Glaucoma Grand Rounds

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1

Disclosure Slide for Dr Eric Schmidt

- Dr Schmidt is an advisor or consultant for the following:
  - Allergan
  - Tarsus
  - Eyenovia
  - Carl Zeiss
  - Thea Pharmaceuticals
  - Topcon
  - B&L
  - Sight Science
  - Avellino Labs

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What Is The difference between a glaucoma suspect and a glaucoma patient?

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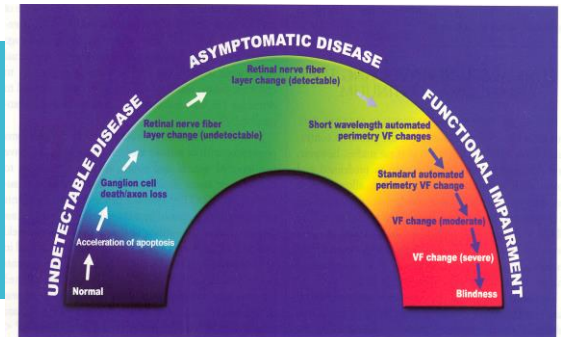

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Glaucoma Risk Factors

- FINDACAR
- The more risk factors one has, the more likely one is to develop glaucoma
- The more risk factors one has, the lower the IOP target should be

5

A Review Of Risk Factors

- FINDACAR
  - Family history
  - IOP
  - Nearsightedness
  - Diabetes/Vascular disease
  - Age
  - Corneal thickness
  - Asymmetry
  - Race

6

A risk factor analysis is critical

- For the diagnosis
- To increase your level of suspicion
- For initiating therapy
- For changing therapy

- BUT…are any of these more important than others?

7

OHTS

- Goal of tx – 20% drop in IOP
  - 24mm target IOP

RESULTS: At 5 years

4.4% of tx group developed POAG

9.5% of no tx group developed POAG

So - lowering IOP in Oc Hx reduced the likelihood of glaucoma by 50% - RIGHT?

8

OHTS – A Closer Look

- 90% of untreated group did not progress
- 95.6% of tx group did not progress

- It proved that ***in those individuals who are going to progress*** to POAG lowering IOP by 22.4% will delay the onset by at least 5 yrs.
- Who are " those individuals at risk"?

9

OHTS – The Nitty Gritty

- The most predictive factors for conversion:
  - Older age
    - 22% increase/ decade
  - Larger horizontal and vertical C/D
    - 32% increase/0.1 larger
  - Higher baseline IOP
    - 10% increase/ mm Hg
  - Thinner corneas
    - 71% increase in risk/ 40 microns thinner

10

Case 1

- 66 y/o Caucasian Female
- PMH: Anemia, Hypothyroid
- FMH: Mother- POAG

- Multiple IOP Readings over 3 year period: 18-25mm Hg
- C/D as shown: ~.8/.8

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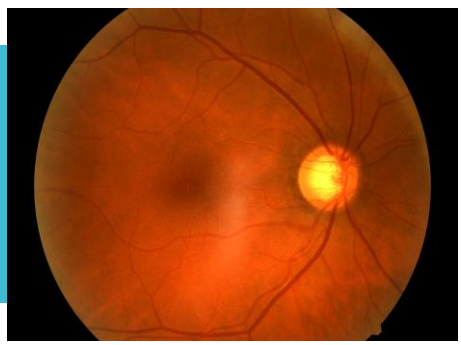

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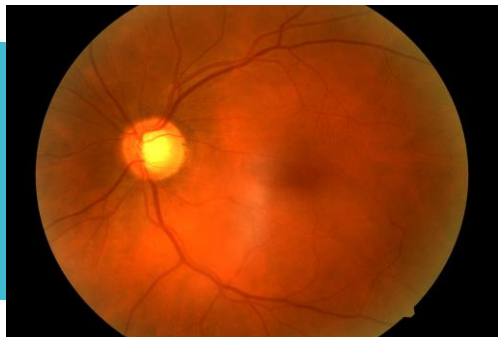

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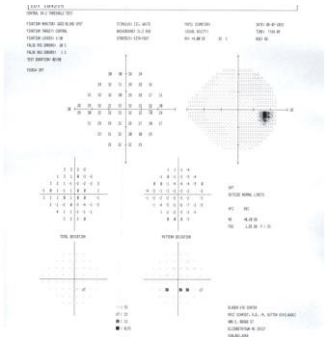

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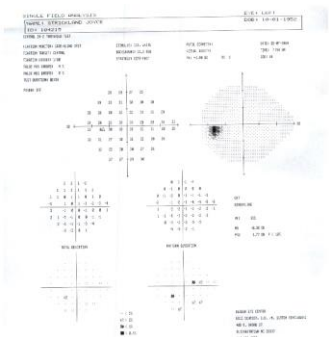

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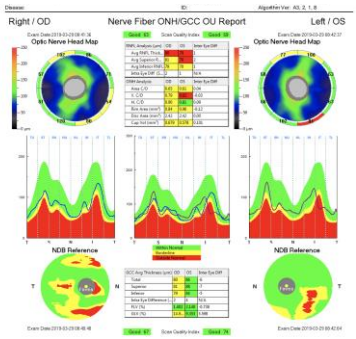

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SO-TREAT or no treat???

