

Decisions in the Medical Management of Glaucoma

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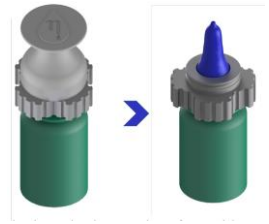
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Disclo\$ure

- Speakers Bureau for Aerie, Novartis, Allergan, Bausch & Lomb, Glaukos, Ivantis, Optovue, Reichert, Syntemed
- Investor: Nanodropper



When to Begin Treatment in Ocular Hypertensive Patients



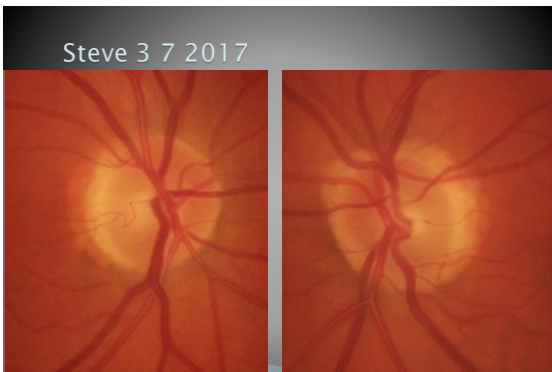
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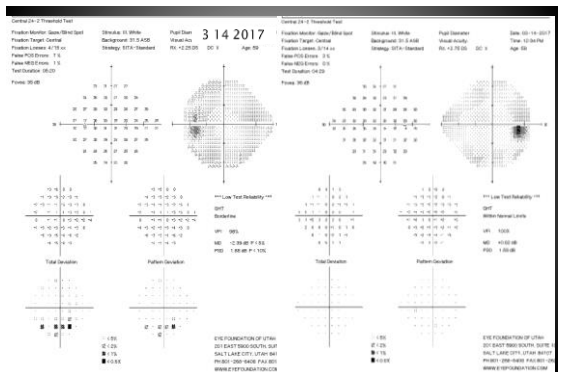
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Hypothetical Steve

- 60yo M
- VA sc OD 20/25 OS 20/30
- SLE Penetrating scar with retained metallic debris
 - From galvanized nail
- IOP R 23 L 25
- CCT R 550 L 545
- SLE Quiet OU

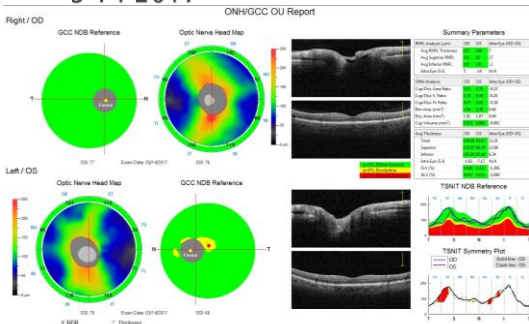


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3 14 2017



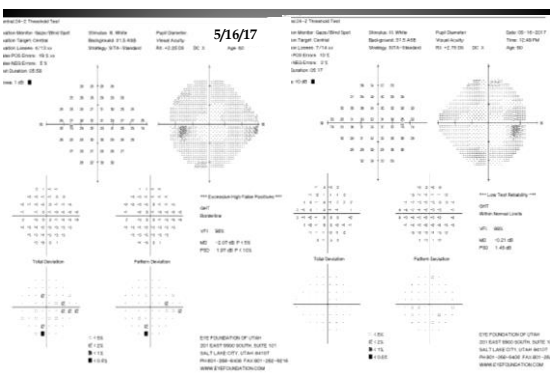
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What is your plan?

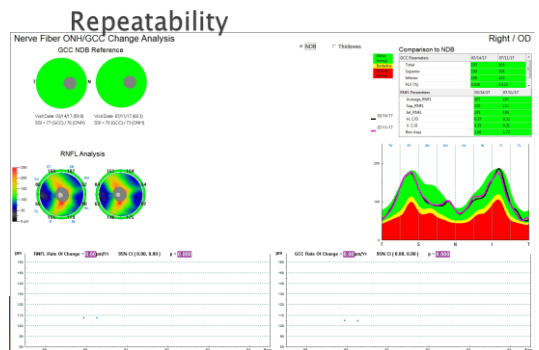
- 1. Follow indefinitely without treatment until definite damage occurs
- 2. Start treatment now



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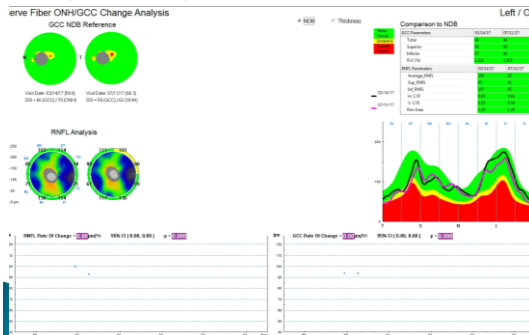


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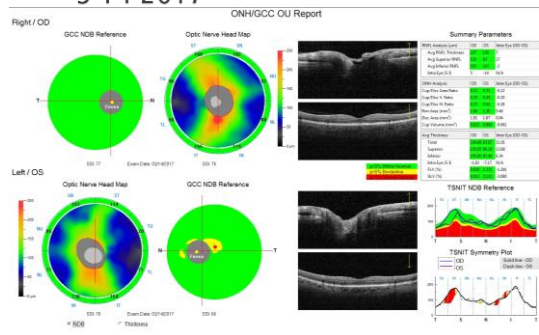
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Repeatability



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3 14 2017



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Risk Assessment

- ▶ IOP^{1,2}
- ▶ Central Corneal Thickness (CCT)^{1,2}
- ▶ C/D ratio¹
- ▶ Age^{1,2}
- ▶ Race²
- ▶ Family history²
- ▶ Corneal hysteresis²
- ▶ Ocular Perfusion Pressure (OPP)^{2,3,4,5,6}

1. Gordon MO et al Arch Oph. 2002; 120(10): 714-720
 2. Diagnosis of POAG pp 127-158 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications
 3. Tzielsch, Katz, Sommer, Quigley, Javitt. Arch Ophthalmol 1996;113:216-21
 4. Bonomi L, Marchini G, Maresella M et al. Ophthalmology 2000;107:1287-93
 5. Leske MC, Wu S-Y, Nemesure B, et al. Arch Ophthalmol 2002;120:954-9 Quigley HA, West SK, Rodriguez J, et al. Arch Ophthalmol. 2001;119:1819-26

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Ocular Hypertension Treatment Study

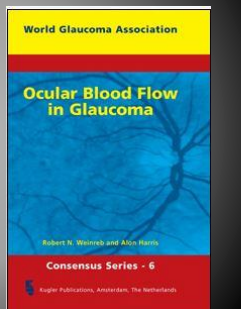
- ▶ Race did NOT increase risk of glaucoma development in the multi-variate analysis
- ▶ Blacks did have an 59% increase in risk in the univariate analysis but blacks had two other risk factors that DID increase risk in the multi-variate analysis
 - Larger vertical C/D ratio
 - Thinner central corneal thickness

Gordon MO et al Arch Oph. 2002; 120(10): 714-720

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World Glaucoma Association

- ▶ 1. Glaucoma Diagnosis 2004
- ▶ 2. Glaucoma Surgery
- ▶ 3. Angle Closure
- ▶ 4. IOP
- ▶ 5. Glaucoma Screening
- ▶ 6. Ocular Blood Flow 2006
- ▶ 7. Medical Treatment
- ▶ 8 Progression
- ▶ 9. Childhood Glaucoma
- ▶ 10. Diagnosis of POAG 2013



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Family History, Genetics

- ▶ First-degree relatives of POAG patients are at increased risk for glaucoma.
- ▶ Although studies have revealed there are multiple associated foci for OAG, there is little value for routine genetic testing to diagnose or predict the development of glaucoma at this time.

