Putting the "Oh" in OCT

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Financial Disclosure - Marrelli

- Allergan
- Bausch & Lomb
- Carl Zeiss Meditec
- Glaukos
- M&S Technologies
- Thea

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Mark Dunbar: Disclosure

- Optometry Consultant/Advisory Board
  - Carl Zeiss
  - Allergan
  - Regeneron
  - Astella
  - Apellis
  - B&L
  - Orasis
  - Visus
  - Tarsus
  - Topcon
  - Avellino
  - Thea

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

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Reports

SCIENCE

Optical Coherence Tomography 1991

David Huang, Eric A. Swanson, Charles P. Lin, Joel S. Schuman, William G. Stinson, Warren Chang, Michael R. Hee, Thomas Flotte, Kenton Gregory, Carmen A. Puliafito, James G. Fujimoto*

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 ~10^{-10} of the incident optical power. Tomographic imaging is demonstrated in vitro in the peripapillary area of the retina and in the coronary artery, two clinically relevant examples that are representative of transparent and turbid media, respectively.

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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

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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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The OCT in Glaucoma

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The OCT in Glaucoma

- When is it glaucoma?
  - Differentiating glaucoma nerves from physiologic nerves
  - Sometime it's very easy but not always
- Following glaucoma suspects
  - Recognizing early change -> **green disease**
  - Recognizing when it's NOT glaucoma – **red disease**
- Determinging progression
- When is the OCT not as helpful?

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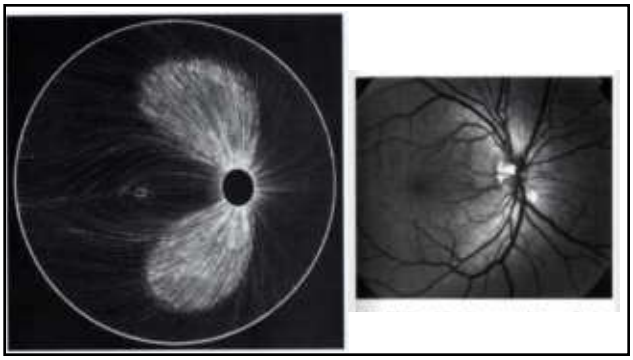

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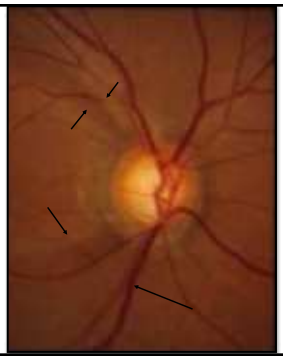

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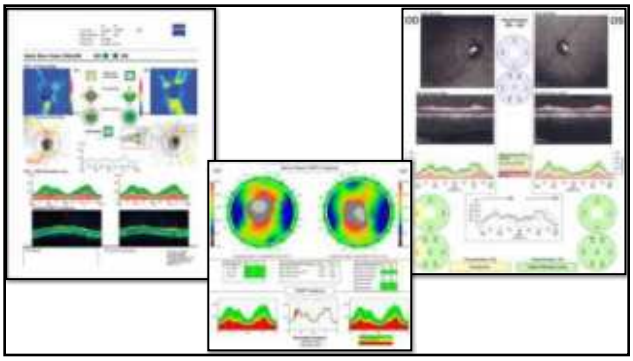

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Quantifiable/Objective Imaging

- "Diagnostic capability":
  - Good for early glaucoma
  - Excellent for moderate to severe glaucoma
  - Improved when more than one parameter is evaluated
- Many of us rely on imaging devices to identify glaucoma (and progression)
- Has imaging become "the answer"?

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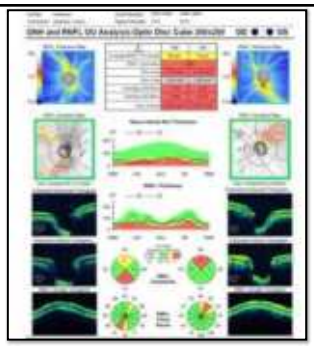
OCT RNFL Basics: How Do I Make Sense of This?



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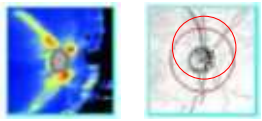
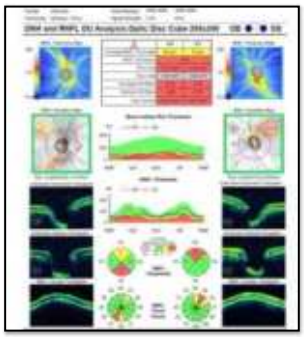
Systematic Strategy

- Quality
  - Signal Strength
  - Circle Placement
  - Movement?





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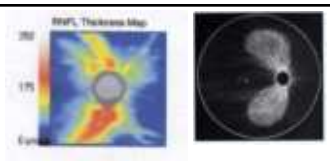
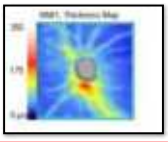
Systematic Strategy

- Thickness Map
- Deviation Map





IMPORTANCE OF BLOOD VESSELS!!!!

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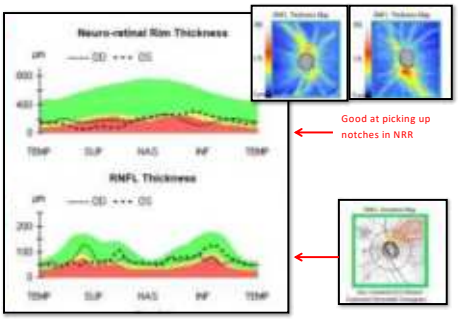
- Thickness Profiles
  - Compared to normative data
- KEYS:
  - SYMMETRY
  - MODULATION



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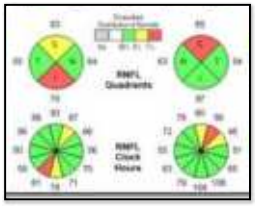
Systematic Strategy

- Quadrant and Clock Hour RNFL analysis



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Do you only do 1 RNFL scan?

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

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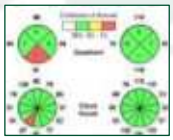
What is the Reproducibility of RNFL OCT Clock Hour Measurements

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



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Where Can We Go Wrong?

- Artifacts
- Interpretation Errors

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Artifacts in Spectral Domain OCT (SD-OCT)

- **Artifacts are common in SD-OCT:**
  - 6-44% of scans will have some type of artifact
  - Artifacts increase in the presence of other pathology
  - Not all artifacts are visible on standard printout
- **Causes of Artifacts:**
  - Technician/Acquisition Errors
  - Software Errors
  - Patient Dependent:
    - Pupil Size
    - Media
    - Concurrent pathology (PVD, ERM)
    - Myopia-related changes*

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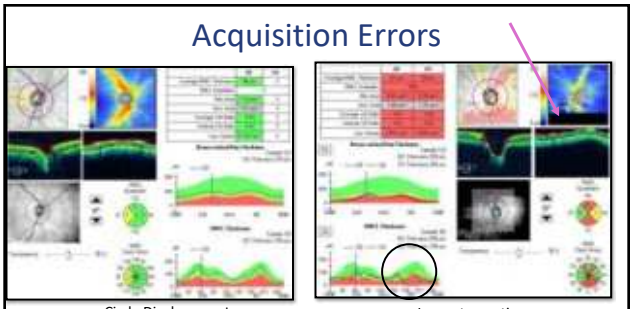
Acquisition Errors



Circle Displacement | Image truncation

Images courtesy of Marcus Gonzales, OD, FAAO

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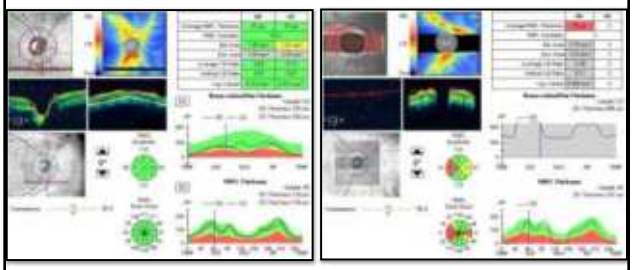
Acquisition Errors – Don't Blink!