- What factors would lead you to monitor rather than treat
  - Or Vice Versa
- Do We Need Any More Data?
- What makes you feel comfortable about monitoring without therapy?

17

The pachymetry issue

Juicy Data

- 36% of pxs w/ IOP >25.75 AND K thickness < 555 microns developed POAG
- 6% of pxs w/ same IOP but K thickness > 588 converted toPOAG

Juicy Data II

- 15% pxs w/ C/D .3/.3 and K thickness < 555 microns converted but
- 4% of pxs w/ same disk parameters and K thickness> 588 microns converted

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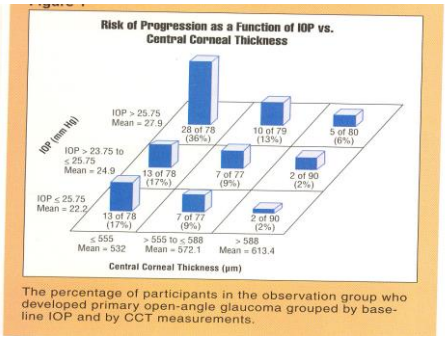

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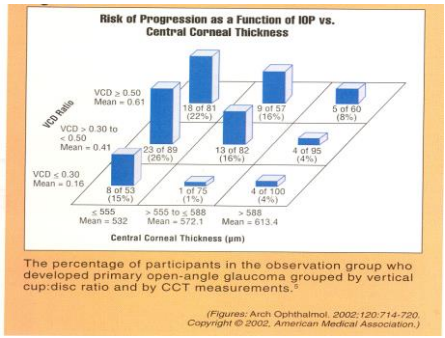

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IOP 30mmHg, CCT 600µ

Glaucoma Risk Estimator

Age 70	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
	1st	2nd	3rd	1st	2nd	3rd
Untreated Intraocular Pressure (mm Hg)	30	30	30	30	30	30
Central Corneal Thickness (microns)	600	600	600	600	600	600
Vertical Cup to Disc Ratio by Contour	0.55			0.55		
Pattern Standard Deviation (Humphrey (dB) / Octopus loss variance (dB))	1.0	1.0		1.0	1.0	

Print | Reset | 9.1% | The patient's estimated 5-year risk (%) of developing glaucoma in at least one eye.

Glaucoma risk is 9.1%

21

IOP 20mmHg, CCT 500µ

Glaucoma Risk Estimator

Age 70	RIGHT EYE MEASUREMENTS			LEFT EYE MEASUREMENTS		
	1st	2nd	3rd	1st	2nd	3rd
Untreated Intraocular Pressure (mm Hg)	20	20	20	20	20	20
Central Corneal Thickness (microns)	500	500	500	500	500	500
Vertical Cup to Disc Ratio by Contour	0.55			0.55		
Pattern Standard Deviation (Humphrey (dB) / Octopus loss variance (dB))	1.0	1.0		1.0	1.0	

Print | Reset | 20.7% | The patient's estimated 5-year risk (%) of developing glaucoma in at least one eye.

Glaucoma risk is 20.7%

22

IOP and Glaucoma

- Which IOP is most important?
  - Mean IOP
  - Peak IOP
  - Trough IOP
  - IOP range

23

24

Assessment of Cumulative Incidence and Severity of Primary Open-Angle Glaucoma Among Participants in the Ocular Hypertension Treatment Study After 20 Years of Follow-up

IMPORTANCE Ocular hypertension is an important risk factor for the development of primary open-angle glaucoma (POAG). Data from long-term follow-up can be used to inform the management of patients with ocular hypertension.

OBJECTIVE To determine the cumulative incidence and severity of POAG after 20 years of follow-up among participants in the Ocular Hypertension Treatment Study.

DESIGN, SETTING, AND PARTICIPANTS Participants in the Ocular Hypertension Treatment Study were followed up from February 1994 to December 2008 in 22 clinics. Data were collected after 20 years of follow-up (from January 2016 to April 2019) or within 2 years of death. Analyses were performed from July 2019 to December 2020.

INTERVENTIONS From 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.

MAIN OUTCOMES AND MEASURES Twenty-year cumulative incidence and severity of POAG in 1 or both eyes after adjustment for exposure time.

RESULTS A total of 1636 individuals (mean [SD] age, 55.4 [9.6] years; 931 women [56.9%]; 1138 White participants [69.6%]; 407 Black/African American participants [24.9%]) were randomized in phase 1 of the clinical trial. Of those, 483 participants (29.5%) developed POAG in 1 or both eyes (unadjusted incidence). After adjusting for exposure time, the 20-year cumulative incidence of POAG in 1 or both eyes was 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, and 41.9% (95% CI, 37.2%-46.3%) among participants in the medication group. The 20-year cumulative incidence of POAG was 55.2% (95% CI, 47.9%-61.5%) among Black/African American participants and 42.7% (95% CI, 38.9%-46.3%) among participants of other races. The 20-year cumulative incidence for visual field loss was 25.2% (95% CI, 22.5%-27.8%). Using a 5-factor baseline model, the cumulative incidence of POAG among participants in the low-, medium-, and high-risk tertiles was 31.7% (95% CI, 26.4%-36.6%), 47.6% (95% CI, 41.6%-53.0%), and 59.8% (95% CI, 53.1%-65.9%), respectively.

