PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Rick Trevino, OD, FAAO

Indiana University School of Optometry

PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

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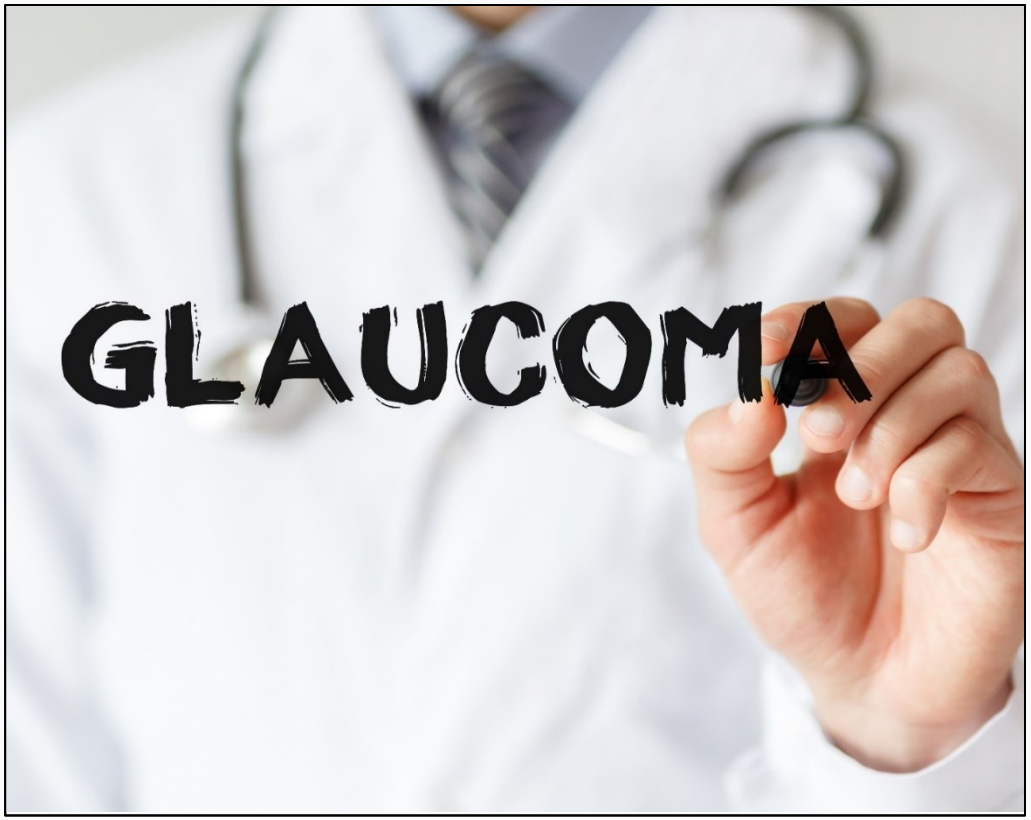
- **Disclosures**
  - None



PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Clinical Decisions in Glaucoma

SECOND EDITION

https://go.iu.edu/4QsN

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PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Welcome to the Iowa Glaucoma Curriculum

About the Iowa Glaucoma Curriculum

This is a teaching site for residents and others interested in learning about glaucoma.

It breaks glaucoma into fifty bite-sized lectures that average 14 minutes in length (range 4 to 37 minutes). In total the curriculum is just under 12 hours long.

It is highly visual with >900 images and >90 movie clips.

Taking care of glaucoma can be very hard, but I am hoping that I have made learning about this family of diseases somewhat easier.

READ MORE

iowaglaucoma.org

PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Factors Affecting OCT Detection of Glaucoma

Differential Diagnosis of Normal Tension Glaucoma

False Positive Diagnosis of Glaucoma

PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Factors Affecting OCT Detection of Glaucoma

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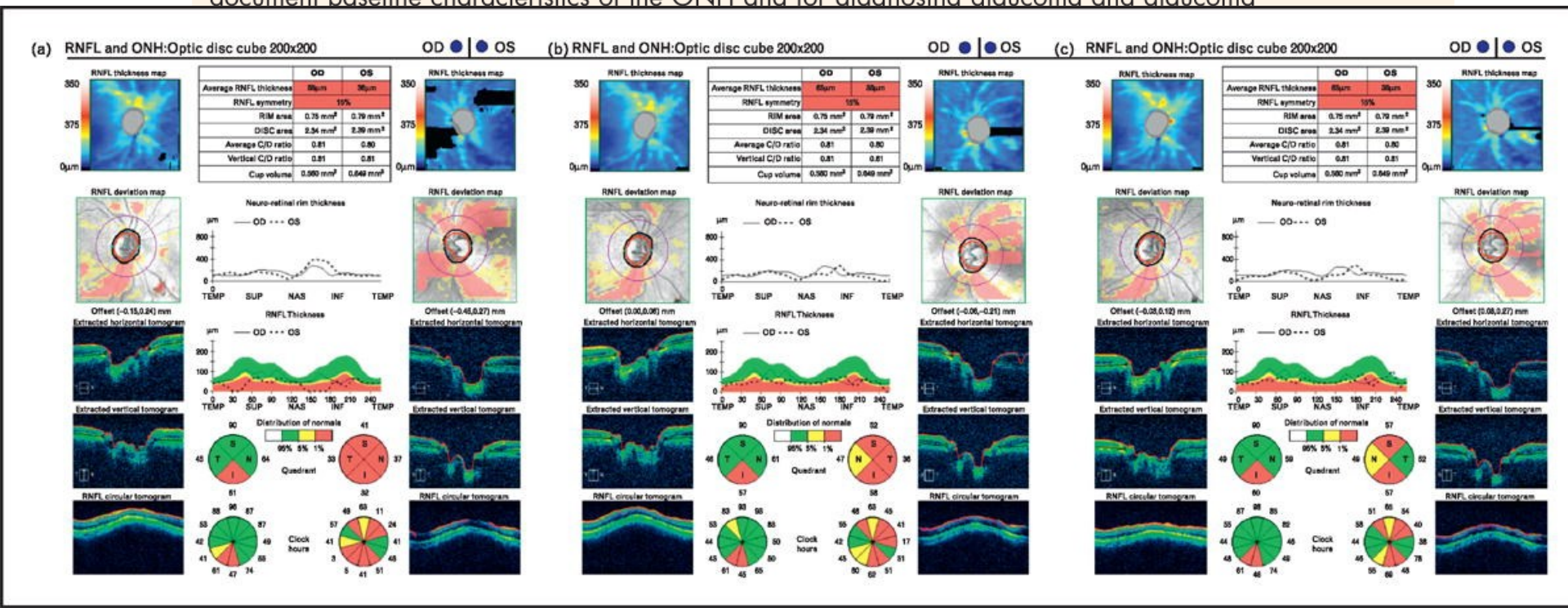
Glaucoma versus red disease: imaging and glaucoma diagnosis

Gabriel T. Chong and Richard K. Lee

PMID: 22262083

Purpose of review

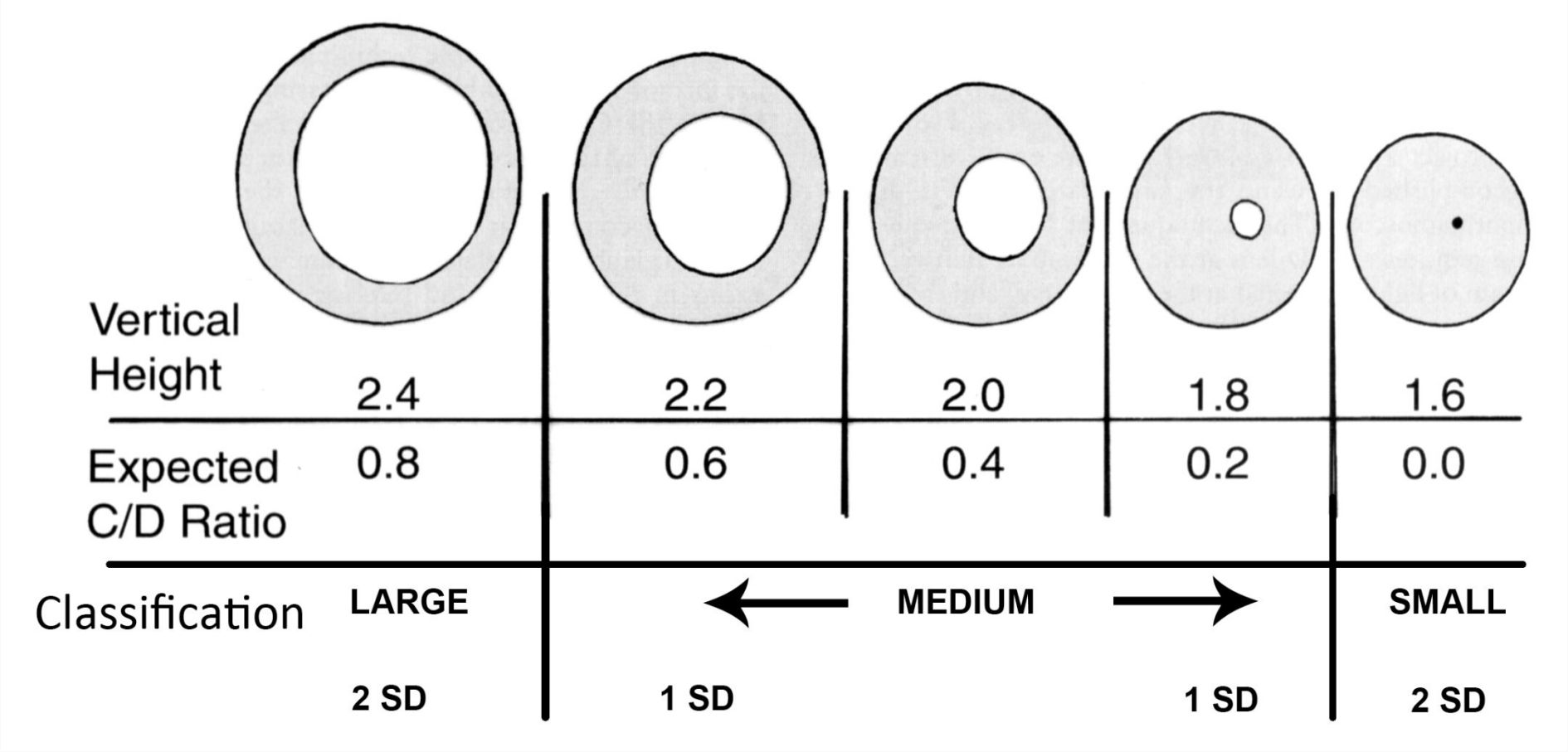
The use of ophthalmic imaging for documentation and diagnosis of ocular disease is rising dramatically. Optical coherence tomography (OCT), confocal scanning laser tomography (CSLT), scanning laser polarimetry (SLP) and photographic imaging of the optic nerve head (ONH) are currently used to document baseline characteristics of the ONH and for diagnosing glaucoma and glaucoma



PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Evaluation of the ONH in Glaucoma

- Physiologic variation in optic disc size
- Cup to disc ratio
- Loss of rim tissue
- Disc hemorrhage
- Peripapillary atrophy
- Retinal nerve fiber layer atrophy

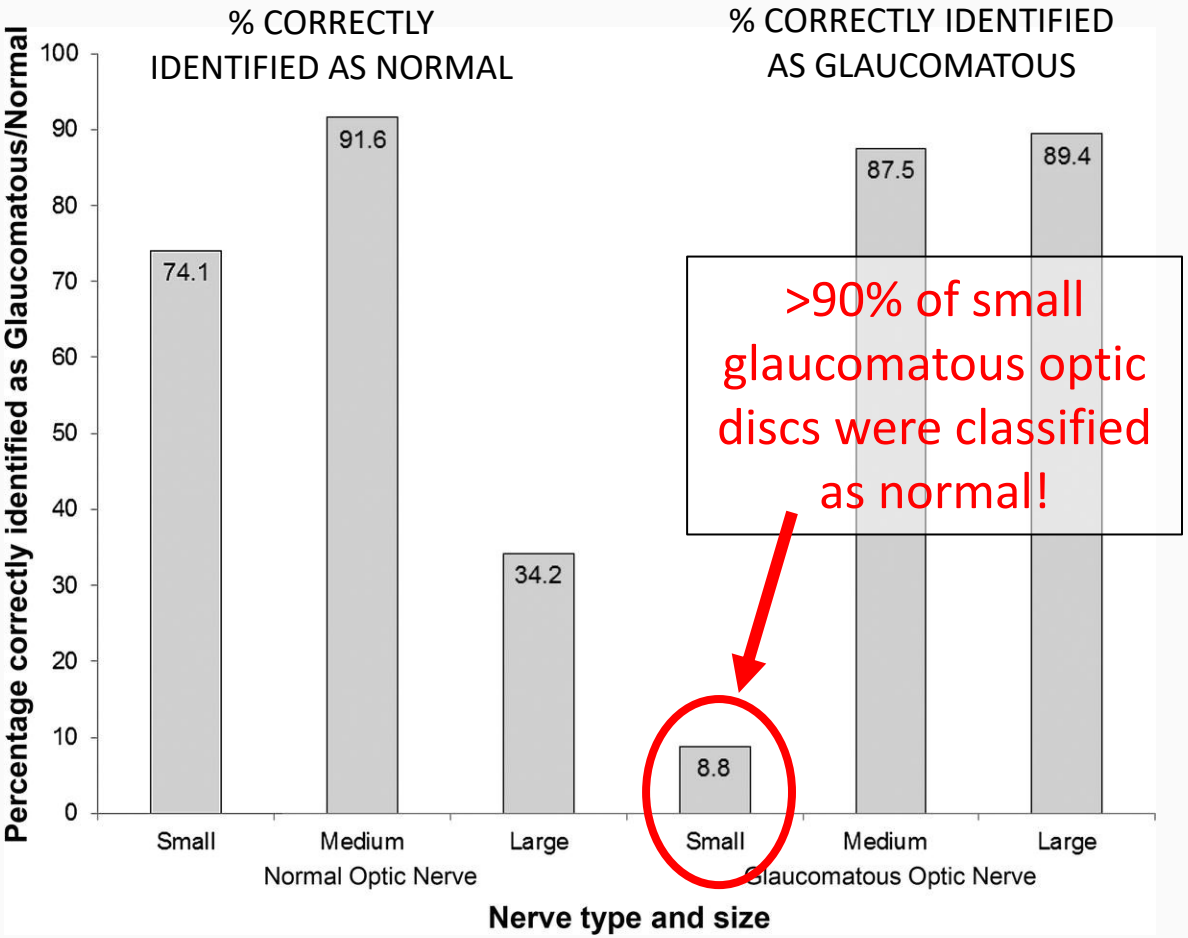


Assessment of disc size is the first step in assessment of optic cup size.

Because the axonal tissue entering the optic disc varies much less than the size of the optic disc itself, the optic cup in the center of the disc can vary a greatly without necessarily reflecting any underlying deficit in the number of ganglion cell axons

Numerous studies have documented the **difficulty of correctly identifying glaucomatous damage in small optic discs**

Nixon (2017): Doctors examined stereophotos of optic nerve heads and were asked to classify them as normal or glaucomatous



Percentage of images where nerve type was correctly identified, by nerve type and size. Size was assessed by OCT (<1.63 mm^2 = small; >1.97 mm^2 = large) (Nixon, 2017)

PMID: 28538334

Cirrus ONH Parameters

	OD	OS
Average RNFL Thickness	73 µm	61 µm
RNFL Symmetry	55%	
Rim Area	1.12 mm^2	0.72 mm^2
Disc Area	1.58 mm^2	1.72 mm^2
Average C/D Ratio	0.53	0.75
Vertical C/D Ratio	0.49	0.77
Cup Volume	0.036 mm^3	0.220 mm^3

Always gray b/c it's not compared to normals!

<1.75 mm^2 = sm

1.75-2.75mm^2 = medium

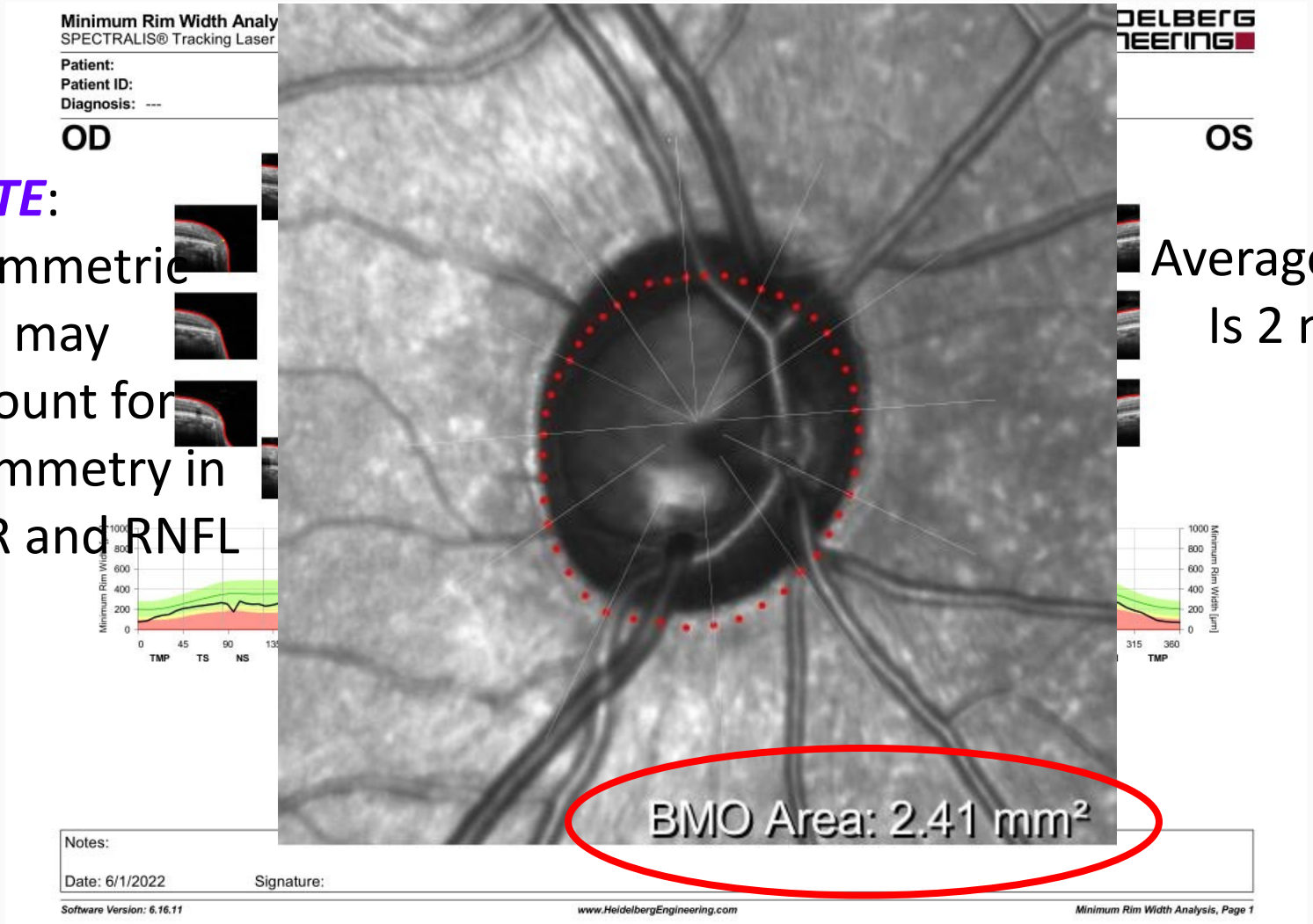
>2.75 mm^2 = lg

ONH morphology

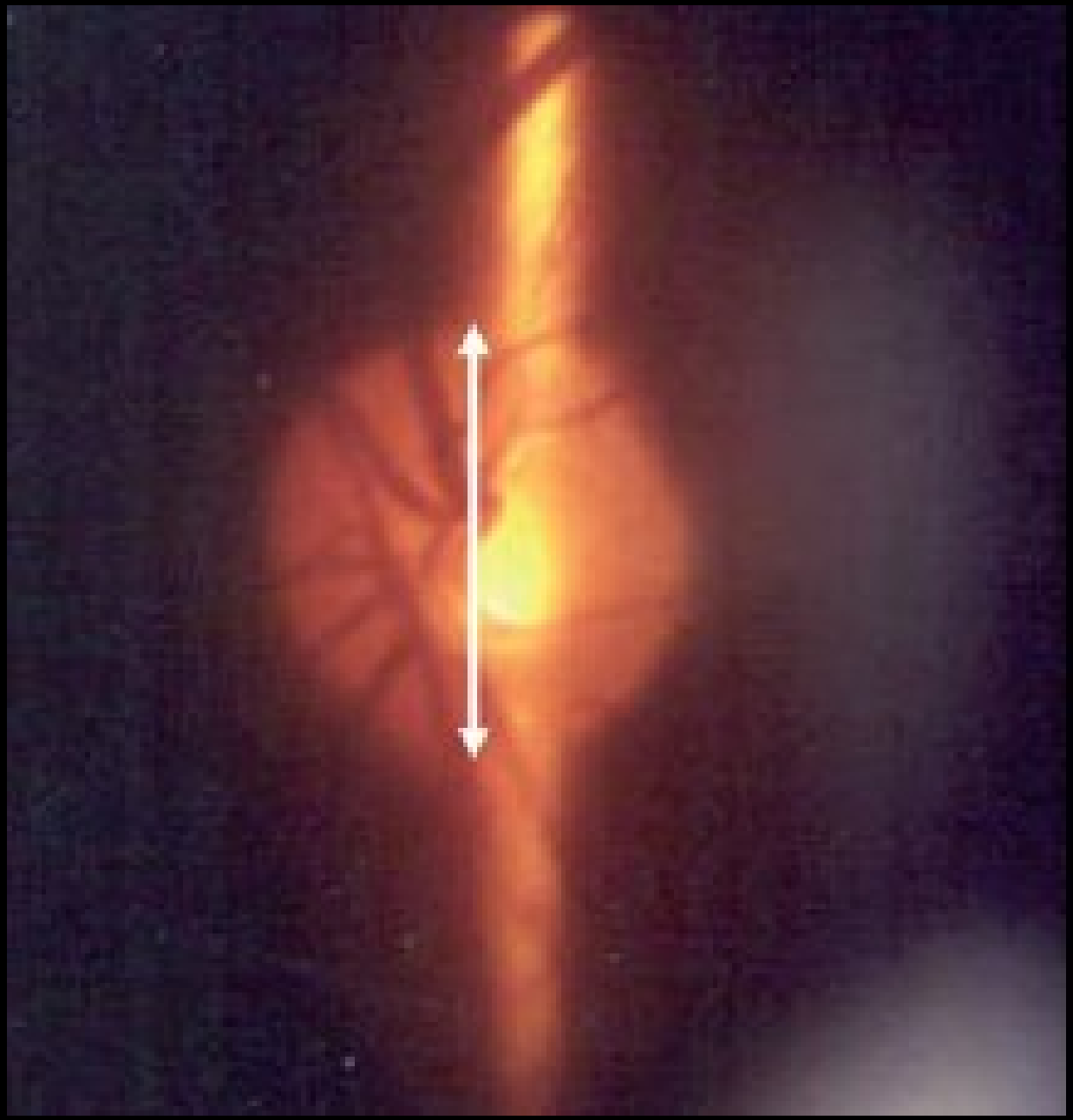
NOTE: Asymmetric size may account for asymmetry in CDR and RNFL

Heidelberg MRW Analysis

NOTE:
Asymmetric size may account for asymmetry in CDR and RNFL



Average BMO Is 2 mm^2

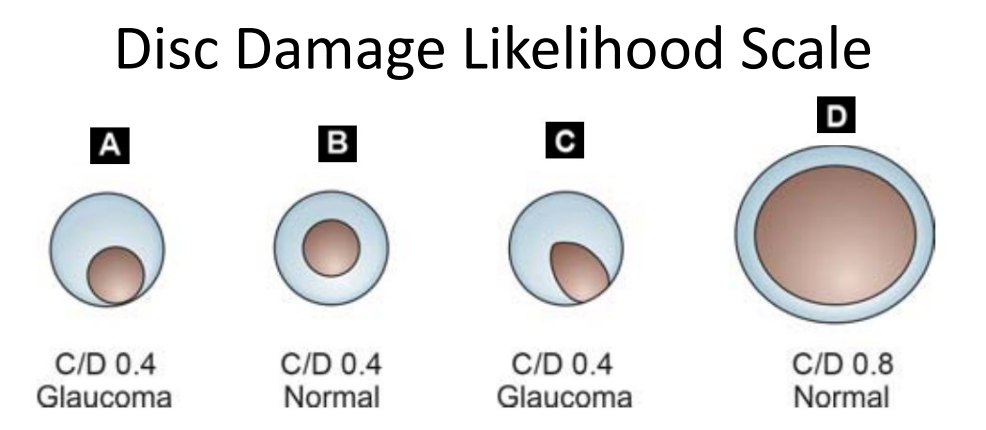


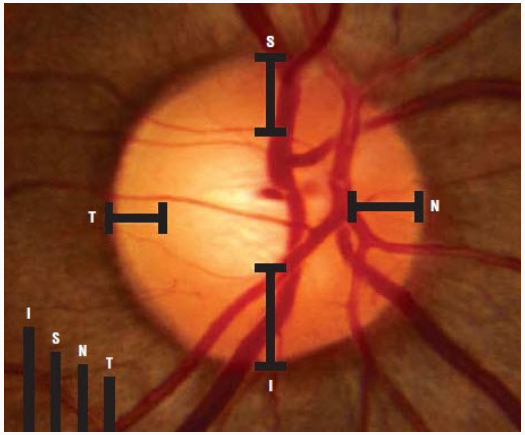
Adjust slit lamp beam height to match disc height to assess whether ONH is unusually large or small

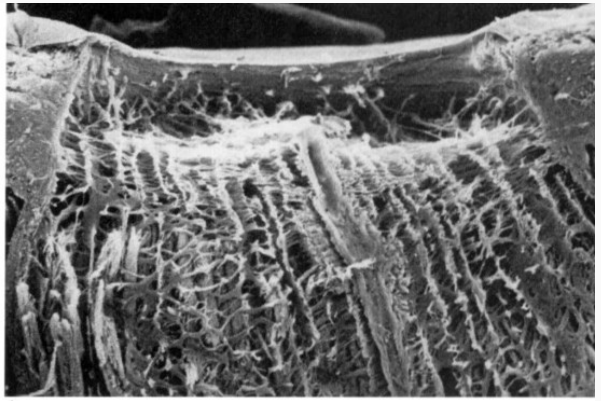
BEWARE SMALL ONH!

