

### When the Pressure is On Get an OCT: A Guide to Retina and Glaucoma

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1

### Mark Dunbar: Disclosure 24 months

- Optometry Consultant/Advisory Board
  - Carl Zeiss
  - Allergan
  - Regeneron
  - Iveric
  - Orasis
  - Visus
  - Tarsus
  - Avellino

Mark Dunbar does not own stock in any of the above companies

2

### JESSICA STEEN FINANCIAL DISCLOSURES 24 MONTHS

- Speaker-Carl Zeiss Meditec, Bausch and Lomb, Oyster Point Pharma
- Advisory Board-Bausch and Lomb, Santen, Peripherex, Ocuphire, OcuTerra, Oyster Point Pharma
- Shareholder-Clearside Biomedical (<0.01% ownership)

▪ All relevant relationships have been mitigated

3

### Reports

1991

**Optical Coherence Tomography**

DAVID Hwang, ERIC A. SWANSON, CHARLES F. J. LIU, JIM S. SCHULTEIS, WILLIAM G. STROBE, WARREN CHANG, MELISSA J. HUB, THOMAS FEITZ, KRISTIN GRABERY, CARRIE A. PULIAFITO, JAMES G. FUERNBERG\*

A technique called optical coherence tomography (OCT) has been developed for noninvasive cross-sectional imaging in biological systems. OCT uses low-coherence interferometry to produce a two-dimensional image of optical scattering from internal tissue microstructures in a way that is analogous to ultrasonic pulse-echo imaging. OCT has longitudinal and lateral spatial resolutions of a few micrometers and can detect reflected signals as small as  $\sim 10^{-18}$  of the incident optical power. Tomographic imaging is demonstrated in vitro in the primate retina and in the coronary artery, two clinically relevant examples that are representative of transparent and turbid media, respectively.

4

OCT 1: 1996

OCT 3: Stratus 2000

SD OCT: 2007

5

### OCTA and Swept Source OCT

6

### The Evolution of OCT Imaging

- OCT has changed how clinicians look at the retina
- OCT has changed how we manage glaucoma
- The assessment of retinal abnormalities and glaucoma based on OCT imaging has advanced eye care
- OCT in Optometry practices ~ 70-85%
- As the technology has evolved -> prices continue to come down

7

### Advances in SD-OCT

- Improving software
- **Faster – virtual angiography**
- Noise reduction/over sampling technology
- Wider and deeper scans
- Greater density in the scans
- Improvements in 3D imaging
- Enhanced depth imaging – imaging choroid
- Progression analysis software

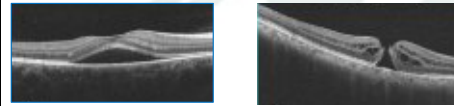
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### Understanding the Fundamentals

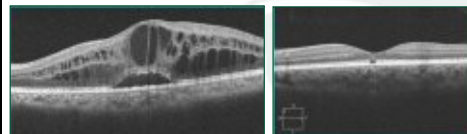
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### Don't Make It More Complicated Than it Needs to be

- Many macular disease conditions have a "signature" OCT feature
- Learn what those are and the diagnosis and interpretation becomes easier

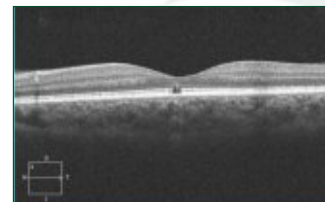


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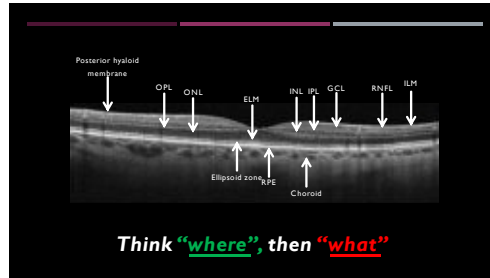


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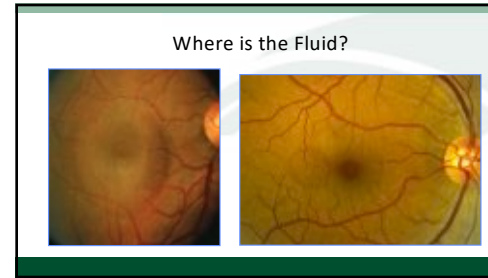
### What does This patient have?



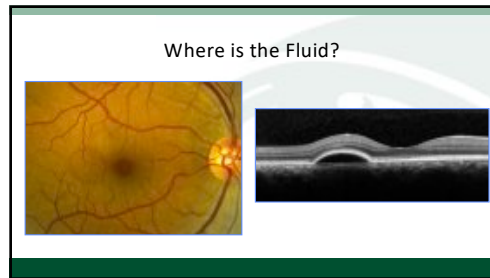
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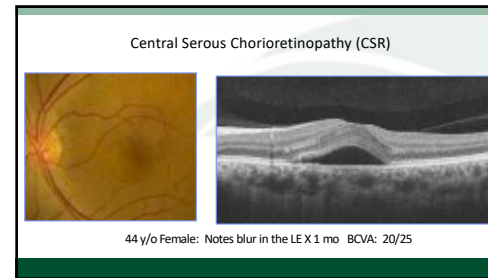
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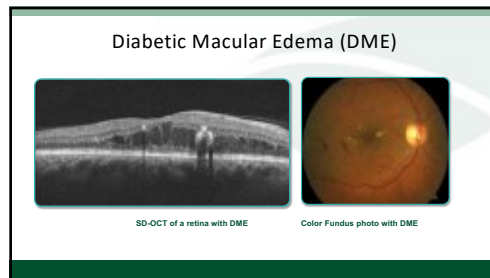
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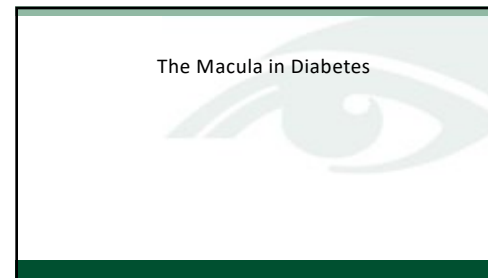
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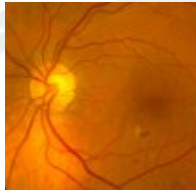
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18

### The Macula in Diabetes

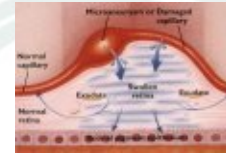
- Is there retinopathy?
- Is there retinal thickening?
- Is there fluid?
- How close is it to the macula?



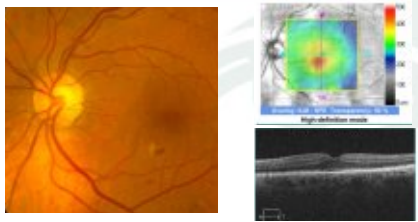
19

### Macular Edema

- Thickening of the retina
- Secondary to leaky microaneurysms
- **90% of visual loss in diabetes**




20



21

### CSME

- Retinal thickening within 500 microns from the center of the FAZ
- Hard exudates associated with retinal thickening 500 microns from center of FAZ
- Zones of retinal thickening > 1 DD in area, any part of which is 1 DD from the center of the fovea



22

### How we diagnose diabetic macular edema is changing

ETDRS definition has been modified in the era of OCT and anti-VEGF therapy

23

### Diabetic Macular Edema (DME)

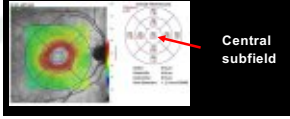
- CSME
- Center involved vs. Not center involved

24

### 2017 DME Classification:

Center Involved or Not?

