

DISCLOSURES

Leo Semes, OD, FAAO, FACMO

Consultant - Maculogix

Speaker Bureau - Regeneron

Scientific Advisory Board - EyePromise, Apellis

Stock options - Eye Promise (< 0.01% ownership), HPO (< 0.01% ownership)

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COURSE OBJECTIVES

- The attendee will be challenged with cases without clear-cut diagnoses
- The attendee will be presented with alternative diagnoses to optic nerve head disorders
- The attendee will gain a perspective on the use of complementary testing in glaucoma diagnoses
- The attendee will be presented with a template for optic disc and RNFL evaluation using clinical observations
- The attendee will appreciate that few cases are straightforward
- The attendee will be offered discussion and input on the conflict that occurs among clinical findings

CONTEMPORARY GLAUCOMA DEFINITION

POAG is a progressive, chronic optic neuropathy in adults in which intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an anterior chamber angle that is open by gonioscopic appearance.

ala AAO PPP

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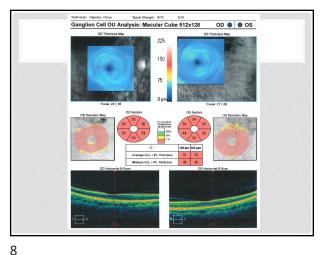
CONTEMPORARY GLAUCOMA DEFINITION...

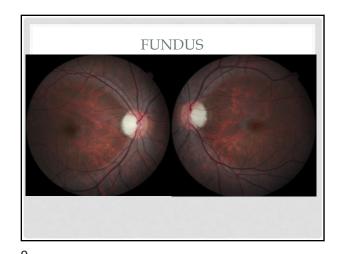
POAG is a progressive, chronic optic neuropathy in adults in which intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an anterior chamber angle that is open by gonioscopic appearance. *ala AAO PPP*

"Can glaucomatous optic neuropathy be induced by a primary <u>non-IOP-related insult</u>... alone??" -Claude Burgoyne

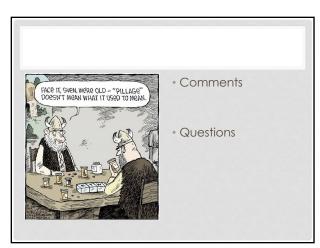
A CASE ILLUSTRATING POTENTIAL CONTAMINATION OF GCC RESULTS

- 40s AA Male
- Longstanding diagnosis of MS with systemic treatment
- BSCVA 20/40, 20/40
- Normal IOP and anterior segment





SUPRATHERSHOLD VF



10 12

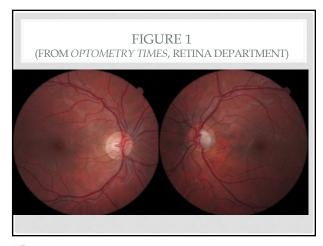
FLD? GLAUCOMA? ???

- A 24 year-old was referred to the Ocular Disease Service at UAB Eye Care for a glaucoma evaluation.
- Spectacle lens correction for myopic refractive error, personal ophthalmic history is otherwise negative.
- Maternal grandfather with glaucoma (unconfirmed).
- He has never smoked and drinks alcohol socially.
- He takes no Rx medications

FLD? GLAUCOMA? ???

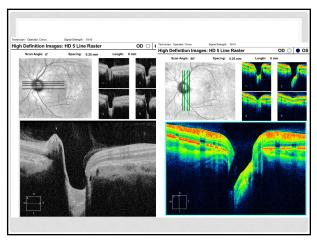
- Visual acuity is correctable to 20/20 in each eye.
- Pupils are round and equally reactive without RAPD.
- Goldmann applanation tonometry: 16 mm Hg in each eye at 9:55 AM.
- Pachymetry: 619 and 622 um OD, OS, respectively.
- The anterior segments were unremarkable in each

13 14



| Comparison | Com

15 16



WHAT'S YOUR DIAGNOSIS?

Congenital/developmental optic pit.

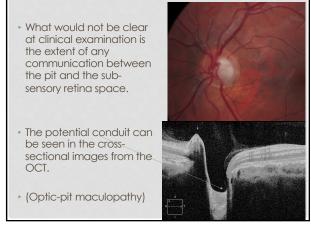
Distinguish from APON

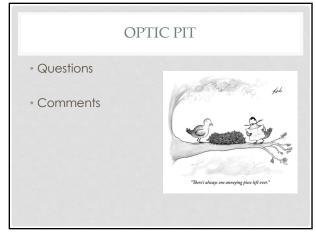
Jovitt JC, Spaeth GL, Katz LJ, Poryzees E, Addiego R. Acquired pits of the optic nerve. Increased prevalence in patients with low-tension glaucoma. Ophthalmology. 1990 Aug;97(8):1038-43: discussion 1043-4.