Diagnosis of POAG pp 161-187 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications

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Relationship Between Ocular Parameters and Progression to POAG

	High Risk	Moderate Risk	Low Risk
IOP (mm Hg)	>25.75	>23.75 to ≤25.75	≤23.75
CCT (µm)	≤555	>555 to ≤588	>588
Vertical C/D	≥0.5	>0.3 to <0.5	≤0.3

Adapted from Gordon MO et al. Arch Ophthalmol. 2002;120:714-720.

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OHTS/EGPS 5-Year Risk Calculator

FACTORS	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
	1 st	2 nd	3 rd	1 st	2 nd	3 rd
? Age <input type="text" value="55"/>						
? Untreated Intraocular Pressure (mm Hg)	25	25	25	25	25	25
? Central Corneal Thickness (microns)	555	555	555	555	555	555
? Vertical Cup to Disc Ratio by Contour	0.50			0.50		
? Pattern Standard Deviation Humphrey <input type="radio"/> Octopus loss variance <input type="radio"/>	2.0	2.0		2.0	2.0	

15.1% The patient's estimated 5-year risk (%) of developing glaucoma in at least one eye.

Gordon MO, Torri V et al; Ophthalmology. 2007;114(1):10-19.

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Level of Risk Over 5 Years

- ▶ **Recommended Action**
- ▶ Low <5% Observe and Monitor
- ▶ Moderate 5% – 15% Consider Treatment
- ▶ High >15% Treat
- ▶ Adapted from Weinreb RN et al. *Am J Ophthalmol.* 2004.5



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OHTS 20-Year Results (OHTS-3)

- ▶ February 28, 1994, to June 2, 2002 (phase 1), participants were randomized to receive either topical ocular hypotensive medication (medication group) or close observation (observation group).
- ▶ From June 3, 2002, to December 30, 2008 (phase 2), both randomization groups received medication.
- ▶ Beginning in 2009, treatment was no longer determined by study protocol.
- ▶ From January 7, 2016, to April 15, 2019 (phase 3), participants received ophthalmic examinations and visual function assessments.

JAMA Ophthalmol. 2021;139(5):558-566.
doi:10.1001/jamaophthalmol.2021.0341



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20-Year Cumulative Incidence of POAG (one or both eyes)

- ▶ 45.6% (95% CI, 42.3%-48.8%) among all participants,
- ▶ 49.3% (95% CI, 44.5%-53.8%) among participants in the observation group
- ▶ 41.9% (95% CI, 37.2%-46.3%) among participants in the medication group
- ▶ 55.2% (95% CI, 47.9%-61.5%) among Black/African American participants
- ▶ 42.7% (95% CI, 38.9%-46.3%) among participants of other races.



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Cumulative Incidence of POAG

- ▶ Low-risk tertiles was 31.7% (95% CI, 26.4%-36.6%),
- ▶ Medium-risk: 47.6% (95% CI, 41.6%-53.0%), and
- ▶ High-risk: 59.8% (95% CI, 53.1%-65.5%), respectively.
- ▶ 20-year cumulative incidence for visual field loss was 25.2% (95% CI, 22.5%-27.8%)
- ▶ 483 patients developed glaucoma
- ▶ 565 patients did NOT develop glaucoma
- ▶ 515 patients died



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More data

- ▶ Of the 1636 participants enrolled, 483 participants (29.5%) developed POAG in 1 or both eyes over a median follow-up of 20.2 years (range, 0-24.5 years).
- ▶ The cumulative incidence of POAG at 20 years, adjusted for exposure time, was 45.6%.
- ▶ Incidence was fairly linear (i.e. no abrupt changes)
- ▶ 62 participants developed bilateral POAG optic disc deterioration without detectable POAG VF loss
- ▶ 91 participants developed unilateral POAG VF loss and POAG disc deterioration in the same eye
- ▶ 63 participants who developed both bilateral POAG VF loss and bilateral POAG disc deterioration



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OHTS Weaknesses

- ▶ Limited baseline IOP range of 21 to 32 mm Hg (mean 24.9)
- ▶ Collection of medical history and family history of glaucoma only by self-report
- ▶ Loss to follow-up over the 20-year study period, missing data on participants (particularly between the OHTS 2 and the OHTS 3)
- ▶ Nonrandomized treatment after the OHTS 2, and
- ▶ **Lack of OCT measurements until the OHTS 3**
- ▶ **Optic nerve photo analysis?**



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Ocular Response Analyzer® G3: Corneal Hysteresis (CH)



Corneal Hysteresis (CH), measured by the **Ocular Response Analyzer® G3**, is a result of a patented, non-contact, *dynamic bi-directional applanation* process.
– Rapid, gentle, in/out corneal deformation

Corneal Hysteresis reflects the ability of the cornea to absorb and dissipate energy...

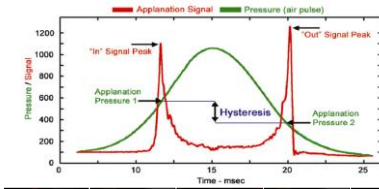
- *“how good of a shock absorber is the cornea?”*
- A surrogate for structural characteristics related to the pathogenesis of glaucoma

(Low) CH has been consistently shown to be **independently associated with or predictive of glaucoma development and rate of progression** and is more significant than other risk factors.

700 publications in the last 15 years

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Ocular Response Analyzer Technology Bi-directional Applanation Signal



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Corneal Hysteresis (CH)

- ▶ There is strong evidence implicating lower CH as a risk factor for glaucoma development and progression.
- ▶ There is insufficient evidence about the mechanisms by which CH is associated with the risk of glaucoma progression.

Diagnosis of POAG pp 127-158 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications

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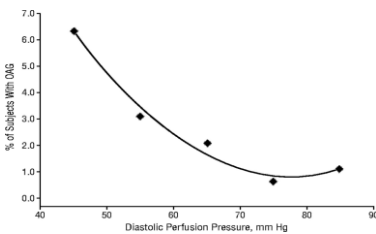
OPP and Glaucoma: Population Studies

- Baltimore Eye Survey
 - AA and Caucasian
- ▶ Egna-Numarkt Study
 - Caucasian
- ▶ Barbados Eye Study
 - African-Caribbean
- ▶ Proyecto Ver
 - Hispanic

Tielsch, Katz, Sommer, Quigley, Javitt. Arch Ophthalmol 1995;113:216-21
Bonomi L, Marchini G, Marraffa M et al. Ophthalmology 2000;107:1287-93
Leske MC, Wu S-Y, Nemesure B, et al. Arch Ophthalmol 2002;120:954-9 Quigley HA, West SK, Rodriguez J, et al. Arch Ophthalmol. 2001;119:1819-26

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OPP: Proyecto VER



Quigley HA, West SK, Rodriguez J, et al. Arch Ophthalmol. 2001;119:1819-26.

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Are Calcium Channel Blockers a Risk Factor for Glaucoma?

- ▶ Methods: Population-based cross-sectional study included UK Biobank participants with complete data (2006–2010) for analysis of glaucoma status, IOP, and OCT-derived inner retinal layer thicknesses
- ▶ Measures: Glaucoma status, corneal-compensated IOP, OCT-derived macular retinal NFL and macular ganglion cell-inner plexiform layer [mGC IPL] thicknesses).
- ▶ Conclusions: CCB users had:
 - 39% higher odds of having glaucoma adjusting for various factors, including the use of other antihypertensives (OR 1.39, 95% CI 1.14–1.69, $P=0.001$),
 - Thinner MRNFL thickness and GC/IPL thickness
 - CCB use was NOT associated with IOP

1. Kastner A, Stuart K, et al JAMA Ophthalmol. Published online September 7, 2023. doi:10.1001/jamaophthalmol.2023.3877

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Conclusion

- ▶ "The lack of association of CCB use with IOP suggests that an IOP-independent mechanism of glaucomatous neurodegeneration may be involved. Although a causal relationship has not been established, CCB replacement or withdrawal may be considered should glaucoma progress despite optimal care."
- ▶ "The risk isn't severe enough to pull patients off CCBs who don't already have glaucoma or who have stable disease, co-author Anthony Khawaja, MBBS, PhD, of University College London, told *MedPage Today*. But it's worth considering alternate medications in patients who are taking the drugs and suffering from worsening glaucoma, he said."