CONCLUSIONS AND RELEVANCE In this study, only one-fourth of participants in the Ocular Hypertension Treatment Study developed visual field loss in either eye over long-term follow-up. This information, together with a prediction model, may help clinicians and patients make informed personalized decisions about the management of ocular hypertension.

25

Key Points

Question Do 20-year follow-up data from the Ocular Hypertension Treatment Study inform the management of patients with ocular hypertension?

Findings In this cohort study of 1636 participants with ocular hypertension who participated in the Ocular Hypertension Treatment Study, the 20-year cumulative incidence of primary open-angle glaucoma was 46% in 1 or both eyes, and the cumulative incidence of visual field loss was 25% after adjusting for exposure time.

Meaning This study's findings, together with a predictive model, may help clinicians and patients make informed personalized decisions about the management of ocular hypertension.

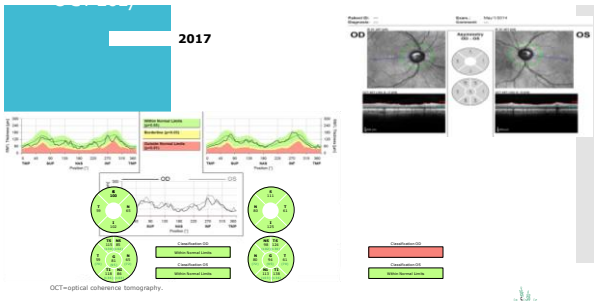
26

Case 2

- 68 y/o African American Male
- PMH: HBP, Hypercholesterolemia
- FMH: Mother POAG
- Initial Presentation:
  BCVA: 20/20 OD, OS
  IOP: OD 21mm Hg, OS 22mm Hg
  C/D: 0.6/0.6 OD, 0.6/0.6 OS

So What Now???

27



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Case 2 (cont)

- FP taken
- VF – wnl
- Pachymetry – OD 505, OS 510
- Hysteresis- OD 8 OS 9

- To Treat Or Not To Treat – That Is The Question!!

29

2 Years Later – No treatment

2019 – IOP: 20mm Hg OD, 21mm Hg OS

Followed for 2 years w/out tx
IOP ranged 19-23mm Hg (5 readings)

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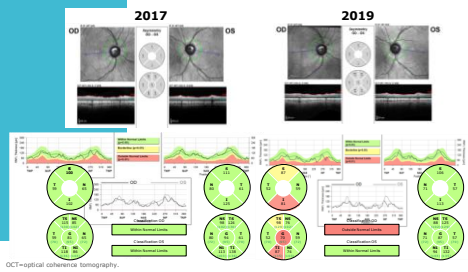

OCT=optical coherence tomography.

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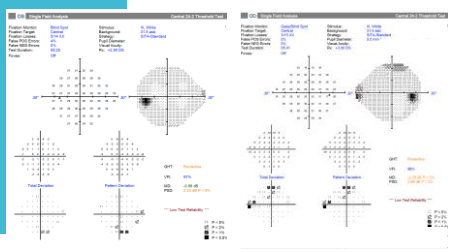
VF Results-20



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Definitely POAG

- Were there any clues that may have led us to treat earlier??
- How Many Risk Factors??
- Time For A Coffee Talk!!!

34

59yoBM

January 16, 2020

- Seen 1 month ago and noted to have suspicious optic nerve appearance
  - IOP at last visit was 15 mm Hg OD/14 mm Hg OS
- Medical history
  - Hypertension using hydralazine (vasodilator), amlodipine (calcium channel blocker), labetolol (beta blocker)
  - Sleep apnea using CPAP
- Eye history and family eye history
  - Negative
  - Gonioscopy
    - Open to CB 360° OD and OS

Examination

- Ta 23/21 9am
- Pachymetry 511/513
- Refraction OD -0.75sph 20/20 OS -1.00sph 20/20
- Optic nerve and imaging
- Visual fields 24-2 SITA Faster

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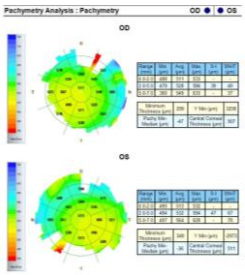

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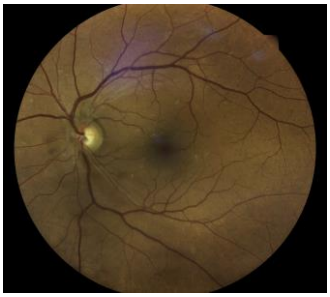

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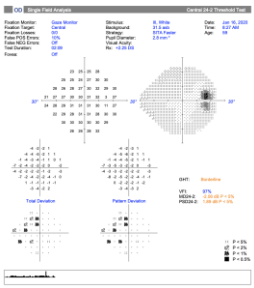

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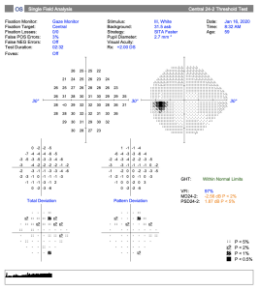

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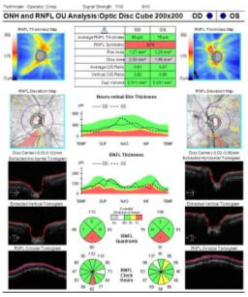

