

AMD A-to-OCT-to-RI-to-Z

What You Need to Know

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Northern Rockies Optometric Conference

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- ~ Lectured for: Alcon, Allergan, Aerie, BioTissue, Kala, Maculogix, Optovue,
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Course Description and Objectives

This course will evaluate Age Related-Macular Degeneration (AMD) from subclinical to advanced AMD. It will emphasize structure (OCT) and function (dark adaptation) testing to provide early detection and proper staging of AMD. Once accurately diagnosed the course will discuss applying current clinical guidelines in the treatment of subclinical to advanced AMD. The course will also call attention to OCT structural changes indicating progression.

Course Objectives:

- ~ Show how to diagnose the often missed subclinical or early AMD
- ~ Increase ones understanding on function testing for AMD
- ~ Increase ones understanding on the structure changes to properly stage AMD
- ~ Show how to treat subclinical or early AMD
- ~ Discuss OCT Angiography utilization in AMD
- ~ Review treatments for Intermediate AMD
- ~ Review treatments for exudative/choroidal neovascular AMD

AMD Dominance

- ~~ In 2010, the World Health Organization estimated that 5% of the world's blindness was due to AMD
- ~~ Leading cause of blindness over 55-year-old in USA
- ~~ 11 million people in USA have AMD, 22 million by 2050
 - * Approximately 1 in 14 people over the age of 40 has some degree of macular degeneration
 - * Over 60, 1 in 8 (12.5%)
 - * Over 80, 1 in 3 (33 %)
- ~~ More cases of AMD than Alzheimer's, breast cancer, and Parkinson's combined
- ~~ The leading cause of blindness and vision loss in Caucasians
- ~~ Affect 1 in 5 families
- ~~ Hereditary strongest genetic linkage of any major diseases

Eye Care Professional Landscape

~58,000 eye care professionals

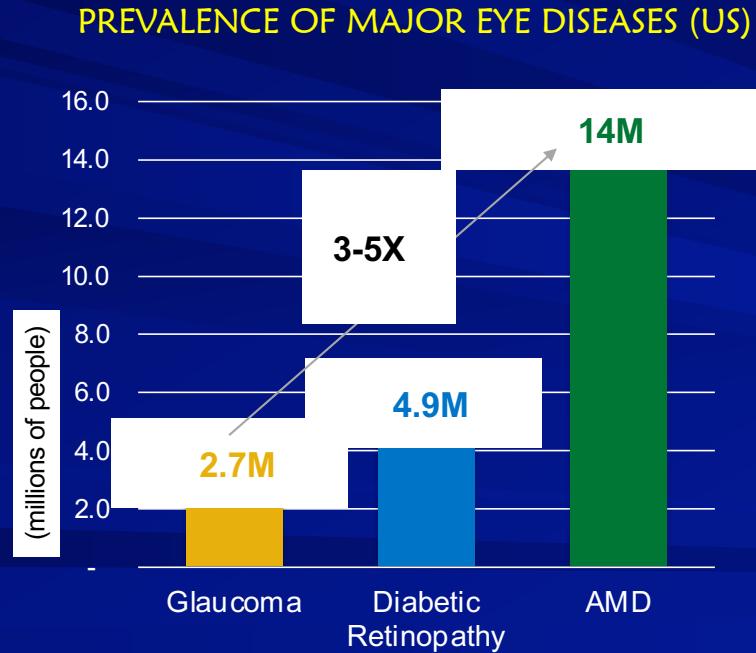
★ 40,000 optometrists

★ 18,000 ophthalmologists

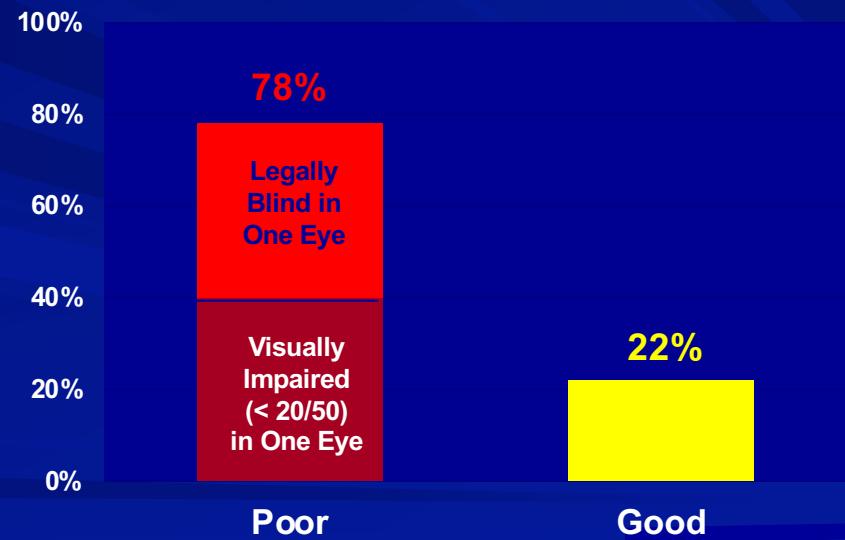
□ About 10% are retinal specialists

Age-Related Macular Degeneration is the Leading Cause of Preventable Blindness in the Western World

~ Clinical AMD is more prevalent than Glaucoma and Diabetic Retinopathy combined



CNV PATIENT OUTCOMES ON 1ST PRESENTATION FOR Anti-VEGF TREATMENT



References: <https://www.aoa.org/newsroom/eye-health-statistics> | Neely D, et al. *Ophthalmol*. Published online April 27, 2017. | Klein R, et al. *Arch Ophthalmology*. 2011;129(1):75-80. | Chevraud, O et al. *Eur J of Ophthalmology*. 2016;26(1):44-47. | Cervantes-Castañeda RA, et al. *Eye (Lond)*. 2008;22(6):777-781. | Olsen TW, et al. *Ophthalmology*. 2004;111(2):250-255.

Primary Eye Care is Missing Visible Disease in 25% of Patients Using Standard Workup

JAMA Ophthalmology | Original Investigation

Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care

David C. Neely, MD; Kevin J. Bray, MD; Carrie E. Huisingsh, MPH; Mark E. Clark, BS;
Gerald McGwin Jr, PhD; Cynthia Owsley, PhD

1288 eyes from 644 people

- Mean age of 69.4
- 36% male

Doctors were aware that they were recruiting patients for an AMD study!!!

- ✓ 25% of eyes had findings consistent with AMD
- ✓ 30% of missed AMD eyes had large drusen (Intermediate AMD)
- ✓ Well-known risk factor for progression to advanced disease
- ✓ ODs and MDs miss AMD diagnosis equally

Reference: Neely DC, Bray KJ, Huisingsh CE, Clark ME, McGwin G, Owsley C. Prevalence of Undiagnosed Age-Related Macular Degeneration in Primary Eye Care. *JAMA Ophthalmol.* 2017;135(6):570–575.

AMD Considerations and Pearls

- ~ There is currently no cure for AMD
 - * Proper detection and care may prevent significant visual acuity loss in many patients
- ~ Are anti-VEGF injections our patients' best hope?
- ~ Late-stage treatments, albeit necessary, they have little impact on central acuity
 - * Impacting our ability to intervene in early to intermediate AMD?

Optometrists and All Eye Care Professionals Responsibility

- ☞ Rethink our responsibility related AMD diagnosis and management
- ☞ Commit to that we will do better in
 - ★ Early detection
 - ★ Treatment
- ☞ Know, execute, and employ current clinically appropriate Practice Guidelines
 - ★ Those that preserve vision
 - ★ Don't wait until vision has been lost
- ☞ Closely monitor and treat the early detected disease
 - ★ If progresses to advanced AMD, better opportunity to save vision

ODs on Facebook

Chad Fellows December 18 at 5:10 PM
Loss of foveal pit with macular traction and drusen appearance which may be vitelliform. Amsler normal OU, VA OD 20/25+, OS 20/30+. Mild cataracts OU. Who sends to retina? Who monitors? Options?



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This community is PRIVATE: ODs, students, Opticians, Industry/Ops... See More

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APR 26 CE in Italy/Europe Bavaria in the Spring 2020 Heidelberg April 26, 2020 - April 28, 2020 Heidelberg Germany James Fane invited you to an event for ODs on Facebook

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ODs on Facebook

Tracy Kimmelman Casten Monitor Like · Reply · 2d

Cibele S. Saporito Monitor Like · Reply · 2d

Steve Burnham what's retina going to do with it? monitor Like · Reply · 2d

Dr. Alan Glazier Monitor q 3 mos with home amsler Like · Reply · 2d

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Azadeh Razmandi Monitor Like · Reply · 2d

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Early Onset Pathogenesis

☞ Drusen small or large are not makers for early stage AMD

- ★ Visible structural evidence of a pathological process
 - Underway for quite some time

☞ Cholesterol deposits exist beneath the surface long before drusen form

- ★ Cannot be seen with structure-based methods
- ★ Cholesterol produced by RPE and deposits into Bruch's membrane
- ★ Continue to layer in Bruch's membrane

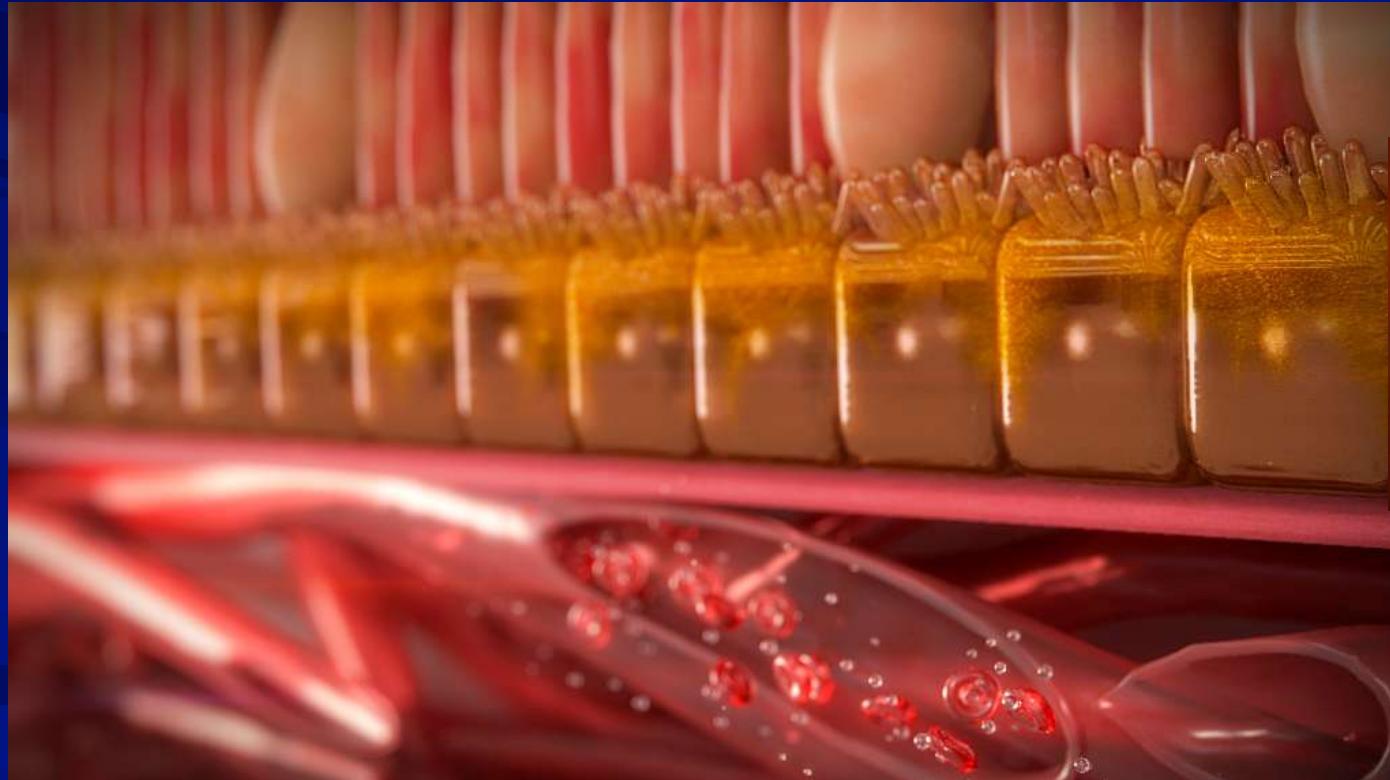
☞ As this cholesterol accumulates the process unfolds with compromise to the outer retina

- ★ Inflammation
- ★ Oxidative stress
- ★ Disruption of oxygen and nutrients
- ★ Drusen formation

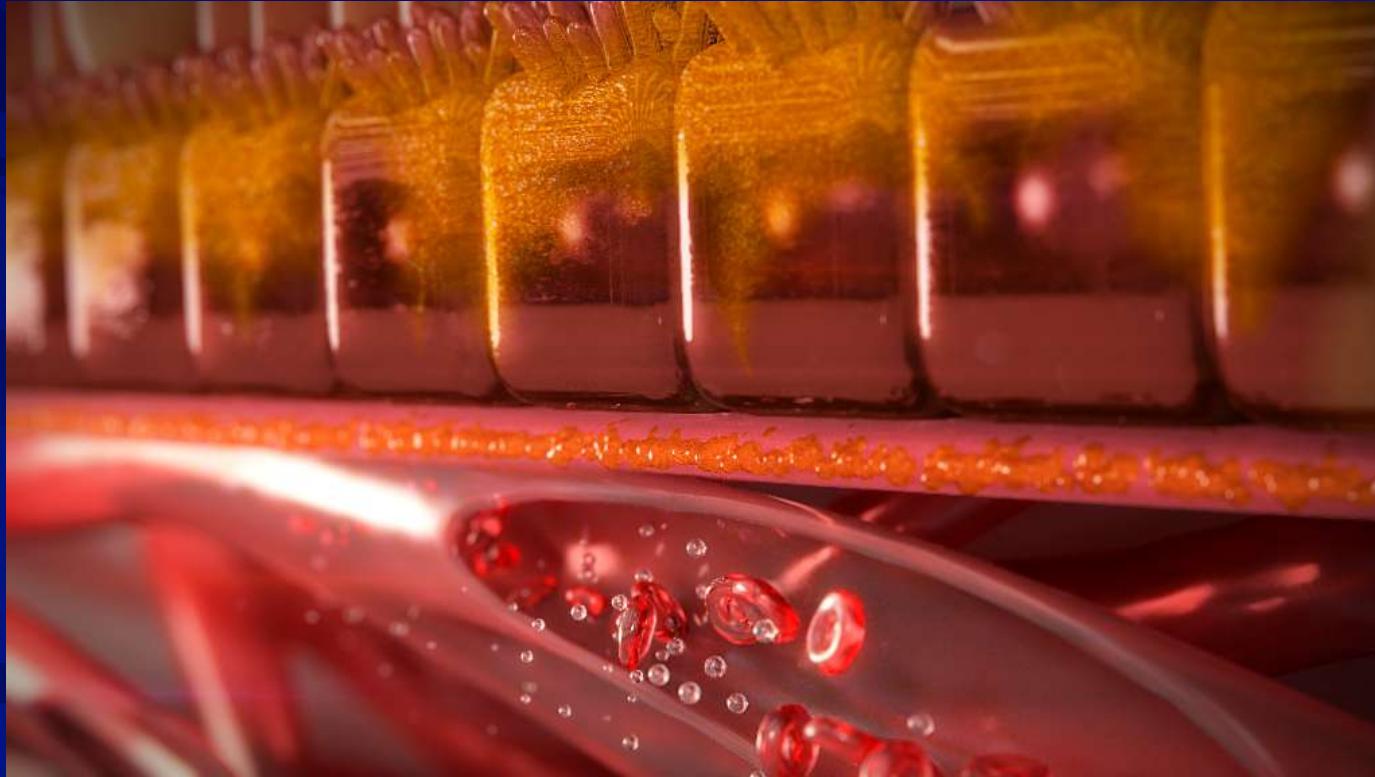
☞ Impaired Vitamin A across Bruch's membrane

- ★ Functional impairment can occur to dark adaptation

Healthy choriocapillaris, Bruch's, RPE, and Photoreceptors



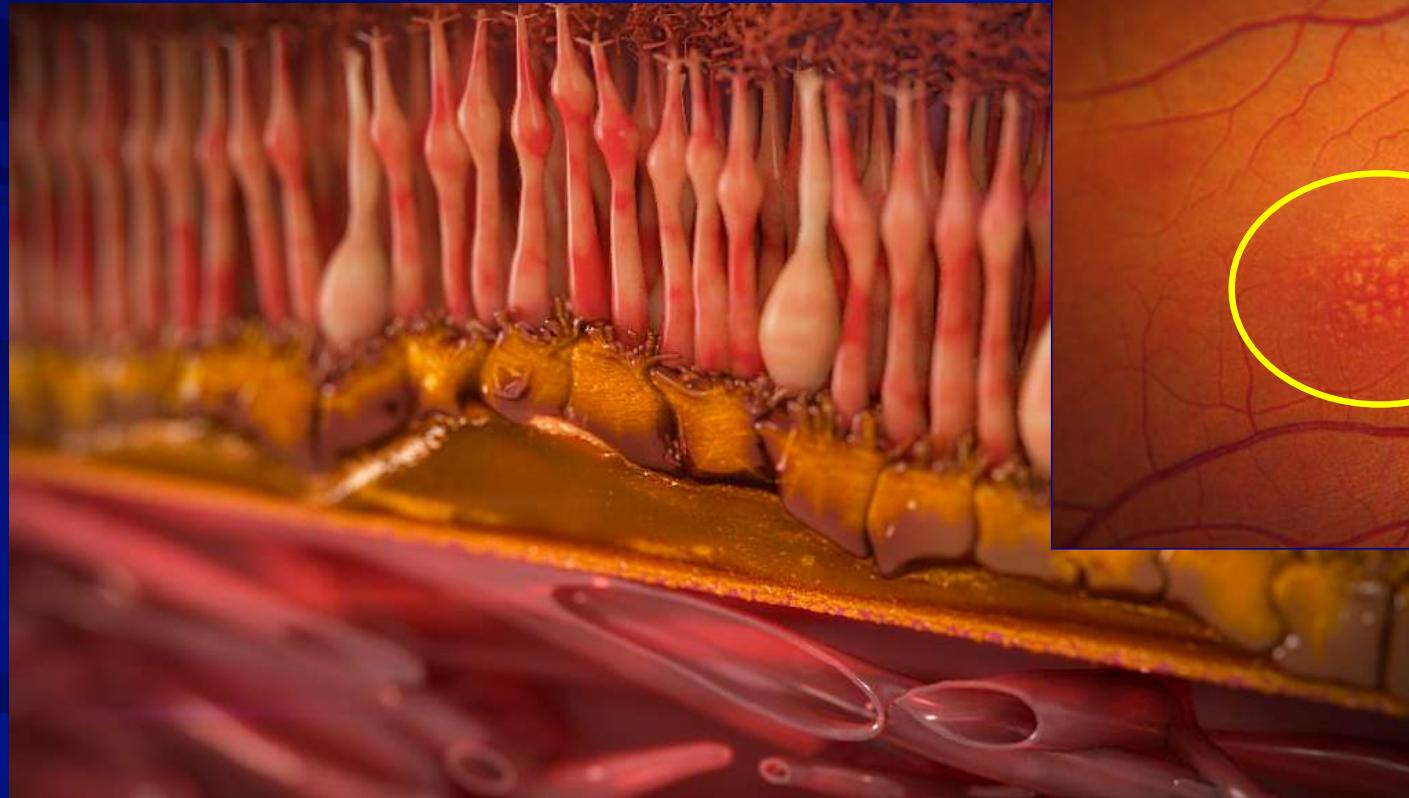
Cholesterol barrier deposited along Bruch's and RPE



