Course # 110

SECO2026
THE EDUCATION DESTINATION™

Glaucoma Challenges: Real Cases, Real Decisions

Jessica Steen, OD

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1

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All relevant relationships have been mitigated.

2

GLAUCOMA CHALLENGES: REAL CASES, REAL DECISIONS

Jessica Steen OD, FAAO, Dipl ABO

3

JESSICA STEEN OD FINANCIAL DISCLOSURES

- Speakers Bureau-Carl Zeiss Meditec, Bausch and Lomb, Viatris, Thea Pharma, Alcon, Allergan, Astellas, Dompé
- Consultant-Bausch and Lomb, Balance Ophthalmics, Carl Zeiss Meditec, Opus Genetics, Viatris, Allergan, Astellas, Alcon, Radius XR, iCare, Glaukos, Eyenovia, Tarsus, Orasis, Topcon, Envision Health Technologies, LKC
- Shareholder-Clearside Biomedical, Annexon Bio (<0.01% ownership)
- *All relevant relationships have been mitigated*

4

Where are we going?

Diagnosis of glaucoma

Management of glaucoma

Detection of progression

5

How quickly are we moving?

How quickly is the patient's disease "moving"?

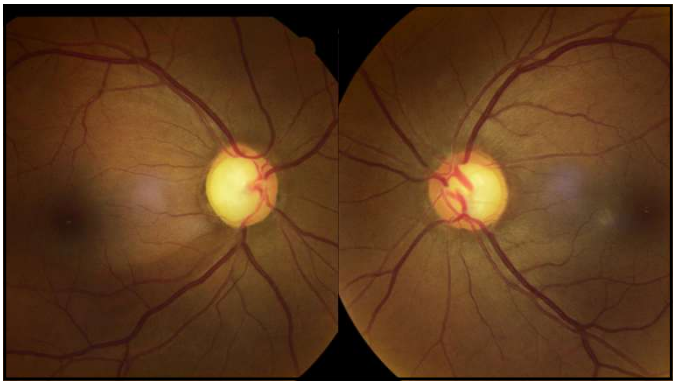
Take the time that you need to determine a diagnosis and if progression has occurred

6

56 YEAR OLD AFRICAN AMERICAN FEMALE

- 56 year old African American female referred for evaluation due to suspicion of glaucoma secondary to optic disc appearance
  - No family history of glaucoma
  - No systemic diagnoses; no systemic medications

7



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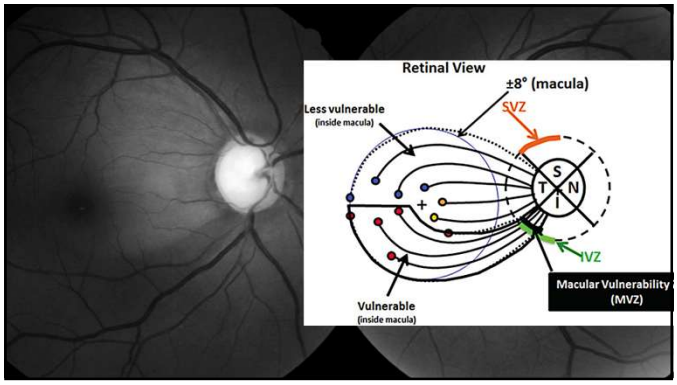

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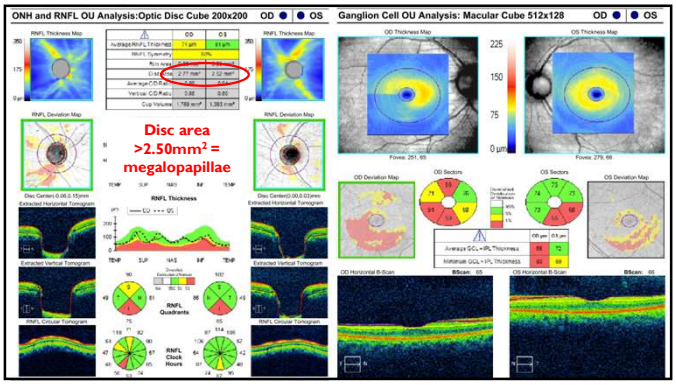

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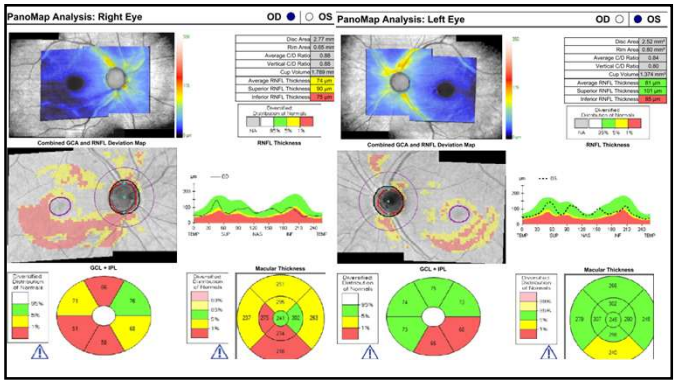

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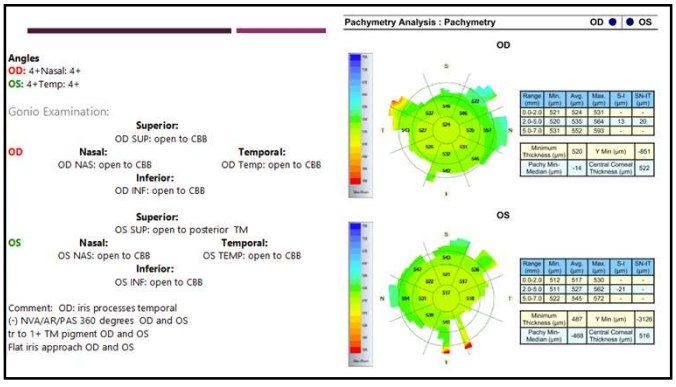

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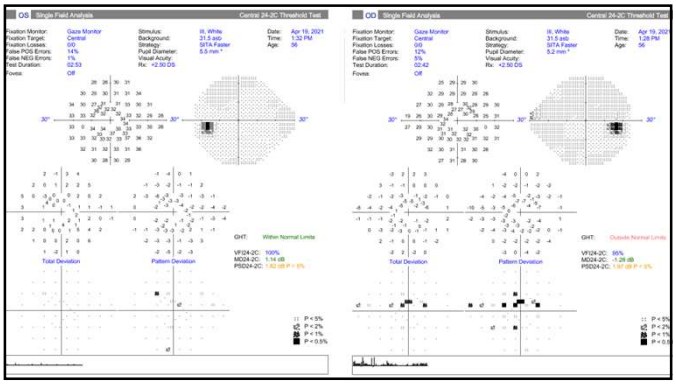
56 year old African American female

Does the imaging reflect typical patterns observed in early glaucomatous optic neuropathy?

What do you think the visual field will look like?

13



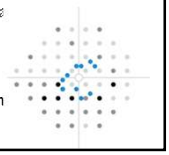
14

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 Standa
  - 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

15

56 year old African American female

How quickly should therapy be initiated?

What is the risk of imminent vision loss?

Ideally 3 IOP measurements prior to initiation of therapy

16

You've diagnosed glaucoma, now what?

Treatment options?

Medication

SLT

17

Efficacy of Repeat Selective Laser Trabeculoplasty in Medication-Naive Open-Angle Glaucoma and Ocular Hypertension during the LiGHT Trial

Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial

*Gus Gazzard, Evgenia Konstantakopoulou, David Garway-Heath, Anurag Garg, Victoria Vickerstaff, Rachael Hunter, Gareth Ambler, Catey Bunce, Richard Wormald, Neil Nathwani, Keith Barton, Gary Rubin, Marta Buszewicz, on behalf of the LiGHT Trial Study Group**

- ***No game-changing data; But did provide good quality evidence for what was already known***

SLT: at target 93% of visits, 91.3% in the medication group (3 years)

18

AMERICAN ACADEMY OF OPHTHALMOLOGY

Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial

Six-Year Results of Primary Selective Laser Trabeculoplasty versus Eye Drops for the Treatment of Glaucoma and Ocular Hypertension

Conclusions: Selective laser trabeculoplasty is a safe treatment for OAG and OHT, providing better long-term disease control than initial drop therapy, with reduced need for incisional glaucoma and cataract surgery over 6 years. *Ophthalmology 2023;130:139-151 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

No difference in health-related quality of life scores: mobility, self-care, usual activities, pain or discomfort.