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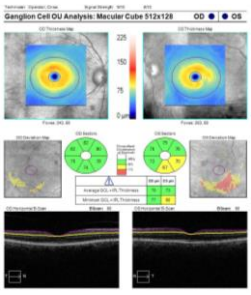

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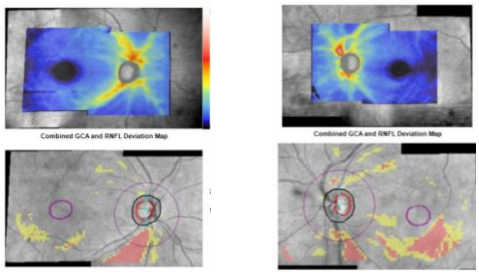

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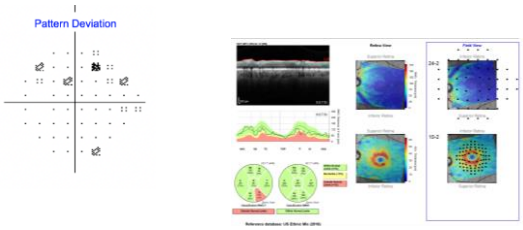

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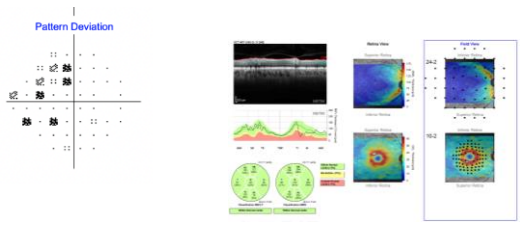

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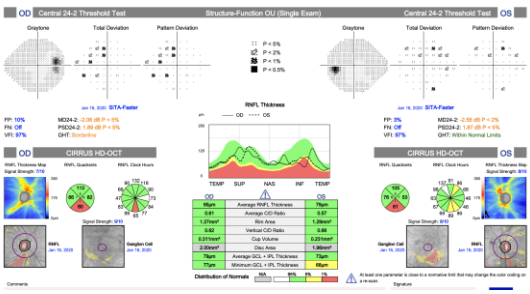

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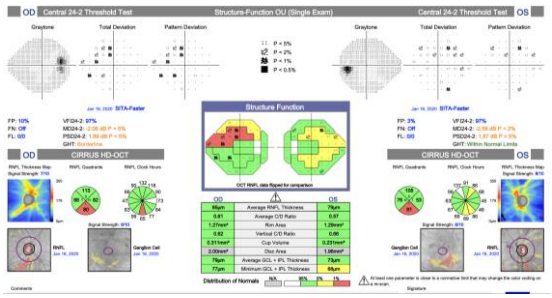

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Assessment

- Primary Open Angle Glaucoma R > L
  - This is not low-tension glaucoma
  - IOP low but thin cornea and using systemic beta blocker
- Young person with dense, focal loss

Plan

48

ARS Questio

- My first choice for therapy would be
  - A. Generic latanoprost
  - B. Lumigan or Travatan Z
  - C. Selective Laser Trabeculoplasty
  - D. Rocklatan
  - E. Vyzulta
  - F. No therapy – monitor further with additional IOP measurements

49

ARS Questio

- My target IOP goal is:
  - 10% reduction
  - 20%
  - 30%
  - 50%

50

ARS Questio

- Once I start therapy, I would bring this gentleman back in
  - 2 weeks
  - 4 weeks
  - 8 weeks
  - 12 weeks

51

ARS Questio

- How often would you do OCT and visual fields after therapy is initiated for the first year?
  - Once per year
  - Twice per year
  - Three times per year
  - Four times per year

52

59yo BM

Assessment

- Primary Open Angle Glaucoma R > L
  - This is not low-tension glaucoma
  - IOP low but thin cornea and using systemic beta blocker
- Young person with dense, focal loss

Plan

- Start PG with target IOP goal of 30% reduction
- Return in 1 month
- Monitor twice yearly with fields and OCT since IOP low

53

What is the expected IOP reduction from SLT in POAG?

- 2-4mm Hg
- 4-6mm Hg
- >6 mm Hg

54

SLT versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicenter randomized controlled trial

- Gus Gazzard, Eugenias Konstantakopoulos, David Garway-Heath et al

www. thelancet.com Vol 393 April 13, 2019

- Pxs had to have mild or moderate glaucoma based on VF criteria
- Target IOP reduction 20-30% (depending on severity)
- Standard SLT energy protocols
- Medicine group – 1st line PGA, 2nd Line Beta blocker, 3rd line CAI or Alpha agonist
- Both groups followed for 36mths

55

LiGHT study outcomes

- Both groups showed similar efficacy in lowering IOP
  - 16.3mm Hg Drop group, 16.6 mm Hg SLT Group
  - 78.2% SLT group required no drops, 12% required 1 drop
  - 64.6% drop group controlled on 1 drop, 18.5% required 2 drops
  - 0% SLT Group required trab, 3.3% Drop group required trab
  - 93% SLT group at target IOP, 95% Drop group
- SLT Group spent 202 pounds less on care
- So what does this mean for us , our clinics and our patients??

56

1) Change your impression of the efficacy of SLT?

