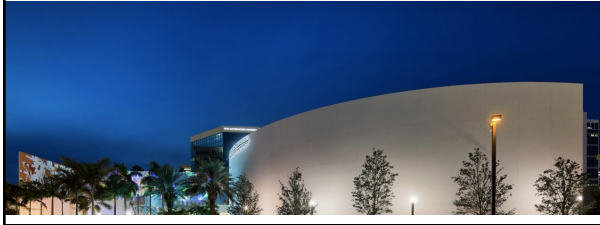**TAKEAWAYS IN GLAUCOMA MANAGEMENT**
JESSICA STEEN OD, FAAO, DIPL ABO

1

FINANCIAL DISCLOSURES

- Speaker-Carl Zeiss Meditec, Bausch and Lomb, Oyster Point Pharma
- Advisory Board-Bausch and Lomb, Santen, Peripherex, Ocuphire, Ocuterra
- Shareholder-Clearside Biomedical (<0.01% ownership)
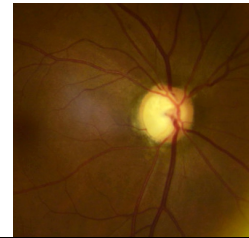
- *All relevant relationships have been mitigated*

2

The foundation of assessment: optic disc evaluation

We're really talking about assessment of the neuroretinal rim

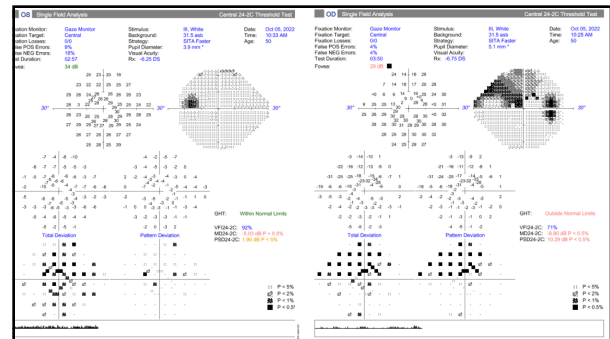*Best assessed binocularly at the slit lamp using a magnified view*

3

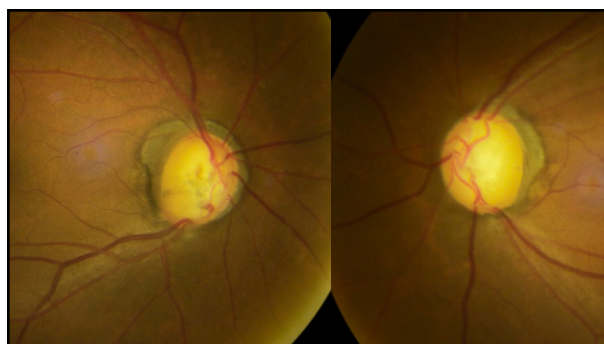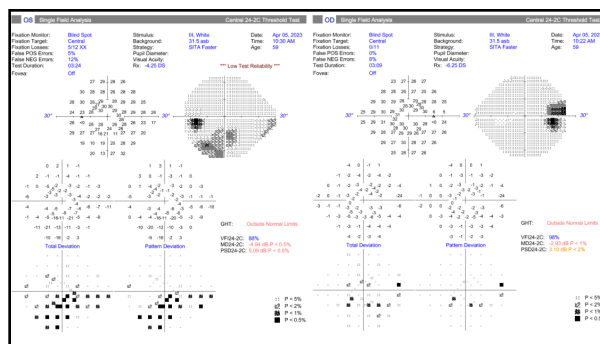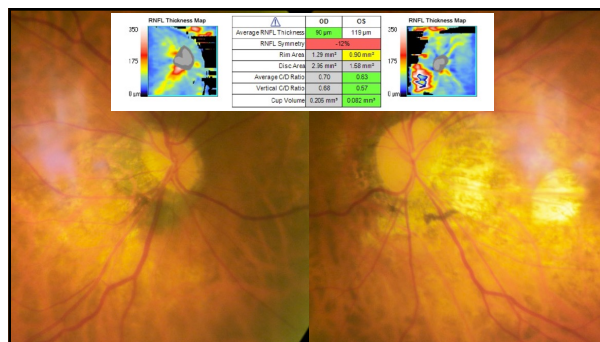*The health of the neuroretinal rim is NOT assessed by a cup to disc ratio*

4

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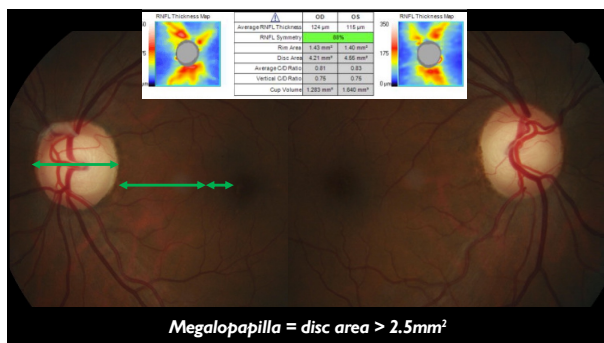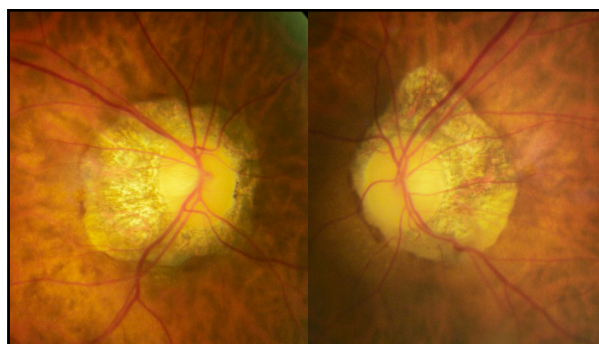
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Peripapillary atrophy or "halo"

Nerve fibers are susceptible to damage when they are passing bare choroid

These eyes may be more sensitive to pressure changes--and this halo can enlarge and change over time

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Glaucoma is a progressive, chronic optic neuropathy

Is there change over time?