Randy Dottinga, MedPage Today September 7, 2023

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Baseline Information (Wooldridge)

- ▶ IOP (at least 2, am and pm)
- ▶ Visual fields (2 within first 6 months)
- ▶ Optic nerve photos
- ▶ Central Corneal Thickness (CCT)
- ▶ Gonioscopy
- ▶ OCT (2 within first six months)

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Initial Evaluations

- ▶ First Visit
 - Comprehensive Examination
 - CCT, Corneal Hysteresis (CH)
 - Visual field
 - Optic nerve photos
- ▶ Second Visit
 - Intermediate exam
 - OCT: NFL and Ganglion Cell Analysis
 - Gonioscopy
 - Initiate treatment

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Damage Assessment

- ▶ Structural
 - Disc damage on examination
 - Dilation still necessary!
 - Cupping > pallor
 - Disc hems
 - Disc photos
 - Still important!
 - Helpful for seeing NFL defects
 - OCT NFL and ganglion cell complex (GCC)
- ▶ Functional
 - Visual fields

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Glaucoma Progression Analysis

Agreement Among Glaucoma Specialists in Assessing Progressive Disc Changes From Photographs in OAG Patients

- ▶ 3 glaucoma specialists looked at stereophotos of 164 eyes
- ▶ Interobserver agreement was slight to fair
- ▶ After masked adjudication, in 40% of the cases in which the optic disc appeared to have progressed in glaucoma severity, the photograph of the "worse" optic disc was in fact taken at the start of the study.
- ▶ "Caution must be exercised when using disc change on photographs as the "gold standard" for diagnosing open-angle glaucoma or determining its progression."

Jampel HD, Friedman D et al AJO 2009;147(1): 39-44

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Knowledge of chronology of optic disc stereophotographs influences the determination of glaucomatous change

- ▶ Two sets of stereo disc photos presented to three glaucoma specialists
 - Photographs of patients enrolled in the Advanced Glaucoma Intervention Study and Collaborative Initial Glaucoma Treatment Study studies from Wills Eye Hospital
 - Five-year interval between photos
- ▶ Evaluated for glaucomatous progression each time
- ▶ First presented in chronologic order with dates shown
- ▶ Presented again three months later with order shuffled so observers did not know sequence

Altangerel U, Bayer, A et al Oph 2005 Jan; 112(1): 40-3

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Results

- ▶ Intra-observer agreement between chronologically masked and unmasked readings was 61%, 64%, and 71% for the 3 observers, respectively
- ▶ The number of cases identified as having deteriorated was significantly higher (101 vs. 54) when the observer knew the chronological order with which the photographs were taken ($P=0.007$)
- ▶ **CONCLUSIONS:**
 - When disc photographs are read with knowledge of the chronology with which they were obtained, the observations differ considerably from when the readings are made without this knowledge.

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Eidon True-Color Confocal Retinal Imager



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Technical Specs

- ▶ Non-mydratic (min pupil 2.5 – 3 mm)
- ▶ Field of View: 60° (horizontal) x 55° (vertical)
- ▶ 14 Mpix CMOS sensor (4608 x 3288)
- ▶ Visible light spectrum 440 to 650 nm
- ▶ Infrared light spectrum 825 – 870 nm
- ▶ Spherical correction -12D and +15D
- ▶ Internal fixation movable across the whole field, for automated multi-field examinations

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Change in Peripapillary Atrophy

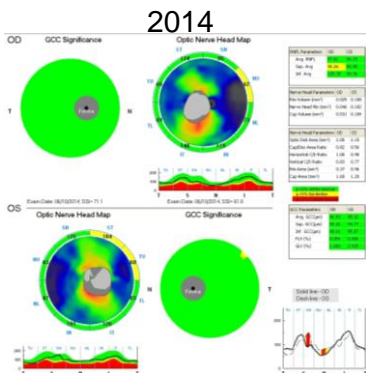


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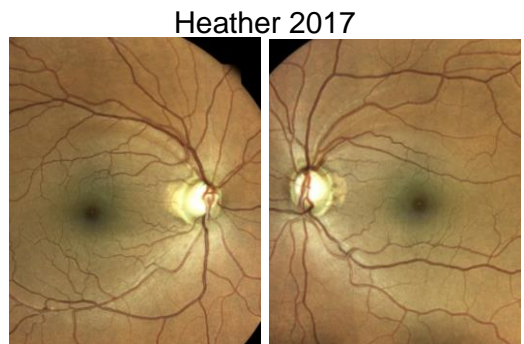
Heather

- ▶ Currently 57yo WF
- ▶ Followed for NTG since 2009
- ▶ Pre-treatment IOP OD 18 OS 19
- ▶ CCT R 595 L 611
- ▶ Monitored without treatment 2009-2011
- ▶ On constant medical treatment since 2011
- ▶ S/P SLT OU 2017

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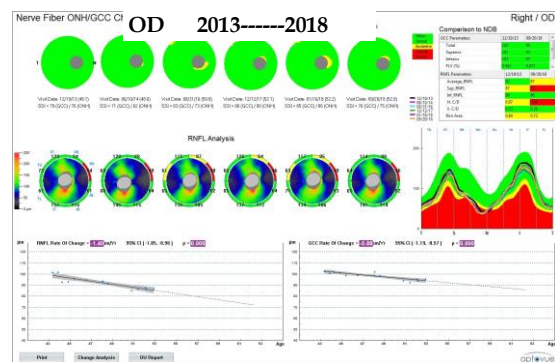
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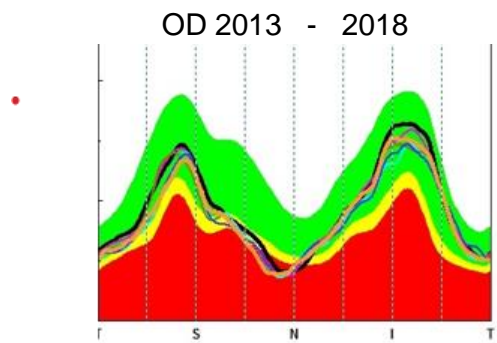
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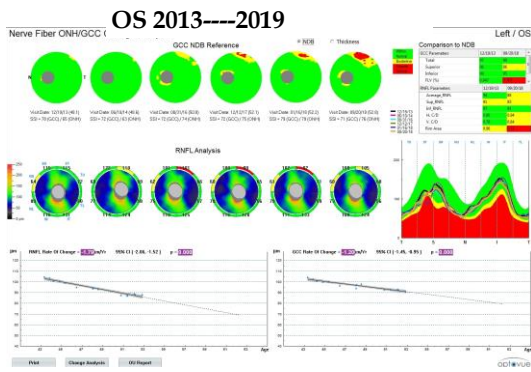
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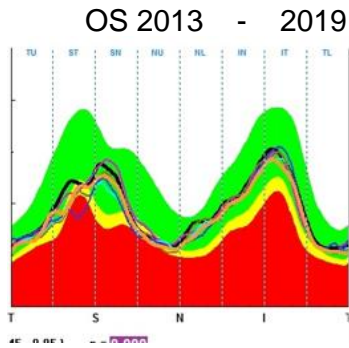
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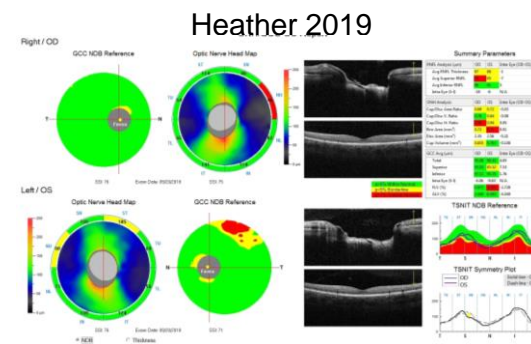
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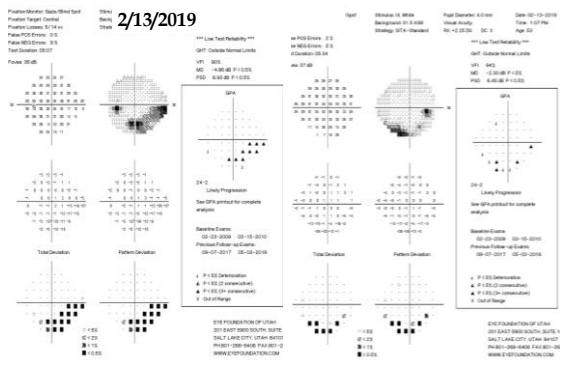
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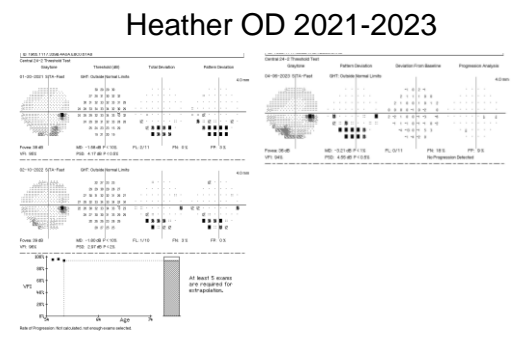
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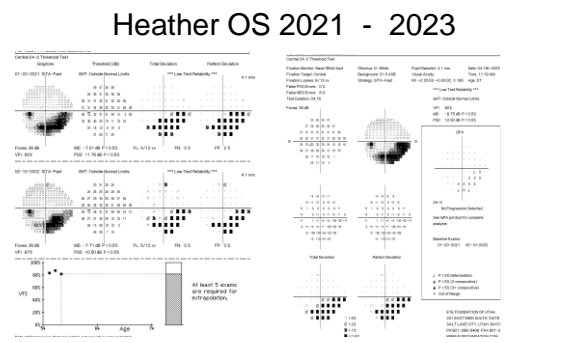
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Heather