2) Change your impression of when you would recommend SLT for your patients?

3) Change your impression on who may be good candidates for SLT?

Does The LiGHT Study…

57

A Tough Inheritance

62 y/o BF, (+) fam hx- treated for POAG for 6 years

VA 20/20 OD, 20/20 OS

Pachs – OD 490, OS 495

No systemic meds

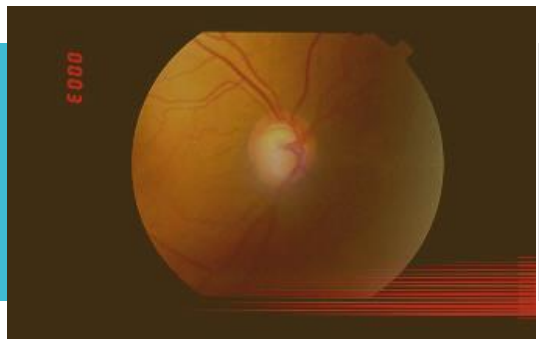
IOP maintained around 18 OU on Lumigan QHS, AlphaganP OU TID, T1/2 OU BID

Initial IOP 28 OD, 29OS

Condition was stable but px developed hypersensitivity (After patient was switched to Brimonidine 0.15%)

IOP 22 OU on Lumigan only

58



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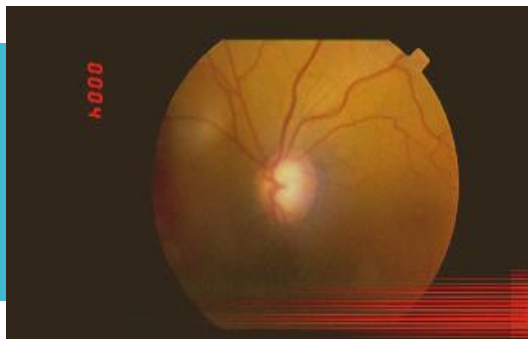

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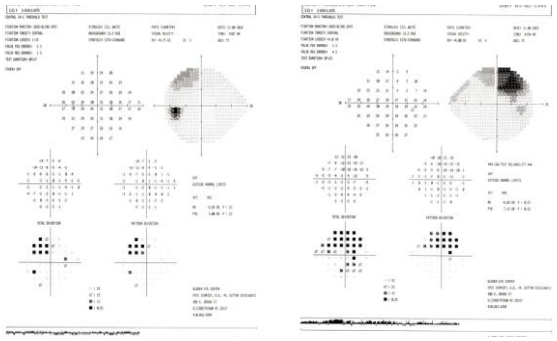

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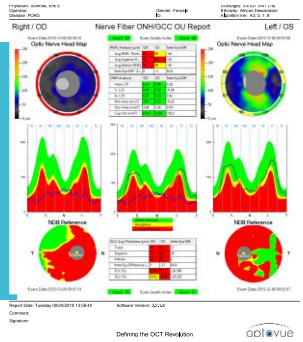

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What is the target IOP?

–18
–15
–12

How Do You Know??

63

What would you recommend?

1. Switch to Rocklatan
2. SLT OU 180
3. Add Azopt OU BID
4. add Timoptic ½ OU BID
5. Trabeculectomy
6. d/c Lumigan, try Travatan Z OU QHS
7. Cosopt OU BID
8. Combigan OU BID

64

SLT OU IOP 19 OD, 20 OS

What would you do now?

65

How Do You Know if the IOP needs to be lower?

What are the risk factors for progression?

- Age
- IOP at diagnosis
- Neuroretinal rim tissue
- Disk hemes
- Corneal hysteresis

Is she progressing?

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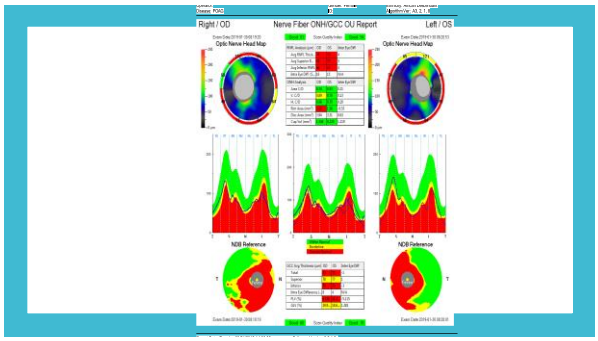

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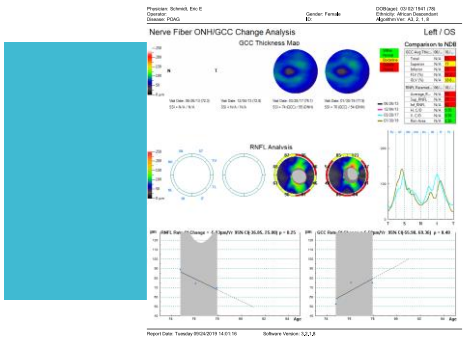

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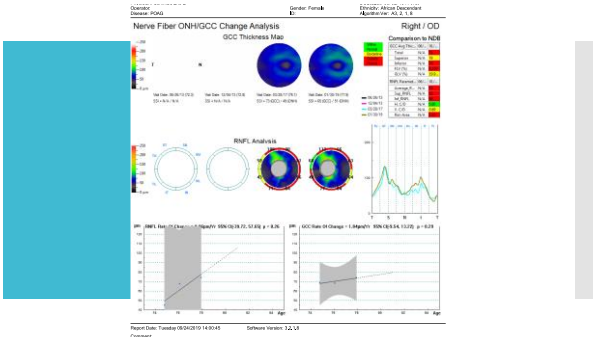