Minimal difference in Glaucoma Symptom Scale-did not translate to difference in HRQoL

19

ARTICLE IN PRESS

AMERICAN ACADEMY OF OPHTHALMOLOGY

Six-Year Rate of Visual Field Progression in the Laser in Glaucoma and Ocular Hypertension Trial

Giovanni Montesano, MD, PhD,[1,2] David P. Crabb, PhD,[2] David F. Garway-Heath, MD, FRCOphth,[1] David M. Wright, PhD,[3] Evgenia Konstantakopoulou, PhD,[1,4] Neil Nathwani, BSc (Hons), DipTp(IP),[1] Giovanni Ometto, PhD,[1,2] Gus Gazzard, MD, FRCOphth[1]

Results: Data from 710 eyes (482 with OAG and 354 in the SLT-first arm) were analyzed. The 2 arms had similar baseline MD ($P = 0.7$). The average intraocular pressure (IOP) during follow-up was 16.1 [14.2–18.2] for the drops-first arm and 16.8 [14.6–18.6] in the SLT-first arm (median [interquartile range], $P = 0.057$). The mean [95% credible interval] MD rate was −0.37 [−0.43 to −0.31] decibels (dB)/year in the drops-first arm and −0.26 [−0.31 to −0.21] dB/year in the SLT-first arm ($P = 0.007$). When stratified by severity, this difference was significant only in mild OAG ($P = 0.035$, the largest sub-group). The secondary analyses largely confirmed the main results. The difference in MPD rate was also significantly slower in the SLT-first arm ($P < 0.001$).

26% of med-first eyes were fast-progressors vs. 15% in SLT-first

20

JAMA Ophthalmology | Original Investigation

Selective Laser Trabeculoplasty After Medical Treatment for Glaucoma or Ocular Hypertension

Evgenia Konstantakopoulou, PhD; Gus Gazzard, MA, MD, MBBChir; David Garway-Heath, MD; Mariam Adeleke, PhD; Gareth Ambler, PhD; Victoria Vickerstaff, PhD; Catey Bunce, DSc; Neil Nathwani, BSc; Keith Barton, MD; for the LiGHT Trial Study Group

Patients were randomized to SLT or medication first (LiGHT)-then after 3 years patients were allowed to have secondary SLT (to reduce medication load) or to escalate therapy if needed

65% of 320 subjects taking drops chose to continue medical therapy!

21

Direct SLT-no lens used!

120 shots, 1.8mJ, 3ns duration, 400 micron spot size, 2 seconds (GLAUrious trial)

22

SLT

Champagne bubbles = explosions at the microscopic level

…this is tissue damage

Damage to TM endothelial cells which allows for new cells to migrate from Schwalbe's line over about 1 week post-treatment

Leads to macrophage recruitment and TM proliferation

23

What's next?

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

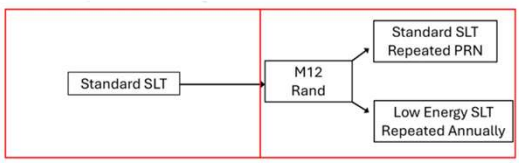
Tony Realini, MD, MPH, Gus Gazzard, MD,†‡ Mark Latina, MD,§ and Michael Kass, MD§‖*

Estimated primary completion date: June 2027

Aims to determine optimal energy level and frequency of SLT

24

Determined that initial low energy (0.4mJ) SLT was not as effective as initial "full strength" SLT starting at 0.8mJ



25

63 year old male

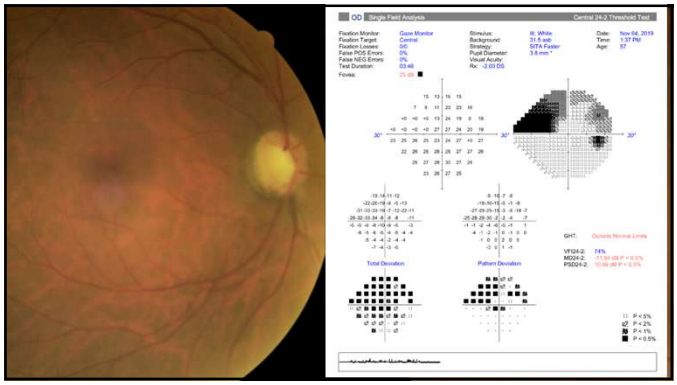
Referred for evaluation of glaucoma: elevated IOP and severe optic disc damage determined at CEE

BCVA 20/20 OD, 20/200 OS

Untreated IOP 25/29mmHg

CCT 512 μm OD 518 μm OS

26



27

Now what?!

Medication?
Laser?
Intracameral drug delivery?
Surgery?

28

You're going to lower the pressure, but what data will change the way you manage the patient on day 1?

29

Gonioscopy.

30

Gonio Examination:

Superior:
OD SUP: open to posterior TM

OD **Nasal:** **Temporal:**
OD NAS: open to posterior TM OD Temp: open to posterior TM

Inferior:
OD INF: open to posterior TM

Superior:
OS SUP: open to posterior TM

OS **Nasal:** **Temporal:**
OS NAS: open to posterior TM OS TEMP: open to posterior TM

Inferior:
OS INF: open to posterior TM

Comment: (-) NVA, angle recession, PAS, blood in Schlemm's canal OD and OS
Flat iris approach 360 OU

2+ pigmented post. TM OU

31

TARGET INTRAOCULAR PRESSURE

- *What is the patient's **peak** pressure?*
  - ***Our patient: 25 mmHg OD; 29 mmHg OS***
- *What is the central corneal thickness?*
  - ***CCT 512µm OD; 518µm OS***
- *What's the diagnosis?*
  - ***Primary open angle glaucoma OD and OS-severe stage***
- *Is there significant family history—if so, how significant?*
- *How much damage is there?*
- *How young is the patient?*
  - *63*

32

TARGET INTRAOCULAR PRESSURE

- Should be at least 25% lower than pretreatment IOP
  - Should be lower if there is more severe disc damage
  - i.e. 40-50% in advanced disease—***or more?!***
- Does not have to be symmetric; does not have to be exact
- Target pressure is an estimate and needs to be individualized and adjusted
  - What if you don't have a target pressure? What if you don't reach target pressure?
    - Not at medicolegal risk
- If progression occurs at the target pressure—think about adherence to therapy and outside of office IOP fluctuation
  - Initially substitute vs. add medication
- Assess the patient for local ocular and systemic side effects

33

Target IOP

Based on this patient's current level of disease, age, risk factors for future progression—with the goal of reducing risk of bilateral blindness

50% reduction? More aggressive?

Add multiple medications at the same visit?

Challenges to assessment of clinical efficacy

Risk of undertreatment and stepwise approach to target pressure

34

Now what?

Latanoprost 0.005% QHS OU; 2 week follow up

IOP 11mmHg OD
12mmHg OS

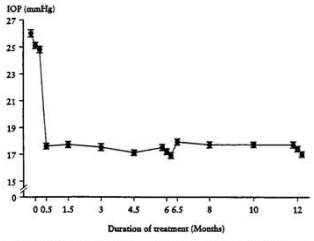


Figure 1. Effect on intraocular pressure (IOP) of 0.005% latanoprost applied once daily to one or both eyes in each of 198 patients with elevated IOP completing 1 year of therapy. Each point represents the mean IOP of 184 to 198 patients, with limits of ± standard error of the mean. All values during treatment were significantly ($P < 0.0001$) reduced compared with baseline measurements.

Camras CB, Alm A, Watson P, Stjernschantz J. Latanoprost, a prostaglandin analog, for glaucoma therapy. Efficacy and safety after 1 year of treatment in 198 patients. Latanoprost Study Groups. Ophthalmology. 1996 Nov;103(11):1916-24.

35

Is this good enough?

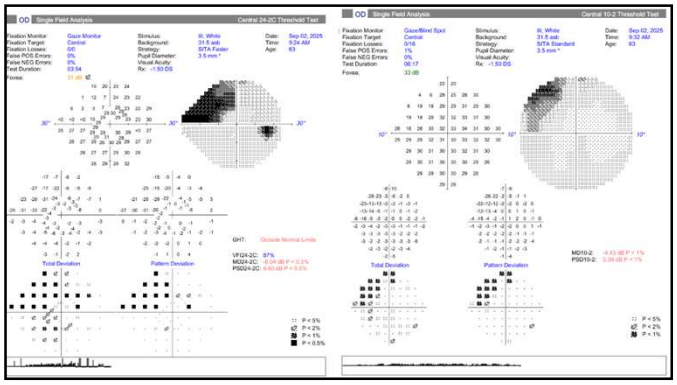
Declines surgical consultation. No medical coverage.

+ Dorzolamide-timolol BID OU (1 month): 9mmHg OD 9mmHg OS.

I would love to get SLT on board (expectations?!)

+ Brimonidine 0.2% BID OU

36



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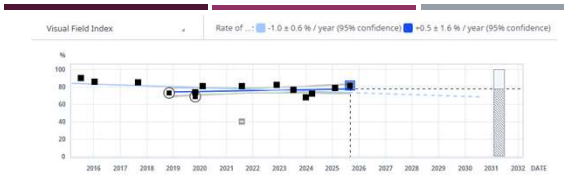


Long-term IOP 7-9mmHg; still no medical coverage

I would still love to get SLT on board; declines SLT and surgical consultation

38

Now what?