Take the time that you need to establish a diagnosis

21

Necessity of data interoperability

How many different devices are utilized for a glaucoma patient?

How many data points are collected—and evaluated at each visit?

How do we share our data with co-managing providers

23

75 YEAR OLD FEMALE

- Diagnosed with POAG OU in 2008
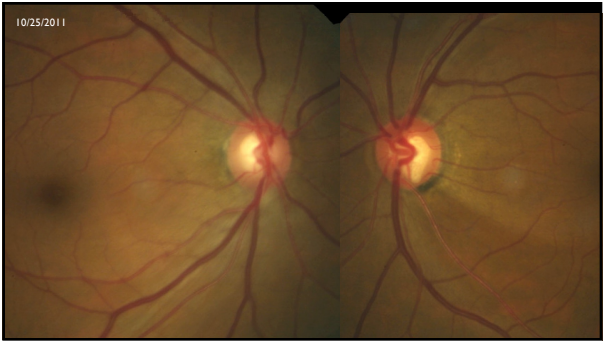 - Medically managed
  - History of adverse event with brimonidine (headache)
- Peak IOP 20mmHg OD and OS
- CCT 540 μm OD and 538 μm OS
- Gonioscopy open to PTM 360 degrees OD and OS
  - No PAS, AR, NVA OD and OS, flat iris approach, 2+ PTM pigment OD and OS
- **Presented taking latanoprost 0.005% QHS OU and dorzolamide-timolol BID OU**
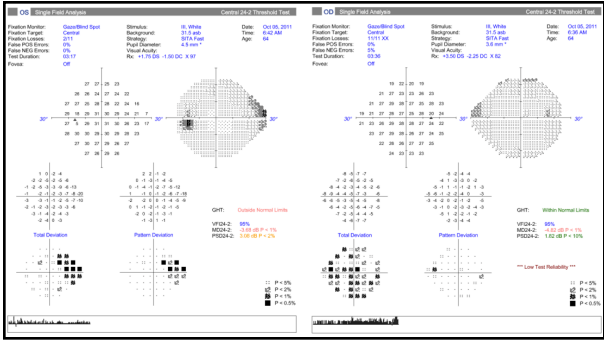 - **IOP 13-16mmHg range OD and OS**

24

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75 YEAR OLD FEMALE

- Hypertension, hyperthyroidism, and hypercholesterolemia
  - **Atenolol**, losartan, thiamazole
- No close family history of glaucoma
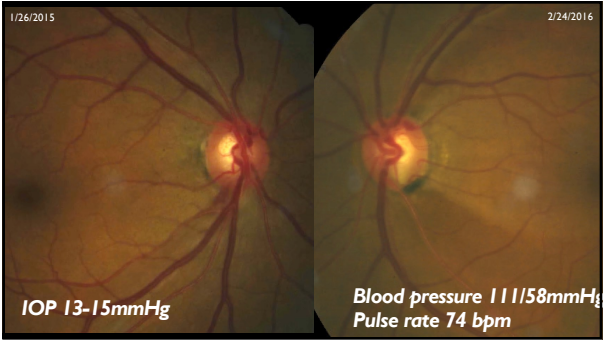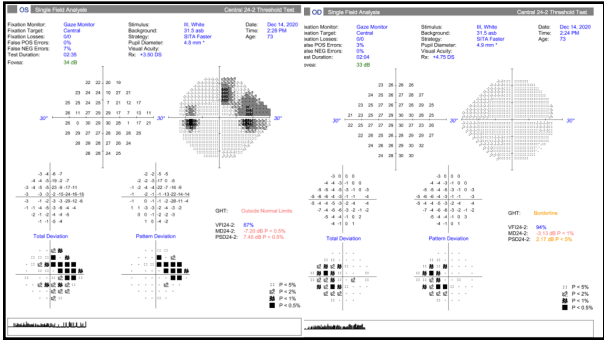 - Maternal uncle, paternal aunt
- BCVA 20/20 OD and OS
  - APD OS
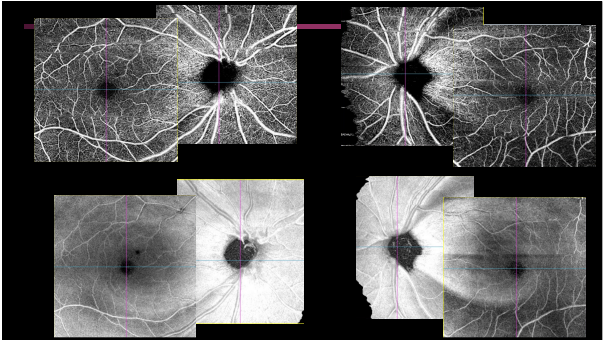
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IOP 13-15mmHg