Images courtesy of Marcus Gonzales, OD, FAAO

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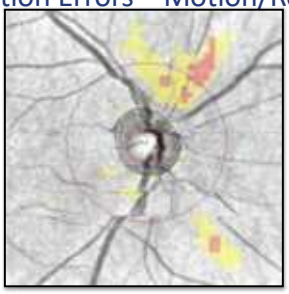
Acquisition Errors – Motion/Rotation



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Software Errors

- **Improper boundaries of optic nerve**
- **Improper segmentation of layers (RNFL, GC-IPL)**
  - Pure segmentation error
  - Poor signal strength
  - Often related to coexisting disease

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Segmentation Errors

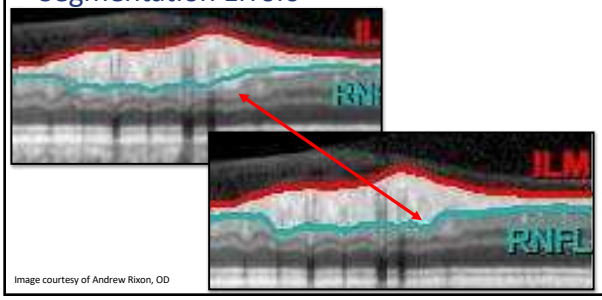

Image courtesy of Andrew Rixon, OD

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Clinical Interpretation Errors

- **Reliance on reference database color indicators**
  - Red Disease
  - Green Disease
- **Failure to recognize non-glaucomatous causes of RNFL thinning**

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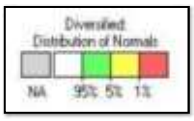
Reliance on Reference Database Color System

- **Reference Database (aka "normative" database):** Reference population without disease in question, to which an individual patient's data will be compared



Question: Does abnormal DATA mean you have DISEASE?

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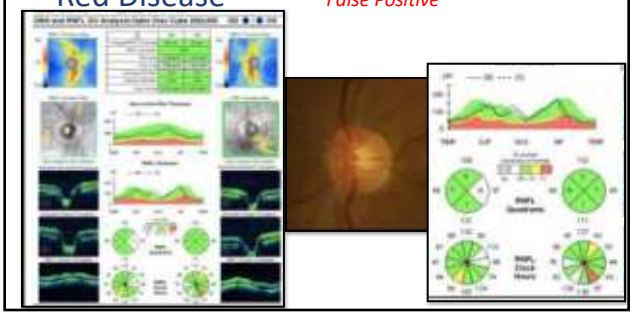
"Red Disease"

False Positive



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REVIEW

Green disease in optical coherence tomography diagnosis of glaucoma

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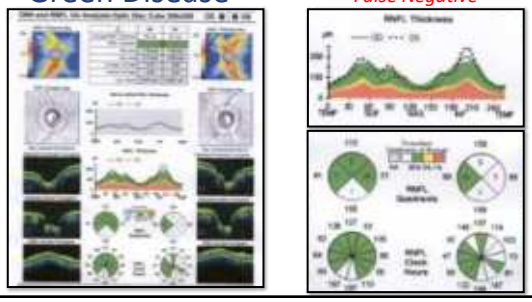
"Green Disease"

False Negative



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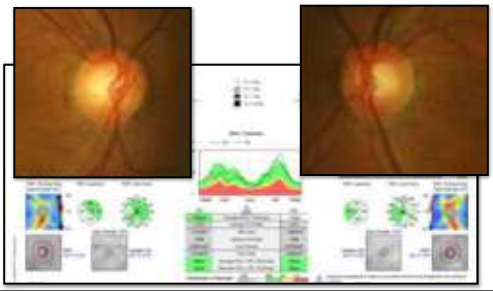
"Green Disease"



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Non-glaucomatous Causes of RNFL thinning

Masqueraders

- **Retinal Disease***
- **Ischemic Optic Neuropathy***
- **Other optic neuropathies**
- **Neuro-degenerative disease**
- **Myopia*****

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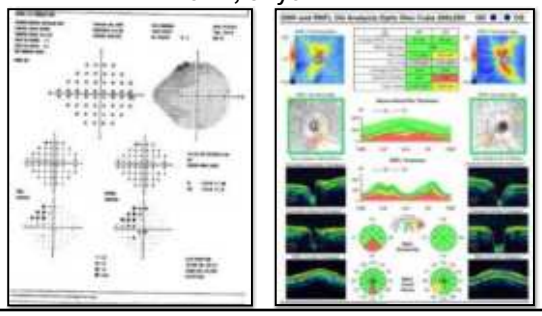
Kevin, 52yo WM



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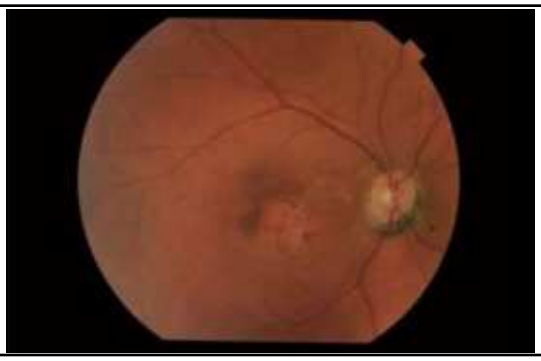

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Newest Addition to Glaucoma Diagnosis Arsenal: Macular Imaging

- 1998: Zeimer et al reported on macular thickness loss in patients with known glaucomatous damage
- 2003: Greenfield reported correlation between total macular thickness and MD on VF in glaucoma patients (time domain OCT)
- 2013: Hood et al – extensive investigation of segmented "RGC+" (RGC + IPL) layer and description of the "Macular Vulnerability Zone" (MVZ)

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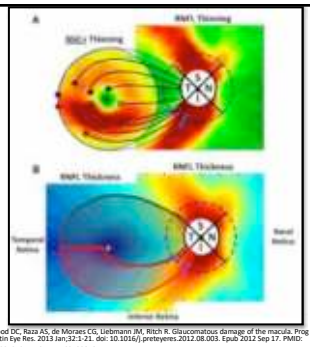

Hood DC, Raza AS, de Moraes CG, Liebmann JM, Ritch R. Glaucomatous damage of the macula. Prog Retin Eye Res. 2013 Jan;32:1-21. doi: 10.1016/j.preteyeres.2012.08.003. Epub 2012 Sep 17. PMID: 22995953; PMCID: PMC3529818.

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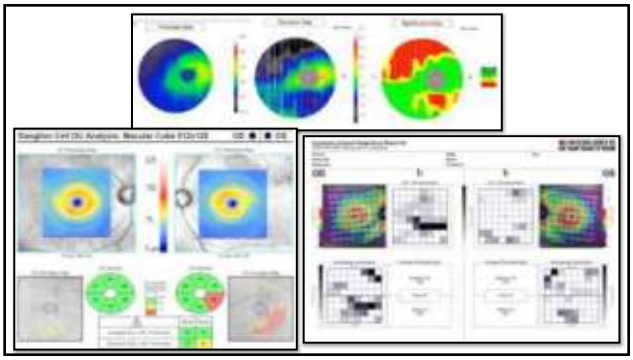

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Advantages of Macular Analysis

- Macula contains ~50% of retinal ganglion cells
  - Glaucoma is a disease of these cells
  - Macular thinning/irregularity cannot be detected during clinical exam
- More reproducible measure (if not using retinal nerve fiber layer) than peripapillary RNFL
  - Fewer blood vessels an other cell components
  - Less anatomic variation compared to optic disc/peripapillary region
- Better superior/inferior symmetry and symmetry between eyes than peripapillary RNFL

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Disadvantages of Macular Imaging

- Macular imaging is not helpful in glaucoma cases in which patients have concurrent macular disease
  - AMD
  - ERM
  - CME
  - DME
  - Macular hole

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Glaucoma and Myopia

A Diagnostic Dilemma

- **Myopia and Glaucoma**
  - Myopic epidemic: 5 Billion myopes by 2050
  - Myopia is a risk factor for glaucoma development
- **Myopic Discs can be difficult to evaluate**
  - Tilt
  - Peripapillary changes
  - Flattening of cup
- **Challenges with OCT in myopic eyes**
  - Difficult to acquire image
  - Higher incidence of segmentation errors
  - RNFL database not typically adjusted for RE or AL
  - RNFL and macular thickness may be affected by increased AL

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Glaucoma and Myopia
A Diagnostic Dilemma

- **RNFL**
  - Decreased RNFL with increasing AL in S, I, N sectors
  - RNFL more temporally located (S/I peaks shifted)
  - Increasing axial length associated with "false positive" (red disease) RNFL OCT
  - Poor agreement with VF
- **Macular Ganglion Cell**
  - Average thickness reduced in high myopia
  - Tend to have diffuse circular thinning with irregular inner margin
  - "GCIPL Hemifield Test" shown to have high sensitivity and specificity in high myopia (Kim YC, et al. IOVS 2016;57:5856-63)

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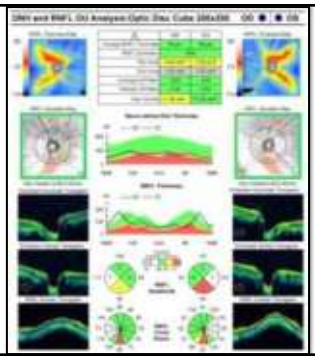
Temporally displaced RNFL peaks