Use R/L asymmetry and ISNT rule violation to decide whether OCT is indicated

EVALUATION OF THE ONH IN GLAUCOMA



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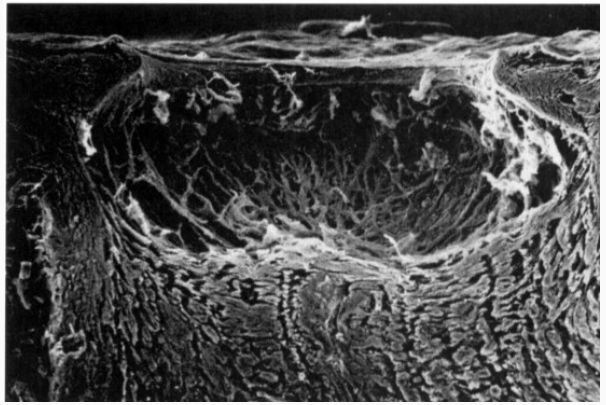


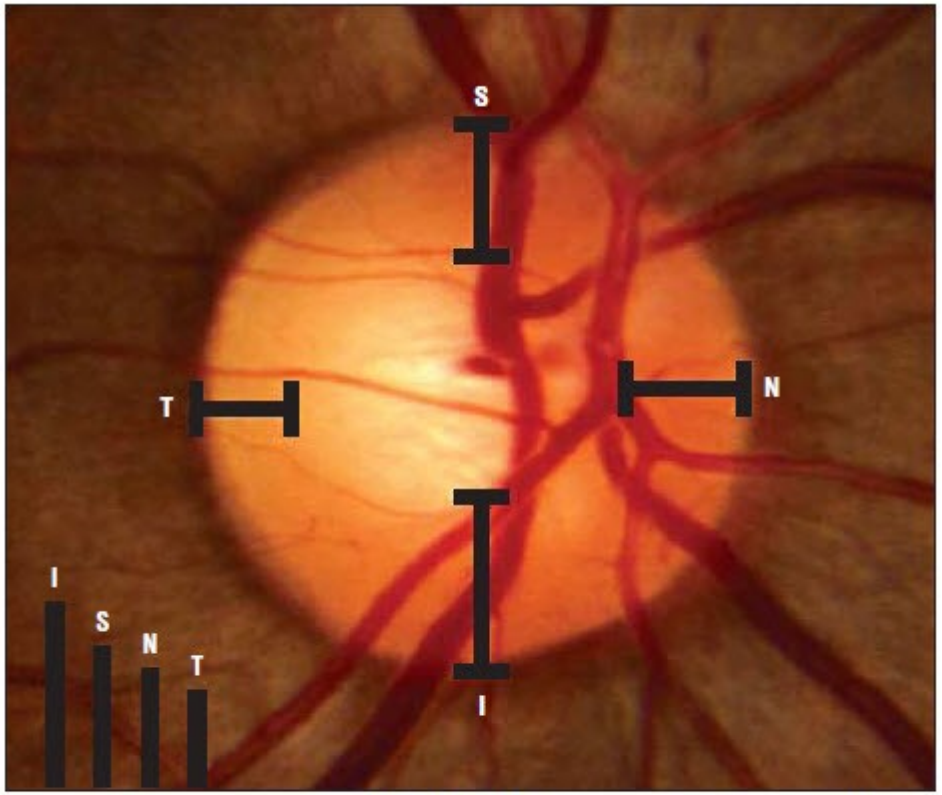


Figure. Clinical assessment of the ISNT rule for a normal optic nerve. The ISNT rule is that disc rim thickness shows a characteristic configuration of inferior (I) greater than or equal to superior (S) greater than or equal to nasal (N) greater than or equal to temporal (T) (or I≥S≥N≥T).

Violation of the ISNT rule

(Inf < Sup)

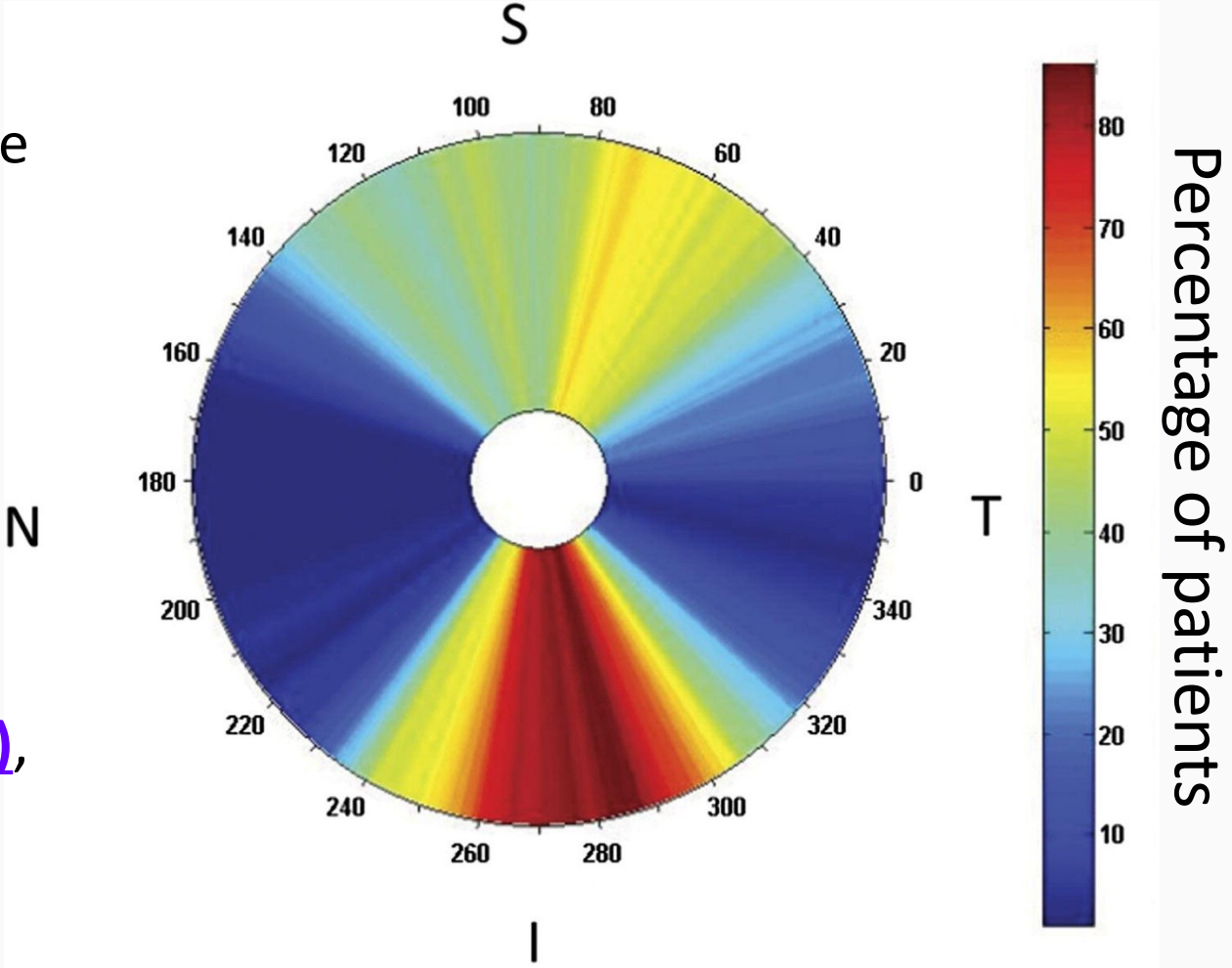
is a significant predictor of glaucoma

Inf ≥ Sup ≥ Nas ≥ Tem

EVALUATION OF THE ONH IN GLAUCOMA

Frequency distribution of the location of RNFL defects in glaucoma patients.

Most common: infero-temporal meridian (80.4%), superotemporal (54.2%)



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PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

- **OCT Detection of Glaucoma**
  - Retinal Nerve Fiber Layer (RNFL)
  - Optic Nerve Head (ONH) Topography
  - Macular Thickness
- **Factors Affecting OCT Detection of Glaucoma**
  - Disease severity
  - ONH size
  - Others

OCT Detection of Glaucoma

Method #1: Retinal Nerve Fiber Layer Thickness

- 3.4mm diameter **measurement circle**
  - Make sure disc is centered in measurement circle
- **Segmentation** of RNFL from other layers
  - **Accuracy dependent upon signal strength**
- Overall, quadrant, sector values
  - Avg and inferior most often affected in early glc
- Compared to age-related norms and fellow eye
  - Average thickness of fellow eyes should be within 10µm
  - **Difference < 5µm is noise** (stable vs change over time)

ONH OCT

The 4 Questions

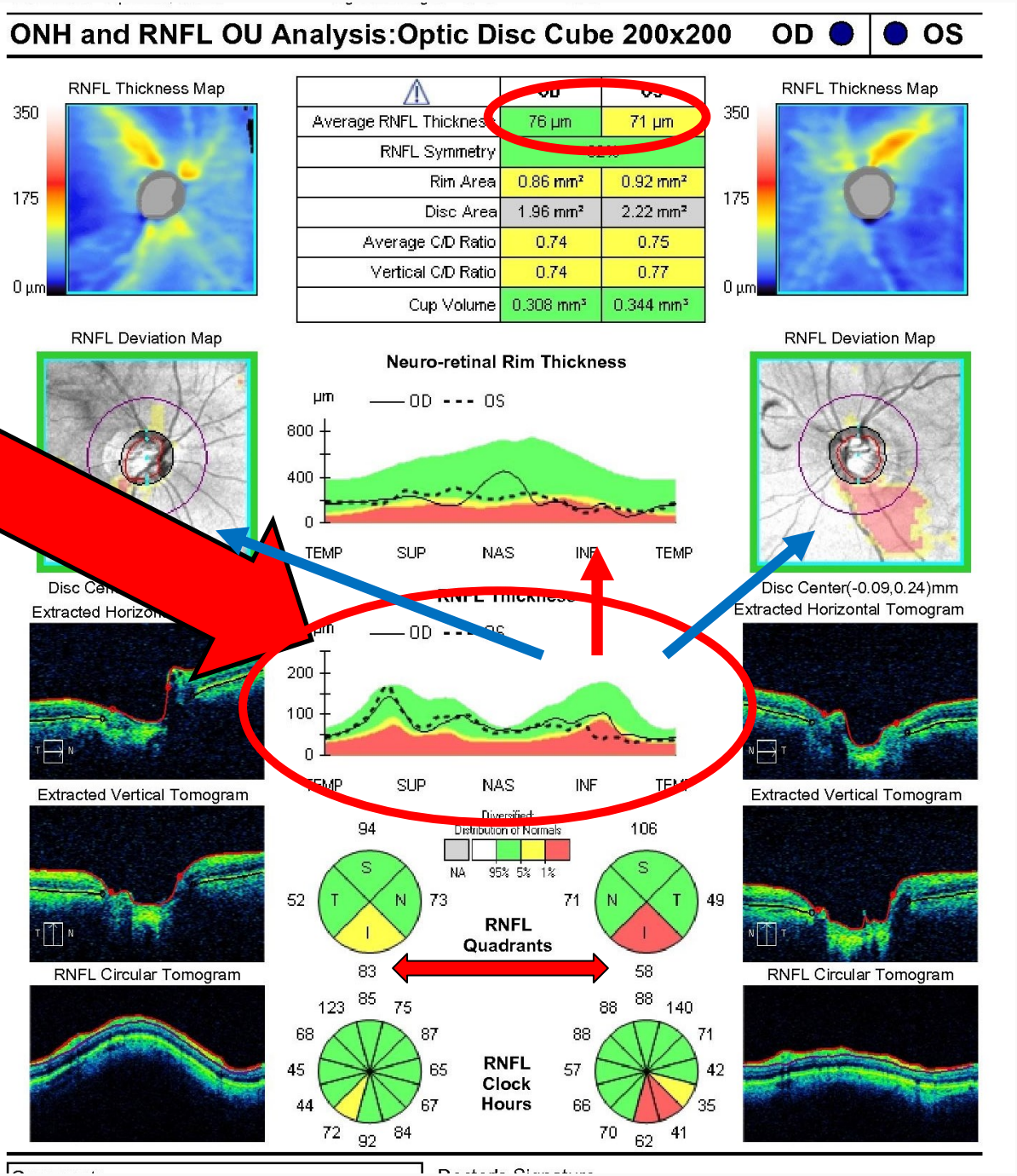
This is where most of the action is!

Is the superior (less common) or inferior (more common) hump depressed?

Is there RE/LE symmetry?

Is there evidence of rim loss corresponding to the RNFL loss?

Does the deviation map show evidence of a NFL defect?



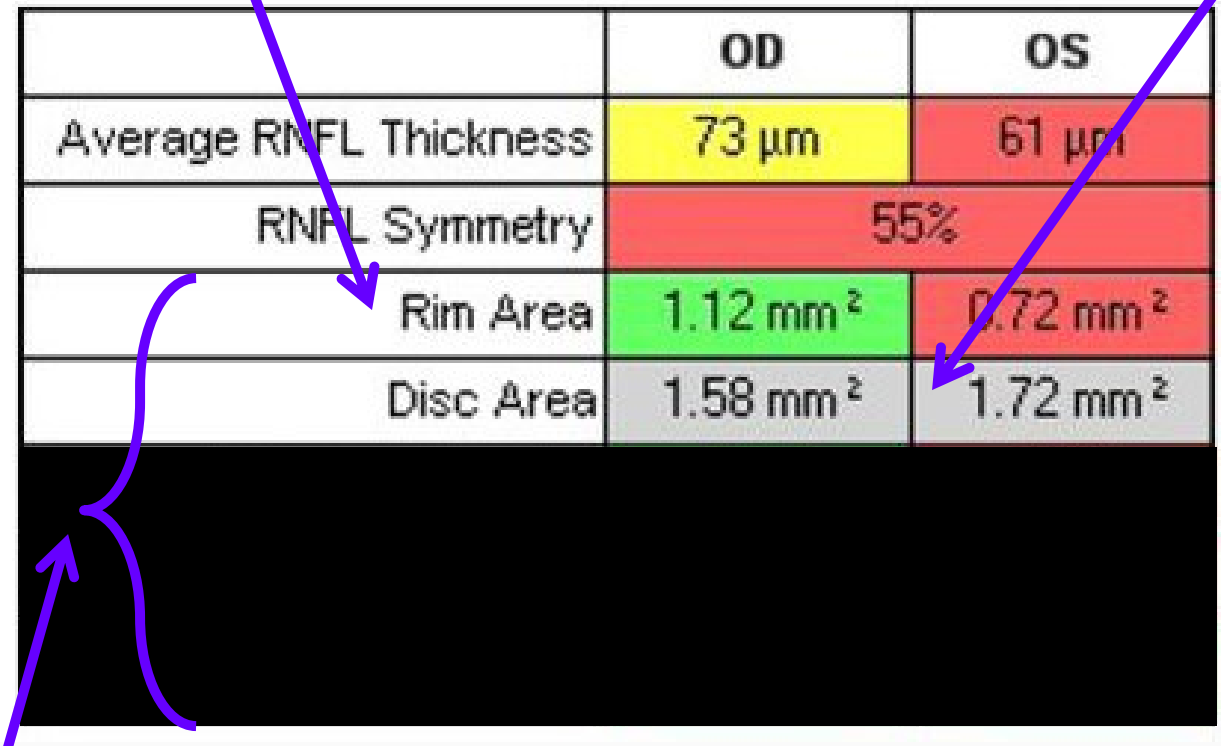
OCT Detection of Glaucoma

Method #2: Optic Disc Morphology

- Compare cup and rim parameters to normals
- Automated detection of disc & cup margins
- ONH margin defined as the termination of Bruch's
  - Analyzed at 255 points around the ONH circumference
  - The shortest perpendicular distance to ILM is the cup margin
- Posterior migration of the lamina

Cirrus ONH Parameters

Rim Area <1.0 mm^2 is *ALWAYS* suspicious



	OD	OS
Average RNFL Thickness	73 µm	61 µm
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Rim Area	1.12 mm^2	0.72 mm^2
Disc Area	1.58 mm^2	1.72 mm^2

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<1.75 mm^2 = sm

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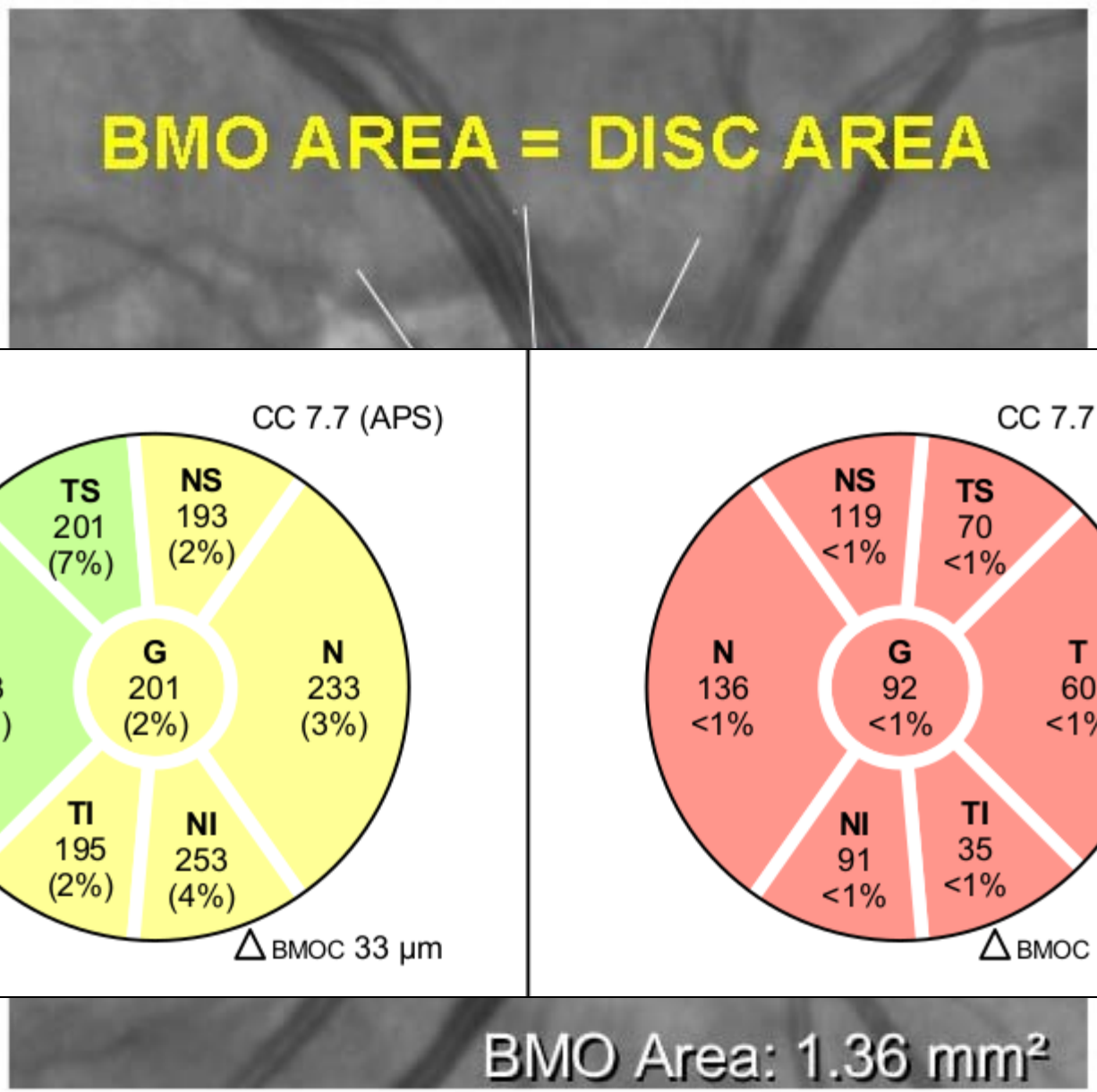
ONH morphology

NOTE: Asymmetric disc size may account for asymmetry in CDR and RNFL

H[illegible]'s


BMO AREA = DISC AREA
Minimum Rim W
SPECTRALIS® Tra
Patient:
Patient ID:
Diagnosis: ---
OD
OS
CC 7.7 (APS)
TS 201 (7%)
NS 193 (2%)
T 143 (5%)
G 201 (2%)
N 233 (3%)
TI 195 (2%)
NI 253 (4%)
ΔBMOC 33 µm
CC 7.7 (APS)
NS 119 <1%
TS 70 <1%
N 136 <1%
G 92 <1%
T 60 <1%
NI 91 <1%
TI 35 <1%
ΔBMOC 25 µm
BMO Area: 1.36 mm²

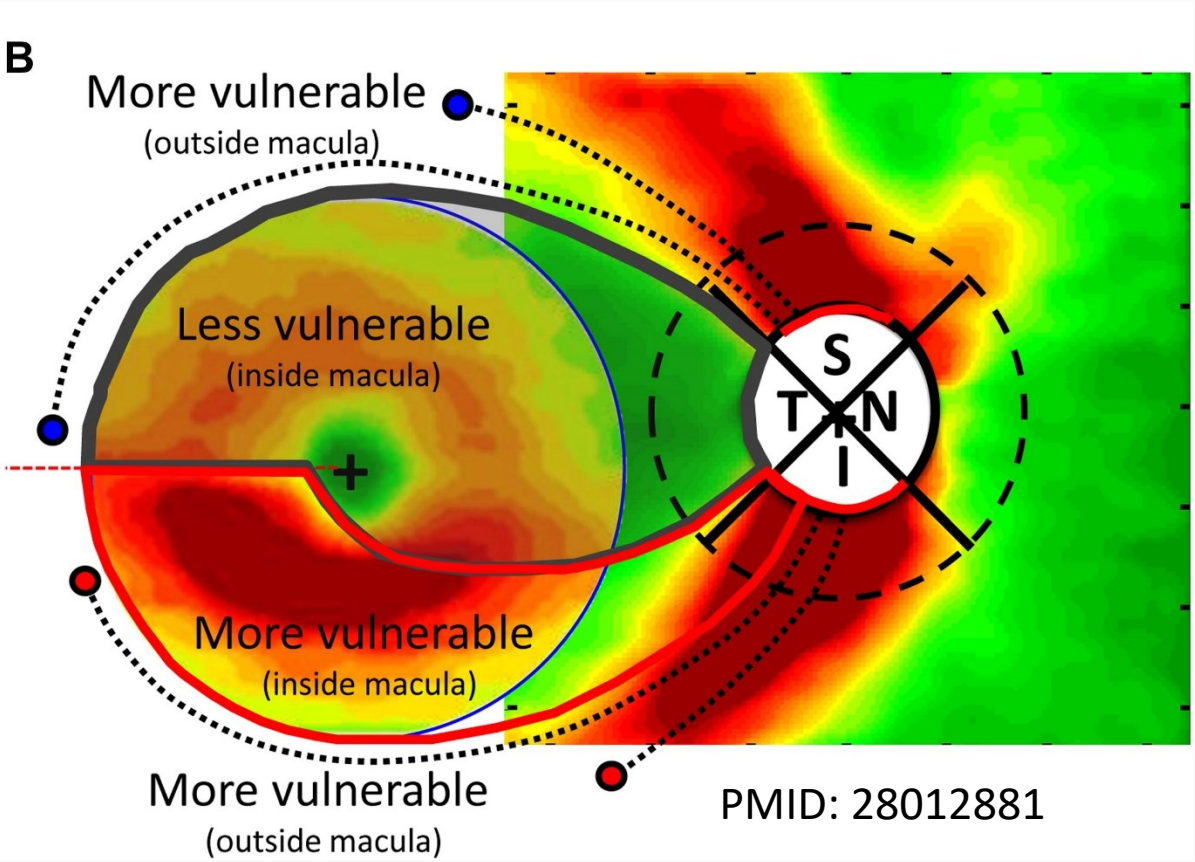
n

OCT Detection of Glaucoma

Method #3: Ganglion Cell Layer Thickness

- Death of ganglion cells leads to macular thinning
  - Localized &/or diffuse loss
  - Can be correlated with changes in RNFL and VF
- Ganglion Cell Complex (GCC)
  - Because it is technically difficult to segment the GCL from the IPL, all instruments include IPL and/or RNFL in thickness measurement
  - GCC = RNFL + Ganglion cells + Inner plexiform (RTVue)
  - NOTE: Cirrus does not include RNFL in its analysis

Because the fovea lies about 10 degrees below the ONH, **ganglion cells inferior and temporal to the fovea are preferentially damaged in glaucoma**



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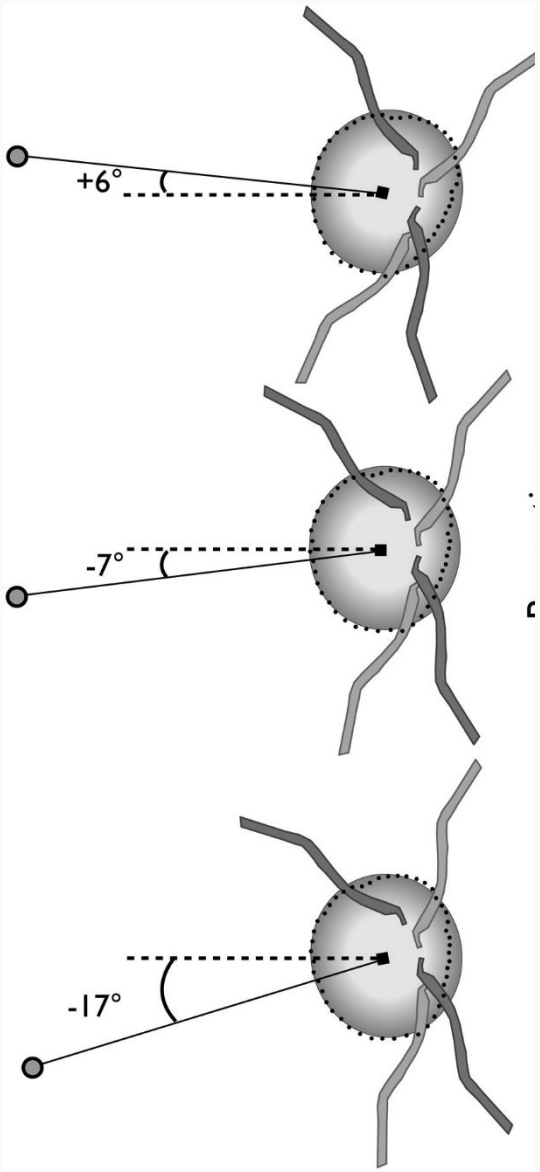
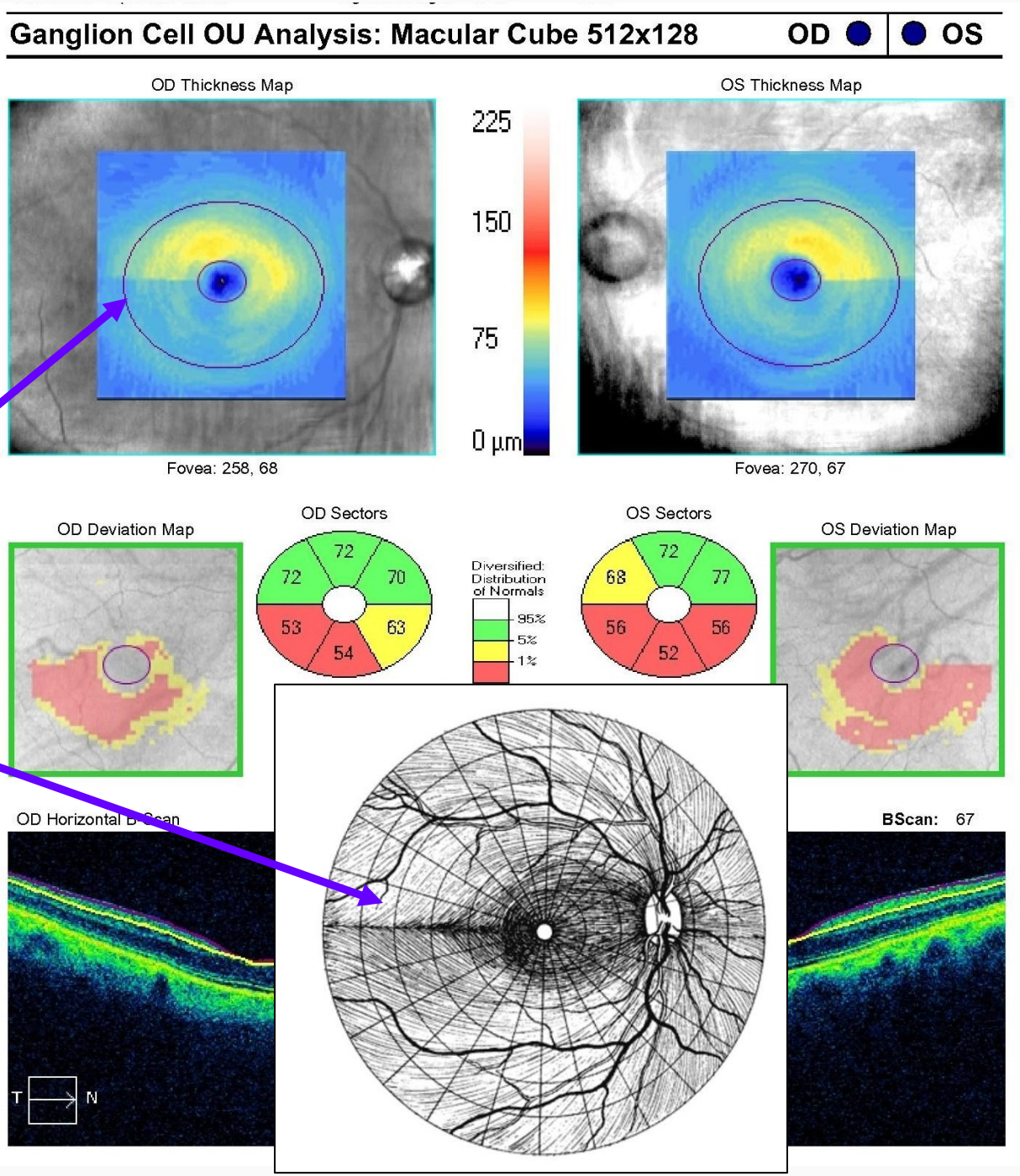


GCC Thickness Data Presentation

- Thickness map
- Sector thickness
- Deviation map
- Data table
- Tomograms

Look for temporal step defect in thickness map and sectors

Are the GCC findings consistent with the RNFL findings?