- ▶ Slowly progressive glaucoma despite aggressive medical therapy and SLT OU
- ▶ With good IOP control!
- ▶ Felt to be compliant
- ▶ Resistant to having surgery



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More tests of your skills!



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Hector 2017

- ▶ 60 yo Hispanic male
- ▶ VA 20/20 OU
- ▶ Pretreatment IOP
- ▶ R 22
- ▶ L 20

- ▶ CCT
- ▶ R 531
- ▶ L 525



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Hector 2017 v 2023



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Heather 2.20.23

- ▶ 34yo WF referred for glaucoma evaluation
- ▶ Referring doctor said recent photos showed drastic change in Rt. Nerve compared to 1 year ago
- ▶ C/O foggy vision OD with patchy spots above and below central fixation
- ▶ Notes good VA OS
- ▶ + FH of glaucoma in great grandmother



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Heather 2.20.23

- ▶ VA CL R 20/25 L 20/15
- ▶ IOP R 50 L 43
- ▶ ORA R 56.7 CH 2.4
- ▶ L 47.6 CH 4.4
- ▶ CCT R 562 L 565
- ▶ SLE NL, quiet OU
- ▶ DFE as seen



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2.20.23



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Heather 2.20.23 Plan

- ▶ Diamox 500mg, Lumigan given in office
- ▶ Rx Rocklatan QHS, Simbrinza BID, Combigan BID samples given
- ▶ See referring OD in a few days
- ▶ RTC 1 week

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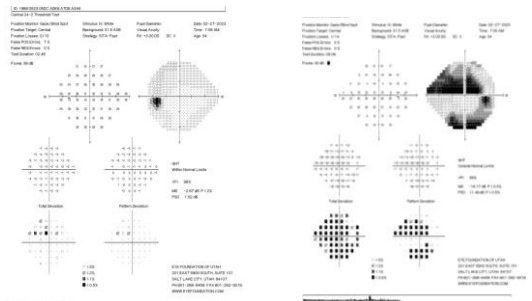
2.27.23

- ▶ VA R 20/25 L 20/15
- ▶ IOP R 17 L 11
- ▶ ORA R 18.4 L 12.7
- ▶ CH R 8.9 L 12.6

- ▶ March-April 2023
- ▶ OD SLT 360 performed
- ▶ OS SLT 180 performed (so far)

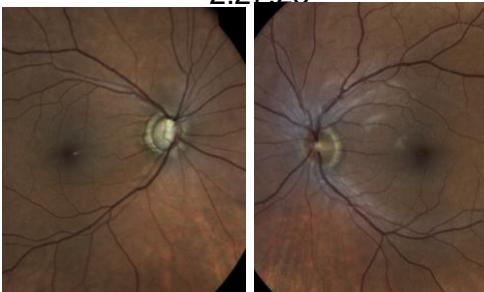
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2.27.23



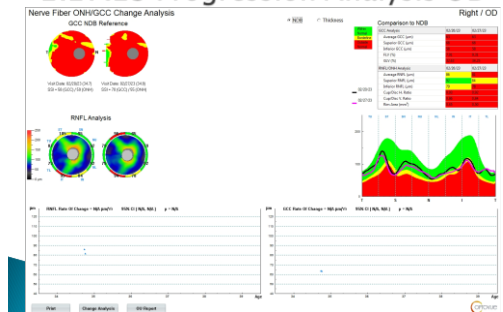
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2.27.23



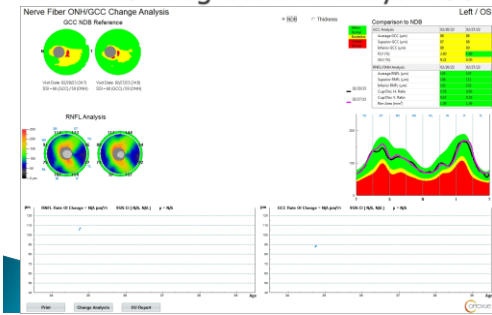
65

2.27.23 Progression Analysis OD



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2.27.23 Progression Analysis OS



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5.2.23

- ▶ Patient now taking latanoprost, dorzolamide-timolol, brimonidine OU
- ▶ Rocklatan denied by insurance
- ▶ IOP R 26 L 22
- ▶ Plan:
 - Continue present meds
 - Complete SLT OU



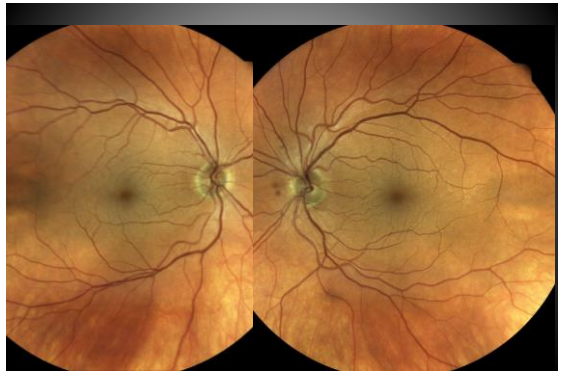
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Chris 2018

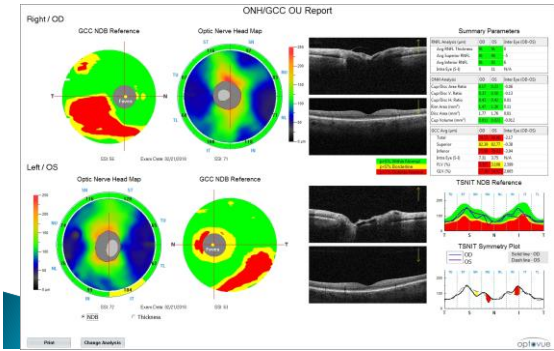
- ▶ 67yo WM
- ▶ Followed for several years for HSK OD
- ▶ Pretreatment IOP R 21 L 17