Blood pressure 111/58mmHg
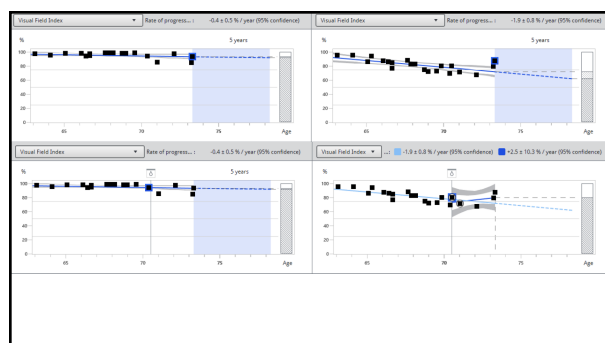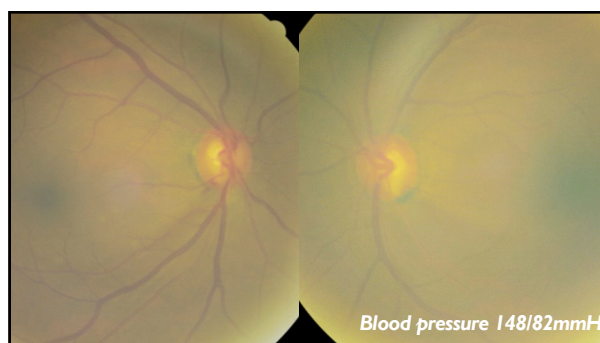Pulse rate 74 bpm

29

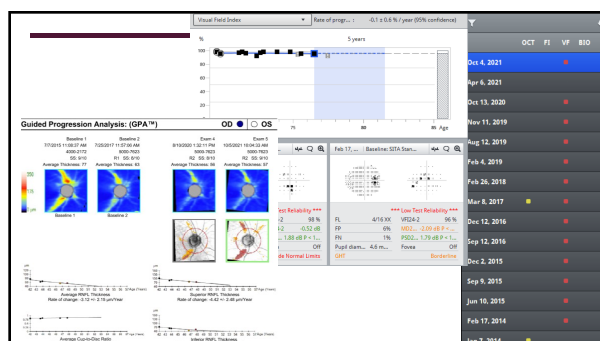

30

31

Blood pressure 148/82mmHg

32

WE'RE AT A TIPPING POINT

- Evaluation of multiple datapoints are needed to determine our management plan
  - Evaluation of current data
  - Meaningful comparison to previous data (including trend analysis)
- Deliver and discuss the plan
  - ….and be ready to adjust the plan based on patient-specific needs

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34

Artificial Intelligence
Human-like tasks including recognition, processing, creating output

What's the difference?

Machine Learning
Development of algorithms that recognize data

Deep Learning
Supervised vs. semi-supervised vs. self-supervised learning
Process large amounts of raw data and determine the most relevant features to use and improve detection
Convolutional neural networks

35

Can we predict disease progression?
We can currently identify features present after the event has occurred

Can we improve efficiency of our clinical structure: who needs to be seen once per year, and who needs to be seen every 3 months?
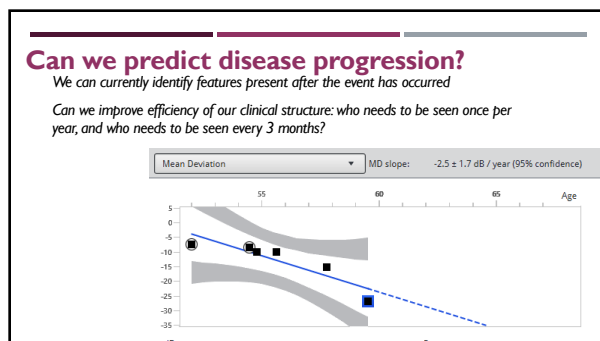
36

OUR NEXT ACT?

- Improved information to make clinical decisions
- Care will become more individualized
- Shift towards counseling

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Issues in imaging

Segmentation error
Inaccuracy of detection of retinal layers or boundaries
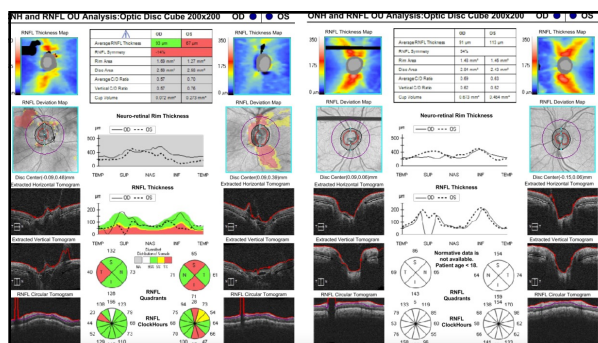*20-46.3% of RNFL scans contain artifacts or segmentation errors*

Y. Liu, H. Simavli, C.J. Que, et al 2015
S. Asrani, L. Essaid, B.D. Alder, C. Santiago-Turla 2014
R.A. Alshareef, S. Dumpala, S. Rapale, et al 2016
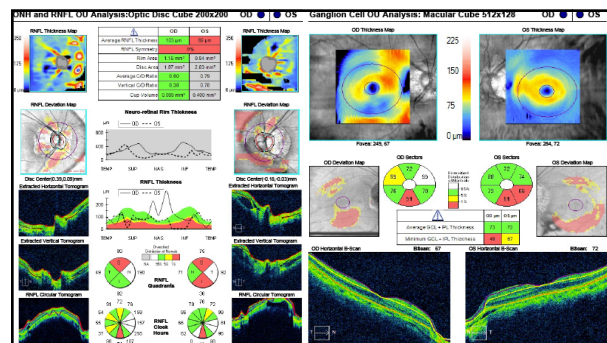K.E. Kim, J.W. Jeoung, K.H. Park, D.M. Kim, S.H. Kim 2015

