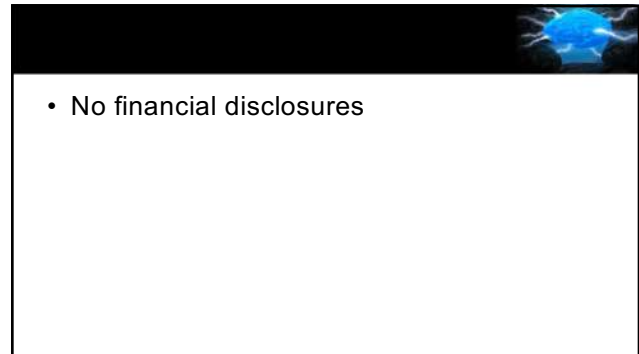
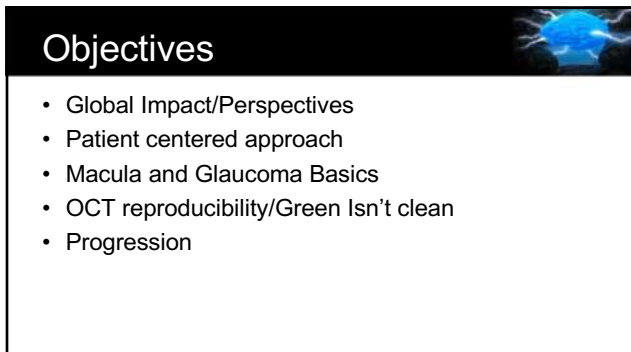




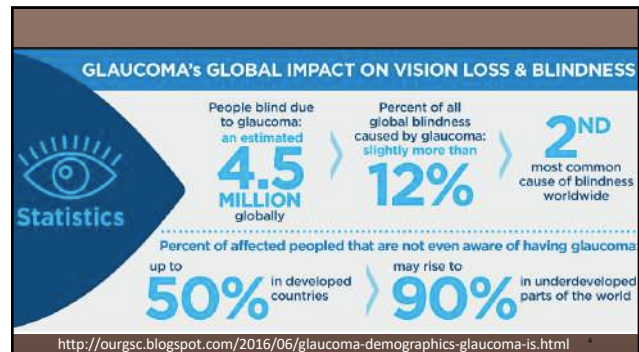
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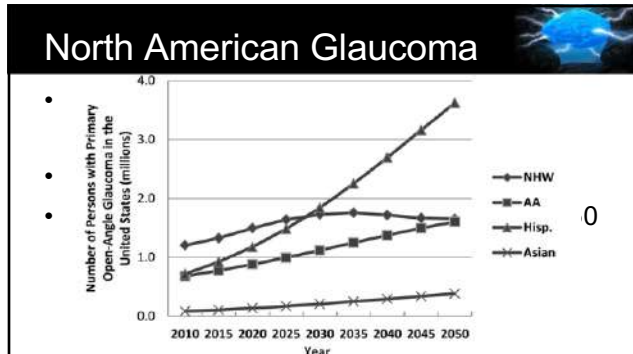
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3



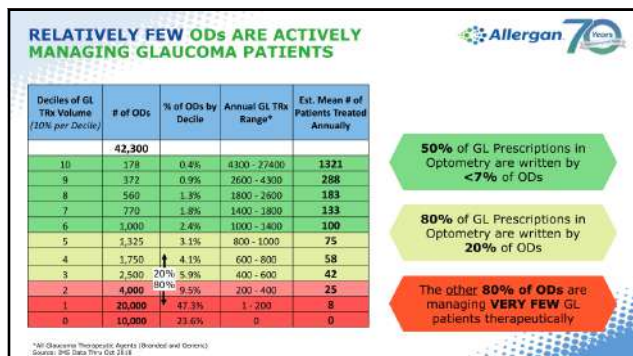
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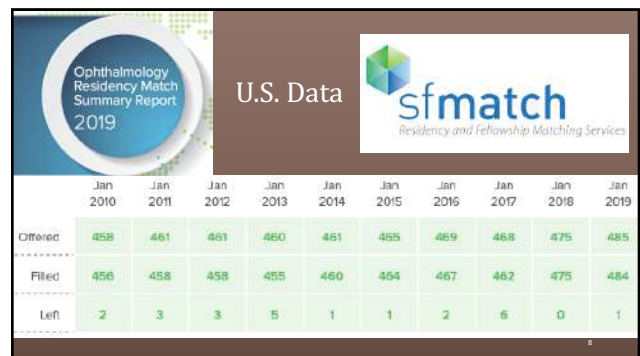
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6

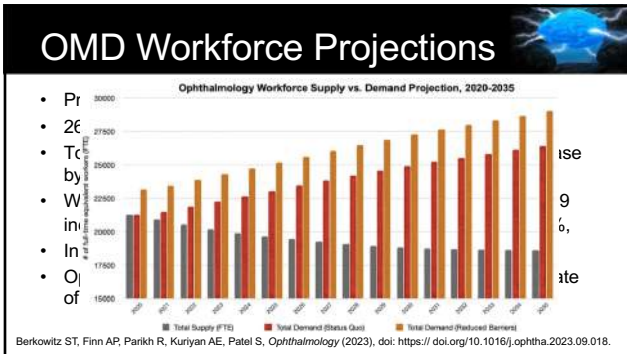


7



8

## OMD Workforce Projections



9

## Definitions



10

### RGC-centric Definition

- Glaucoma is characterized by loss of retinal ganglion cells (RGCs) and their axons that manifests clinically as structural changes to the optic nerve head (ONH) and circumpapillary retinal nerve fiber layer (cpRNFL). These changes are accompanied by a reduction in visual field sensitivity, which without adequate treatment, may progress to visual impairment and blindness.

Zhang C, et al *PLoS ONE* 2016 Aug 18;11(8):e0160549

11

### What is elevated IOP

Historical=over 21mmHg (Leydhecker 1959)

Modern Definition= The IOP at which the optic nerve sustains damage

IOP susceptibility is more important than the number

12



13



14

**January 2020**

80 year AAM in for Glaucoma F/U


- Dx: November 2019
- NO Visual Complaints
- NO mobility Issues/Falls

**November A and P**

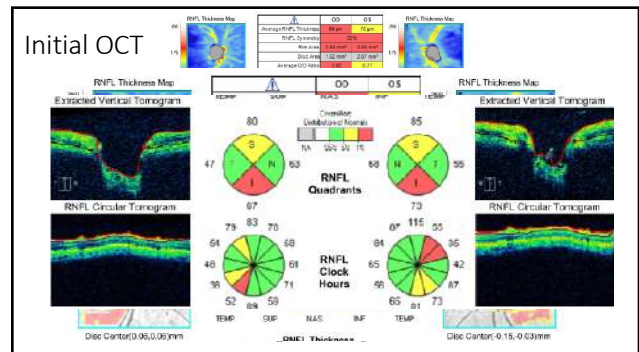
A: POAG mild OU....HVF does not match CVF or v

P: Rx Latanoprost qevening

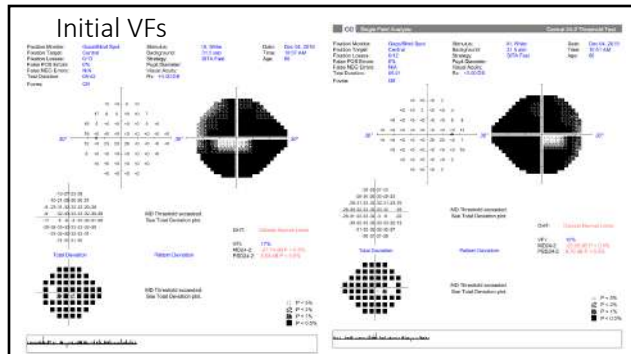
Occupation: Drives cars for auto auctions.....



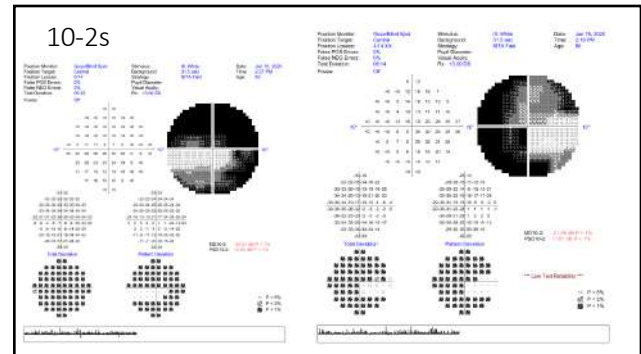
15



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17



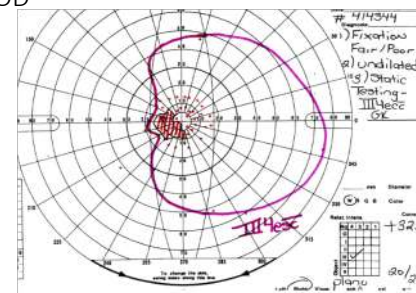
18

### Our A and P

- POAG, severe OU
- (-) mobility issues or perceived blur
- Ed pt about glaucoma and s/s of disease progression. Discussed Crabb forced choice images. Patient asymptomatic.
- Refer for surgical consultation
- Refer for LV evaluation/Goldmann with Dr. Squier

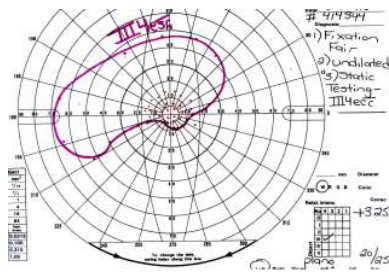
19

### LV exam OD

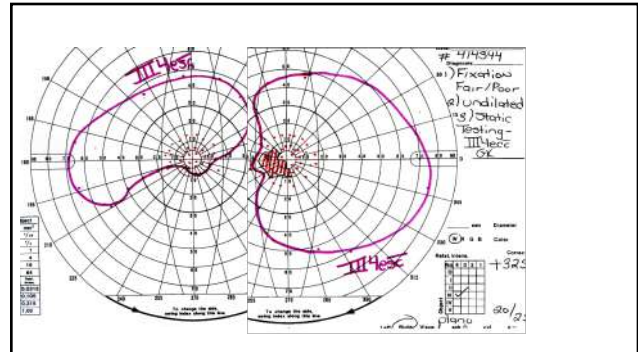


20

## LV Exam OS



21



22

## How Does Glaucoma Look?

## Patient Perception of Visual Field Loss

David P. Crabb, PhD,<sup>1</sup> Nicholas D. Smith, PhD,<sup>1</sup> Fiona C. Glen, PhD,<sup>1</sup> Robyn Burton, BSc,<sup>1</sup>  
David F. Garway-Heath, MD<sup>2</sup>

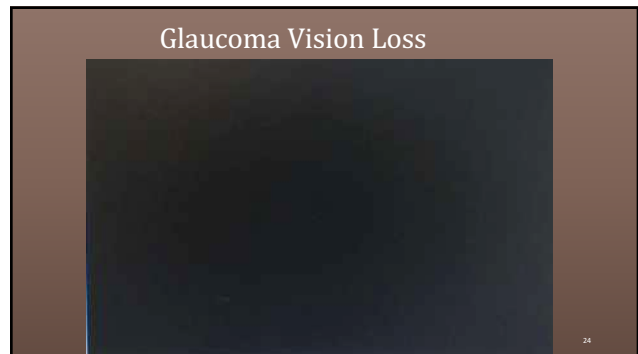
Eye (2016) 30, 304–313  
© 2016 Macmillan Publishers Limited. All rights reserved. 0950-2228/16  
www.nature.com/eye

A view on glaucoma—  
are we seeing it  
clearly?