Low vision consultation; most effective early in the course of disease

39

63 YEAR OLD WHITE MALE

- History of "narrow angles" and bilateral LPI
  - 25 years ago (1999)-at the age of 38
- Latanoprost QHS OU (teal cap)
  - Reported peak untreated IOP high 20s
- Systemic hypertension and anxiety
  - Lisinopril
  - Clonazepam
    - No events of significant blurred vision, haloes around lights, significant nausea, or headache

40

63 YEAR OLD WHITE MALE

- BCVA 20/20 OD and OS
  - +2.00D OD and OS
- Patent LPI 1:00 OD and OS
  - What does LPI do?!
    - ***Reverse or prevent pupil block***
- Moderately deep central anterior chamber
  - Anterior trabecular meshwork 360 degrees OD; 270 degrees OS with no structures temporal
    - Convex iris approach; no PAS, AR, NVA
    - 1+ pigment with compression

41

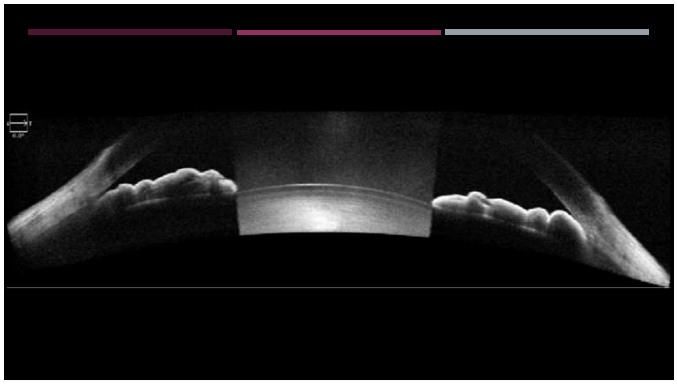
OCT Evaluation of the Anterior Chamber

No inadvertent compression

May be performed in complete darkness

Most valuable to determine if the angle is open or closed

42



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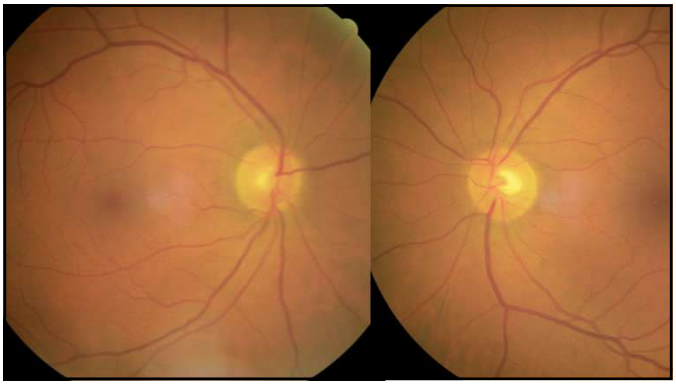

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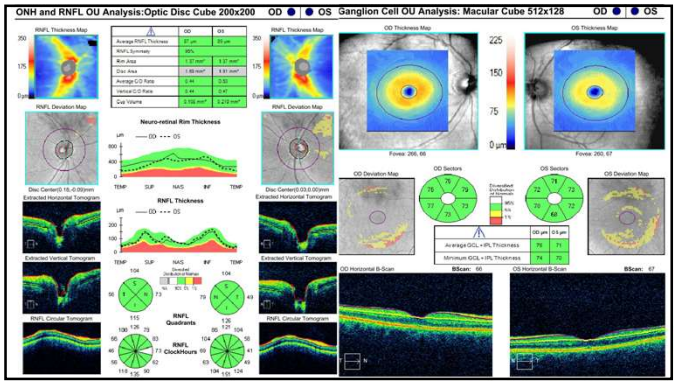

45

Does this patient need to be on treatment?

46

TERMINOLOGY

- **1) Primary angle closure suspect**
- 2) Primary angle closure
- 3) Primary angle closure glaucoma
- 4) Acute angle closure crisis

Either open or closed
There is no such thing as "narrow angle glaucoma"

47

PRIMARY ANGLE CLOSURE SUSPECT

- Discontinue latanoprost: 18mmHg OD/17mmHg OS at follow up
- Advocate for early cataract surgery

- ***Does this patient meet EAGLE inclusion criteria?***

48

Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial

Augusto Azuara-Blanco, Jennifer Burr, Craig Ramsay, David Cooper, Paul J Foster, David S Friedman, Graham Scotland, Mehdi Javanbakht, Claire Cochrane, John Norrie, for the EAGLE study group

- Removal of clear lenses in eyes with PACG with IOP > 21 mmHg or eyes with PAC (without glaucoma) and IOP >30mmHg vs. LPI (and medications); greater than 50 years of age
  - Clear lens extraction patients had greater IOP control and improved quality of life
  - Patients who underwent lens extraction had fewer IOP lowering medications
    - Only 1 needed trabeculectomy after phaco whereas 24 patients in the LPI group needed trabeculectomy
  - Cost-effective at 3 years; savings by 10 years
    - Fewer procedures, fewer office visits
- Clear lens extraction can be considered

49

Local Coverage Determination (LCD)

Cataract Surgery

L34413

In general, cataract surgery is performed to alleviate visual impairments attributable to lens opacity.

"There are uncommon situations when lens extraction becomes medically necessary for anatomic reasons rather than optical reasons"

"These include induced angle closure (e.g. microspherophakia)"

50

Laser peripheral iridotomy for the prevention of angle closure: a single-centre, randomised controlled trial

Mingguang He, Yuzhen Jiang, Shengsong Huang, Dolly S Chang, Beatriz Munoz, Tin Aung, Paul J Foster*, David S Friedman*

- Zhongshan Angle Closure Prevention (ZAP) trial
- Purpose: to determine if laser iridotomy is superior to observation in primary angle closure suspects in China over a 6 year period
  - PACS = 6 or more clock hours where posterior trabecular meshwork was not visible
    - Without elevated IOP, disc change, or peripheral anterior synechiae
- Endpoint: elevated IOP--used dark-room prone provocative testing (compared pre-test IOP to IOP measured after 15 minutes in a dark room in prone position), PAC, acute angle closure
- Outcome: 889 eyes treated. 50% reduction in risk for development of primary angle closure over 6 years, but only 4% of untreated eyes progressed to primary angle closure
  - Acute angle closure: 5 patients untreated, 1 treated (3 control eyes and one LPI eye were after dilation)
  - Authors determined that laser peripheral iridotomy was not justified in smaller populations

51

14-Year Outcome of Angle-Closure Prevention with Laser Iridotomy in the Zhongshan Angle Closure Prevention Study: Extended Follow-Up of a Randomized Controlled Trial

Results: During the 14 years, 390 LPI-treated eyes and 388 control eyes were lost to the follow-up. A total of 33 LPI-treated eyes and 105 control eyes reached primary endpoints (P <0.01). Within them, twelve eyes developed AAC or primary angle closure glaucoma (AAC: five control eyes and one LPI-treated eye; PACG: four control eyes and two LPI-treated eyes). The hazard ratio for progression to PAC was 0.31 (95% confidence interval, 0.21–0.46) in LPI-treated eyes compared with control eyes. At the 14-year visit, LPI-treated eyes had severer nuclear cataract, higher IOP, larger angle width and limbal anterior chamber depth (LACD) than control eyes. Higher IOP, shallower LACD, and central anterior chamber depth (CACD) were associated with an increased risk of developing endpoints in control eyes. In the treated group, eyes with higher IOP, shallower LACD, or less IOP elevation after dark room–prone provocative tests (DRPPT) were more likely to develop PAC after LPI.

Yixiong Yuan, MD, Wei Wang, PhD, Rulin Xiong, MD, Jian Zhang, MPH, Cong Li, MD, Shaopeng Yang, MD, David S. Friedman, PhD, Paul J. Foster, PhD, Mingguang He, PhD

Endpoint: PAC, PAS, IOP>24mmHg or AAC

NNT: 12-13

52

EMERGENCY VISIT

- IOP determined to be 30mmHg OD and 32mmHg OS at a comprehensive eye examination
- ***What is the mechanism for elevated intraocular pressure?***

53

What about the clonazepam?

CONTRAINDICATIONS

Klonopin should not be used in patients with a history of sensitivity to benzodiazepines, nor in patients with clinical or biochemical evidence of significant liver disease. It may be used in patients with open angle glaucoma who are receiving appropriate therapy but is contraindicated in acute narrow angle glaucoma.

54

Now what?

1. *Lower the pressure*
   - *Is this an acute emergency?*
   - *Medical therapy is NOT disease-modifying*
2. *Arrange for cataract surgery?*
   - *How soon?*

55

73 year old female

History of POAG; diagnosed in her 40s, treated with topical medications

"Small bottle and a big bottle with a blue cap"

IOP consistently in the 30-40mmHg range despite treatment

IOP 42mmHg OD 28mmHg OS

56

Gonio Examination:

	Superior: OD SUP: no structure seen		
OD	**Nasal:** OD NAS: no structure seen	**Temporal:** OD Temp: no structure seen	
	Inferior: OD INF: no structure seen		
	Superior: OS SUP: no structure seen		
OS	**Nasal:** OS NAS: open to anterior TM	**Temporal:** OS TEMP: no structure seen	
	Inferior: OS INF: open to anterior TM		

Comment: appositional touch OD and OS; convex iris approach OD and OS, with very difficult compression no AR, NVA OD and OS
1-2+ PTM pigment with compression OD and OS.