38

RETINAL NERVE FIBER LAYER & GANGLION CELL COMPLEX

- **We use both**
- Ganglion cell complex (not just the cell layer-usually IPL-may also include RNFL)
  - Difficult to segment ganglion cell layer ONLY
  - Retinal ganglion cells most dense at the macula
    - More than 30%; 2% of retinal area
  - Lack of retinal blood vessels and support cells
- Retinal nerve fiber layer contains non-neuronal elements
  - Thickness impacted by blood vessels, glial elements
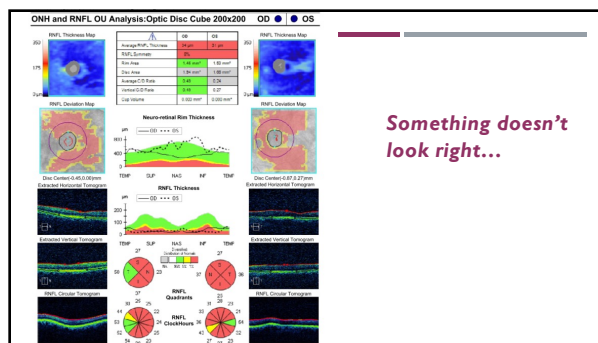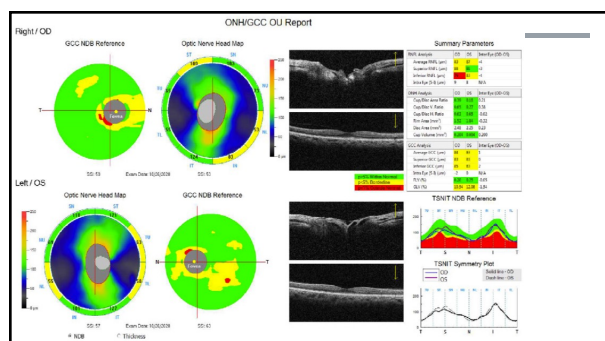 - BUT-contains **all** (100% of) retinal ganglion cell axons
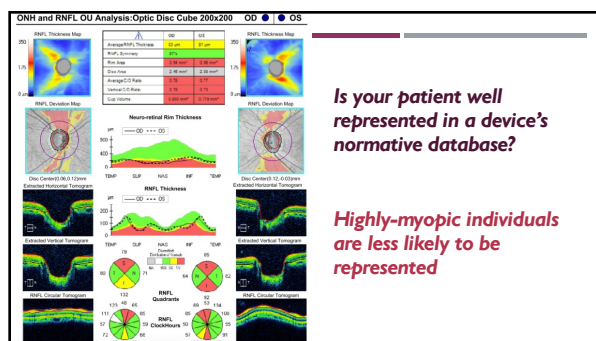
39

40

41

Something doesn't look right...

42

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43

Is your patient well represented in a device's normative database?

Highly-myopic individuals are less likely to be represented

44

45

ISSUES IN IMAGING

- Poor image quality
- Incorrect scan performed
- Uploaded to the wrong patient's chart
- Incorrect identifying information

46

What is a "glaucoma workup in 2023?"

…it depends on the patient— and their clinical features which had them 'labeled' as a glaucoma suspect to begin with

47

Assessment of a newly referred patient

What features will be most valuable to assess to allow us to make a meaningful management decision that day?

Prioritization of testing

48

## Evaluation of history (risk assessment)

Helps to guide testing day one

Suspicion of glaucoma secondary to:
Optic disc appearance
Intraocular pressure
Family history
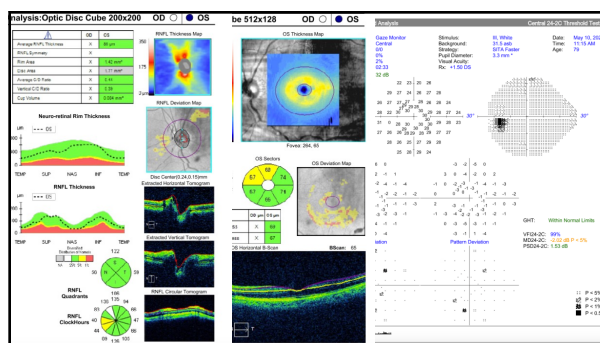### Visual field defect
…Something else?