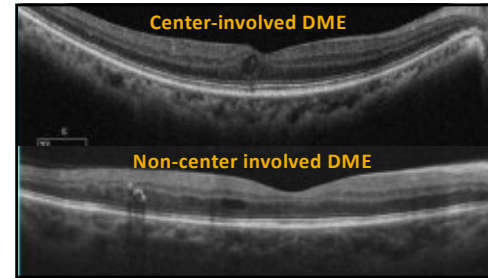
- ETDRS definition of "clinically significant macular edema" modified in era of OCT
- Randomized clinical trials of anti-VEGF agents used presence of DME in **OCT central subfield**



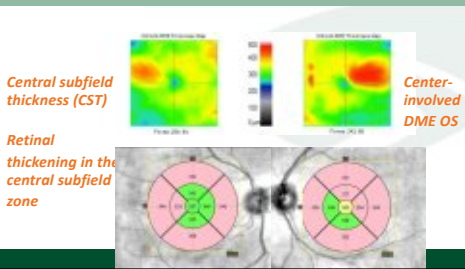
**Central subfield**

Notes: 1. Center of the fovea is the center of the central subfield. 2. The central subfield is defined as the area within 1 mm of the fovea. 3. The central subfield is defined as the area within 1 mm of the fovea. 4. The central subfield is defined as the area within 1 mm of the fovea. 5. The central subfield is defined as the area within 1 mm of the fovea. 6. The central subfield is defined as the area within 1 mm of the fovea. 7. The central subfield is defined as the area within 1 mm of the fovea. 8. The central subfield is defined as the area within 1 mm of the fovea. 9. The central subfield is defined as the area within 1 mm of the fovea. 10. The central subfield is defined as the area within 1 mm of the fovea. 11. The central subfield is defined as the area within 1 mm of the fovea. 12. The central subfield is defined as the area within 1 mm of the fovea. 13. The central subfield is defined as the area within 1 mm of the fovea. 14. 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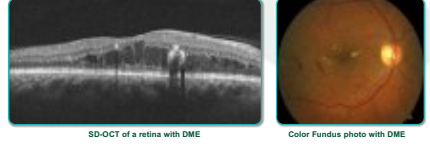
**Central subfield thickness (CST)**

**Center-involved DME OS**

**Retinal thickening in the central subfield zone**

27

### Diabetic Macular Edema (DME)



**SD-OCT of a retina with DME**

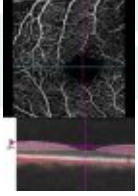
**Color Fundus photo with DME**

28

### OCT Angiography (OCTA)

The Basic Idea of How it Works:

- Capturing motion** in the retina
- Scans at 68,000 A-scans per second
  - Traditional SD OCT scan at 28,000 to 40,000 A-scans per second
- Compares **repeat scans** acquired at the **same position** in the retina to look for changes - motion



29

### OCT ANGIOGRAPHY

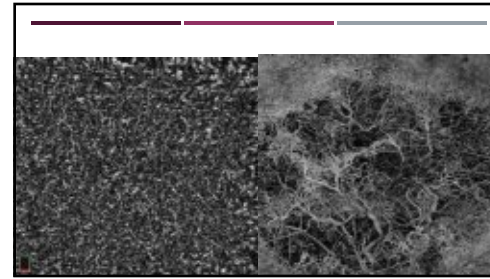
- The only thing that moves in the retina over time are red blood cells
- Take the 'difference' between multiple B scans at the same location to produce a 'decorrelation signal'

30

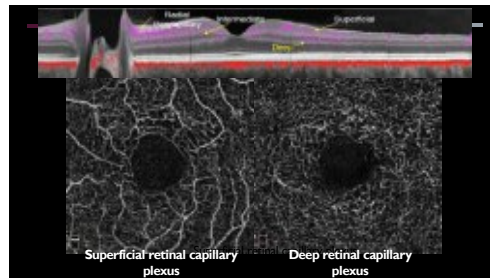
**OCT ANGIOGRAPHY**

- En face flow formation and cross sectional structural information
- Not a replacement for FA/OCT
  - Provides new information
- Valuable for detection of choroidal and retinal neovascularization, macular ischemia, segmentation of the deep and superficial capillary plexi—and maybe early glaucoma?

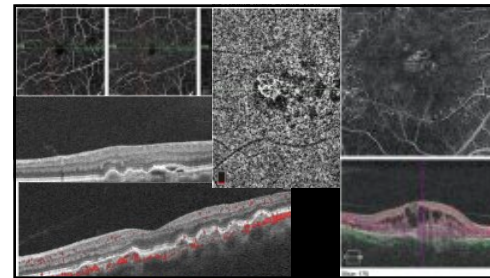
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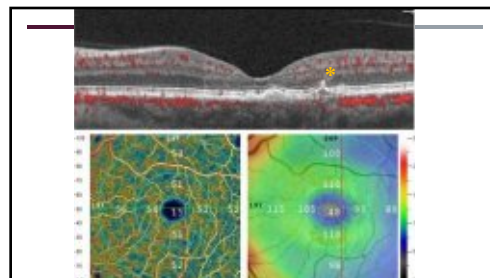
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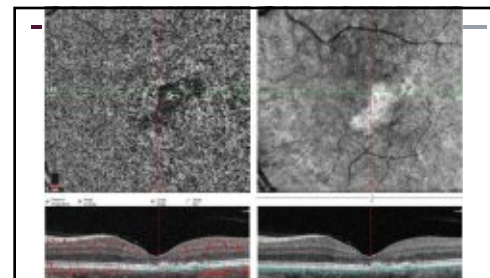
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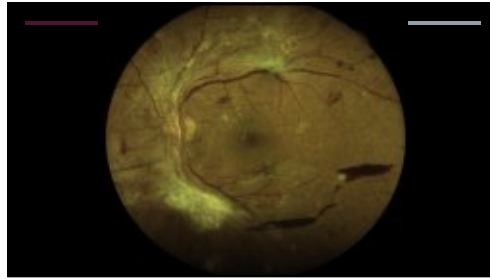
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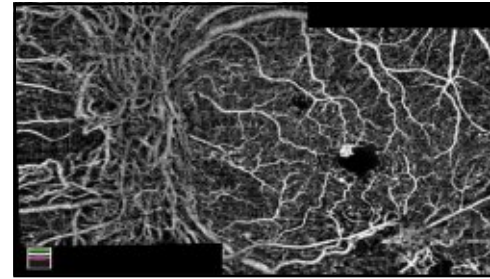
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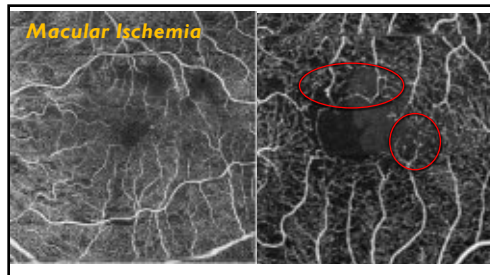
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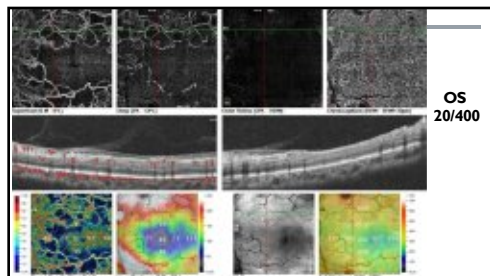


39

**MACULAR ISCHEMIA**

- Vision loss either due to fluid within the macula or a poorly perfused macula
  - **Macular ischemia** in the absence of DME/hemorrhage/exudate
  - Enlargement of the foveal avascular zone is a sign of ischemia

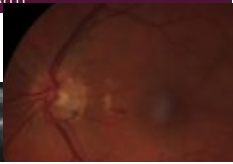
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41

**ISCHEMIA IN DIABETIC RETINOPATHY**

- Cotton wool spot
- Really *not* an "infarct"



42

### Challenges in OCTA


Static blood flow information  
**No leakage, pooling or staining**

Small field of view 3x3mm; 6x6mm; 8x8mm (or 12x12mm) with current systems

Motion artifacts are a big deal

Sensitivity is a challenge in eyes with pathology

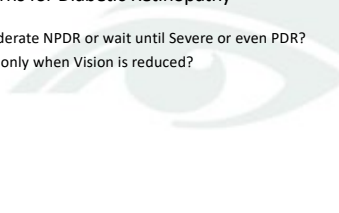
Quantification of blood flow-not yet



43

### Referral Patterns for Diabetic Retinopathy

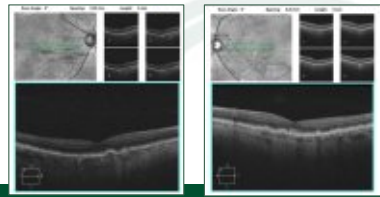
- More than moderate NPDR or wait until Severe or even PDR?
- Any CI-DME or only when Vision is reduced?