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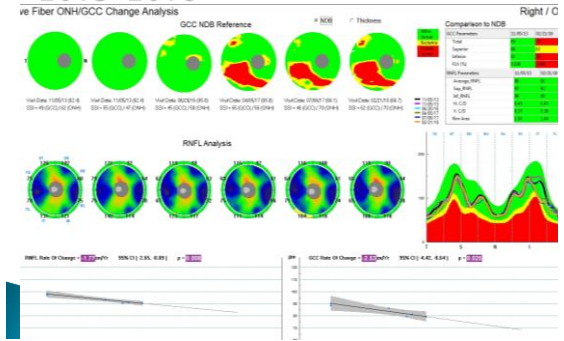


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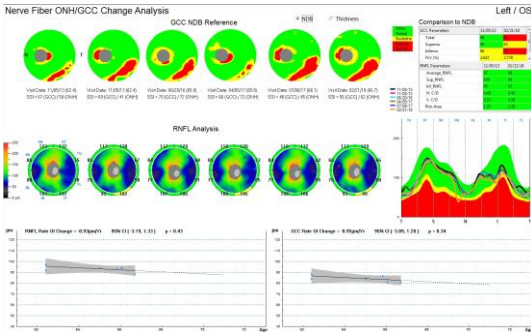
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2013-2018



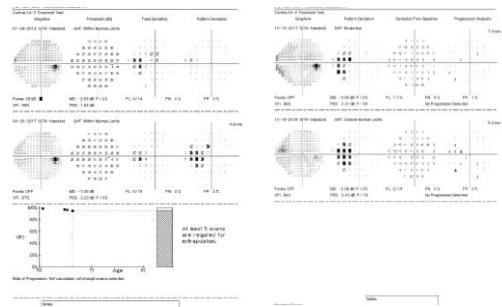
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OS 2013-2018



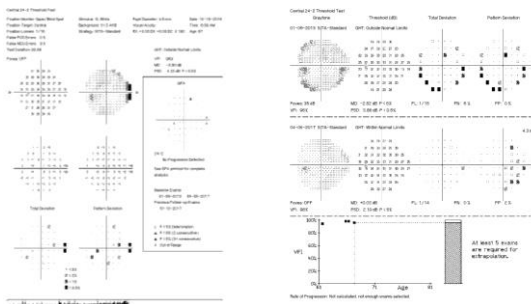
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Chris VF OD 2013----- 2018



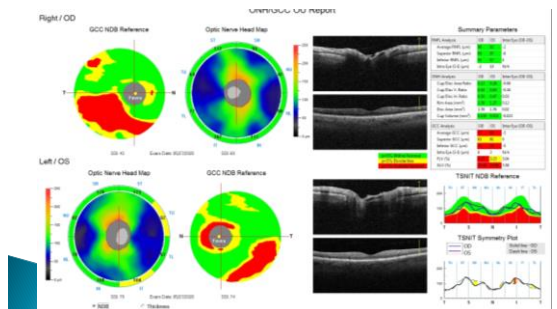
74

Chris 10 19 2018



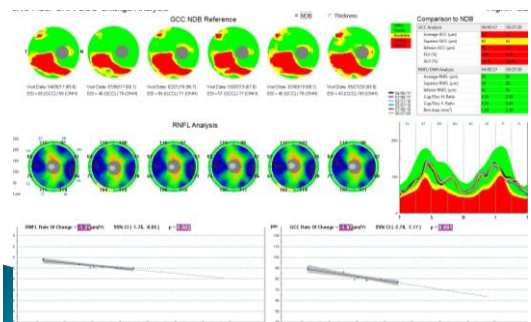
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Chris 5 27 2020



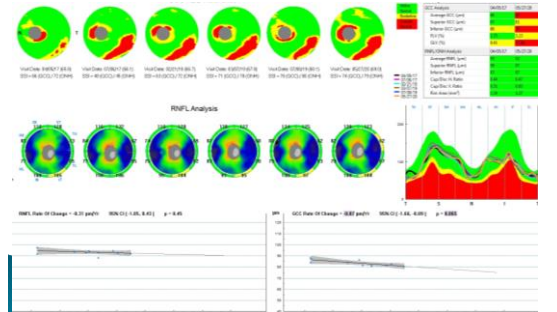
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Chris 2017---2020



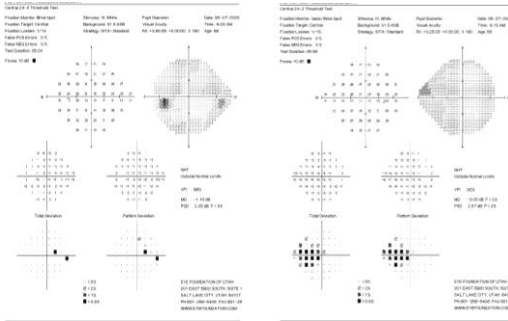
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Chris 2017-----2020



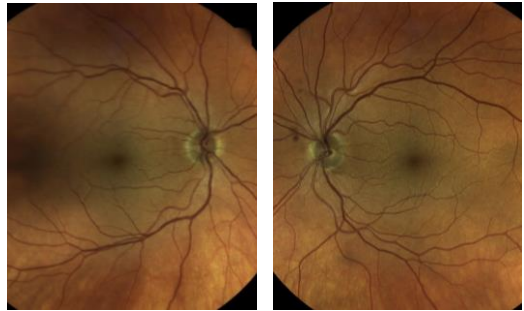
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Chris 5 27 2020



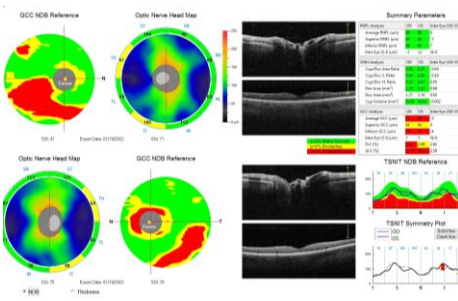
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Chris 3 3 2021



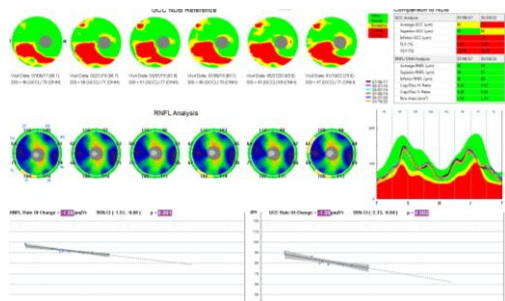
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Chris 1 19 2022



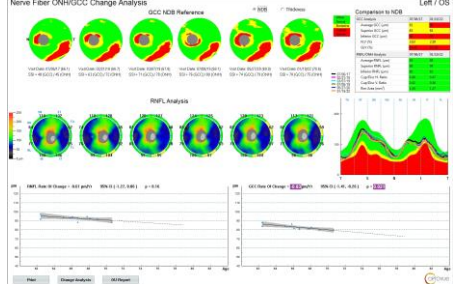
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2017-----2022



82

2017-----2022



83

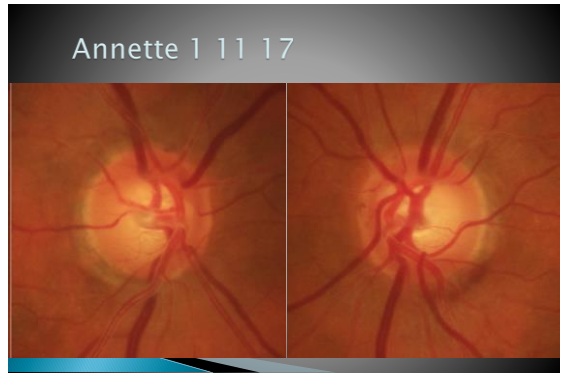
Chris Moral of the Story
Sometimes "healthy" nerves aren't so healthy!