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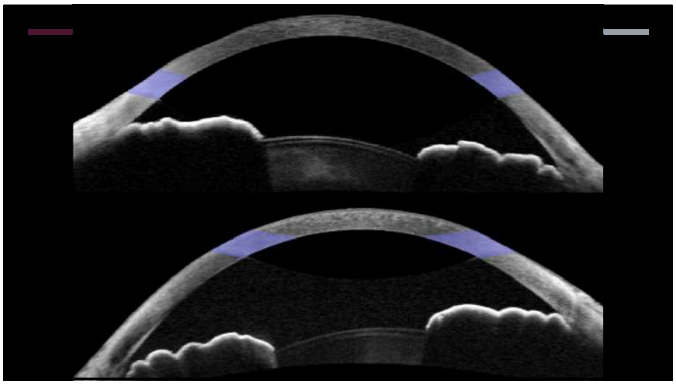

58

56-YEAR-OLD MALE

- Diagnosis of pigmentary glaucoma left eye
- Presents for second opinion; he is cautious about SLT—but wishes to reduce medication load
  - Significant symptoms of DED (SPEED 15)
    - Failed on an immunomodulator and serum tears
- Non-Hodgkin's lymphoma (2017), CMML (2023)
- History of bilateral LASIK
- Latanoprost 0.005% QHS OU, dorzolamide-timolol BID OU, brimonidine 0.2% BID OS
  - IOP 17mmHg OD, 21mmHg OS

59

56-YEAR-OLD MALE

- Gonioscopy: open to CBB 360 degrees OD and OS
- 3+ dense Sampaolesi line right eye; 4+ dense Sampaolesi line left eye
- Flat iris approach
- Peak IOP 27mmHg OD 33mmHg OS
  - Average CCT

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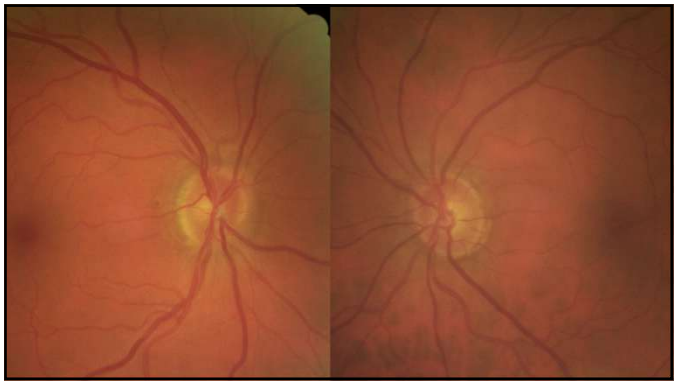

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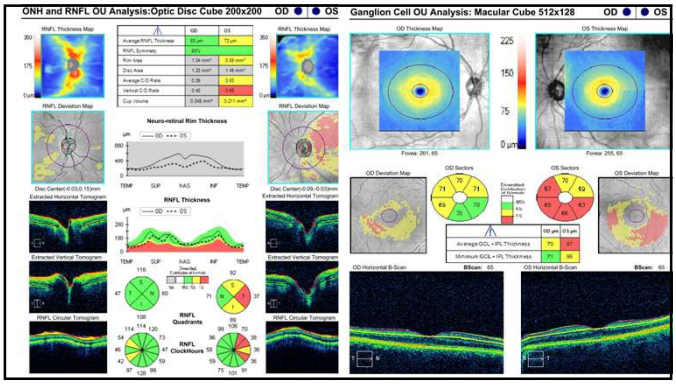

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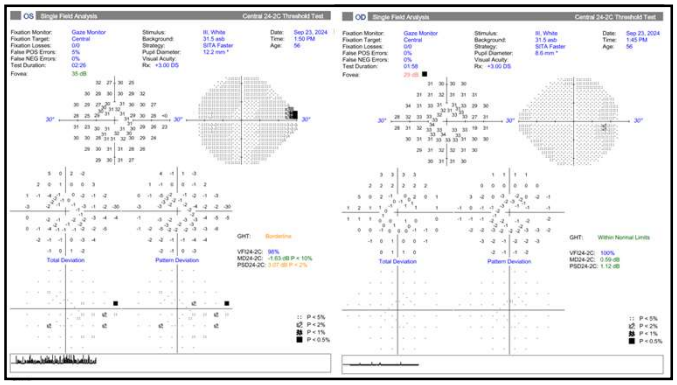

63

MORE phase 4 trial

Multicenter, prospective, open-label study
No comparator; treated IOP =>20mmHg

Latanoprost, latanoprost + 1, latanoprost +2
Switch to netarsudil/latanoprost

Latanoprost → -4.9mmHg
Latanoprost + 1 → -3.6mmHg
Latanoprost +2 → -3.7mmHg

64

56-year-old male

IOP check on netarsudil/latanoprost QHS OU for 16 days OU
Should we be waiting 4 weeks?!
IOP 15mmHg OD, 21mmHg OS

6 months later; bilateral SLT
IOP 14mmHg OD, 18mmHg OS

65

48 YEAR OLD FEMALE

- Recently relocated and presented to establish ongoing glaucoma care
  - POAG OU (diagnosed about 15 years ago)
    - Latanoprost QHS OU
    - Dorzolamide-timolol BID OU
    - Brimonidine BID OU
- IOP 10mmHg OD and OS
  - CCT 481 µm/504 µm
- Gonioscopy
  - Open to ciliary body 360 degrees and unremarkable
    - Best repeated every 1-2 years—or with an unexpected IOP measurement

66

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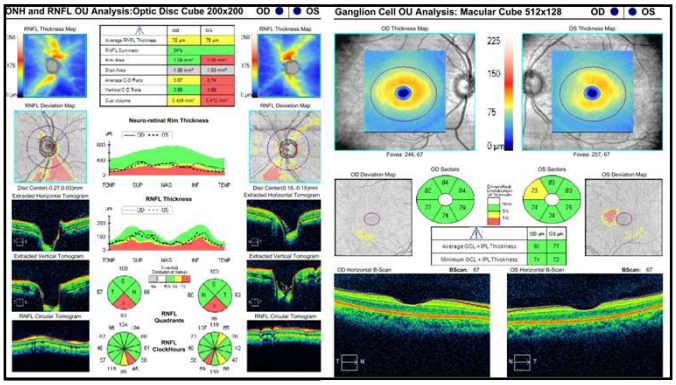

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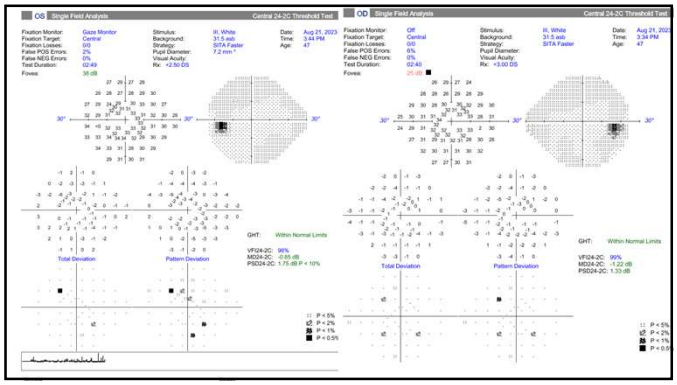

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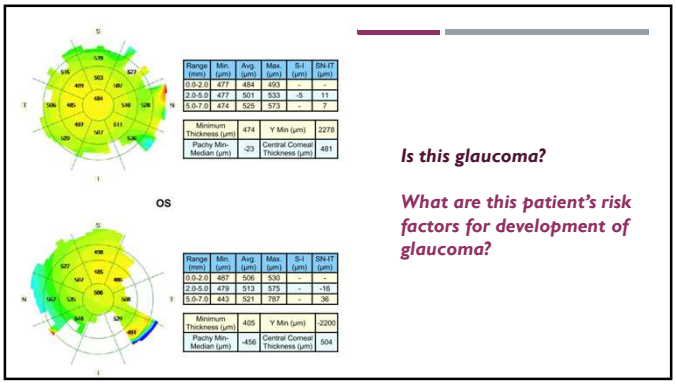


70

48 YEAR OLD FEMALE

- Now what?
  - Discontinue medication?
  - What is the risk of continuing therapy and carrying over the previous diagnosis?