Tan, et al. Br J Ophthalmol 2019;103:1347-1355

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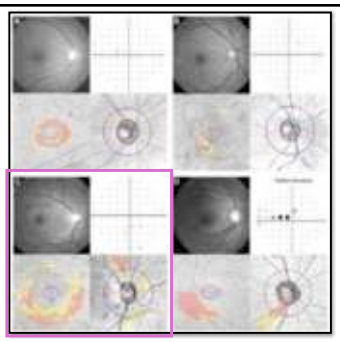
GCIPL False+



Kim, et al. Ophthalmology 2015;122(3):502-510

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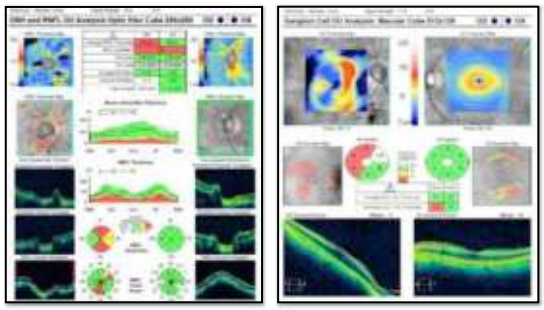

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Case for Discussion
CM, 51yo HM

- **Referred for glaucoma suspicion due to ONH appearance**
- **POH:**
  - LASIK OU (2000), PRK OS (2014)
- **FOH:**
  - (+) glaucoma (maternal gm)
- **PMH:**
  - unremarkable

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Case for Discussion
CM, 51yo HM

- **BCVA: 20/20 OD, OS**
- **Normal pupils, motility, CVF**
- **SLE: LASIK flaps visible, otherwise normal**
- **Gonioscopy: open to CB 360° OD, OS**
- **Tmax: 18mmHg OU**
- **CCT: 523 OD 489 OS**

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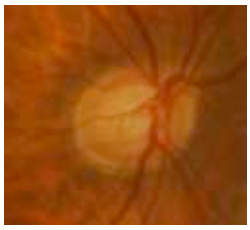
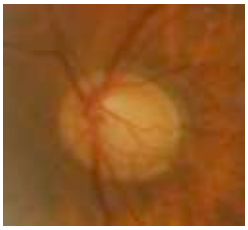
Case for Discussion

CM, 51yo HM





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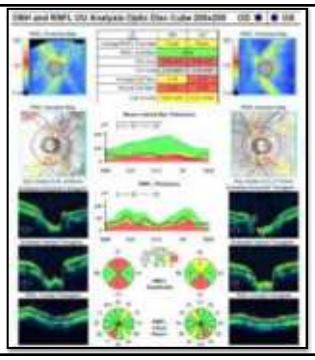
CM, 51yo HM



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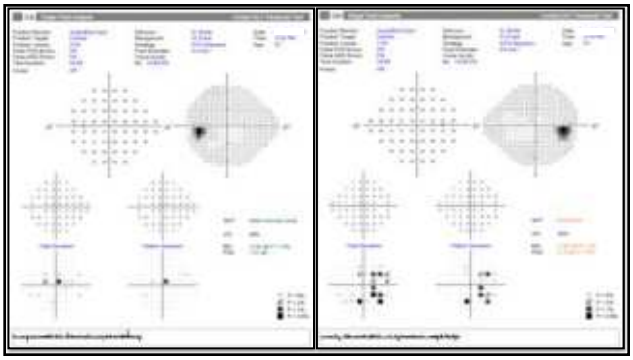

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Case for Discussion

CM, 51yo HM

- **Do you think this is glaucoma?**
- **What else should we do?**

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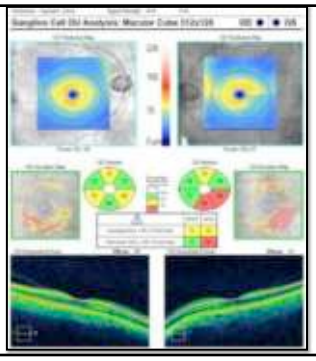
CM, 51yo HM



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What about the 10-2 VF?

- Central 8 degrees from the center of the foveal contains more than 30% of retinal ganglion cells
- 24-2 and 30-2 test strategies use a 6 degree test grid pattern; these points fall outside of the densist region of ganglion cells
- 10-2 test strategy uses a 2 degree test grid
- Recent research has shown that in some patients with small regions of macular gangion cell loss, 10-2 testing may be better able to detect VF loss

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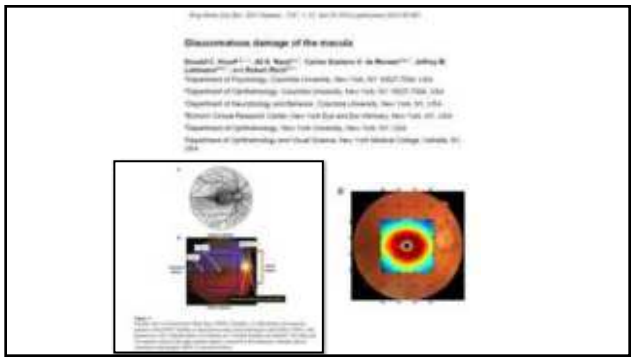

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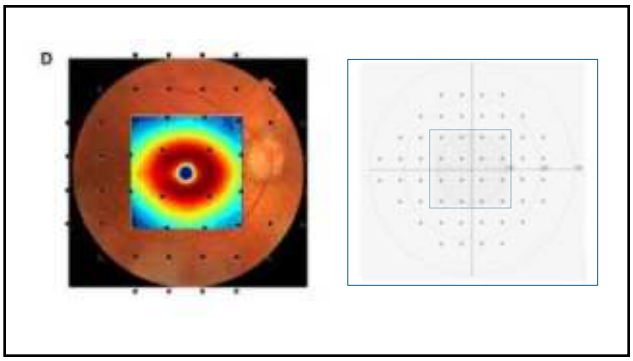

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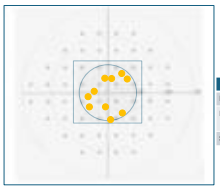
SITA Faster 24-2C Pattern on HFA3



The 24-2C test pattern combines all 24-2 points + ten selected 10-2 points (shown in OD orientation)

Large Gray	24-2 pattern
Large Orange	Ten additional 24-2C points
Small Gray	10-2 pattern

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24-2C: The newest pattern on the HFA

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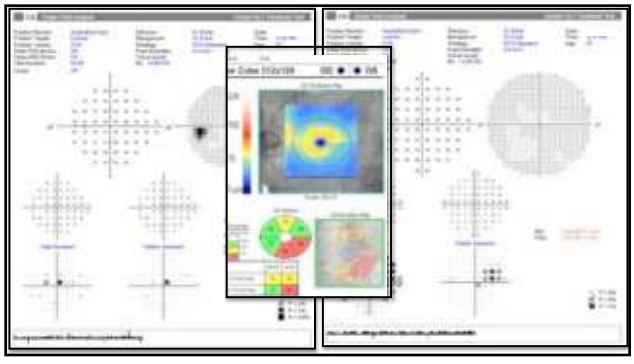

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The OCT in Retina

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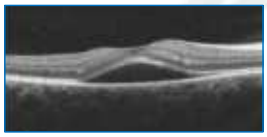
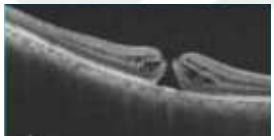
Don't Make It More Complicated Than it Needs to be

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





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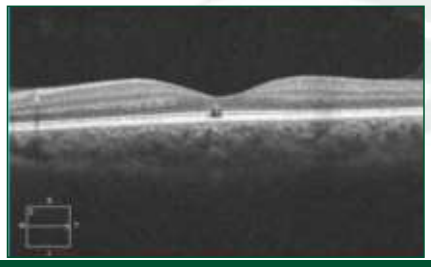
What does This patient have?



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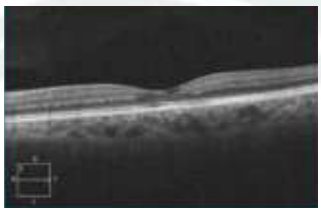
What does this "signature" OCT represent?



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Where is the Fluid?

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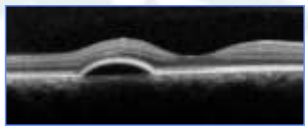
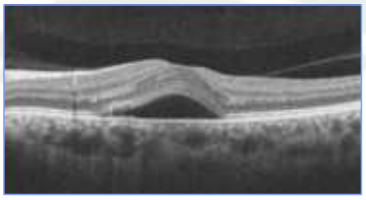
Where is the Fluid?