Careful stereoscopic observation may lead to the diagnosis but additional testing, such as the OCT images are helpful.

Stereoscopically, the pit is evident.

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19 20

62 WM

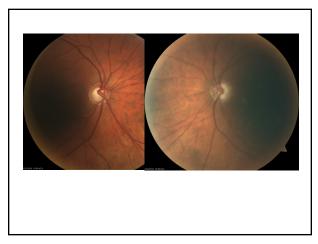
- Complained of vision loss superiorly in the left eye.
- VA 20/20 OD, OS; (L)RAPD 2+; IOP 11,9 mmHg.
- Seen by primary-care OD Dx = NTG, initiated on latanoprost qhs.

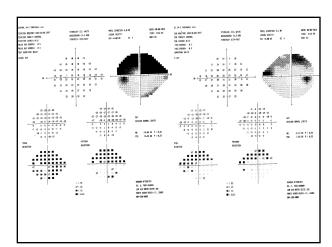
62 WM

- • Complained of vision loss superiorly in the left eye VA 20/20 OD, OS; (L)RAPD 2+; IOP 11,9 mmHg.
- Seen by primary-care OD Dx = NTG, initiated on latanoprost qhs.
- Sent for consultation/SLT due to significant VF depressions.

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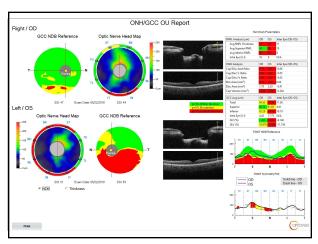
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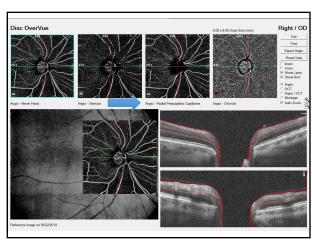




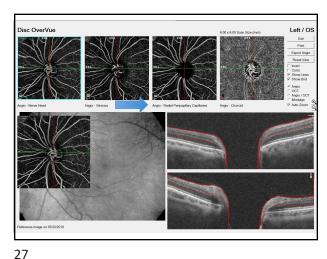
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Additional information

• Patient reveals in social conversation the he suffers from Reynauds syndrome

28

Additional information

- Patient reveals in social conversation the he suffers from Reynauds syndrome
- Patient further reveals in casual conversation that he takes a prescription medication for ED, and that it makes his vision blurry!

Cryo-EM structure of phosphodiesterase 6 reveals insights into the allosteric regulation of type I phosphodiesterases Sahil Gulati^{1,2,3}, Krzysztof Palczewski^{1,2,3}*, Andr Henning Stahlberg⁴*, Lubomir Kovacik⁴

Gulati et al., Sci. Adv. 2019; 5 : eaav4322 27 February 2019

SCIENCE ADVANCES | RESEARCH ARTICLE

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SCIENCE ADVANCES | RESEARCH ARTICLE

the PDE family (4, 5) and other related enzymes (6). In particular, inhibitors of PDE5, including sildenafil and vardenafil, are widely used for the treatment of erectile dysfunction and pulmonary hypertension (7). However, PDE5 inhibitors have been associated with several ocular side effects, including blurred vision, changes in color vision, transient alterations in the electroretinogram, conjunctival hyperemia, ocular pain, photophobia, and, in extreme cases, damage to the optic nerve (8). These secondary effects are mediated

Gulati et al., Sci. Adv. 2919: 5: eaav4322 27 February 2019

But not all data support the risk for AION

- Analysis included reports from MEDLINE, EMBASE, Toxline and VigiBase for NAION and PDE-5 inhibitors
 - Four observational studies, [3 had good methodological protocols]
 - 50 case reports, 12 of which did not have risk factors for NAION, but regular administration was observed in 24/50 (48%) & 39 (78%) were treated for ED
 - 608 spontaneous reports

Conclusion: According to the available evidence, the treatment with phosphodiesterase - 5 inhibitors was not found to be associated with

Penedones A, Alves C, Batel Marques F. Risk of nonarteritic ischaemic optic neuropathy with phosphodiesterase type 5 inhibitors: a systematic review and meta-analysis. Acta Ophthalmol. 2020 Feb;98(1):22-31. doi: 10.1111/jos.14253. Epub.2019 Sep 27.