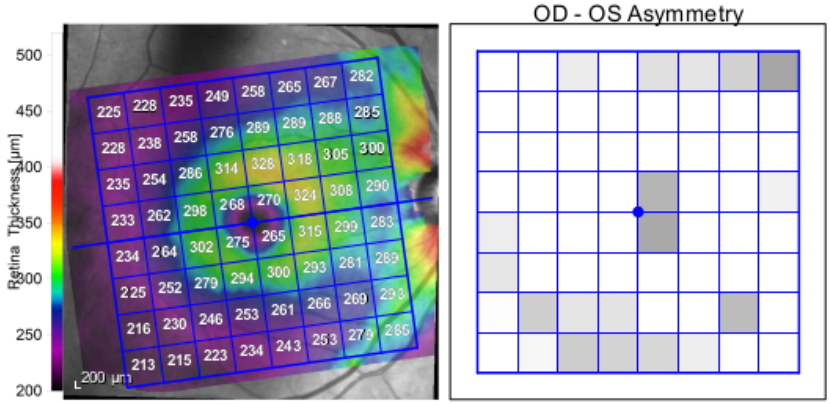
Right-Left Asymmetry

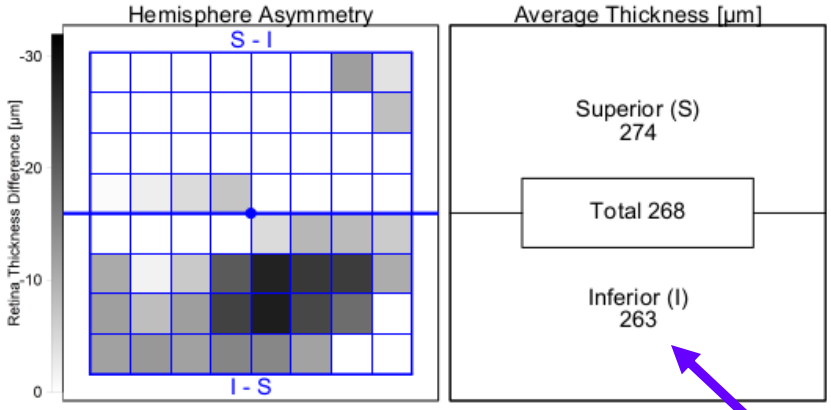
Asymmetry Analysis Single Exam Report OU
SPECTRALIS® Tracking Laser Tomography

HEIDELBERG ENGINEERING

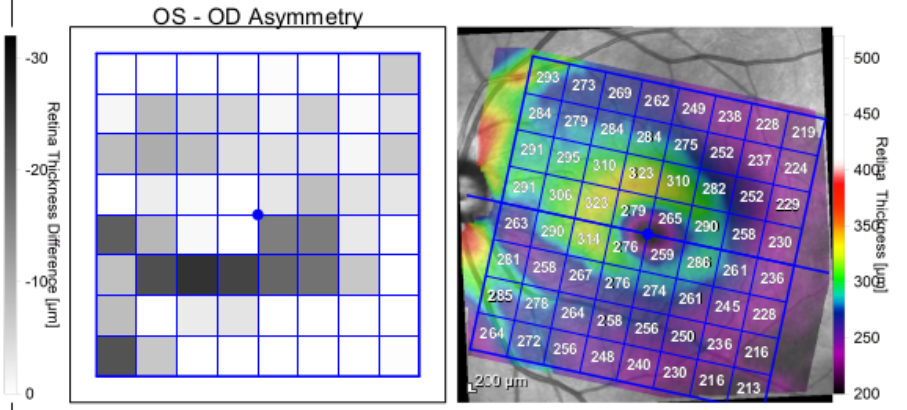
Patient:	Sherfield, Karen	**DOB:**	Sep/20/1955	**Sex:**	F
Patient ID:	67680	**Exam.:**	Sep/19/2022		
Diagnosis:	---	**Comment:**	---		

OD

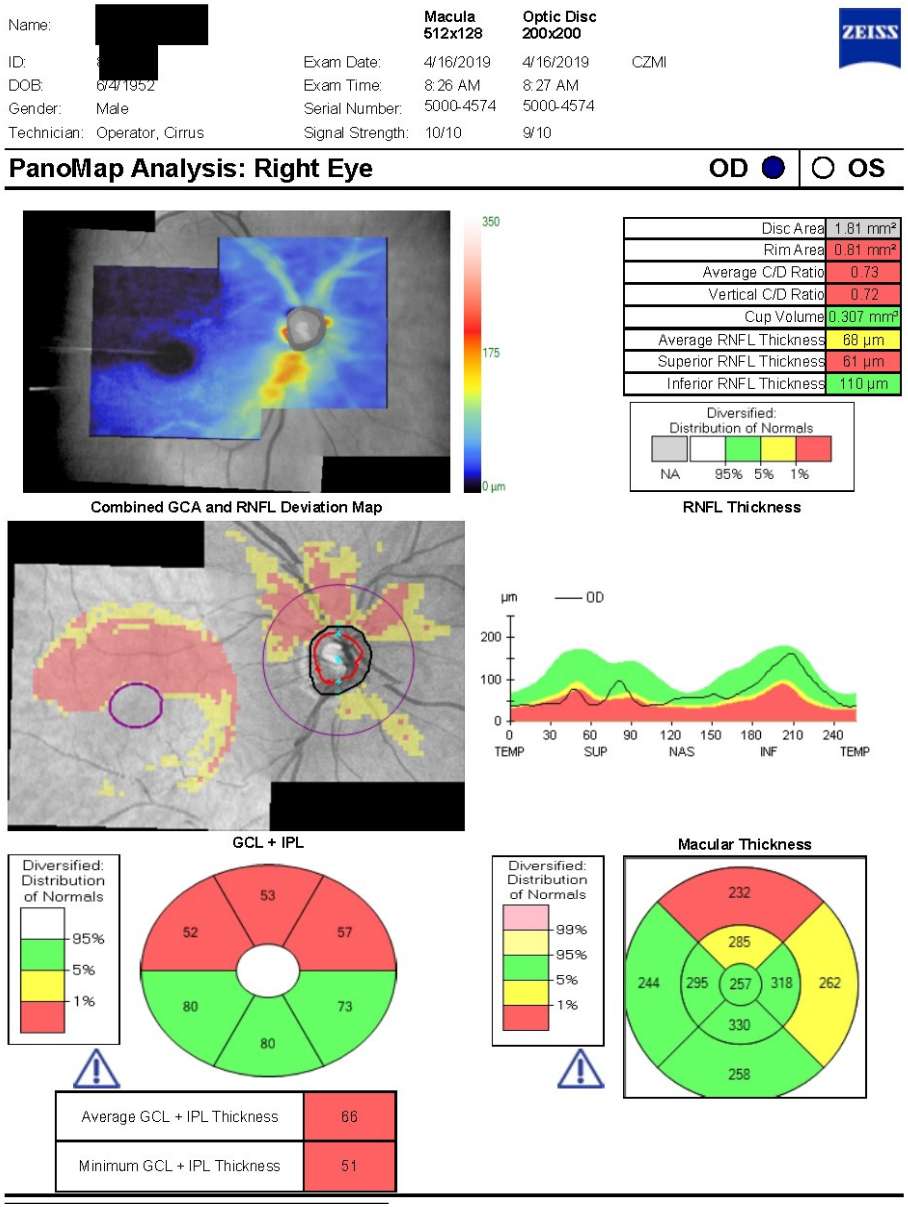


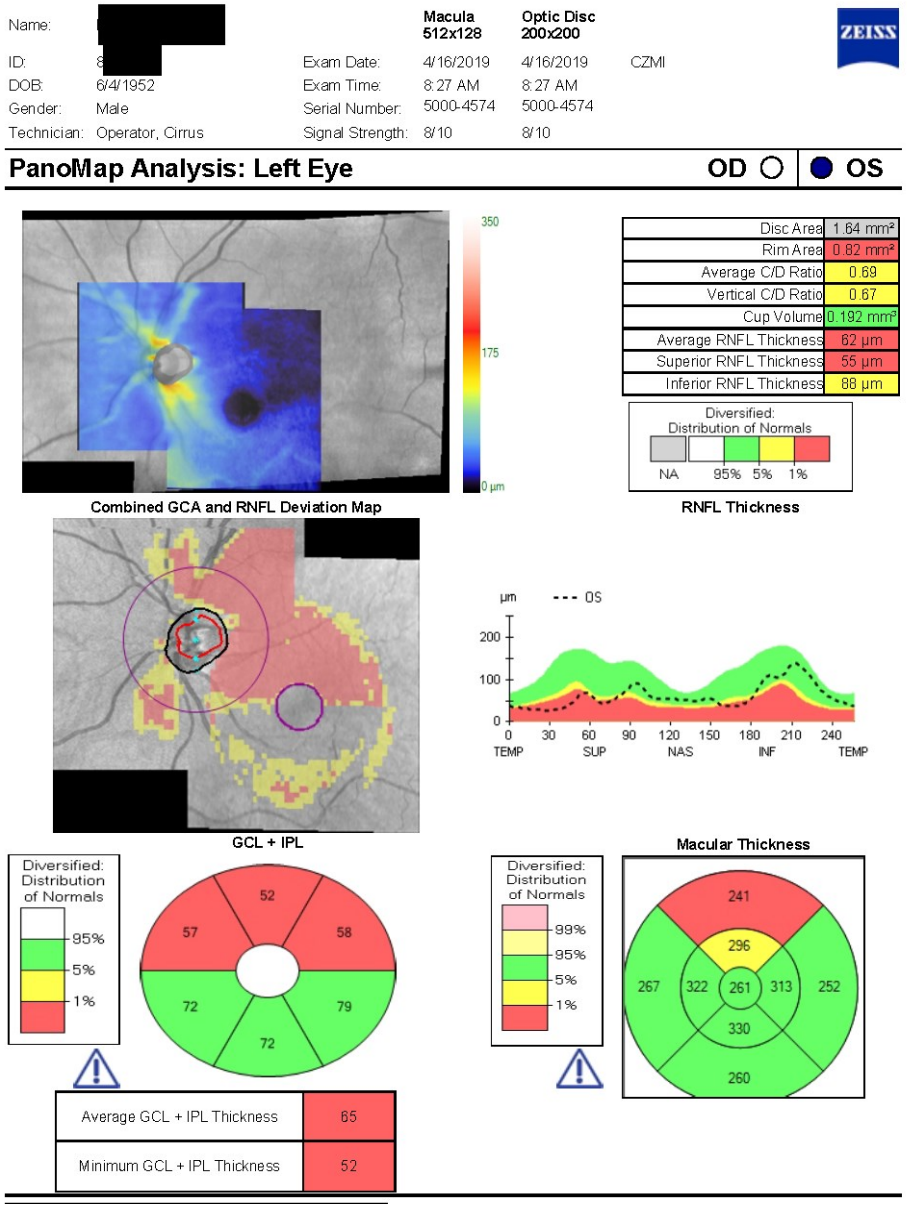


OS



Superior-Inferior Asymmetry



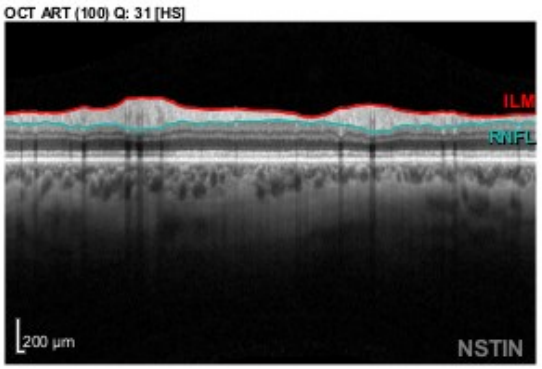


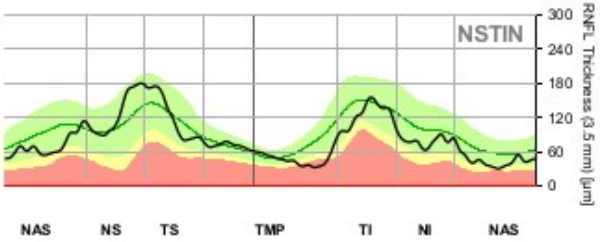
PanoMap Analysis: *PRO*: See correlation between RNFL and GCC damage. *CON*: Loss of right-left eye comparisons

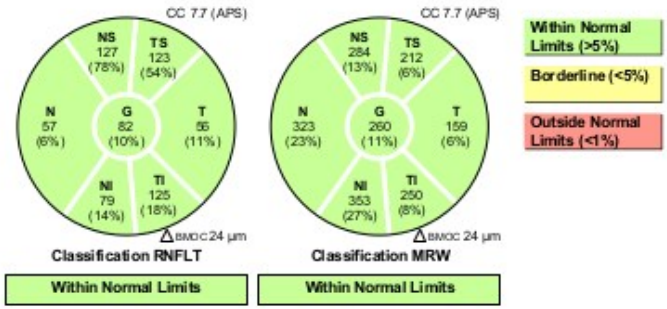
Hood Glaucoma Report
SPECTRALIS® Tracking Laser Tomography

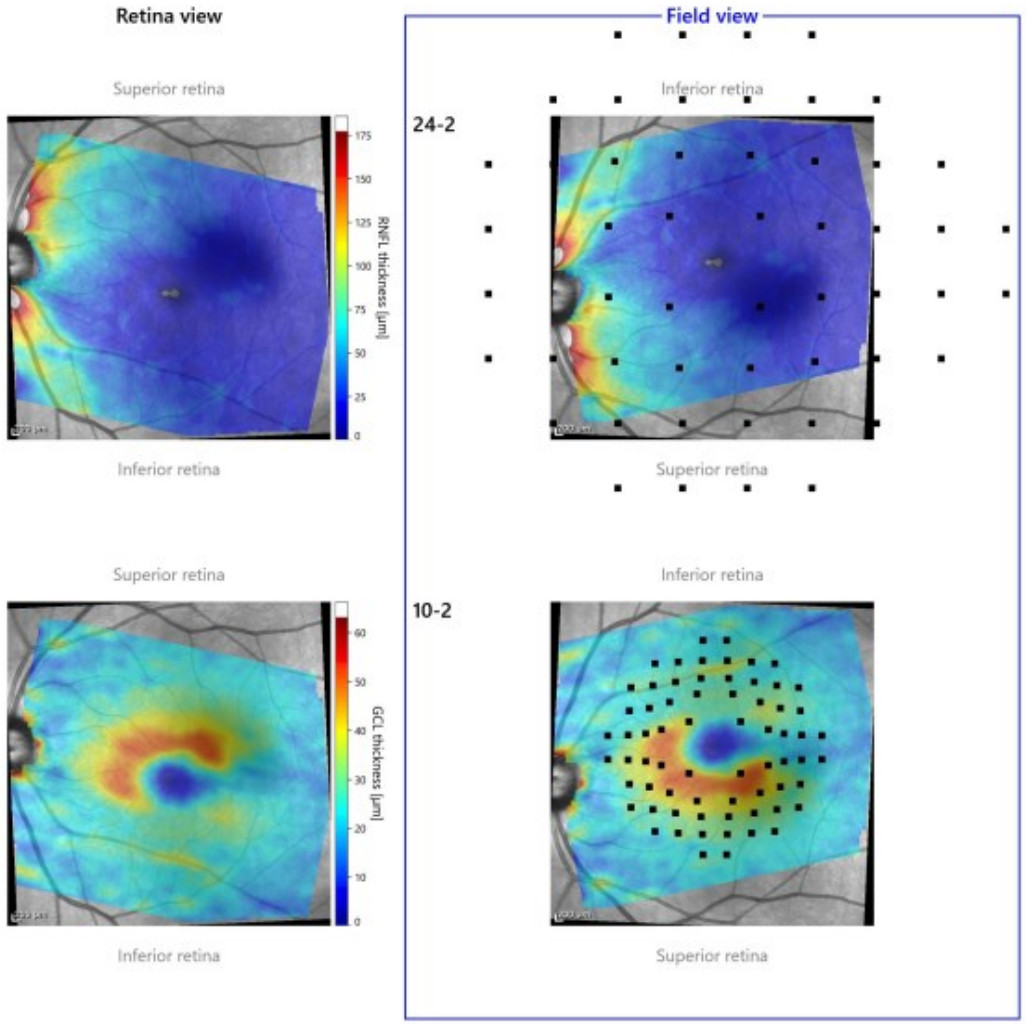
HEIDELBERG ENGINEERING

Patient:		**DOB:**	Sep/20/1955	**Sex:**	F
Patient ID:		**Exam.:**	Sep/19/2022		**OS**
Diagnosis:	---	**Comment:**	---		









Reference database: US Ethnic Mix (2016)

Hood Report – VF overlay missing in USA
due to FDA concerns regarding misinterpretation

Optical coherence tomography retinal ganglion cell complex analysis for the detection of early chiasmal compression

Richard J. Blanch[1,2,3] · Jonathan A. Micieli[1] · Nelson M. Oyesiku[4] · Nancy J. Newman[1,4,5] · Valérie Biousse[1,5]

Abstract

Purpose To report patients with sellar tumors and chiasmal compression with normal visual fields, who demonstrate damage to the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) on optical coherence tomography (OCT).

Methods Seven patients with sellar tumors causing mass effect on the optic chiasm without definite visual field defect, but abnormal GCC are described. GCC/RNFL analyses using Cirrus-OCT were classified into centiles based on the manufacturer's reference range.

Results In seven patients with radiologic compression of the chiasm by a sellar tumor, OCT-GCC thickness detected compressive chiasmopathy before visual defects became apparent on standard automated visual field testing. Without OCT, our patients would have been labelled as having normal visual function and no evidence of compressive chiasmopathy. With only OCT-RNFL analysis, 3/7 patients would still have been labelled as having no compression of the anterior visual pathways.

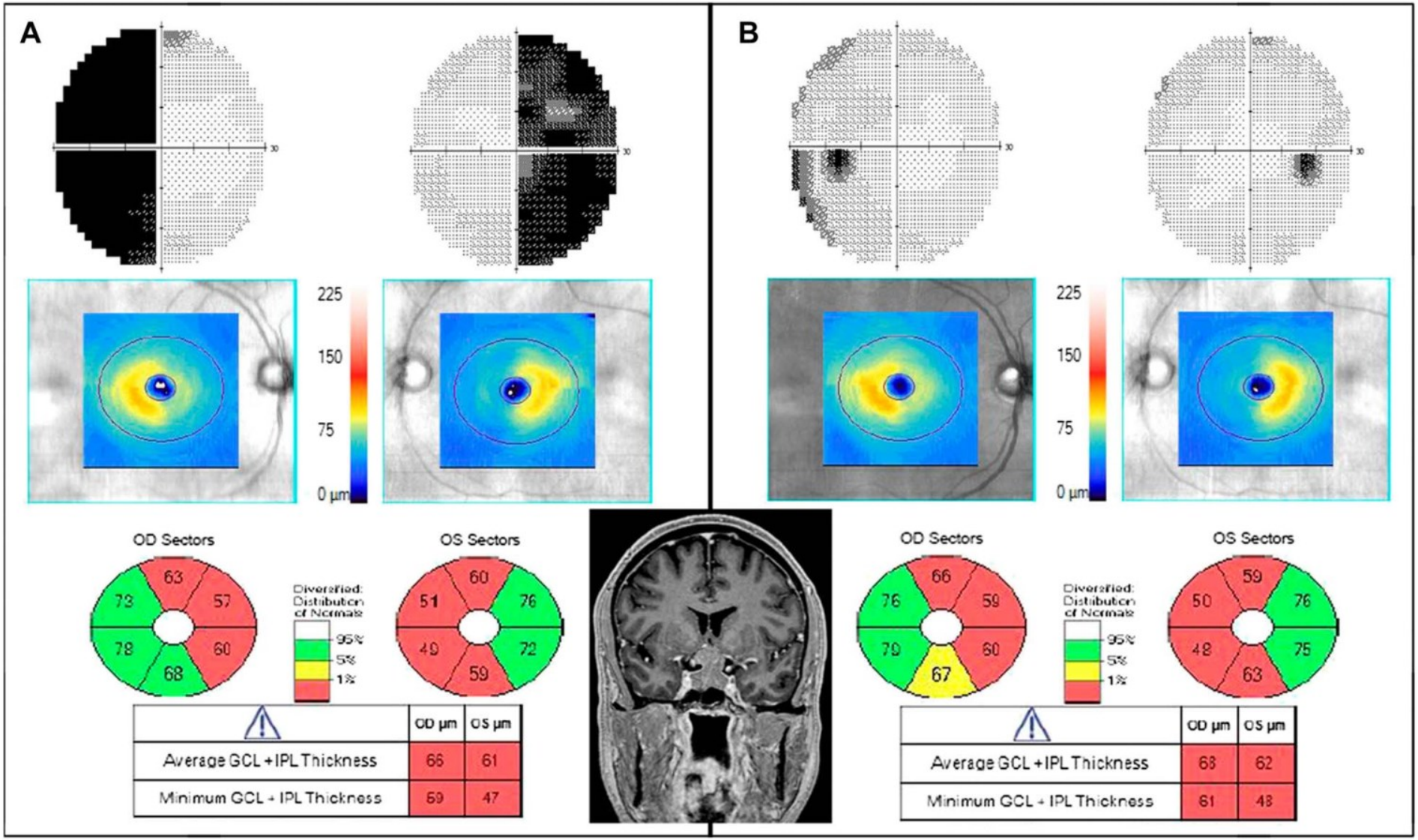
Conclusions These patients show that OCT-GCC analysis is more sensitive than visual field testing with standard automated perimetry in the detection of compressive chiasmopathy or optic neuropathy. These cases and previous studies suggest that OCT-GCC analysis may be used in addition to visual field testing to evaluate patients with lesions compressing the chiasm.

OCT can detect chiasmal compression before VF loss occurs

PMID: 30097827

Pre-Op

Post-Op



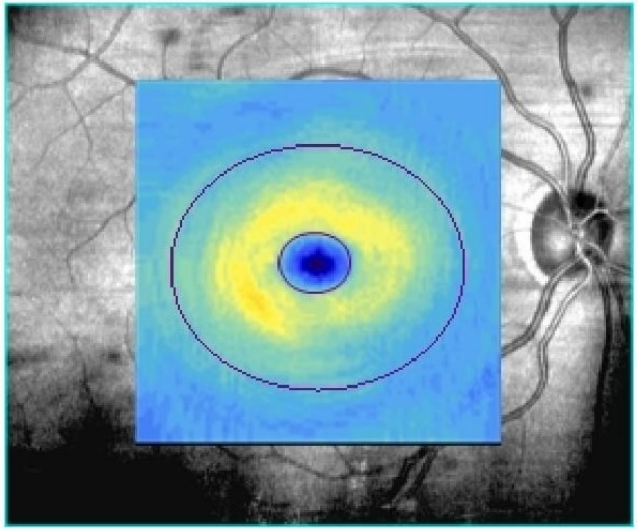
PMID: 30097827

		OD	OS	
Name:				
ID:		Exam Date:	3/6/2017	3/6/2017 CZMI
DOB:	10/2/1961	Exam Time:	1:59 PM	2:02 PM
Gender:	Male	Serial Number:	5000-7099	5000-7099
Technician:	Operator, Cirrus	Signal Strength:	8/10	8/10

Ganglion Cell OU Analysis: Macular Cube 512x128

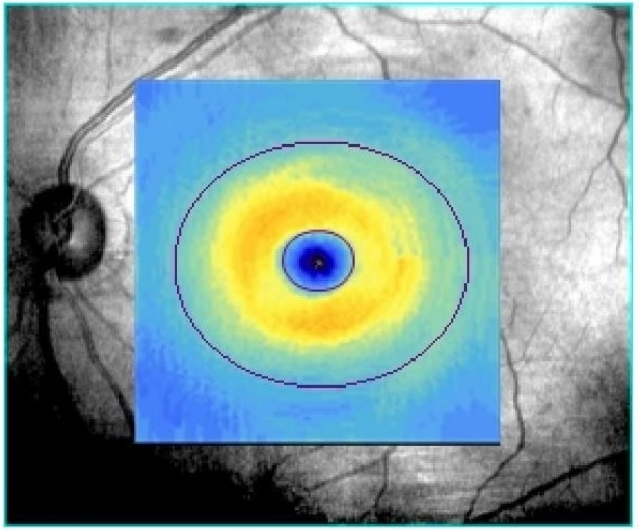
OD ● | ● OS

OD Thickness Map



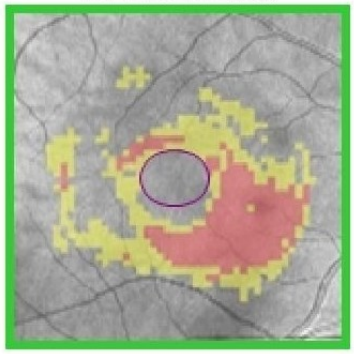
Fovea: 253, 65

OS Thickness Map

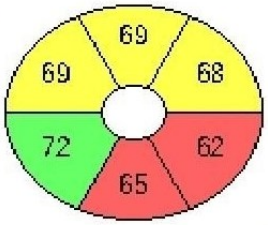


Fovea: 259, 64

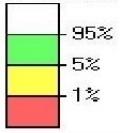
OD Deviation Map



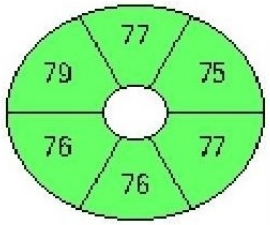
OD Sectors



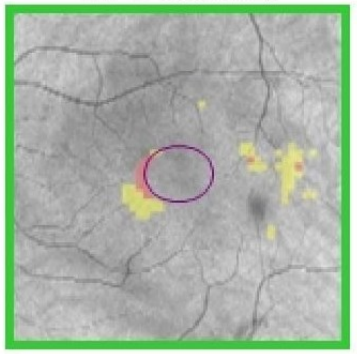
Diversified Distribution of Normals



OS Sectors



OS Deviation Map



	OD µm	OS µm
Average GCL + IPL Thickness	68	77
Minimum GCL + IPL Thickness	63	76

Factors Affecting Glaucoma Detection

1. Disease severity
2. Optic disc size
3. Signal strength / Errors
4. Artifacts / Ocular anomalies
5. Axial length
6. Blood vessel position
7. Age
8. Race

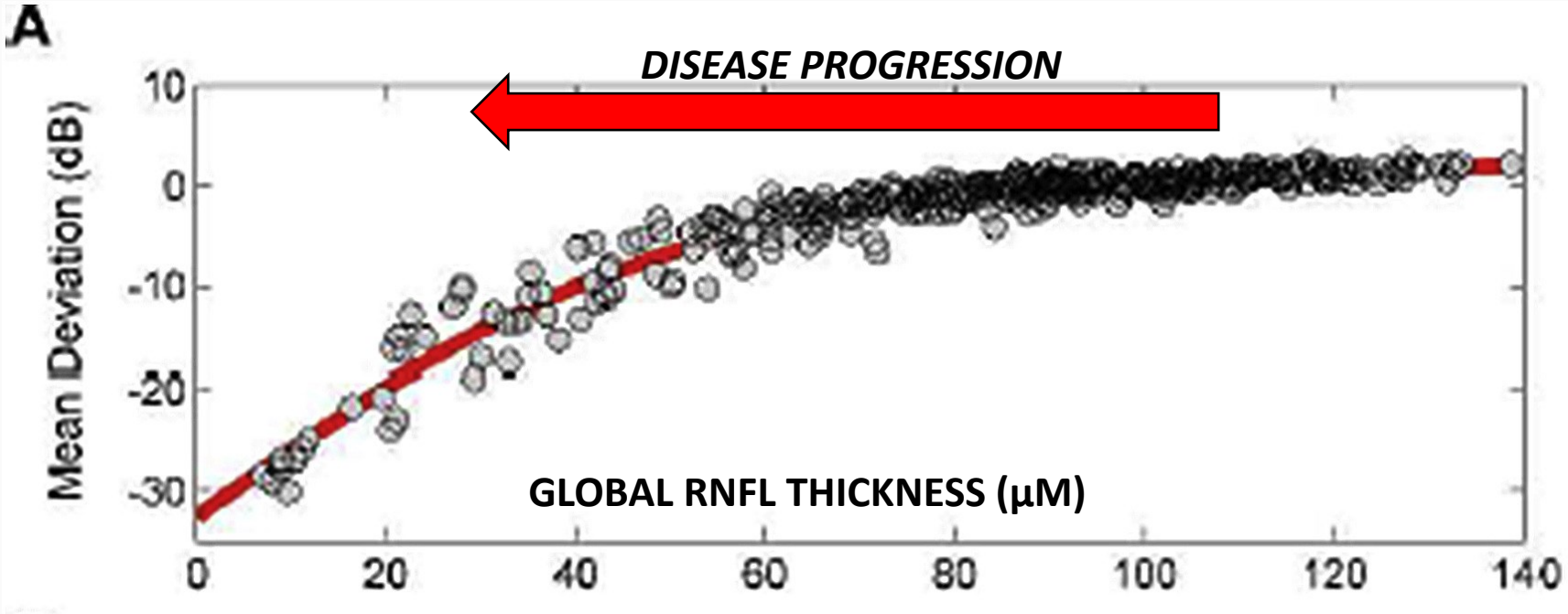
Factors Affecting Glaucoma Detection

- Disease Severity: Early glaucoma
  - **OCT more sensitive than perimetry** in detection of early glaucoma.
  - Large overlap between normal and mildly glaucomatous findings makes diagnostic determination upon a single test result difficult
  - Detection of ***change over time*** may be the most reliable means of confirming the presence of preperimetric disease