65

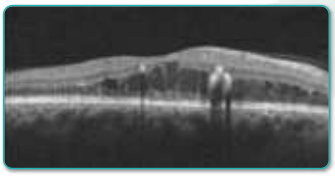
Central Serous Chorioretinopathy (CSR)



44 y/o Female: Notes blur in the LE X 1 mo BCVA: 20/25

66

Diabetic Macular Edema (DME)



SD-OCT of a retina with DME

Color Fundus photo with DME

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The Macula in Diabetes

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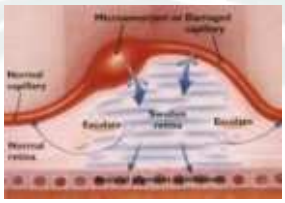
The Macula in Diabetes

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

69

Macular Edema

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



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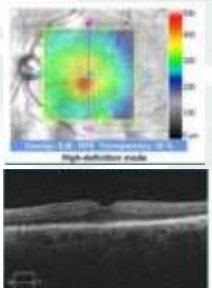


71

CSME

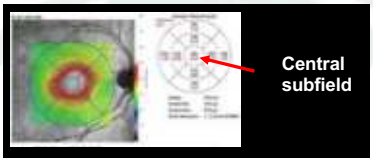
- Retinal thickening within 500 microns from the center of the FAZ
- Hard exudates associated with retinal thickening 500 microns from center of FAZ
- Zones of retinal thickening > 1 DD in area, any part of which is 1 DD from the center of the fovea

72

2017 DME Classification:

Center Involved of Not?

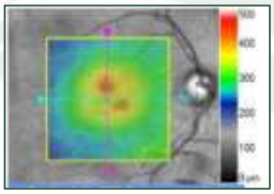
- ETDRS definition of "clinically significant macular edema" modified in era of OCT
- Randomized clinical trials of anti-VEGF agents used presence of DME in **OCT central subfield**



Nguyen, Quan Dong, et al. "Ranibizumab for diabetic macular edema: results from 2 phase III randomized trials: RISE and RIDE." Ophthalmology 119.4 (2012): 789-801.

Brown, David M., et al. "Intravitreal aflibercept for diabetic macular edema: 100-week results from the VISTA and VIVID studies." Ophthalmology 122.10 (2015): 2044-2052.

73



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Diabetic Macular Edema (DME)

SD-OCT of a retina with DME

Color Fundus photo with DME

75

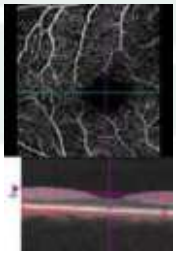
OCT Angiography (OCTA) is a great non-invasive tool to view the microvascular

76

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



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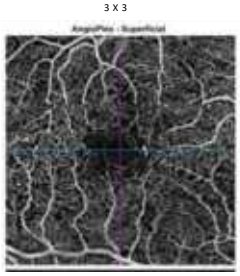

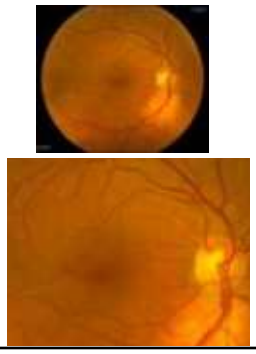

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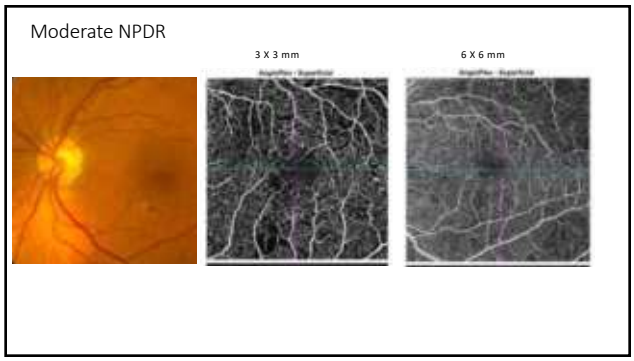

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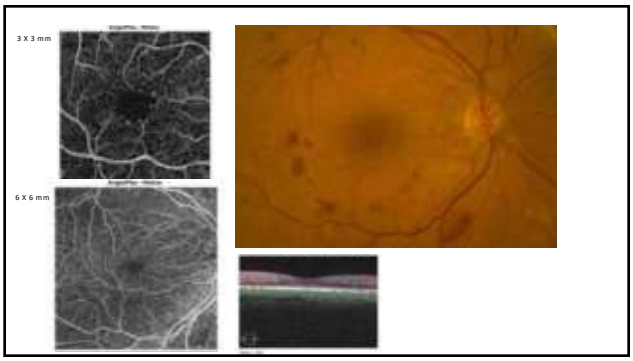

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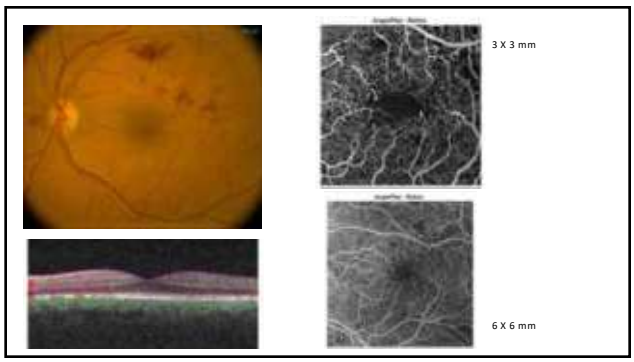

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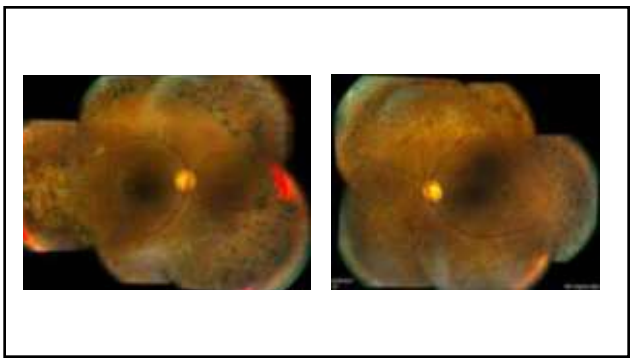

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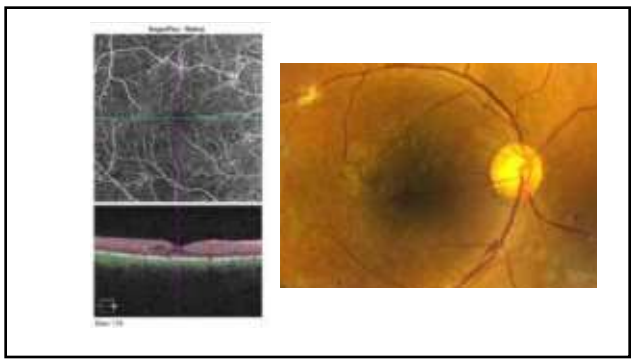

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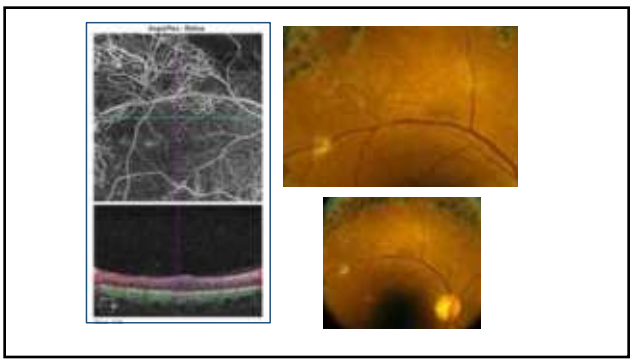

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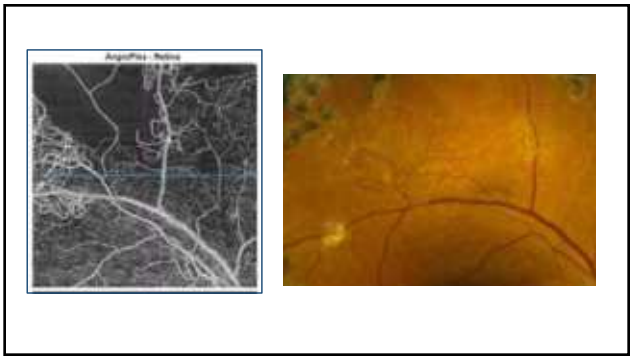

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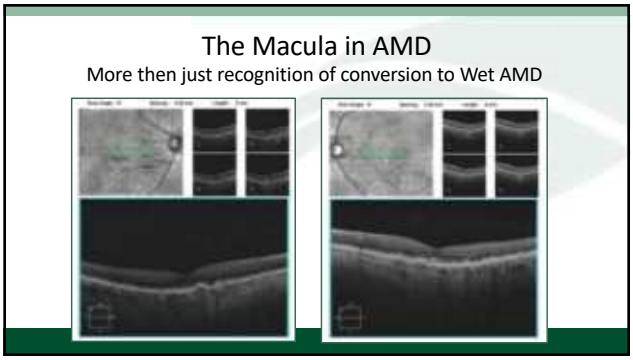