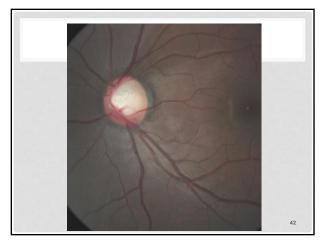
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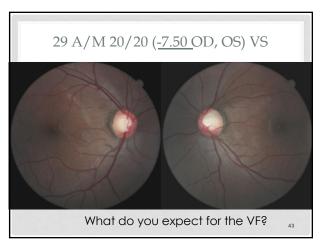
Presents for periodic ophthalmic evaluation
Unremarkable ocular [ex. myopia] and family history
Noncontributory medical history
BSCVA 20/20 (OD, OS)
Anterior segment – unremarkable (OD, OS)
IOP 16, 17 mmHg, (OD, OS); (Pachymetry not obtained)

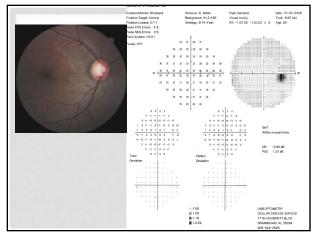
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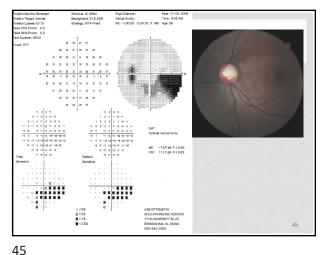


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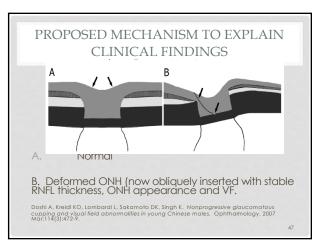


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CLINICAL GUIDANCE FOR THE PRESENT CASE Doshi A, Kreidl KO, Lombardi L, Sakamoto DK, Singh K. Nonprogressive glaucomatous cupping and visual field abnormalities in young Chinese males. Ophthalmology. 2007 Mar;114(3):472-9. http://www.ncbi.nlm.nih.gov/pubmed/17123617

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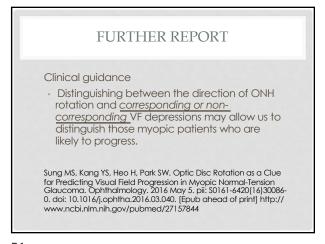


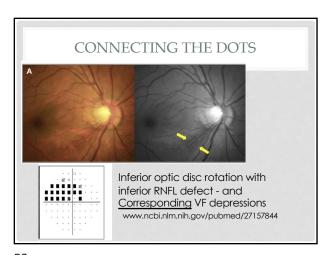
Stable over 8 years 42 – 50 Kreidl KO, Lombardi L, Sakamoto DK, Singh K. Whyrogressive glaucomatous cupping and visual field abnormalifies in young Chinese males. Ophthalmology, 2007 Mar;114(3):472-9.

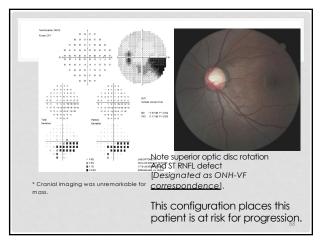
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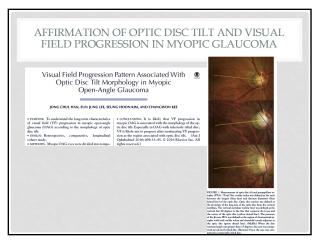
FOLLOW-UP DATA AND GUIDANCE (2011) Treated and untreated patients suspected of having glaucoma should be followed for several years to determine progression regardless of whether their condition is related to Among young Chinese myopes, the best course may be to initiate treatment "gently" [1 or 2 meds] unless or until there is demonstration of rapid progression. http://www.ncbi.nlm.nih.gov/pubmed/21623224 Kumar RS, Baskaran M, Singh K, Aung T. Clinical Characterization of Young Chinese Myopes With Optic Nerve and Visual Field Changes Resembling Glaucoma. J Glaucoma. 2011 May