DP Crabb

23

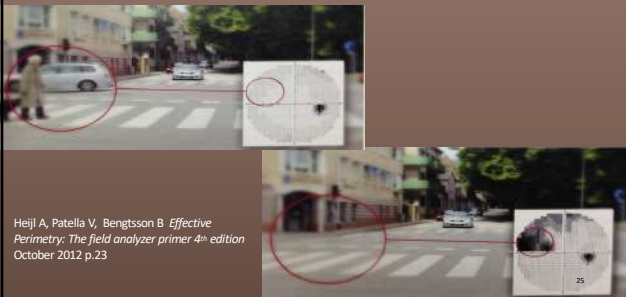
## Glaucoma Vision Loss



24



## Glaucoma=Negative Scotoma?



25

## What Does The Patient Perceive?



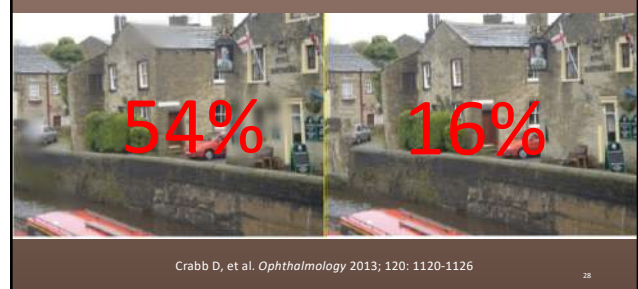
26

## Patient Perception



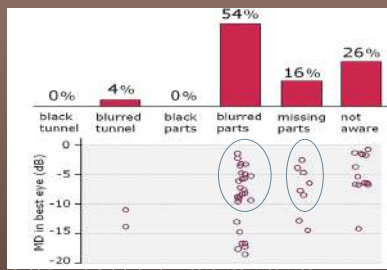
27

## Patient Perception



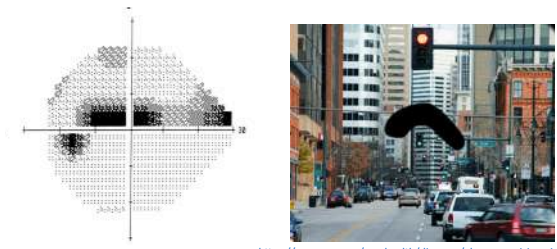
28

### Only the Advanced Cases?



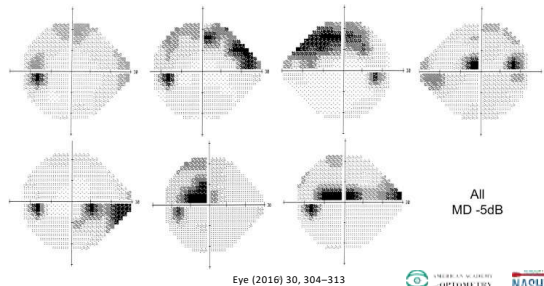
29

### Are we biased to believe these are the same?



30

### SAP Bias Can Cause Flawed Perceptions of Function



31

### Patient Self Reported Descriptors



32





### Current Evaluation/SAP Problems

- Substantial variability in psychophysical testing<sup>1</sup>
- Requires high volume of tests to detect change during followup<sup>2</sup>
- Substantial number of RGCs may be lost prior to detection<sup>3</sup>
- Retinal loci/RGC receptive fields sampled poorly by current strategies<sup>4</sup>
- Highly trained Perimetrist Required<sup>5</sup>
- Lacks portability\*



1) Susanna R, et al. TVST. 2015 2) Abe RY, et al. IOVS 2016;57(9):421-8  
 3) Kerrigan-Baumrind LA, et al. IOVS. 2000;41:741-748  
 4) Ashimatey BS, Swanson WH. IOVS. 2016;57:502-507 5) Patella et al. Effective Perimetry 2012



37

JAMA Ophthalmology | Original Investigation

### Use of Virtual Reality Simulation to Identify Vision-Related Disability in Patients With Glaucoma

Alexander K. N. Lam, PhD; Elaine To, MSc; Robert N. Weinreb, MD; Marco Xu, PhD; Heather Mak, PhD; Gilda Lai, BSc; Yvonne Chiu, BSc; Ken Wu, PhD; Xujiao Zhang, PhD; Timothy P. H. Cheng, BSc; Philip Yawen Guo, MSc; Christopher K. S. Luong, MD, MB, ChB

**CONCLUSIONS AND RELEVANCE** These findings suggest that vision-related disability is associated with lighting condition and task in patients with glaucoma. Virtual reality may allow eye care professionals to understand the patients' perspectives on how visual impairment imparts disability in daily living and provide a new paradigm to augment the assessment of vision-related disability.

<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2762850>



40

### Simulations

- Shopping <https://edhub.ama-assn.org/in-learning/video-player/18315135>
- City <https://edhub.ama-assn.org/in-learning/video-player/18315141>
- City Day vs Night <https://edhub.ama-assn.org/in-learning/video-player/18315143>
- Night Stairs <https://edhub.ama-assn.org/in-learning/video-player/18315137>
- Day vs Night Stairs <https://edhub.ama-assn.org/in-learning/video-player/18315139>



41

### Medication Adherence/ Criticality of Doctor-Patient Dialogue



42

## Medication Adherence Reality Check

- 30-70% of mean doses are taken across multiple studies
- 30-50% of medications are D/C in the first months of therapy
- Patients report far higher medication use than reality
- Patients DO NOT want to acknowledge undesirable behavior
- Ophthalmologists do a poor job of detecting nonadherence
- IOP and Cap Color DO NOT capture medication adherence
- Many patients DO NOT believe reduced vision is a risk of Not using drops

Doctor-Patient communication DOES contribute to patient adherence!!!

1) Friedman DS, et al. *IOVS*. 2007;48:5052-5057 2) Savitz ST, et al. *Med Care*. 2017;55:500-505 3) Okeke C, et al. *Ophthalmology* 2009;116:191-199 4) Okeke C, et al. *Ophthalmology* 2009;116:2286-2293 5) Slota C, et al. *OVS* 2015;92:537-543 6) Dawkins R, et al. *Ophthalmology* 2015;122:2373-2379. 7) Robin A, Grover D. *Indian J Ophthalmol*. 2011;59:593-96



43

## We can improve.....

### Effect of Patient-Centered Communication Training on Discussion and Detection of Nonadherence in Glaucoma

- Ophthalmologist communication is physician centered, NOT patient-centered
- Videotaped doctor-patient communication before and after educational intervention
- Substantial improvement post education
- 4 steps to improved adherence assessment
  - 1) Open-ended questions
  - 2) Non-judgmental environment
  - 3) Shared Decision Making/Patient Understanding
  - 4) Ask about missed doses last



Hahn SR, et al. *Ophthalmology* 2010;117:1339-1347



44

## So....Are you nonadherent????

- IOP and Cap Color DO NOT capture medication

- Cho et al. A subjective pharmacy refills objective adherence

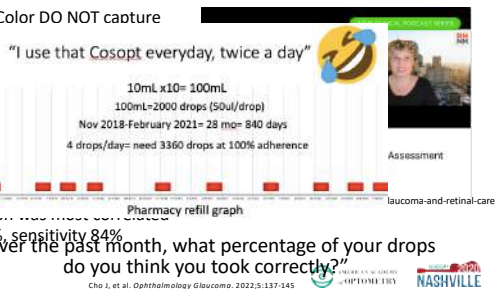
- 95 patients
- 56% were nonadherent

- Pharmacy refills with nonadherence

- Single question was more sensitive

- Accuracy 71%, sensitivity 84%

Over the past month, what percentage of your drops do you think you took correctly?"