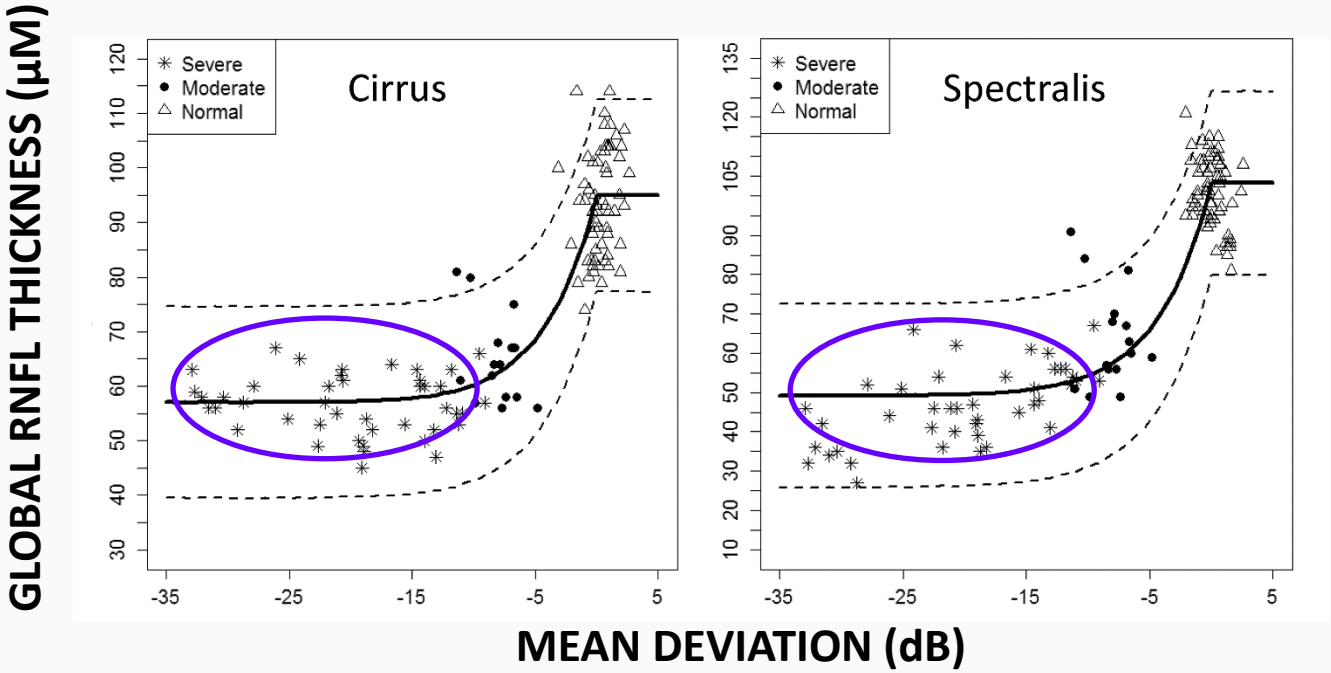
Factors Affecting Glaucoma Detection

- Disease Severity: Severe glaucoma
  - **OCT less sensitive than perimetry** in detection of progression due to “floor effect”
  - **Floor effect**: Residual RNFL tissue (blood vessels, glia) masks continued loss of ganglion cell axons
  - OCT not reliable in detecting progression once global RNFL thickness <60um

PERIMETRY



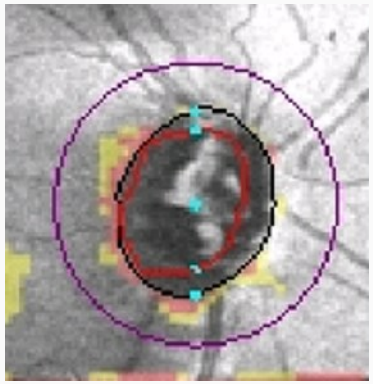
OCT

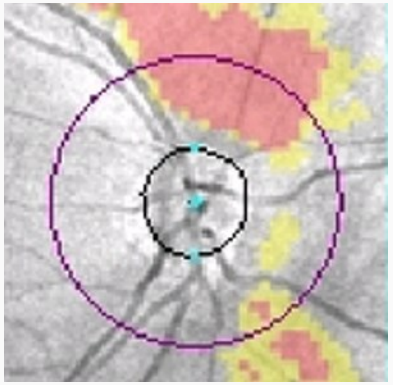


FLOOR EFFECT

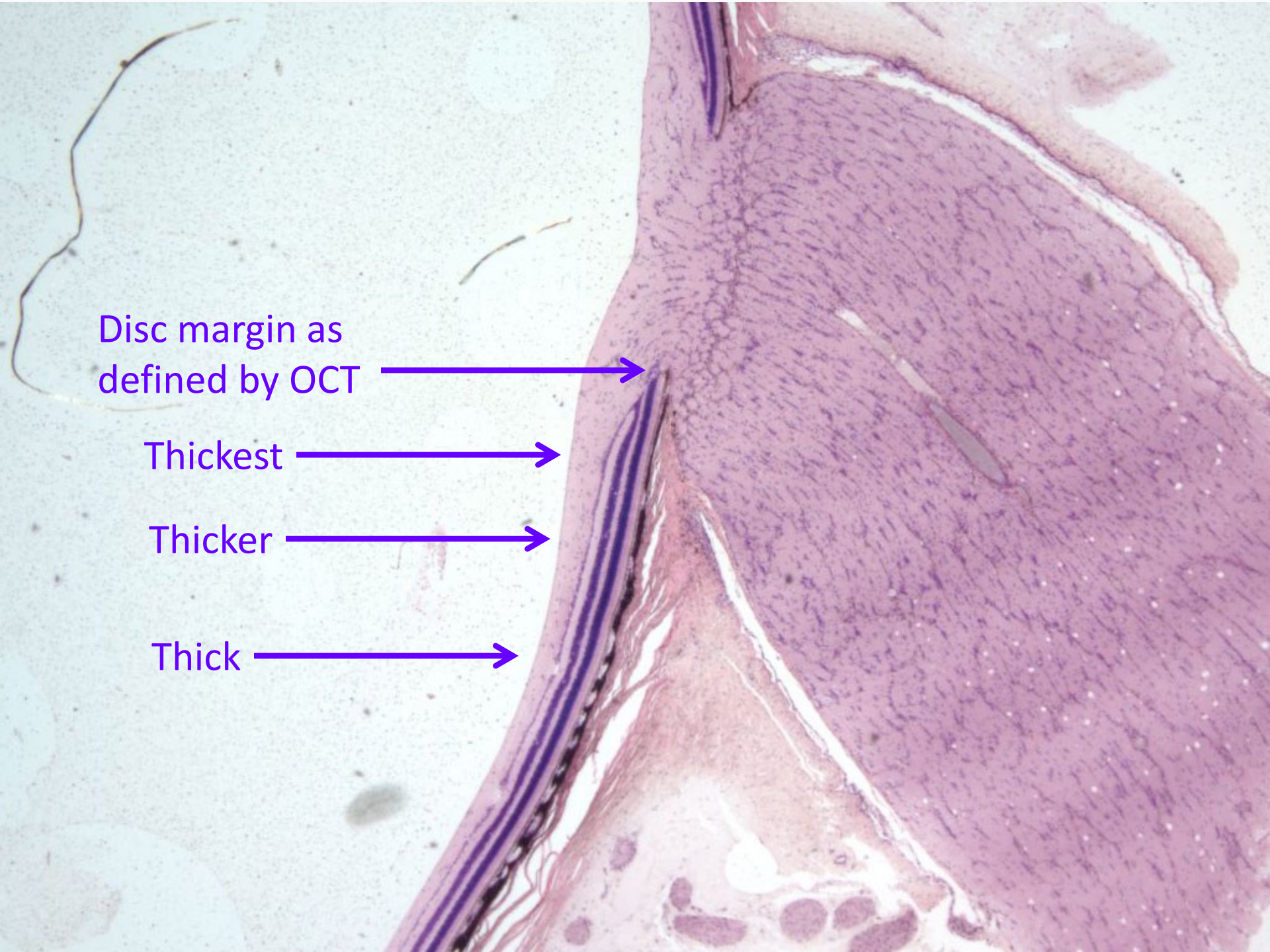
Factors Affecting Glaucoma Detection

- Optic Disc Size
  - **Larger discs have thicker RNFL measurements**



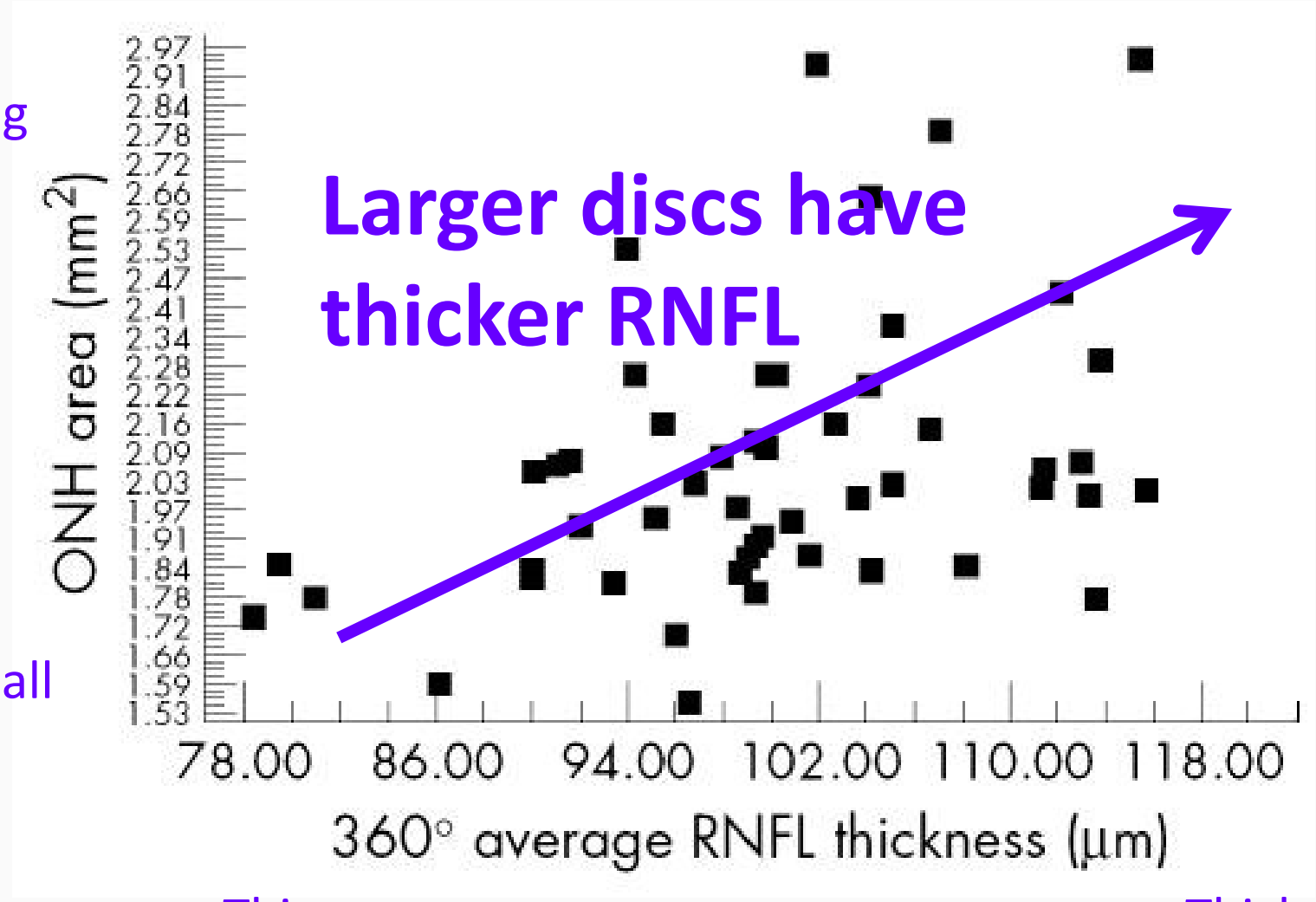


    - May contain more nerve fibers
    - May be an artifact of fixed measurement circle
  - Larger discs have lower sensitivity for early glaucoma detection
    - Because larger discs start with thicker RNFL measurements, they must suffer more damage before registering as abnormal on OCT

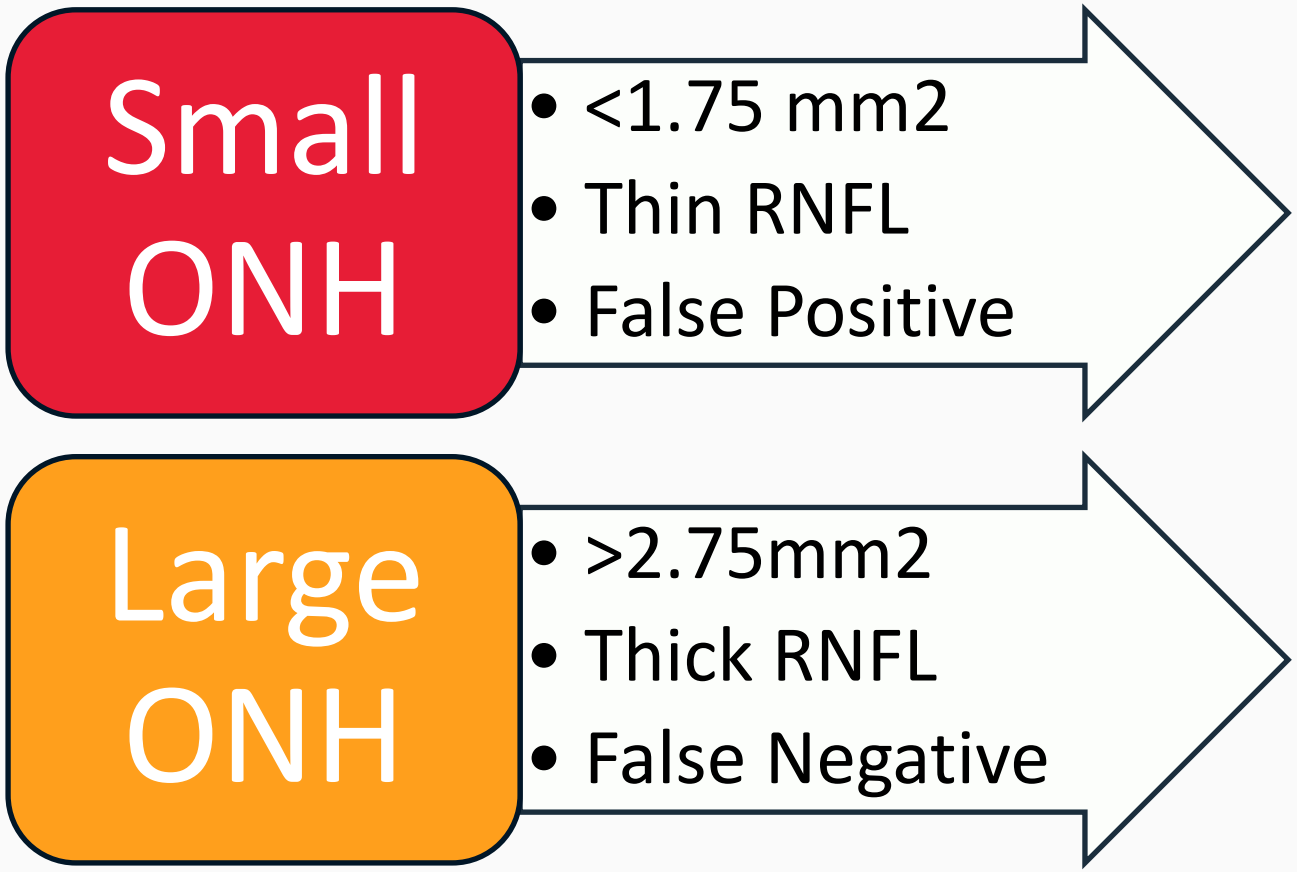

Disc margin as defined by OCT
Thickest
Thicker
Thick

Relationship between ONH size and measured RNFL thickness

PMID: 15774930



Factors Affecting Glaucoma Detection



PMID: 21550120

Factors Affecting Glaucoma Detection

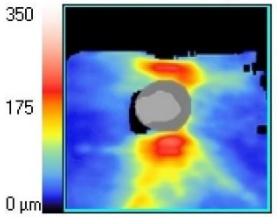
- Signal Strength
  - Scan quality affects OCT performance, even when within manufacturer recommended limits
    - Effect greater on RNFL than ONH and GCC
  - Pupil dilation does not affect signal strength, RNFL measurement or reproducibility in *normal eyes*
    - Pupil dilation may improve signal strength with cataract
  - **Technical errors**
    - Disc centration, capture window displacement
    - Blinks & eye movements

		OD	OS
Name:			
ID:		Exam Date:	4/23/2018	4/23/2018
DOB:	5/1/1957	Exam Time:	12:47 PM	12:49 PM
Gender:	Male	Serial Number:	[illegible]	[illegible]
Technician:	Operator, Cirrus	Signal Strength:	3/10	8/10

ONH and RNFL OU Analysis:Optic Disc Cube 200x200

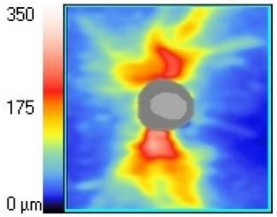
OD ● | ● OS

RNFL Thickness Map

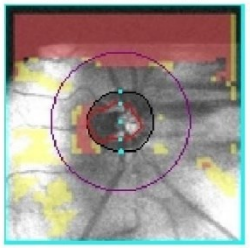


	OD	OS
Average RNFL Thickness	68 µm	101 µm
RNFL Symmetry	41%	
Rim Area	1.03 mm²	1.33 mm²
Disc Area	2.00 mm²	2.05 mm²
Average C/D Ratio	0.69	0.58
Vertical C/D Ratio	0.60	0.54
Cup Volume	0.301 mm³	0.146 mm³

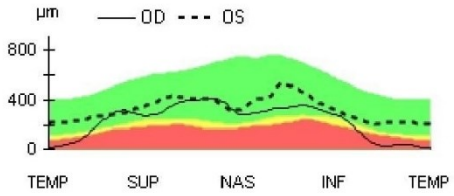
RNFL Thickness Map



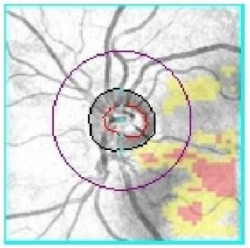
RNFL Deviation Map



Neuro-retinal Rim Thickness

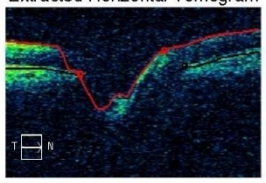


RNFL Deviation Map

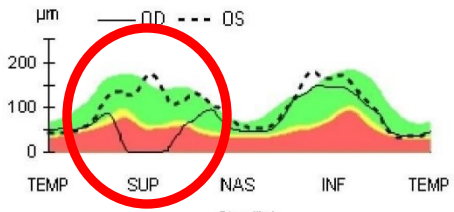


Disc Center(-0.12,0.09)mm

Extracted Horizontal Tomogram

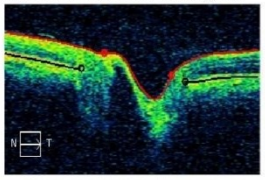


RNFL Thickness

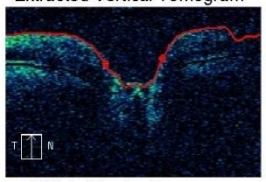


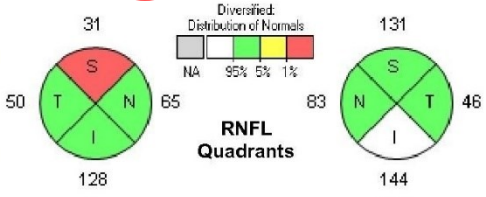
Disc Center(-0.09,0.12)mm

Extracted Horizontal Tomogram

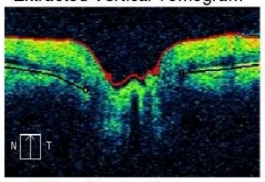


Extracted Vertical Tomogram

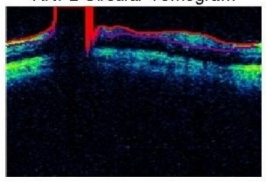


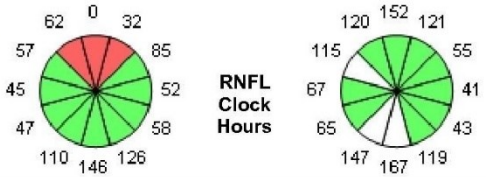


Extracted Vertical Tomogram

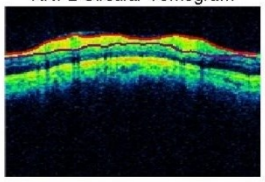


RNFL Circular Tomogram

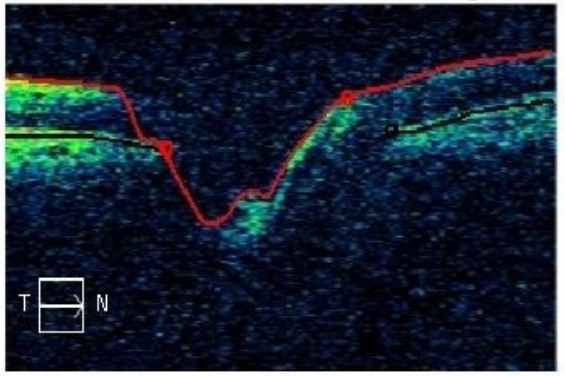




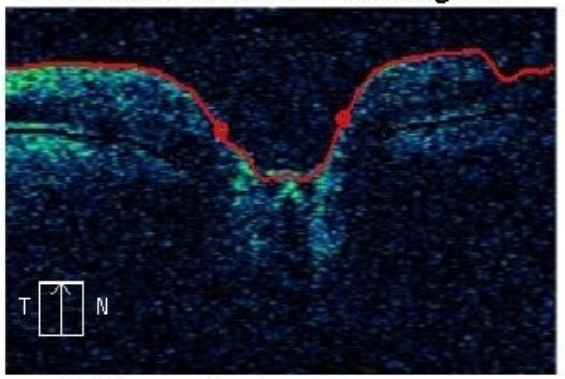
RNFL Circular Tomogram



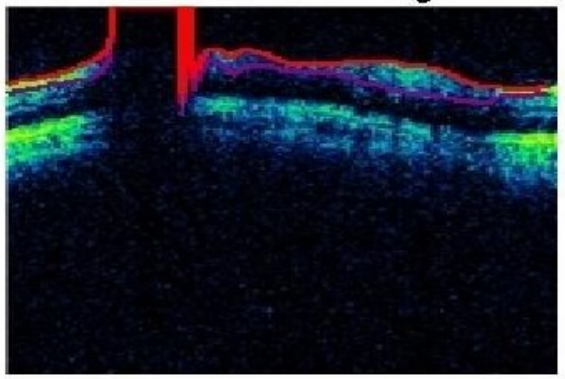
Extracted Horizontal Tomogram



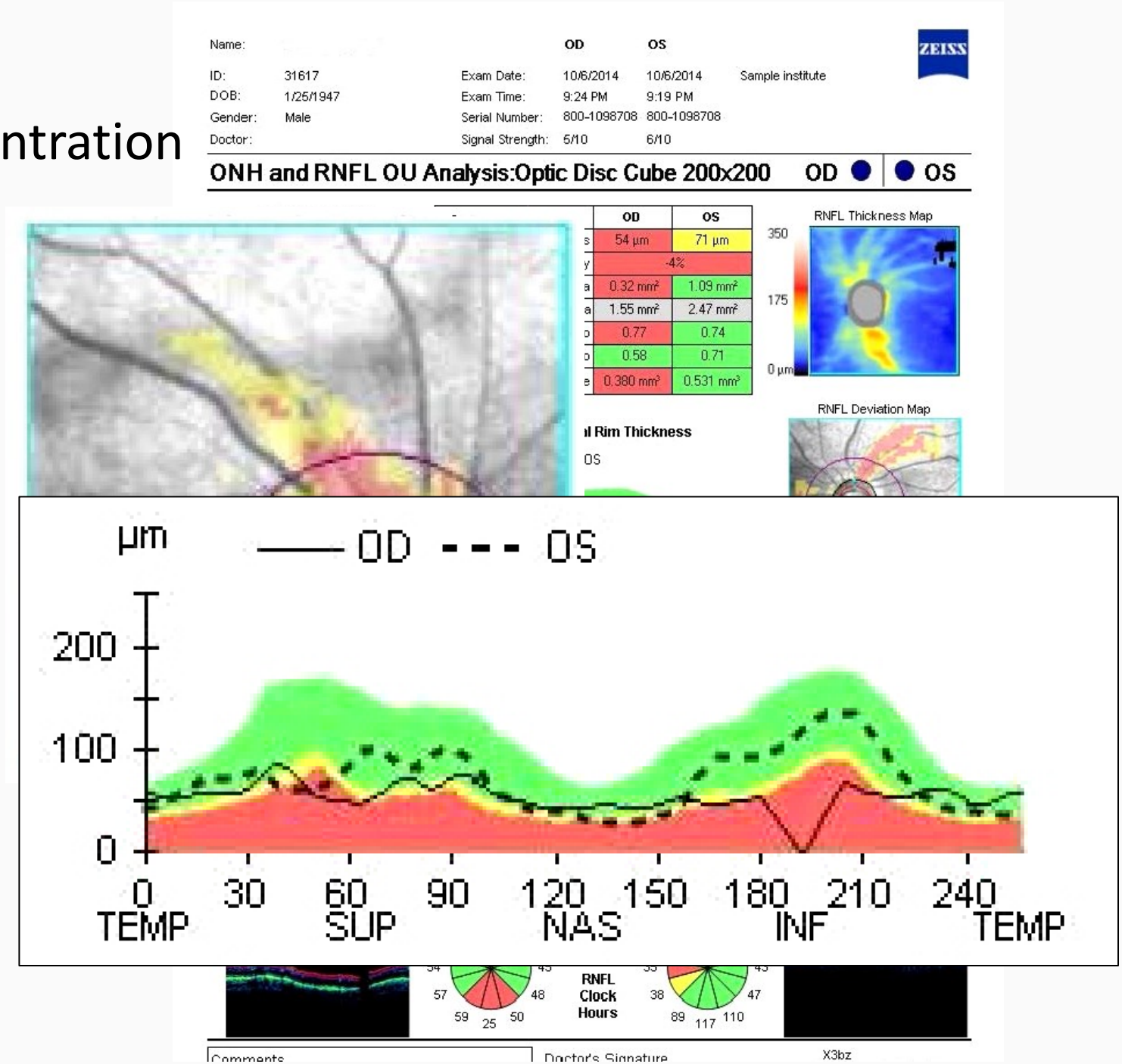
Extracted Vertical Tomogram



RNFL Circular Tomogram



Decentration Error



Factors Affecting Glaucoma Detection

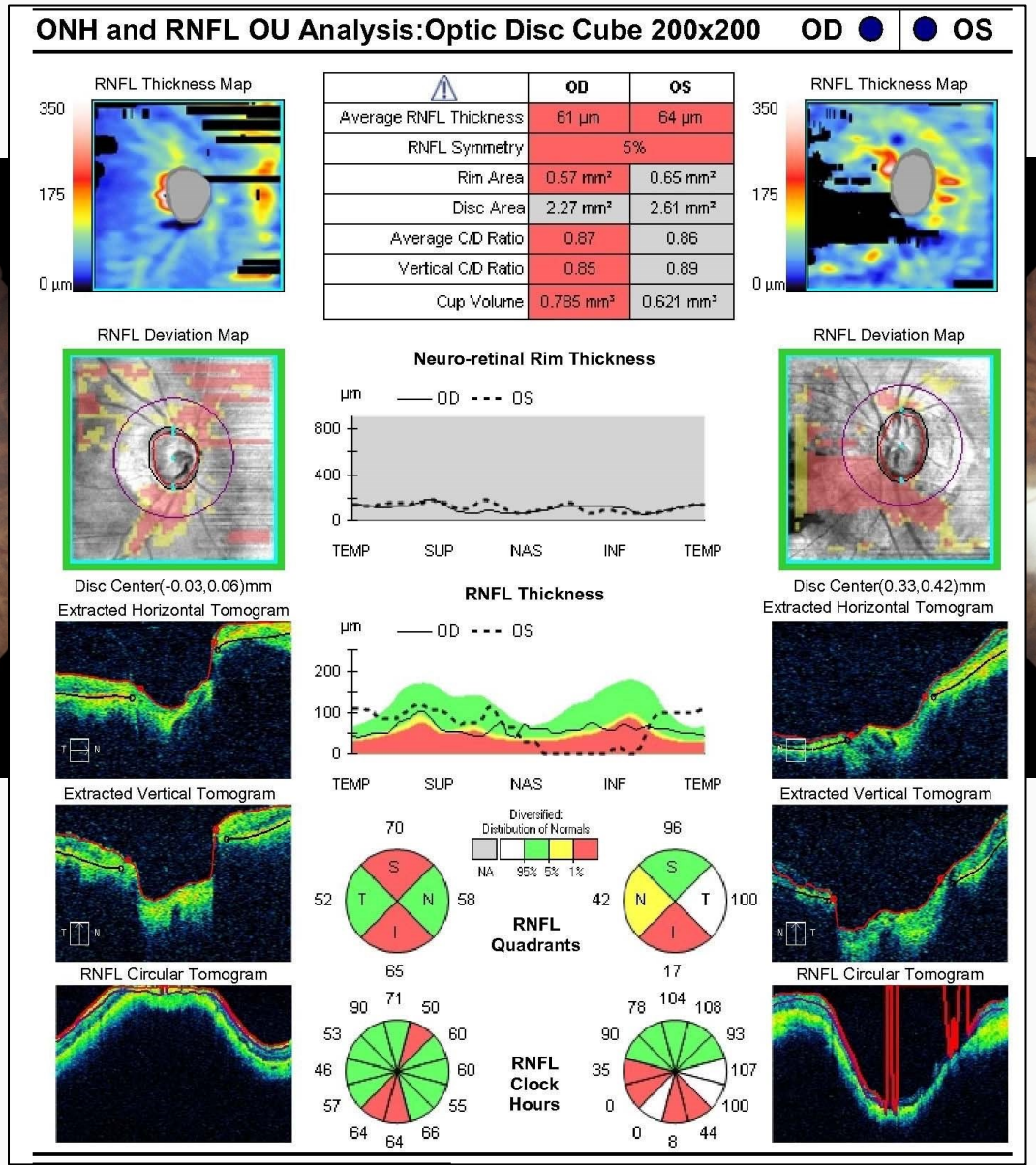
- Ocular Anomalies
  - Cataracts can decrease signal strength
    - May be improved with pupil dilation
  - Epiretinal membrane is a common artifact on RNFL and GCC scans
    - **ERM may inflate RNFL and macular thickness measurements**
  - Partial PVD will also inflate the thickness measurements until detachment occurs
    - **Decrease in thickness following PVD may simulate glaucoma progression**