44


### The Macula in AMD

More than just recognition of conversion to Wet AMD



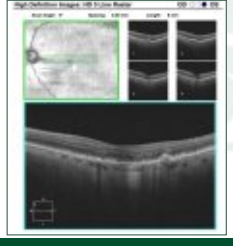
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46

Inf scan through GA:  
 Hypertension defect  
 IRDRA



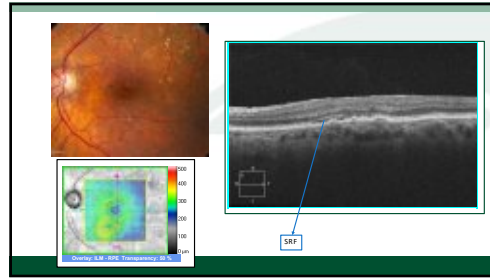
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### Conversion from Dry to Wet

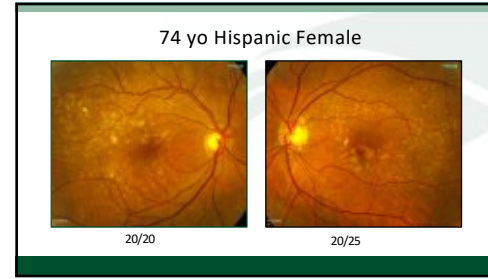


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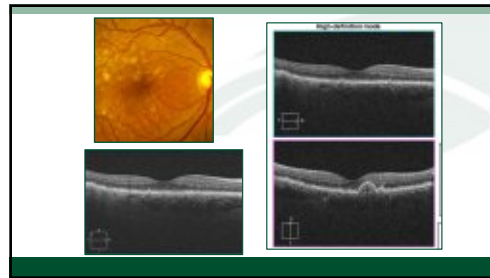




49



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51



52

### Risk Factors for Progression to Wet AMD

- Traditionally based on clinical appearance
- Intermediate AMD
  - Large drusen > 125 microns
  - RPE mottling/pigmentary abnormalities
- Risk of conversion to wet AMD over 5 years > 50%

53

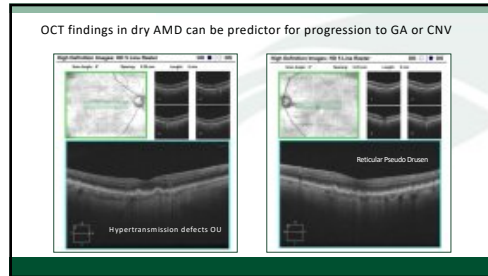
AMD is the Leading Cause of Blindness for Caucasians in the US<sup>1</sup>

Stage	10-year risk of progression for the highest risk category (AREDS simple scale) <sup>2</sup>
Early AMD	53.9%
Intermediate AMD	47.6%
Advanced AMD	-

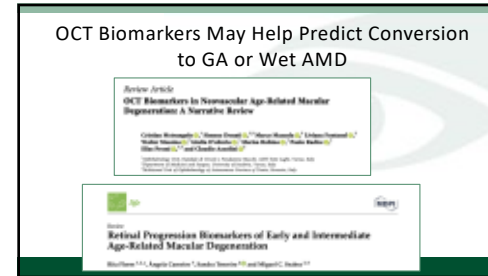
Neovascular AMD (nAMD)

AREDS, age-related macular degeneration; AREDS2, Age-Related Eye Disease Study 2; GA, geographic atrophy; nAMD, neovascular AMD. 1. Eye Disease Prevalence Research Group. Arch Ophthalmol. 2004;122(10):1471-1477. 2. Ferris FL, et al. Ophthalmology. 2013;120(10):1664-1671. 3. Chew EY, et al. JAMA Ophthalmol. 2014;132(3):272-277. 4. Age-Related Eye Disease Study Research Group. Arch Ophthalmol. 2002;120(11):1050-1059.

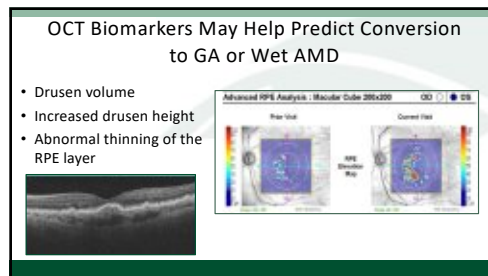
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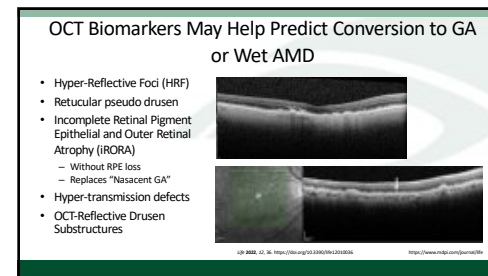
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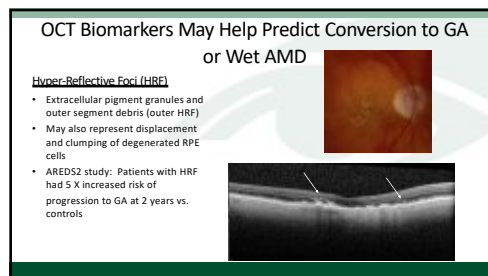
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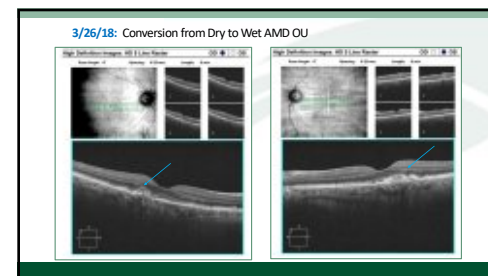
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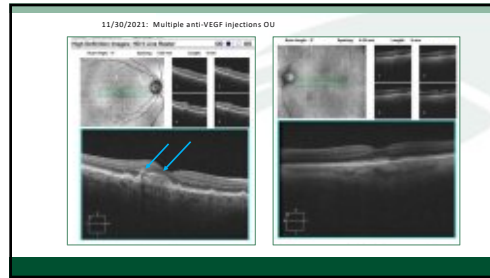
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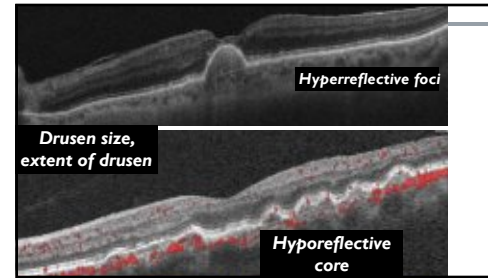
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62

### Hyperreflective Retinal Foci (HRF)

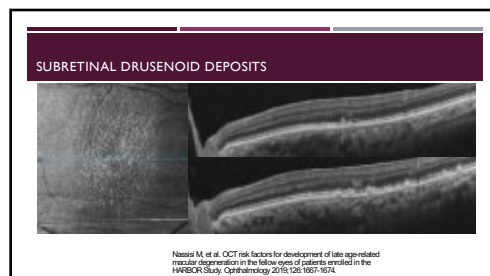
- Secondary to:
  - DR/DME, RVO, AMD, CSR, Uveitis, MacTel; IRD
- Most likely activated inflammatory microglia cells
- **Biomarker for disease progression**

63

### Reticular Pseudo Drusen

- Subretinal collections of granular, interlacing, hyper-reflective material located above RPE
- Commonly found in the superior macula or close to superotemporal arcade
- Undergo a characteristic lifecycle of growth, invasion into the ellipsoid zone, and finally regression
- Reticular pseudodrusen is associated **with an additional 2-6-fold increased risk of progression to nAMD or central GA**,  
 — Risk of progression higher for reticular pseudodrusen located outside the macula

64



65

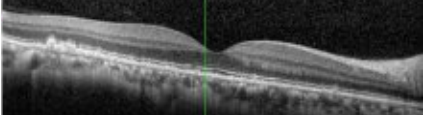
### SUBRETINAL DRUSENOID DEPOSITS

- Distinctive type of drusen aka reticular pseudodrusen
- Subretinal space extending to the outer segments of photoreceptors
- Not just drusen above the RPE
- Include immune-reactive cells (macrophages, microglia)
  - Impact dark adaptation; choriocapillaris flow impairment
- Increased risk of progression to late stage AMD
- Finger et al. 2014