Cho J, et al. *Ophthalmology Glaucoma*. 2022;5:137-145

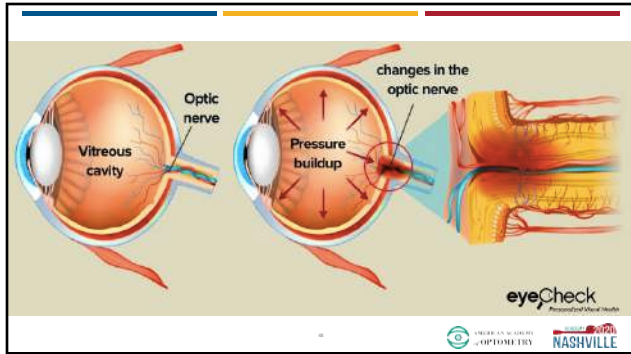


45

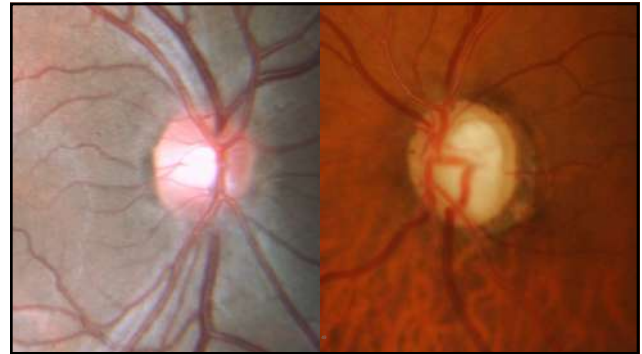
## Glaucoma Patient Education Deck



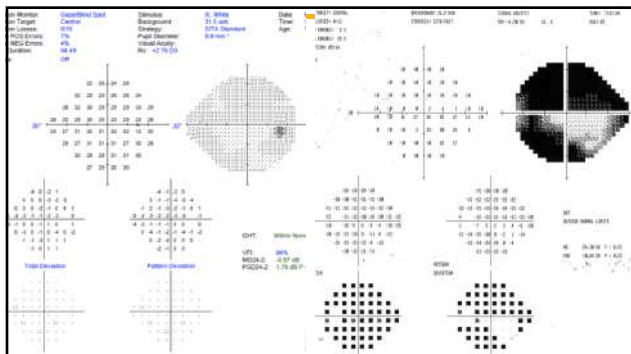
47



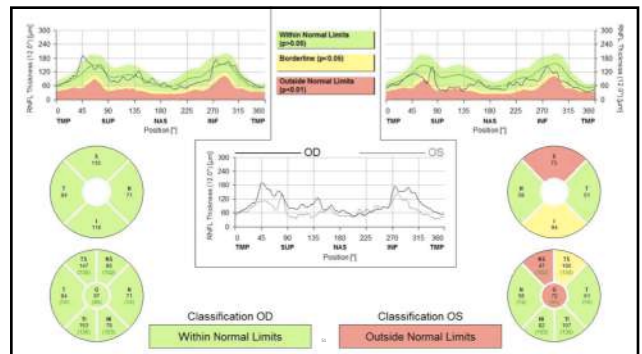
48



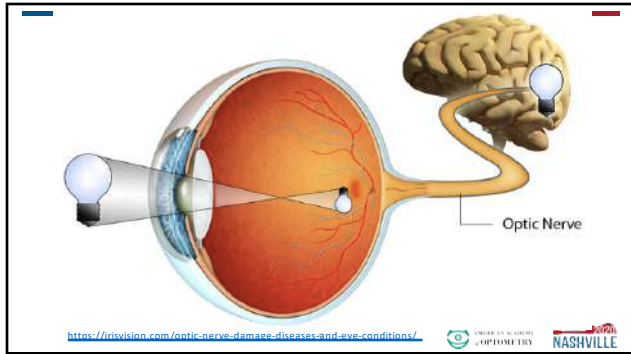
49



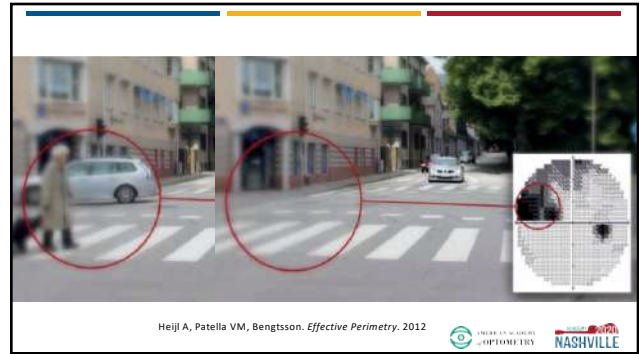
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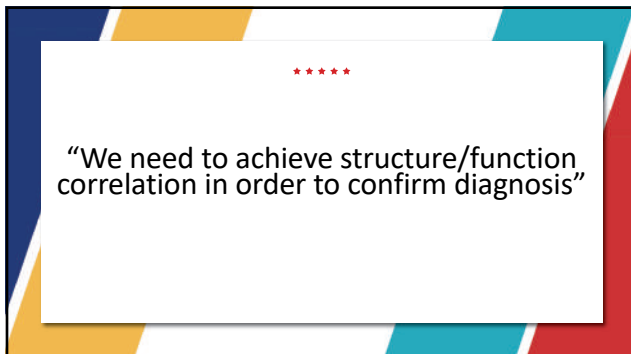
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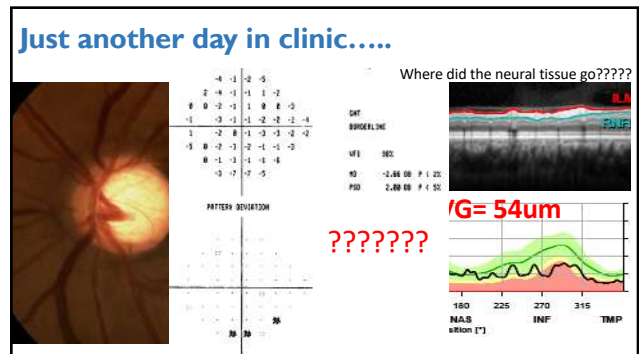
52



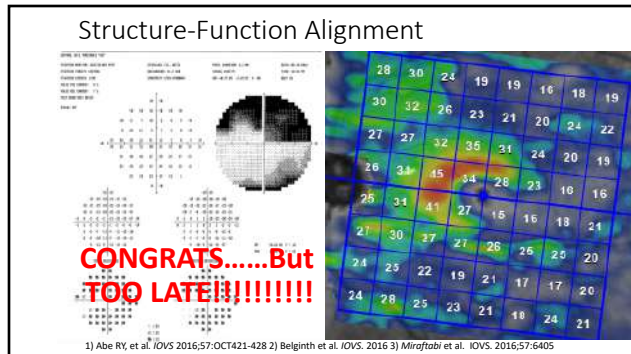
53



54



55



56

### Structure-Function Relationship....

- Linear vs non-linear units of measurement<sup>1</sup>
- Between subject test-retest variability<sup>3</sup>
- Retinal loci/RGC receptive fields poorly sampled<sup>3</sup>
- Tissue thickness  $\neq$  RGC function<sup>2</sup>
- Lower variability in structural testing<sup>4</sup>
- Disease severity and number of tests run<sup>1</sup>

Relationship Status:

Interested in: ☐ Single ☐ In a Relationship ☐ Engaged ☐ Married ☒ **Relationship** ☐ In an Open Relationship ☐ Widowed

Looking for: ☐ Dating ☐ A Relationship ☐ Networking

1) Abe RV, et al. IOVS. 2016 2) Malik, Swanson, Garway-Heath. Clin Exp Ophthalmol. 2012  
3) Ashimatey BS, Swanson WH. IOVS. 2016; 4) Raza, Hood IOVS. 2015

57

### RGC estimates and MD loss in Humans based on disease stage

MD, dB	Stage of Disease	Estimated RGC Count	Change in MD, dB, for a Change of:		
			10,000 RGCs	35,000 RGCs	100,000 RGCs
0.4 <sup>*</sup>		1,020,000	0.04	0.11	0.33
-2		710,000	0.15	0.56	1.79
-5		560,000	0.25	0.94	2.98
-10		405,000	0.39	1.34	3.99
-15		281,000	0.47	1.78	5.78
-20		193,000	0.64	2.35	7.02
-25		121,000	0.71	2.53	7.25

<sup>\*</sup> Average MD of the healthy eyes included in the study.  
Medeiros F. IOVS. 2012;53(11):6939-46

59

### Progression in EMGT: Structure vs Function

- 306 eyes of 249 glaucoma pts
- Followed by SAP and Monoscopic Disc Photos over median 8 years
- SAP detected progression first in...
  - 80% with Early Field loss
  - 79% with Moderate
  - 100% with advanced
- Simultaneous Progression in 0.003% (1/306)

Ohnell HM, et al. Ophthalmology. 2016;123(6):1173-80

Ohnell HM, et al. Acta Ophthalmol. 2017; 95: 281-287

60



### Structure versus Function in Glaucoma: The Debate That Doesn't Need to Be

Felipe A. Medeiros, MD, PhD - San Diego, California  
Andrew J. Tatham, FRCOphth, FRCSEd - Edinburgh, United Kingdom

- Agreement is the EXCEPTION rather than the rule

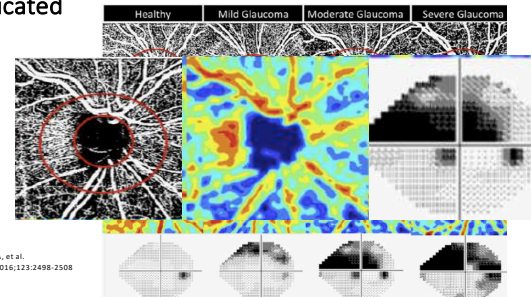
“The disagreement between structural and functional changes may seem puzzling, because the death of a RGC and axonal loss obviously should be accompanied by the loss of function. However, it can be easily understood when considering the properties of the tests available to measure structure and function, such as their different scales, variability, and dynamic range”

- Both have value, both are needed, Integration is key!

Medeiros FA and Tatham AJ. *Ophthalmology*. 2016;123(6):1171-72

61

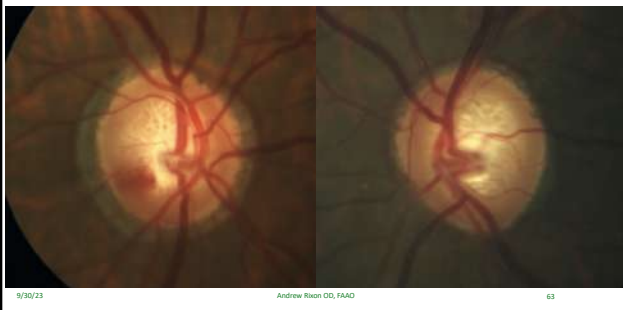
### Function-Vascular Relationship May Not Be Complicated



Yarmohammadi A, et al.  
*Ophthalmology* 2016;123:2498-2508

62

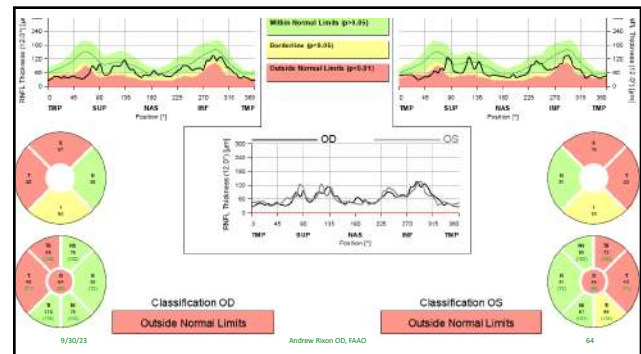
### Arch Case



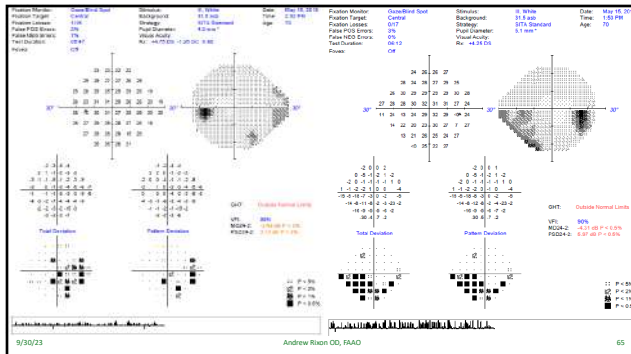
9/30/23

Andrew Roon OD, FAAG

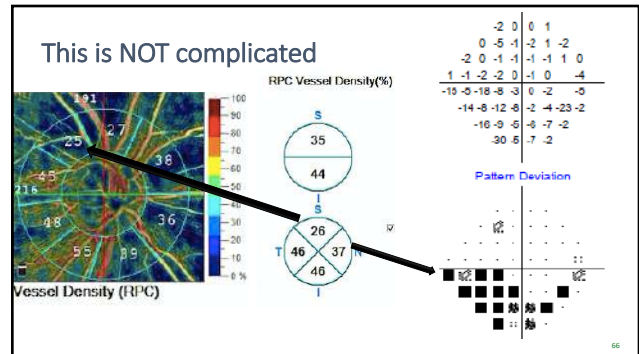
63



64



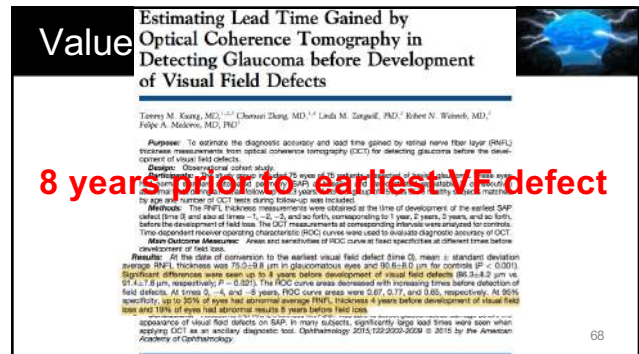
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67



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DISCLOSURE STATEMENT  
"No disclosure statement"

**SECO2018**  
WHERE SIGHT MEETS VISION™

Course Title: **OCT in the management of Glaucoma: Green Isn't always Clean**

COPE #56199-GL

Lecturer: **Andrew Rixon OD, FAAO**


**SECO UNIVERSITY**

Please silence all mobile devices.