49

80 YEAR OLD BLACK MALE

- History of POAG OU diagnosed 2-3 years ago
- Latanoprost QHS OU, dorzolamide-timolol BID OU
- NLP OD, 20/40 OS
  - 4+ APD OS
- Band keratopahy OD
- PCIOL in good position OD; 2-3+ opalescent NS OS
- IOP 28mmHg OD, 8mmHg OS

50
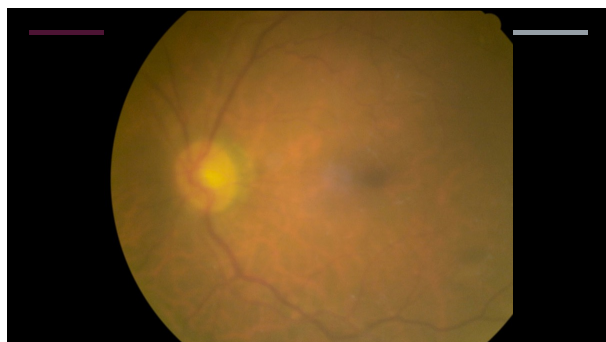
51

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Sometimes the best action is seemingly "inaction"
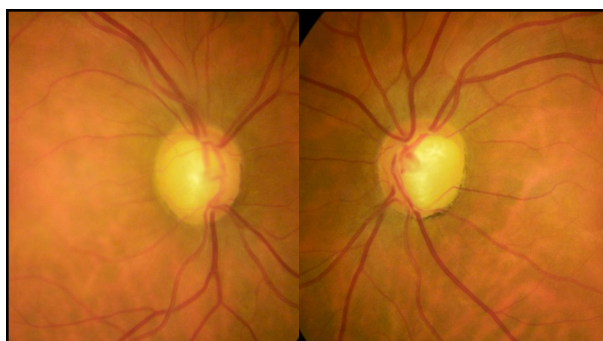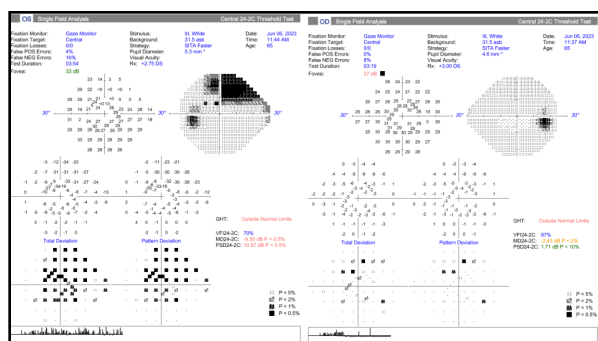
53

65 YEAR OLD FEMALE

- Diagnosed with glaucoma in 2008; unknown peak pressure
  - With spotty adherence reported, IOP has been measured as high as 20mmHg OD and OS
- Latanoprost (teal cap) QHS OU; IOP 15mmHg OD 16mmHg OS
- CCT 466um OD 471um OS

- Gonioscopy open to CBB 360 degrees
  - No PAS, AR, NVA OD and OS
  - 1+ PTM pigment OD and OS, flat iris approach
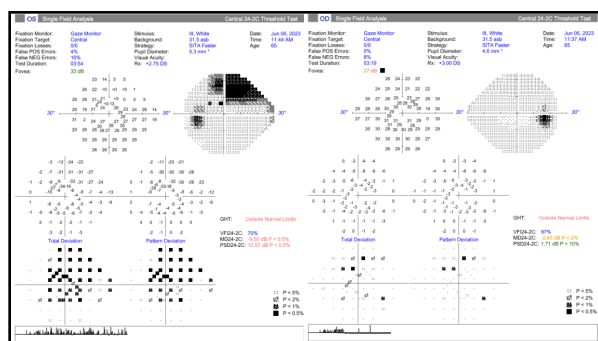
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Is 15-16mmHg good?!

...it depends
Ideally 3 measurements prior to making a treatment decision

In this case, what are the risks/benefits of:
1) **Continuing current therapy**
2) **Escalating therapy**

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A Comparison of the Visual Field Parameters of SITA Faster and SITA Standard Strategies in Glaucoma

- Removes 'dead time' during the test
- No blind spot, no false negatives
  - Gaze monitoring and false positives
    - Unless you manually adjust settings
- Slightly increased overall threshold sensitivity (is this bad?!)
- More difficult testing situation vs. 'positive start bias' of SITA Standard
  - No 'easy' answers
- *Clinically* equivalent to SITA Standard(?)

Lavanya R et al. A Comparison of the Visual Field Parameters of SITA Faster and SITA Standard Strategies in Glaucoma. J Glaucoma. 2020 Sep;29(9):783-788.

Thulasidas M, Patyal S. Comparison of 24-2 Faster, Fast, and Standard Programs of Swedish Interactive Threshold Algorithm of Humphrey Field Analyzer for Perimetry in Patients With Manifest and Suspect Glaucoma. J Glaucoma. 2020 Nov;29(11):1070-1076.

24-2C Testing pattern: an additional 10 points in the paracentral area overlaid on the the 24-2 pattern
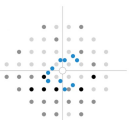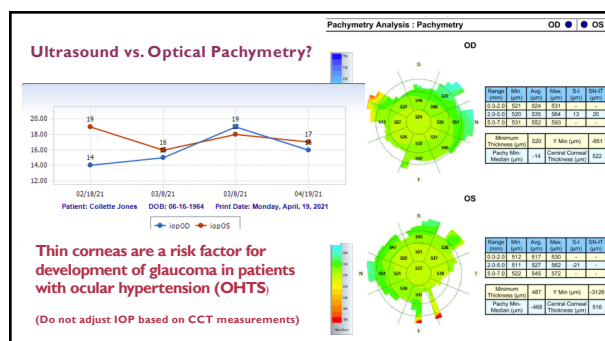
60

How often do we perform testing?

It depends on how we may best (most quickly) be able to detect change

Pachymetry: Once*

Gonioscopy: Every 1-2 years
Necessary for diagnosis

61

9

6/10/23

Slide 62

Ultrasound vs. Optical Pachymetry?