71

Discontinuation of therapy

Step-wise, logical approach

1. Stop dorzolamide-timolol
IOP 15/15mmHg
2. Stop brimonidine
IOP 17/18mmHg
3. Stop latanoprost
IOP 29/28mmHg

72

Discontinuation of therapy

4. Diagnose ocular hypertension

5. Restart latanoprost → switch to latanoprostene bunod 0.024%
14mmHg OD 13mmHg OS

73

Sometimes the best action is <u>seemingly</u> "inaction"

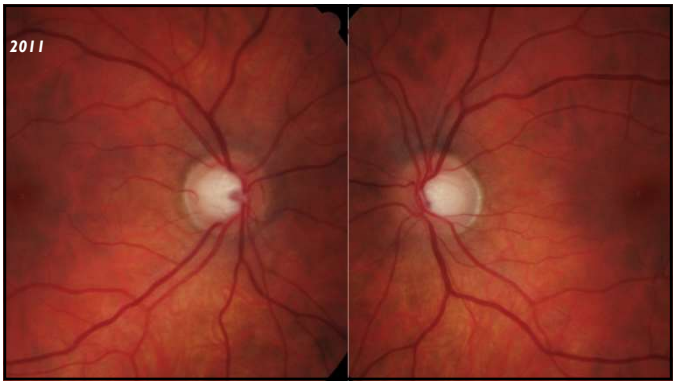
Taking the time you need you need to evaluate a treatment, repeat a test, or observe an individual over time will clarify unexpected or equivocal findings

74

55 YEAR OLD WHITE MALE

- Suspicious of glaucoma since 2003 (33 years old) based on optic disc appearance

75



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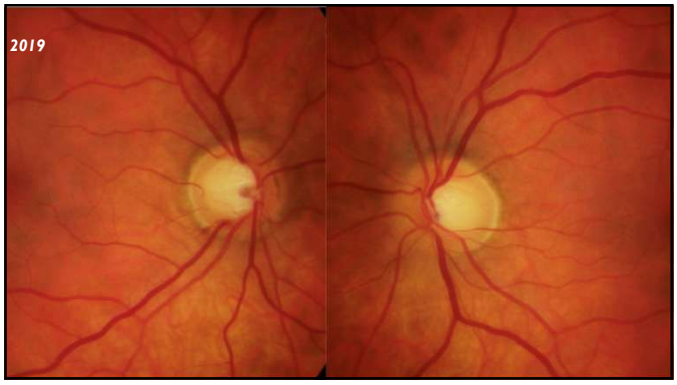

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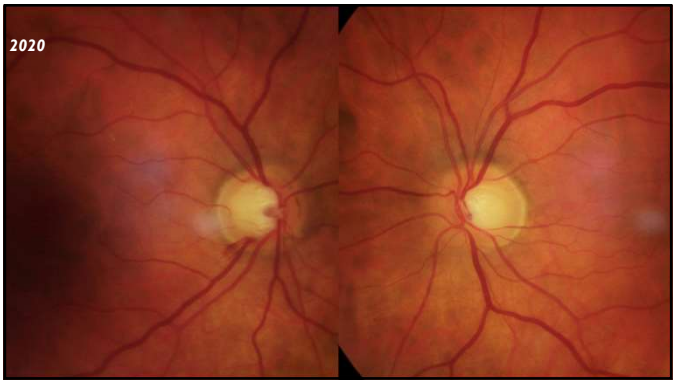

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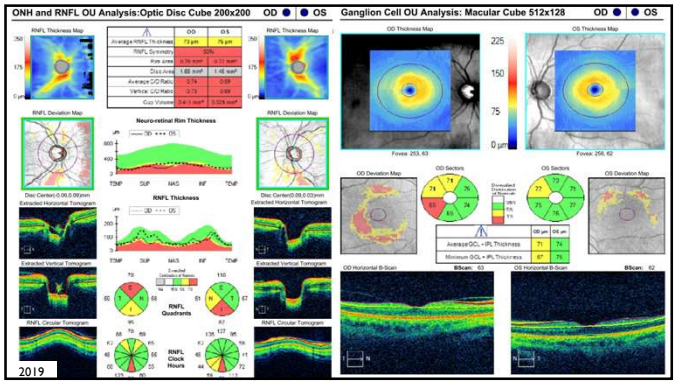

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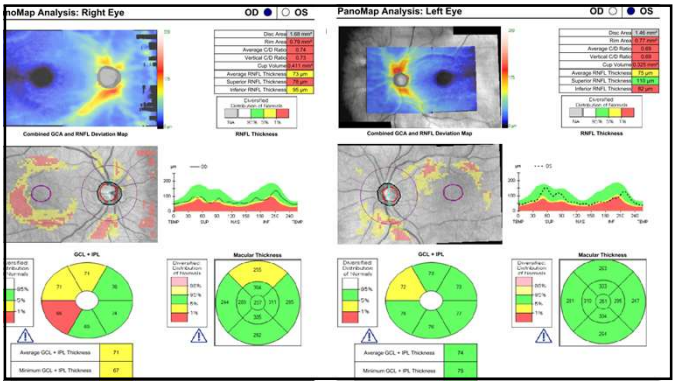

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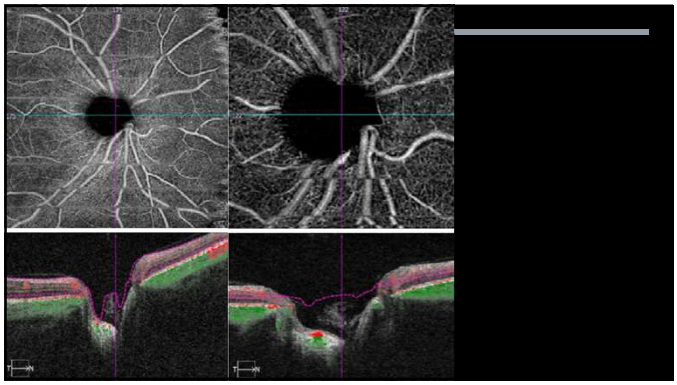

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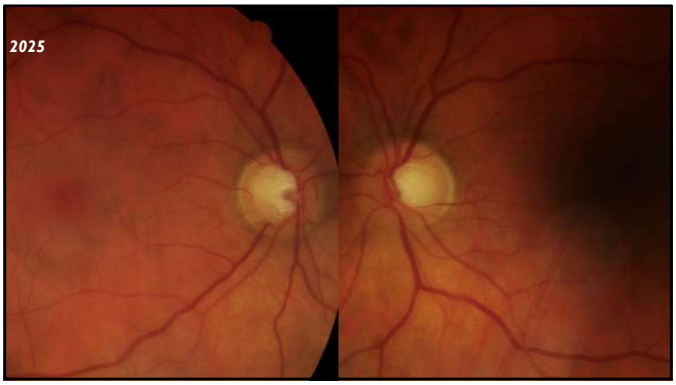

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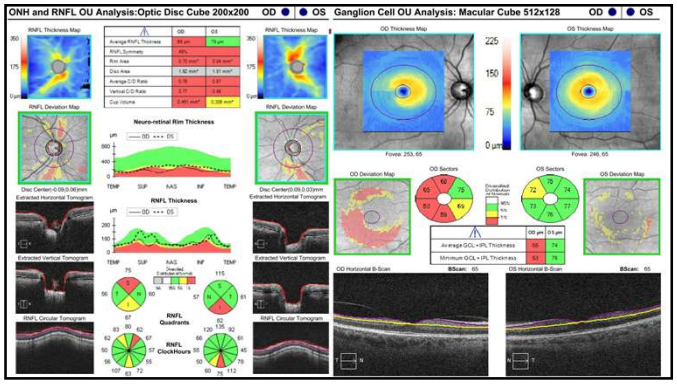

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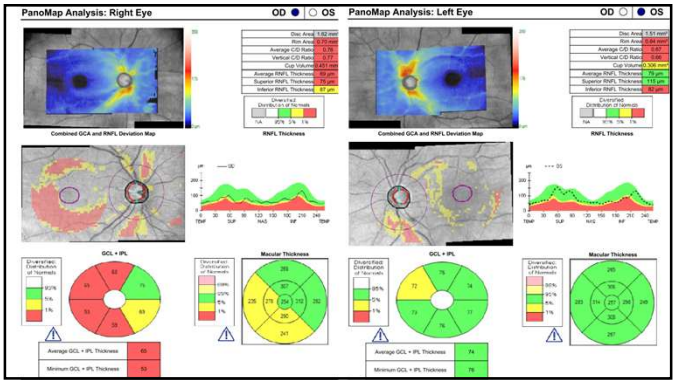

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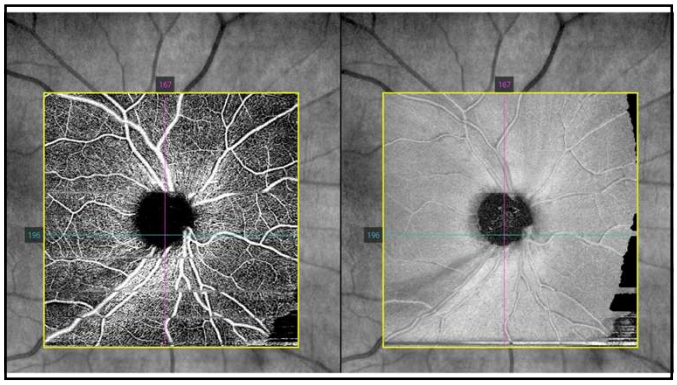