69

### Cirrus RNFL/Macula Normative Database

- 284 Subjects included
- 527 subjects screened
- 43% caucasian, 24% asian, 18% african american, 12% hispanic
- -12D to +8D
- 19-84
- Red, Green, Yellow based in databases



Knight OJ, et al Arch Ophthalmol 2012 Mar;130(3):312-8  
[http://www.accessdata.fda.gov/cdrh\\_docs/pdf8/k083291.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf8/k083291.pdf)

70

### Range of values in database-69yo

**90% in the Green**

- We can measure multiple steps of statistically significant change while a glaucoma suspect still is in the green normal range.

Excellent Perimetry 2021

IN NORMAL SUBJECTS

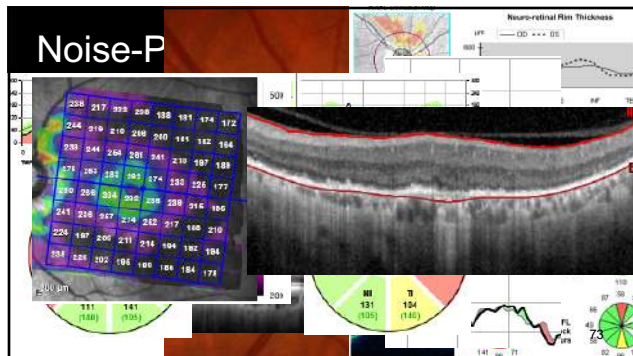
95 <sup>th</sup> percentile = 107 microns
50 <sup>th</sup> percentile = 89 microns
5 <sup>th</sup> percentile = 75 microns
1 <sup>st</sup> percentile = 67 microns
Risk of Disability = 55 microns

(values shown are for a 69 year old normal)

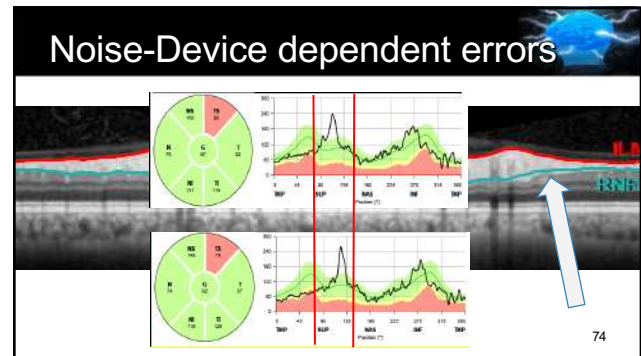
71

### QUALITY IS CRITICAL!

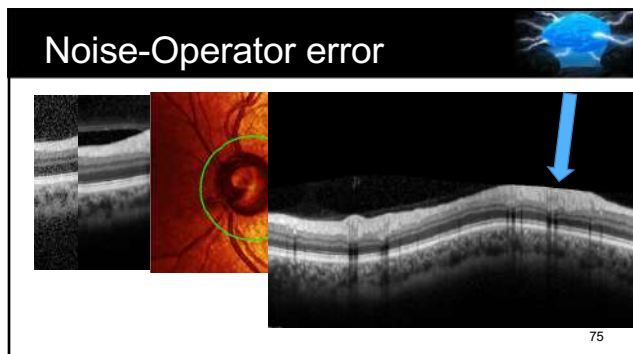
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74



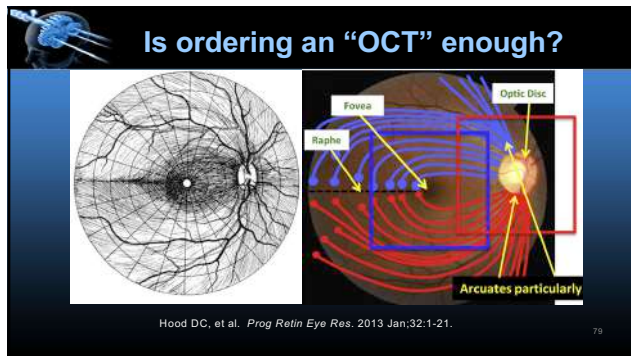
75

### The Macula and Glaucoma

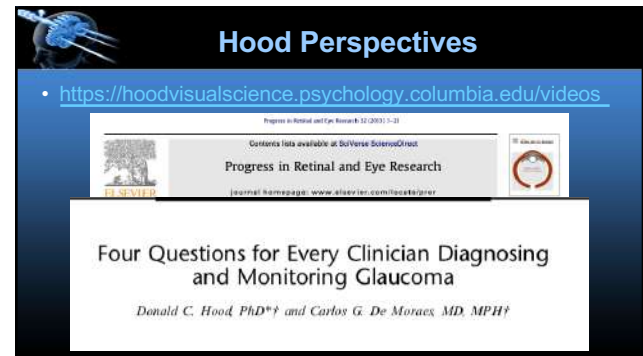
- Macula= $\pm 8^\circ$  from the foveal center
- Constitutes ~50% of all RGCs
- Represents less than 2% of the retinal area
- Ganglion Cell layer is most dense at the macula (6-12 layers)
- In combo with RNFL constitutes 30-35% of retinal thickness in that region
- Macula involved in ALL stages of Glaucoma

1) Hood DC, et al. *Prog Retin Eye Res* 2013 Jan;32:1-21  
2) Um TW, et al. *IOVS* 2012; 53:1139-1144

78



79



80

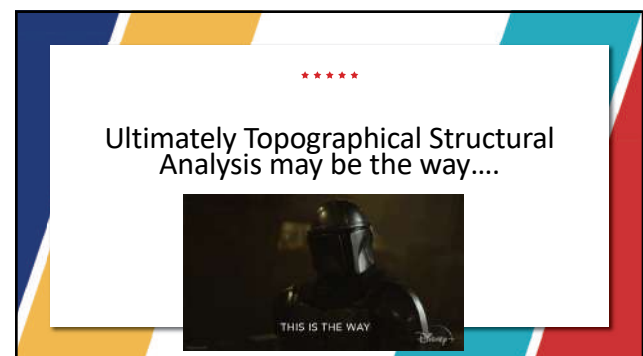
Article  
DOI: 10.1117/tvst.4.6.4

#### Central Glaucomatous Damage of the Macula Can Be Overlooked by Conventional OCT Retinal Nerve Fiber Layer Thickness Analyses

- 143 OAG patients
- 10-2s, Macula and Disc Cubes
- Combined RNFL (TQ, CH 7-10), RGC+, 10-2s
- Experts graded as Abnormal or Normal macula
- TQ missed 77%, TQ+CH7 39%, CH7-10 36%
- Need more than cp-RNFL!!!

Wang DL, et al. *Trans Vis Sci Tech.* 2015; 4(6):4

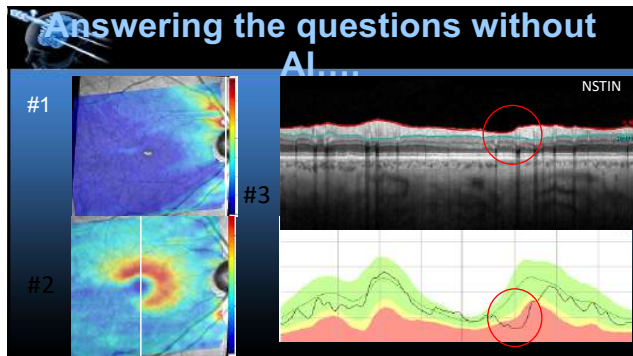
81



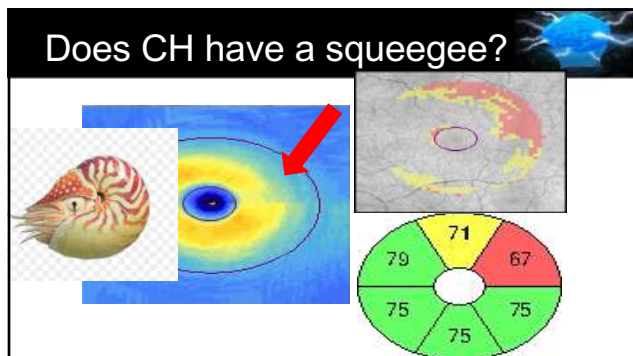
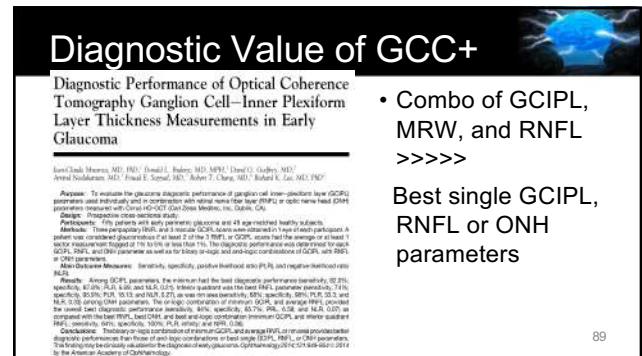
82