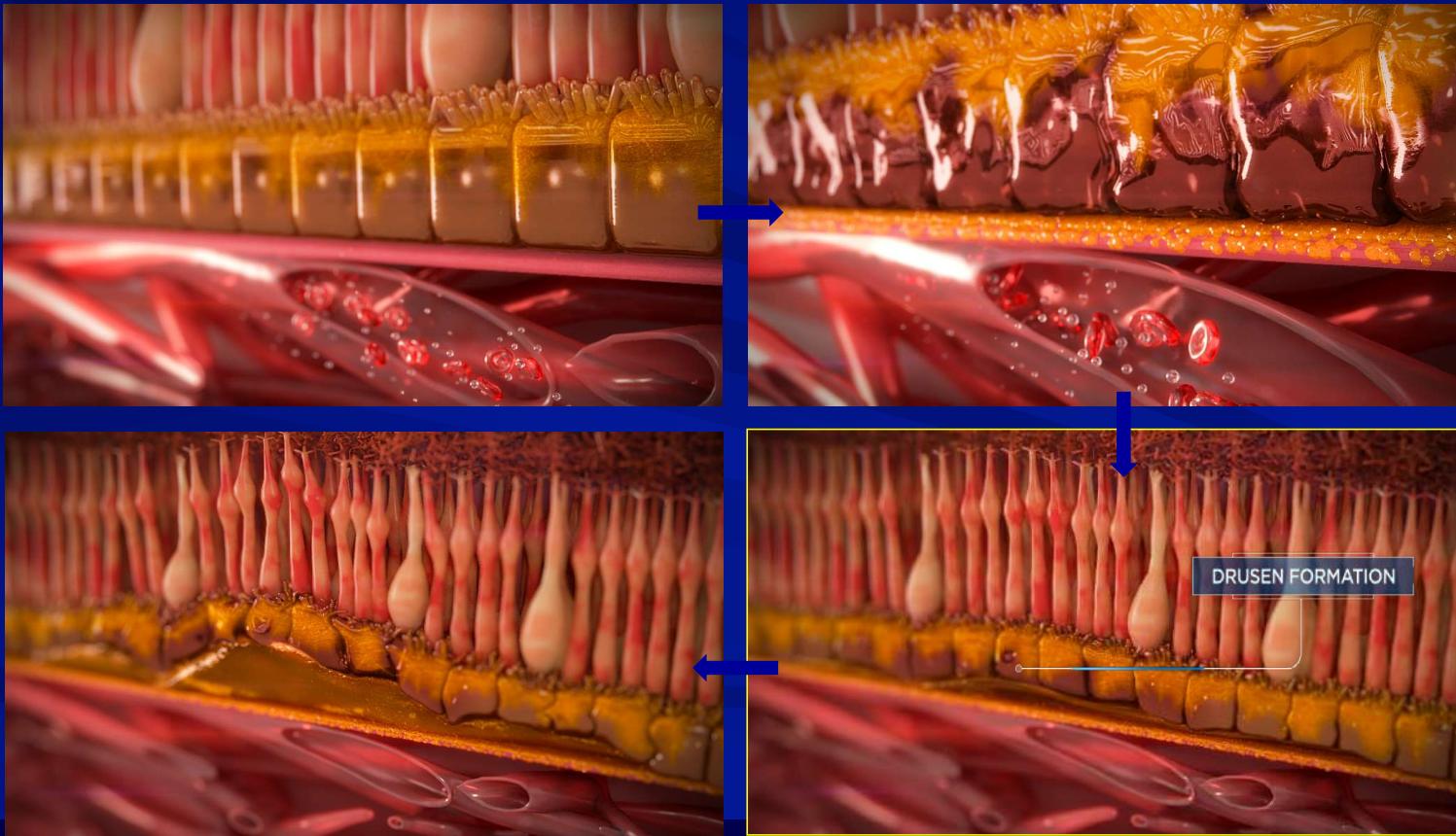
RPE Secretes even more cholesterol and degenerates



Finally, visibly evident drusen on fundus evaluation



AMD is a Disease Process that Starts Below the Surface



Staging of Drusen

What method to detect?

- | | |
|---|----------------------|
| ☞ Subclinical or sub-structural – cholesterol layer | Functional |
| ☞ Small drusen < 63 microns | Exam, photos, SD-OCT |
| ☞ Medium drusen > 63 – <125 microns | Exam, photos, SD-OCT |
| ☞ Large drusen > 125 microns | Exam, photos, SD-OCT |

Beckmann Committee Classification of AMD

Based on presence of lesions within 2 DD of fovea in either eye

* No AMD

- ☐ None or few small drusen, < 63 microns
- ☐ No AMD pigmentary abnormalities

* Early AMD

- ☐ Medium drusen, > 63 – <125 microns
- ☐ No AMD pigmentary changes

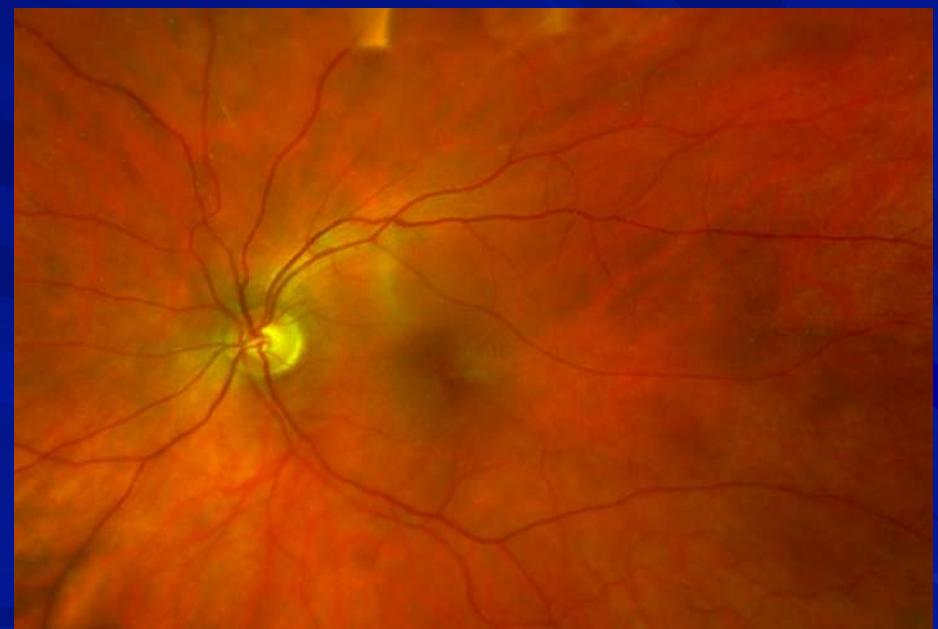
* Intermediate AMD

- ☐ 1 large drusen, > 125 microns
- ☐ Any AMD pigmentary changes

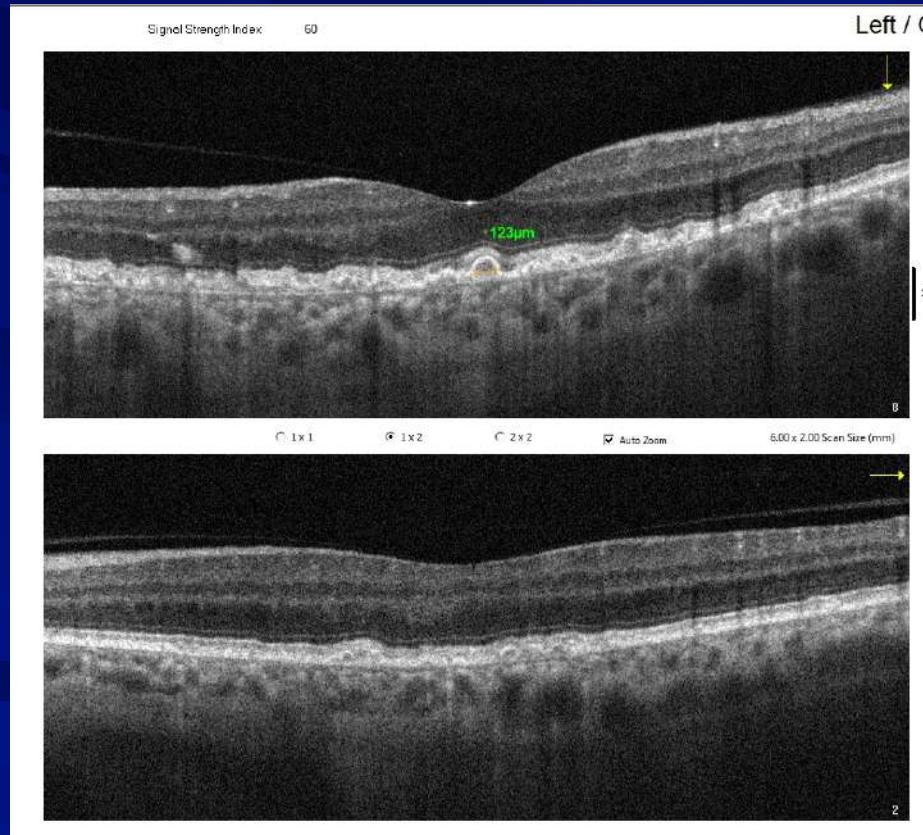
* Advanced AMD

- ☐ Any geographic atrophy
- ☐ Choroidal neovascularization (CNV)

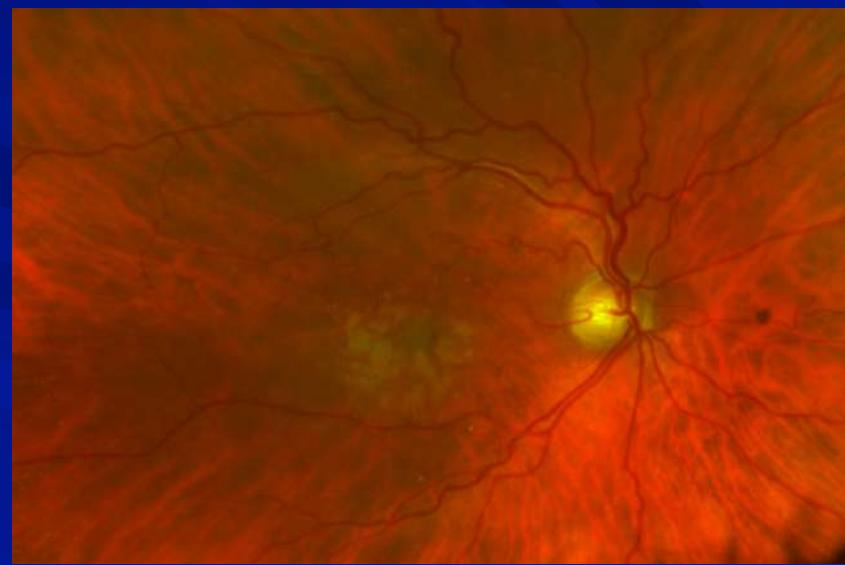
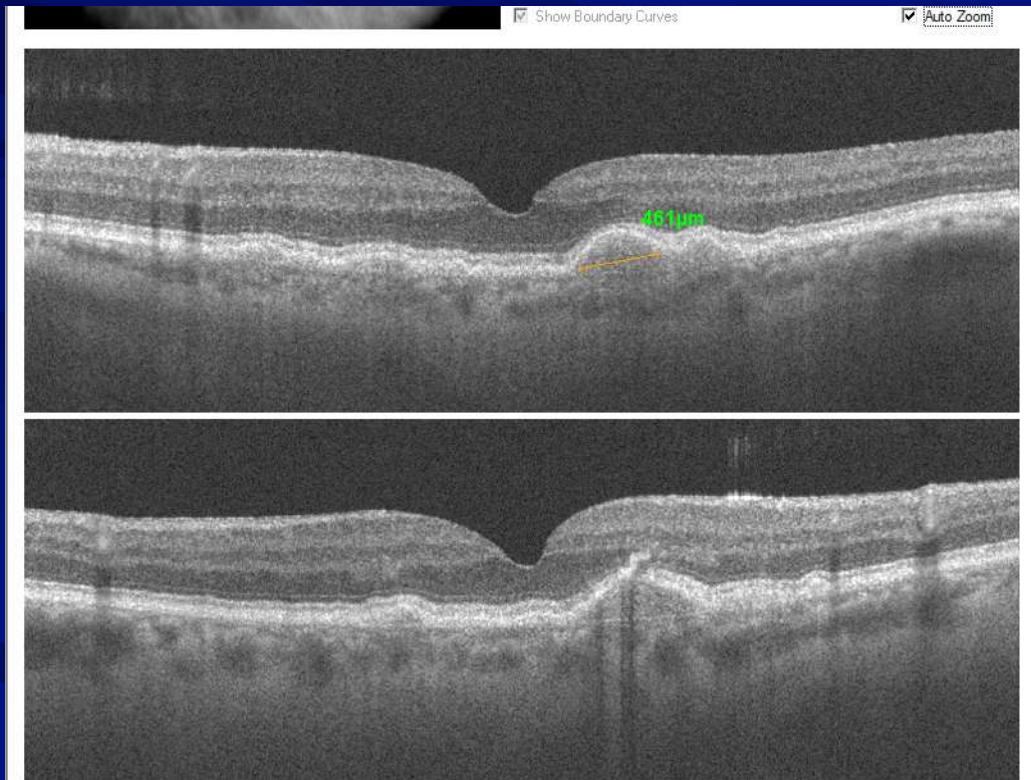
Measure the Drusen with Your OCT



Measure the Drusen with Your OCT



Measure the Drusen with Your OCT



Choroidal Neovascularization (CNV)

- ☞ Type 1 – Occult
- ☞ Type 2- Classic
- ☞ Type 3- RAP
- ☞ Type 4- Mixed

Predictors of Progressing to Advance Disease

- ☞ Hyper-reflective foci
- ☞ Reticular pseudodrusen
- ☞ Nascent geographic atrophy
- ☞ Sub-RPE hyper-reflective columns
- ☞ Drusen substructures
- ☞ Drusen load and regression
- ☞ Vision loss from geographic or exudative/CNV

Tools for Diagnosis, Management, and Treatment of AMD

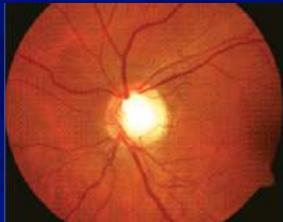
- ~~ Comprehensive eye exam – structural, some functional
- ~~ Fundus photography and FAF - structural
- ~~ OCT and OCT Angiography – structural
- ~~ Dark adaptation – functional

- ~~ How about macula pigment density testing

Applying a Familiar Standard of Care: *Two Multifactorial Diseases*

Glaucoma

Structure



Cup-to-disc
Ratio

Function



Visual Field

Risk

Intraocular Pressure (IOP)
Corneal Thickness
Age/race
Family history/etc.
Health and Lifestyle (Diabetes)



AMD

Drusen



Dark Adaptation



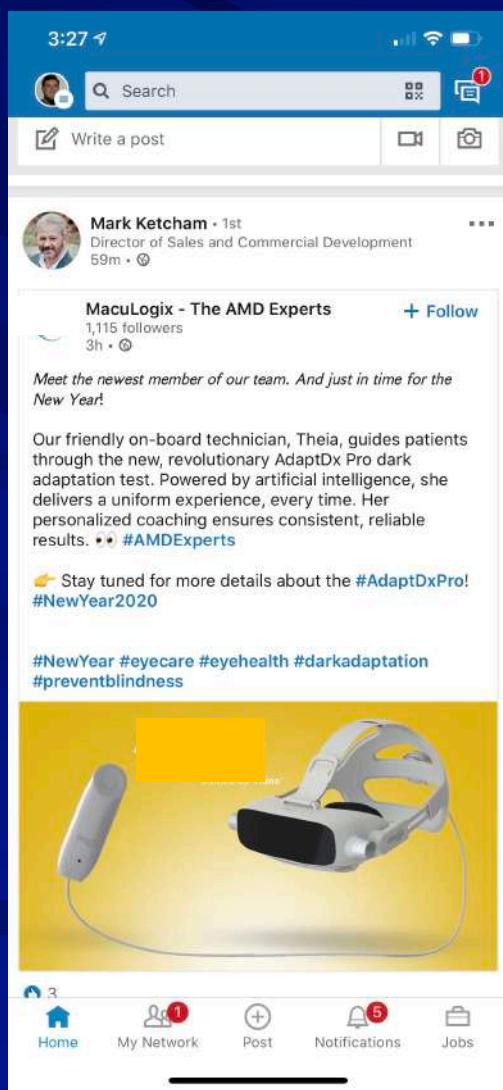
Age
Genetic Testing
Health and Lifestyle (Smoking)
Macular Pigment Optical Density (MPOD)
Contrast Sensitivity.