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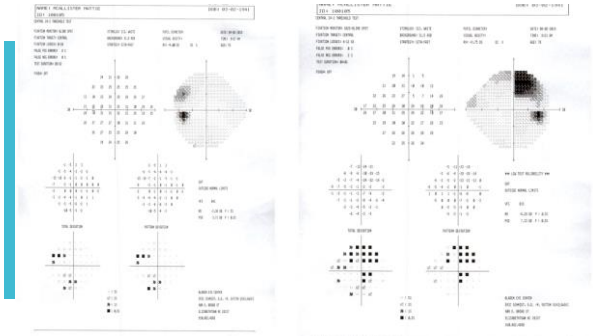

70

Estimating the Lead Time Gained by Optical Coherence Tomography in Detecting Glaucoma before Development of Visual Field Defects

Tammy M. Kuang, MD,[1,2,3] Chanwei Zhang, MD,[1,4] Linda M. Zangwill, PhD,[1] Robert N. Weinreb, MD,[1] Felipe A. Medeiros, MD, PhD[1]

At 95% specificity, up to **35% of eyes had abnormal average RNFL thickness** 4 years before development of visual field loss and **19% of eyes had abnormal results 8 years before field loss**.

Conclusions Assessment of RNFL thickness with OCT was able to detect glaucomatous damage before the appearance of VF defects on SAP. In many subjects, significantly large lead times were seen when applying OCT as an ancillary diagnostic tool.

71

When Progression Is Detected, How Do We Know…

- How Low the IOP Should be…
- Which agent(s) should we use…
- When Surgery is Indicated…
- The Rate Of Their Progression…

72

4 Major questions surrounding progression

- 1. Why Do Patients Progress?
- 2. How Do We Best Detect Progression?
- 3. How Can We Improve Compliance?
- 4. Once Progression Occurs, What Is Our Best Strategy?

73

Rate Of Progression

- RGC loss in normals ~0.5% /yr
- RGC loss in Glaucoma – 3.5% / yr
- RGC loss in treated G – 1.5%/yr

74

Rate of Progression for Various Glaucomas

- NTG- 56% progression at 6 yrs
- POAG -74% progression rate (6 yrs)
- PXG – 93 % - progression rate at 6 yrs
- Pxs older than 68 progressed much faster compared to younger pxs

75

How Low should We Go?

- AAO Preferred Practice Guidelines
  - "Lowering the pretreatment IOP by 25% or more has been shown to slow progression of POAG"
  - Based upon age of px, time of occurrence and other risk factors
    - Prum et al, Ophthalmology. 2016

76

AGIS Results

- Diurnal Curve Is Real Important
  - Avg IOP of 15mm with a curve btwn 13mm – 17mm progresses less than if curve is btwn 11mm – 19mm
- The peak IOP is important
- Which tx best affect the diurnal curve?
- Also remember risk/benefit ratio

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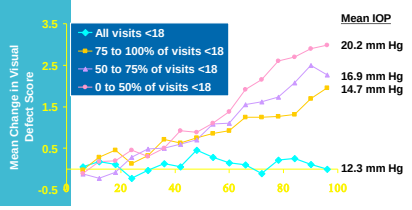
Consiste



AGIS 7, AJO, 2000

78

Progression according to CIGTS

- Seen in 56.7% in 6 years
  - Biggest risk factors
    - Inadequate IOP control
    - Disk hemorrhage
- Proving once again that if you diagnose a px with POAG REALLY treat them!

79

- For pxs who showed progression of glaucoma despite IOP at acceptable range
  - 3% showed a peak IOP >21mm
  - 35% showed a range of IOP >5mm
    - Collaer, Caprioli, et.al, J Glaucoma 2005;14(3): 196-200
- Underscores the importance of serial tonometry *even in well controlled pxs*

80

Treatment Paradigm Summary

- Heijl et al. *Arch Ophthalmol.* 2002; Kass et al. *Arch Ophthalmol.* 2002; Lichter et al. *Ophthalmology.* 2001; AGIS Investigators. *J. Am J Ophthalmol.* 2000.

Mean IOP in study populations	IOP in individual patient	New predictors of progression	Treatment goal
• Early treatment to lower IOP reduces and delays progression • NEI trials show better outcomes at lowest IOP	• To preserve vision, every mm Hg matters • Individualized, low target IOP recommended	• Diurnal fluctuation and long-term variation in IOP within individual patients can cause glaucomatous damage	• get IOP low, and keep it low

81

Glaucoma Damage

- Occurs in a curvilinear/logarithmic plot as opposed to a linear fashion
- The further the disease has progressed the more rapid the RGC loss is
- Early glaucoma rate of RGC loss is 1.5%dB change/yr
- Late stage rate translates to 10%dB change/yr)

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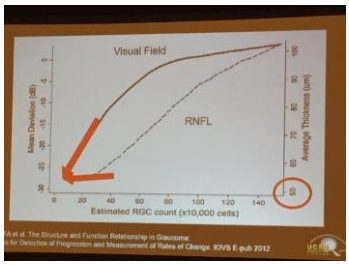

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Predictive Factors For Progressing POAG

- Older age
- Advanced VF damage
  - Worsening MD (-4)
- Smaller neuroretinal rim
- Larger zone Beta
  - Martus, Jonas, et.al. AJO, June 2005
- Baseline IOP, *but not Mean IOP*
  - Martinez-Bello, et al, AJO March 2000.
- Lower CH

84

So Let's Talk About Compliance

85

What are the biggest barriers to proper compliance?