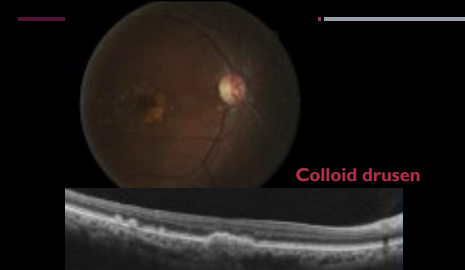
66

**CUTICULAR DRUSEN**

- Drusen subtype
- AKA basal laminar deposits
  - Between the basal lamina of RPE and the inner collagenous layer of Bruch's membrane
- Can progress to geographic atrophy and MNV

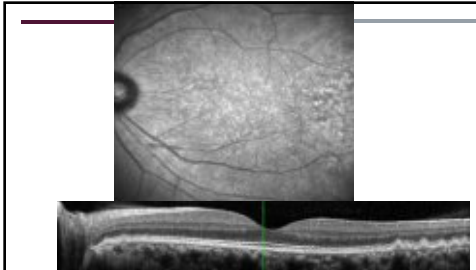


67



**Colloid drusen**

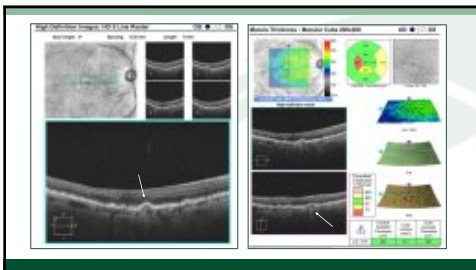
68



69



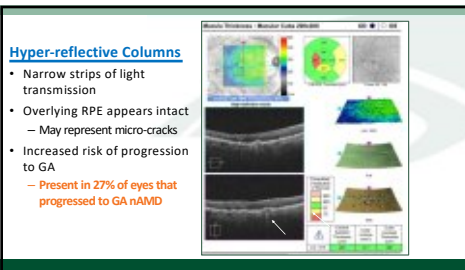
70



71

**Hyper-reflective Columns**

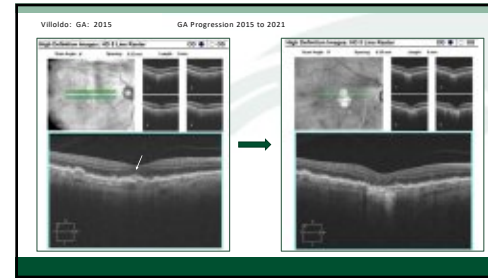
- Narrow strips of light transmission
- Overlying RPE appears intact
  - May represent micro-cracks
- Increased risk of progression to GA
  - Present in 27% of eyes that progressed to GA nAMD



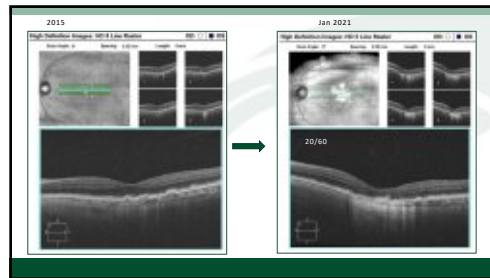
72



73



74



75



76

### CRORA VS IRORA

- CAM (classification of atrophy meetings) classification
  - Consensus on nomenclature
- Complete RPE and retinal atrophy (cRORA) which occurs in AMD
  - $\geq 250 \mu\text{m}$  choroidal hypertransmission on OCT B-scans vs. iRORA (incomplete)
  - Loss of retinal layers, RPE disruption of at least  $250\mu\text{m}$

The slide includes an OCT B-scan showing a large area of choroidal hypertransmission, characteristic of complete RPE and retinal atrophy (CRORA).

77

### OCT BIOMARKERS FOR PROGRESSION TO NAMD

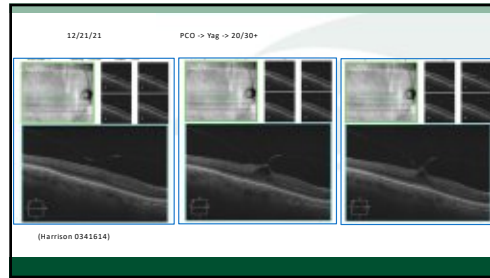
- Thick double layer sign, intraretinal hyperreflective foci, fellow eye exudative macular neovascularization

The slide includes an OCT B-scan showing a thick double layer sign and intraretinal hyperreflective foci, which are biomarkers for progression to neovascular AMD (NAMD).

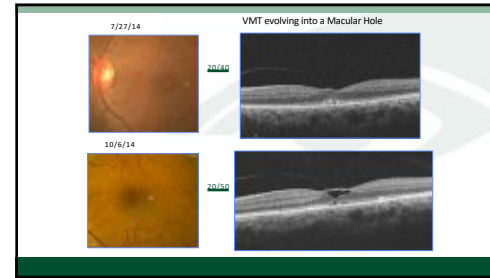
Wilkenski Y et al. Optical Coherence Tomography Biomarkers for Conversion to Exudative Neovascular Age-related Macular Degeneration. J Ophthalmol. 2023;207:137-144

78

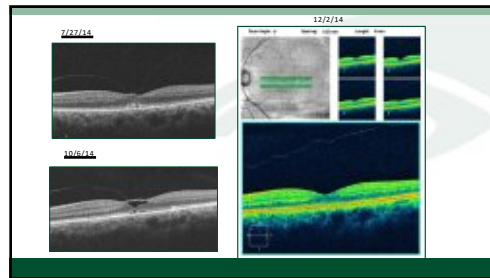




85



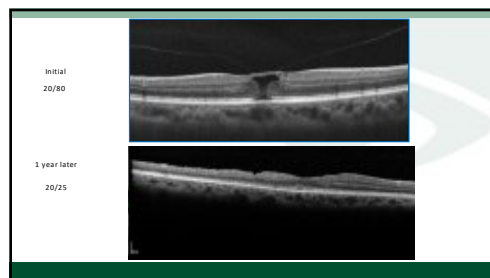
86



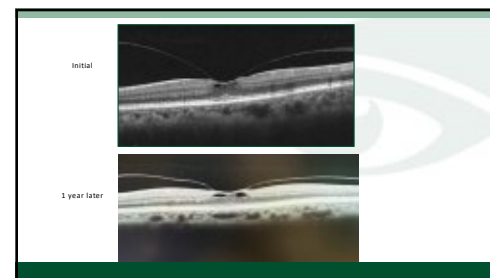
87



88



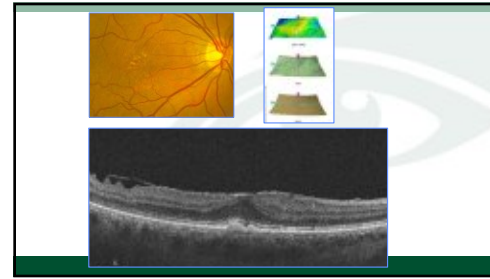
89



90



91



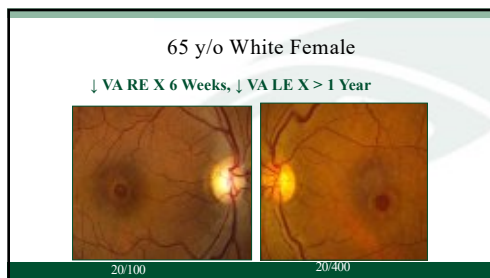
92



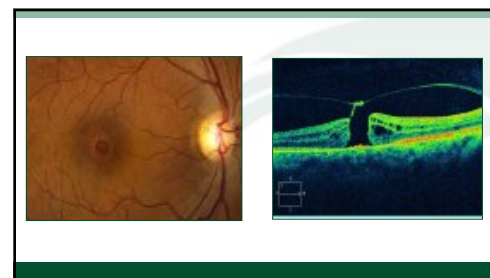
93



94



95

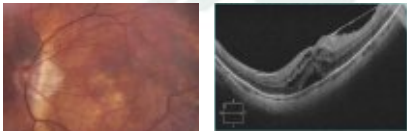


96





Jeff: (66 yo) High Myopia, Pseudophakia and VMT  
 5/11/20  
 • Notes a paracentral defect in the LE X 2 weeks  
 – Starting to invade the central vision: VA: 20/150



103

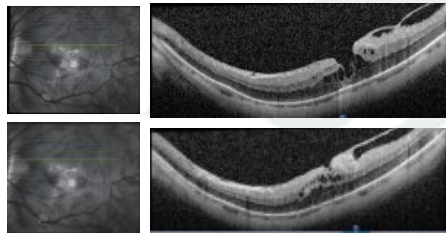


104

9/27/2021: Vision is better: 20/50



105



106

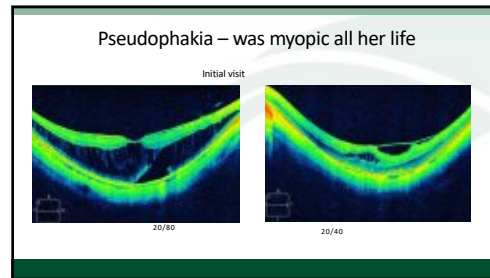
2/14/22  
 20/40



107

What is going to happen?  
 Will he progress to macular hole  
 Would he benefit from a vitrectomy?

