma suspect
 General health - OSA, Seizures*
 Family ocular history - none
 Refractive error: +1.00

	GAT	CH	CCT
OD	20	9.5	535
OS	21	9.5	540



Pretreatment IOP average

	TA
OD	20
OS	21

Treatment initiated with timolol 0.25% qAM OS

	TA
OD	23
OS	15

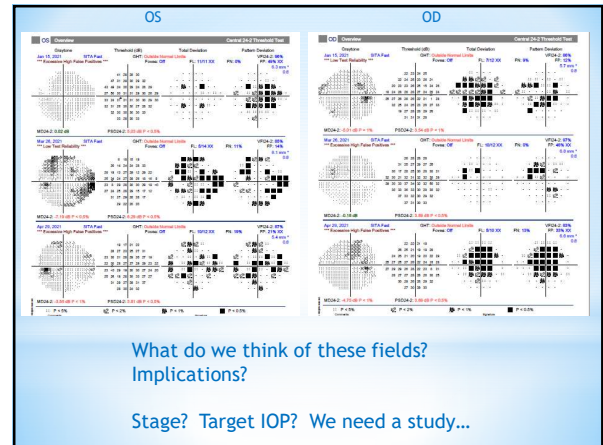
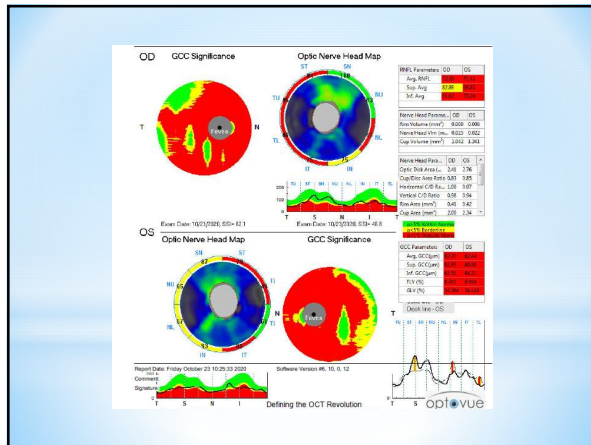
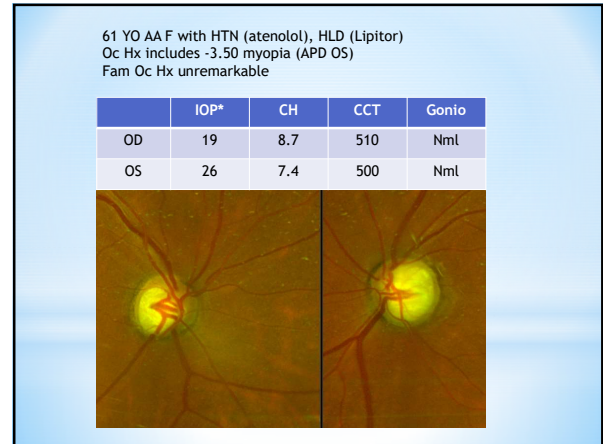
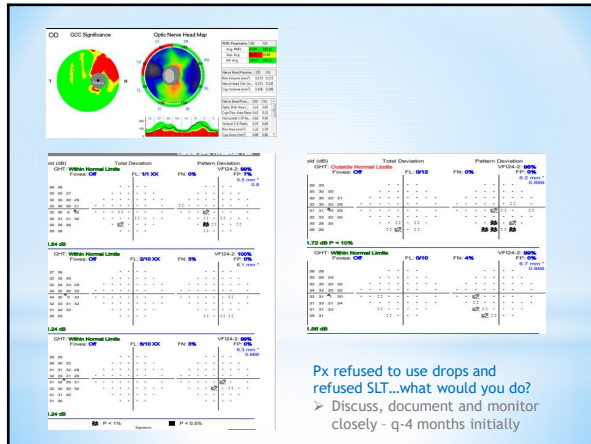
What's the approximate efficacy?
 $21+3=24$; $24-15=9$; $9/24=37.5\%$

Is that good enough?