FURTHER REPORT Key conclusions Optic disc rotation-VF defect correspondence may be an important prognostic factor for patients with myopic NTG for predicting progression. (ONH hemorrhage and IOP reduction may contribute as well) Sung MS, Kang YS, Heo H, Park SW. Optic Disc Rotation as a Clue for Predicting Visual Field Progression in Myopic Normal-Tension Glaucoma. Ophthalmology. 2016 May 5. pii: S0161-6420(16)30086-0. doi: 10.1016/j.ophtha.2016.03.040. [Epub ahead of print] http:// www.ncbi.nlm.nih.gov/pubmed/27157844

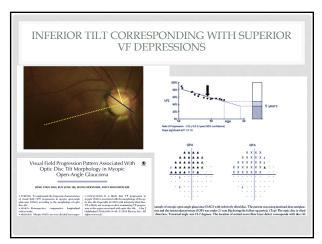








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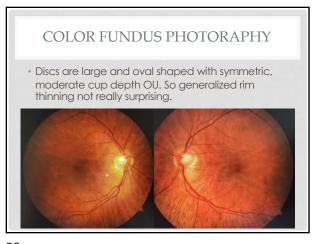




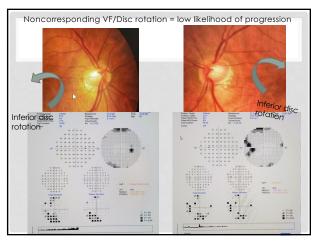
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FROM A FORMER STUDENT LAST MONTH

- 59 year old white female.
- H/o high myopia.
- Post-LASIK CCT 482/472.
- Dad and PGF have glaucoma.
- T_{app} at 1:44 pm: 10/11, Tmax 17/16.



57 58



OCT 9/10 signal strength OD/OS.
Inferior VF defects correspond to OCT thinning but Opposite to disc appearance/direction of tilt by observation.

Inferior disc rotation

Noncorresponding VF/Disc rotation = low likelihood of progression

59 60

WORLDWIDE SUPPORT FOR THE RELATIONSHIP OF MYOPIA & GLAUCOMA

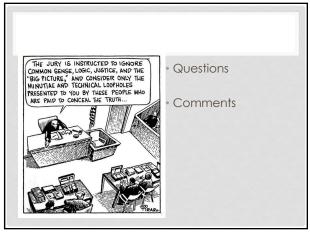
- Grødum K, Heijil A, Bengtsson B. Refractive error and glaucoma. Acta Ophthalmol Scand 2001;79:560–6. (Sweden)
- Mitchell P, Hourihan F, Sandbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. Ophthalmology 1999;106:2010–5. [Australia]
- Suzuki Y, Iwase A, Araie M, et al. Risk factors for open-angle glaucoma in a Japanese population: the Tajimi Study.
 Ophthalmology 2006;113:1613–7. [Japan]
- Yoshida M, Okada E, Mizuki N, et al. Age-specific prevalence of open-angle glaucoma and its relationship to refraction among more than 60,000 asymptomatic Japanese subjects.
 J Clin Epidemiol 2001;54:1151–8. [Japan]

WORLDWIDE SUPPORT FOR THE RELATIONSHIP OF MYOPIA & GLAUCOMA

- Mastropasqua L, Lobefalo L, Mancini A, et al. Prevalence of myopia in open angle glaucoma. Eur J Ophthalmol 1992;2: 33–5. [Italy]
- Leske MC, Connell AM, Wu SY, et al. Risk factors for openangle glaucoma. The Barbados Eye Study. Arch Ophthalmol 1995;113:918– 24 (Barbados)
- Perera SA, Wong TY, Tay WT, et al. Refractive error, axial dimensions, and primary open-angle glaucoma: the Singapore Malay Eye Study.
 Arch Ophthalmol 2010;128: 900-5. [Singapore]
- Xu L, Wang Y, Wang S, et al. High myopia and glaucoma susceptibility the Beijing Eye Study. Ophthalmology2007;114:216–20.
 (China)
- Jiang X, Varma R, Wu S, et al. Baseline risk factors that predict the development of open-angle glaucoma in a population: the Los Angeles Latino Eye Study. Ophthalmology 2012;119:2245–53. [USA]