Pachymetry Analysis : Pachymetry   OD ● | ● OS

Patient: Collette Jones   DOB: 06-16-1964   Print Date: Monday, April, 19, 2021

Thin corneas are a risk factor for development of glaucoma in patients with ocular hypertension (OHTS)

(Do not adjust IOP based on CCT measurements)

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Slide 63

OCT

Frequency of Optical Coherence Tomography Testing to Detect Progression in Glaucoma

Bruna Melchior, MD,*† Carlos G. De Moraes, MD, PhD, MPH,*
Jayter S. Paula, MD, PhD,† George A. Cioffi, MD,*
Christopher A. Girkin, MD, MSPH,‡ Massimo A. Fazio, PhD,‡
Robert N. Weinreb, MD,§ Linda M. Zangwill, PhD,§
and Jeffrey M. Liebmann, MD*

(*J Glaucoma* 2022;31:854–859)

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Slide 64

Visual fields

Practical recommendations for measuring rates of visual field change in glaucoma

B C Chauhan,[1] D F Garway-Heath,[2] F J Goñi,[3] L Rossetti,[4] B Bengtsson,[5] A C Viswanathan,[2] A Heijl[5]

Br J Ophthalmol 2008;**92**:569–573. doi:10.1136/bjo.2007.135012

6 visual fields within the first 2 years—to identify "fast" progressors

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Slide 65

What __else__ can we blame glaucoma on?

Elevated IOP
Older age
Black or African race or Latino or Hispanic ethnicity
Family history of glaucoma
Thin central corneal thickness
Low ocular perfusion pressure
Myopia
Type 2 diabetes mellitus
Low systolic and diastolic blood pressure
Hypothyroidism

Migraine
Sleep apnea
Peripheral vasospasm (Raynaud's syndrome)
Cardiovascular disease
Low corneal hysteresis
Systemic hypertension
Low cerebral spinal fluid pressure
Genetics

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Slide 66

Glaucoma and Genetics

Currently, more than 150 loci have been identified

In most patients, complex genetics are involved

Each gene contributes a small amount of risk, but none of which cause disease on their own
- *Direct contribution to disease development*
- *Influence biological pathways*
- *Contribute to other risk factors (IOP)*

Polygenic risk score; one more parameter to consider (not yet)

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Slide 67

ROUTINE GENETIC TESTING FOR GLAUCOMA RISK ALLELES IS NOT RECOMMENDED FOR PATIENTS WITH POAG

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JUVENILE OPEN ANGLE GLAUCOMA

- Developmental immaturity of the trabecular meshwork
- Essentially normal appearance by gonioscopy
  - Open anterior chamber angle without significant abnormality
- **There is no such thing as 'normal tension' JOAG**
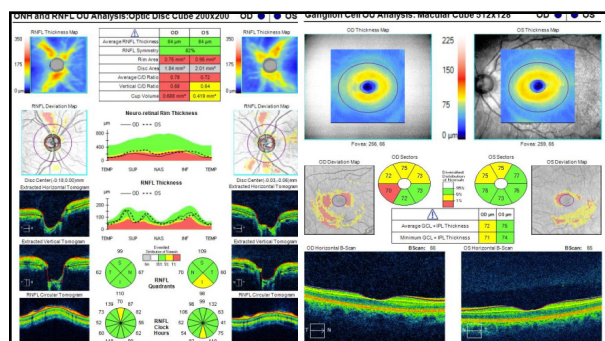- Often considered to be inherited as an autosomal dominant trait

69

39 YEAR OLD FEMALE

- Knows she needs to be followed because her mother has glaucoma
  - Mother-medication, no surgery, no vision loss
- BCVA 20/20 OD and OS
- No APD
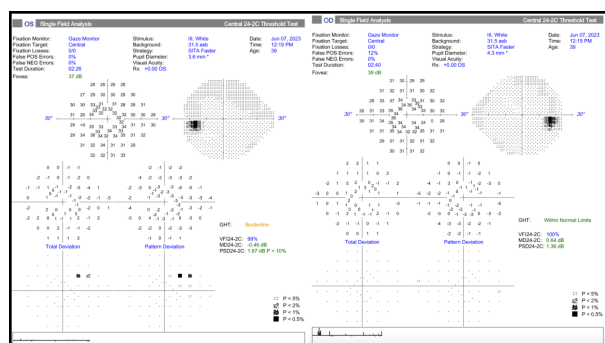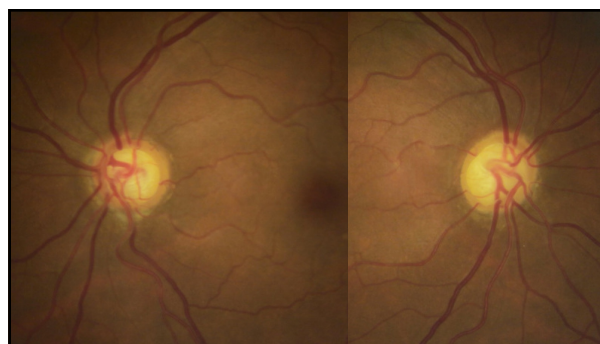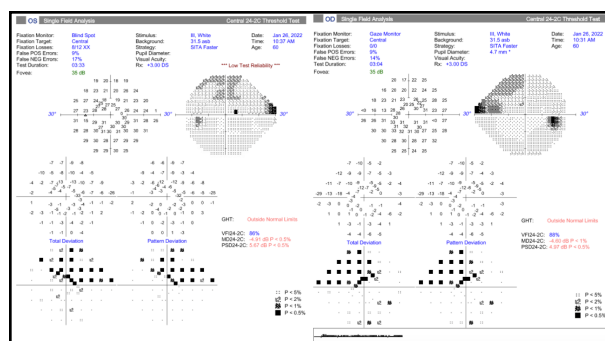- Peak IOP 22mmHg OD and OS
  - CCT 522/530