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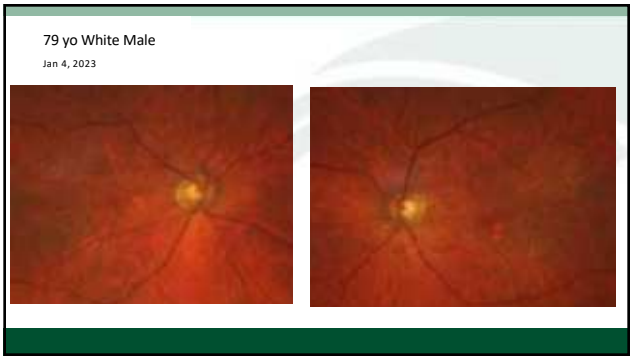

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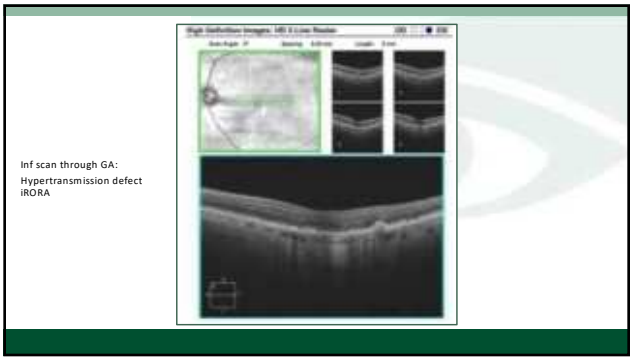

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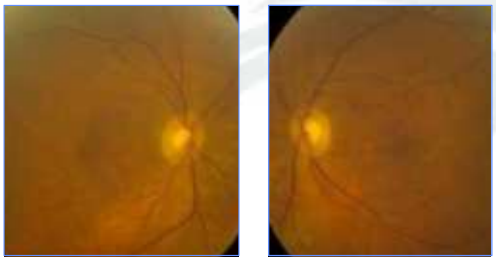
AMD and a Cataract
Can you be sure there is no fluid/thickening?



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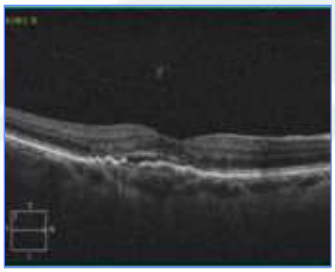

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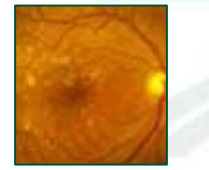

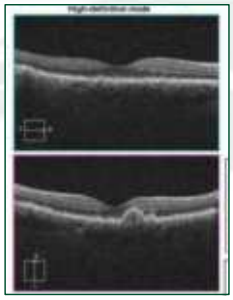

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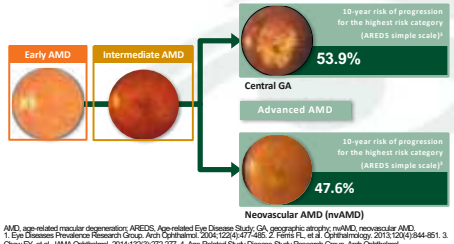
Risk Factors for Progression to Wet AMD

- 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%**

95

AMD Is the Leading Cause of Blindness for Caucasians in the US[1]



AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study; GA, geographic atrophy; nvAMD, neovascular AMD.
1. Eye Diseases Prevalence Research Group. Arch Ophthalmol. 2004;122(4):477-485. 2. Ferris FL, et al. Ophthalmology. 2013;120(4):844-851. 3. Chew EY, et al. JAMA Ophthalmol. 2014;132(3):272-277. 4. Age-Related Study Disease Study Research Group. Arch Ophthalmol. 2005;123(11):1570-1574.

96

OCT findings in dry AMD can be predictor for progression to GA or CNV

97

OCT Biomarkers May Help Predict Conversion to GA or Wet AMD


Review Article

OCT Biomarkers in Neovascular Age-Related Macular Degeneration: A Narrative Review


Retinal Progression Biomarkers of Early and Intermediate Age-Related Macular Degeneration

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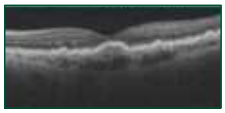
OCT Biomarkers May Help Predict Conversion to GA or Wet AMD

- Drusen volume
- Increased drusen height
- Abnormal thinning of the RPE layer



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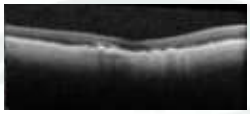
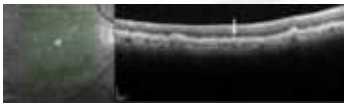
OCT Biomarkers May Help Predict Conversion to GA or Wet AMD

- Hyper-Reflective Foci (HRF)
- Retucular pseudo drusen
- Incomplete Retinal Pigment Epithelial and Outer Retinal Atrophy (iRORA)
  - Without RPE loss
  - Replaces "Nasacent GA"
- Hyper-transmission defects
- OCT-Reflective Drusen Substructures





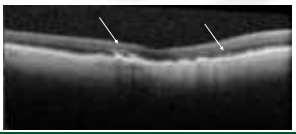
Life **2022**, *12*, 36. https://doi.org/10.3390/life12010036 https://www.mdpi.com/journal/life

100

OCT Biomarkers May Help Predict Conversion to GA or Wet AMD

Hyper-Reflective Foci (HRF)

- Extracellular pigment granules and outer segment debris (outer HRF)
- May also represent displacement and clumping of degenerated RPE cells
- AREDS2 study: Patients with HRF had 5 X increased risk of progression to GA at 2 years vs. controls



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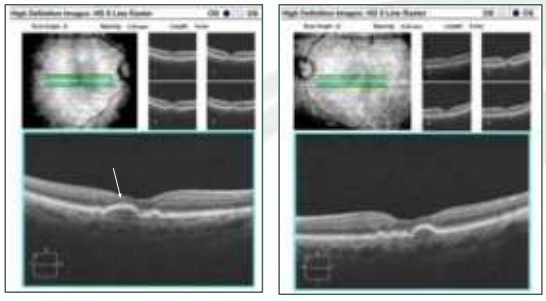

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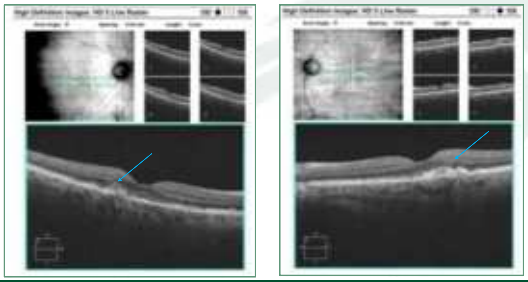
3/26/18: Conversion from Dry to Wet AMD OU



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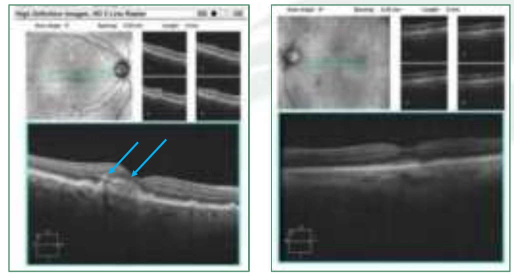
11/30/2021: Multiple anti-VEGF injections OU



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Hyperreflective Retinal Foci (HRF)

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

Lara-Medina FJ, Esteban O, Bartolome I, Ispa C, Mateo J, and Ascaso FJ. "New landmarks, signs, and findings in optical coherence tomography." Clin. App. of OCT in Ophthamol. Feb 2019; 10.5772
Coscas G, De Benedetto U, Coscas F, Li Calzi CI, Vismara S, Roudot- Thoraval F, et al. Hyperreflective dots: A new spectral-domain optical coherence tomography entity for follow-up and prognosis in exudative age-related macular degeneration. Ophthalmologica. 2013;229(1):32-37
Ogino, Ken et al. "Characteristics of Optical Coherence Tomographic Hyperreflective Foci in Retinal Vein Occlusion." Retina (Philadelphia, Pa.) 32.1 (2012): 77–85.
Fragiotta, Serena et al. "Significance of Hyperreflective Foci as an Optical Coherence Tomography Biomarker in Retinal Diseases: Characterization and Clinical Implications." Journal of ophthalmology 2021 (2021): 6096017–10.