Factors Affecting Glaucoma Detection

- Axial Length
  - RNFL thickness is influenced by axial length—**the longer the eye, the thinner the mean RNFL**
    - Every 1mm ↑axial length = 2.2µm ↓RNFL thickness
  - High myopes may also have lateral shifts in the RNFL thickness profile
  - Longer axial length associated with significantly higher risk of OCT **false positive**

PMID: 17210181, 21550120

Pathologic Myopia

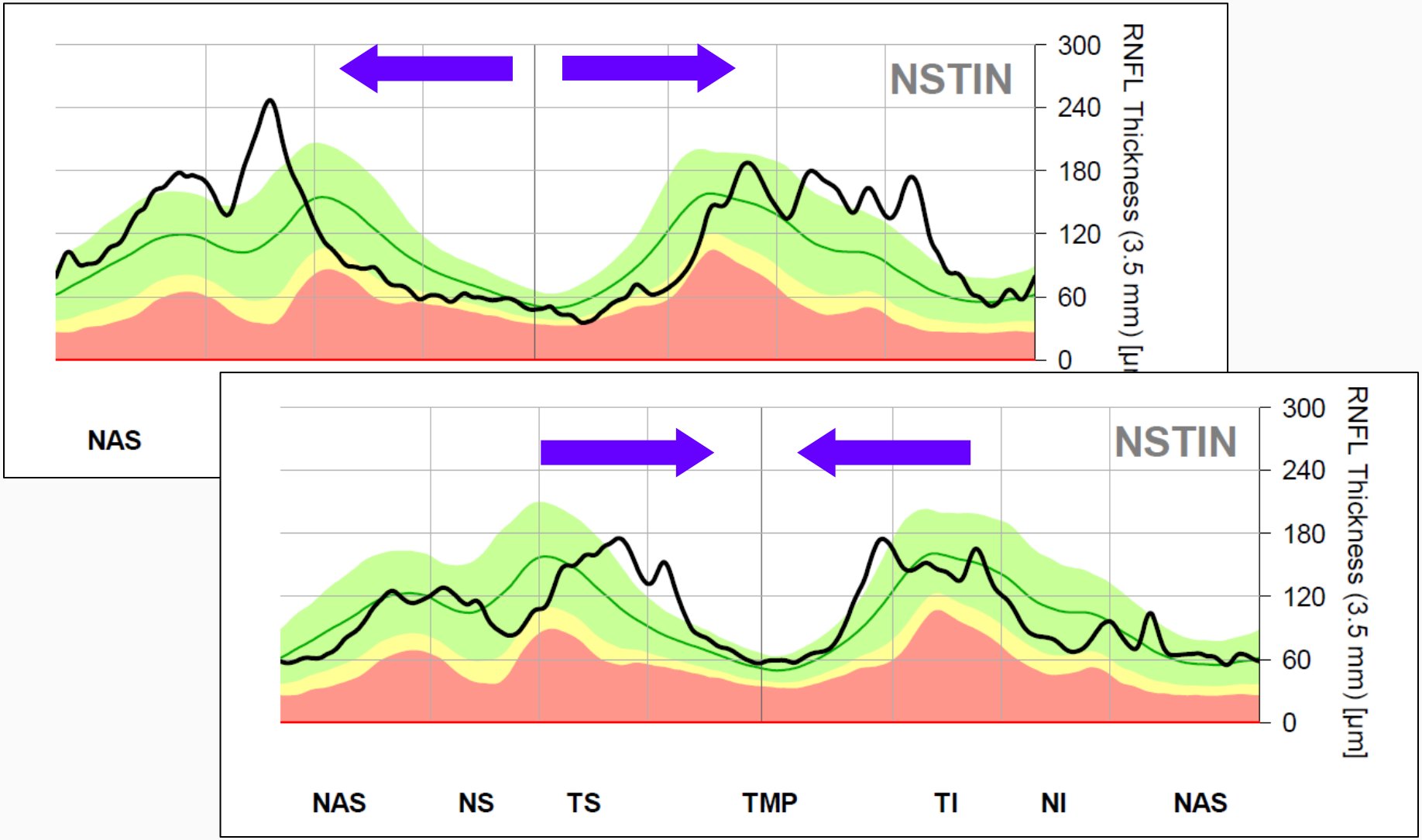


Factors Affecting Glaucoma Detection

- Blood Vessel Position
  - The thickest RNFL region is usually at the location of the temporal vascular arcades.
  - **Variations in normal RNFL profiles are often due to variation in blood vessel location**
  - Split bundles: When the RNFL bundles traveling with the nasal and temporal arcades are distinctly separated. May simulate a wedge defect

PMID: 18854727

Factors Affecting Glaucoma Detection



Factors Affecting Glaucoma Detection

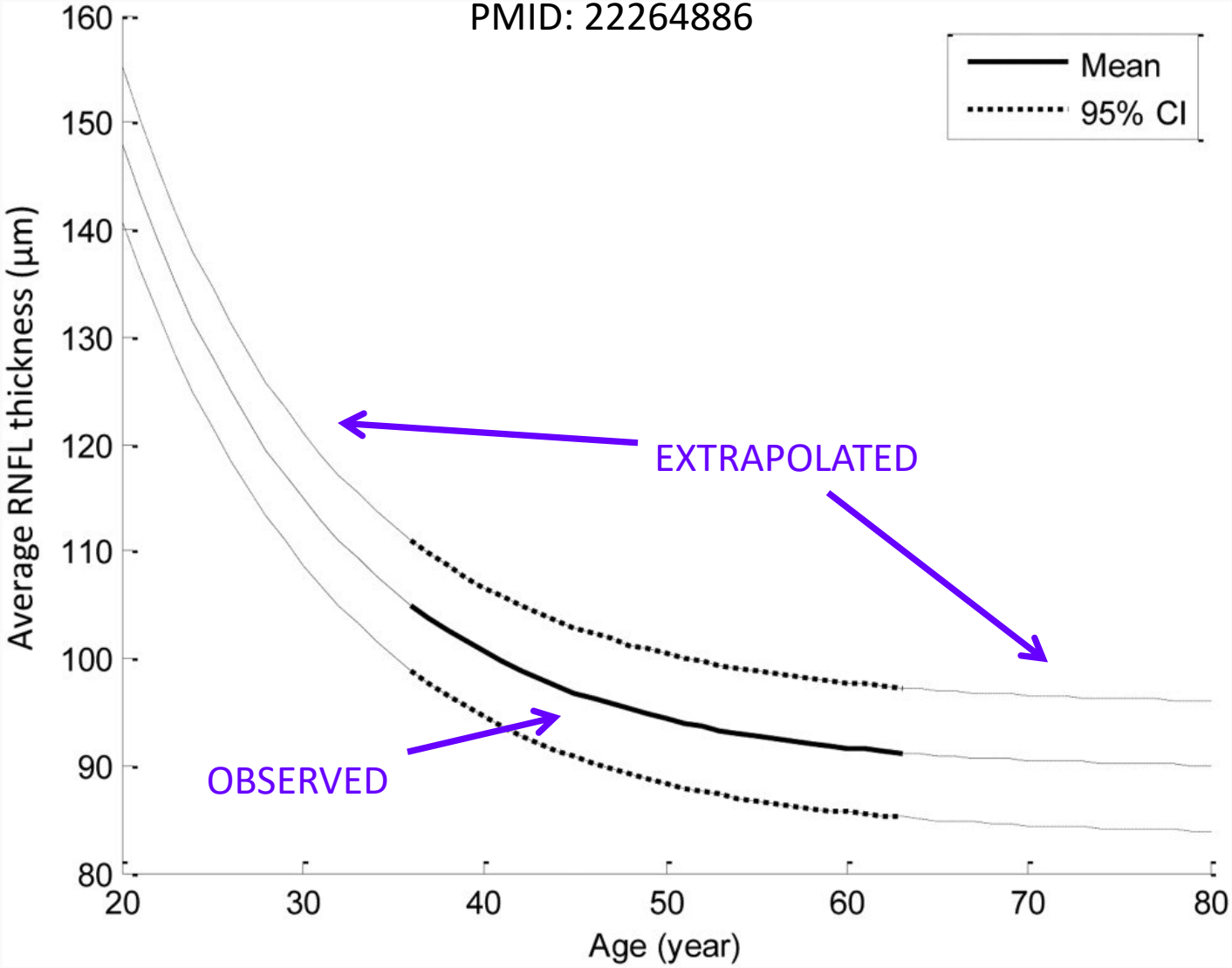
- Age
  - **RNFL thickness declines with age**, but not linearly
  - **Rate of loss declines with age**
  - The rate of decline is greater in eyes with thicker baseline RNFL thickness
  - Rate of decline is greater at the poles than laterally
  - All OCT normative data is age-related

PMID: 22264886

Decline in Average RNFL Thickness with Age

(Assumes 100 µm thickness at age 40 yrs)

PMID: 22264886



Take Home Messages

- **Focus on the data, not just the colors**
  - Analyze RNFL, ONH morphology and GCC
- **Recognize confounding effect of disc size, refractive error, blood vessel position**
  - Red disease ***and*** Green disease
- **Beware of errors and artifacts**
  - Signal strength, centration, blinks, ERM, PVD
- **Attempt to correlate OCT with perimetry**
  - Focus on OCT in early disease and VF in advanced

PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

Differential Diagnosis of Normal Tension Glaucoma

Rick Trevino, OD, FAAO

Indiana University School of Optometry

Key Features of Primary Open Angle Glaucoma

1. **ONH**
   - Cupping. ISNT rule. ONH hemorrhages. *No pallor!*
2. **VF**
   - Respect horizontal midline. *No vertical midline cuts!*
   - Nasal loss > Temporal loss
3. **IOP**
   - >21 mmHg on at least one occasion

- Other
  - **Normal visual acuity** (R/O optic n. & retinal dx)
  - Unoccludable angles (R/O ACG with gonioscopy)

Differential Diagnosis of NTG

ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

ONH: ONH appearance and OCT findings

VF: Defects on SAP consistent with glaucoma

IOP: IOP >21mmHg on at least 1 occasion

Differential Diagnosis of NTG

ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

Two abnormal findings increase the likelihood of the patient having glaucoma

Patients with elevated IOP and either VF defects or optic nerve findings characteristic of glaucoma should have their IOP lowered

Differential Diagnosis of NTG

ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

Differential Diagnosis:

- Classic NTG
- Other optic nerve disease (AION, tumors, etc)
- POAG with undetected diurnal peak

Differential Diagnosis of NTG

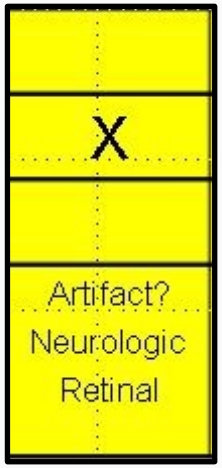
ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

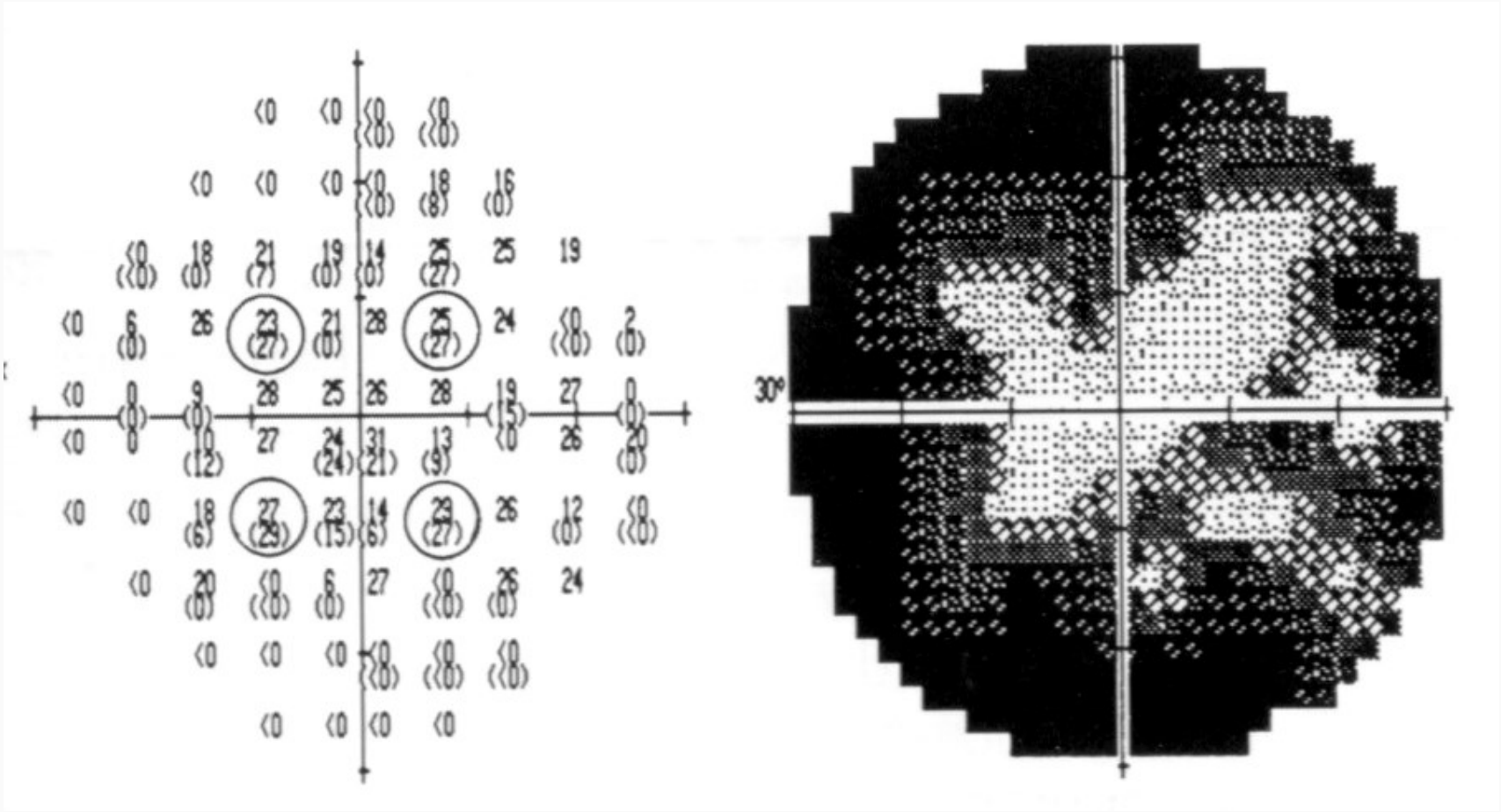
Having **only 1 abnormal finding** decreases the likelihood of glaucoma

Patient may be completely normal or have non-glaucomatous optic nerve disease

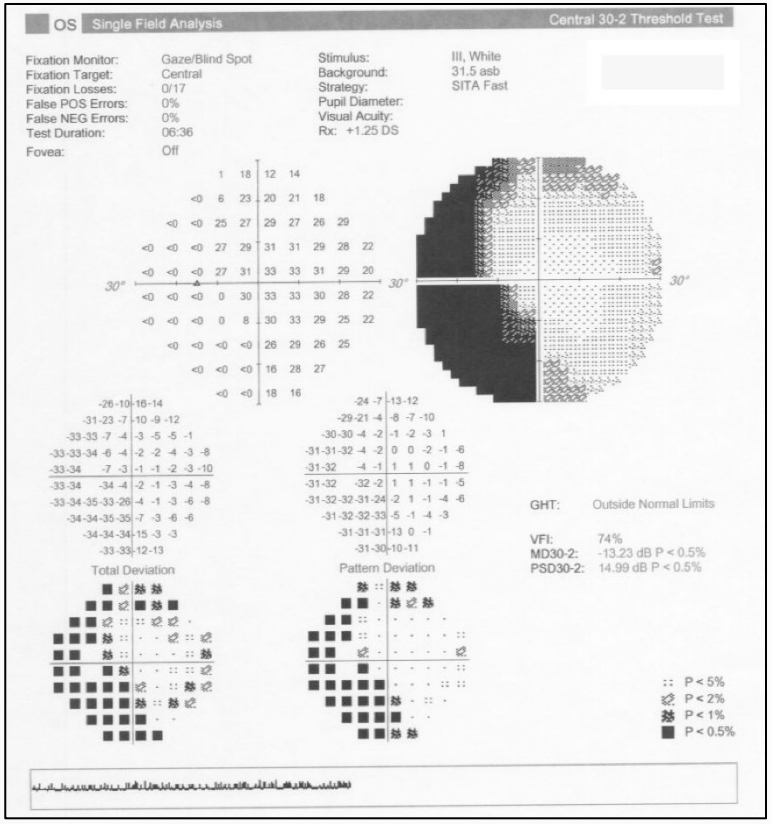
NTG Suspect #1

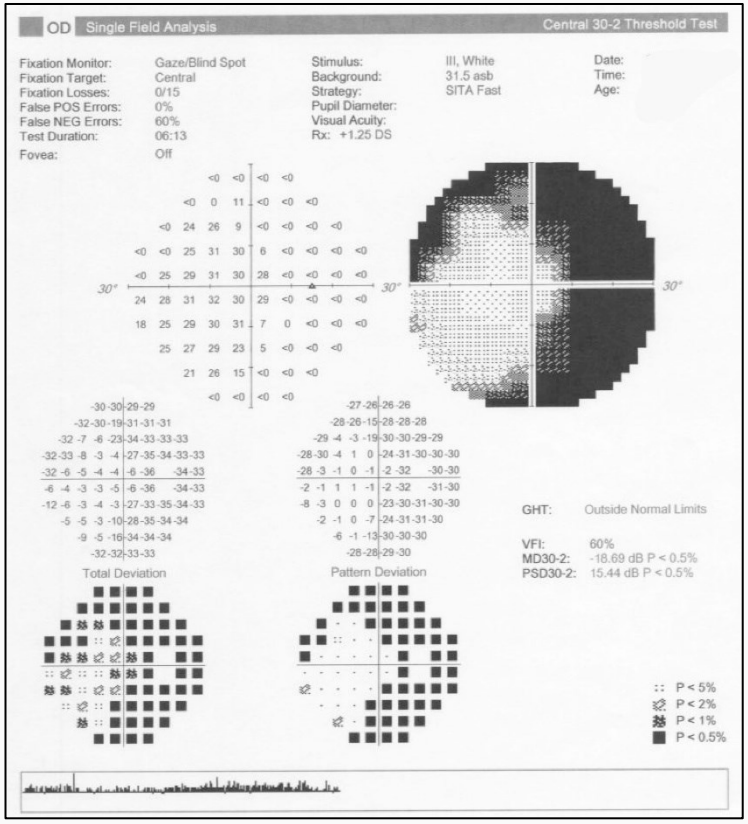
- VF defects only
  - Need to confirm **reproducibility** of defect
    - Avoid artifacts: trial lens, lids, etc
    - Watch for signs of fatigue (clover leaf pattern)
  - Is the ONH really normal?
    - **Pseudo-normal ONH**: small discs with small cups
    - **Green disease**: Large ONH with thick RNFL
  - Is the VF defect characteristic for glaucoma?
    - **Beware vertical midline respect!**
    - Temporal loss greater than nasal loss → not glaucoma
    - Chorioretinal scars, old retinal vascular occlusions, etc
  - **Plan**: Neuroimaging and/or monitor





Cloverleaf pattern of loss on Humphrey automated perimetry could be misinterpreted as severe glaucomatous loss

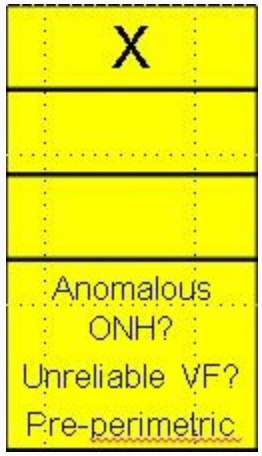




Glaucomatous defects **always** respect the horizontal midline and are typically **greater nasally** than temporally

These defects are greater temporally, and do not respect the horizontal

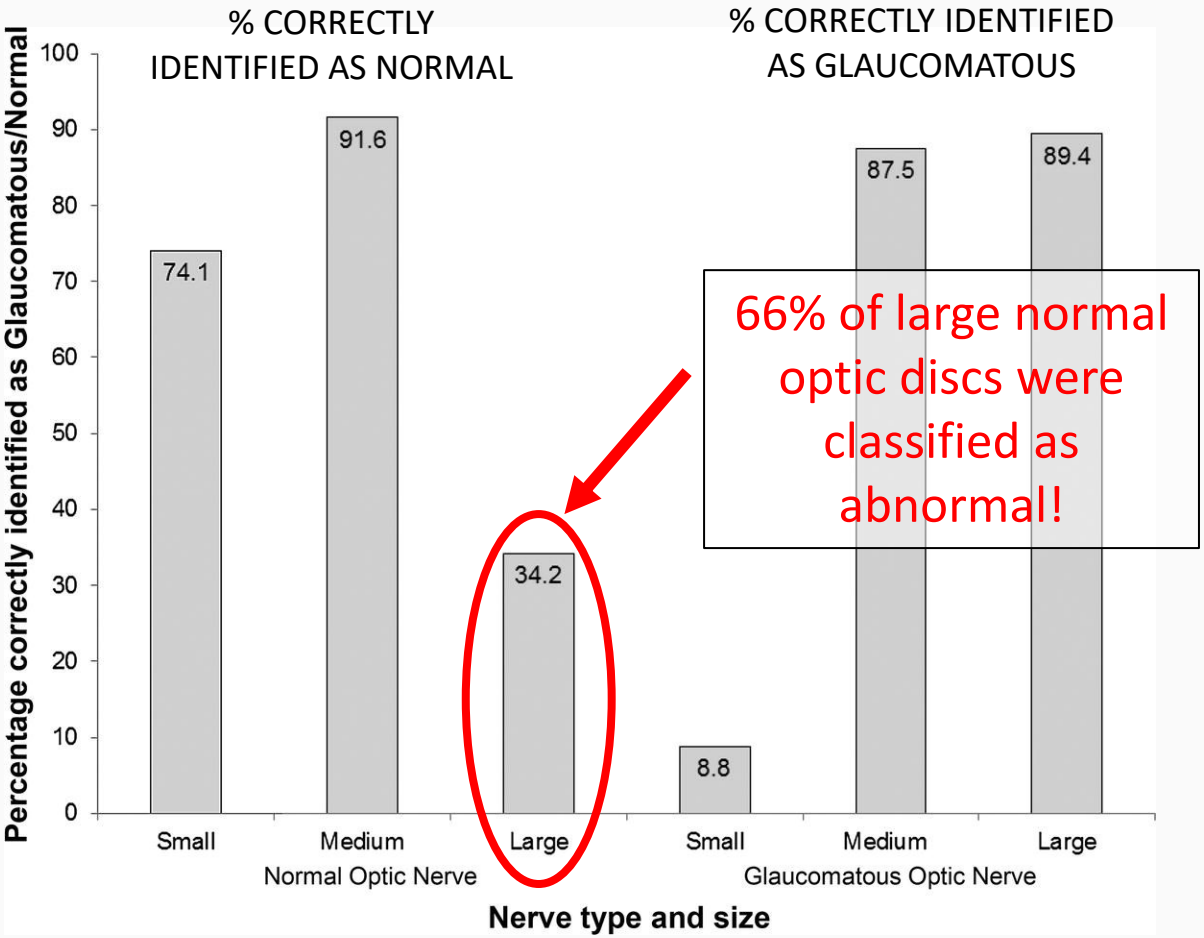
NTG Suspect #2



- ONH only
  - **Anomalous optic nerves are common and many appear glaucomatous**
  - Most patients with ISNT rule violation, asymmetric cupping, etc are normal
  - **Recognizing suspicious ONH cupping is the key to diagnosing NTG!**
  - **Plan**
    - If OCT is normal: Just another FLN → annual exams
    - If OCT suggests glaucoma but VF is normal: Monitor

Numerous studies have documented the **difficulty of correctly identifying glaucomatous damage in small optic discs**

Nixon (2017): Doctors examined stereophotos of optic nerve heads and were asked to classify them as normal or glaucomatous



Percentage of images where nerve type was correctly identified, by nerve type and size. Size was assessed by OCT (<1.63 mm^2 = small; >1.97 mm^2 = large)
(Nixon, 2017)

PMID: 28538334

NTG Management

Natural History of Normal-Tension Glaucoma

Collaborative Normal-Tension Glaucoma Study Group

Objective: A recently reported randomized study described the role of intraocular pressure (IOP) in normal-tension glaucoma (NTG) pathogenesis and the effect of therapeutic lowering of IOP. This is a report of an analysis of the natural course of NTG during the time eyes were not receiving therapy, either in the time interval awaiting randomization or after being randomly assigned not to receive treatment to lower the IOP.