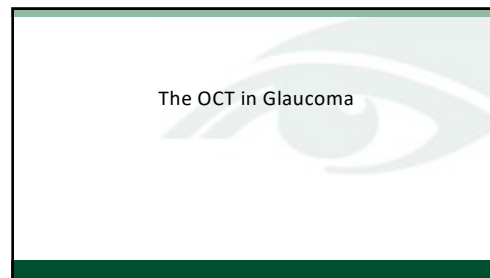
108



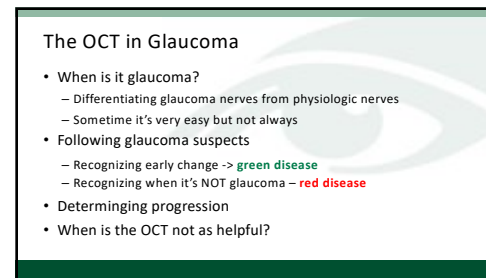
109



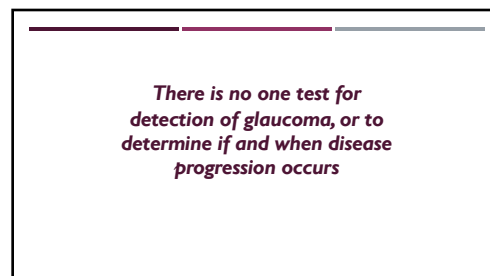
110



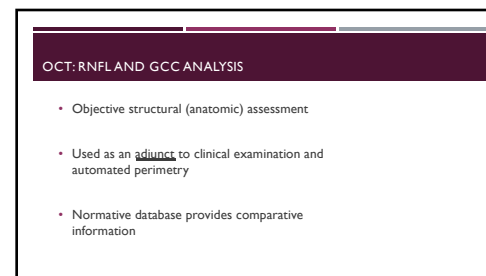
111



112



113



114

**RETINAL NERVE FIBER LAYER VS. GANGLION CELL COMPLEX**

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

115

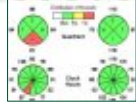
**Do you on do 1 RNFL scan?**

- How do you know how accurate/reliable that scan is?
- Instead do 3 RNFL scans at a time
  - at a minimum do 2 scans
- Ensures consistency/reliability

116

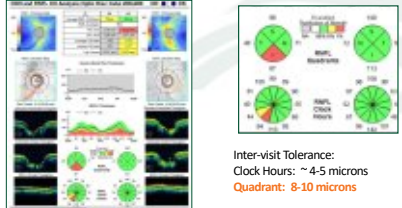
**What is the Reproducibility of RNFL OCT Clock Hour Measurements**

A. 0-3 microns  
 B. About 4-5 microns  
 C. About 10 microns  
 D. > 10 microns



117

**RNFL Quadrants and Clock Hours**



Inter-visit Tolerance:  
 Clock Hours: ~ 4-5 microns  
 Quadrant: 8-10 microns

118

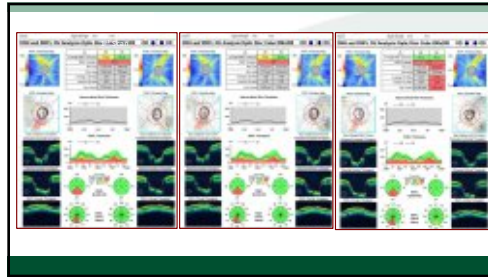
**How much change needs to occur on an OCT RNFL for it to be significant?**

119

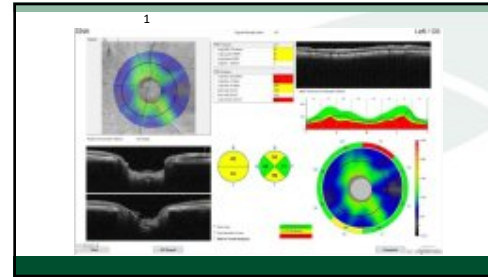
**How much change needs to occur on an OCT RNFL for it to be significant?**

- 5 microns
- 10 microns
- 20 microns
- 25 microns

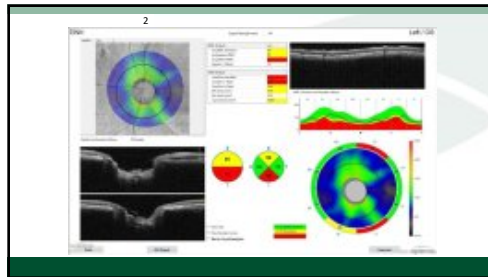
120



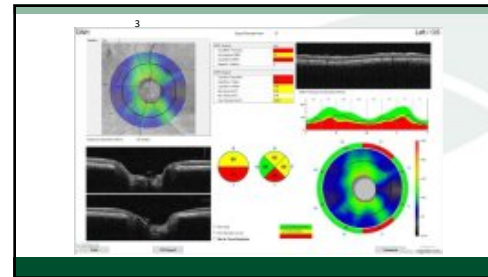
121



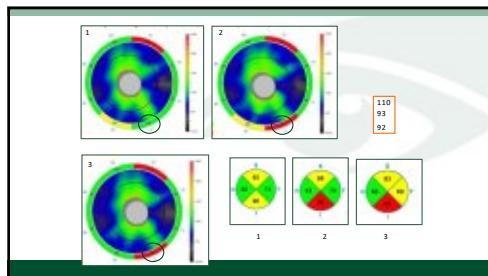
122



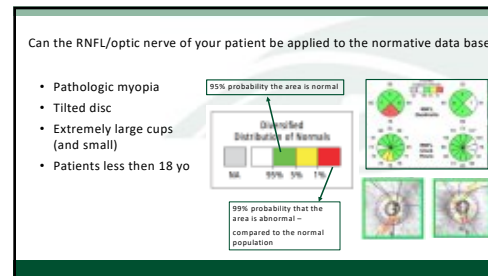
123



124



125



126

**Do normative databases help--or hurt us?**


*Group of normal individuals to which your images (and therefore patient) are compared to "Healthy" patients can be labeled as abnormal and vice versa if they don't "fit the mold"*

Heidelberg Spectralis: 330 eyes  
 218 non-Hispanic white, 45 Hispanic white, 41 Black, 23 Asian, 3 American Indian  
 Age 18-78

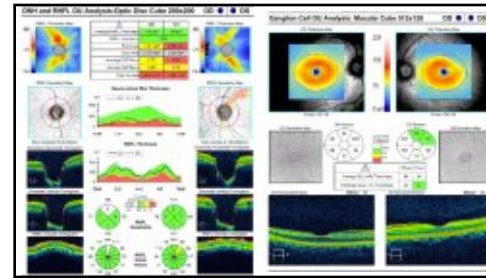
Zeiss Cirrus: 282 eyes  
 Age 19-94; 6 US sites, 1 in China  
 122 males, 149 females; 43% Caucasian, 24% Asian, 18% African American, 12% Hispanic, 1% Indian, 6% mixed ethnicity