Dark Adaptation in AMD

Function Test

- ❖ Measures how long to recover from bright light to darkness
 - ★ Rod intercept line (RI) time
- ❖ Functional test that can help overcome the challenges in diagnosing AMD
- ❖ Alabama Study on Early Age-Related Degeneration (ALSTAR)
 - ★ Able to detect subclinical 3 years before clinically visible
 - ★ 325 adults without clinically detectable AMD
- ❖ Rod deterioration happens in earliest stages of AMD
 - ★ Earlier detection before visual acuity
- ❖ AdaptDx 92284
 - ★ Sensitivity 90.6%
 - ★ Specificity 90.5%





Dark Adaptation in AMD

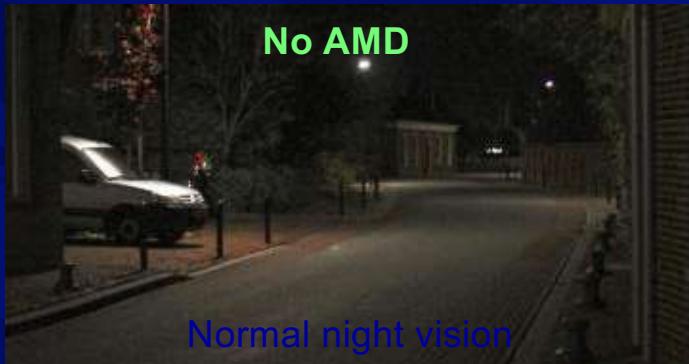
Function Test

January 1st, 2020

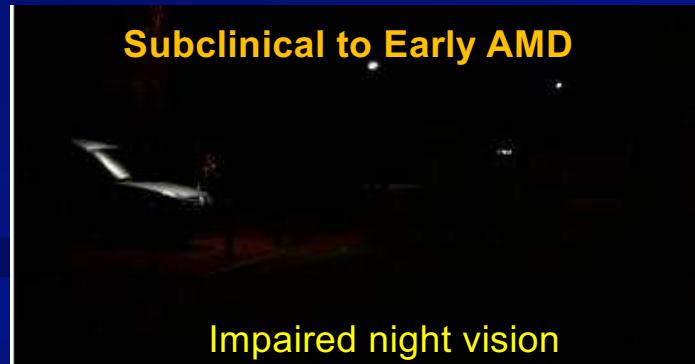
AdaptDx Pro Now Available for Clinical Use



This Means We Now Have an *Early Symptom* We Can Use to Help Diagnose AMD



- Night vision impacted in early AMD: 30+ studies
- AMD patients often give up driving at night
- Night vision is impaired before day vision
- Typically ECP's chalk this complaint up to cataracts

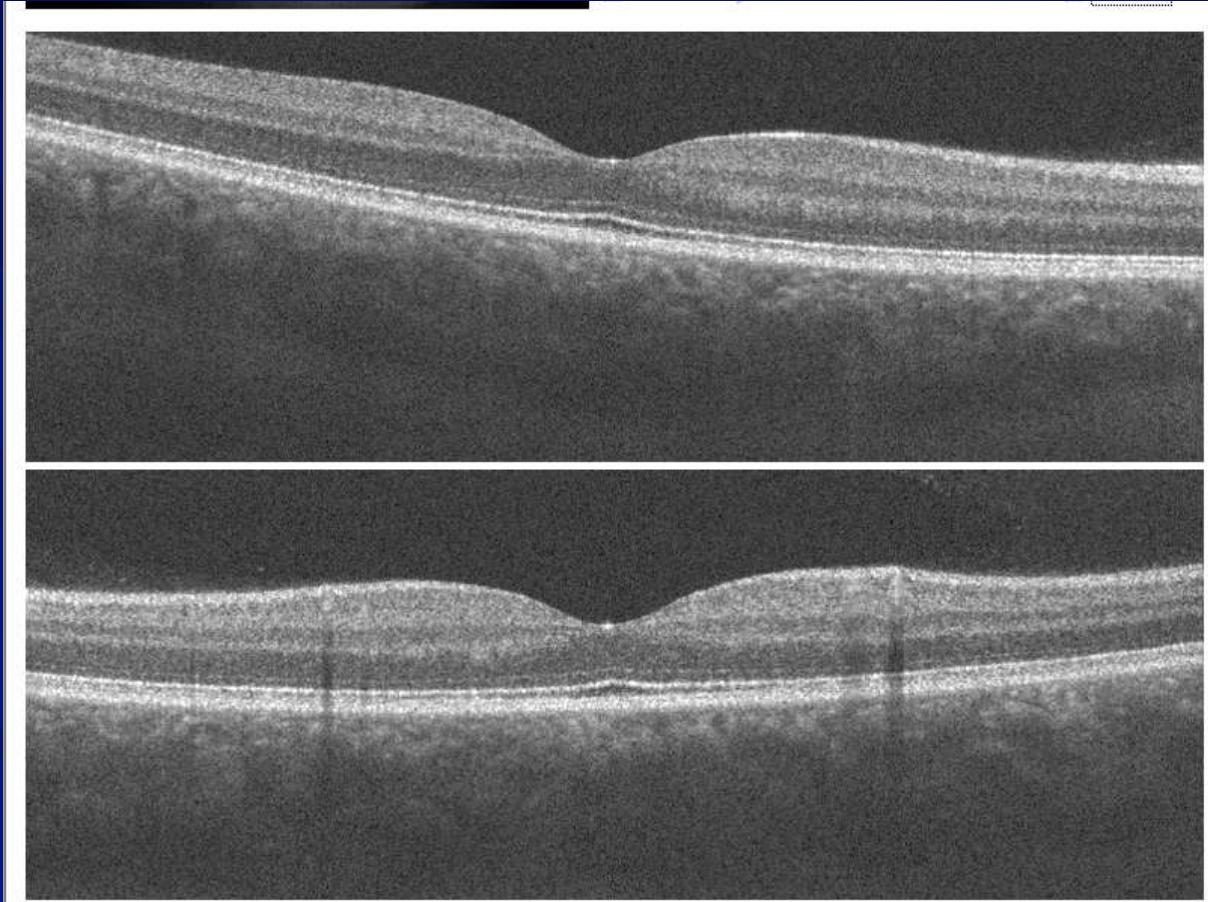


*Ask Every Patient Over 50
About Their Night Vision*

OCT in AMD

- ☞ Need spectral domain to follow intermediate or worse AMD
- ☞ Able to identify OCT predictors of progression
- ☞ Especially in identifying OCT predictors of progression
 - ★ Hyper-reflective foci
 - ★ Reticular pseudodrusen
 - ★ Nascent geographic atrophy
 - ★ Sub-RPE hyper-reflective columns
 - ★ Drusen substructures
 - ★ Drusen load and regression

Hypo versus Hyper Reflectance



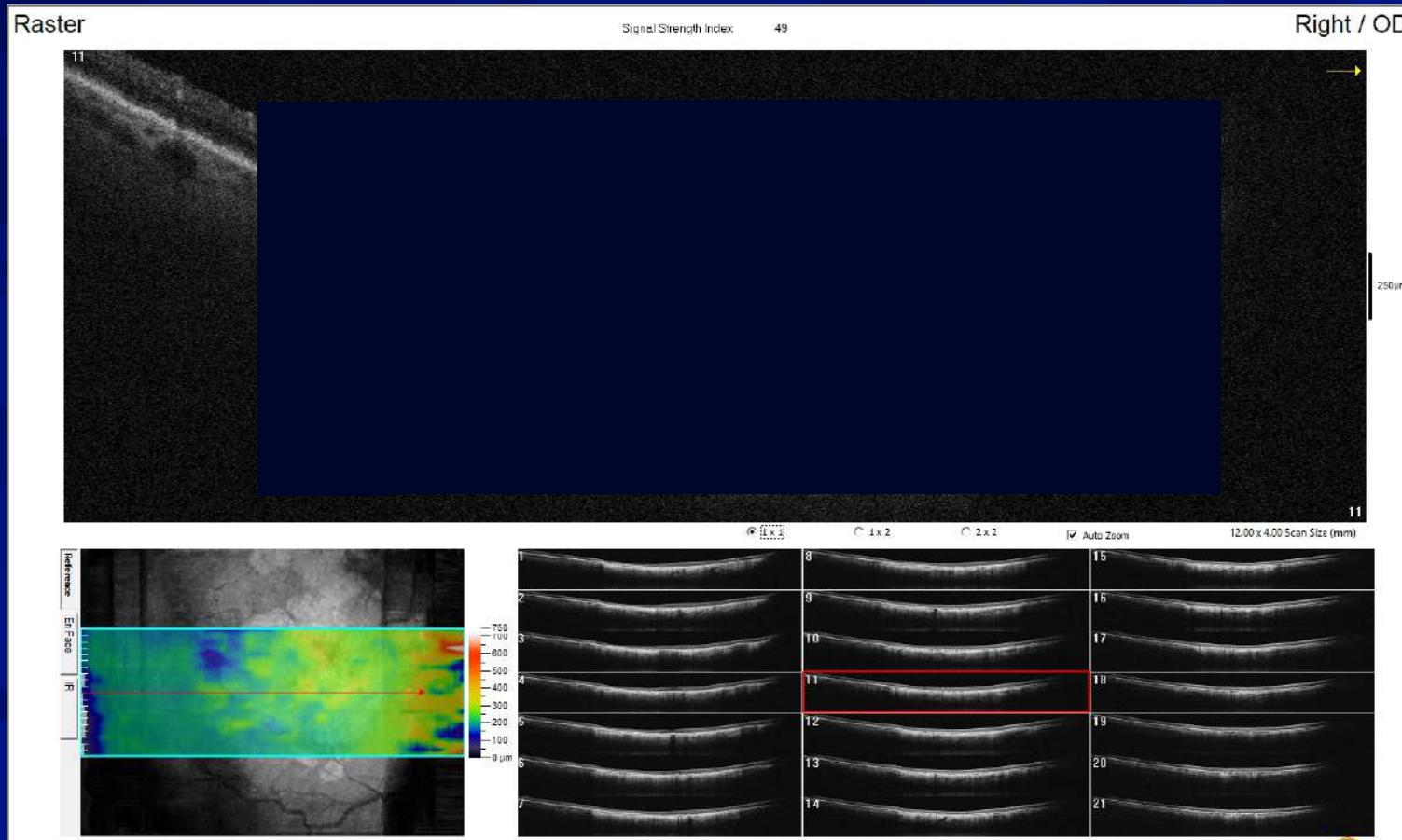
Can We Learn From These Pictures?



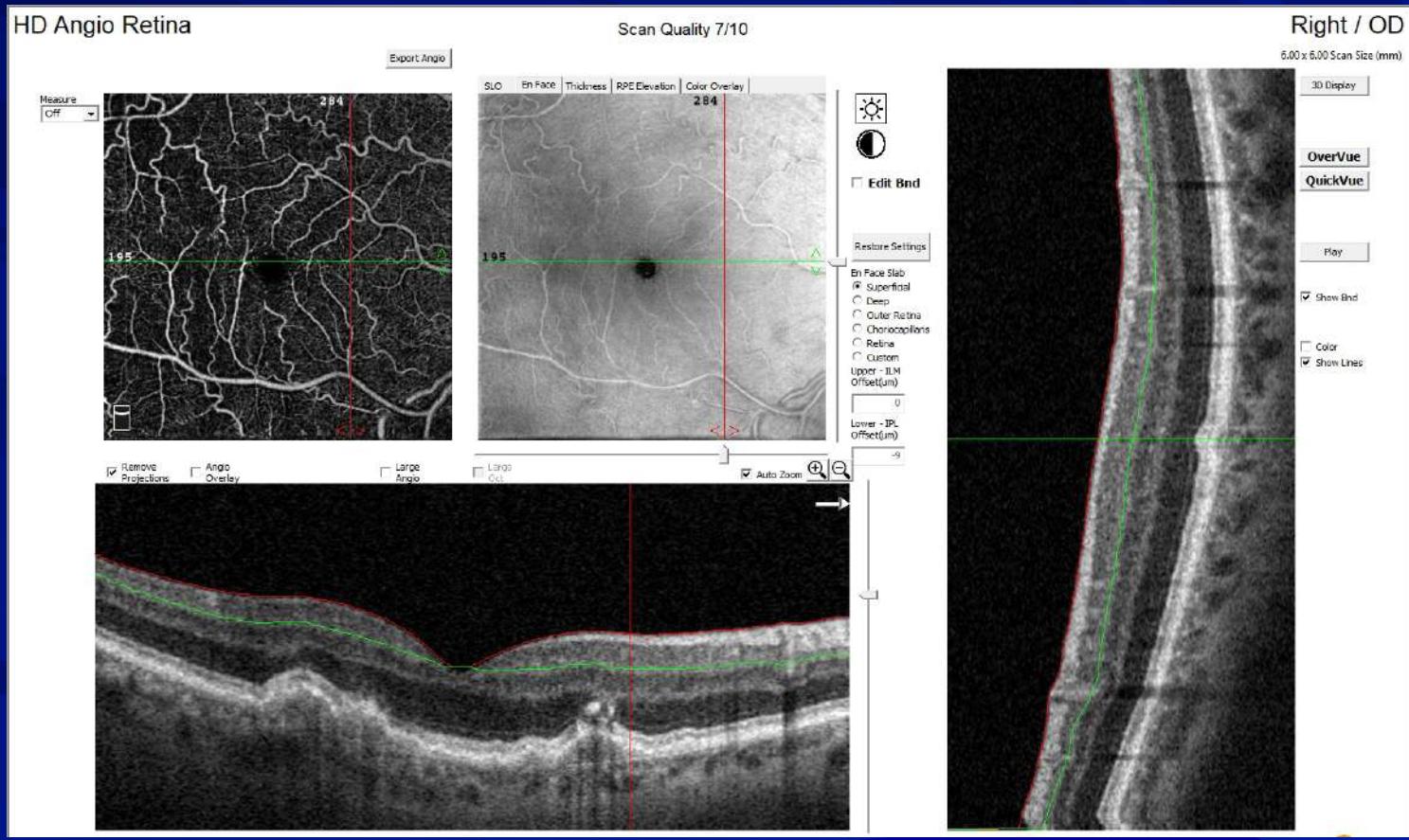
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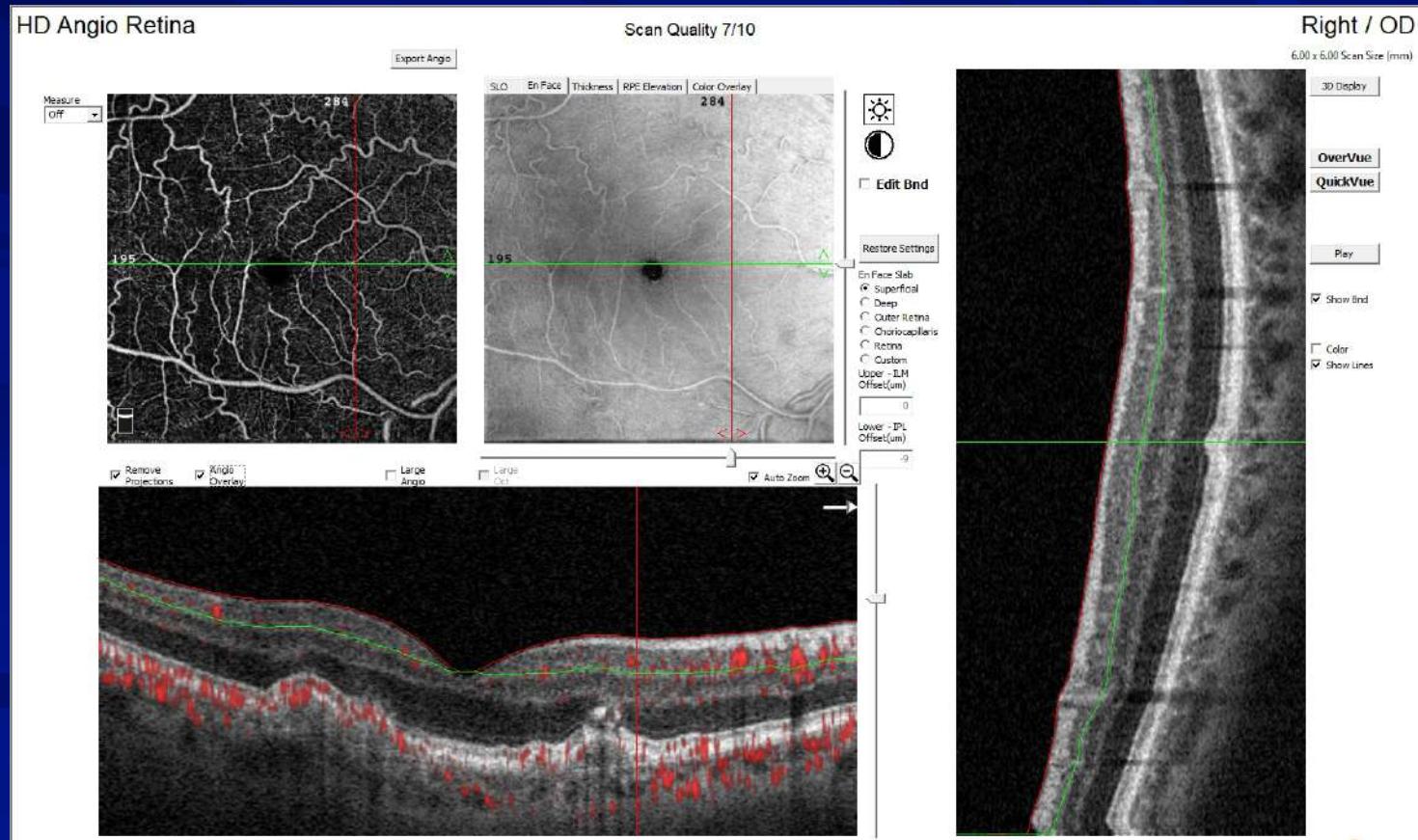
Hypo versus Hyper Reflectance