84

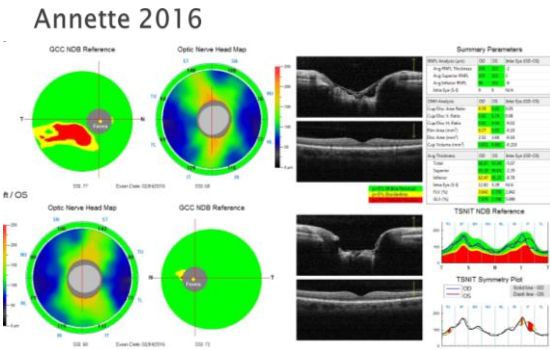
Annette

- ▶ 69yoWF referred with large cups
- ▶ IOP
 - R 16, 11, 14 mmHg
 - L 18, 13, 16 mmHg
 - (three separate exams)
- ▶ ORA IOP R 15.3 L 17.5
- ▶ CH R 9.8 L 9.9
- ▶ CCT R 599 L 603

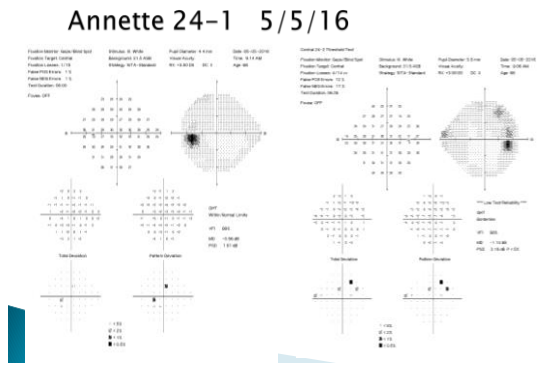
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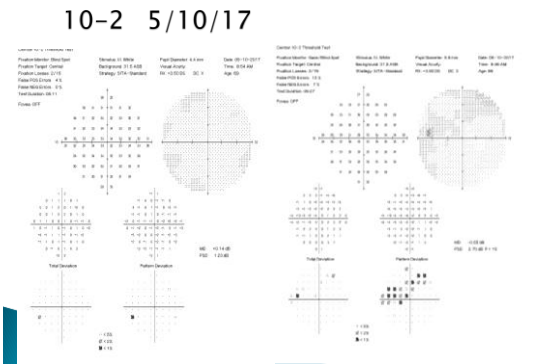
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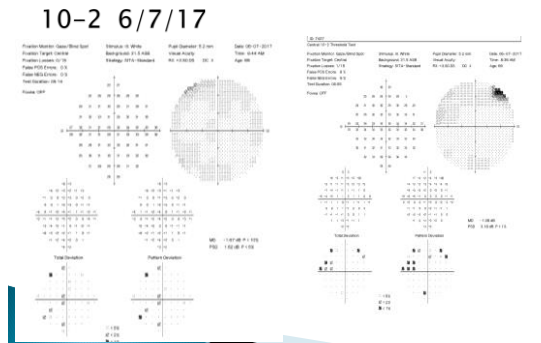
87



88



89



90

When to do 10-2 VF

- ▶ Standard of care is 1-2 VF's per year
- ▶ Still use 24-2 as standard test
- ▶ Periodically use 10-2 to "spot check" glaucoma suspects with normal 24-2
- ▶ Use 10-2 as primary test in severe, late-stage glaucoma



91

Long-Term Follow Up

- ▶ Exam every 3-4 months
 - 3-4x/year
- ▶ VF, ON photos or OCT each visit
- ▶ Each assessment for possible progression is done every 6-12 months
- ▶ More frequent exams and damage assessments with indication of possible change



92

More Frequent Visits if:

- ▶ Early in course
- ▶ Poor control
- ▶ Severe disease
- ▶ Questionable compliance



93

Which medication do I start with?

- ▶ Beta Blocker?
 - Timolol
- ▶ Alpha Agonist?
 - Alphagan
- ▶ Carbonic Anhydrase Inhibitor?
 - Azopt/Trusopt
- ▶ Prostaglandin?
 - Lumigan, Travatan, Xalatan, Zioptan
- ▶ Combination Agent?
 - Combigan, Cosopt, Simbrinza
- ▶ Rocklatan?



94

Initial Response to Treatment

- ▶ Is the patient using the drops?
- ▶ Tolerating the drops?
- ▶ Is the medication affordable??
- ▶ Ascertain IOP Reduction
- ▶ Any questions, problems or concerns?



95

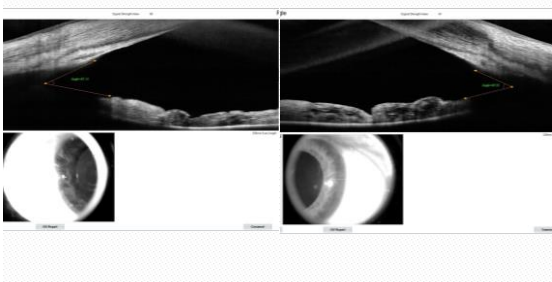
Jeff

- ▶ 54yo M referred for glaucoma evaluation
- ▶ VA 20/40 OU
- ▶ IOP
 - OD 44mm Hg
 - OS 36mm Hg
- ▶ CCT
 - OD 542
 - OS 546
- ▶ Slit lamp exam reveals corneal endothelial pigment dusting OU
- ▶ Gonioscopy confirms Pigmentary Dispersion Syndrome OU



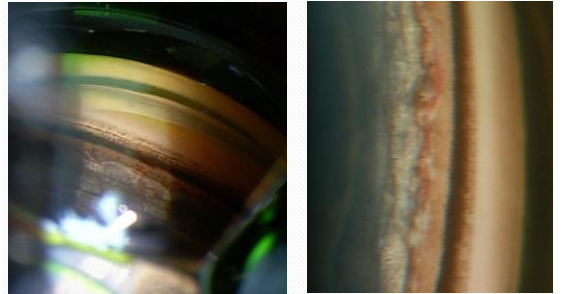
96

OCT shows iris concavity OU

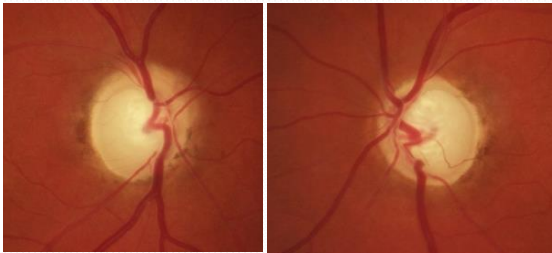


97

Gonioscopy

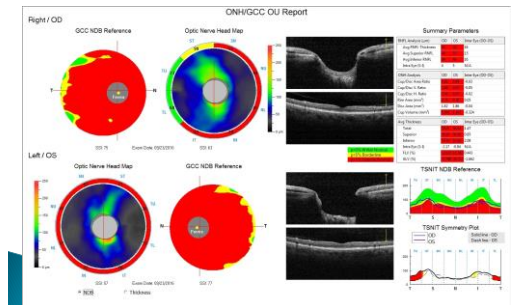


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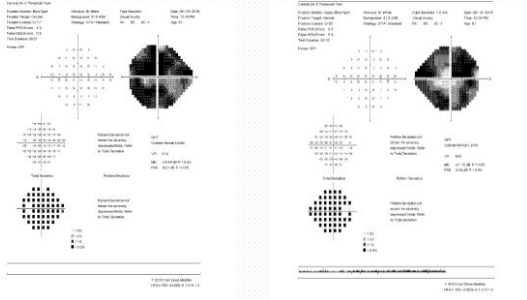
99

Initial OCT



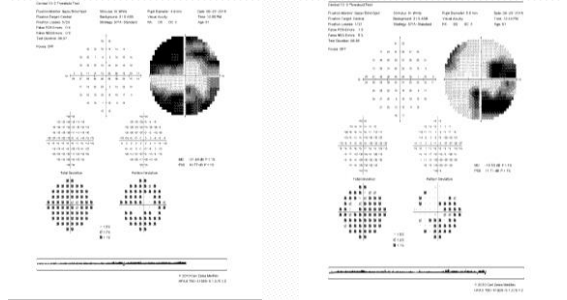
100

24-2 VF



101

10-2 VF



102

What is your plan?