70

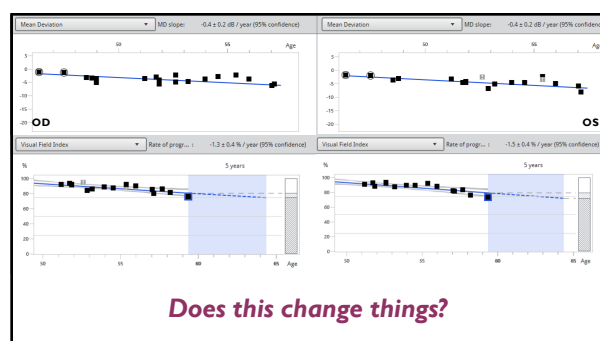
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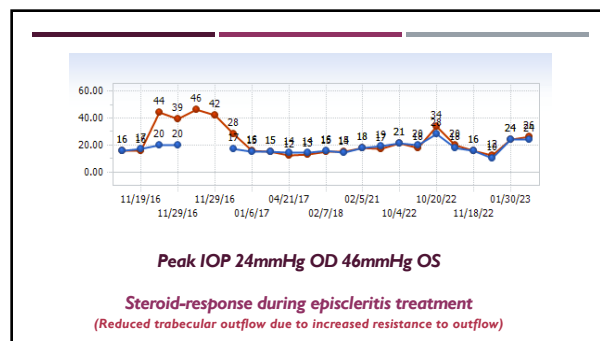

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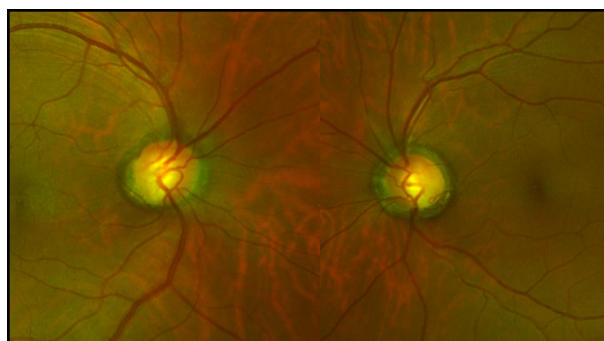*Does this change things?*
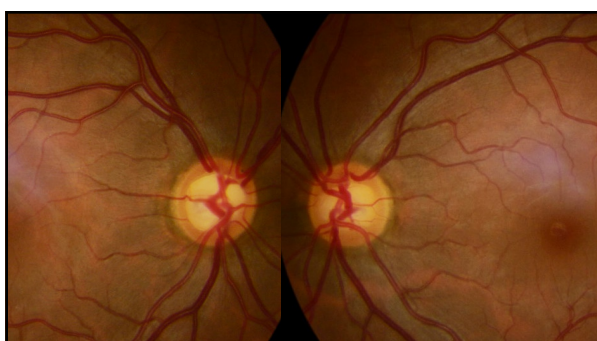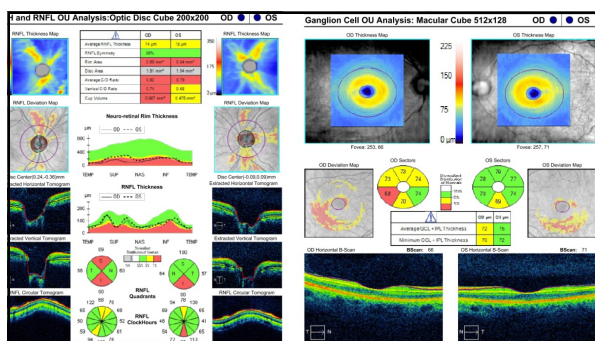
77

41 YEAR OLD BLACK FEMALE

- Sjogren Syndrome, suspected Lupus
- History of scleritis, episcleritis
- BCVA 20/20 OD and OS
- No APD
- No IOP-lowering medications
- IOP 24mmHg OD, 26mmHg OS
  - CCT 530um OD, 540um OS
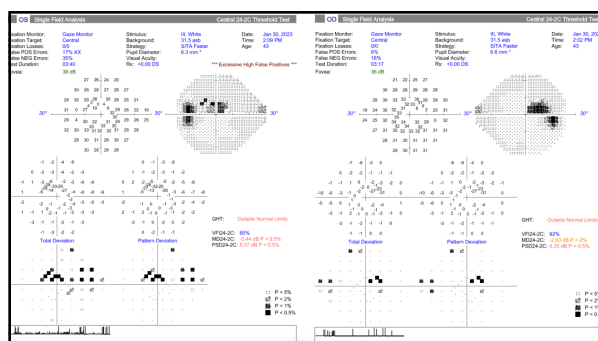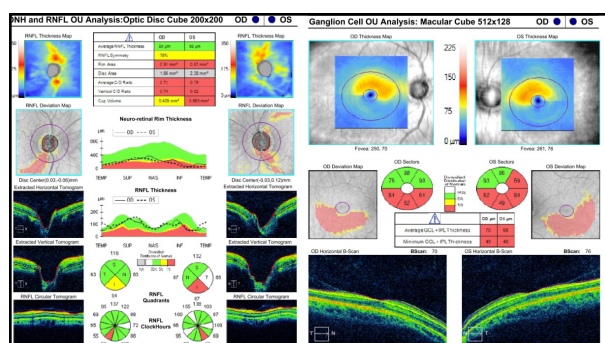- Recent oral steroid pulse due to increased inflammatory markers