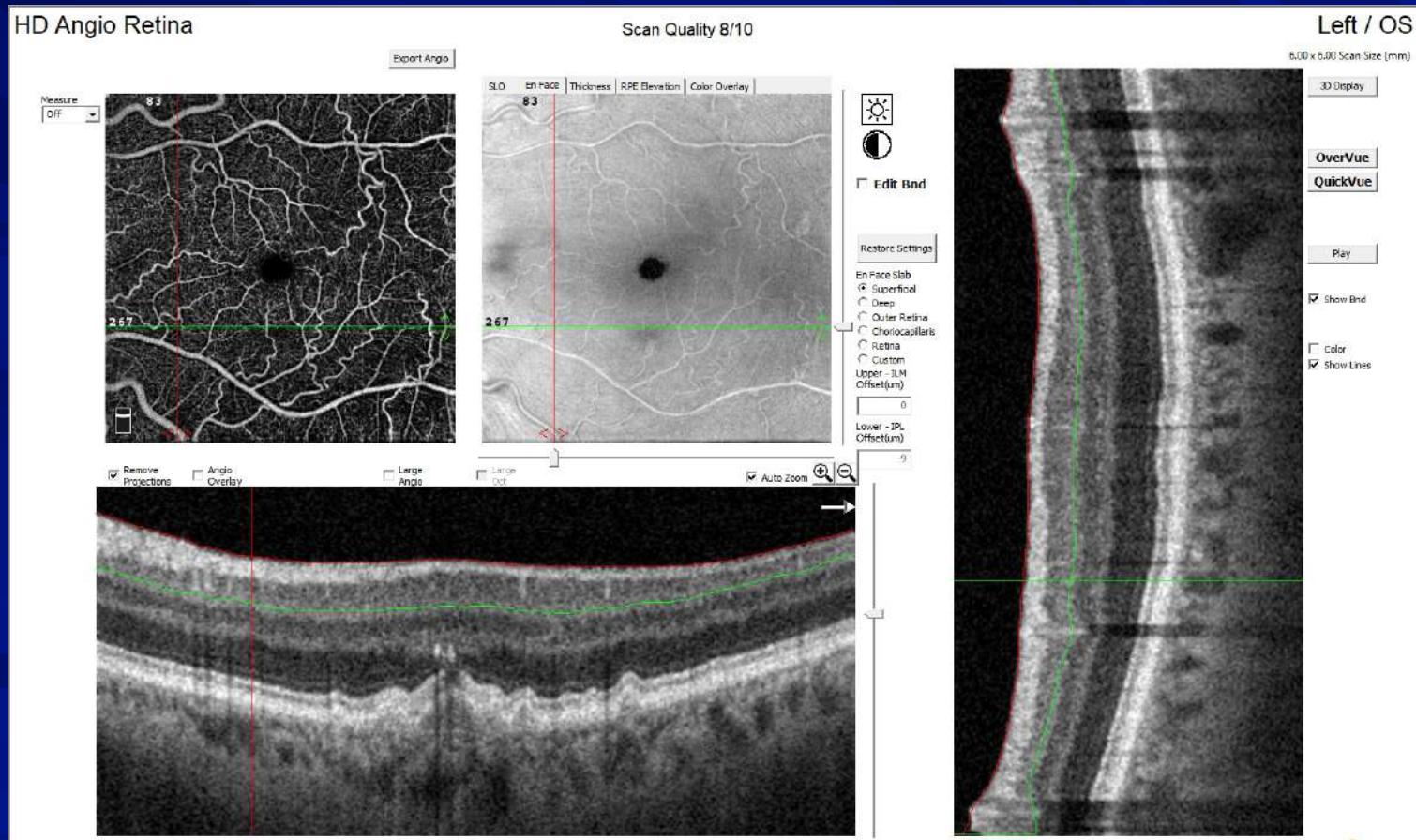
Case 1 - OCT Predictors of Progression



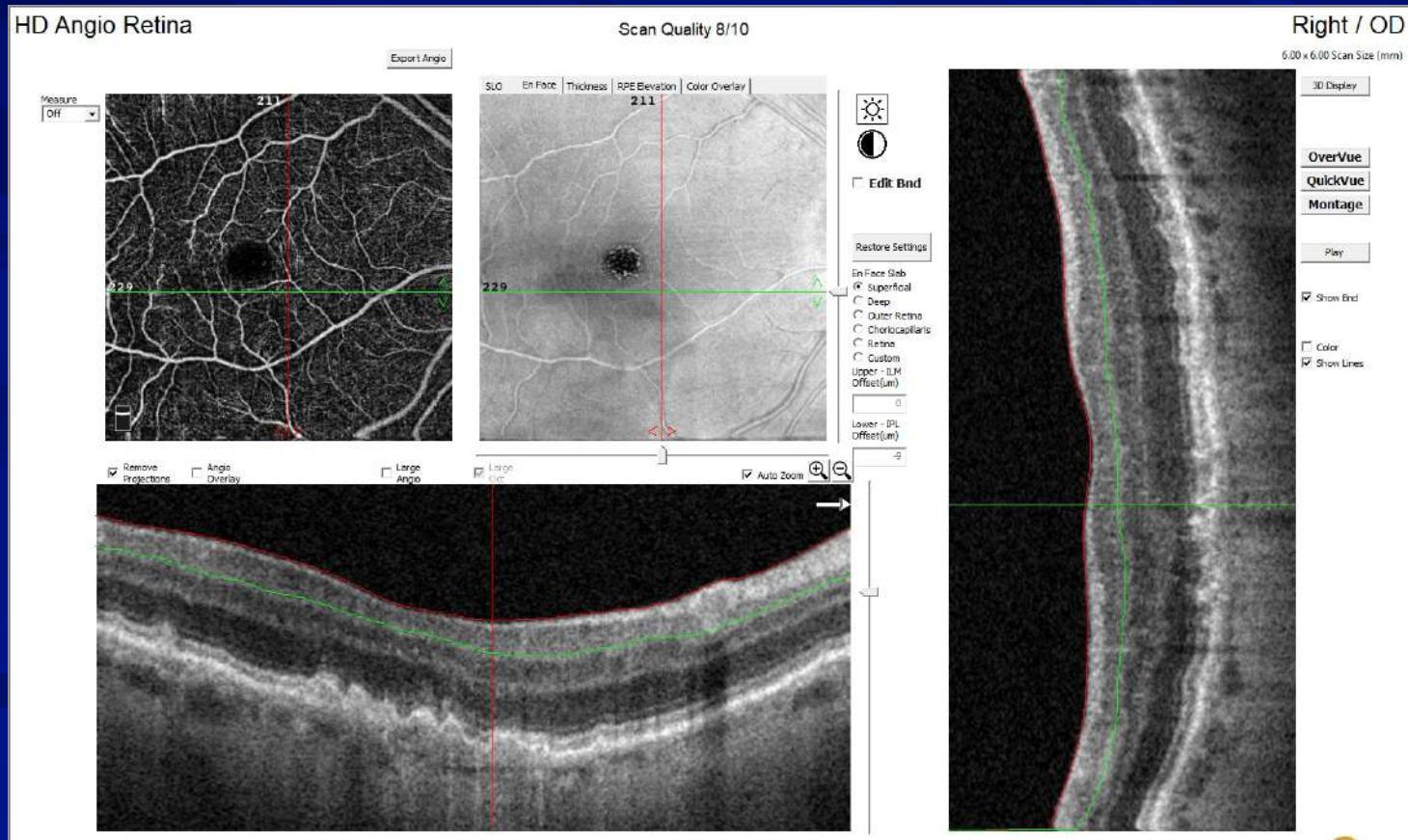
Case 1 - OCT Predictors of Progression



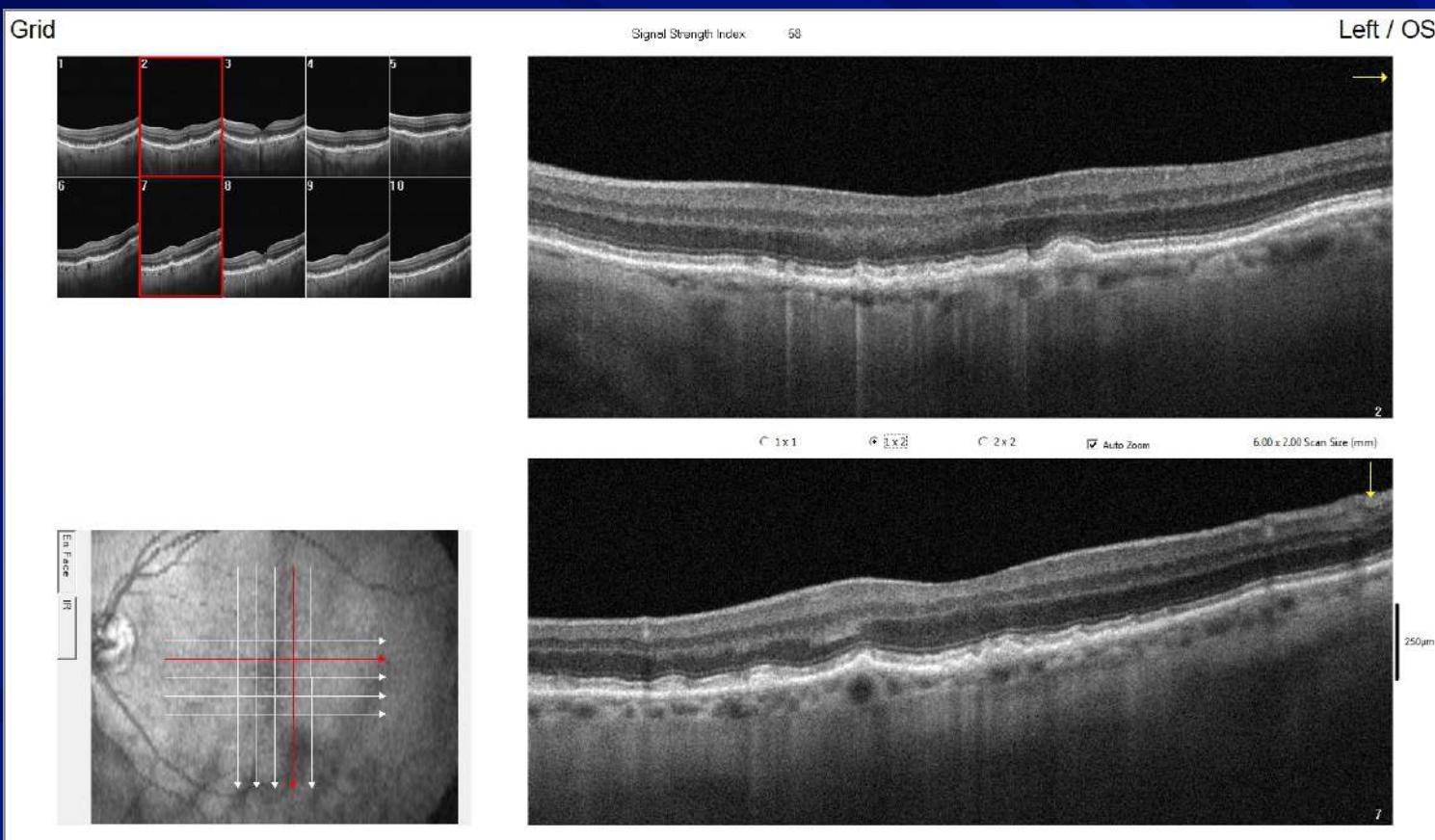
Case 1 - OCT Predictors of Progression



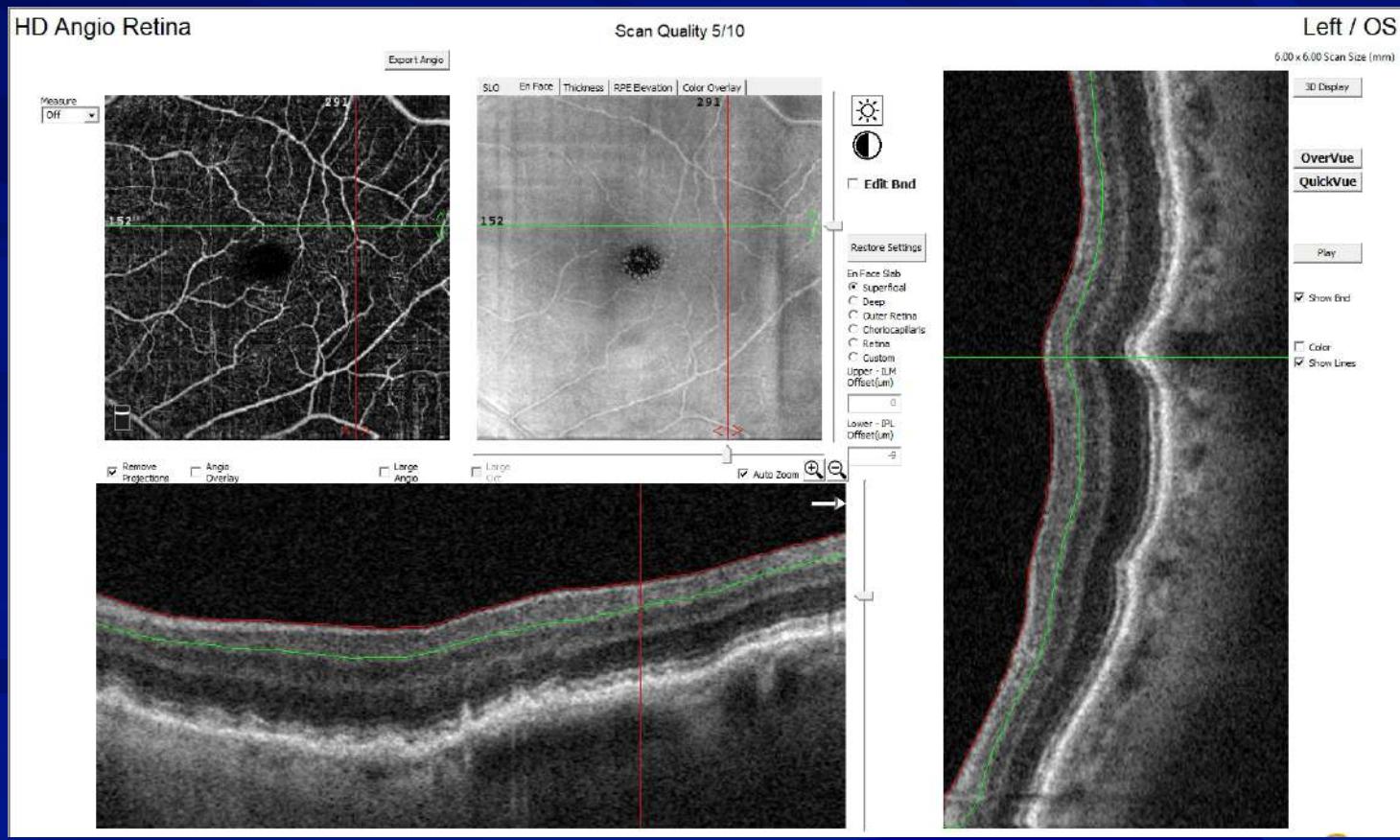
Case 2 - OCT Predictors of Progression



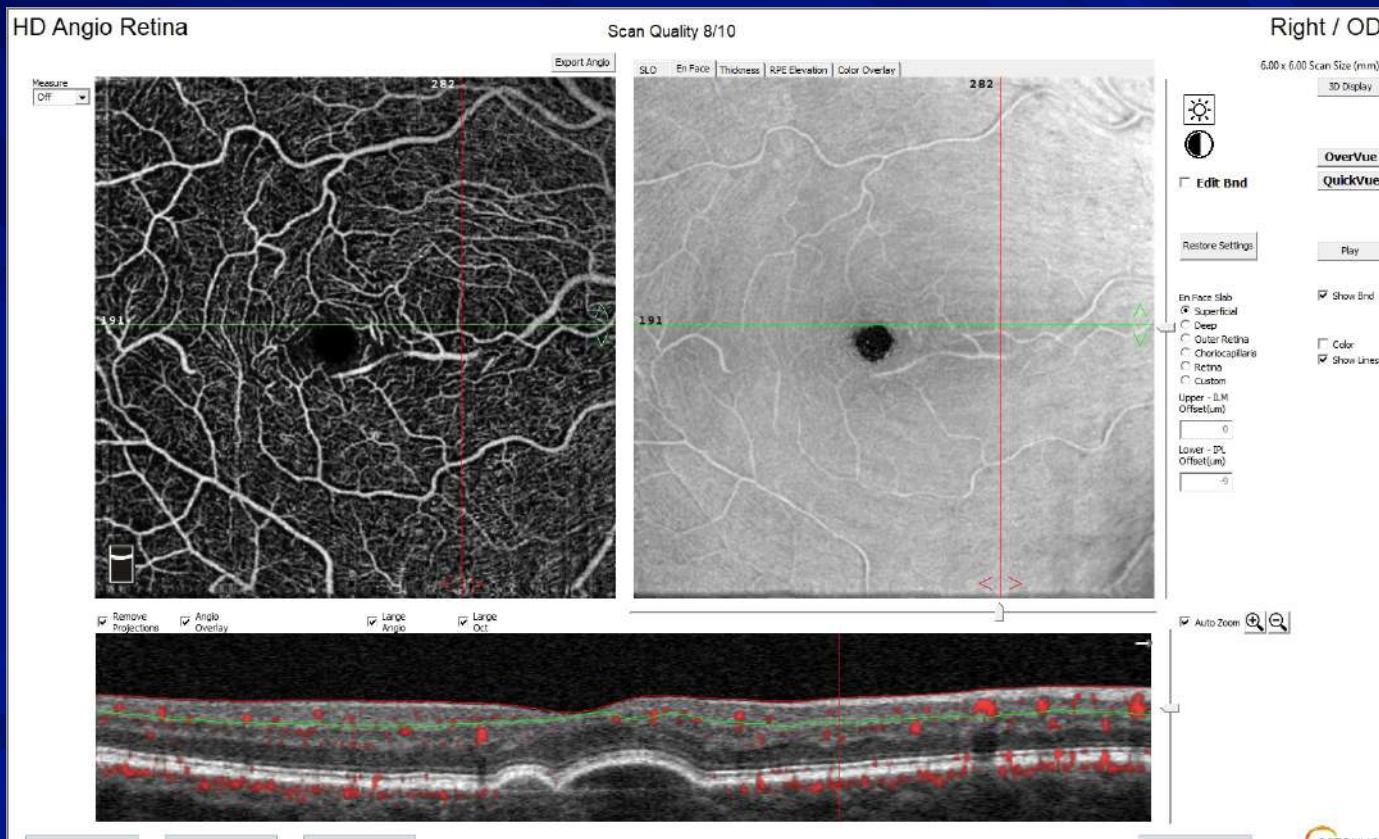
Case 2 - OCT Predictors of Progression



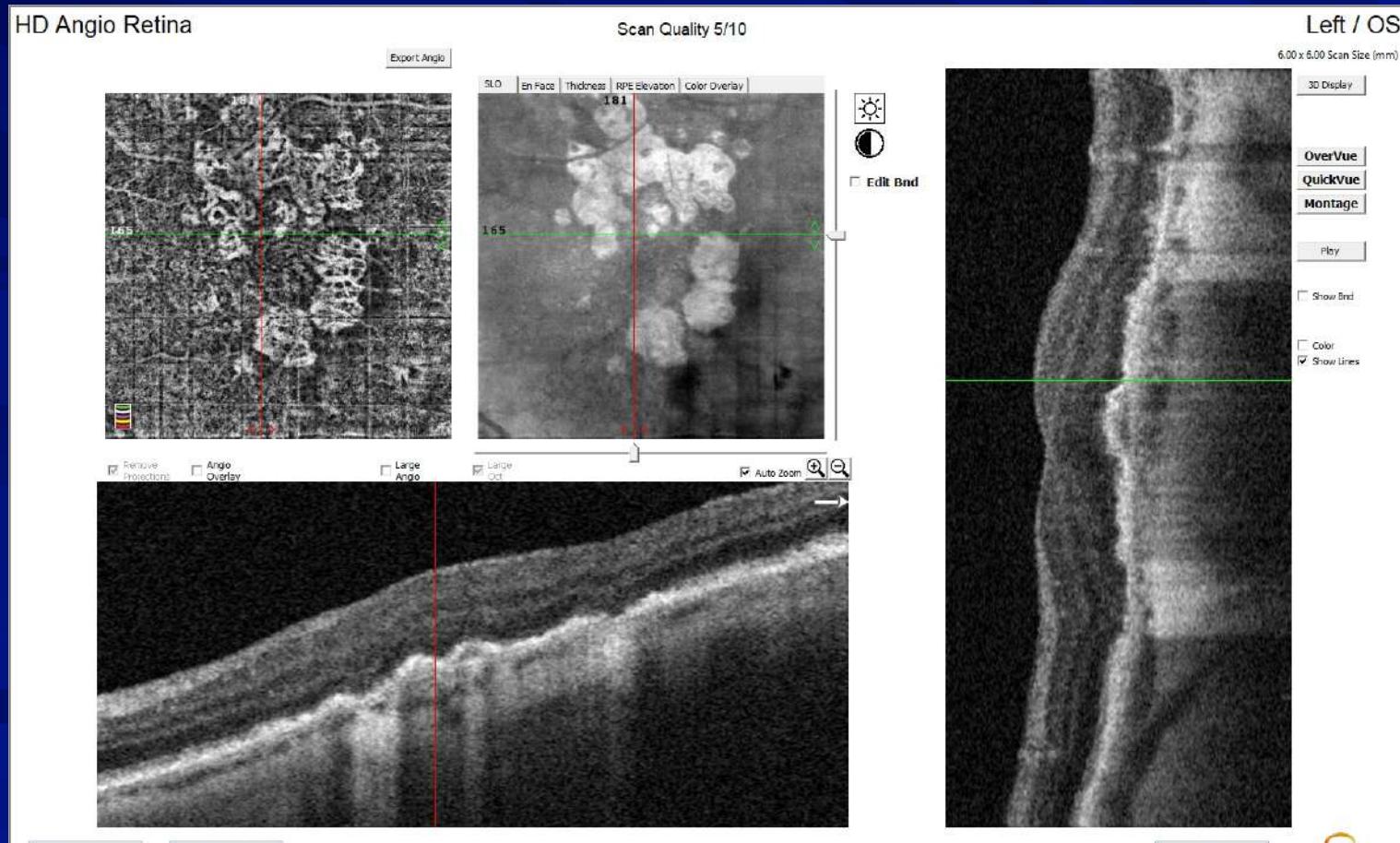
Case 2 - OCT Predictors of Progression



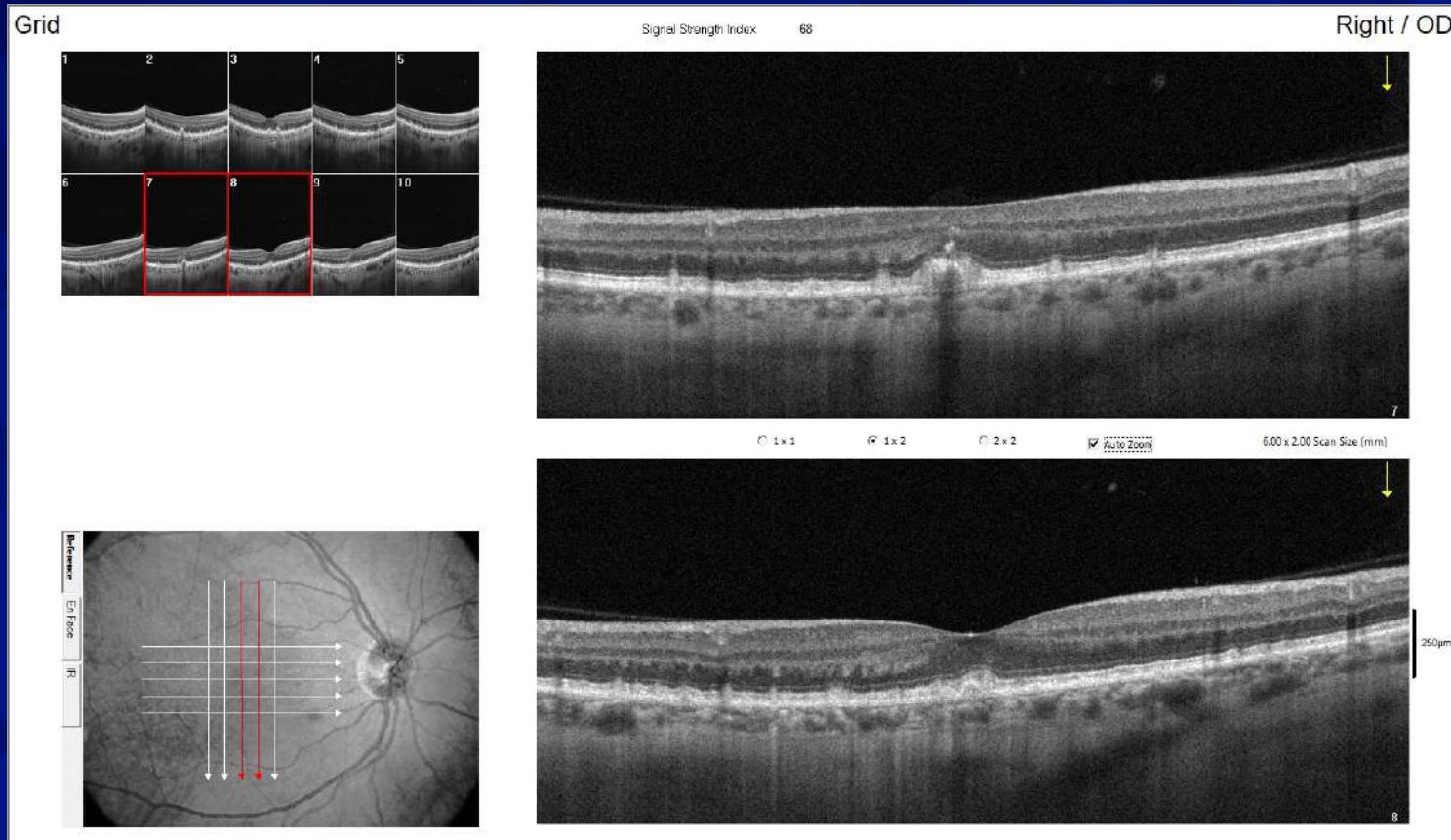
Case 3 - OCT Predictors of Progression



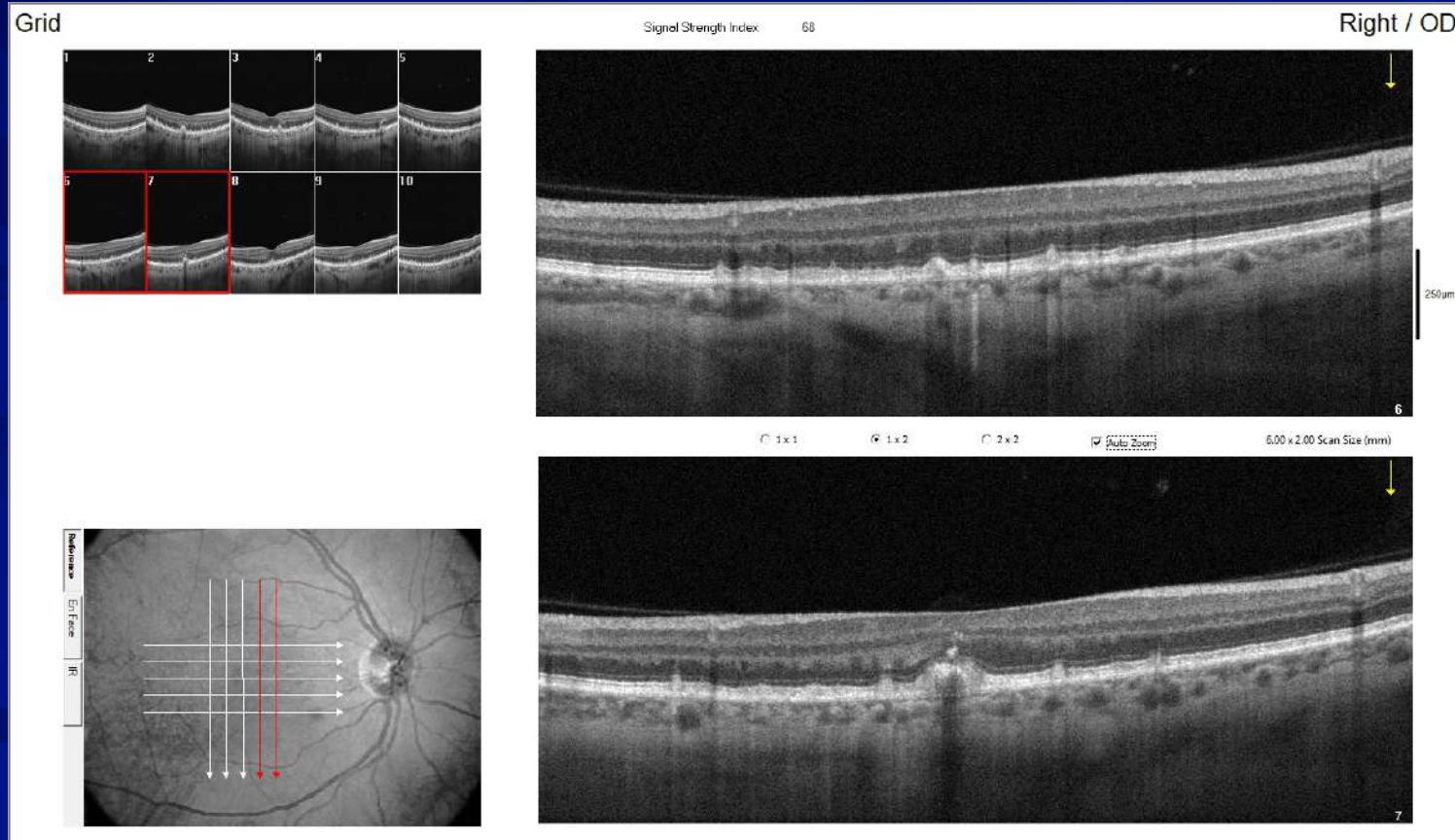
Case 4 - OCT Predictors of Progression



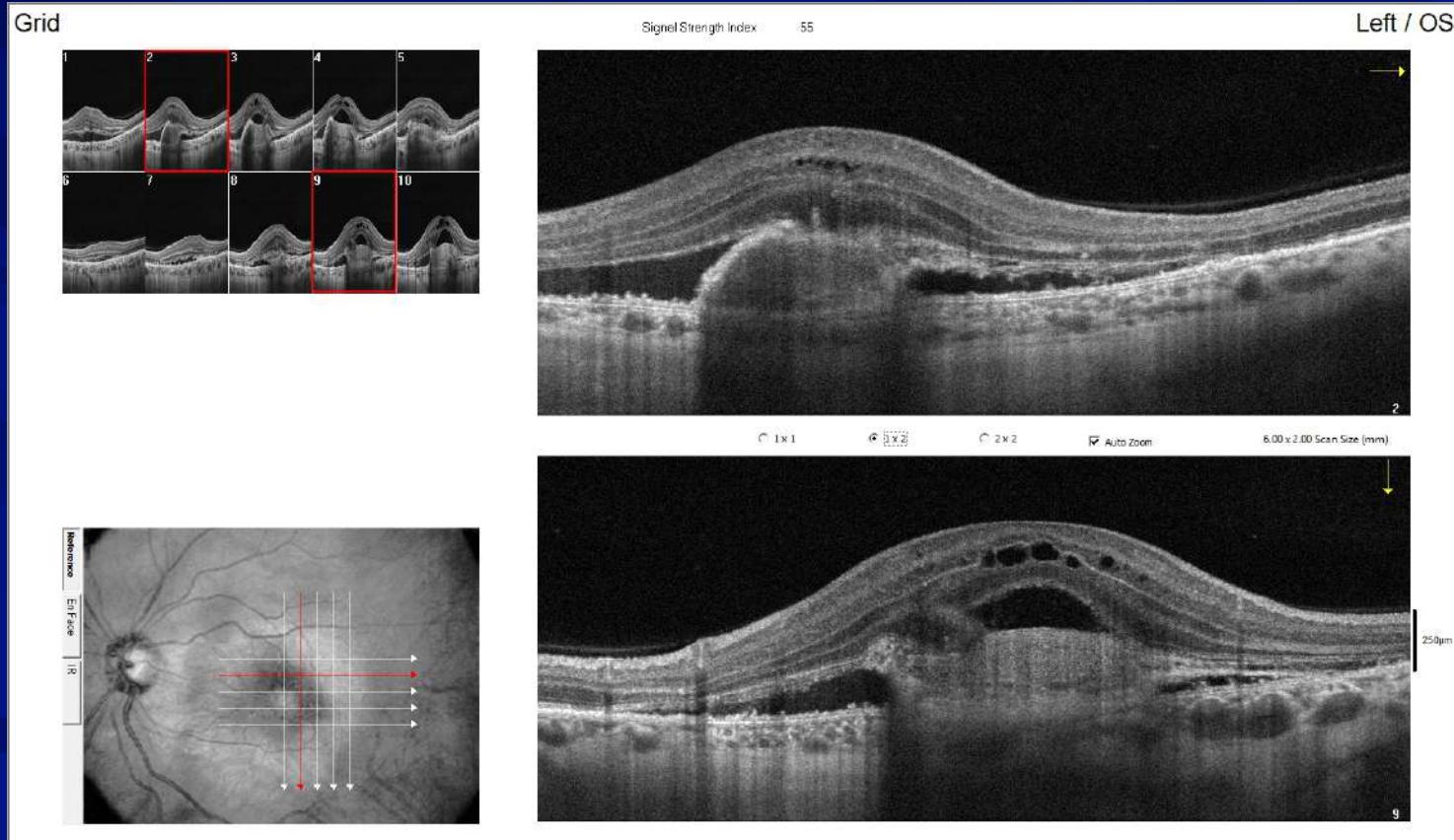
Case 5 - OCT Predictors of Progression



Case 5 - OCT Predictors of Progression



Case 5 - OCT Predictors of Progression