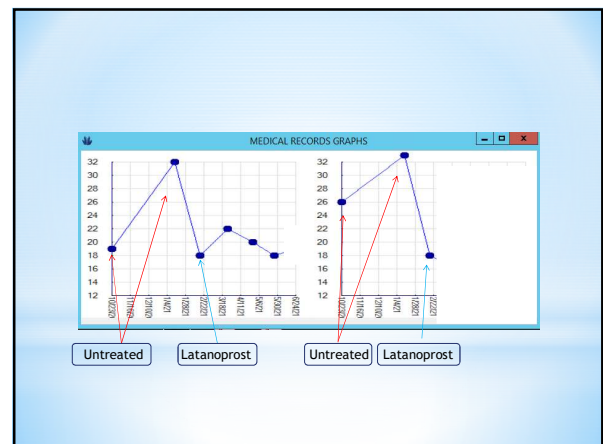
59 YO AA F - Stephanie

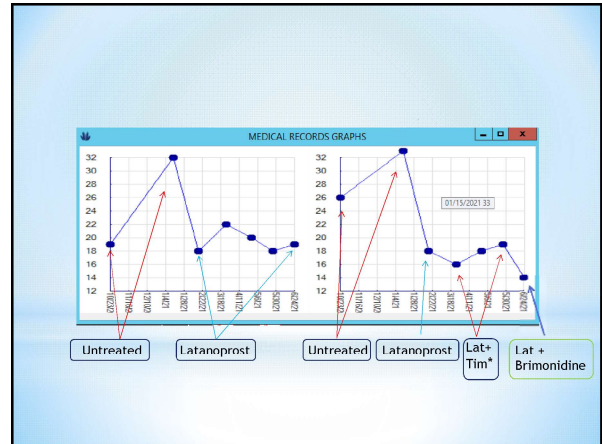
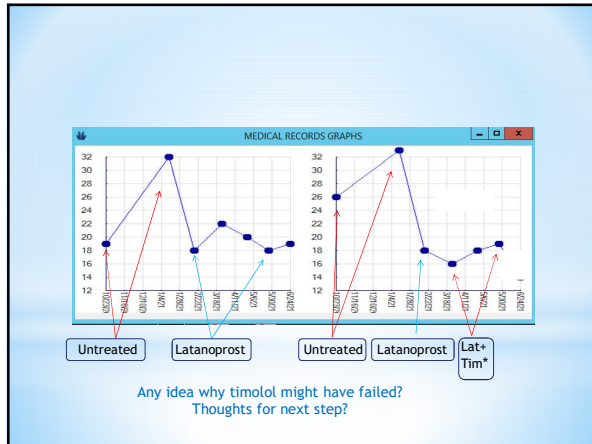
- General health history - DM 18, Hypertension, Smoker, RA, MHD, Seasonal Allergies, HLD
- Ocular history - negative
- Family ocular history - negative
- 1.25 myope

	GATs	CH	CCT	Gonio
OD	21	10.5	495	nml
OS	20	10.5	495	nml



- AGIS - Advanced Glaucoma Intervention Study
- An average IOP greater than 17.5 mm Hg had significant worsening of visual field progression compared with an IOP of less than 14 mm Hg
 - Eyes observed at 100% of follow-up visits to have an IOP of less than 18 mm Hg over 6 years had essentially no change in visual field deterioration
 - Eyes with an IOP of less than 18 mm Hg at fewer than 50% of visits had significant field deterioration





- ### Proposed Glaucoma Surgical Referral Protocols
- o Intolerance or noncompliance with drops
 - o Noncompliance with appointments
 - o Px prefers SLT
 - o Inability to achieve target pressure despite maximal meds- my personal limit is QJD: BB in AM, Simbrinza BID, and PGA (Vyzulta, Rocklatan) HS
 - o Progressive field loss despite normally adequate IOP
 - o Severe POAG in at least 1 eye*
 - o Advanced, moderate OAG OU in a patient <50*
 - o Px anticipating cataract surgery(consider MIGS)

Natty Dread - 72 YO AAM
Oc Hx - cataract
Gen Hx - HTN (HCTZ)
Fam Oc Hx - negative

Rx: -2.50

	GAT	CH	CCT	Gonio
OD	32	9.4	525	CBB P2
OS	38	9.4	535	CBB P2