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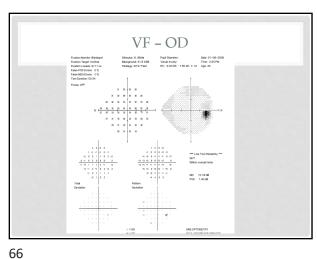
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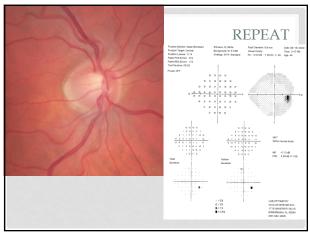


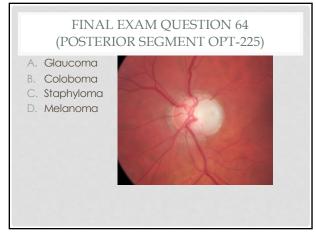
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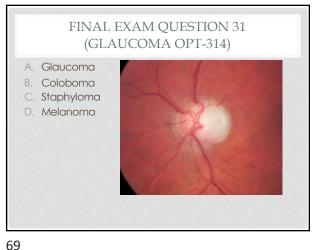


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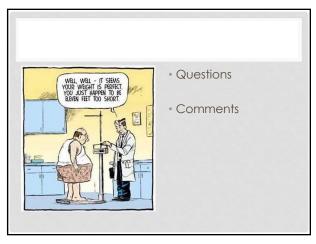


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Myopia as a Risk Factor for Open-Angle Glaucoma: A Systematic Review and WHAT IS THE RELATIONSHIP BETWEEN MYOPIA AND GLAUCOMA (2011) Meta-Analysis Michael W. Marcus, MSc, ¹ Margriet M. de Vries, MD, ¹ Francisco G. Junoy Montolio, MD, ¹ Nondo M. Jansonius, MD. PhD^{1,2} Conclusion: Individuals with myopia have an increased risk of déveloping open-angle glaucoma.

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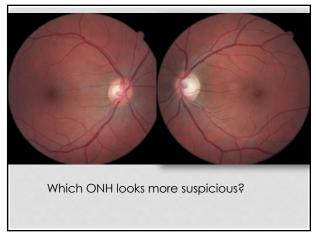
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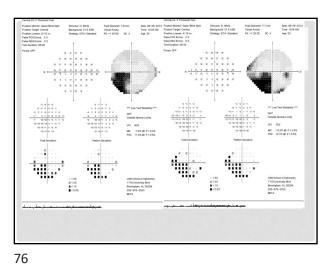
33 F (NURSE) • Referred to UAB Eye Care as a glaucoma suspect Medical history non-contributory • Family history positive for "glaucoma" • Ocular history: refractive correction and mention of amblyopia.

33 F (NURSE) BSCVA 20/20 OD, OS. Minimal hyperopic refraction • IOP: 16 mm Hg OD and 18 mm Hg OS Pachymetry:m567 microns OD and 562 microns OS Angles open with visible CB 360 OS, OS Anterior segment unremarkable

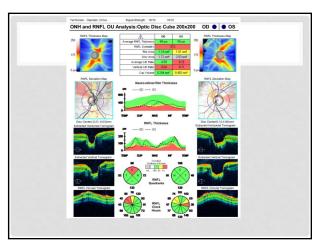
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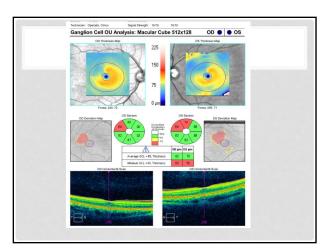
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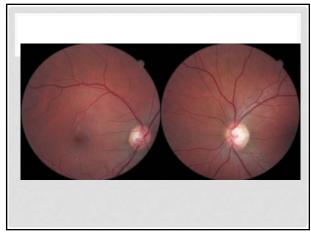


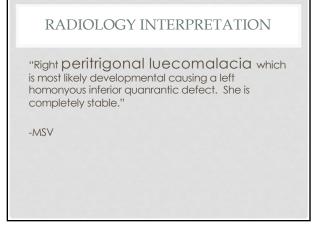
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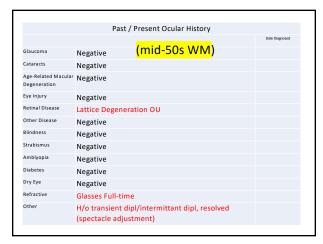