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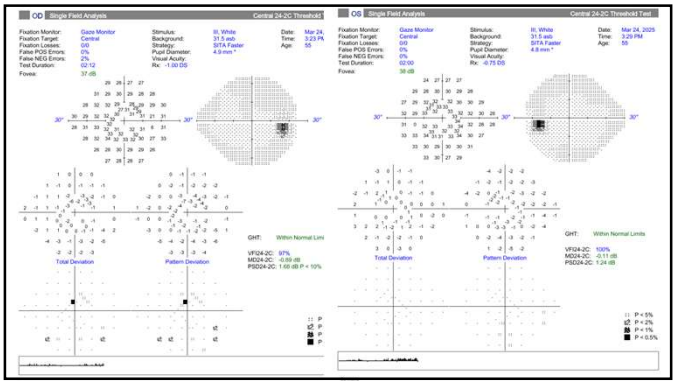

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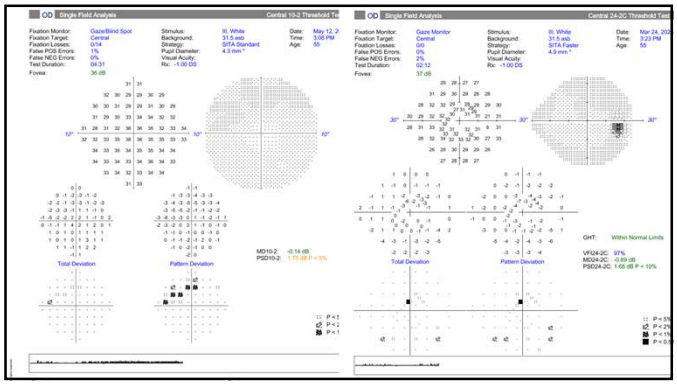

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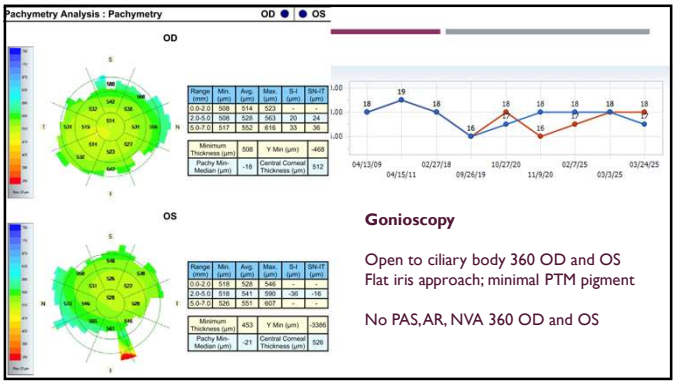

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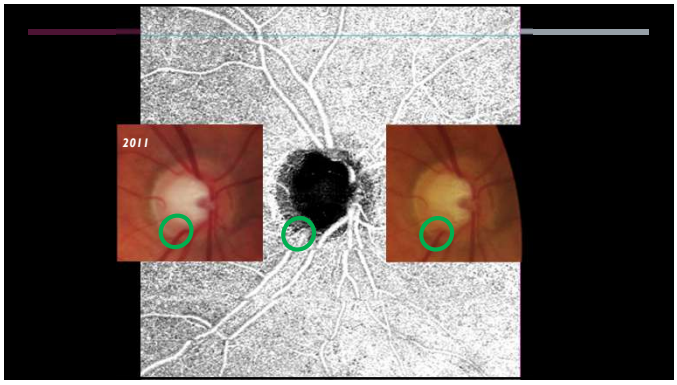

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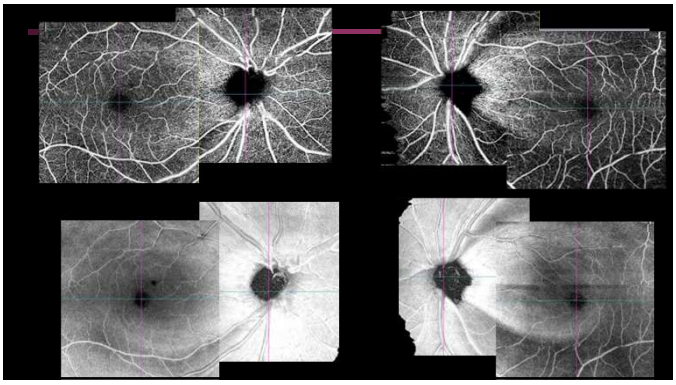
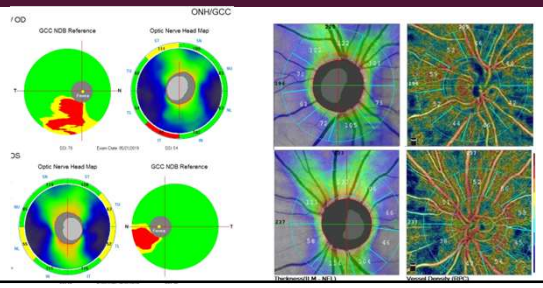


90

RNFL & OCTA OF THE PERIPAPILLARY REGION



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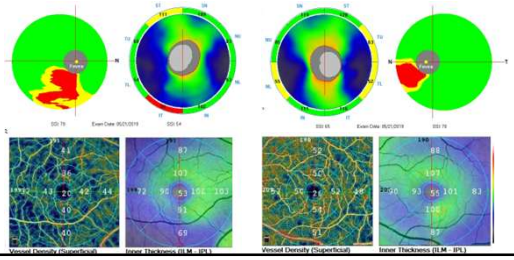
GANGLION CELL COMPLEX ANALYSIS



92

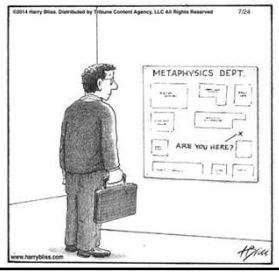
WHAT HAPPENS FIRST?

- Glaucomatous eyes have reduced ocular blood flow
- Reduced peripapillary capillary density may be observed in glaucomatous eyes
- **Does decreased ocular blood flow cause optic neuropathy--or does optic disc damage cause decreased blood flow?**
  - A) Ischemia leads to ganglion cell death
  - B) GC loss results in reduced metabolic demand

93

CHICKEN OR EGG?

- Metaphysical questions have metaphysical answers
- We're clinicians.



94

IT'S NOT ACTUALLY THAT SIMPLE

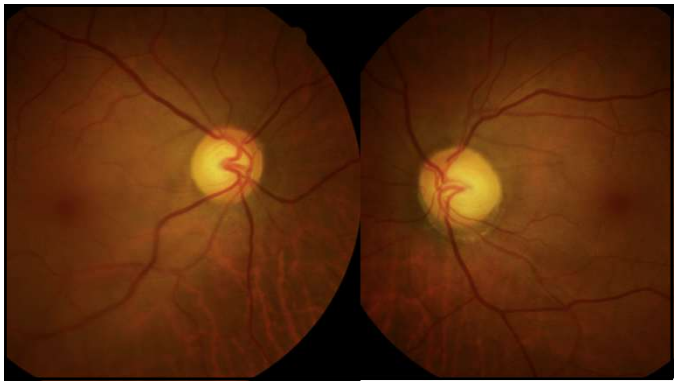
- Neurons, glial cells, cerebral microvascular endothelium function together = neurovascular unit
- Remember, we are limited in a clinical environment by the parameters that we are provided by a device
  - Velocity of blood flow (not yet)
    - Variation of interscan time
  - *Research parameters are developed into clinical parameters-eventually*

95

67 YEAR OLD FEMALE

- History of primary open angle glaucoma of the left eye in 2022
- Presented taking latanoprost 0.005% QHS OU
- IOP in office 16mmHg OD 17mmHg
  - CCT 554 µm OD 560 µm OS
- ***Is this good?***

96



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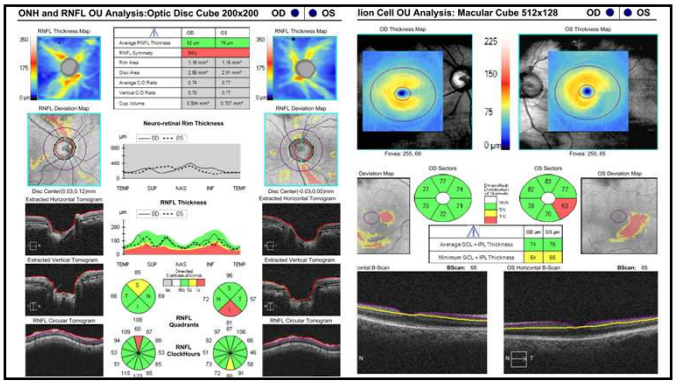