OCT Angiography in AMD Structure Test

- ❖ Able to identify occult or classic CNV before they leak
- ❖ Non-invasive technique
- ❖ Subclinical CNV or “Occult non-exudative CNV”
 - ★ Risk of exudation at 12 months is 15.2 times greater compared to eyes without subclinical CNV

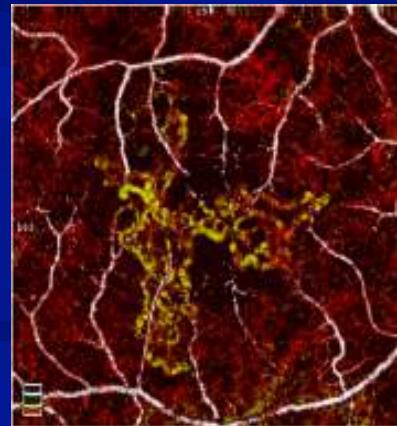
OCT Angiography

A New Approach to Protecting Vision

- ▶ Non-invasive visualization of individual layers of retinal vasculature
- ▶ Pathology not obscured by fluorescein staining or pooling
- ▶ Image acquisition requires less time than a dye-based procedure
- ▶ Reduced patient burden allows more frequent imaging to better follow disease progression and treatment response

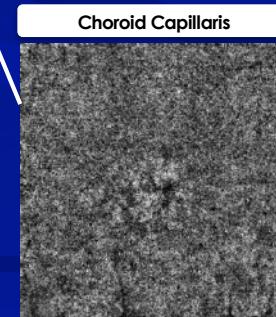
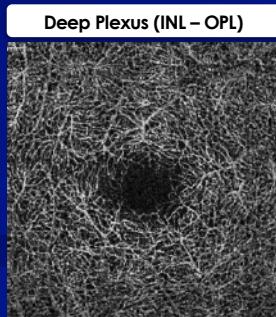
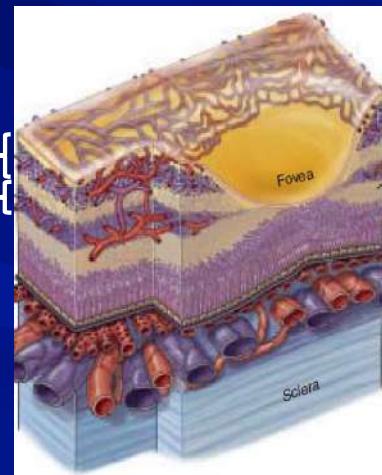
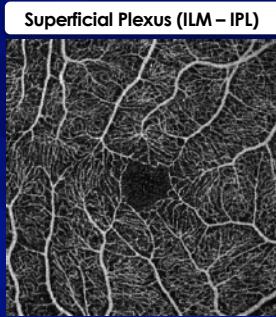