1. Forgetfulness
2. Ability to put drops in
3. Unaware of the importance of the drops
Cost was not in the top 5!!!

86

Predictors of Poor Adherence – Friedman 2019

- Gaps In Visits
- Patients Don't Understand Severity Of Disease
- Cost of Drops (25%)
- Those who Travel A Lot
- Younger Pxs and Very Old Pxs
- African-Americans
- Those In Poor Health

• These drop adherence to <60%

87

Tricks To Increase Compliance

- Improved and increased Dr/Px Communication
- Improve px education as to what Glaucoma is
- Discussion on consequences of untreated glaucoma
- Be a partner with your patients
- Medication review at EVERY VISIT
- More frequent visits??

88

What Does This Mean To Doctors?

- Rethink Maximum Medical Therapy
- Rx Fewer Bottles?
- SLT Earlier
- Doctors must do more to stress adherence and look for side effects

89

Case 5?

- 71 y/o WM
- No ocular symptoms, seen initially for comprehensive exam
- VA 20/30-2 OD, 20/40-2 OS
- Meds: ASA, HCTZ, Lisinopril
- Initial findings:
  - IOP 32mm OD, 34mm OS
  - Pachs 543 OD, 534 OS
  - C/D OD .5/.5, OS .8/.8
- Other tests as shown

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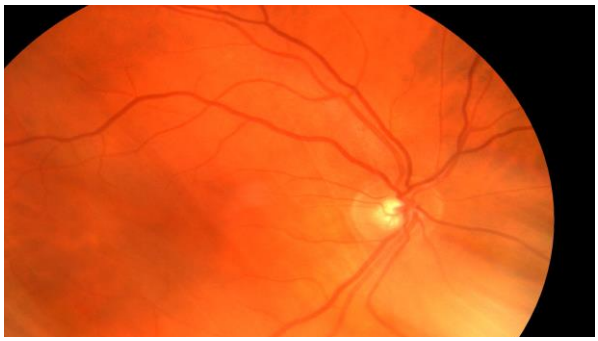

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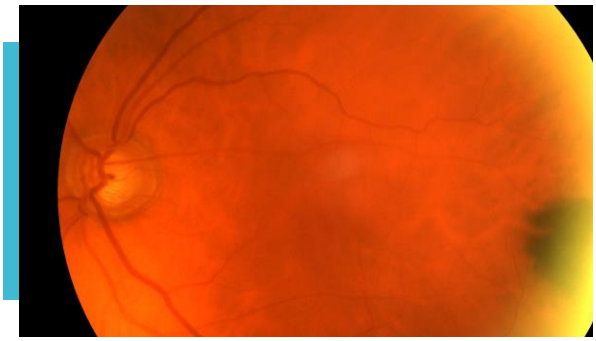

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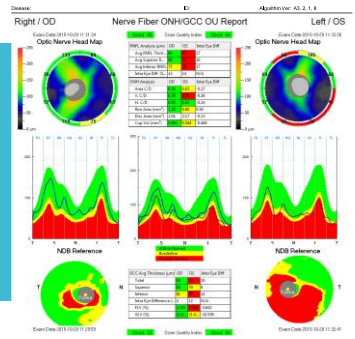

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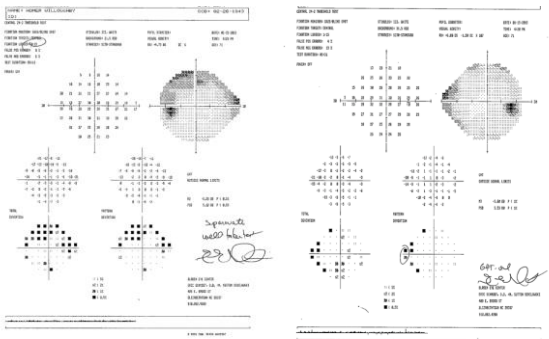

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SO Let's Work Through This …

- Initial Therapy Choice?
- Target IOP?
- Follow Up?

95

3 Months later…

- IOP 23mm OD, 24mm OS on PGA (latanoprost)
- Added Timolol ¾% OU QAM
  - Tolerated drops well but IOP 19mm OD, 20mm OS
- Low Enough?- If not what's the next step?

96

Eventually settled upon:

- Latanoprost OU QHS , Cosopt (generic) OU BID
- IOP stabilized between 17- 20mm Hg OD and OS
- Condition stable for 3 years…

- Or was it?