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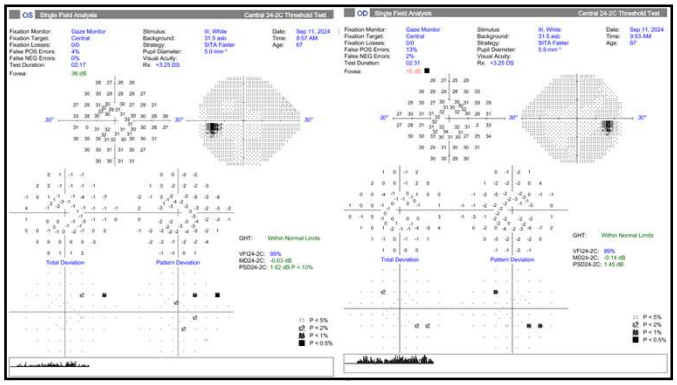

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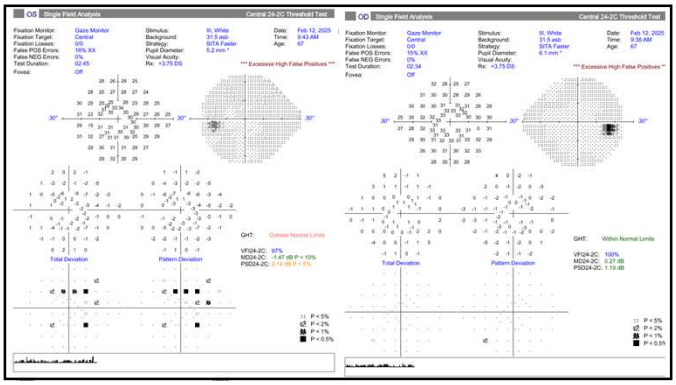


100

Is this good?!

Peak untreated IOP 18mmHg OD and 18mmHg

Treated IOP 16mmHg and 17mmHg OS

Blood pressure: 115/80mmHg on treatment

History of TIA 2011, stroke 2010
Bilateral hip replacement: 2016 & 2017
Fibromyalgia 2018

101

Now what?

Adherence?

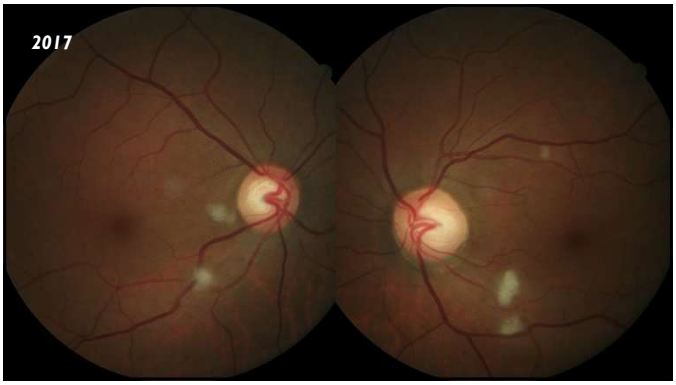
Discontinue treatment

IOP 1 month later: 16mmHg OD 15mmHg OS

102

Evaluation of data gathered on that day—and <u>most</u> importantly, compared to previous data for change over time

103



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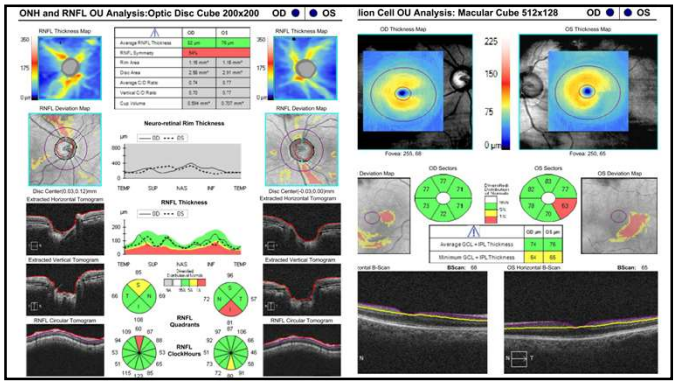

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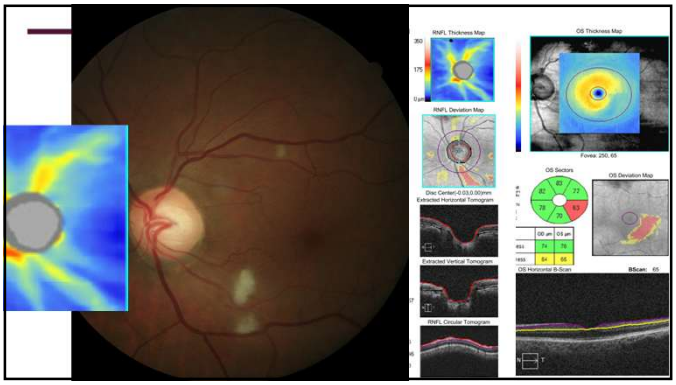

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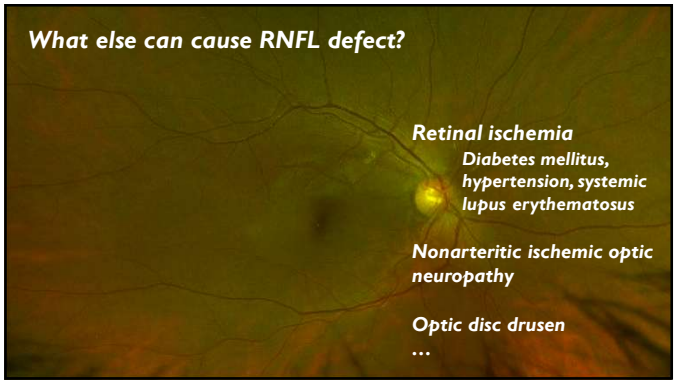

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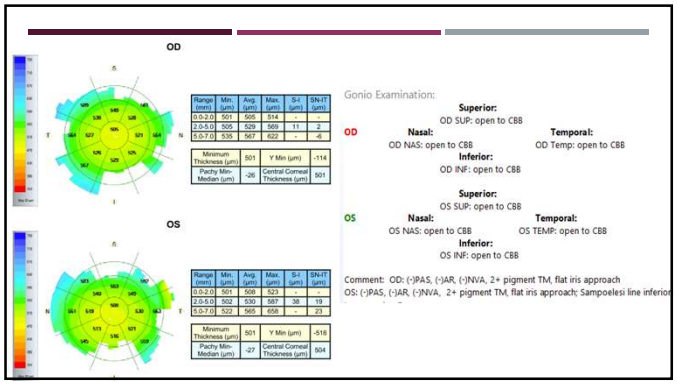


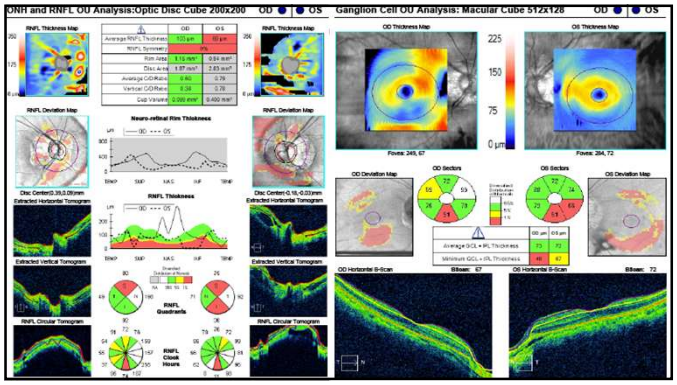
109

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

110



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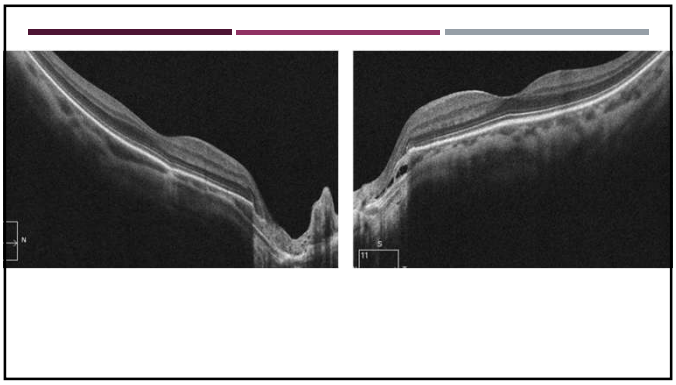

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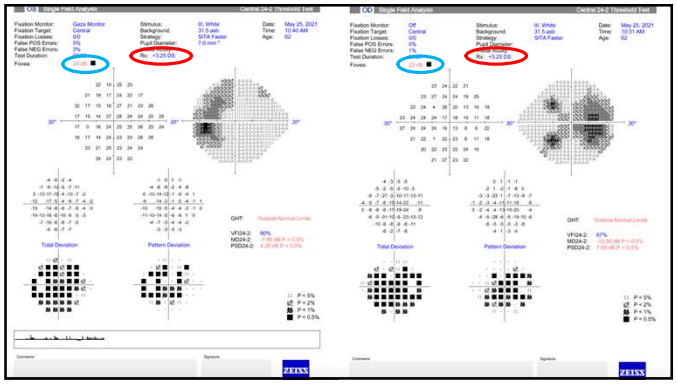