FA of CNV



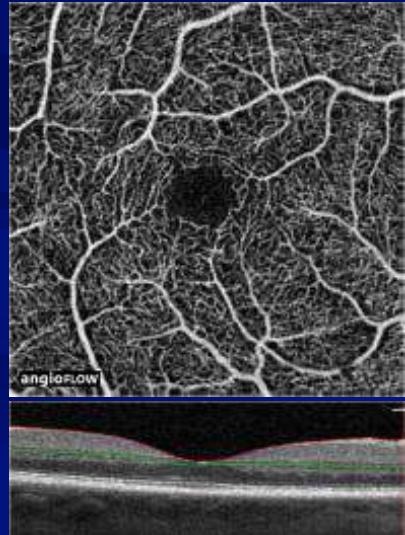
OCTA of CNV

Enface OCT-A Slabs Based on Retinal Anatomy



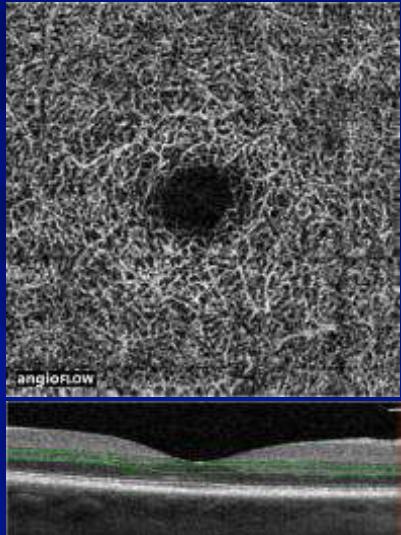
En Face Visualization of Layers
Based on Retinal Anatomy

Normal Retinal Vasculature



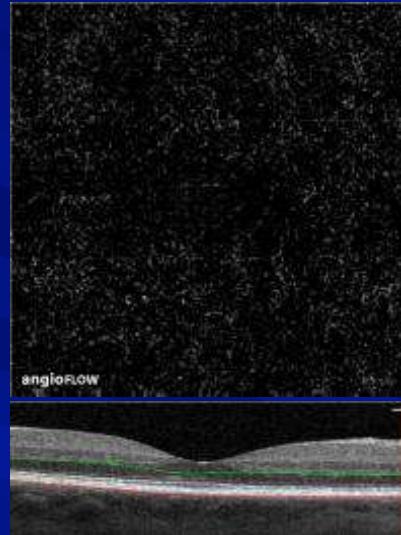
Superficial Capillary Plexus

3 μ m Below ILM → 15 μ m
Below IPL



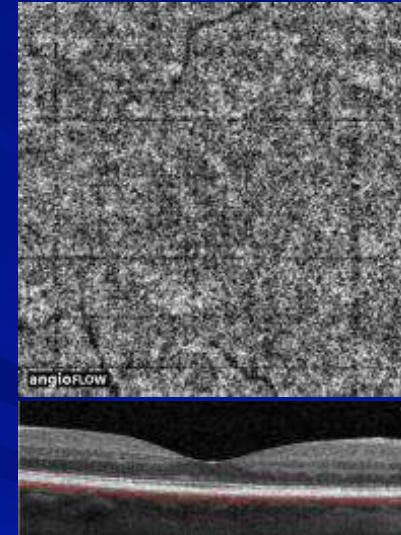
Deep Capillary Plexus

15 μ m Below ILM → 70 μ m
Below IPL



Outer Retina

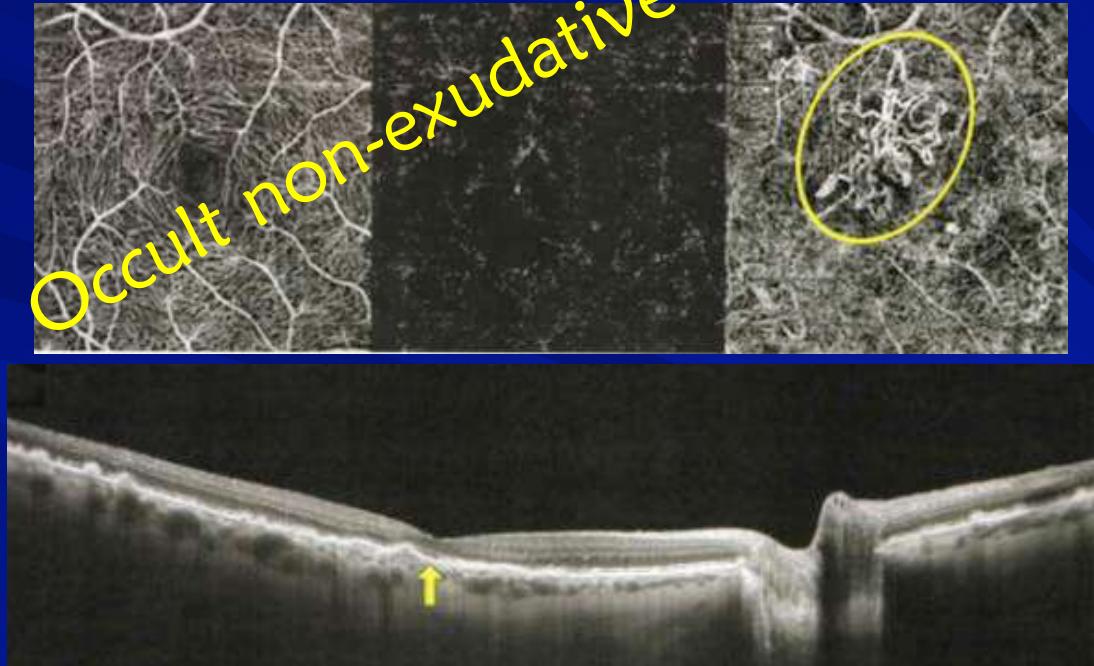
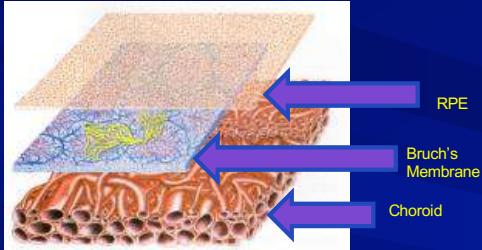
70 μ m Below IPL → 30 μ m
Below RPE Reference



Choriocapillaris

30 μ m Below RPE Reference → 60 μ m
Below RPE Reference

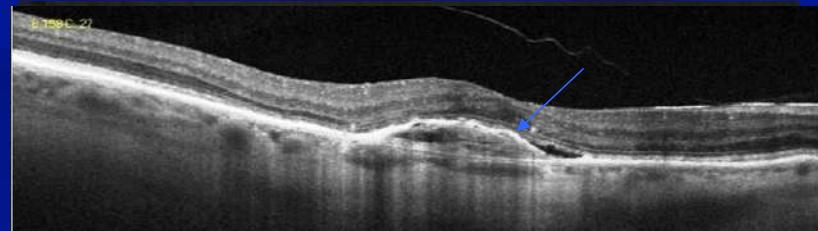
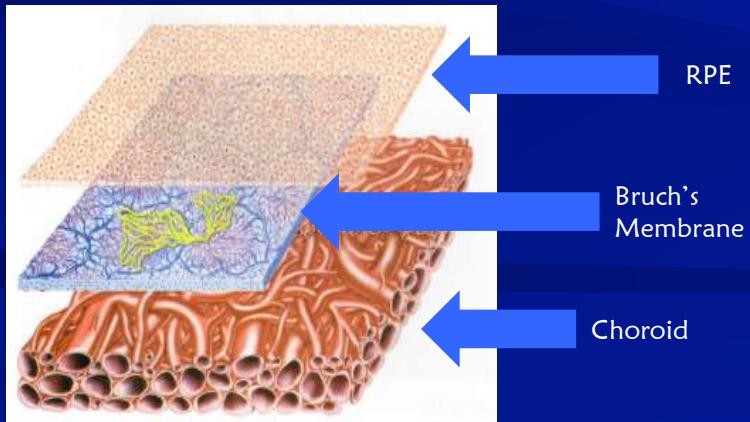
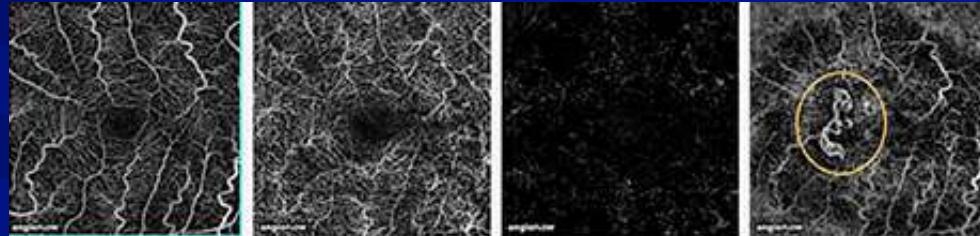
Type 1 “Occult” CNV



- ▶ New vessels develop in the choroid
- ▶ New vessels located below RPE and above Bruch's membrane

Type 1 “Occult” CNV

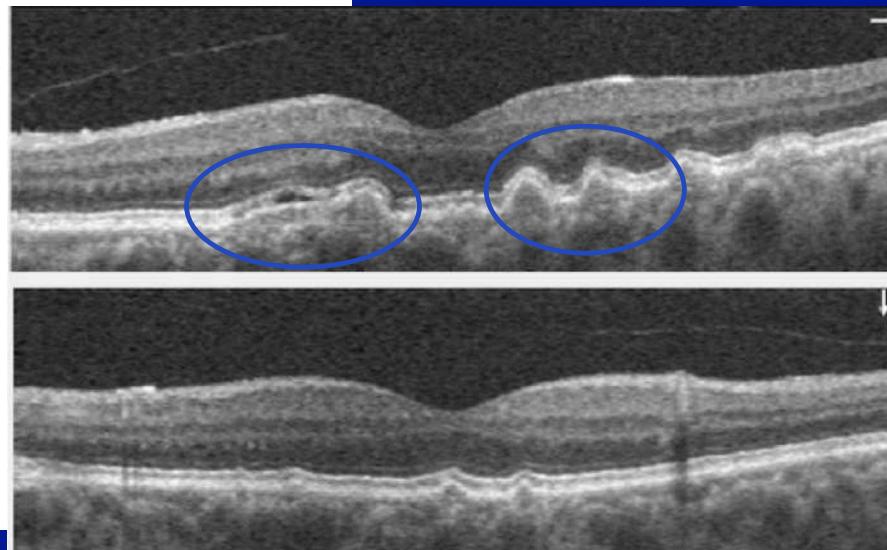
- ~~ New vessels develop in the choroid
- ~~ New vessels located **BELOW RPE** and **ABOVE Bruch's membrane**



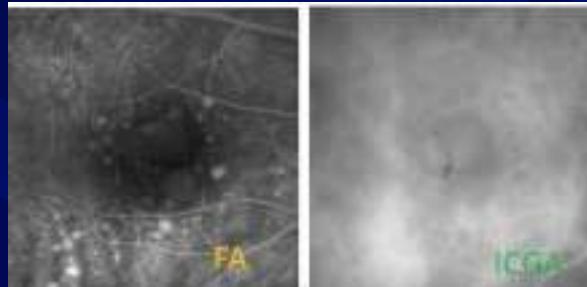
CNV?



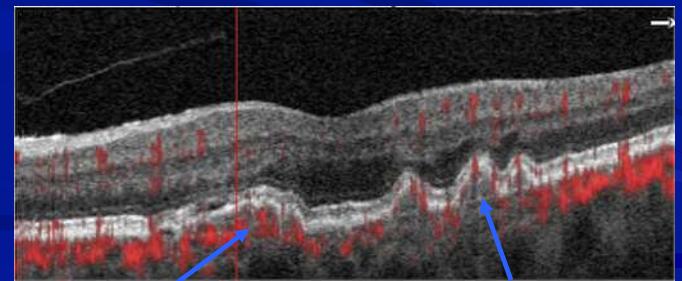
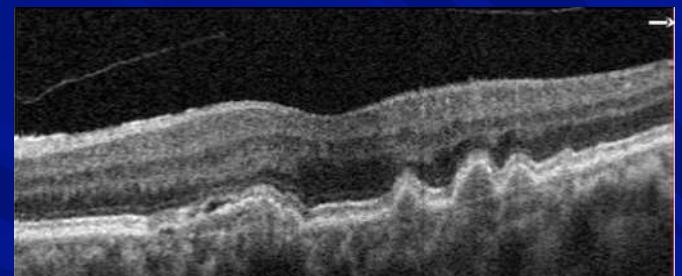
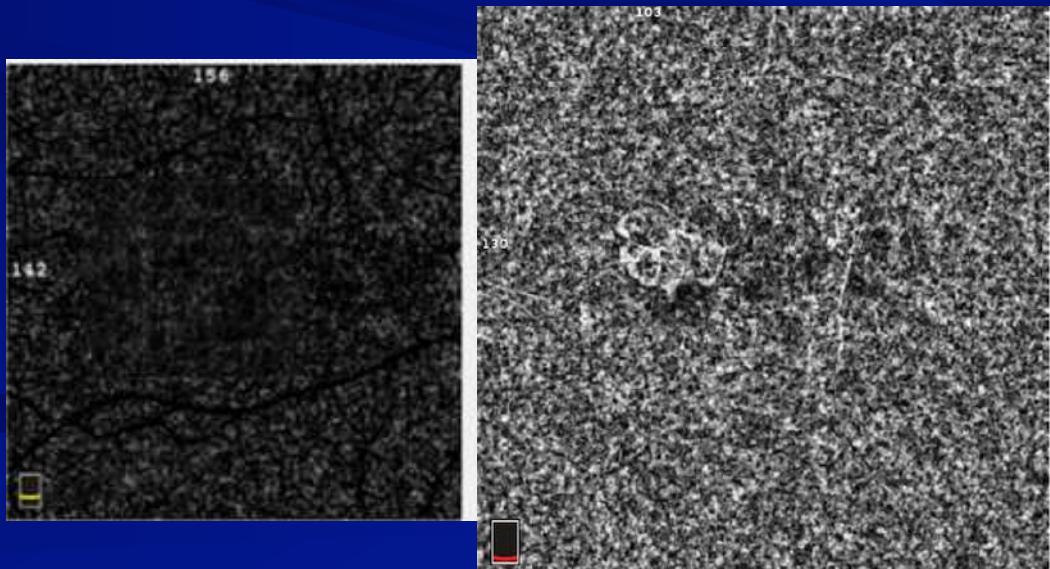
72 y/o Hispanic male
20/30
History of "Dry AMD"



Multimodal imaging and OCTA

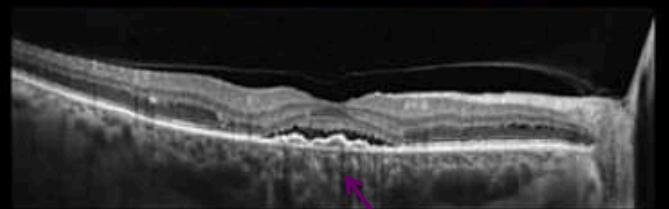
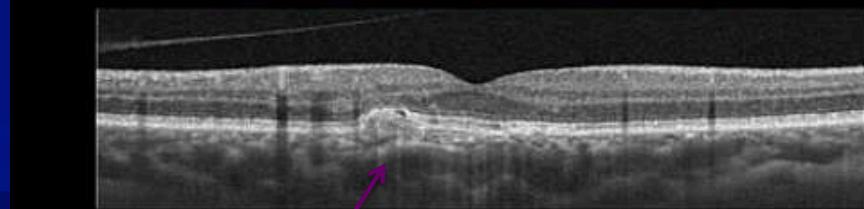
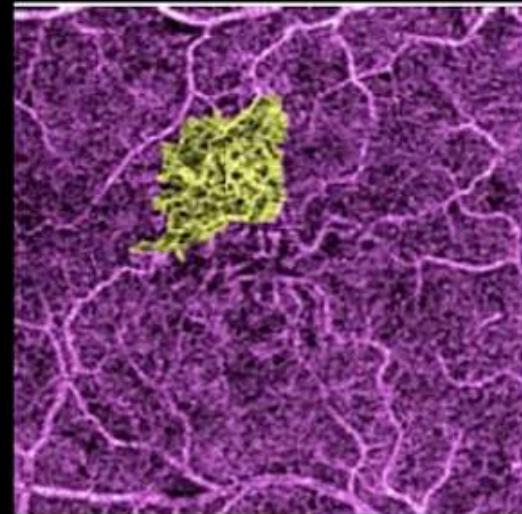
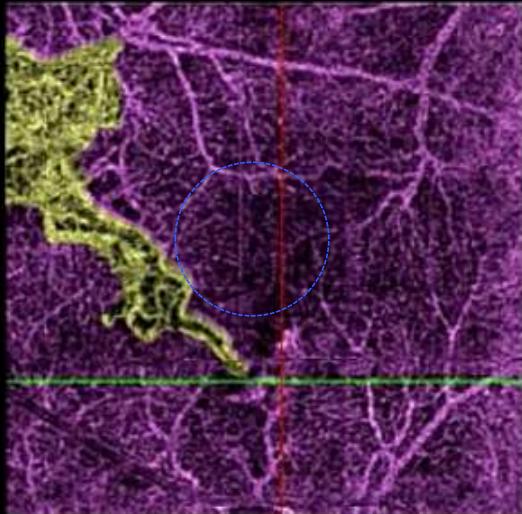


VAGUE???