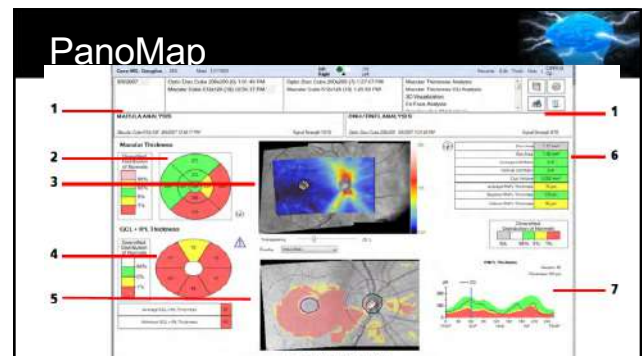




88

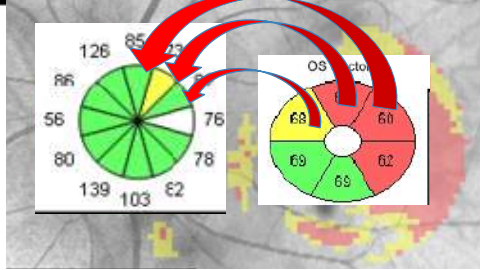


90

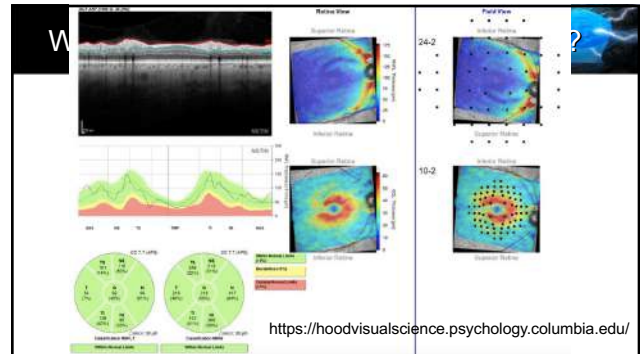


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## Panomap Example



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## VariabilityToolTip

	OD	OS
Average RNFL Thickness	78 $\mu\text{m}$	82 $\mu\text{m}$
RNFL S	At least one parameter is close to a normative limit that may change the color coding on a re-scan. Click for detailed information.	
Disc Area	1.56 $\text{mm}^2$	1.35 $\text{mm}^2$
Average C/D Ratio	0.53	0.31
Vertical C/D Ratio	0.66	0.33
Cup Volume	0.107 $\text{mm}^3$	0.030 $\text{mm}^3$

94



- **Normative Data Details Report**
- There is measurement variability for the macula parameters which may impact the normative database color coding. If the true value is near the limit of what the software uses to determine the normative database color code, then it is possible that the color code could vary from exam to exam. When at least one parameter is close to a normative limit, a blue icon button displays. When your cursor hovers over this icon button, the tooltip appears as shown below.

95

## Illustrative Case

- October 2015
- 65yo AAM in for routine examination
- “Borderline” Glaucoma findings at last exam in 2014
- IOP: 20mmHg/20mmHg
- ONHs: Large discs .55/.60 OD  
.60/.65 OS

96

2014

- “Some inferior thinning noted OS, and some asymmetry b/w eyes. However, changes are subtle and not too concerning at this point.”
- 4 mo VF needed to assess whether the pt. has undergone any significant changes.

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## Normative Data Details OD 2014

Parameter	Value	Percentile Value	Value Minus Reproducibility Limit	Value Plus Reproducibility Limit	Percentile Value
RNFL Parameters					
Average Thickness	78	9	14	4	22
Superior Thickness	70	80	94	63	76
Superior Thickness	92	7	82	1	102
Superior Thickness	63	36	57	18	69
Inferior Thickness	88	3	79	1	97

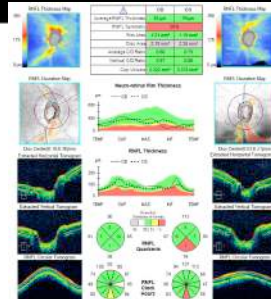
Parameter	Value	Percentile Value	Value Minus Reproducibility Limit	Value Plus Reproducibility Limit	Percentile Value
CH12	89	19	71	5	107
CH13	83	17	66	4	97
CH14	89	23	66	8	92
CH15	59	66	52	36	67
CH16	59	41	50	14	66
CH17	59	4	47	1	72
CH18	89	6	78	1	104
CH19	114	29	100	14	128
CH20	84	00	56	35	73

Note: All units in micrometers.

Download  
Distribution of Results

98

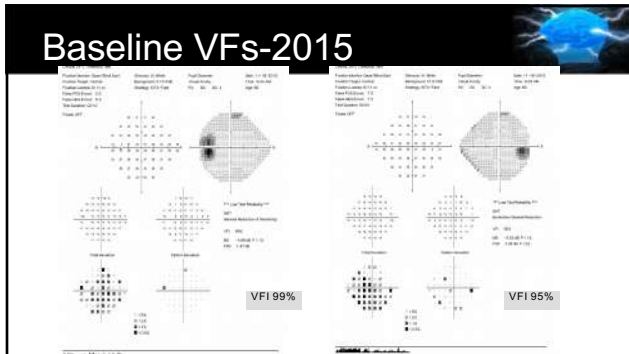
2015



Parameter	Value	Percentile Value	Value Minus Reproducibility Limit	Value Plus Reproducibility Limit	Percentile Value
RNFL Parameters					
Average Thickness	85	35	70	18	87
Superior Thickness	81	50	66	21	71
Superior Thickness	98	8	80	1	99
Superior Thickness	66	35	50	8	68
Superior Thickness	78	3	69	1	94
Superior Thickness	48	45	23	18	71
Superior Thickness	79	17	64	20	81
Superior Thickness	100	25	81	9	110
Superior Thickness	40	33	34	1	100
Superior Thickness	26	49	71	4	88
Superior Thickness	30	84	76	27	80
Superior Thickness	46	87	30	29	89
Superior Thickness	44	87	30	29	89
Superior Thickness	75	23	60	8	88
Superior Thickness	78	3	69	1	94
Superior Thickness	130	35	110	19	142
Superior Thickness	88	48	70	26	71

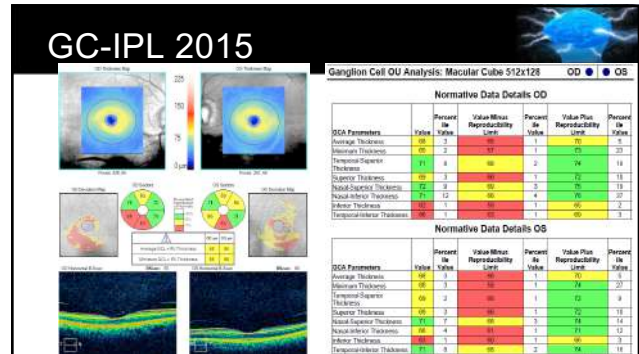
99

## Baseline VFs-2015



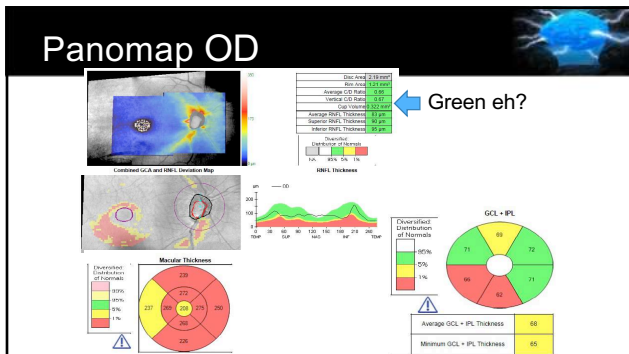
100

## GC-IPL 2015



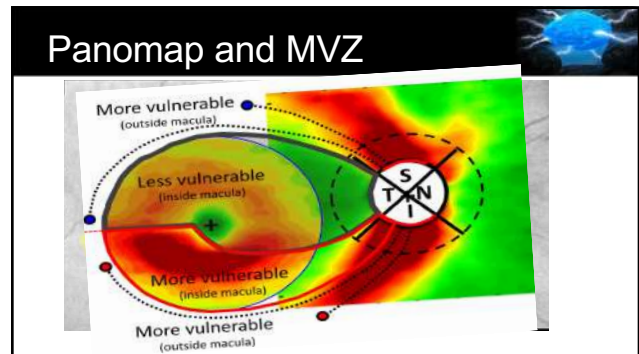
101

## Panomap OD

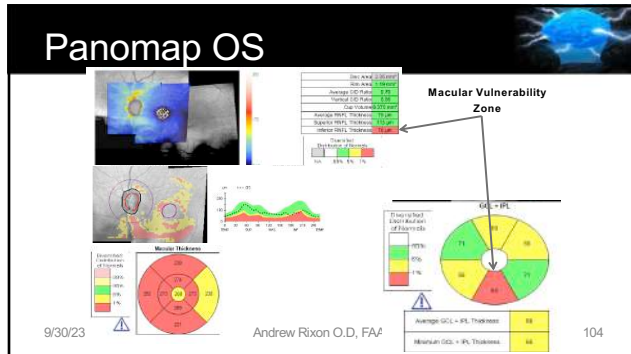


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## Panomap and MVZ



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\*\*\*\*\*

Are historical assumptions/behaviors correct?  
Is There a better way to make decisions?  
How do we gauge success or failure??

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But first the static.....

\*\*\*\*\*

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#ACADEMY19

## IOP peaks and Means are not adequately assessed

#academy19 CHICAGO

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## IOP is NOT static, it is Dynamic!



- Treated POAG patients do NOT manifest a reproducible short or long term diurnal IOP pattern<sup>1,2</sup>
- Any difference <6.8mmHg from pre treatment IOP is indistinguishable from nontherapeutic variation<sup>3</sup>
- "Snapshot" readings are most common way of assessing IOP<sup>4</sup>
- Taking a single IOP measurement between 7am and 9pm has a >75% chance of missing the highest point of the diurnal curve<sup>5</sup>

1) Realini T, et al. Ophthalmology. 2011;118:47-51 2) Japfel T, et al. Ophthalmology 2014;121:1998-2003  
3) Kuchard A, et al. BMJ. 2012;36(7):967-970 4) Metcher B, et al. Br J Ophthalmol. 2012;106:229-233  
5) Jonas J, et al. AJO. 2005;139:1136-1137 6) Clement CL, et al. Surv Ophthalmol. 2014;59(8):615-26

109

## The current paradigm is a problem

- Paradigm of single "IOP" by GAT every 3-4 months
- "In a patient seen 3 to 4 times a year, we obtain about 12 seconds worth of IOP data. Realizing there are more than 31 million seconds in a year, we are not even looking at the tip of the iceberg when it comes to measuring IOP"-Kaweh Mansouri M.D., M.P.H.