RTVue: 600 eyes  
 19-84 years of age; 11 sites, USA, Japan, India, England

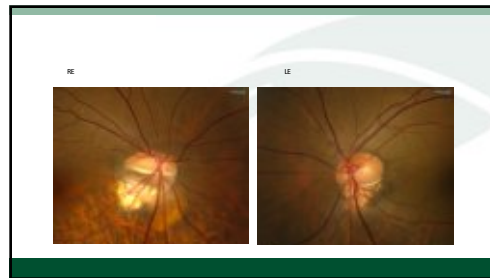
Green = 95% thickness percentile  
 Yellow = <5%  
 Red = <1%



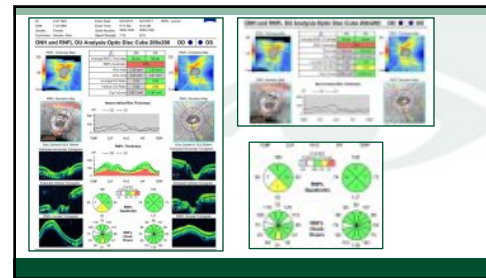
127



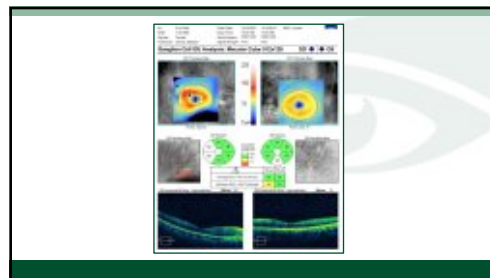
128



129



130

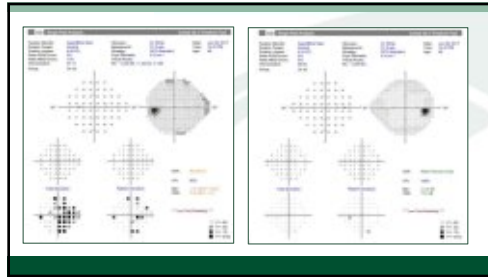


131

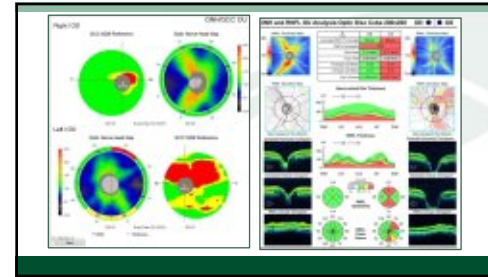


132

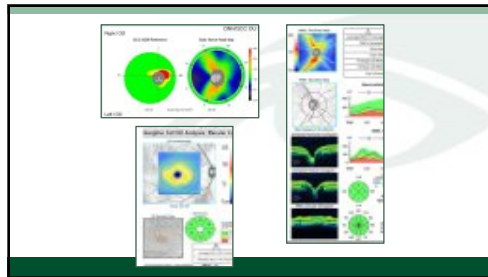




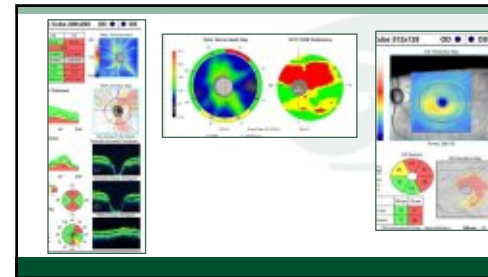
139



140



141



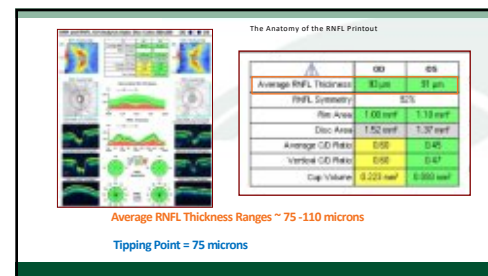
142

When is it Glaucoma?

There is a large range of "normal" before the RNFL reaches the "tipping point"

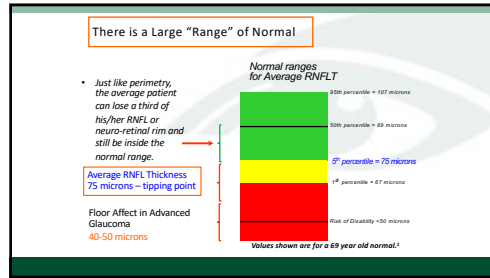
Be on the lookout for Green Disease!!

143

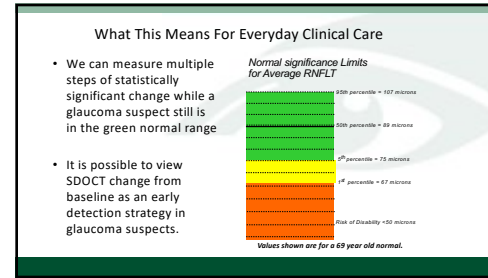


144

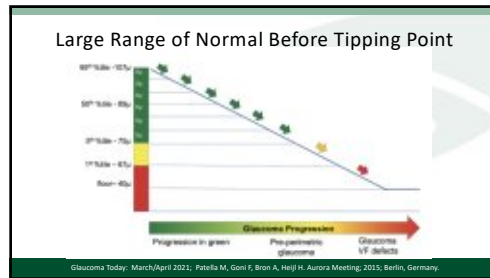




145



146

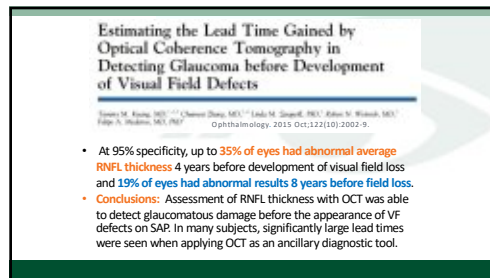


147

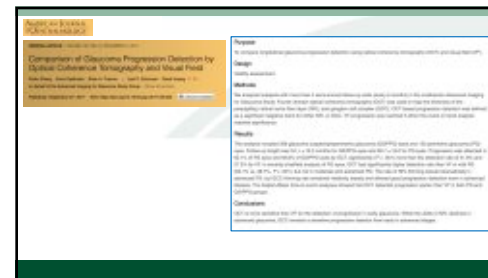
The OCT can show glaucomatous change **BEFORE** it is seen on visual fields

In fact – may be MORE sensitive than visual fields in detecting progression

148



149



150

### OCT Detects Progression Before VF

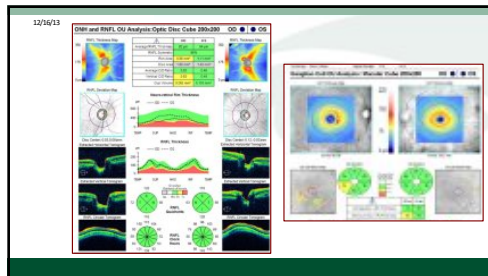
- OCT can detect progression 1-2 years before it shows up on VF
- Both NFL and GCC outperform VF in detecting progression in early glaucoma
- In moderate and advanced GL, RNFL loses sensitivity due to floor effect
- GCC continues to detect progression in moderate and advanced glaucoma

151

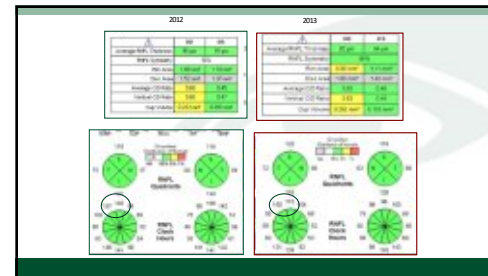
### Arturo

- Followed without treatment for 4-5 years
- Varying IOP's: Tmax 32/17
  - RE fluctuated 18 -> 29 (32 max on initial visit)