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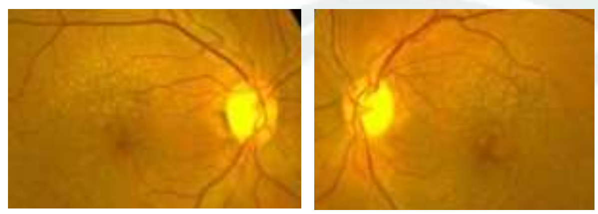
Intermediate AMD with Drusenoid PED's



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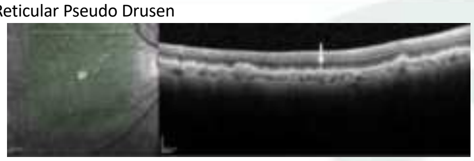
Reticular Pseudo Drusen



- 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

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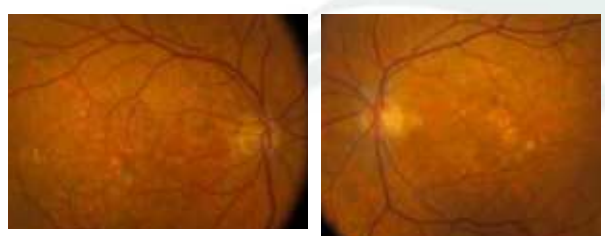
69 yo Hispanic Male



Dec 2017

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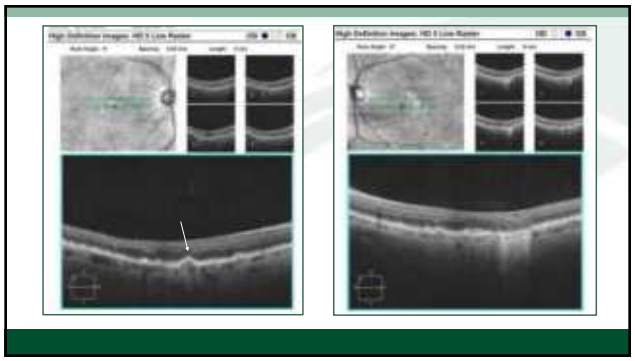

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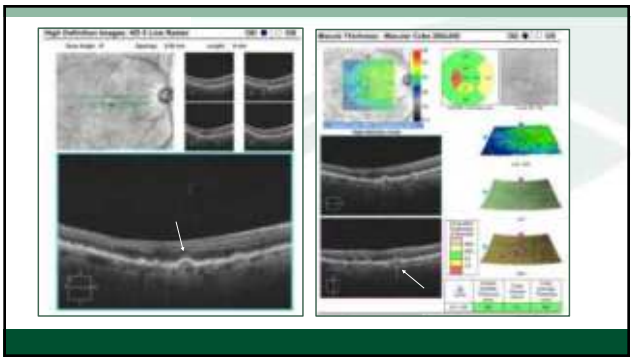

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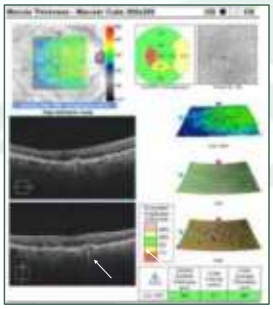
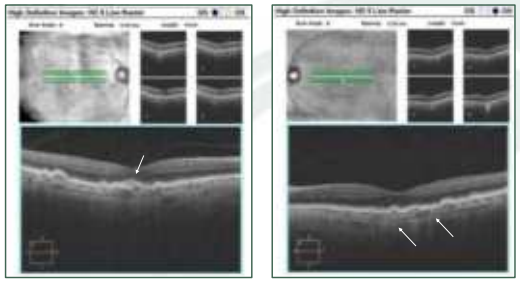
Hyper-reflective Columns

- 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**



111

Villoldo: GA: 2015 Sub-RPE hyper-reflective columns



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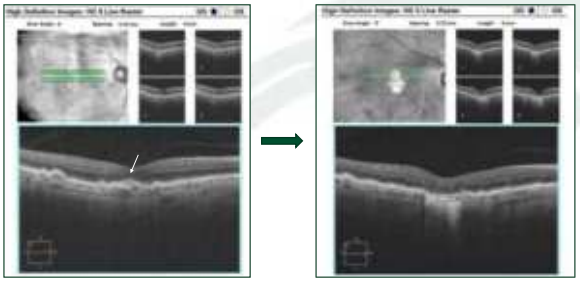
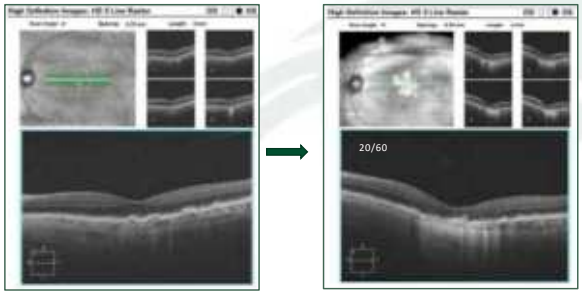
Villoldo: GA: 2015 GA Progression 2015 to 2021



113

2015 Jan 2021



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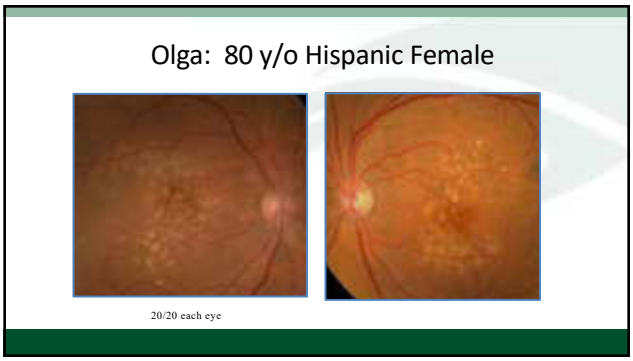

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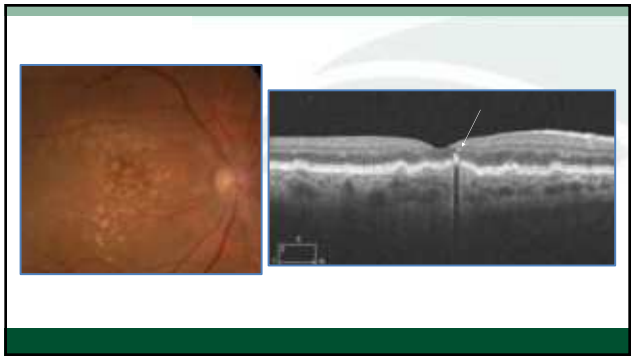

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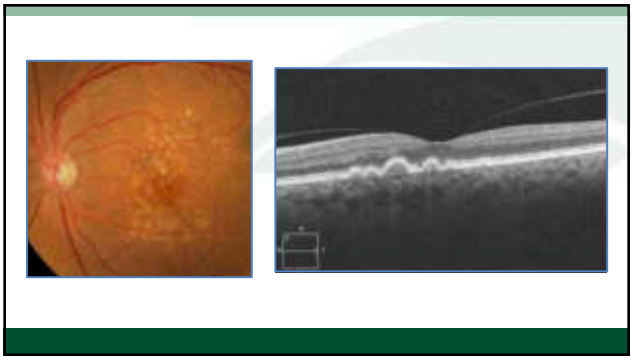

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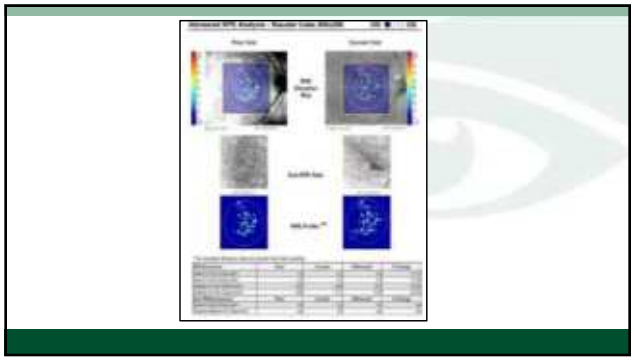

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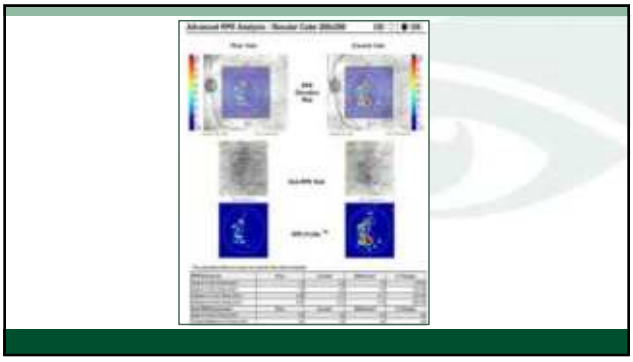

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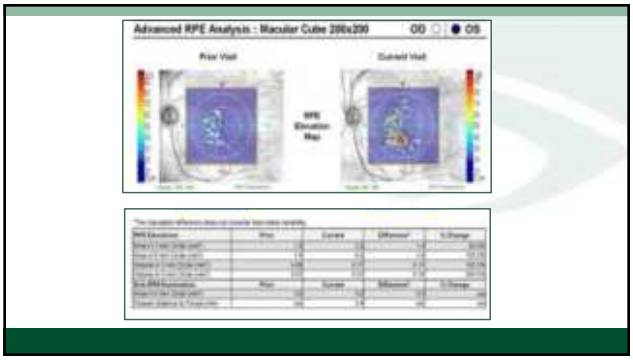