Design: Analysis of prospectively collected data on the long-term course of a cohort of untreated subjects with normal-tension glaucoma, a subset of subjects enrolled in a randomized controlled clinical trial.

Randomization and Subject Selection: If the field defect in the study eye threatened the point of fixation, the subject was randomly assigned to start on treatment immediately or to be observed without treatment until progression was documented. Otherwise, an eye was randomly assigned only when and if, subsequent to enrollment, it showed visual field progression, progression of optic disc cupping, or a new disc hemorrhage.

Participants: Data were collected for this report on 160 subjects observed without treatment among a total enrollment of 260. They consist of 49 subjects who were randomly assigned on enrollment not to receive therapy,

Study of the **natural course of NTG while eyes were not receiving therapy**

- Awaiting randomization
- Randomized to not receive treatment

Conclusions: *Some cases of NTG progress more rapidly than others. Although* ***approximately half of cases showed a confirmed localized visual field deterioration by 7 years****, the change is typically small and slow, often insufficient to measurably affect the MD index.*

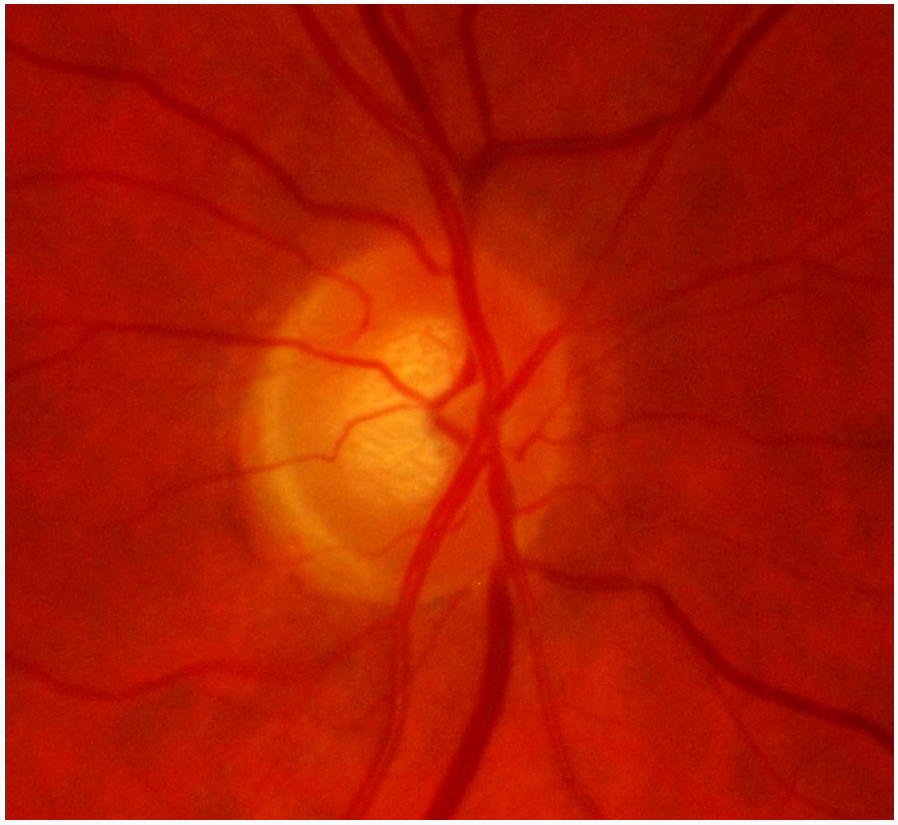
PMID: 11158794

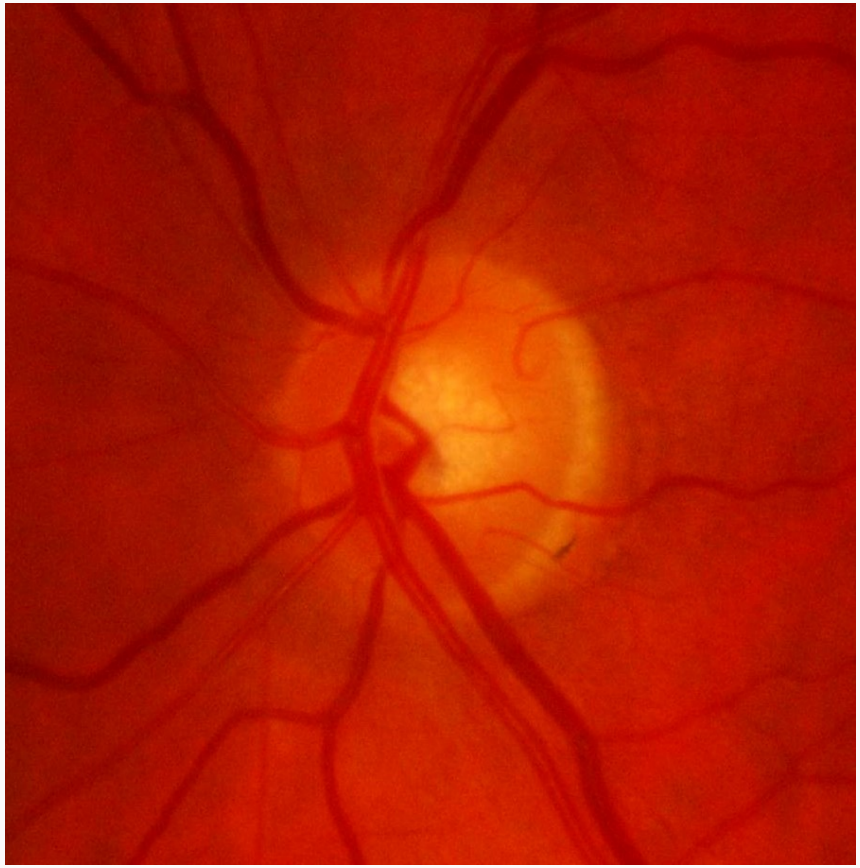
Case Report

- **44yo WM** presents for routine eye exam
- LLE: 7-8yrs ago
- PMH: migraines, smoker, no meds
- FOH: No glaucoma
- Refraction:
  -4.00-0.75x060 **20/25**
  -4.75 **20/20**
- PERRL, (-)APD

- BP: 130/84
- **GAT: 20/20 3pm**
- **C/D: 0.6 OD, 0.5 OS**

- IMP: Borderline IOP
- Plan: Schedule VF





Case Report

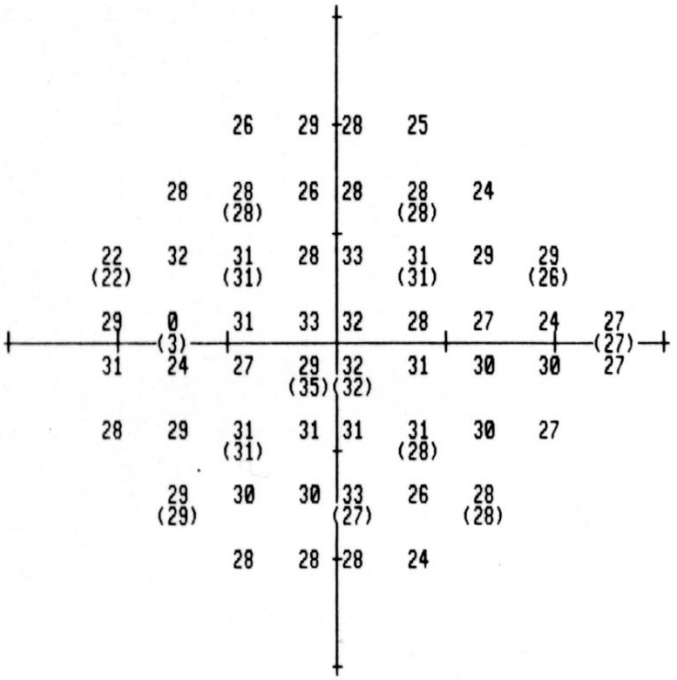
Slight asymmetry of optic cupping

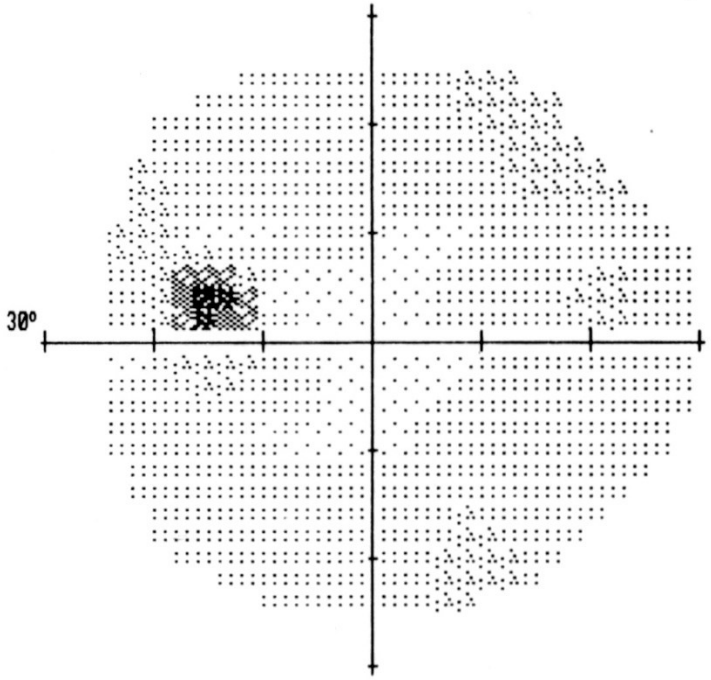
LEFT EYE

AGE 44
FIXATION LOSSES 0/12
FALSE POS ERRORS 0/9
FALSE NEG ERRORS 0/6
QUESTIONS ASKED 210
FOVEA: 37 DB
TEST TIME 05:55

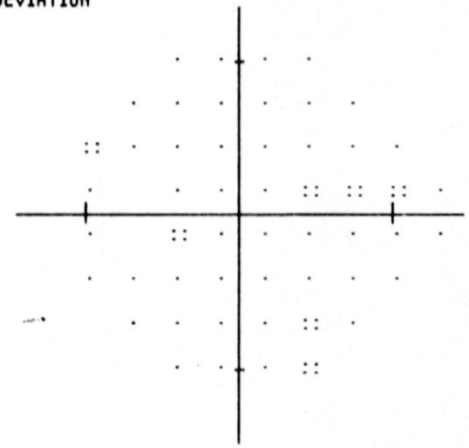
HFA S/N 607-1382

MD - 1.56 DB
PSD 1.96 DB
SF 1.60 DB
CPSD 0.96 DB

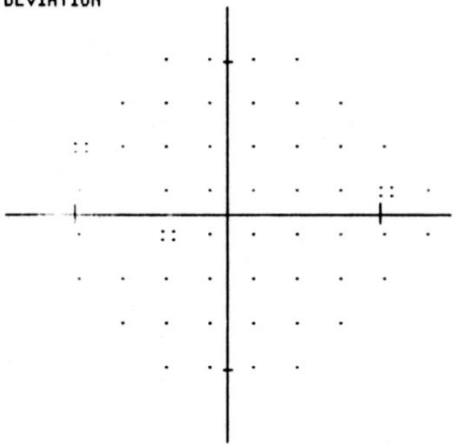




TOTAL DEVIATION



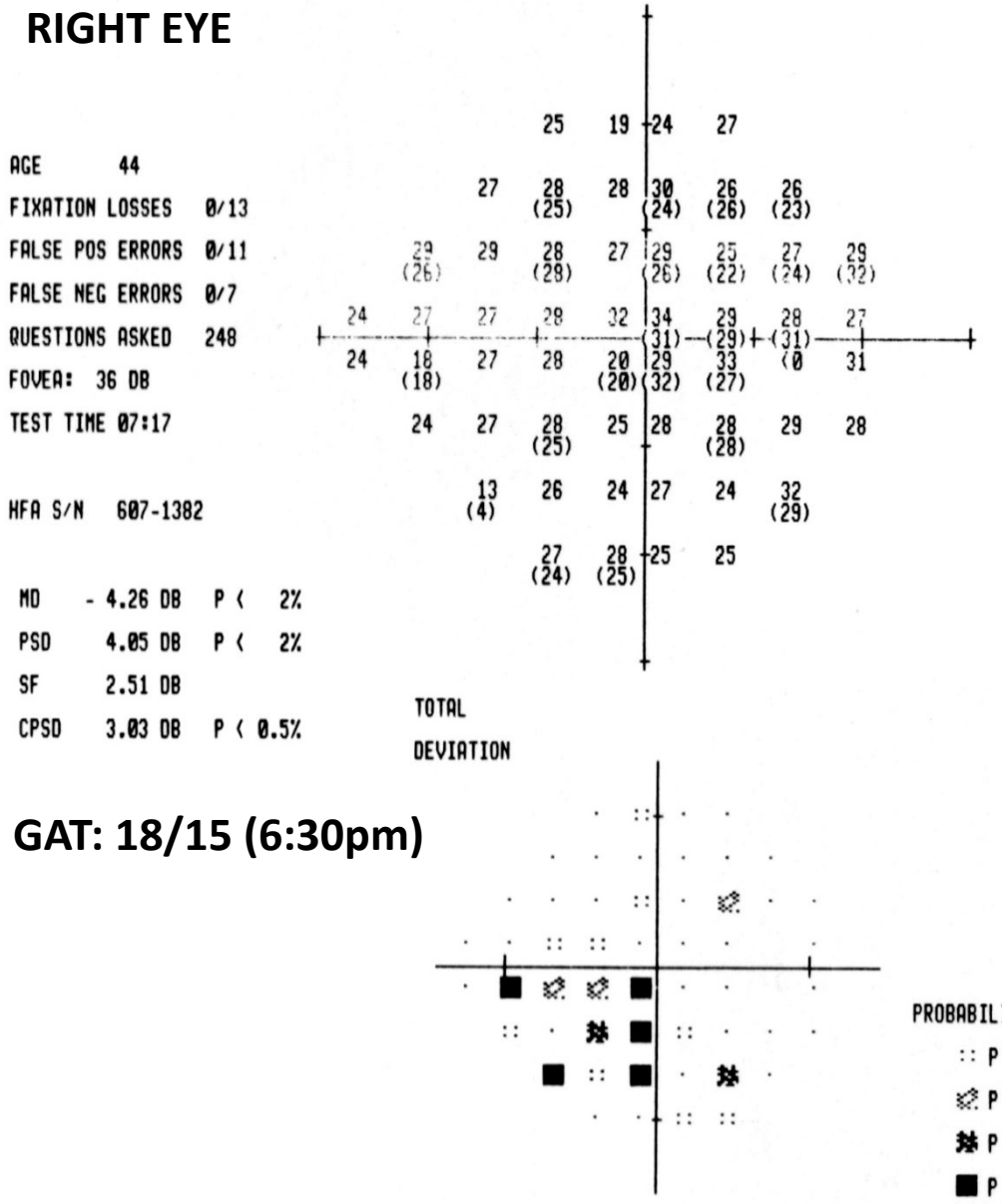
PATTERN DEVIATION

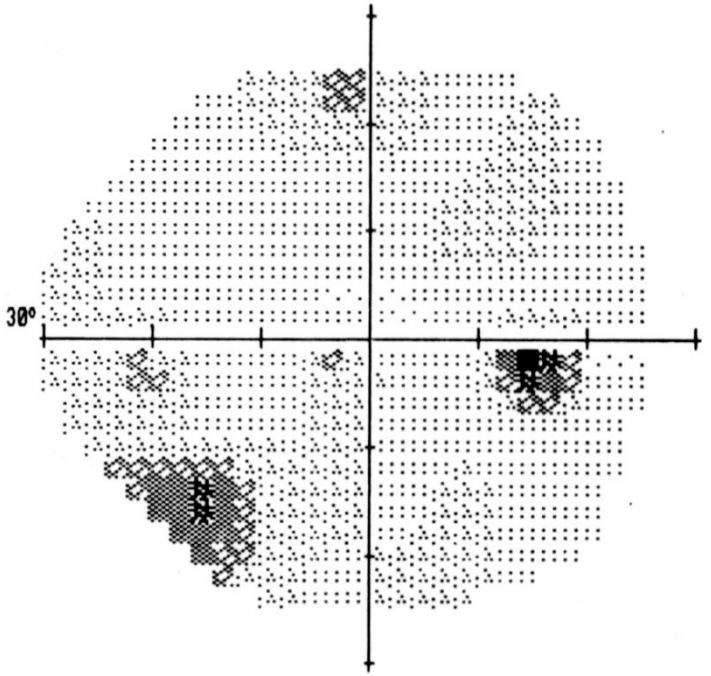


PROBABILITY SYMBOLS

:: P < 5%
P < 2%
P < 1%
■ P < 0.5%

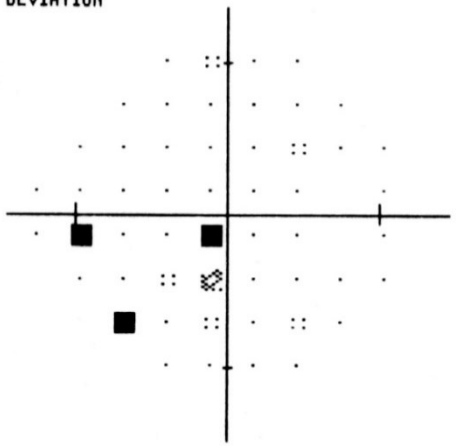
RIGHT EYE





TOTAL DEVIATION

PATTERN DEVIATION



PROBABILITY SYMBOLS

:: P < 5%

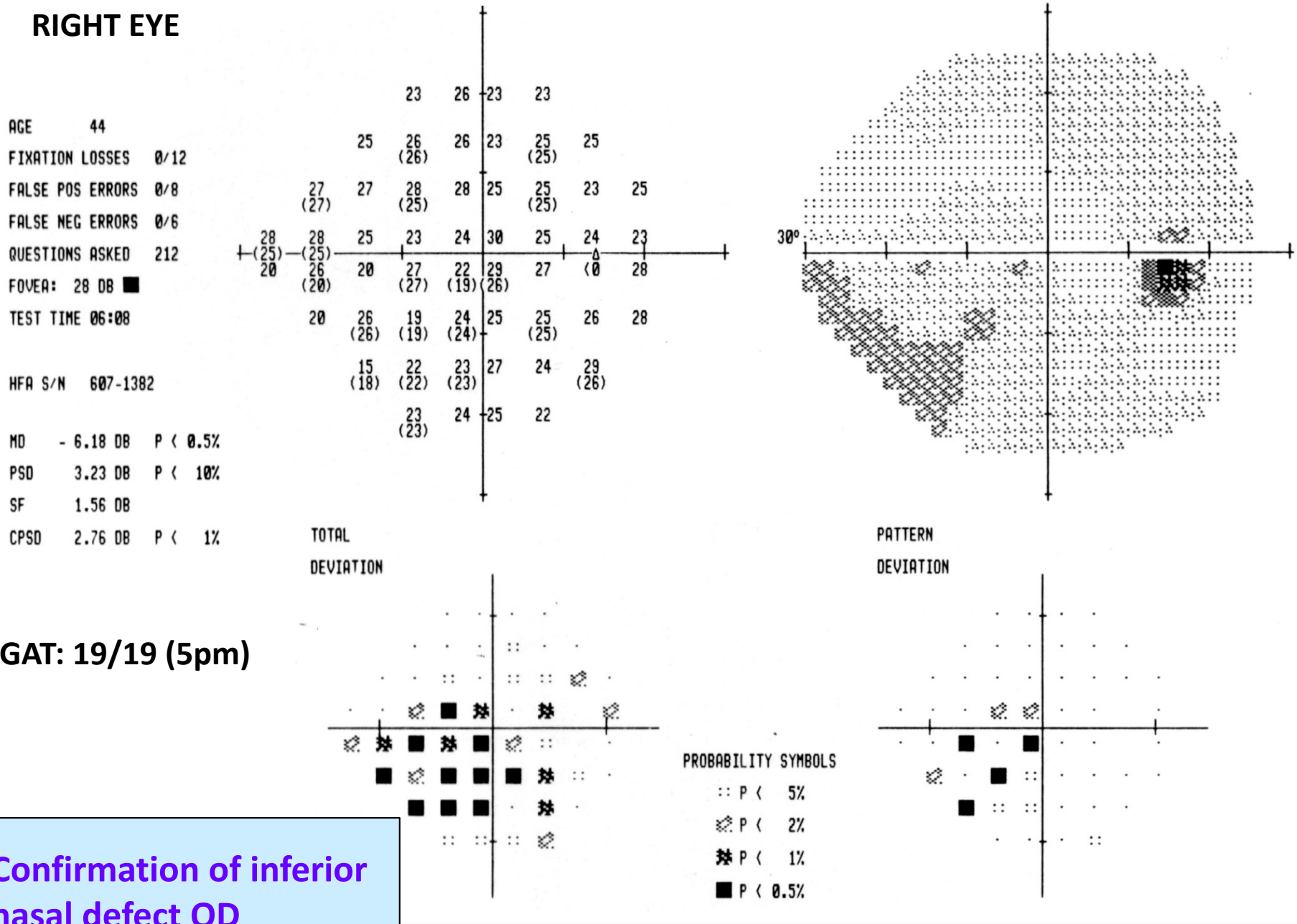
P < 2%

P < 1%

P < 0.5%

GAT: 18/15 (6:30pm)

RIGHT EYE



GAT: 19/19 (5pm)

Confirmation of inferior nasal defect OD

What is it?

ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

What is it?

ONH	X		X		X		X
VF	X		X	X		X	
IOP	X	X				X	X
	POAG	OHT	NTG Neurologic Diurnal IOP	Artifact? Neurologic Retinal	Anomalous ONH? Unreliable VF? Pre-perimetric	Pseudo-normal ONH?	Unreliable VF? Pre-perimetric

- **ONH**: 0.1 difference in CDR. *Not frankly glaucomatous* (obeys ISNT rule). No pallor
- **VF**: Reproducible VF defect, suggestive of inferior nasal step
- **IOP**: Consistently below 21 mmHg

Normal Tension Glaucoma

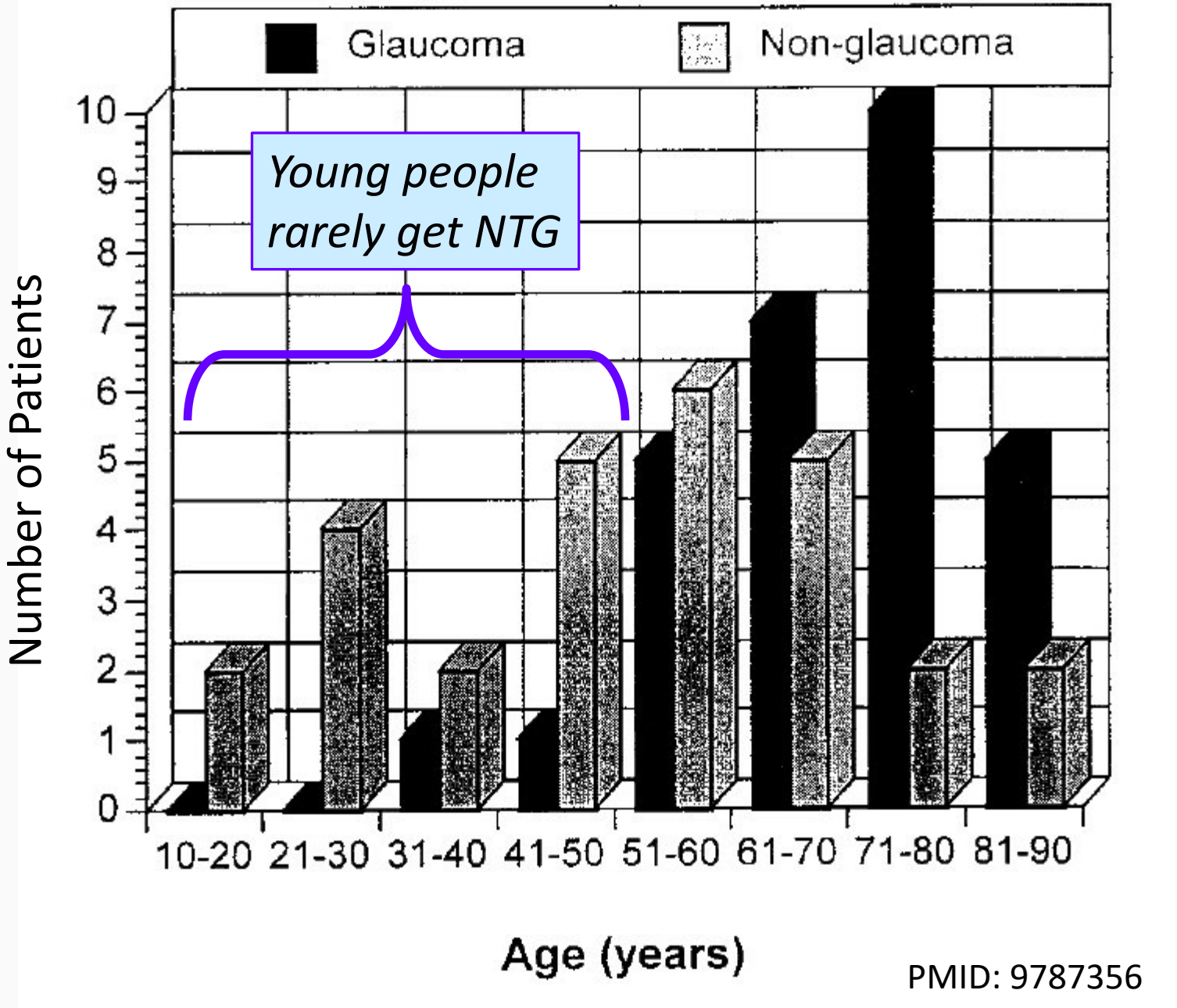
- Differential Diagnosis
  - **NTG**
  - **Undetected high-tension glaucoma**
    - Diurnal variation, Intermittent elevation (eg. subacute ACG), Previous elevation (eg. steroid use, PDS)
    - Tonometric error (thin cornea, S/P LASIK)
  - **Non-glaucomatous causes for VF defect**
    - Optic nerve lesions (eg. retrobulbar optic nerve lesions, anomalous optic disc, disc drusen, AION)
    - Retinal lesions (eg. old retinal vascular occlusions, chorioretinal scars, retinal detachments)

Non-Glaucomatous Cupping

- Physiologic
- Congenital anomalies
- Hereditary optic atrophy
- Ischemia (arteritic > nonarteritic)
- Inflammation
- Toxic/Trauma
- Retrograde degeneration
- Compression

Findings Suggestive of Non-Glaucomatous Optic Neuropathy

- Young age (<50yo)
- VA & color vision loss
- Afferent pupillary defect / Unilateral disease
- Retinal findings (vasc attenuation, exudates)
- Vertically aligned VF defects
- ONH rim pallor / Shallow cupping
- Neurologic abnormalities (HA, diplopia, etc)