- ▶ 1. Refer him to someone I don't like
- ▶ 2. Treat him myself
- ▶ 3. Just call Rob



103

What is the best test for monitoring?

- ▶ 1. Optic nerve photos
- ▶ 2. OCT NFL, GCC
- ▶ 3. 24-2 VF
- ▶ 4. 10-2 VF



104

What is your target IOP?

- ▶ 1. 18mm Hg
- ▶ 2. 15mm Hg
- ▶ 3. 12mm Hg
- ▶ 4. 10mm Hg



105

Should Jeff be driving?

- ▶ 1. Sure, he's 20/40, why not?
- ▶ 2. Sure, but only in Wyoming
- ▶ 3. Oh, Hell no!



106

Treatment history

- ▶ Recently managed with latanoprost QHS OU, dorzolamide-timolol FDC BID OU
- ▶ Developed allergy to brimonidine earlier
- ▶ Also had SLT OU
- ▶ IOP running 14–16mm Hg OU on multiple visits
- ▶ Target IOP 10–12mm Hg
- ▶ Discussed option, risks and benefits of surgery
- ▶ Later changed to Rocklatan QHS OU and dorzolamide-timolol FDC BID OU
- ▶ IOP now 8–10mm Hg OU without surgery



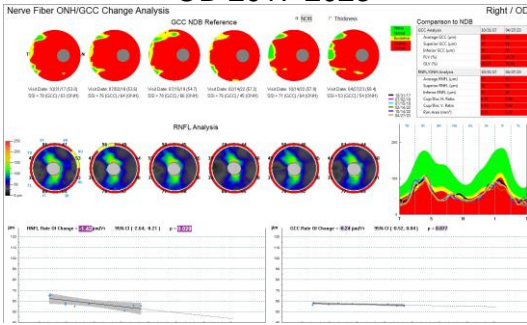
107

Jeff 2018-2023



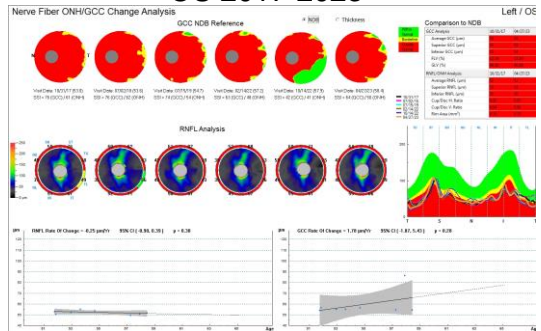
108

OD 2017-2023



109

OS 2017-2023



110

Lessons from Jeff's Case

- ▶ Young patient with severe glaucomatous damage
- ▶ Needs LOW target IOP
- ▶ Until advent of Netarsudil, he would likely have needed a trabeculectomy or tube shunt with risk of complications
- ▶ Addition of Rocklatan allowed patient to get to a very low target IOP without surgery
- ▶ Shows the benefit of Rocklatan's unique MOA, including ability to decrease episcleral outflow pressure, thereby getting IOP to 10 or below.

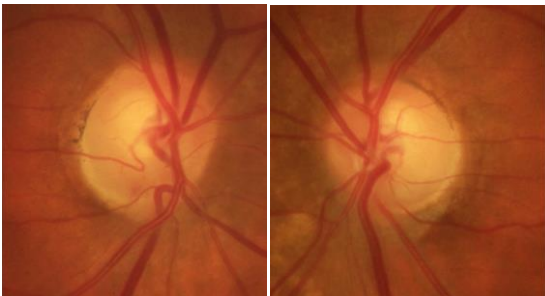
111

Cindy

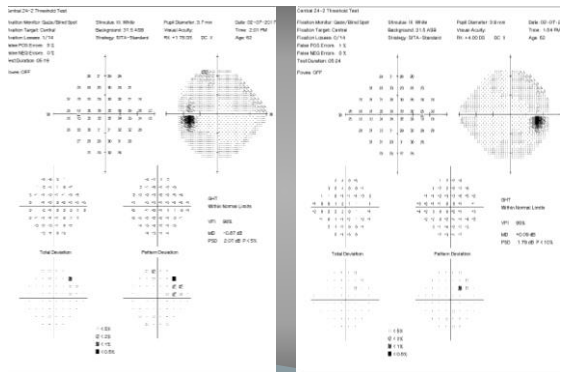
- ▶ 62yoF referred as glaucoma suspect
- ▶ S/P LASIK OD only
- ▶ VAcc 20/15 OU
- ▶ GAT R 18 L 19
- ▶ CCT R 628 L 635
- ▶ ORA R 14, L 17
- ▶ CH R12.6 L13.1

112

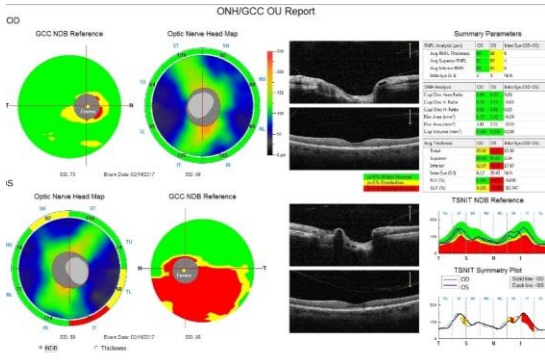
Cindy



113



114

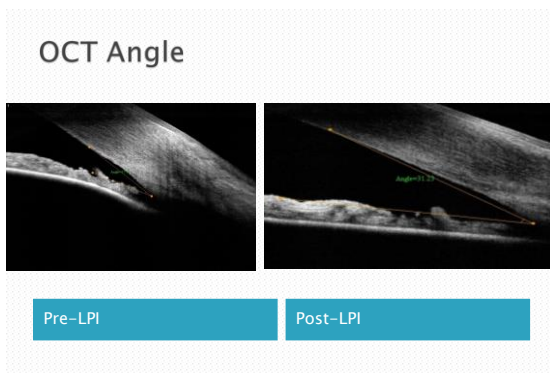


115

Cindy's Morals of the Story

- Look carefully at all optic nerves!
- Younger patient (62yo)
- Normal IOPs
 - GAT R 18 L 19
- THICK corneas even after LASIK
 - CCT R 628 L 635
- Normal IOP with ORA!
 - ORA R 14, L 17
- High Hysteresis!
 - CH R12.6 L 13.1
- And she still has glaucoma

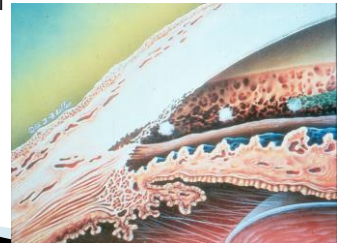
116



117

Medication v. SLT?

- Glaucoma Laser Trial
- Medical history
- Age
- Cost
 - Insurance?
- 24 hour effect?



118

SLT v Drops for 1st Line treatment of OHTN and Glaucoma (LiGHT Study)

- Observer-masked RCT
- 718 treatment naïve patients
 - 356 randomized to SLT
 - 362 randomized to drops
- Objective target IOP set according to severity
- Outcomes measured:
 - Health-related QoL at 3 years
 - Cost, cost-effectiveness, clinical effectiveness, safety

Gazzard C, Konstantakopoulou E, Garway-Heath D et al on behalf of the LiGHT Trial Study Group. Lancet. April 13, 2019. pp1505-1516

119

Results

- No significant difference in HRQoL
 - Average EQ-5D score was 0.89 (SD 0.18) in the SLT group versus 0.90 (SD 0.16) in the eye drops group, with no significant difference (difference 0.01, 95% CI -0.01 to 0.03; p=0.23).
- 74.2% (95% CI 69.3-78.6) of patients in the SLT group required no drops to maintain IOP at target.
- Eyes of patients in the SLT group were within target IOP at more visits (93.0%) than in the eye drops group (91.3%)
- Eyes requiring surgery to maintain IOP at target
 - 0 in SLT group
 - 11 in drops first group
- 97% chance of SLT first group being more cost effective
- Conclusion: SLT should be offered as a first-line treatment for OAG and OHTN, supporting a change in clinical practice.