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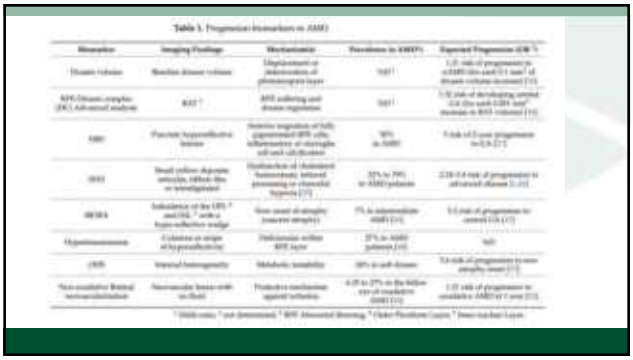

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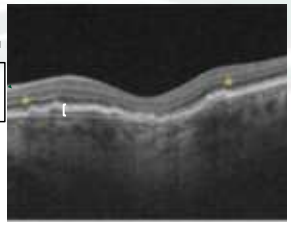
Double Layer Sign

- Shallow, irregular retinal pigment epithelium (RPE) elevation, or **SIRE**
  - Stemmed from the double-layer sign initially described in polypoidal choroidal vasculopathy.
- When the RPE is elevated due to (macular neovascularization), the underlying hyperreflective Bruch's membrane becomes visible
  - Creates 2 hyperreflective lines or a double-layer sign
- In patients with nonexudative AMD - SIRE may predict that 1 in 4 of these patients have an underlying MNV that is not yet exudative
- Features of SIRE include:
  - length of more than 1000 mm
  - RPE elevation < less than 100 mm (resulting in shallow morphologic features),
  - Irregular overlying RPE layer,
  - Nonhomogenous reflectivity



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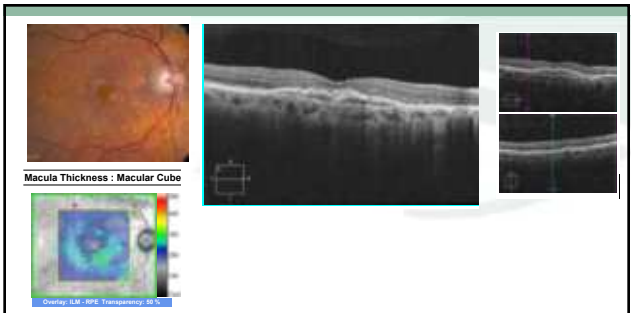

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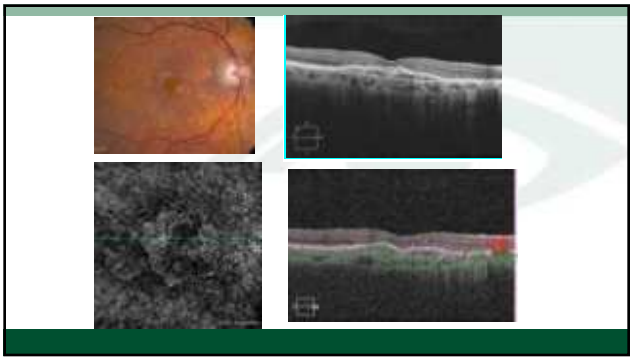
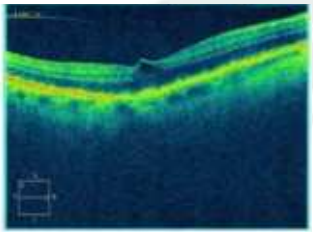


125

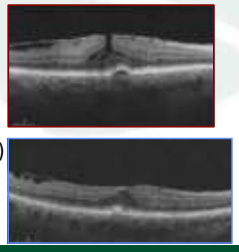
Pay Attention to the Vitreoretinal Interface



126

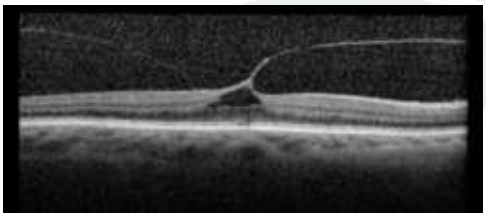
5 Diseases Arising from the Vitreomacular Interface (VMI):

- Vitreomacular traction (VMT)
- Full Thickness macular hole (FTMH)
- Lamellar macular hole
- Epiretinal membrane (ERM)
- Myopic tractional maculopathy (MTM)
  - Myopic macular schisis



127

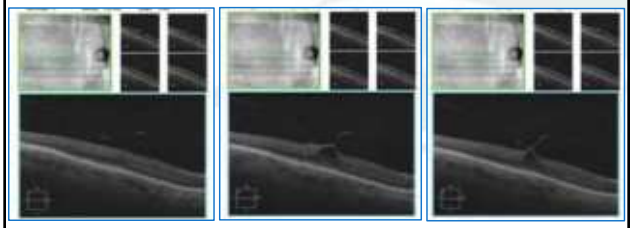
10/30/2018 20/40



Harrison

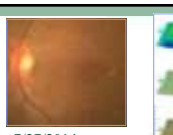
128

12/21/21 PCO -> Yag -> 20/30+



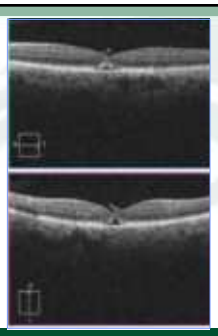
(Harrison 0341614)

129



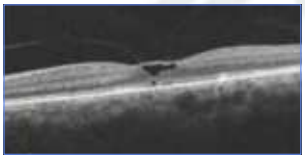
7/27/2014

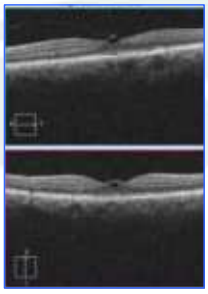
65 y/o Hispanic Female
VA: 20/40



130

9 weeks Later
Worse!
20/50

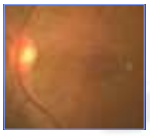




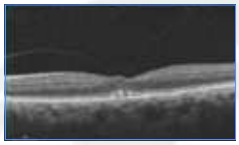
131

VMT evolving into a Macular Hole

7/27/14

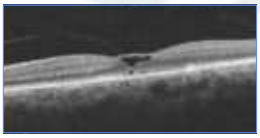


20/40



10/6/14

20/50



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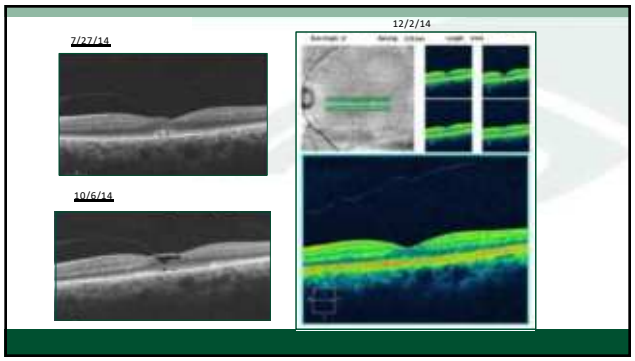
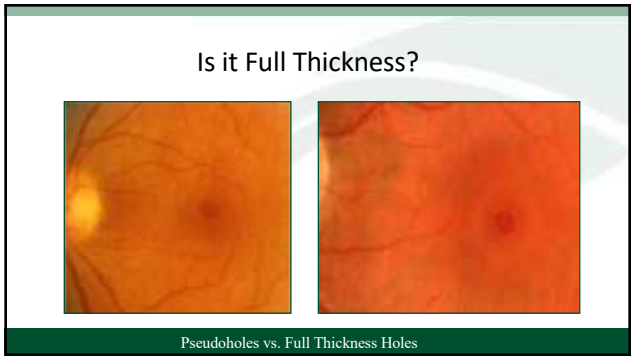


133

134



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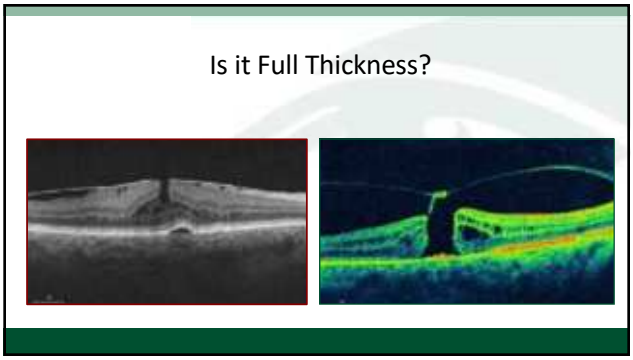