PMID: 9787356

Case Report Continued

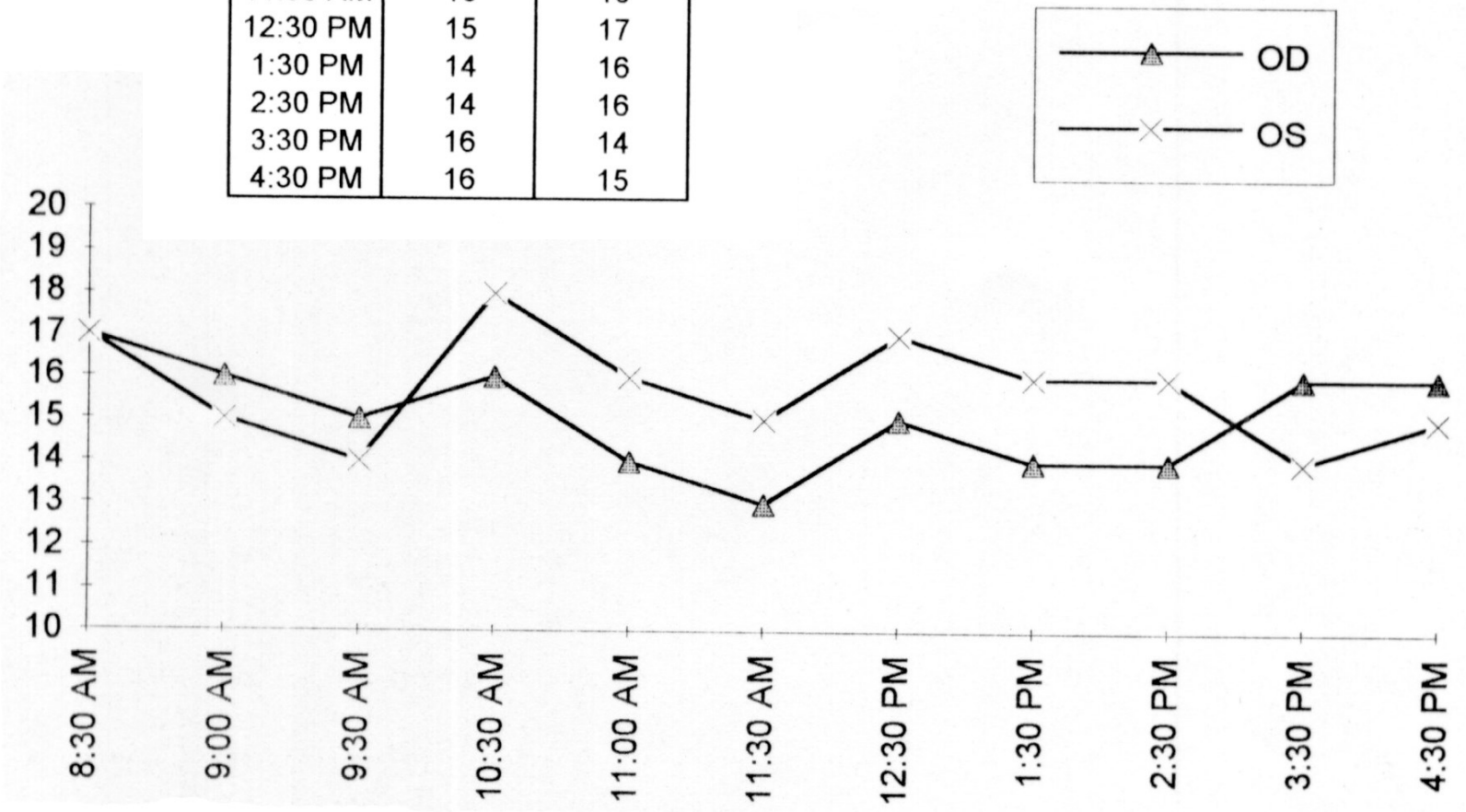
- Ophthalmology consult
  - Hx: No head/eye trauma, (+) migraine HA
  - GAT: 19/19 (3:30pm)
  - Gonio: normal OU
  - Pupils normal
  - Color vision: normal
  - DFE: normal OU, no pallor

  - IMP: Abnormal VF with normal IOP and ONH
  - PLAN: **Get diurnal curve**

Diurnal Curve

APPLANATION TONOMETRY READINGS

TIME	OD	OS
8:30 AM	17	17
9:00 AM	16	15
9:30 AM	15	14
10:30 AM	16	18
11:00 AM	14	16
11:30 AM	13	15
12:30 PM	15	17
1:30 PM	14	16
2:30 PM	14	16
3:30 PM	16	14
4:30 PM	16	15



Diurnal IOP FAQ

- How to monitor diurnal IOP over 24 hours
  - Sleep lab, Triggerfish
  - iCare HOME tonometer

- **Water Drinking Test**
  - NPO 2 hours prior to exam
  - Measure baseline IOP
  - Pt consumes 1L H_2O in <5 min
  - Check IOP every 15 min x 1 hr
  - **IOP peak approximates diurnal peak**

PMID: 28164419

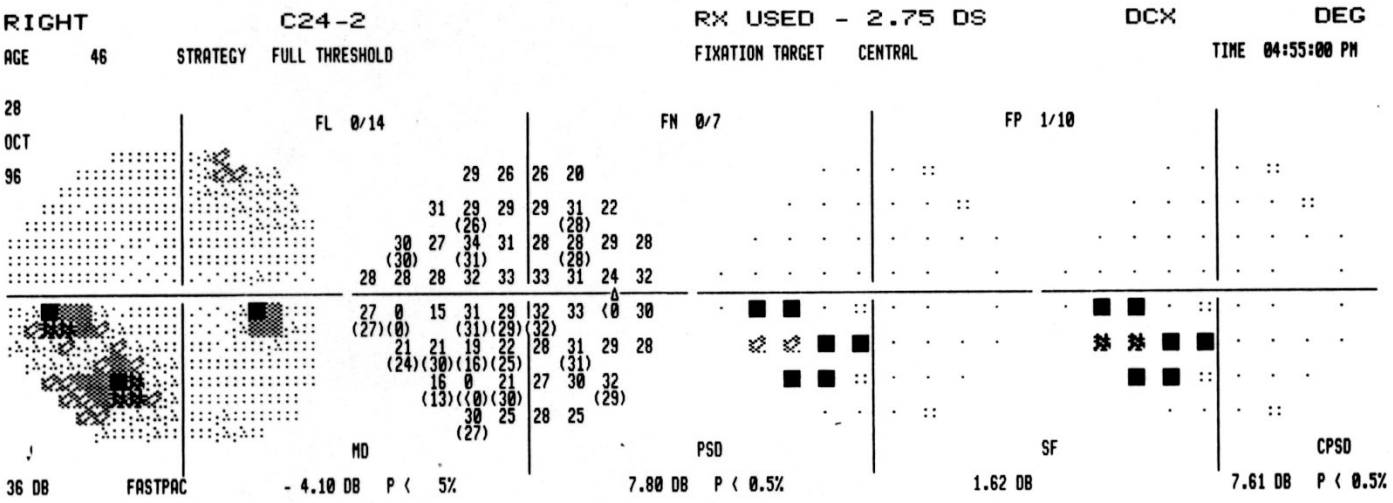
Case Report Continued

- **Lost to follow-up for 2 years**
- Returns with c/o blurry vision
- Vcc
  -4.00-0.75x060 20/40
  -4.75 20/40
- Refraction
  -5.25-1.00x075 **20/30**
  -5.25-0.50x105 **20/20**

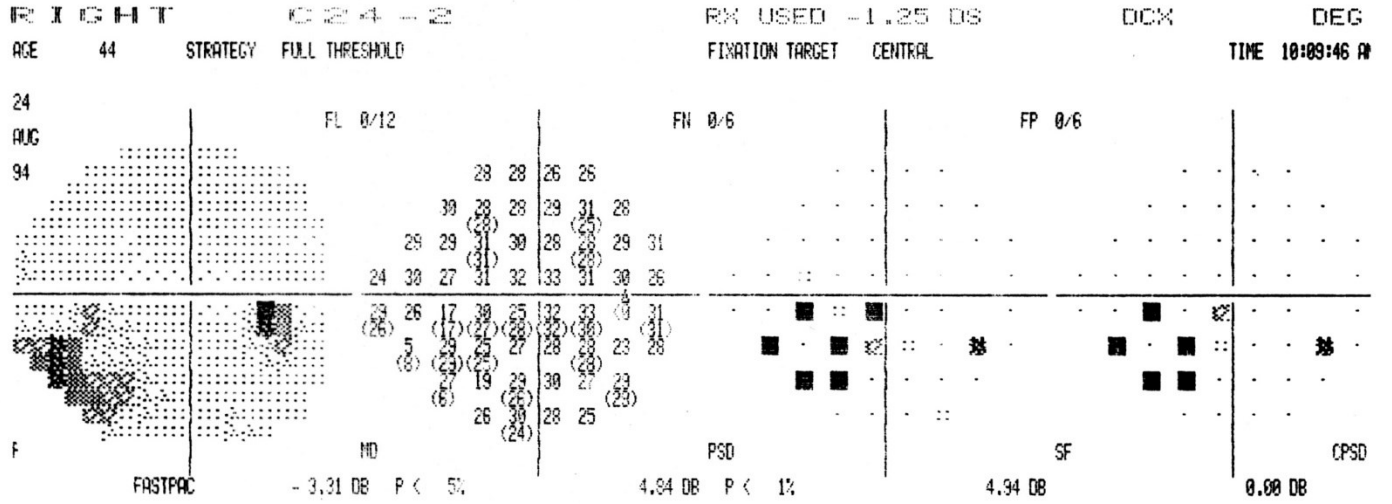
- GAT: 18/18 (3:30pm)
- PERRL, **Trace APD** OD
- C/D: 0.6/0.5

- IMP: Optic neuropathy OD
- Plan: Repeat VF, get CT scan

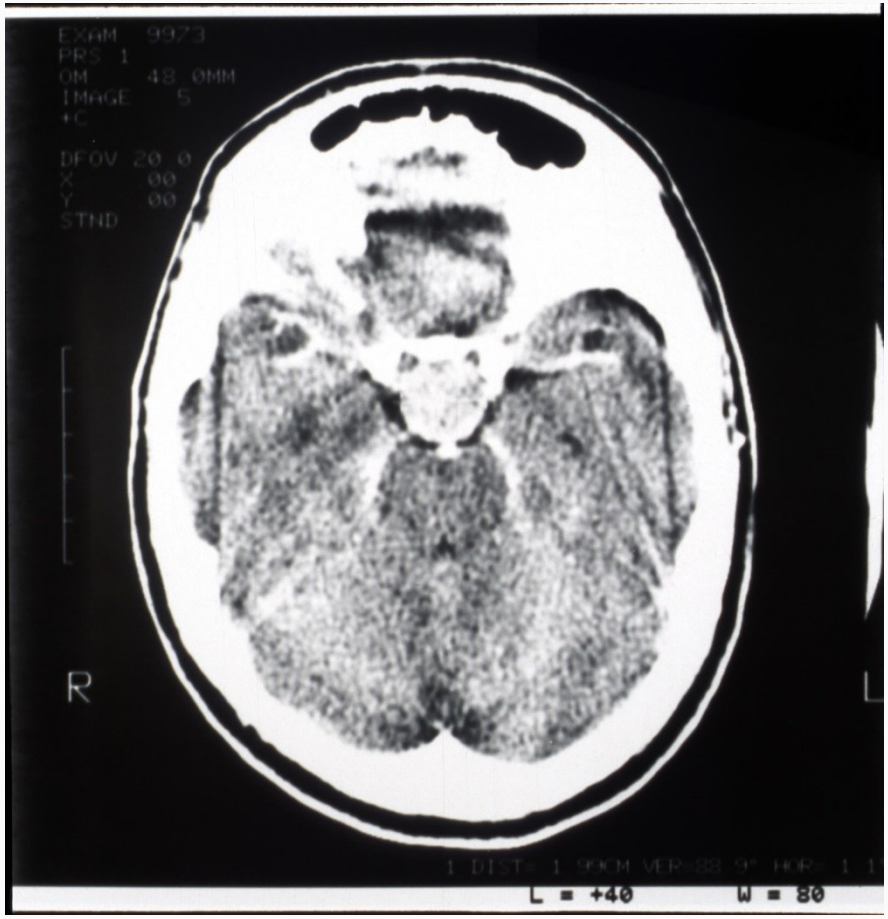
1996

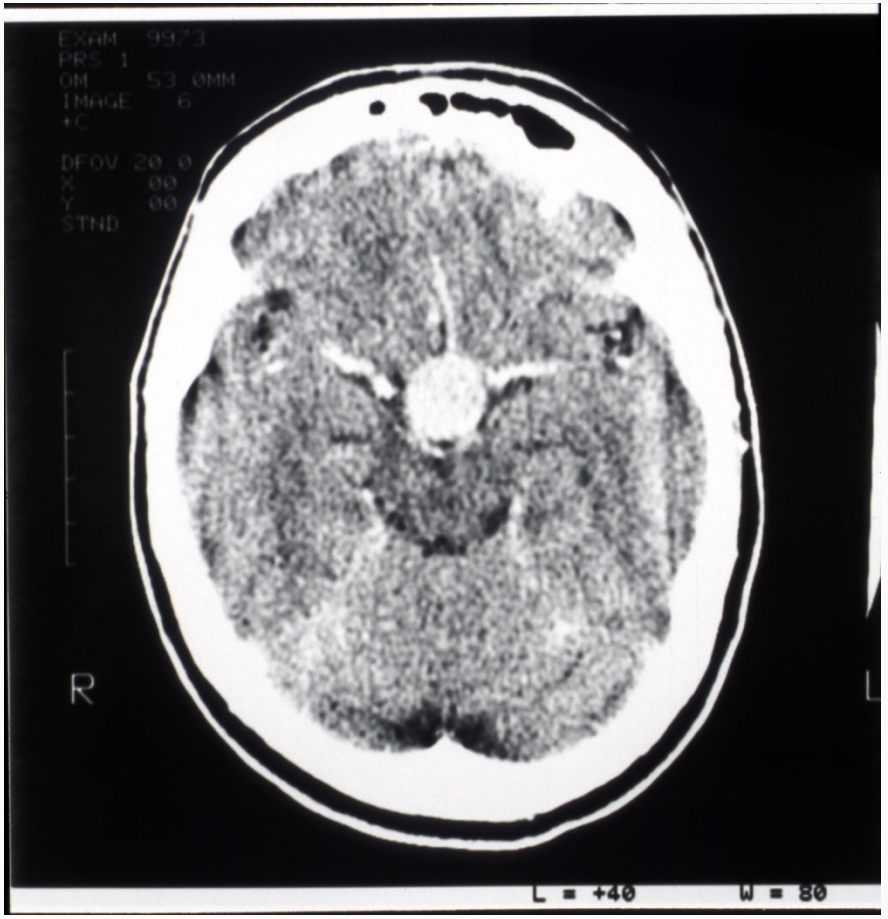

RIGHT
C24-2
RX USED - 2.75 DS
DCX
DEG
AGE 46
STRATEGY FULL THRESHOLD
FIXATION TARGET CENTRAL
TIME 04:55:00 PM
28 OCT 96
FL 0/14
FN 0/7
FP 1/10
MD
PSD
SF
CPSD
36 DB
FASTPAC
- 4.10 DB P < 5%
7.80 DB P < 0.5%
1.62 DB
7.61 DB P < 0.5%

1994


RIGHT
C24-2
RX USED -1.25 DS
DCX
DEG
AGE 44
STRATEGY FULL THRESHOLD
FIXATION TARGET CENTRAL
TIME 10:09:46 AM
24 AUG 94
FL 0/12
FN 0/6
FP 0/6
MD
PSD
SF
CPSD
FASTPAC
- 3.31 DB P < 5%
4.94 DB P < 1%
4.94 DB
0.00 DB

CT Scan





Pituitary adenoma.

Non-Glaucomatous Cupping

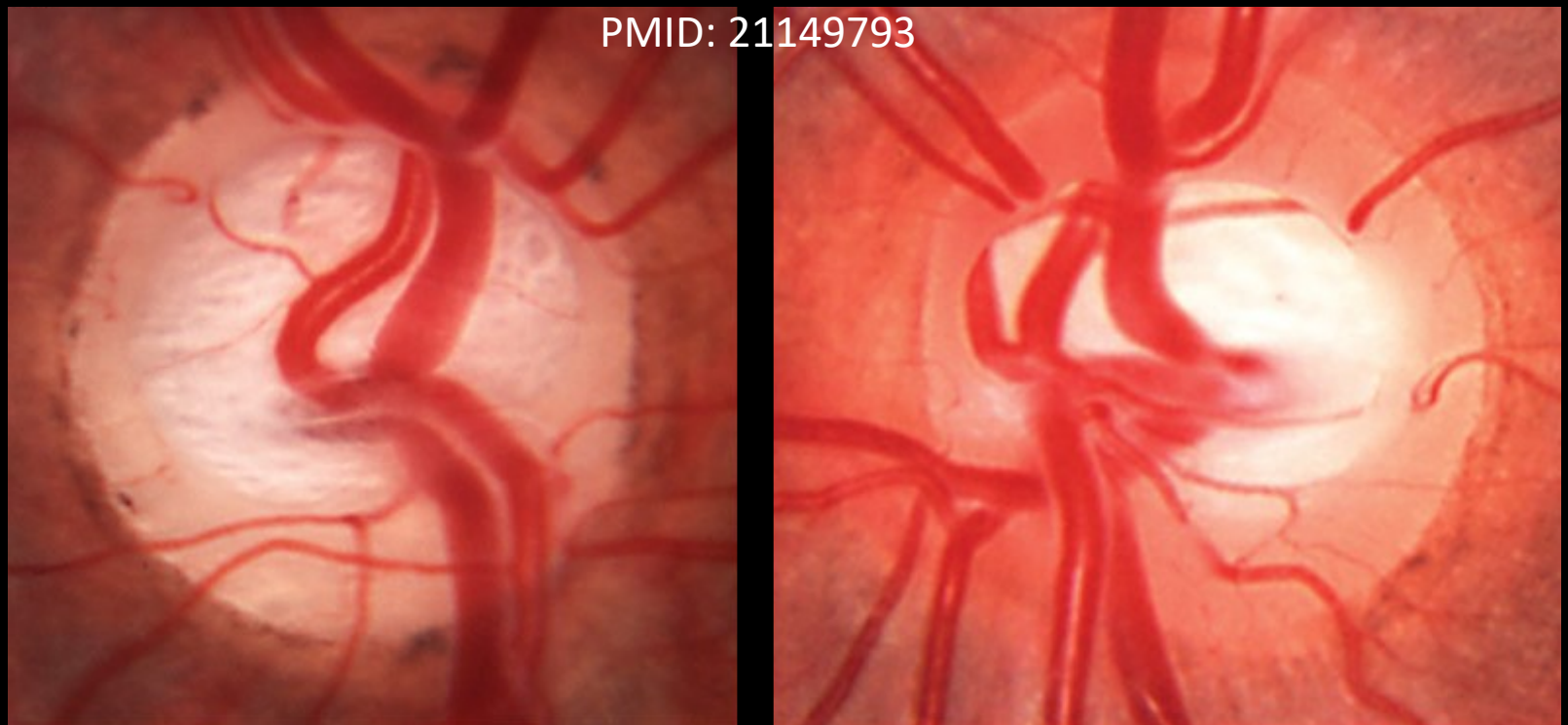
- Physiologic
- Congenital anomalies
- Hereditary optic atrophy
- Ischemia (arteritic > nonarteritic)
- Inflammation
- Toxic/Trauma
- Retrograde degeneration
- Compression ← **pituitary adenoma**

Band (or bow-tie) pattern of pallor is characteristic of optic tract and chiasmal lesions

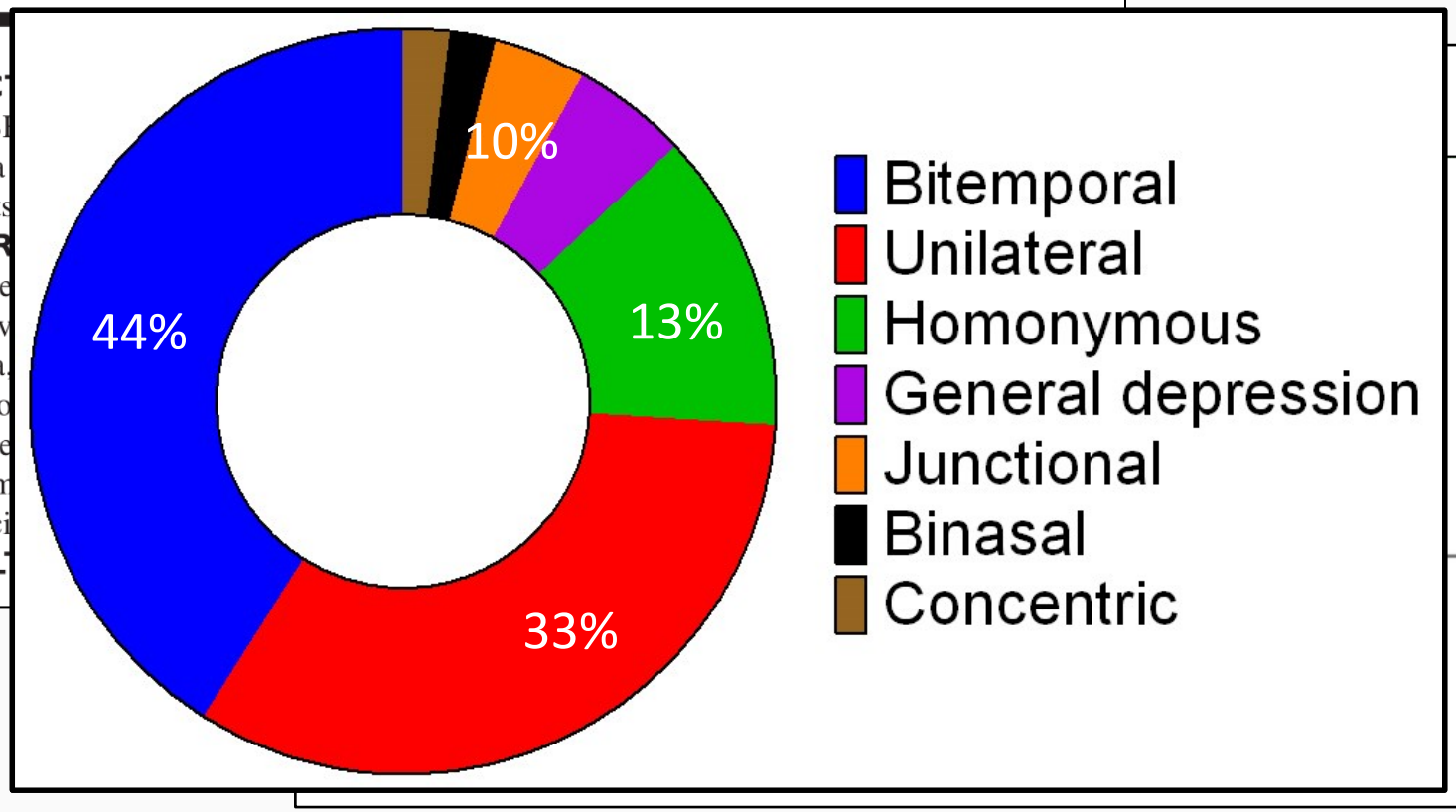
PMID: 23964192

Enlarged optic cupping with tumor compressing chiasm and right optic nerve

PMID: 21149793



Visual Defects in Patients With Pituitary Adenomas: The Myth of Bitemporal Hemianopsia



Bitemporal hemianopia accounts for ≈40% of VF defects caused by chiasmal compression

PMID: 26496573, 23563861

When Should I Order an MRI?

Findings that increase the likelihood of an intracranial mass lesion

- **Age <50yrs**
  - NTG is rare in young people
- **VA worse than 20/40**
  - Beware unexplained reduction in BVA
- **Vertically aligned visual field defects**
  - Glaucomatous defects do not respect the vertical
- **Optic disc pallor**

PMID: 9787356

Take Home Messages

- **Be a skeptic**
  - NTG is a diagnosis of exclusion
- **Embrace uncertainty**
  - You may never know if you have made the correct diagnosis
  - Did the 50% of NTG suspects that never showed progression have glaucoma, or something else?
- **Know the indications for neuroimaging**
  - Age < 50yo, vertically aligned VF defects, unexplained loss of VA, ONH pallor

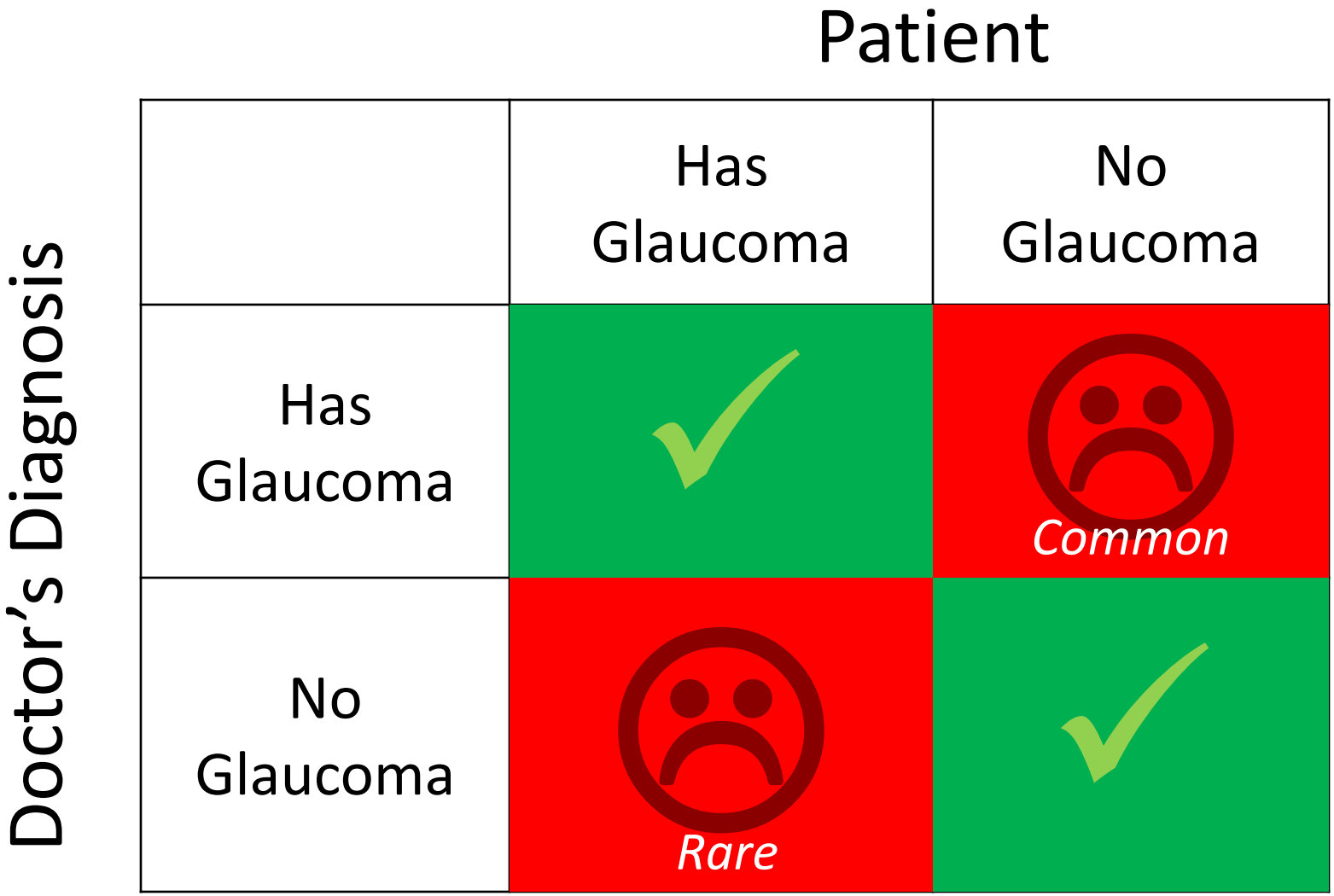
PITFALLS IN THE DIAGNOSIS OF GLAUCOMA

False Positive Diagnosis of Glaucoma

Rick Trevino, OD, FAAO

Indiana University School of Optometry

What is a False Positive Diagnosis?



Are False Positive Diagnoses a Problem Worth Worrying About?

- **Patients misdiagnosed with glaucoma** or as a glaucoma suspect may be subjected to many years of unnecessary treatment and/or surveillance
  - Economic costs: Medications, office visits, time off work, laser procedures
  - Patient safety: Adverse effects & complications of therapy
  - Psychological trauma: Fear of blindness

How Common are False Positive Diagnoses of Glaucoma?

- No data from USA
  - All published studies are from countries with single-payer national health insurance schemes
- Definition of false positive referral
  - **Pt is discharged by the glaucoma specialist after the first visit** without a diagnosis of glaucoma and without future follow-up visits scheduled
  - **Glaucoma suspects** are not considered false positive (they are typically given follow-up appointments)

How Common are False Positive Diagnoses of Glaucoma?

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DOI: 10.1111/opo.13183

OPO THE COLLEGE OF OPTOMETRISTS

REVIEW ARTICLE

Assessment of optometrists' referral accuracy and contributing factors: A review

Josie Carmichael[1,2] | Sarah Abdi[1] | Konstantinos Balaskas[2] | Enrico Costanza[1] | Ann Blandford[1]

2023 review article
All studies from UK

Relevance to USA?