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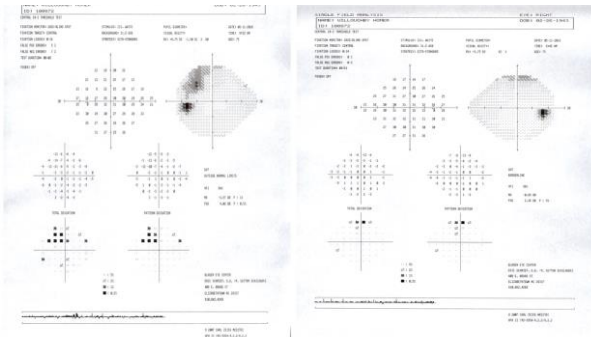

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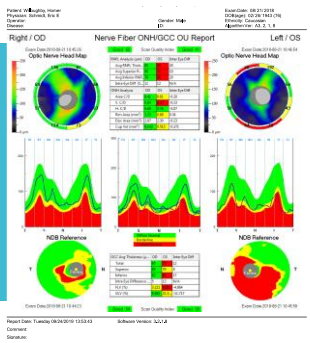

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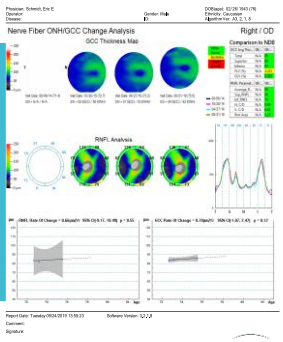

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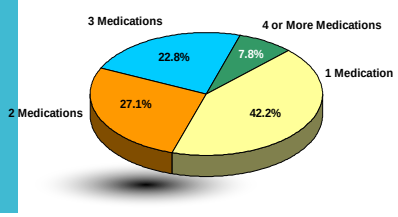
Patients on More Than One IOP-Lowering Medication



Schappert. National Center for Health Statistics. 1995.

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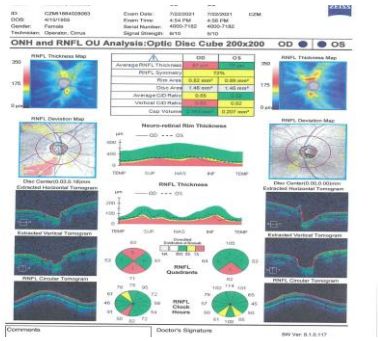

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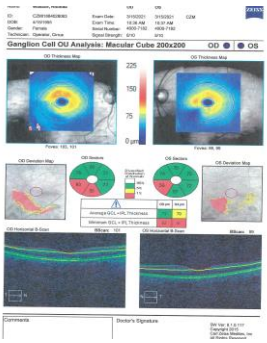

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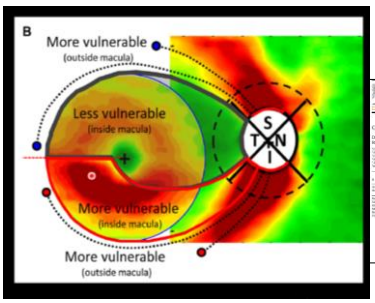

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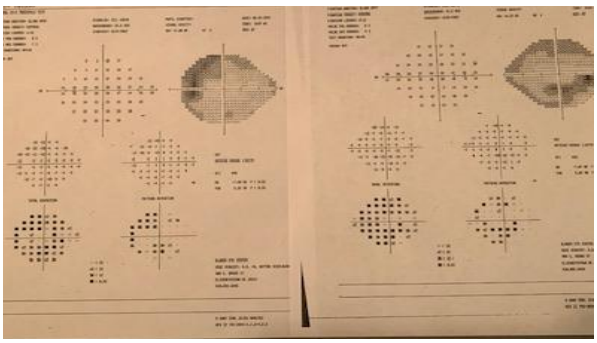

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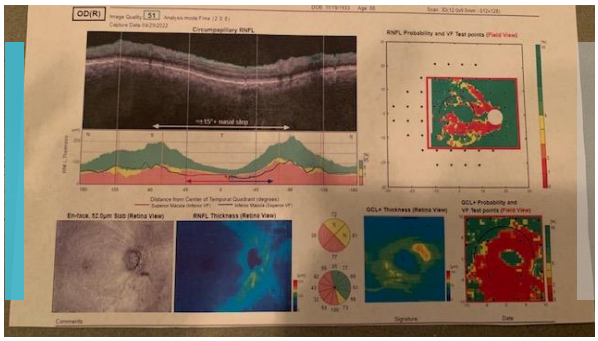
OD(R)
Circumpapillary RNFL
RNFL Probability and VF Test points (Field View)
En-face, 52.0µm Slab (Retina View)
RNFL Thickness (Retina View)
GCL+ Thickness (Retina View)
GCL+ Probability and VF Test points (Field View)

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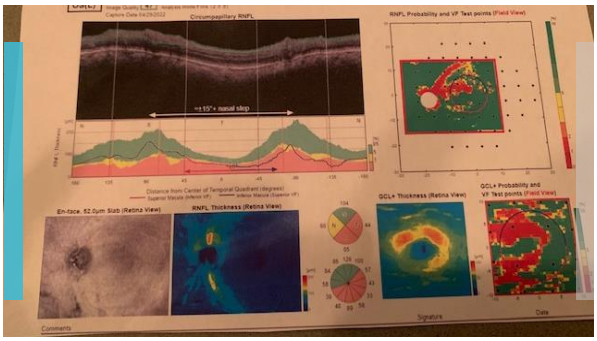
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