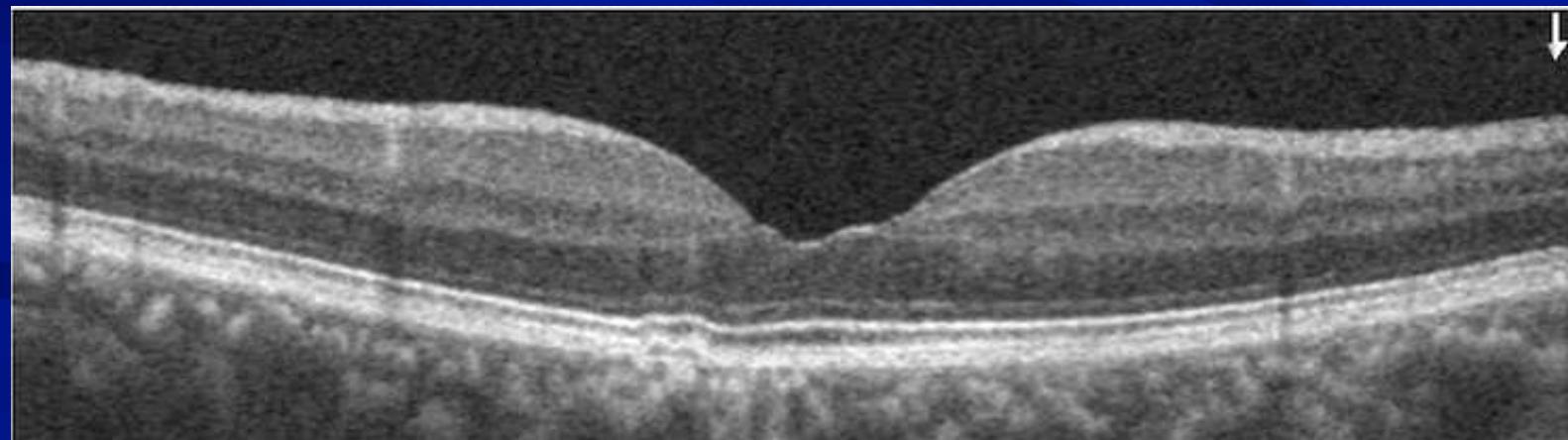
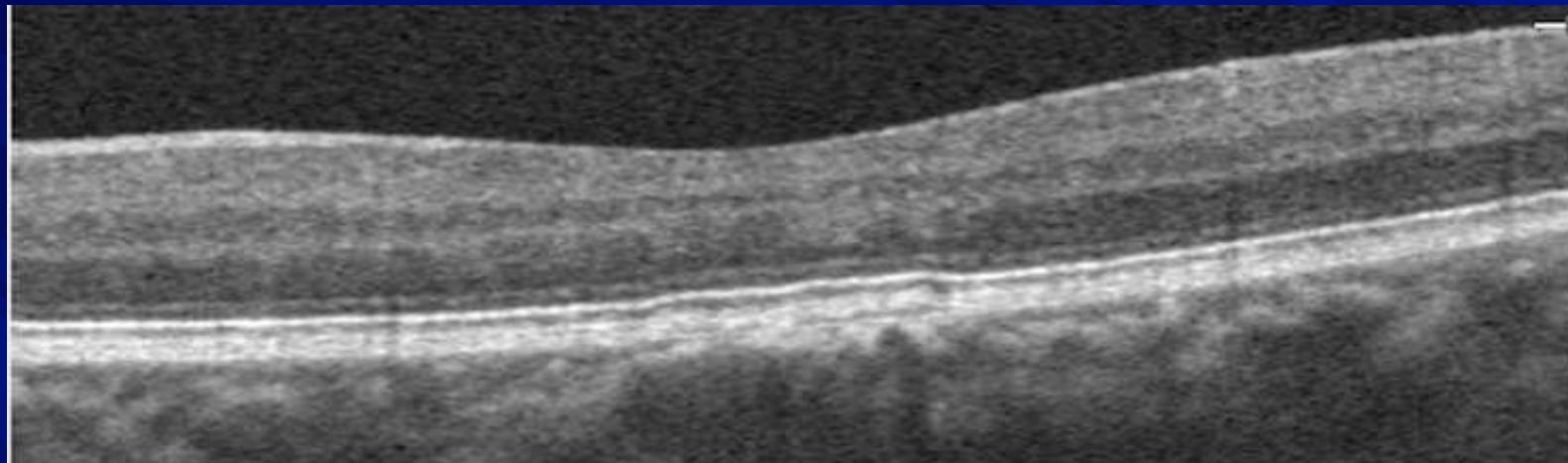


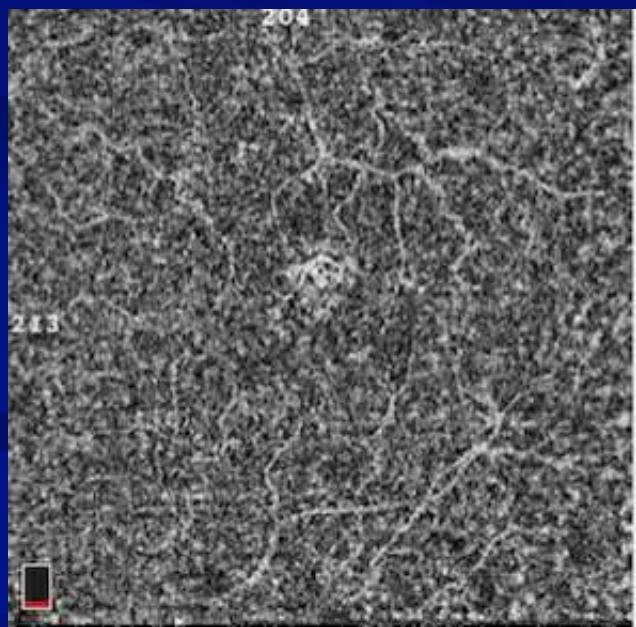
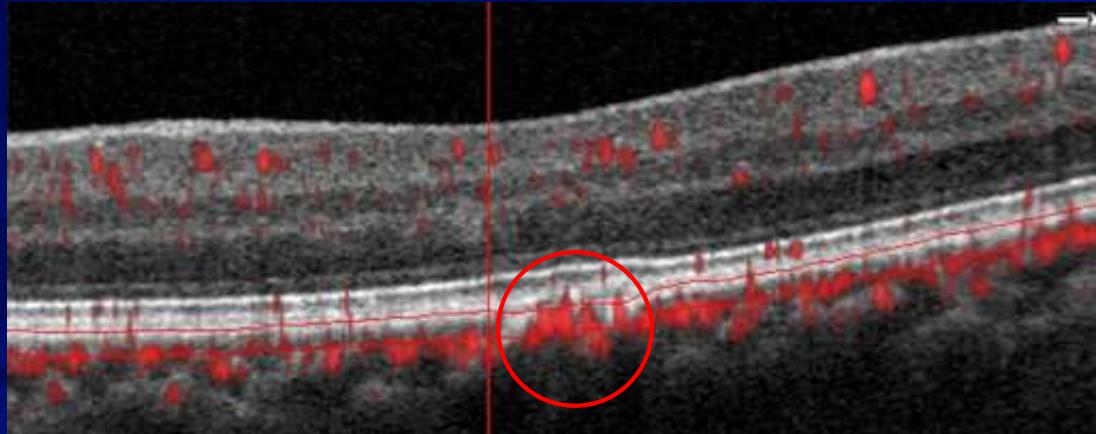
Vascularized Non-vascularized

Type 1 CNV: Below RPE, Wider than Type 2, Avascular Zone Usually Not Involved



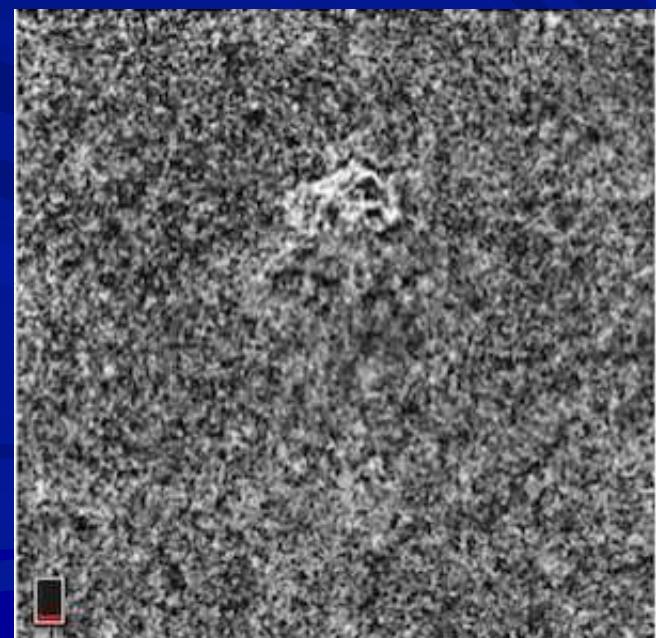
And the not so obvious ones...



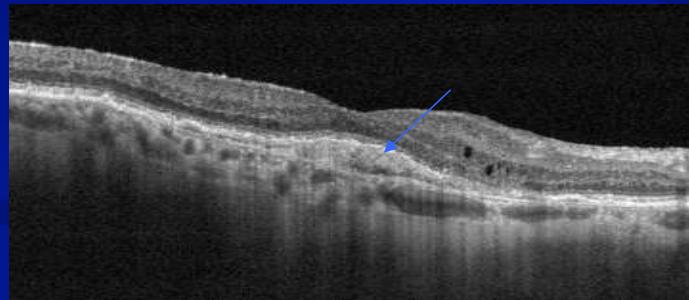
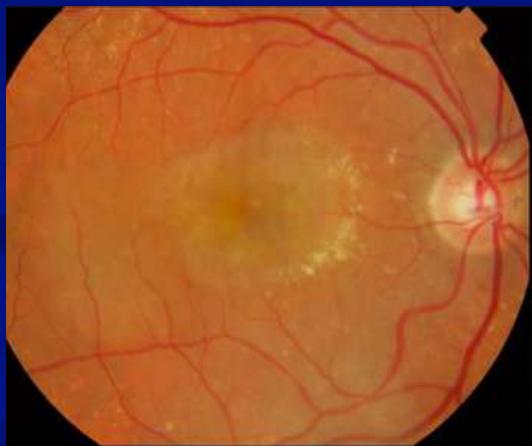
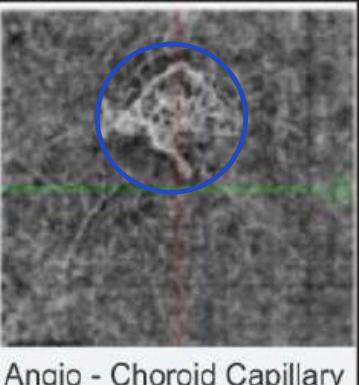
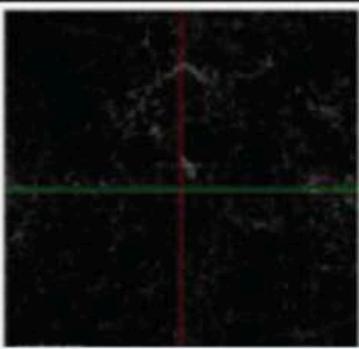
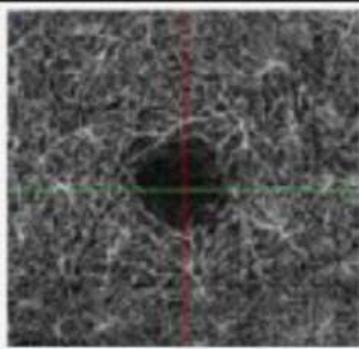
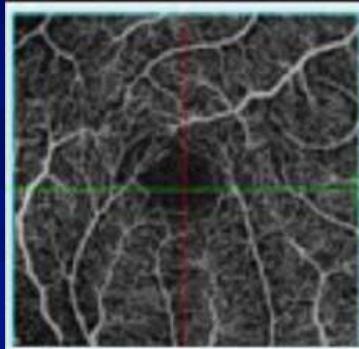
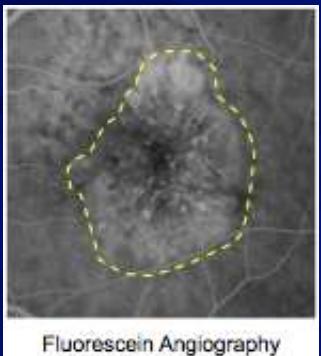


6×6

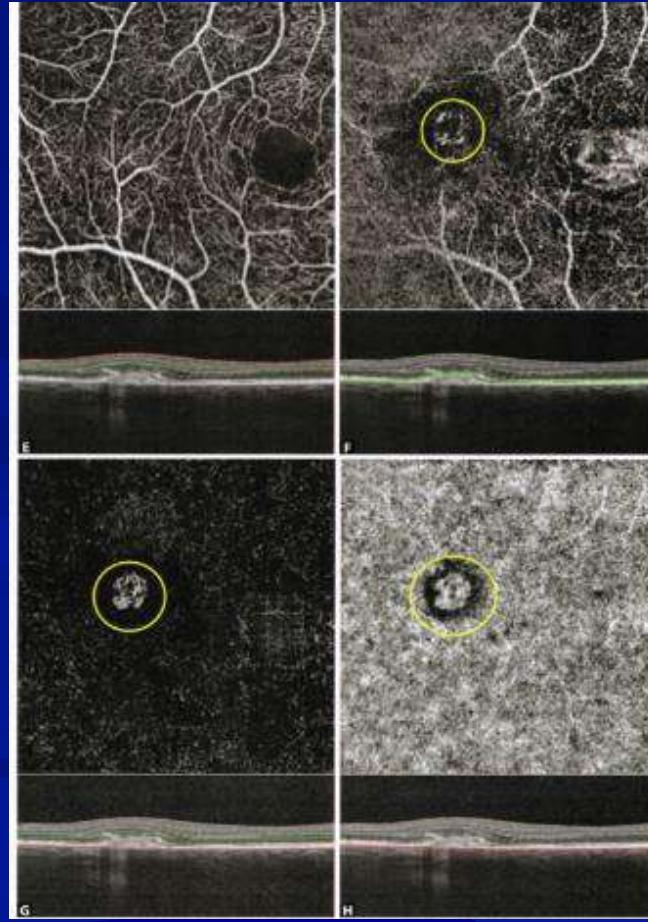
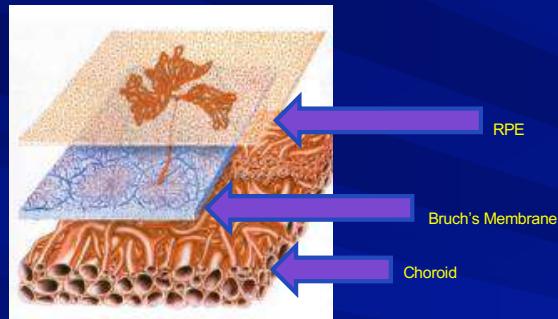
3×3



Case example: 70 y/o WM, AMD



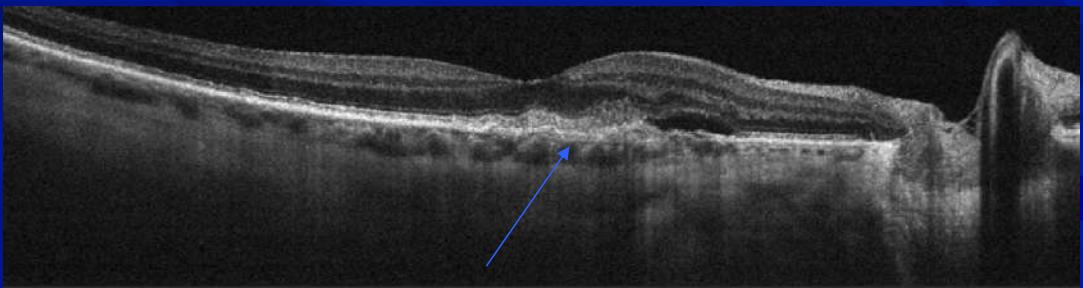
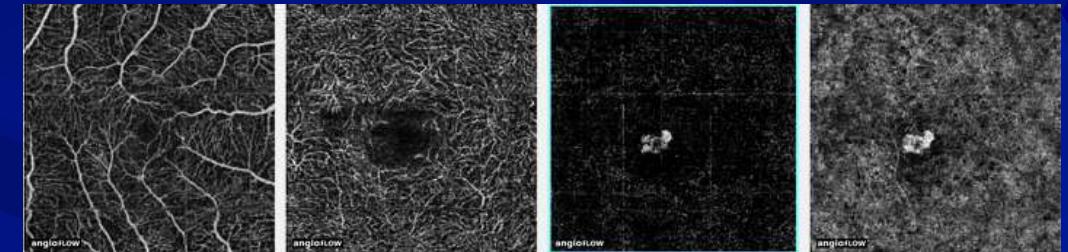
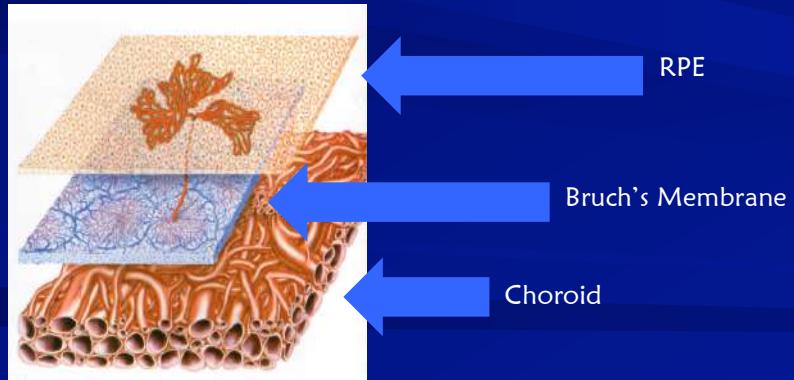
Type 2 “Classic” CNV



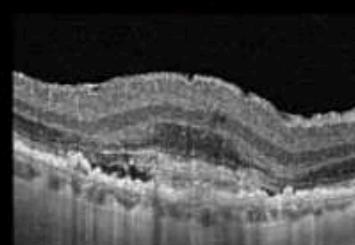
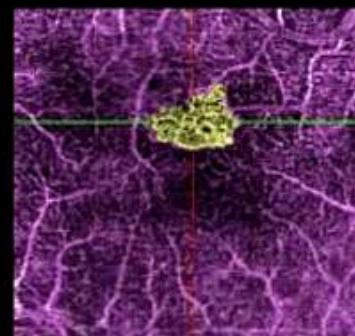
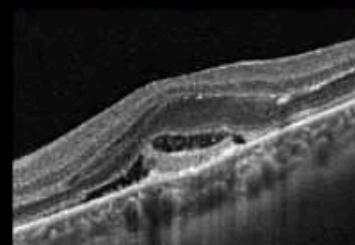
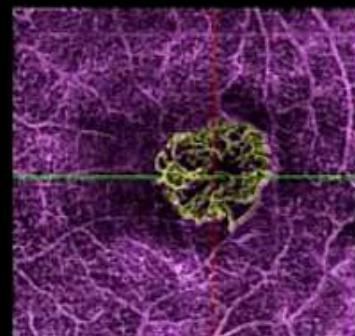
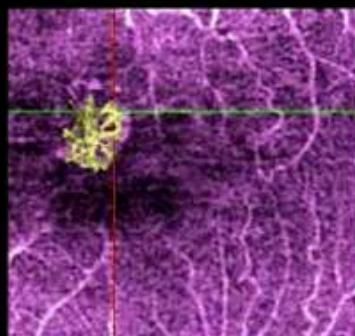
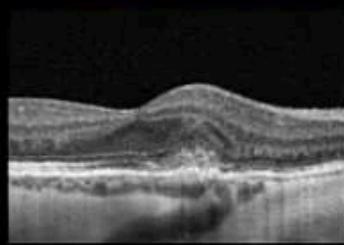
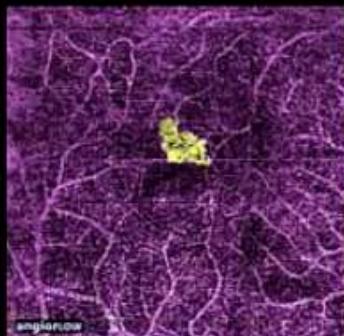
- ~~ New vessels develop in choroid
- ~~ New vessels located above the RPE and above Bruch's membrane