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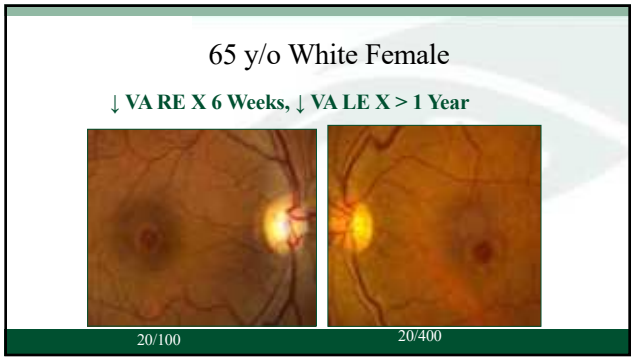
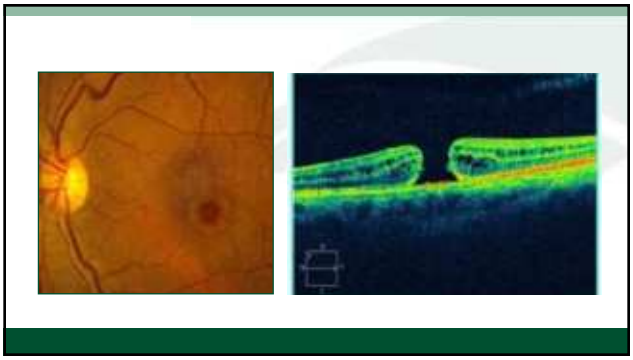


137

138



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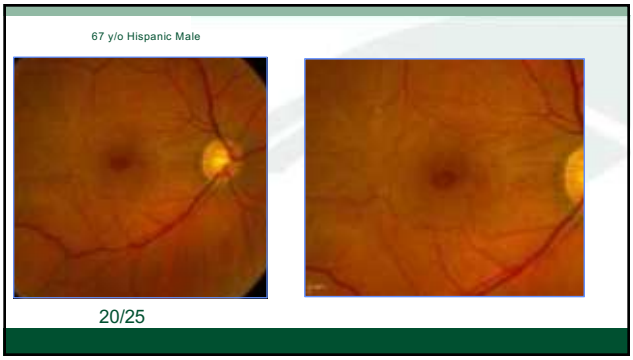

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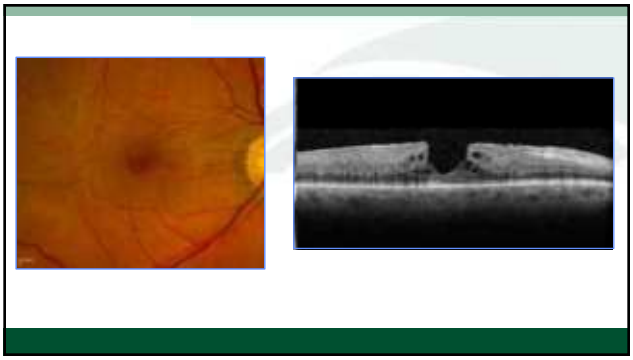
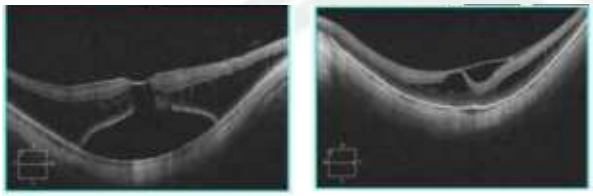


141

The Macula in High Myopia

Scan your high myopes!



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Myopic Macular Retinoschisis
Myopic Tractional Maculopathy

- Seen in 9% of highly myopic eyes with posterior staphyloma
- 50% progress to macular hole formation or macular detachment within 2 years
- **Caused by rigidity of ILM that induces traction**

143

Jeff: mid-50's Attorney, High Myopia

Hx of RD Repair in both eyes: RE: 1985 LE 1989

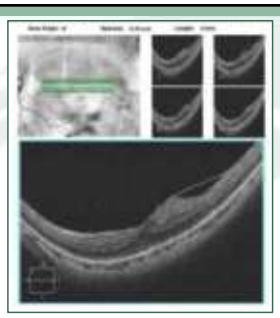
- Never recovers vision in the RE
- He is followed through the 90's with a progressive NS and declining Va ~ 20/70
  - 1 eyed patient and reluctant to have CE
- Eventually has CE/IOL 90's-early 2000's and does well
  - VA 20/25 low refractive error

144

11/22/13
20/30

145

11/22/13

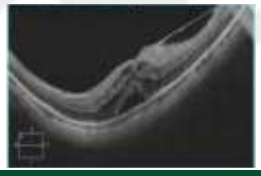


146

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**



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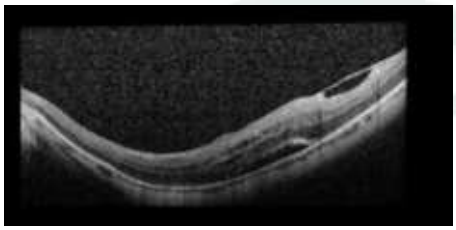
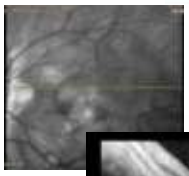
Hybrid Visit

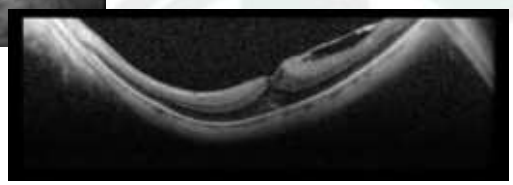
5/26/2020 Feels his vision has improved: now 20/70



149



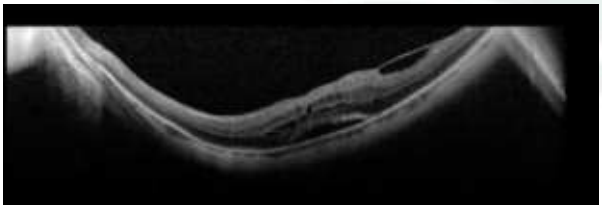
7/27/20
Back to 20/40



150

1 Year Later

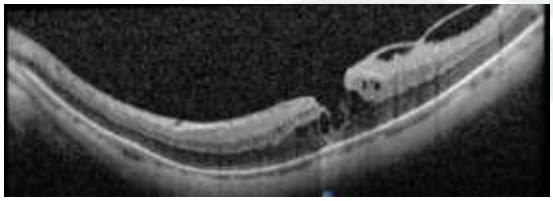
8/9/21: 1 week ago felt a change in the VA: 20/60



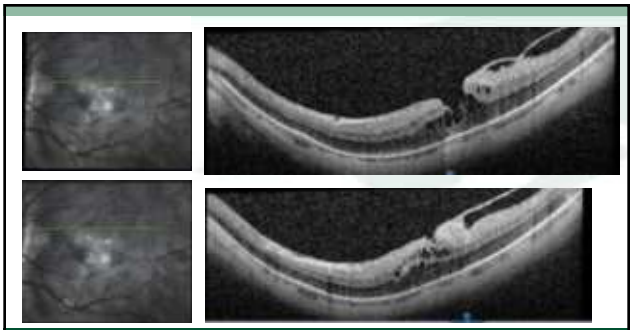
OCT worse -> Va worse -> observe: RTC 6 weeks

151

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



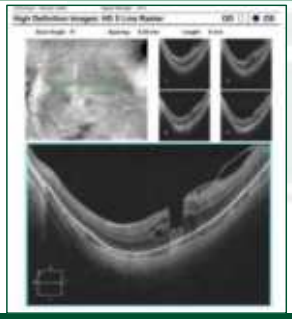
152



153

2/14/22

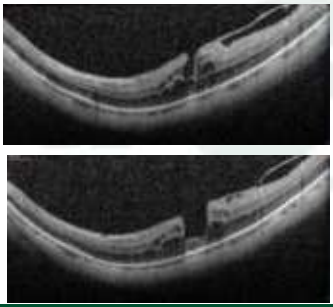
20/40



154

3/28/2022

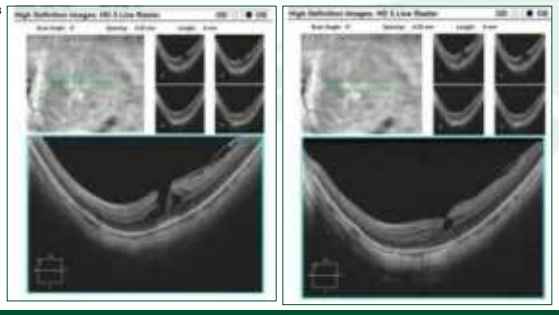
20/50



155

7/19/23

20/30+



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

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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 ophthalmoscopy
- Advancing software has provided expanded uses OCT
- OCT Angiography has taken OCT to the next level

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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

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