152



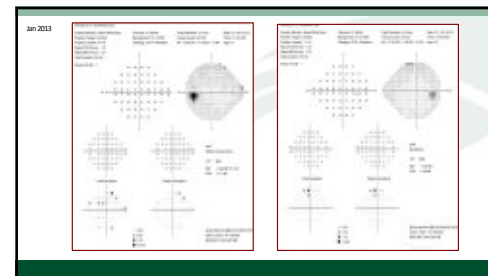
153



154



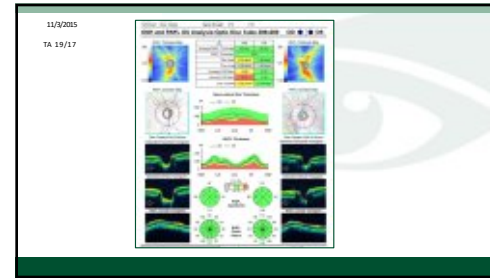
155



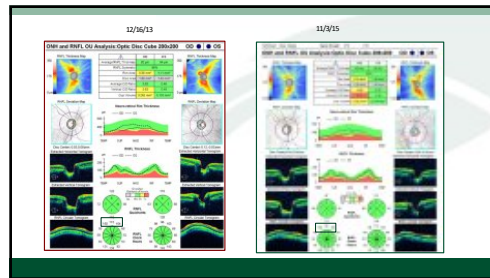
156



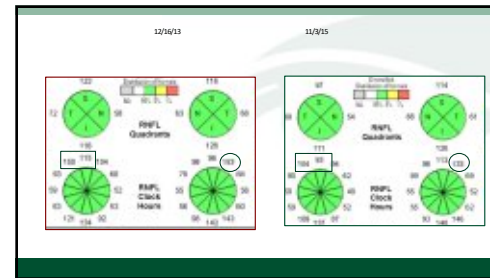
157



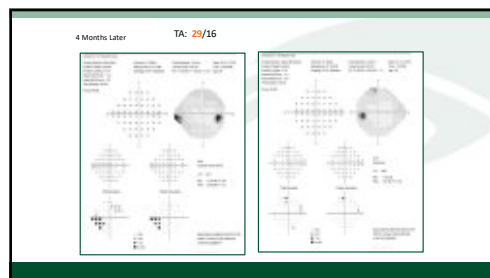
158



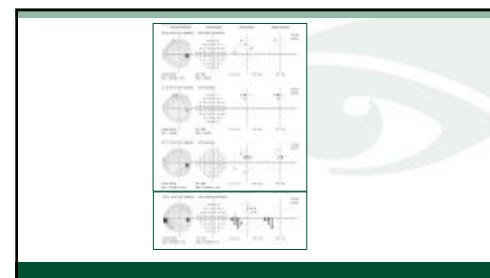
159



160



161



162

### Arturo

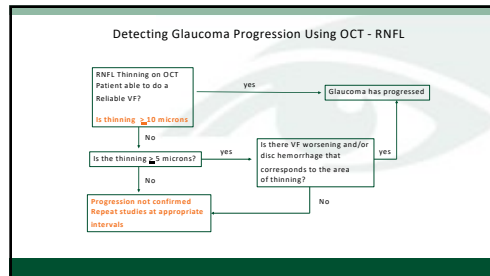
- Being followed for OHTN
  - History of RK
- Variable IOP spikes RE
  - 3/1/16 visit - TA 29
    - Suggestion of VF defect
    - OCT - probably normal...NOT
- What do you do?

163

### Arturo

- Being followed for OHTN
  - History of RK
- Variable IOP spikes RE
  - 3/1/16 visit - TA 29
    - Suggestion of VF defect
    - OCT - Thinning in the normal range
- What do you do?
  - Latanoprost qhs RE started
- Returned 4/2/16 - TA 20/16

164

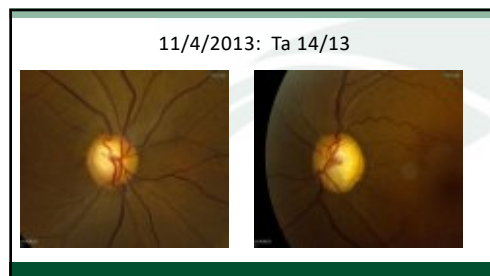


165

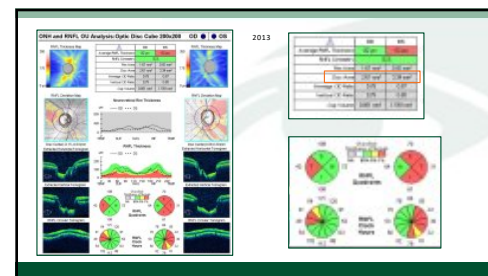
### When is it glaucoma?