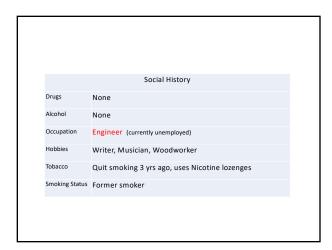
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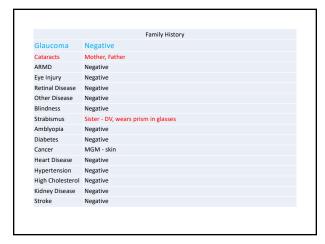


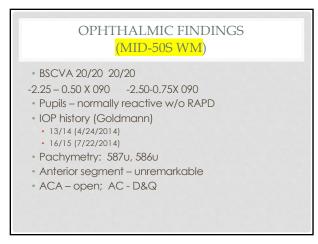


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OPHTHALMIC FINDINGS

* Lens (LOCSIII): NO 1 / NC2 CS 0 PSC 0 (OD = OS)

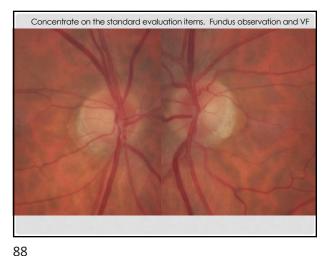
* Optic disc

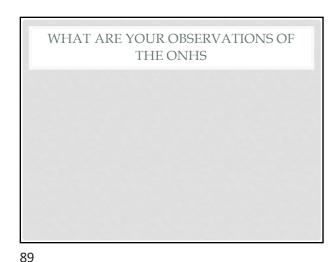
* VF

* OCT

* What do you expect?

86 87

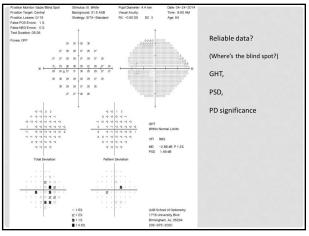




WHAT ARE YOUR OBSERVATIONS OF THE ONHS Small • Temporal crescent consistent with RE • OBL insertion OS > OD • Inferior notch OD > OS • β-zone PPA (OD where rim tissue is thinnest; OS greater temporally than inferiorly)

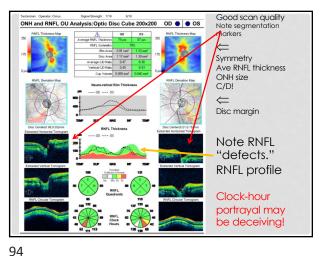
Reliable data? (Where's the blind spot?) GHT, PSD, PD significance

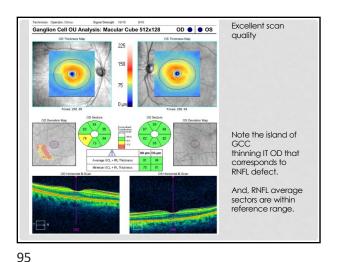
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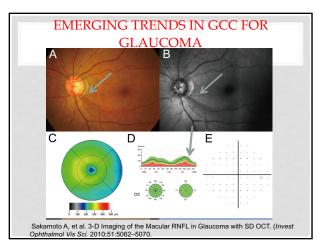
WHAT IS YOUR INTERPRETATION OF THE VF • Left Right Correct testCorrect eyeAppropriate correction Correct testCorrect eye Appropriate correction Reliable dataGHT – WNL Reliable dataGHT – WNL PSD – not flagged • PSD – not flagged PD significance – no clusters in areas suspicious for glaucoma PD significance – ? clusters in areas suspicious for glaucoma

92 93

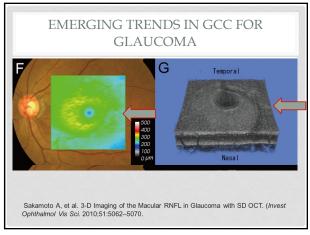


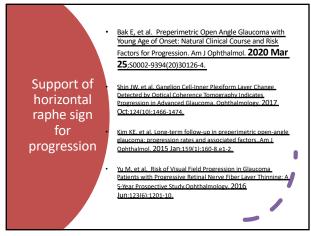


OCT AND GLAUCOMA Utility · Confirming or ruling out he diagnosis of glaucoma Monitoring progression Capabilities RNFL thickness* ONH profile ONH "topography" Macular RNFL**



96 97





98 99

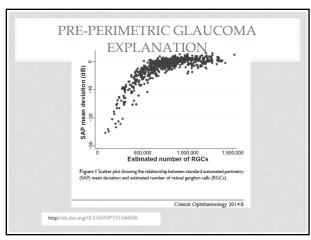


WHAT ARE OUR NEXT STEPS?