78
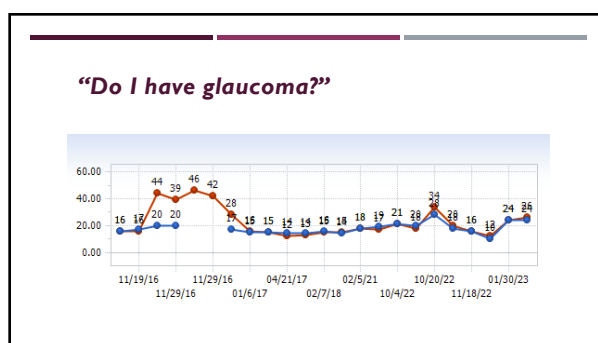

Peak IOP 24mmHg OD 46mmHg OS

Steroid-response during episcleritis treatment
(Reduced trabecular outflow due to increased resistance to outflow)

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"Do I have glaucoma?"

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What is maximum medical therapy?

It depends on what the patient can comfortably manage (tolerate)

Zero medications…6 medications…or somewhere in between

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70 YEAR OLD SOUTH ASIAN FEMALE

**History of Present Illness**

1. glaucoma
   67 F presents with POAG in both eyes diagnosed in 2011. Patient currently is taking Azarga 1 gtt BID OU. Patient reports irritation, pigmentation, and fatigue on Azarga. Patient brought records of OCT of NFL OU and VF 24-2C from Oct 28, 2020. Patient reports occasional headaches after lying down at night. Relief for the headaches when the patient sits up. Patient denies itching, redness, tearing, blurry vision, and double vision.

- **SLT OD and OS in 2012, repeated in 2016**
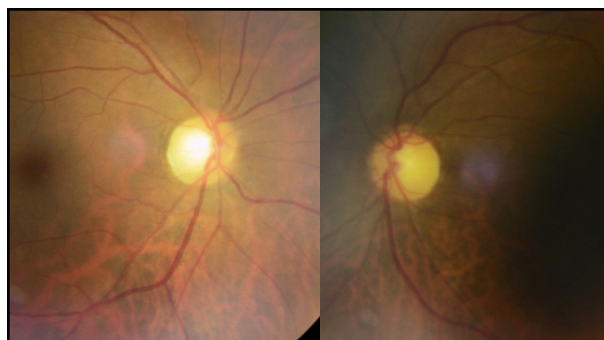
- **IOP 19mmHg OD 16mmHg OS**
  - **CCT 500um OD, 497um OS**

89
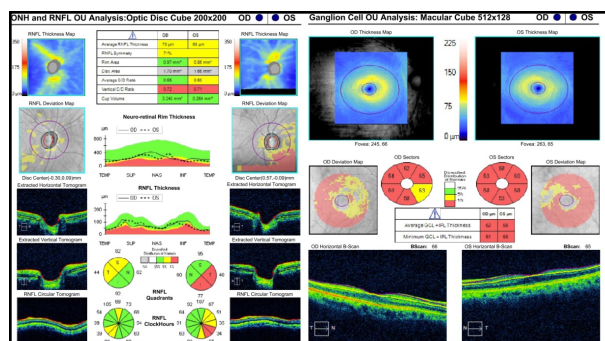
90
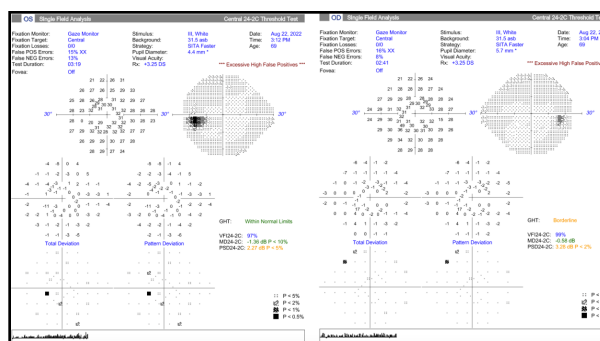
91

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Can she have a THIRD SLT?

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Low-Energy Selective Laser Trabeculoplasty Repeated Annually: Rationale for the COAST Trial

Tony Realini, MD, MPH[1], Gus Gazzard, MD[2], Mark Latina, MD[3], Michael Kass, MD[4]

ORIGINAL RESEARCH

Repeat Selective Laser Trabeculoplasty for Glaucoma Patients: A Systematic Review and Meta-analysis

Hyunsoo J Jang[1], Brian Yu[2], William Hodge[3], Monali S Malvankar-Mehta[4]

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BOTTOM LINE

- Management of glaucoma is *highly* individualized
- Careful assessment of the optic nerve is crucial
- Take the time that you need to establish a diagnosis
- Adjust treatment, (target pressure), evaluation intervals, and testing frequency as supported by data—with the patient on board
- New tools are being developing to meet the needs of clinicians—and patients

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480.289.0613

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