**Red Disease**

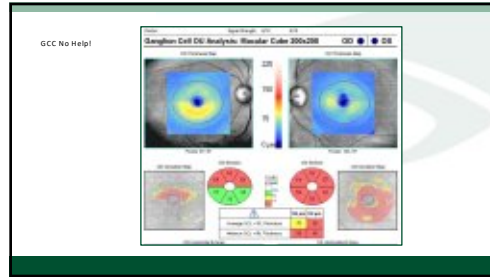
166



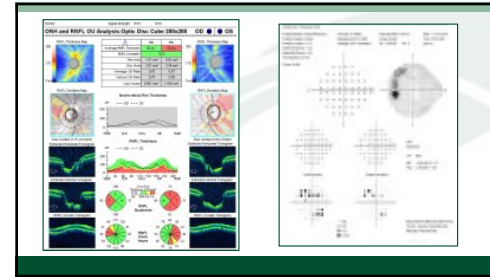
167



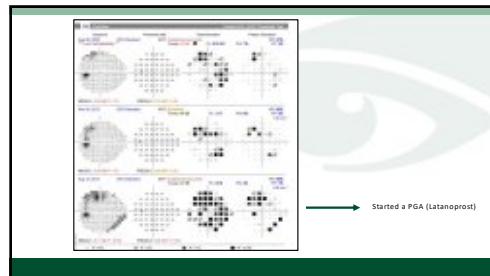
168



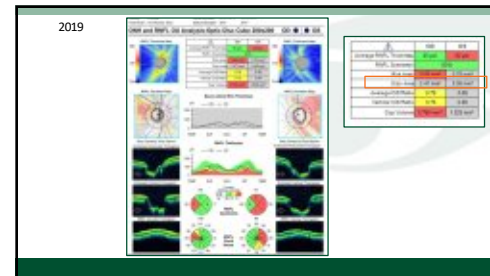
169



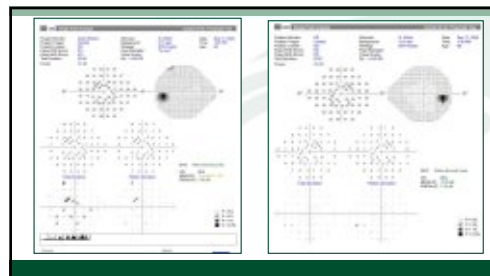
170



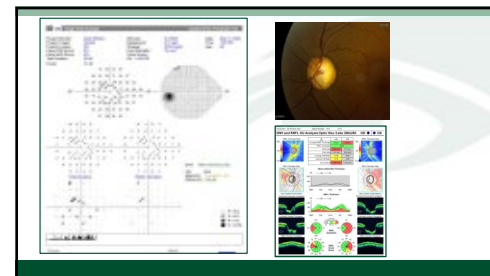
171



172

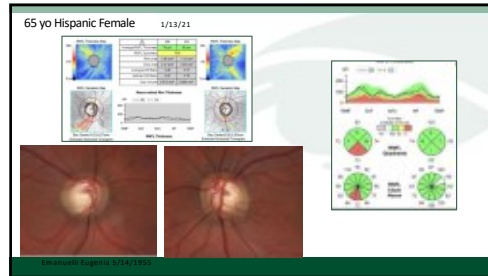


173

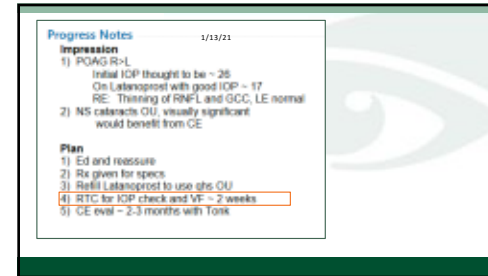


174

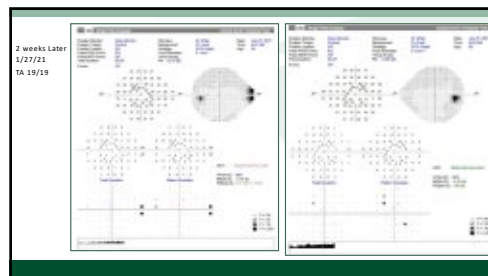




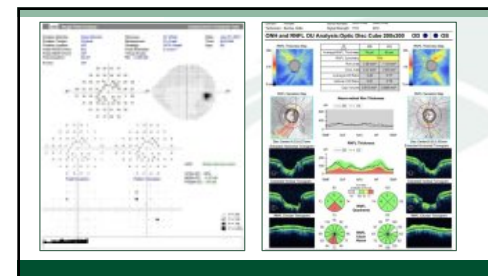
181



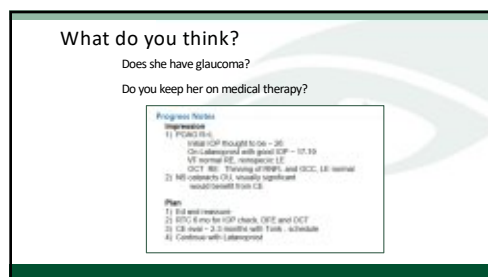
182



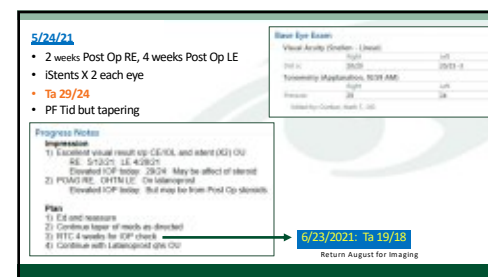
183



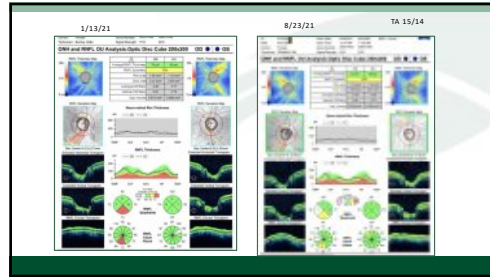
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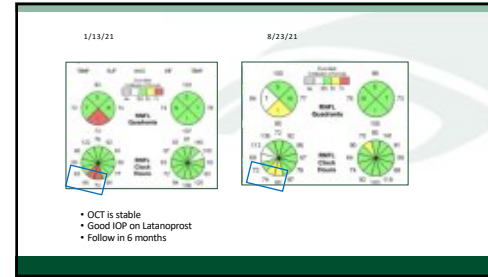
185



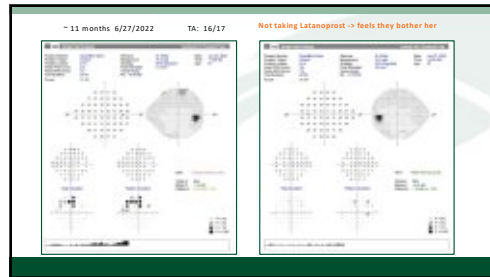
186



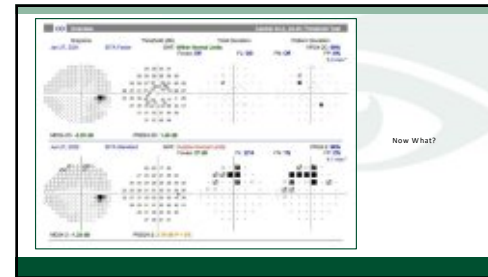
187



188



189



190

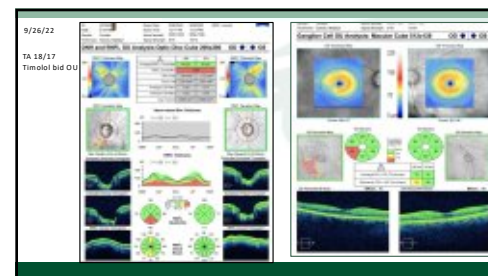
**Emanuelli: 66 yo Hisp Female**

June 27, 2022

- **VF Worse RE but OCT is stable**
  - Progression vs artifact ?
  - If progression - is this due to episodes of elevated IOP during Post OP?
- Dermatochalasis BUL:
  - Wants referral to OCP

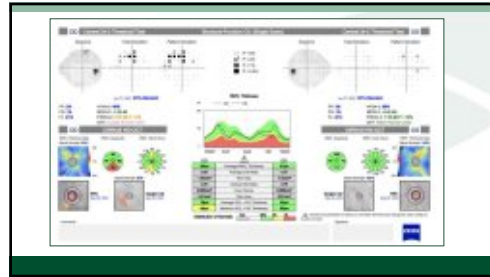
Switch to Timolol bid OU

191

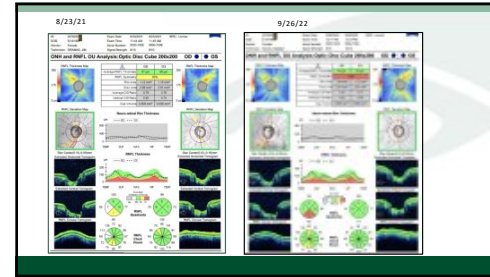


192

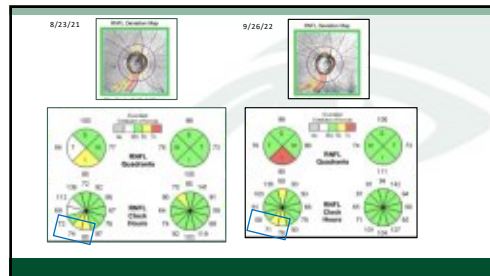




193



194



195

### Final Thoughts...

- RE: POAG – stable; LE: OHTN
  - Appeared progression based on VF but not on OCT
- Needs a VF – scheduled for 6 months
  - I wish I would have done it on the recent visit
- Using Timolol bid...
  - Does she need it in only RE or both?
- Could you consider stopping....?
- Could you consider SLT RE only?

196

When the OCT is not helpful

197

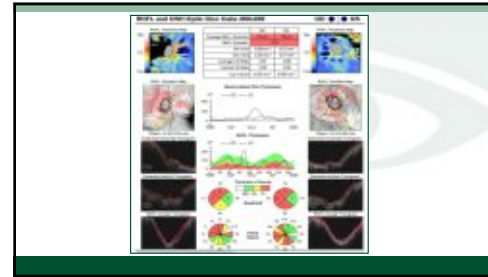
### When the OCT is not helpful

- Severe glaucoma
  - Floor Affect in Advanced Glaucoma ~40-50 microns
  - Difficult to use the OCT to measure progression
- High Myopia
- Tilted Discs

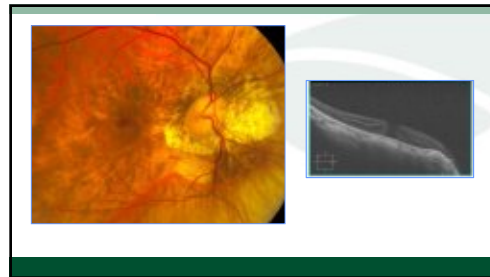
198



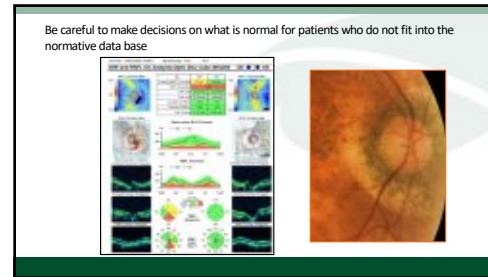
199



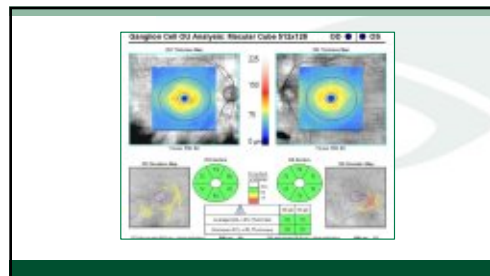
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202



203

### Summary OCT in Glaucoma

- OCT provides another piece information for the "glaucoma puzzle"
  - Along with IOP, visual fields and clinical appearance of the nerve
- It provides an objective means of comparing "glaucomatous" nerves from normal or physiologic optic nerve
- It provides an objectives means of determining progression

204

### Summary: OCT in Retina

- SD OCT has emerged as a critical tool in the diagnosis and treatment of retinal disease
- It has changed how we evaluate the macula
- Helps establish a diagnosis that is difficult to determine with only standard ophthalmology
- Advancing software has provided expanded uses OCT
- OCT Angiography has taken OCT to the next level

205