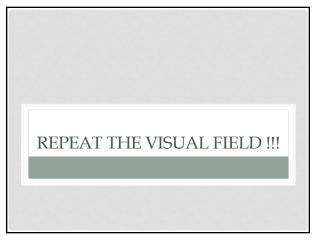
Reviewing the data
Good VA
Good VA
Good VA
Solution
Soluti

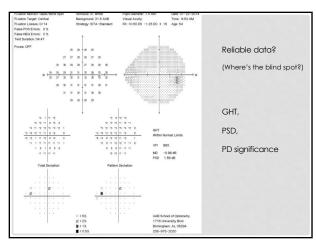
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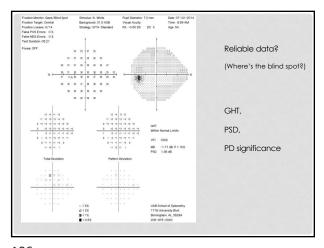


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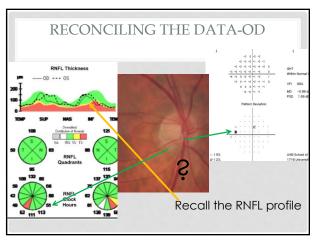


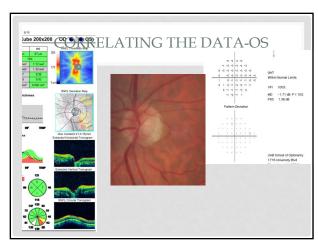
8/18/22



WHAT IS YOUR INTERPRETATION OF THE VF Right • Left Correct test Correct test Correct eyeAppropriate correction Correct eyeAppropriate correction Reliable dataGHT – WNL • Reliable data • GHT - WNL • PSD – not flagged PSD – not flagged • PD significance -? cluster • PD significance - no clusters in areas suspicious for glaucoma in nasal step region

106 107





108 109

MANAGEMENT

Critical questions
Degree of damage
Burden of treatment
Life span

MANAGEMENT

Critical questions
Degree of damage
Burden of treatment
Life span

No treatment at this time
Follow, repeating all tests X 6 mo
Alternatives?

110 111

8/18/22



- IOP = 19/20
- Updated disrupted sleep status diagnosed with SAS and using CPAP device. Reportedly, "...feeling much better."
- Does this change our thinking?

• Questions
• Comments

Got up at 5am, 8km run completed, came back prepared a vegetable smoothie for breakfast....

Don't remember the rest of the dream....

112 117



RS - FOLLOWED X 7 YRS

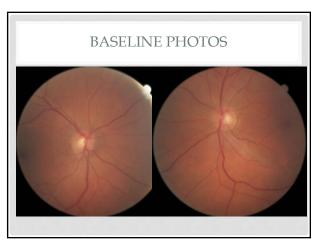
• Non-contributory medical and family histories

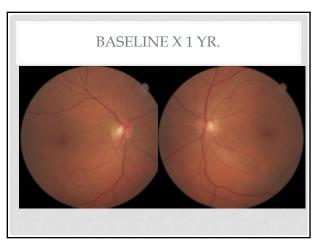
• IOP averages 23 (narrow range: 2-3 mm fluctuation)

• DDX?

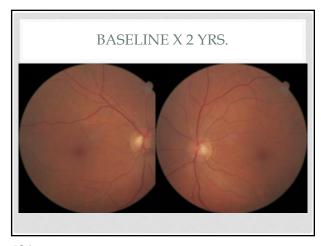
• Glaucoma suspect
• Ocular hypertensive

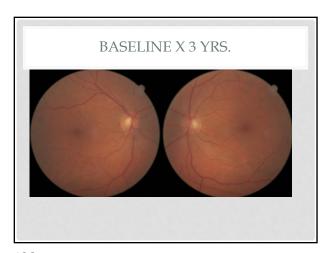
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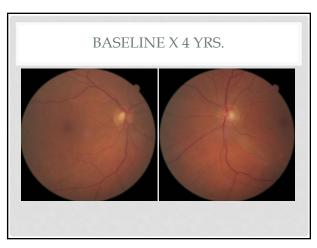