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SLT Considerations

- ▶ Medical side effects
- ▶ Laser side effects
- ▶ Compliance
- ▶ COST
- ▶ Convenience
- ▶ Duration of effect
- ▶ Diurnal effect



121

Surgical Considerations

- ▶ Disease severity
- ▶ Age of patient
- ▶ Medical history
- ▶ Compliance
- ▶ Costs
- ▶ RISKS vs. BENEFITS



122

What Have We Learned?

- ▶ Make careful observations
- ▶ Utilize *proven* new technologies
- ▶ Monitor carefully for change
- ▶ Be aggressive with damage/progression
 - Consider damage vs. patient age
 - Consider risks vs. benefits
 - 1mm decrease = 10% decrease risk of progression
- ▶ Prostaglandins first in most cases
- ▶ SLT a reasonable first line treatment option
- ▶ Many options for second line treatment



123

Review of literature and Consensus of experts



124

Intraocular Pressure (IOP)

- ▶ Although POAG may develop at any IOP, there is strong evidence supporting higher mean IOP during FU as a risk factor for development and progression of glaucomatous damage.
- ▶ There is insufficient evidence... to elucidate which IOP parameter (mean, peak and/or fluctuation,... etc.) is most important in determining risk...
- ▶ There is insufficient evidence implicating IOP fluctuations as an independent risk factor for glaucoma development or progression.

Diagnosis of POAG pp 127-158 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications



125

Central Corneal Thickness (CCT)

- ▶ There is strong evidence supporting the role of CCT as an important predictive factor for OAG development in OHTN and glaucoma suspects. Baseline CCT measurements should be obtained in patients suspected of having glaucoma.
- ▶ Algorithms to correct IOP based on CCT are not recommended for routine use in clinical practice.
- ▶ There is insufficient evidence to conclude whether or not CCT is a true independent risk factor or whether its effect is related to a tonometric artifact.

Diagnosis of POAG pp 127-158 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications



126

Age, Race

- ▶ POAG occurs at all ages, and the incidence and prevalence accelerates with age.
- ▶ Older age is a risk factor for glaucoma onset and progression.
- ▶ Populations with the highest incidence and prevalence of OAG have African ancestry.
 - Due to the earlier age of disease onset, the average duration of OAG may be greatest in individuals of African Ancestry.
- ▶ Hispanics may have higher incidence and prevalence of OAG than individuals of European ancestry (non-Hispanic whites).

Diagnosis of POAG pp 161-187 Weinreb RN, Garway-Heath D et al. 2016 Klugler Publications

127

Blood pressure, perfusion pressure, and glaucoma

- ▶ Summaries of the pertinent literature and input from glaucoma researchers and specialists
- ▶ METHODS: Review and interpretation of selected literature and the results of a 1-day group discussion involving glaucoma researchers and specialists with expertise in epidemiology, blood flow measurements, and cardiovascular physiology.

Carmoli P, Coleman AL. Blood Flow in Glaucoma Discussion. *AO* 2010 May;149(5):704-12.

128

Results

- ▶ Accurate, reproducible, and clinically relevant measurements of blood flow within the optic nerve head and associated capillary beds are not fully achievable with current methodology.
- ▶ Autoregulation of blood flow in the retina and ONH occurs over a large range of IOP's and BP's.
- ▶ Regulation of choroidal blood flow is provided by a mix of neurohumoral and local mechanisms.
- ▶ Vascular factors may be important in a subgroup of patients with POAG, and particularly in patients with NTG and evidence of vasospasm.

129

Results (cont.)

- ▶ Low OPP and low BP are associated with an increased risk of glaucoma in population-based studies.
- ▶ The physiologic nocturnal dip in blood pressure is protective against systemic end-organ damage, but its effects on glaucoma are not well elaborated or understood.
- ▶ Large-scale longitudinal studies would be required to evaluate the risk of glaucomatous progression in non-dippers, dippers, and extreme nocturnal BP dippers.

130

Conclusions

- ▶ There is no evidence to support the value of increasing a patient's blood pressure as therapy for glaucoma.
- ▶ We lack crucial information about the microvascular beds in the optic nerve, and the appropriate methods to evaluate their blood flow.
- ▶ Cardiovascular safety concerns associated with increasing OPP and blood flow by increasing BP, especially in elderly patients.
- ▶ It is unlikely that safe and effective glaucoma treatments based on altering optic nerve perfusion will soon be available.

131

Early Manifest Glaucoma Trial

- ▶ To compare the effect of immediately lowering the IOP, vs. no treatment or later treatment, on the progression of newly detected OAG.
- ▶ 255 patients with mild glaucoma
 - ½ treated
 - ½ followed without treatment
- ▶ Treatment group
 - ALT plus Betoptic 0.5% bid
 - Xalatan if necessary (IOP > 25)
- ▶ Control group
 - No treatment

Heijl A, Leske MC et al. *Arch Ophthalmol*. 2002; 120(10):1268-1279.

132

Progression (median FU 6 yrs.)

- ▶ Control group: 62%
 - Median time: 48 months
- ▶ Treatment group: 45%
 - Median time: 66 months
 - Significantly later (18 month delay)
- ▶ Median FU: 6 years (at least 4 yrs.)
- ▶ Average IOP reduction: 25% (5.1 mm)
- ▶ Control group: No change in IOP



133

So What?

- ▶ For every 1 mm IOP lowered, risk of progression decreases by 10%
- ▶ Relative risk of progression decreased by 50% with treatment
- ▶ No significant adverse effects



134

Selective Laser Trabeculoplasty as Primary Treatment for Open-angle Glaucoma A Prospective, Nonrandomized Pilot Study

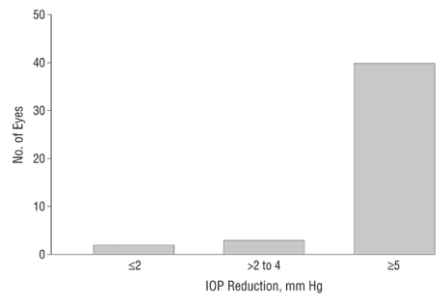
- ▶ Objective: To examine the safety and efficacy of SLT as primary treatment for OAG
- ▶ Methods: 45 eyes of 31 patients with OAG or OHT
 - (IOP ≥23 on 2 consecutive measurements) underwent SLT as primary treatment.
- ▶ IOP measured 1 hour, 1 day, 1 week, and 1, 3, 6, 12, 15, and 18 months postoperatively. During FU, patients were treated with glaucoma medications as required

Melamed S et al Arch Ophthalmol. 2003;121:957-960.



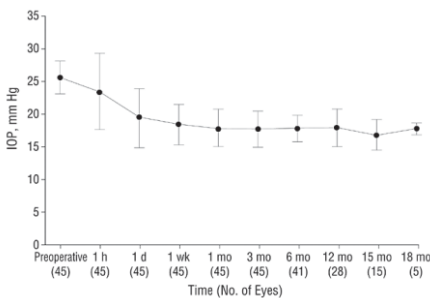
135

IOP Reduction (mm Hg)



136

POST SLT IOP Sustained



137

Results

- ▶ An IOP reduction of at least 20% after SLT was defined as a successful treatment.
- ▶ Mean decrease in IOP: 7.7 ± 3.5 mm Hg (30%).
- ▶ Forty-three (95%) of 45 eyes treated had IOP reduction on 2 consecutive visits (±2 mm Hg).
- ▶ When successful, the IOP reduction was sustained after SLT

Melamed S et al Arch Ophthalmol. 2003;121:957-960.



138

Who is a good candidate for Durysta? (Wooldridge)

- ▶ Noncompliant patients
 - Forgetful
 - Unmotivated
- ▶ Patients who cannot instill their drops
 - Arthritis, dementia, etc.
- ▶ Patients who hate drops!
 - New patient?
- ▶ Patients with OSD



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