**What is happening when we aren't looking?????**

<http://www.ophtalmologytimes.com/modern-medicine-cases/continuous-iop-monitoring-tools-addressing-unmet-need/> last accessed Nov 5, 2018

KEEP CALM AND BURY YOUR HEAD IN THE SAND

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## Mrs. Smith your pressure is

**Peak IOP will be missed in ~75% of cases**


TABLE. Frequency of the Highest Intraocular Pressure (IOP) Measurement and Lowest IOP Measurement During 3,028 Diurnal / Nocturnal Pressure

Time	Highest IOP Measurement		Lowest IOP Measurement	
	n	Percentage	n	Percentage
7 am	616	20.4%	365	12.1%
Noon	539	17.8%	365	12.1%
5 pm	643	21.3%	468	15.1%
9 pm	419	13.8%	740	24.5%
Midnight	808	26.7%	1,077	35.6%

For the parameters "Difference from Mean Value" and "Difference from Maximal Value" measurement is lower than the mean and the maximum, respectively.

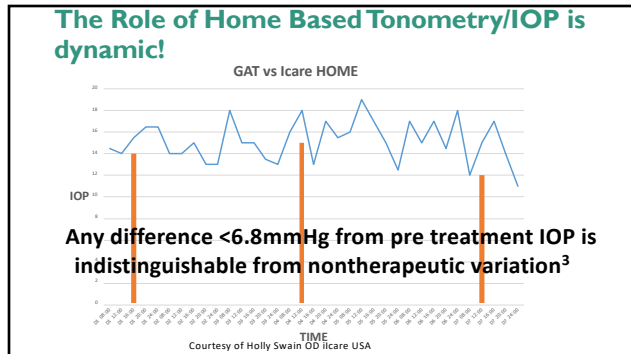
**Highest at midnight!!!!**      **Wait it's lowest at 9pm!!!!**

Jonas J, et al. AJO. 2005;139:1136-1137.

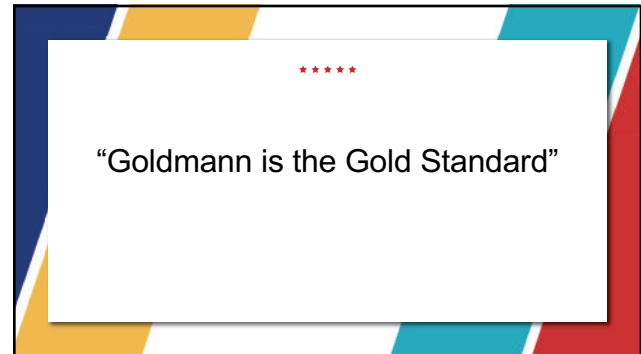


111





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113

**So is it time to move on?**

**When gold standards change: time to move on from Goldmann tonometry?**

Gus Gazzard,<sup>1,2</sup> Hari Jayaram,<sup>2,3</sup> Ana M Roldan,<sup>4</sup> David S Friedman<sup>5</sup>

“The technique is widely integrated within clinical practice, and a certain amount of inertia has prevented clinicians from shifting to newer, possibly better, technologies.”

“Why are we persisting in using GAT clinically?”

*Br J Ophthalmol* January 2021 Vol 105 No 1

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**Correcting with CATS**

**CATS™ TONOMETER PRISM**

Your Goldmann. Better Pressure.

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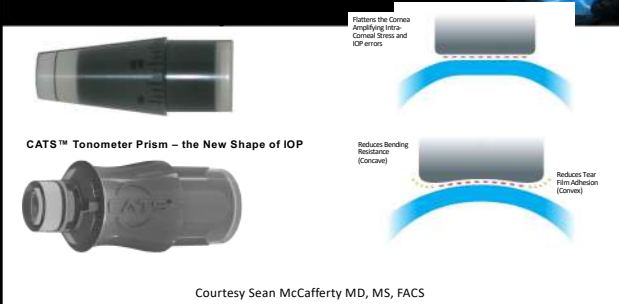
## CATS core

- Sean McCafferty MD, MS (optical engineering)
- FDA cleared 2018
- Correcting applanation tonometry surface (CATS)
- Optimizes historical goldmann prism to minimize mechanical stress induced by the prism and reduce tear film adhesion
- Tear film error can  $\pm$  induce up to 4.5mmHg of error

McCafferty S, et al. *BMC Ophthalmology*. 2017;17:215

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## CATS: Correcting Applanation Tonometry Surface

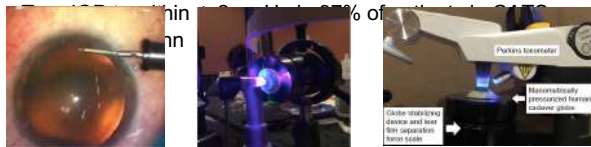


Courtesy Sean McCafferty MD, MS, FACS

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## True IOP....

- Goldmann type prism was 7.9 +/- 2.3 mmHg lower than intracameral pressure in the supine position in vivo
- Cadaveric eyes were 3.1 +/- 2.5 mmHg in seated and 5.4 +/- 3 mmHg than intracameral in supine positioning



McCafferty S, et al. *BMC Ophthalmology*. 2017;17:215

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## Evidence for CATS

- Aligns with GAT on "nominal" corneas
- CATS minimally affected by CCT or CH
- Expected to align with IOPcc\*
- Reduced non-responder label from 36.1% to 13.8%
- CATS IOP better correlation with glaucoma progressors than GAT
- IOP accuracy 50% less affected by PRK and LASIK

1) McCafferty SJ, et al. *BJO*. 2019;103:1840-1844 2) McCafferty S, Lim G, Duncan W, et al. *TVST*. 2016;5:4-5.  
 3) McCafferty S, Tetraut K, McColgin A, et al. *Am J Ophthalmol*. 2018 Dec;196:145-153.  
 4) McCafferty S, Levine J, Schwiegerling J, et al. *BMC Ophthalmol* 2018;18. 5) Ang ET, et al. *BMC Ophthalmol*. 2022;22:503  
 6) Radcliffe N, et al. *Clin Ophthalmol*. 2020;14:2245-2253

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## How easy is it to use?

### Self Centration?



Courtesy of Sean McCafferty MD, MS, FACS and CATS Tonometer LLC

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## Insufficient IOP reduction Remains a reason for why Patients Still Go Blind from Glaucoma



121

### Insufficient IOP reduction

- Reducing IOP is the only known effective treatment for glaucoma
- None of the major studies have specifically addressed what the ideal pressure should be for individual patients or groups
- Simply reducing IOP is not good enough, reduction must be effective
- Lack of change or diminished velocity only way to confirm effectivity

Susanna R, DeMoraes CG, Cioffi GA, Ritch R. TVST. 2015;4(2):1  
Singh K, Shrivastava A. Surv Ophthalmol. 2008;53:333-38



122

### Percentage Based IOP Reduction in Major Trials

Study	Target IOP	Actual IOP Reduction %	Outcome
OHTS <sup>1</sup>	20% reduction or 18mmHg	22.4%	POAG risk reduced by >50% in treated group at 5yrs
EMGT <sup>2</sup>	No target	25%	55% of treatment group did NOT progress vs 35% of control at 6yrs
AGIS <sup>3</sup>	<18mmHg (associative analysis)	30-37%	Mean of 12.3mmHg resulted in minimal progression at ≥6yrs
CNTGS <sup>4</sup>	30% reduction	37%	12% treated eyes progressed vs 35% of control eyes in 5-7yrs
CIGTS <sup>5</sup>	35-50% (Formula based)	48% (surgery) 37% (medicine)	Minimum Δ to VF in either group at 4yrs

<sup>1</sup>Kass MA, et al. Arch Ophthalmol. 2002;120:701-713 <sup>2</sup>Heijl et al. Arch Ophthalmol. 2002;120:1268-1279 <sup>3</sup>AGIS Investigators. 2000;130:429-440 <sup>4</sup>CNTG Study Group. AJO. 2003;133:699-708 <sup>5</sup>Musch DC, et al. Ophthalmology. 2009;116:200-207

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## Therapeutic Failure Facts

- Hyporesponders/Non-responder
- Definitions vary
  - <3-5mmHg decrease
  - <10%, <15%, <20%
- Phase III Latanoprost trials 5% of patients had IOP reduction <10%
- Non-responder rate was 5% when low adherence minimized (Cardiff Model of Glaucoma Care)



1) Hedman K, et al. *Eur J Ophthalmol* 2000;10:95-104 2) Waterman H, et al. *Br J Ophthalmol* 2020;104:1704-1709

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## The Trouble with Targets

- Adherence to Target IOP guidelines (Canadian and European Glaucoma Society) has been recently questioned by VF progression (ADAGES cohort)
- IOP dynamics/Goldmann errors lead to misdiagnosis
- Target IOPs can lead to IOP obsession
- None of the major studies have specified what the ideal pressure should be for individual patients
- Often treated by practitioners as static

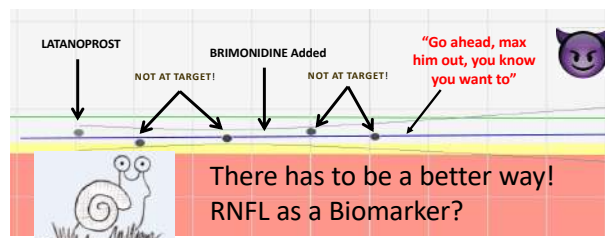


1) Susanna R, DeMoraes CG, Croft GA, Ritch R. *TVST* 2015;4(2):1 2) Singh K, Shrivastava A. *Surv Ophthalmol*. 2008;53:533-38  
3) Jonas JB, et al. *Lancet*. 2017; 390:2183-2193 4) Melchior B, et al. *Br J Ophthalmol*. 2022;106:229-233 5) Clement CJ, et al. *Surv Ophthalmol*. 2014;59(6):615-26 6) Hedman K, et al. *Eur J Ophthalmol* 2000;10:95-104 7) Waterman H, et al. *Br J Ophthalmol* 2020;104:1704-1709

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## Re-Evaluating Target IOP

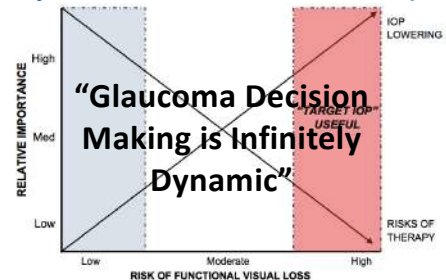
"This patient is not meeting target, I'd like to add another med"



<https://enterfea.com/difference-between-static-and-dynamic-analysis/>

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## Dynamic Market IOP concept



Singh K, Shrivastava A. *Surv Ophthalmol*. 2008;53:533-38.

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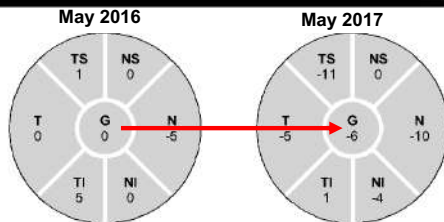
130

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### If Machine variance is 10 $\mu$ m Global...