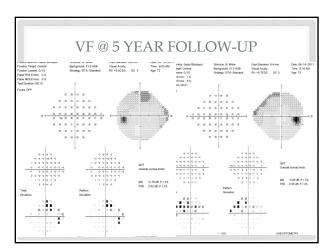


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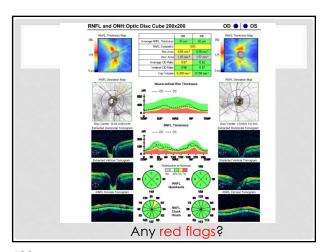








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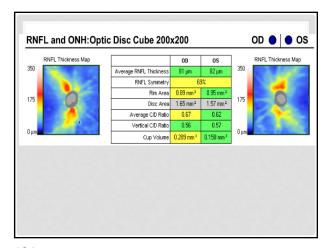


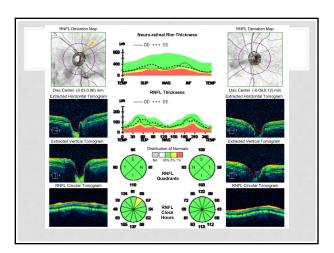
And this just in . . .

Journal Pre-proof
The Weiss ring, a major confounding factor for measurements of peripapillary retinal nerve fiber layer thickness
PII: S0002-9394(22)00003-4
DOI: https://doi.org/10.1016/j.ajo.2022.01.001
To appear in: American Journal of Ophthalmology
Accepted date: January 1, 2022

Highlights
Eyes with a Weiss ring showed thinner mean and inferior pRNFL thicknesses than normal controls, which could be a major confounding factor for analyses of pRNFL changes, especially in glaucoma patients.

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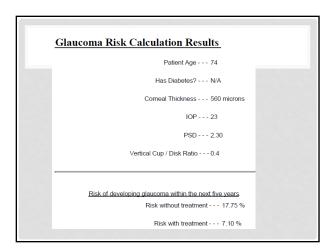
OHT RISK CALCULATIONS
(FROM OHTS DATA MINING)
Glaucoma Risk Calculation Results

Patient Age --- 74

Has Diabetes2--- N/A

Risk of developing glaucoma within the next five years
Risk without treatment --- 17.75 %
Risk with treatment --- 7.10 %

Vertical Cup / Disk Ratio --- 0.4



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Glaucoma Risk Calculation Results

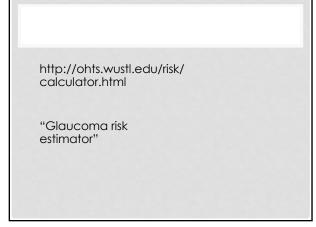
Patient Age - - - 74

Has Diabetes? - - - N/A

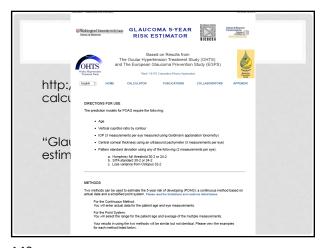
Risk of developing glaucoma within the next five years
Risk without treatment - - - 19.21 %
Risk with treatment - - - 7.69 %

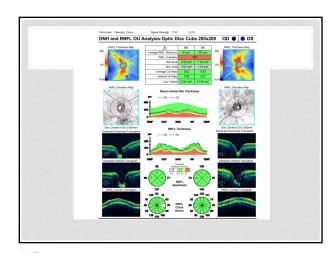
Vertical Cup / Disk Ratio - - - 0.4

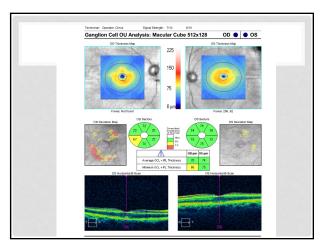
Using just the latest PSD [mean OD + OS] and IOP, note the difference

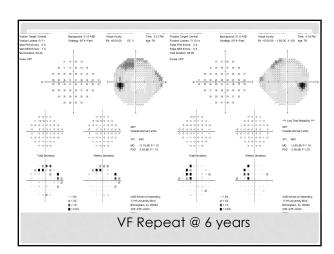


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OHT FOLLOW-UP - MOST RECENT

Treatment option offered and pt started on PGA ghs

F/U @ 2 weeks IOP = 16mm Hg in each eye.

Continued on treatment with low teens IOP

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 The Ocular Hypertension Study Group

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

Published online April 15, 2021. Corrected on July 22, 2021.

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

CONCLUSIONS AND RELEVANCE In this study, only one-fourth of participants in the OHTS 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.

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