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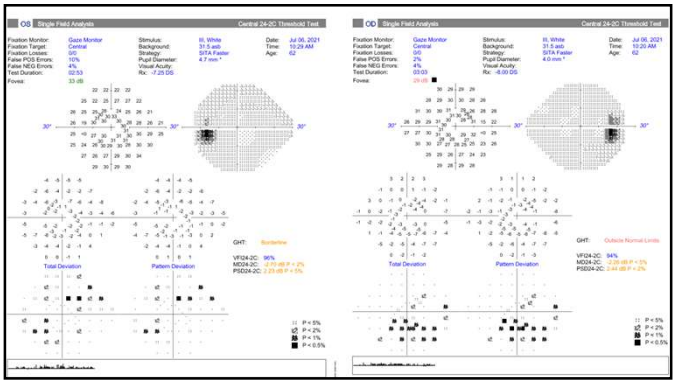

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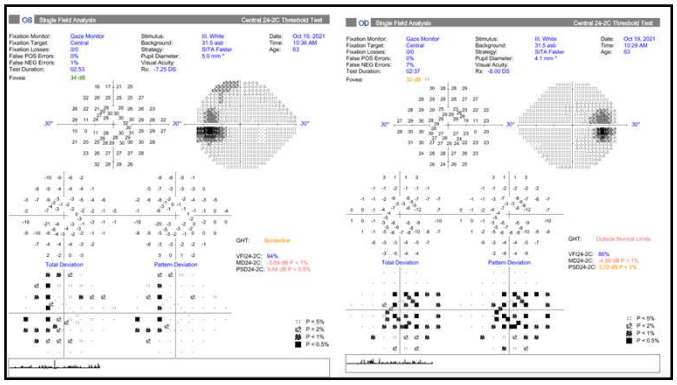

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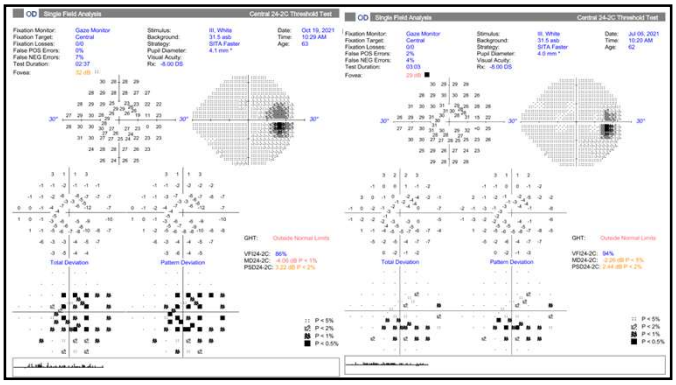

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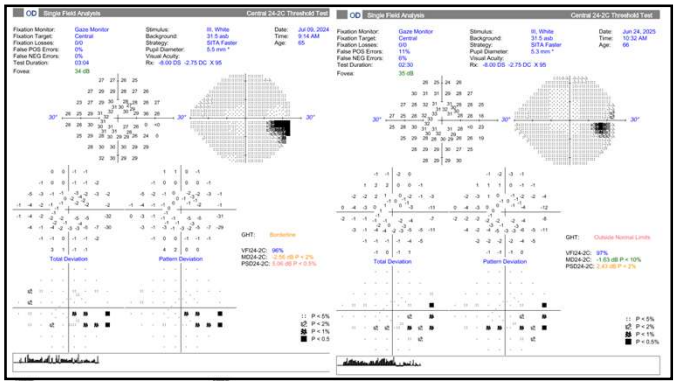
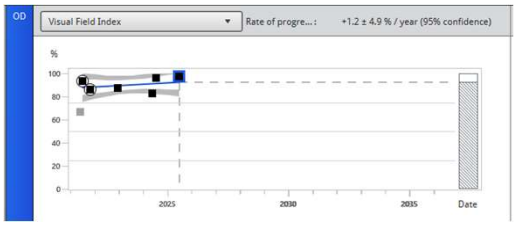


117

Have her fields changed?!



118

61 year old male

Diagnosed with POAG in 2008; SLT bilateral (2018), tube shunt OD 2022

Dorzolamide-timolol BID OU, latanoprost QHS OU

BCVA 20/200 OD, 20/100 OS

IOP 7mmHg OD 15mmHg OS

119

61 year old male

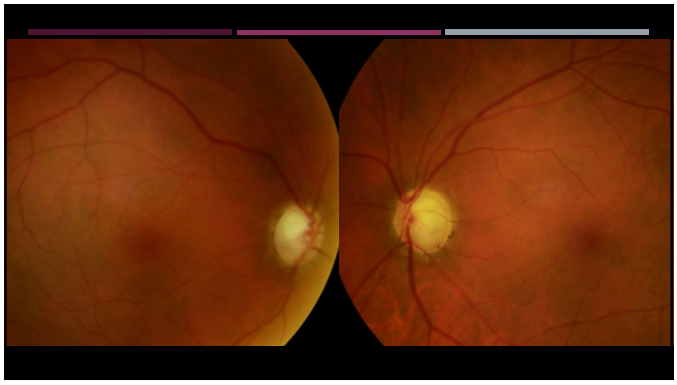
Medication adjustment: Netarsudil-latanoprost QHS OU, dorzolamide-timolol BID OU

Maximally tolerated medical therapy is patient-dependent

IOP 7-9mmHg OD 8-10mmHs OS

"Doc, is there anything else that I can do?"

120



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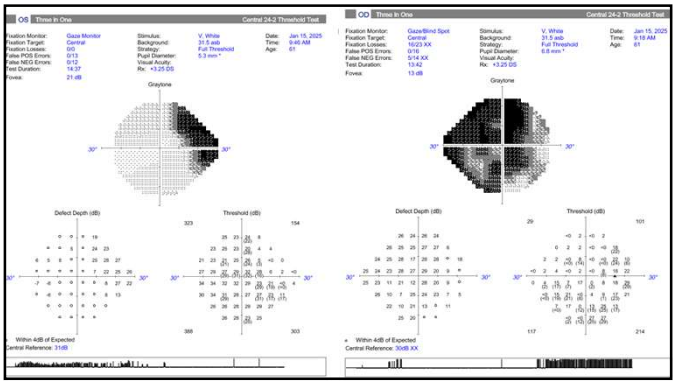

122

Unmet needs in glaucoma management

Nocturnal IOP lowering

Neuroprotection…

Nicotinamide (3g daily) and pyruvate

123

Nicotinamide and Pyruvate for Neuroenhancement in Open-Angle Glaucoma
A Phase 2 Randomized Clinical Trial

Carlos Gustavo De Moraes, MD, MPH, PhD[1]; Simon W. M. John, PhD[1,2,3]; Pete A. Williams, PhD[4]; et al
Author Affiliations | Article Information

JAMA Ophthalmol. 2022;140(1):11-18. doi:10.1001/jamaophthalmol.2021.4576

ARVO Annual Meeting Abstract | June 2024

Restoration of Blood-Retinal Barrier Integrity Prevents Neurodegeneration in Glaucoma

Isaac Alejandro Vidal Paredes; Jorge Luis Cueva Vargas; Nicolas Belforte; Yukihiro Shiga; Florence Dotigny; Heberto Quintero; Adriana Di Polo

ARVO Annual Meeting Abstract | June 2024

A Phase 1 Trial of Topical Insulin for Patients with Glaucoma

Zac Wennberg Smith; Gala Beykin; Mariella Saludares; Mariana Nunez; QianQian Wang; Adriana Di Polo; Jeffrey Louis Goldberg

124

Neuroprotection (and neurorecovery?!)

- *Translation from RGC culture models → experimental models → RCTs*
- *Mitochondrial dysfunction drives RGC degeneration (mouse)*
- *NAD (precursor of nicotinamide) demonstrated to be neuroprotective in mice (Williams 2017)*
- *Ongoing clinical trials—target enrollment over 1300*
  - *Swedish Nicotinamide Trial: newly diagnosed OAG; 3g oral nicotinamide without standard IOP-lowering therapy*
- *Primary endpoints 20 months or longer; safety: liver function (ALT, AST, and bilirubin)*

125

American Glaucoma Society-American Academy of Ophthalmology Position Statement on Nicotinamide Use for Glaucoma Neuroprotection

Aakriti Garg Shukla, MD, MSc, George A. Cioffi, MD, Simon W.M. John, PhD, Qing Wang, MD, PhD, Jeffrey M. Liebmann, MD, on behalf of the American Glaucoma Society and American Academy of Ophthalmology

Accepted Date: 7 January 2025

- *300 patients dosed across trials; 2 have developed drug-induced liver injury*
- *73 year old woman with POAG and normal liver function*
- *69 year old Chinese woman in Singapore; BMI 15*
- *Changed study protocol to LFT at baseline, 1 week, 2 months, 4 months, every 4-6 months*

126

Bottom line

Set reasonable expectations for yourself
- *Of what someone can manage*
- *Of effectiveness of therapy*
- *Of the disease process*

Individualize management.

Take the time that you need to establish a diagnosis, determine effectiveness of treatment, and determine progression

127

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128