PMID: 37395045

		CASES	FP	
1	Huang (2020)	74	19	26%
2	Sii (2019)	312	91	29%
3	Kamel (2019)	98	35	36%
4	Annoh (2019)	715	156	22%
5	Founti (2018)	28	12	43%
6	Kahn (2012)	102	31	30%
7	Lockwood (2010)	441	257	58%
8	Salmon (2007)	1106	531	48%
9	Bowling (2005)	2506	1148	46%
		5382	**2280**	**42%**

26%

47%

How Common are False Positive Diagnoses of Glaucoma?

- Keenan (2014) – Australia 
  - Retrospective review of glaucoma referrals by specially trained ODs between 2010 and 2013.
    - ODs underwent didactic and clinical training in the Glaucoma Clinic and were required to have automated perimetry, pachymetry and optic disc photography

Glaucoma	Glc Suspect	OHT	Other	Normal	Total
153 (8.8%)	185 (10.7%)	113 (6.5%)	192 (11.1%)	1090 (62.9%)	1733

26%

PMID: 25070417

How Common are False Positive Diagnoses of Glaucoma?

- Verma (2014) – Canada 
  - Retrospective study of referrals to a teleglaucoma program in Alberta from 2008-2012
  - Referring practitioners completed a training session on glaucoma diagnosis.

Glaucoma	Glc Suspect	Normal	Total
77 (31.2%)	104 (42.1%)	66 (26.7%)	247

  - Conclusion: A key factor for success is using stringent referral criteria

PMID: 24767217

How Common are False Positive Diagnoses of Glaucoma?

- Founti (2018) – UK 
  - Prospective study of 50 consecutive referrals to a glaucoma specialist
  - **Optometrist** referrals: **43%** false positive
  - **Ophthalmologist** referrals: **50%** false positive
  - Overall, only 10% of newly referred patients had glaucoma
  - 32% of referrals were due to elevated IOP only
  - Conclusion: Elevated IOP only is a poor predictor of glaucoma

PMID: 28774936

How Common are False Positive Diagnoses of Glaucoma?

- False positive diagnoses of glaucoma are a **common problem**
  - Affects both ODs and general ophthalmologists
- **What should the false positive rate be?**
  - No consensus. Lowest report is 22%
- **Problems associated with attempts to decrease the false positive rate**
  - More false negatives (missed glaucoma)
  - Reason for current false positive rate is unclear

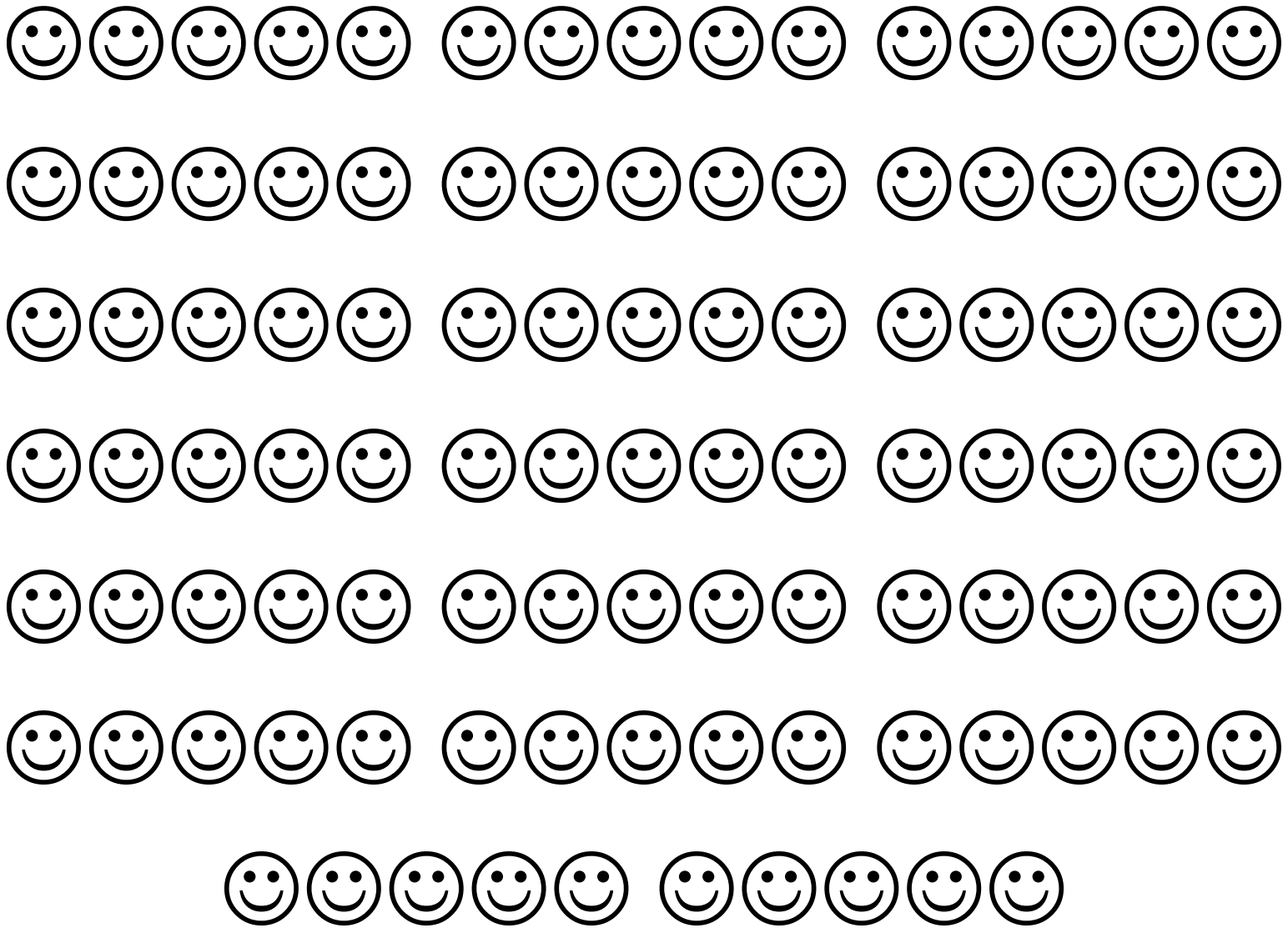
Why is the False Positive Rate so High?

1. Low prevalence of glaucoma
2. Medicolegal pressure
3. Financial and time constraints
4. Clinical skills required for glaucoma diagnosis
5. Excessive reliance on technology
6. Clinical decisions made on the basis of a single abnormal finding

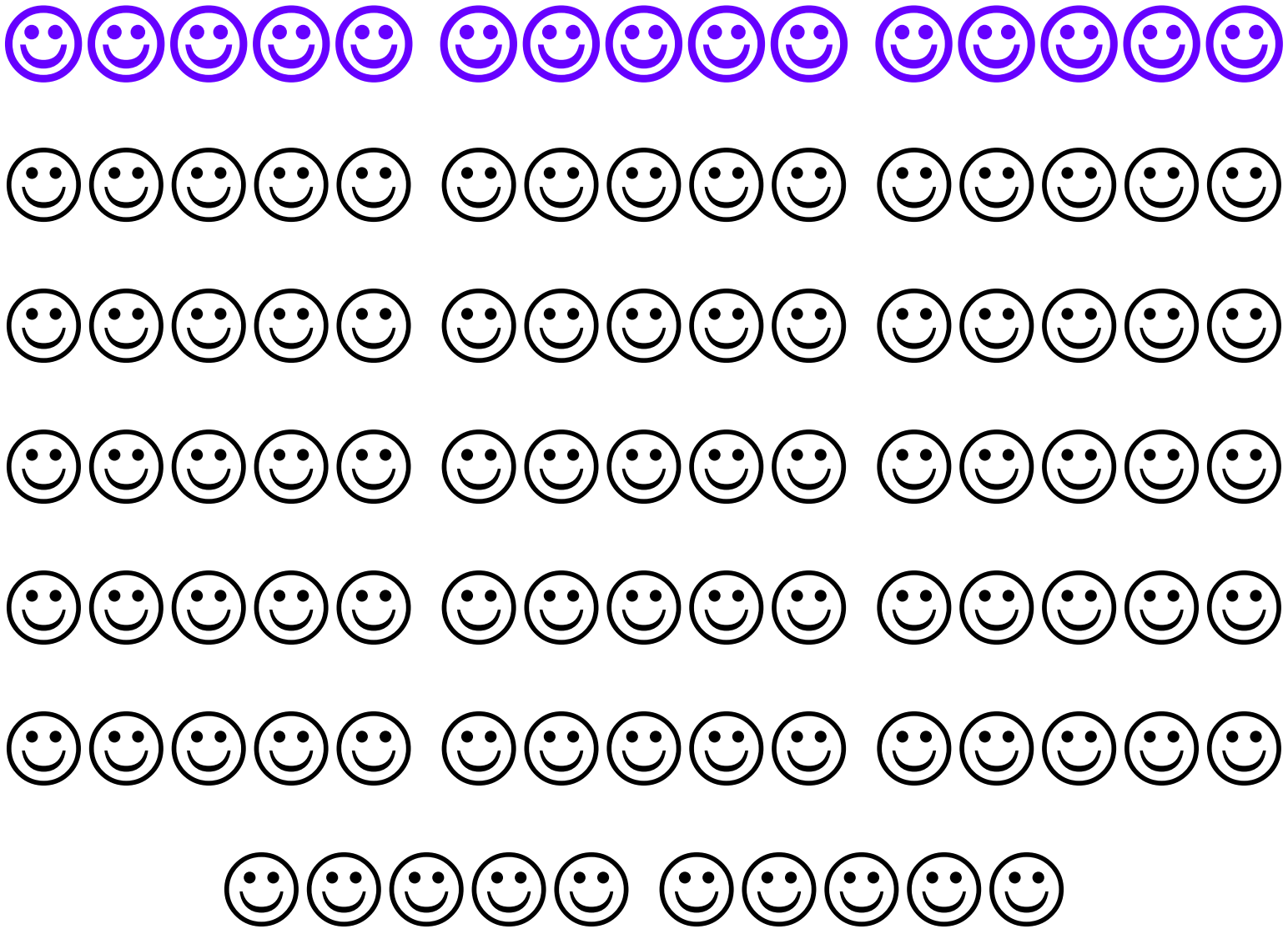
Low Prevalence of Glaucoma

- Diagnosing glaucoma is difficult
  - No pathognomonic sign of glaucoma
- **Findings we associate with glaucoma have a certain prevalence in the normal population**
- Because glaucoma is so rare (2-3%), these suspicious findings will turn up ***more frequently*** in normal people than in glaucoma patients

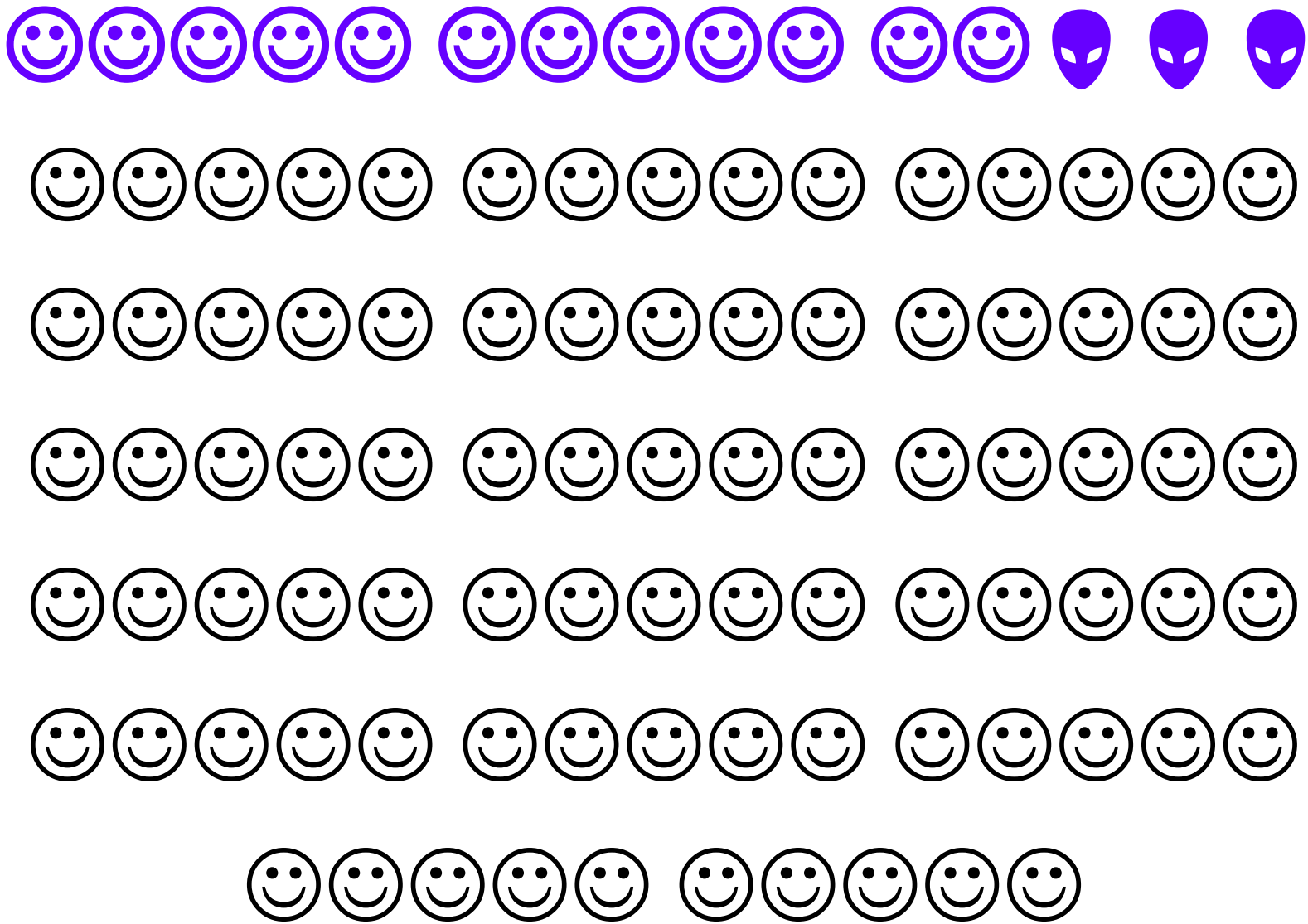
Random Sample of 100 People from the General Population



15 people will have an optic disc that violates the ISNT Rule



80% of the people with an ISNT Rule violation are normal



Medicolegal Pressure

- The most common source of lawsuits against optometrists involve misdiagnosis or missed diagnosis of glaucoma
- **Defensive Medicine**
  - The incentive to aggressively diagnose glaucoma is greater than the incentive to take a more conservative approach

Financial & Time Constraints

- For some practitioners, there are incentives to refer patients with suspicious findings rather than doing a complete work-up themselves
  - Retail settings, optometric specialty practices (contact lens, low vision, etc)
- **Most commonly cited barrier to glaucoma detection**
  - Survey of 1,680 ODs in the UK
  - Cited by 50-60% of ODs

PMID: 21205271

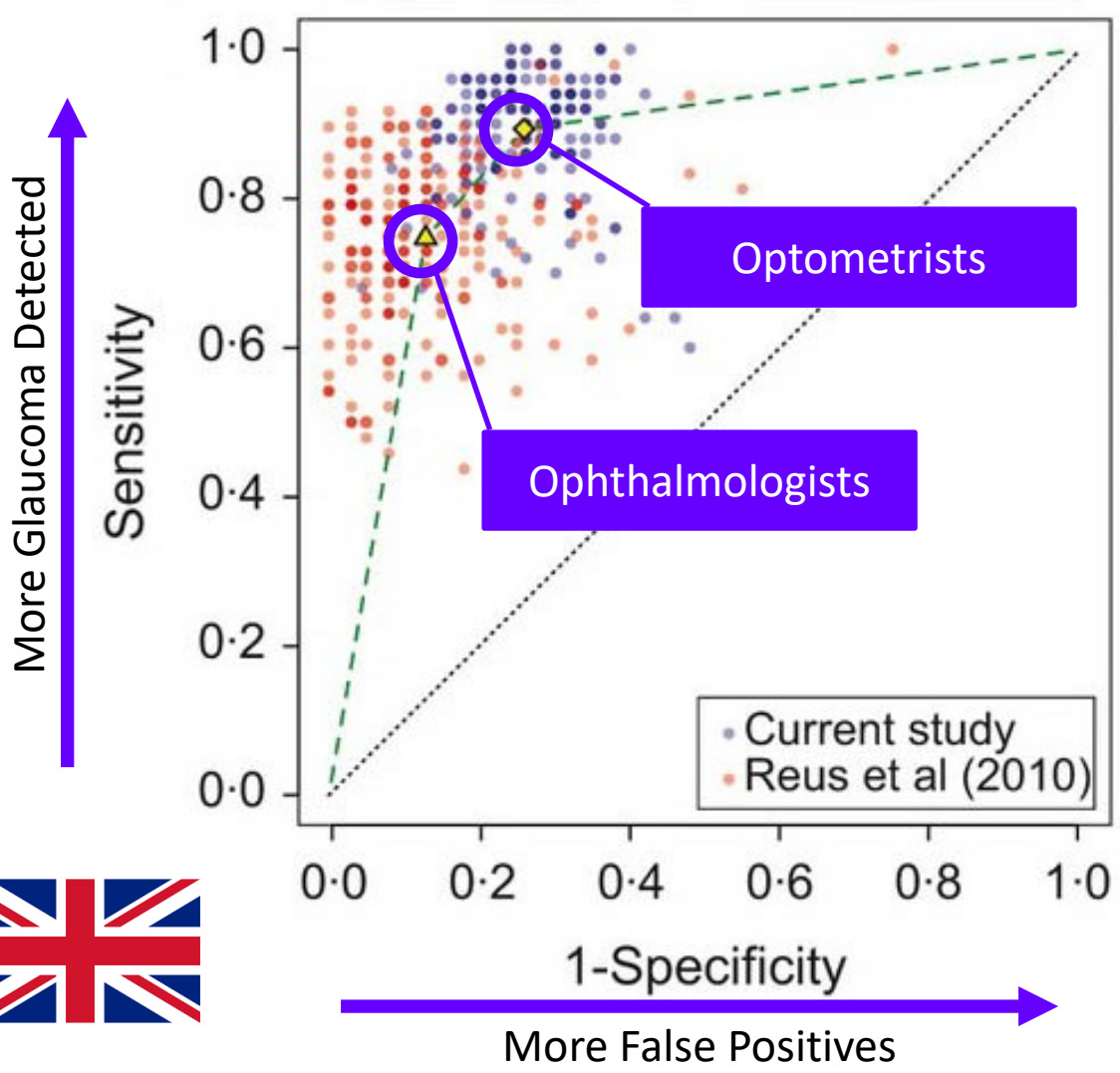
Clinical Skills

- **How well are ODs able to identify signs of glaucoma?**
  - How good are they at detecting abnormality (**sensitivity**) and normality (**specificity**)
- Abrams (1994)- USA  (PMID: 7936564)
  - Compare interpretation of 75 stereo ONH photos

ONH Assessment	OD (n = 6)	OMD (n = 6)	Residents (n = 6)
Sensitivity	56%	78%	78%
Specificity	53%	60%	47%

  - Conclusion: OMDs are more sensitive at detecting glc. **All had poor specificity (high false positives)**

Clinical Skills



Assessment of 110 stereophotos by 208 ODs and 243 OMDs to detect glaucoma. **ODs correctly identified more glaucoma cases than OMDs**, but also had more false-positives (Hadwin, 2013)

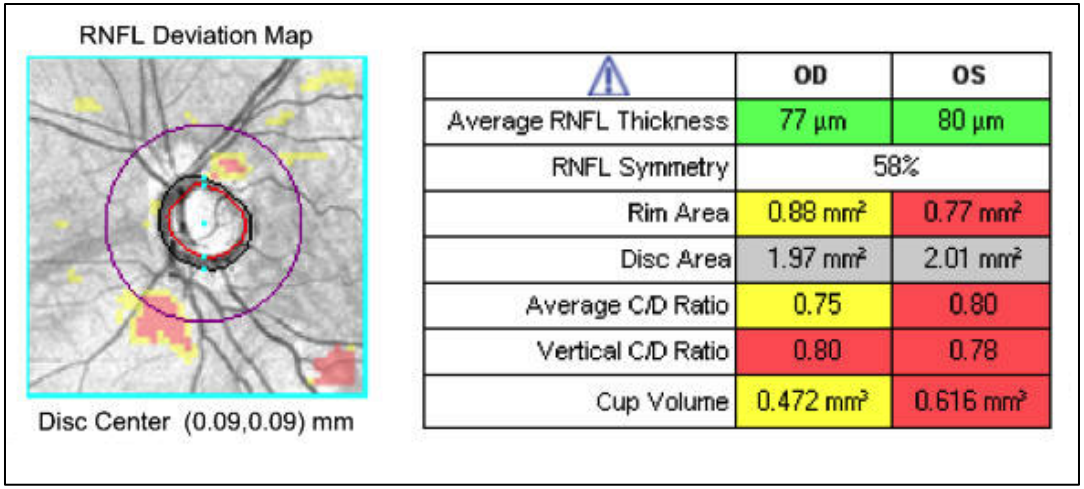
PMID: 23634792

Clinical Skills

- How well are ODs able to identify signs of glaucoma?
  - **Studies indicate that ODs perform at least as well as general OMDs**
  - **Optometrists tend to favor sensitivity over specificity in their diagnostic evaluation**
  - Conclusion: Optometric clinical skills are probably **not a major factor** in the high false positive glaucoma diagnosis rate

Excessive Reliance on Technology

- "Red Disease" vs Glaucoma
  - **Growing reliance on technology** to determine whether a patient is normal (imaging, perimetry)
  - **When an instrument has documented an apparent abnormality, doctors are unlikely to ignore it**
  - Rigorous highly sensitive screening tests can lower overall referral accuracy as it produces a high number of false positive results



	OD	OS
Average RNFL Thickness	77 µm	80 µm
RNFL Symmetry	58%	
Rim Area	0.88 mm²	0.77 mm²
Disc Area	1.97 mm²	2.01 mm²
Average C/D Ratio	0.75	0.80
Vertical C/D Ratio	0.80	0.78
Cup Volume	0.472 mm³	0.616 mm³

Clinical Decisions Made on the Basis of a Single Abnormal Finding

- There is a great deal of overlap between findings that are associated with glaucoma and those that occur in the normal population
  - Examples: Cup-Disc ratio, IOP, ISNT rule
- A comprehensive eye exam will likely uncover many normal individuals with at least 1 suspicious finding
- **Patients with 2 or more suspicious findings are more likely to have glaucoma**

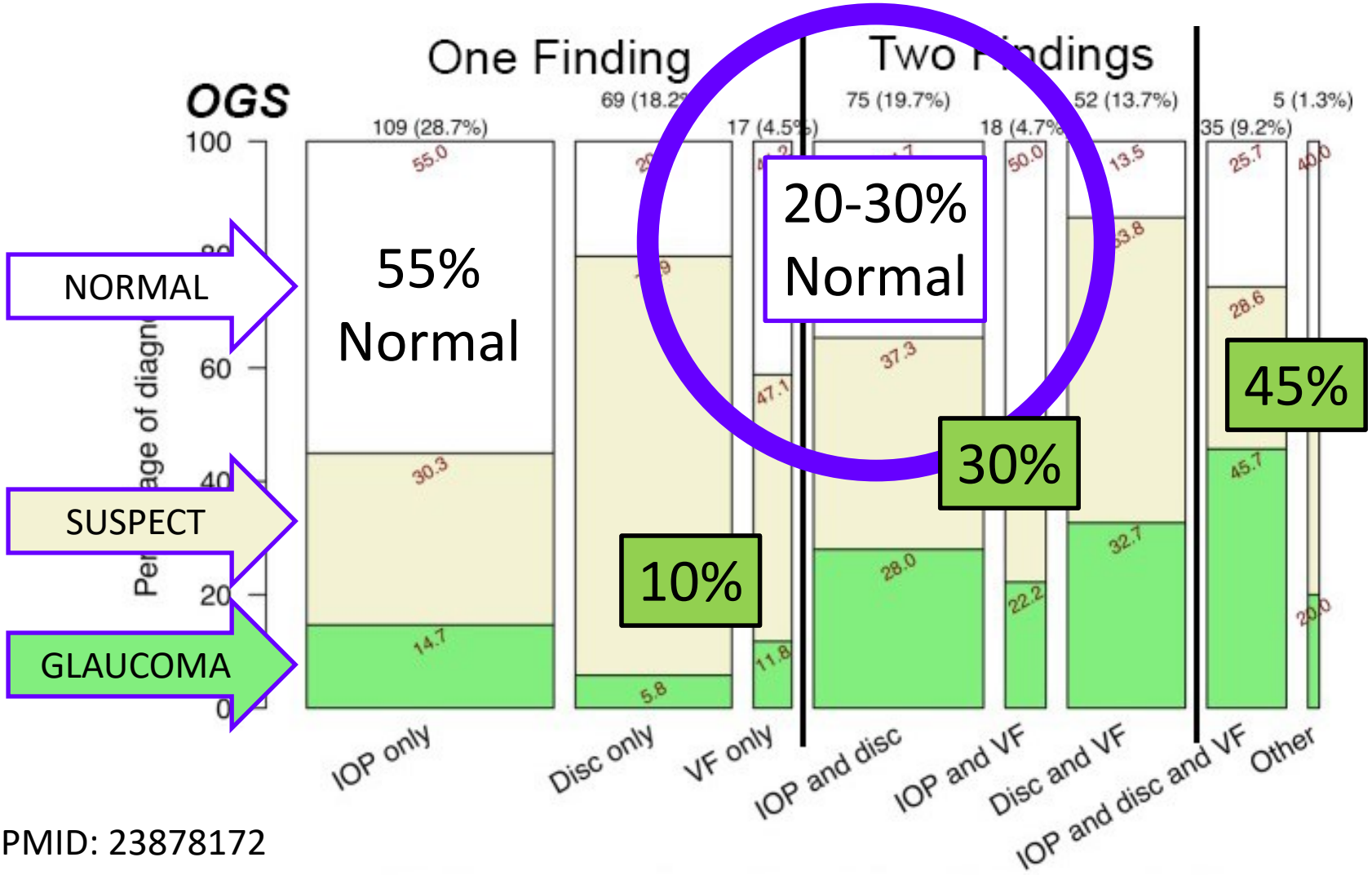
Clinical Decisions Made on the Basis of a Single Abnormal Finding

- Ratnarajan – UK  (PMID: 23878172)
  - Retrospective analysis of 1,086 glaucoma referrals from ODs, comparing those with special training in glaucoma ("optometric glaucoma specialists") to those without

	Non-OGS	OGS
Total referrals	703	380
False positive rate	473 (67.3%)	134 (35.3%)
Dx with glaucoma	66 (9.4%)	81 (21.3%)
P	<0.0001	

OGS's had 23% more glaucomas detected with 45% fewer referrals

Clinical Decisions Made on the Basis of a Single Abnormal Finding



PMID: 23878172

Clinical Decisions Made on the Basis of a Single Abnormal Finding

- Ratnarajan – UK

  - Conclusions
    - Multiple criterion referrals resulted in a higher percentage of patients being diagnosed with glaucoma
- Bottom Line…
  - **IOP is a very poor indicator of glaucoma**
  - **Glaucoma more likely to be present in patients with >1 abnormal finding**

PMID: 23878172

Why is the False Positive Rate so High?

1. Low prevalence of glaucoma
2. Medicolegal pressure
3. Financial and time constraints
4. Clinical skills required for glaucoma diagnosis
5. Excessive reliance on technology
6. Clinical decisions made on the basis of a single abnormal finding

All of the above appear to contribute

How to Minimize False Positive Diagnosis of Glaucoma

1. **Glaucoma diagnostic skills improve with training and experience**
   - General OD has similar skill level as general OMD
   - ODs with more glaucoma experience improve in specificity and overall diagnostic accuracy
2. **Balance sensitivity and specificity**
   - Beware of “Red Disease”
   - Do not start treatment until confident of the diagnosis
3. **Search for multiple signs of the disease**
   - IOP alone has extremely high false positive rate
   - ONH appearance has highest specificity

Thank you!