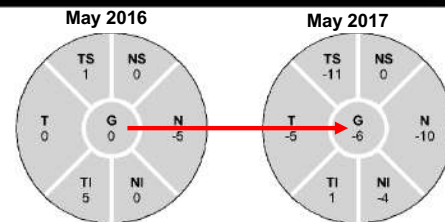


Cannot attribute change to pathological progression....  
NOT a Significant Change.....

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### If Machine variance is 3 $\mu$ m Global...



Change IS significant.....  
This change could be attributable to pathological progression....

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### RNFL Reproducibility-Database

measured on 32 normal subjects.

	Mean Thickness ( $\mu$ m)	Repeatability SD ( $\mu$ m)	Reproducibility SD ( $\mu$ m)	Repeatability Limit <sup>a</sup> ( $\mu$ m)	Reproducibility Limit <sup>b</sup> ( $\mu$ m)
Average	93.1	1.33	1.35	3.72	3.78
Temporal	64.6	2.03	2.05	5.68	5.74
Superior	118.8	3.42	3.45	9.58	9.66
Nasal	68.6	2.19	2.24	6.13	6.27
Inferior	123.6	3.01	3.14	8.43	8.79

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### Clock Hours Reproducibility

	Mean Thickness ( $\mu$ m)	Repeatability SD ( $\mu$ m)	Reproducibility SD ( $\mu$ m)	Repeatability Limit <sup>a</sup> ( $\mu$ m)	Reproducibility Limit <sup>b</sup> ( $\mu$ m)
Clock hour 6	133.5	4.93	5.21	13.80	14.59
Clock hour 7	134.7	5	5.01	14.00	14.03
Clock hour 8	66.1	3	3	8.40	8.40
Clock hour 9	59.0	1.71	1.78	4.79	4.98
Clock hour 10	76.3	3.53	3.53	9.88	9.88
Clock hour 11	125.2	4.75	4.77	13.30	13.36
Clock hour 12	121.6	6.43	6.51	18.00	18.23

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## GC-IPL Reproducibility

	Repeatability		Reproducibility	
	Repeatability SD	Repeatability Limit <sup>a</sup>	Reproducibility SD	Reproducibility Limit <sup>b</sup>
<b>GCA Parameters (µm)</b>				
Average GCL + IPL Thickness	0.5839	1.6348	0.7479	2.0942
Minimum GCL + IPL Thickness	2.8630	8.0165	2.8935	8.1018
Temporal-Superior GCL + IPL Thickness	0.8394	2.3502	0.9496	2.6590
Superior GCL + IPL Thickness	0.9115	2.5522	1.0723	3.0024
Nasal-Superior GCL + IPL Thickness	0.9198	2.5753	1.0412	2.9154
Nasal-Inferior GCL + IPL Thickness	1.6735	4.6857	1.7330	4.8525
Inferior GCL + IPL Thickness	0.9962	2.7894	1.1907	3.3339
Temporal-Inferior GCL + IPL Thickness	0.8196	2.2948	0.9177	2.5696

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## What is significant change?

- Global/Average RNFL 4-5µm<sup>1</sup>
- Inf/Sup RNFL Sectors=9-15µm<sup>2,3</sup>
- RNFL Clock hrs (Cirrus)=5-18µm<sup>4</sup>
- Inferior/Superior regions more sensitive/greater variability
- Average GC IPL=2-3µm<sup>5</sup>
- Average minGC IPL=7-8µm<sup>5</sup>
- Change MUST BE REPRODUCIBLE

1) Mwanza JC, et al. *IOVS*. 2015;56(11):6344-6351. 2) Tan BB, et al. *J Glaucoma*. 2012;21:266-273  
 3) Toscano DA, et al. *Arq Bras Oftalmol*. 2012, 75(5):320-3 4) Zeiss Cirrus HD-OCT User Manual 2017<sup>142</sup>  
 5) Kim KE, et al. *IOVS*. 2015;56:4857-4864

142

## What is 5µm worth?

- Loss of 70,000 axons if axon=1µm diameter
- 141,500 axons if axon=0.7 (Fortune)
- Baseline 848,827±167,928 in progressors (Medeiros)
- Baseline 1,026,569±158,081 in nonprogressors (Medeiros)
- 7500 axons/yr over age 50 normal (Quigley)
- ~19,000 per/yr in progressors, 8,800 per/yr in non progressors
- Every 10,000 cells/yr faster =2.7x risk of progression

*IOVS* 2013 Jun;54(6):4174-4183

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## Age Related Attrition

- Mean loss of Global Cp-RNFL  
-0.26—0.92µm/yr<sup>1,2,6</sup>
- Mean loss of Macular Thickness -0.42µm/yr<sup>1</sup>
- ~1.5-2µm per decade<sup>3,4</sup>
- 7500 axons/yr over age 50 ~0.75%/yr<sup>5</sup>

1) Sung KR, Wollstein G, et al. *Ophthalmology*. 2009;116:1119-1124.  
 2) Leung CK, et al. *Ophthalmology*. 2012;119:731-7  
 3) Alsalil, T et al. *J Glaucoma*. 2012  
 4) Budenz DL, et al. *Ophthalmology*. 2007 Jun; 114(6): 1046-52  
 5) Quigley HA, et al. *Am J Ophthalmol* 1989;107:453-64  
 6) Wu Z, et al. *Am J Ophthalmol* 2017

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## Rates of Progression

Age-related	Slow	Moderate	Fast
-0.54µm/year	<-1µm/year	Between -1 and -2µm/year	Between -2 and -4µm/year
-0.06dB/year	-0.5-1dB/year	-1-1.5dB/year	-1.5-2dB/year

Cottrill, Maxey, Rixon. *RevOptom* July 2023

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## Confirm!!! before Initiating or Reinforcing

- Up to 56% of abnormal scans were not abnormal on F/U
- Consider test-retest variability
- Minimally 2 consecutive follow-up exams
- Trend analysis performs better than event analysis
- May take 4.5-4.8yrs to exceed test-retest if only 1 test per year

Yu M, et al. *IOVS* 2011

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## Performance of the Rule of 5 for Detecting Glaucoma Progression between Visits with OCT

### Comparing the Rule of 5 to Trend-based Analysis for Detecting Glaucoma Progression on OCT

**Results:** 5-µm or more eyes were progression by cumulative that only 15

**Conclusions:** Trend-based analysis was superior to the simple rule of 5 for identifying progression in glaucoma eyes and should be preferred as a method for longitudinal assessment of global SD-OCT RNFL change over time. *Ophthalmology* Glaucoma 2020;3:414-420 © 2020 by the American Academy of Ophthalmology

based on glaucoma true progression (1%). The suggesting its is not proportion of false-positive results over time, which could lead to unnecessary interventions in patients without glaucoma.

**Results:** After 5 years, the simple rule of 5 identified 37.5% of eyes as progressing at a specificity of 81.1%. At the same specificity, the hit rate for trend-based analysis was significantly greater than that of the rule of 5 (62.9% vs. 37.5%;  $P < 0.001$ ). If the rule of 5 was required to be repeatable on a consecutive test, specificity improved to 93.4%, but hit rate decreased to 21.0%. At this higher specificity, trend-based analysis still had a significantly greater hit rate than the rule of 5 (47.4% vs. 21.0%, respectively;  $P < 0.001$ ).

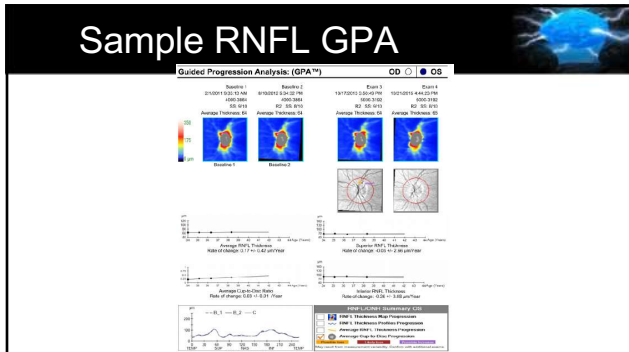
147

## GPA

- Provides Event and Trend analysis
- Each "event" is compared to baseline and flagged on the RNFL thickness map
  - Yellow "possible loss"
  - Red "likely loss"
  - Lavender "Possible increase"
- If events show repeatable statistical change over baseline the likelihood description escalates
- Trend can analyze from 3 to 8 exams

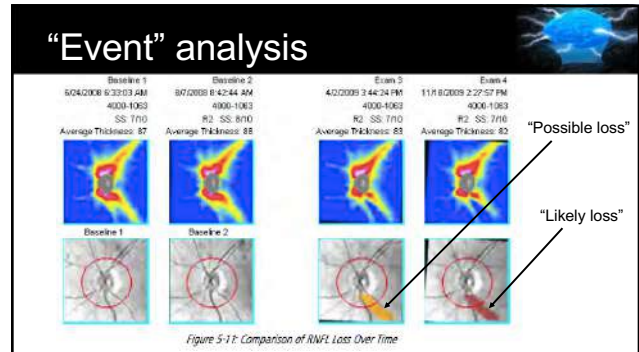
148

## Sample RNFL GPA



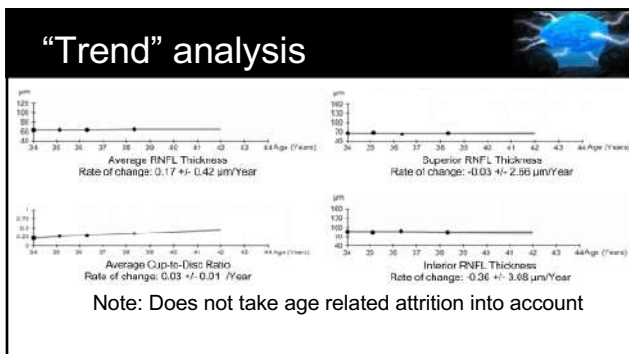
149

## "Event" analysis



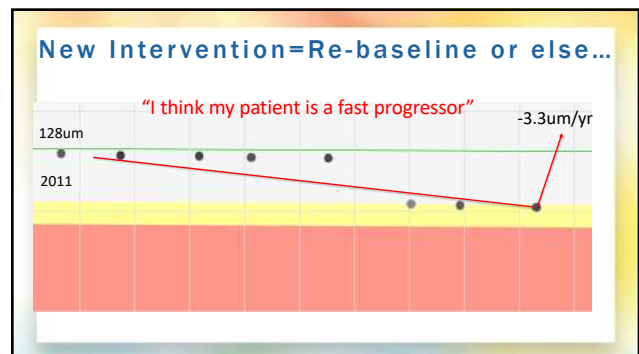
150

## "Trend" analysis



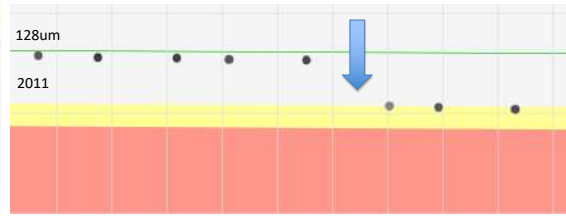
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## New Intervention=Re-baseline or else...



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You're looking at this all wrong.....  
When did we start treatment????



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Perspective/Vantage Point Matters



No Re-baseline=No Perspective

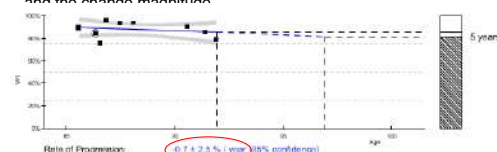
154

## Visual Fields and Progression

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## Trend Analysis

- Provides evidence that there is change and estimates its rate
- Presumed to be directly related to the underlying damage or disease mechanism
- The significance is determined by the variability of the measurement and the change magnitude



- 1) WGA Consensus Series 8: Progression of Glaucoma. 2011
- 2) Hu R, Racette L, Chen KS, Johnson CA. *Surv Ophthalmol*. 2020 Nov-Dec;65(6):639-661.

156

## Local Variability

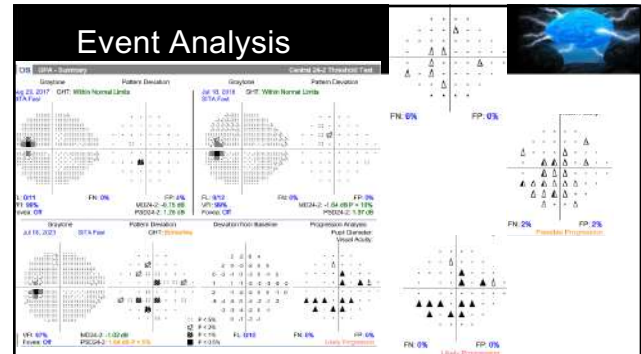


- Variability (Overall and local) increases as level of VF sensitivity decreases
- Test-Retest variability is  $\pm 3\text{dB}$  in loci with threshold of 30dB
- Test-Retest variability  $\pm 15\text{dB}$  in loci with baseline threshold of 10dB

1) Artes PH, Hutchinson DM, Nicolaie MT, et al. *Invest. Ophthalmol. Vis. Sci.* 2005;46(7):2451-2457  
 2) DeMoraes CG, et al. *Surv Ophthalmol.* 2016;61:597-615  
 3) DeMoraes CG, et al. *Prog Ret Eye Res.* 2017;56:107-147  
 4) Russell RA, Garway-Heath DF, Crabb DP. *Prog ONE.* 2013;8(12):e83595

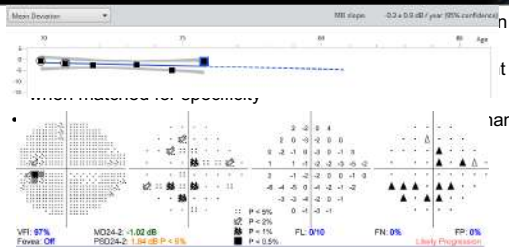
157

## Event Analysis



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## Trend Vs Event



1) Casas-Llera P, et al. *Br J Ophthalmol.* 2009 Dec;93(12):1576-9.  
 2) Zhichao Wu, Felipe A. Medeiros. *Trans. Vis. Sci. Tech.* 2018;7(4):20.  
 3) Hu R, Racette L, Chen KS, Johnson CA. *Surv Ophthalmol.* 2020 Nov-Dec;65(6):639-661

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## Clinical Judgment

- Clinician compare grayscale, dB series and pattern deviation across a series
- Viswanathan et al. (5 glaucoma experts) graded 27 VF series (19 VF per series) for progression<sup>1</sup>  
 $\kappa=0.32$
- Tanna et al. using 5 glaucoma specialists found  $\kappa=0.45$  but intra-observer agreement as high as 0.78<sup>2</sup>
- GPA did not improve inter-observer, but altered decisions on 11/100\*
- Lack of standardization, Not intra-observer variability may be the issue
- WGA rec for Us=Use the available software support!<sup>3</sup>

1) Viswanathan AC, Crabb DP, et al. *Br J Ophthalmol.* 2003 Jun;87(6):726-30. 2) Tanna A, et al. *Ophthalmology.* 2012 Mar;119(3):468-73.  
 3) WGA Consensus Series 8. Progression of Glaucoma. 2011

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## Rates of Visual Field Progression\*

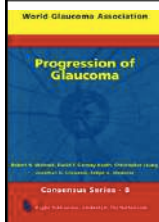
	Age Related	Slow	Moderate	Fast	Catastrophic
SAP in MDs 24-2	-0.06dB/yr	-0.3-1.0dB/yr	-1.0-1.5dB/yr	-1.5-2.0dB/yr	≥ -2.0dB/yr

- 5-13% of patients under routine care as reported to be Fast Progressors<sup>4</sup>

1. Jammal AA, Thompson AC, Mariotti EB, et al. *Am J Ophthalmol*. 2021;222:238-247  
 2. Spry PG, Johnson CA. *Optom Vis Sci*. 2001; 78(6):436-41  
 3. Saunders L, Medeiros FA, Weinreb RN, Zangwill LM. *Expert Review of Ophthalmology*. 2016;11(3):227-234  
 4. Jackson AB, Martin KB, Coote MA et al. *Ophthalmology*. 2023 May;130(5):462-468  
 5. Chauhan BC, et al. *IOV* 2014. 55:4135-4143

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## VF Recommendations-How many?



### Foundation

- 2 reliable fields in the first 6mo
- At least 2 VF in the next 18mo if low risk of disability
- 4 in the next 18mo if high risk of disability<sup>1,2</sup>

### Framing

- Employ an "Adaptive" test strategy
    - Adapt testing based on the context of the patient i.e. test intervals shortened if progression suspected
- SO.....2 VF per year post progression should be the minimum (After new baseline)

1) WGA Consensus Series 8: Progression of Glaucoma. 2011 2) Wu Z et al. *Ophthalmology* 2017;124:786-792  
 3) Chauhan B, et al. *Br J Ophthalmol*. 2008;92:569-573 4) Melchior B, et al. *J Glaucoma*. 2023 Sep 1;32(9):721-724  
 5) Sabouri S, et al. *J Glaucoma*. 2023 May 1;32(5):355-360

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## How Many Fields do we need?

(a) Total MD change (dB)	Progression rate (dB/year)		
	2 years	3 years	5 years
-1.0	-0.5	-0.3	-0.2
-2.0	-1.0	-0.7	-0.4
-4.0	-2.0	-1.3	-0.8

(b) Total MD change (dB)	Annual examinations		
	2 years	3 years	5 years
-1.0	7	6	4
-2.0	5	4	3
-4.0	3	3	2

Chauhan B, et al. *Br J Ophthalmol*. 2008;92:569-573

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## Contingent on Variability

(a) 1 examination/year	Variability		
Progression rate (dB/year)	Low	Moderate	High
-0.25	13	19	30
-0.5	9	13	19
-1.0	6	9	13
-2.0	5	6	9 yrs

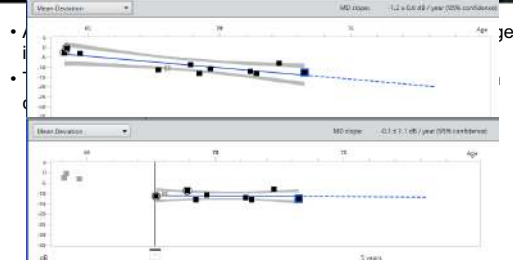
(b) 2 examinations/year	Variability		
Progression rate (dB/year)	Low	Moderate	High
-0.25	6.5	8.5	15
-0.5	4.5	6.5	8.5
-1.0	3	4.5	6.5
-2.0	2.5	3	4.5 yrs

- Newly diagnosed COAG patients receive <3 VFs in the first 2yrs
- Then average 0.7 VF over minimum 2yrs of f/u (Glc Specialist Offices)

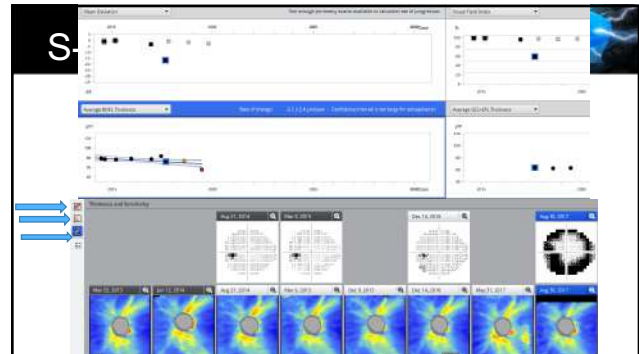
1) Chauhan B, et al. *Br J Ophthalmol*. 2008;92:569-573 2) Fung SSM, et al. *Br J Ophthalmol* 2013;97:843-847

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## Re-baselining provides perspective



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## Progression Pearls

- There is a lack of linearity in progression<sup>1</sup>
- Risk of progression in the real world is much greater than in RCTs<sup>2</sup>
- No consensus on average length of time required to prove intervention is working (12mo?)
- Confirmation of progression/stability requires vigilance
- 2 Baseline VFs, followed by 2-4 in the next 18 mo is WGA recommendation<sup>4</sup>
- 2 OCT/OCT scans per year are likely sufficient to detect progression<sup>5</sup>
- A target rate of progression may be >>> target IOP<sup>3</sup>

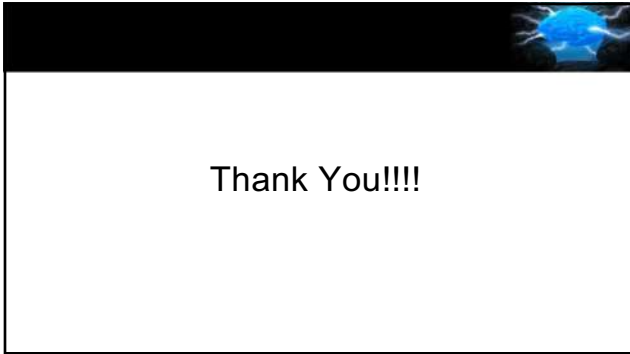
1) Heijl A, et al. *Acta Ophthalmol.* 2013;91:406-412. 2) Peters, Bengtsson, Heijl *Am J Ophthalmol* 2013; 156:724-730  
3) Melchior B, et al. *Br J Ophthalmol.* 2022;106:229-233 4) Weinreb R et al. World Glaucoma Association Consensus Series-8  
Progression of Glaucoma 2011 p.5 5) Mahmoudinezhad G, et al. *AJO.* Online Sept 2022

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## Resources

- <https://hoodvisualscience.psychology.columbia.edu/videos>

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