Type 2 “Classic” CNV

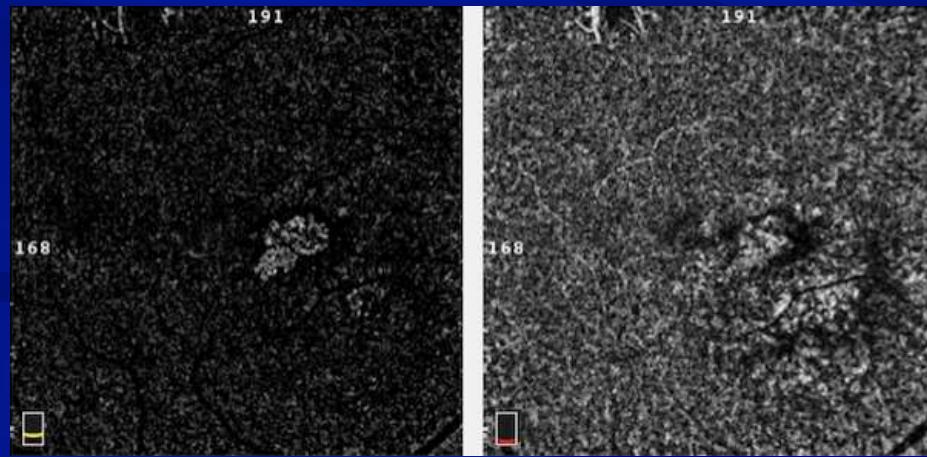
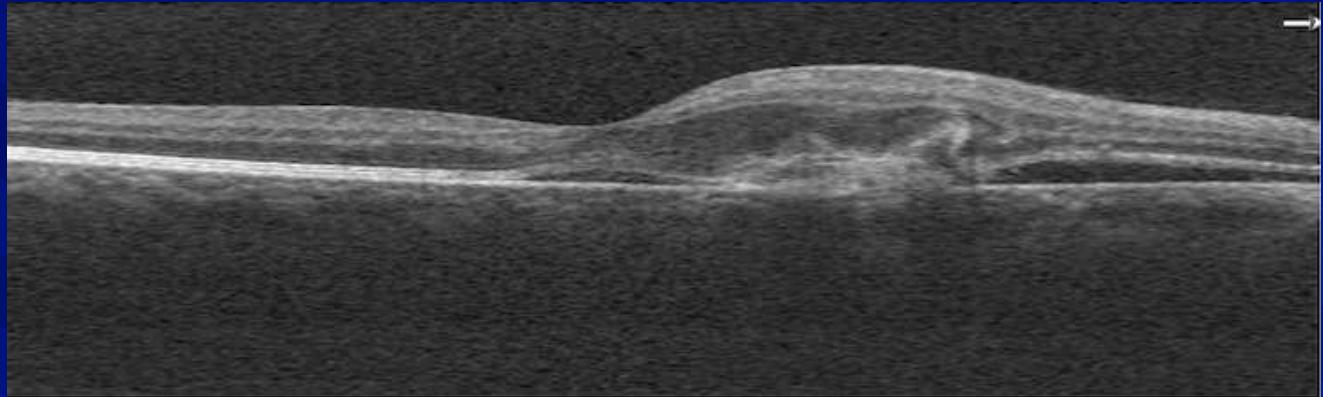
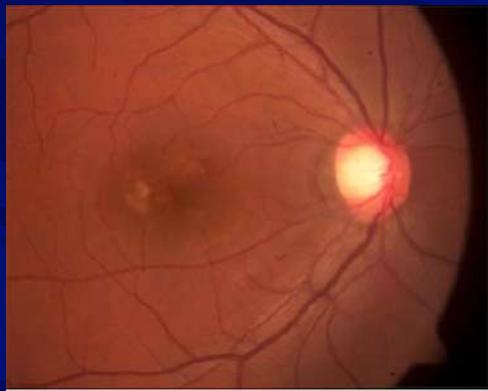
- ~ New vessels develop in choroid
- ~ New vessels located **ABOVE** the RPE and **ABOVE** Bruch's membrane



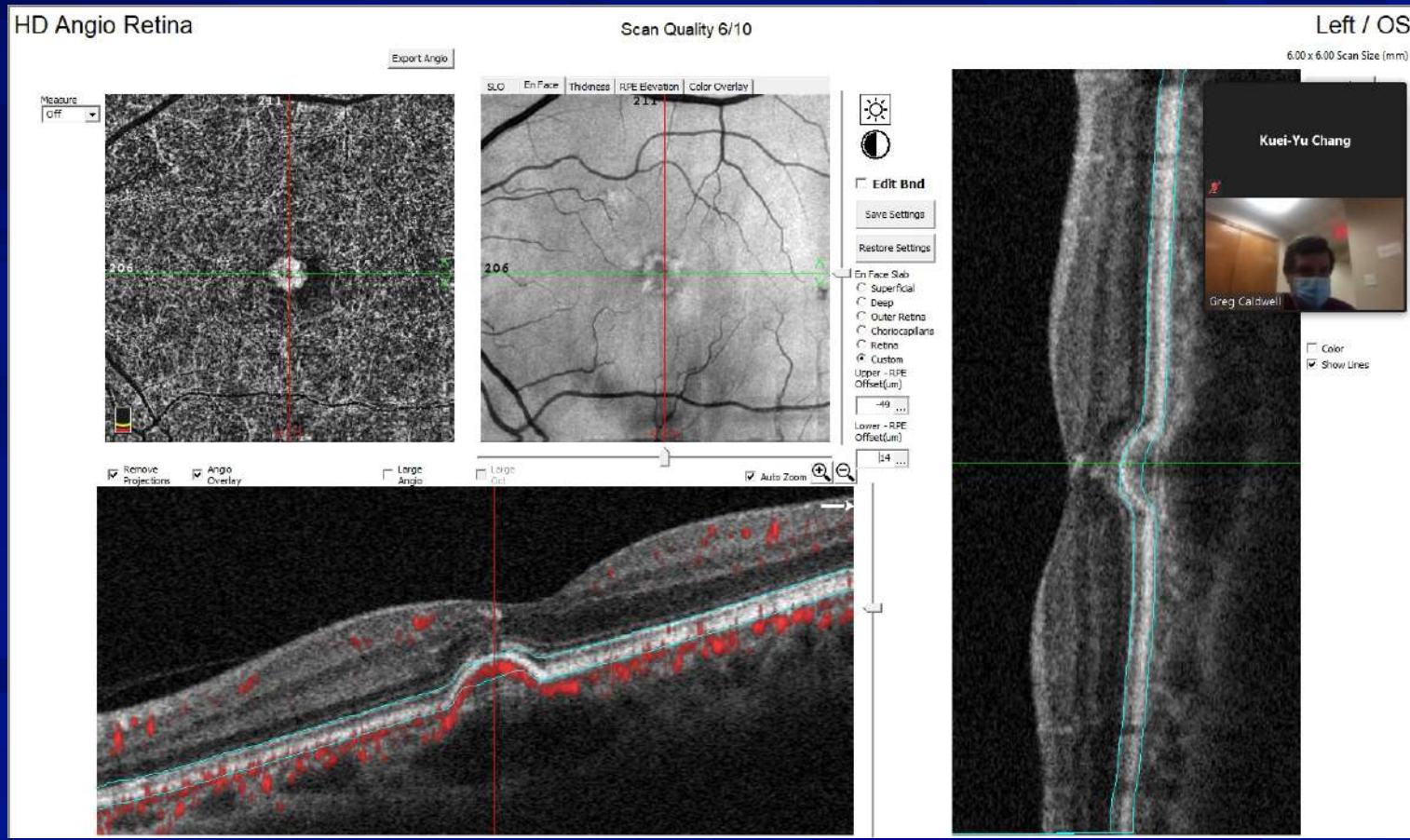
Type 2 CNV: Above RPE, Smaller than Type 1, Avascular Zone Always Involved.
Very Heterogeneous Shapes



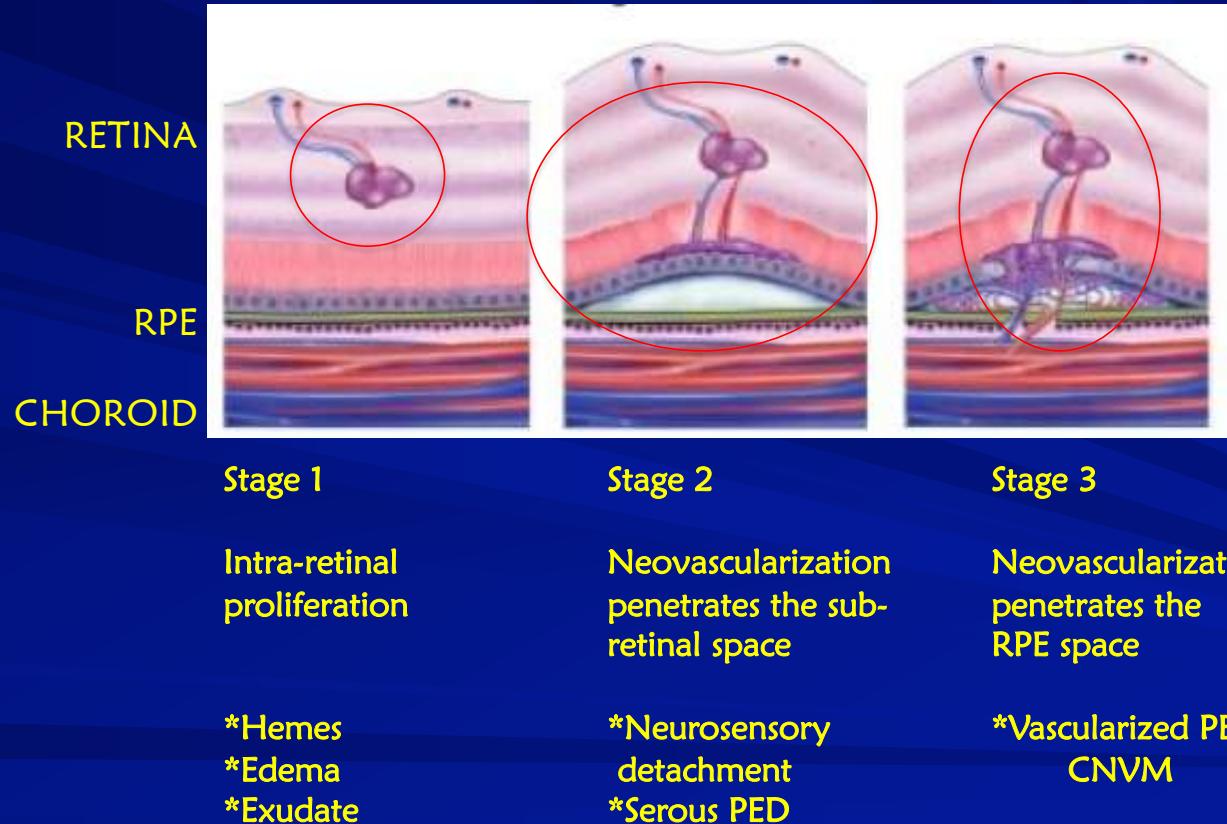
48 y/o WM 2 week history of “dark spot” OD

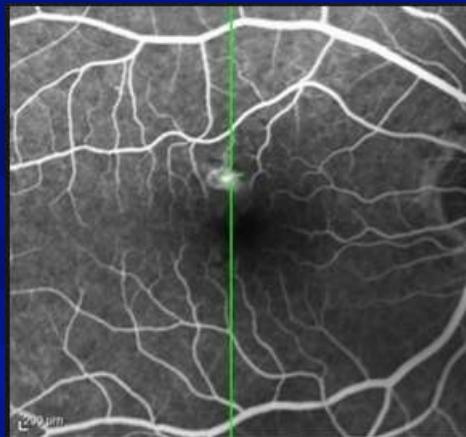
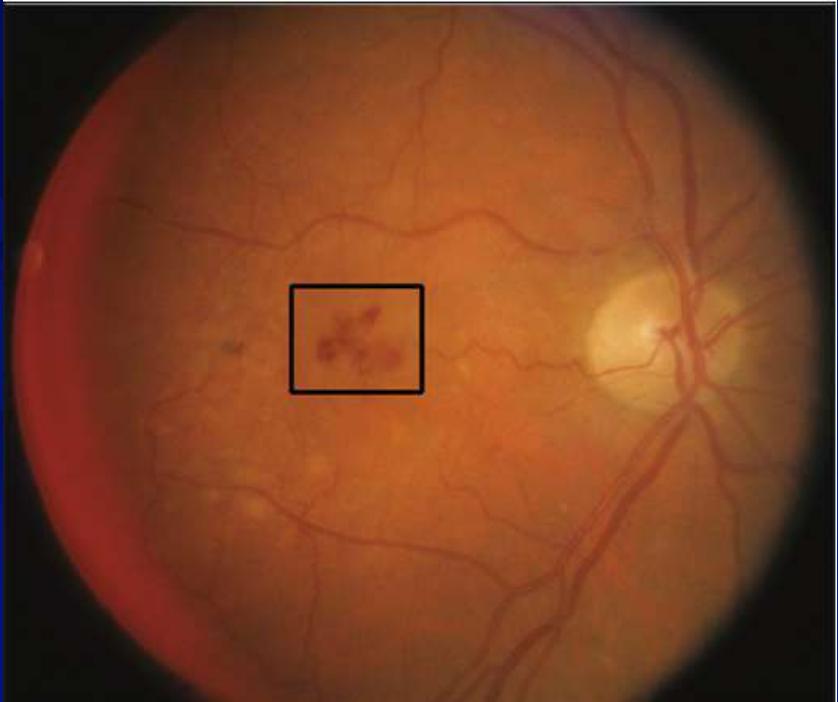


Why I Love to Teach



Retinal Angiomatous Proliferation

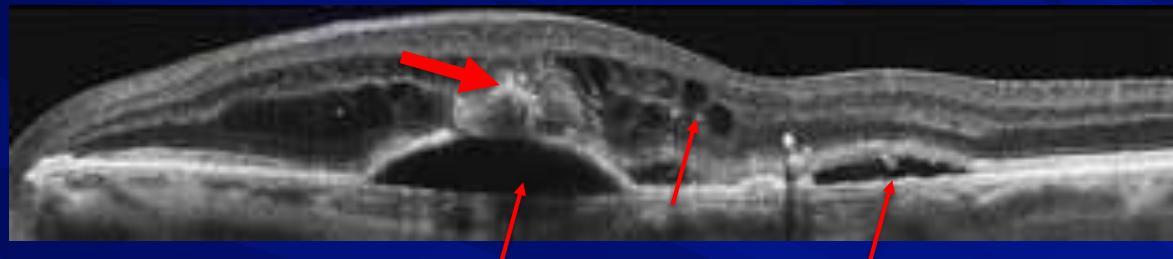




https://www.researchgate.net/figure/In-retinal-angiomatous-proliferation-fluorescein-angiography-FA-shows-a-hot-spot-in_fig8_264903506

<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/42089>

Inspect the SD-OCT carefully!!



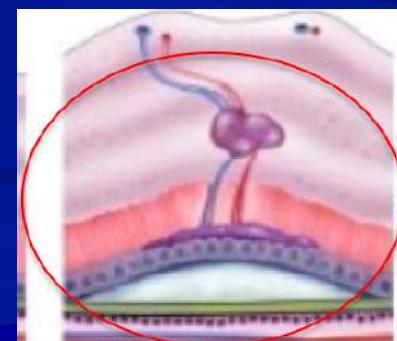
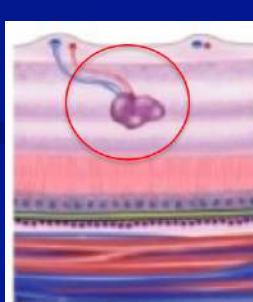
VA 20/40

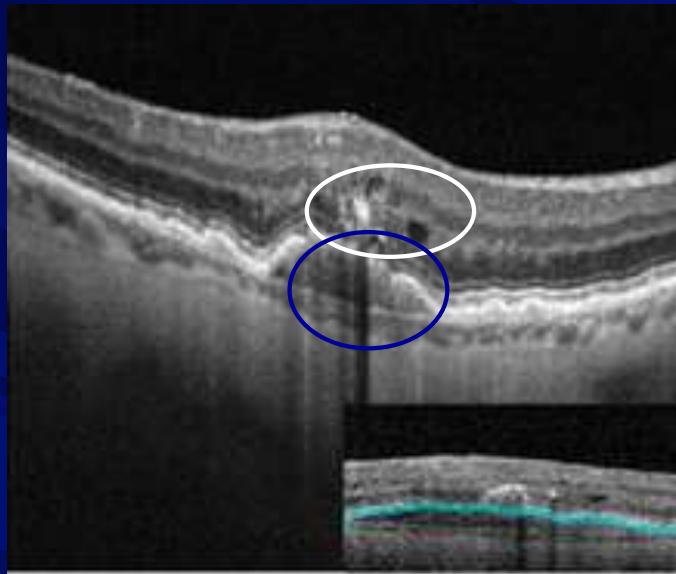
HYPER-REFLECTIVE lesion above
pigment epithelial detachment

Intraretinal cysts

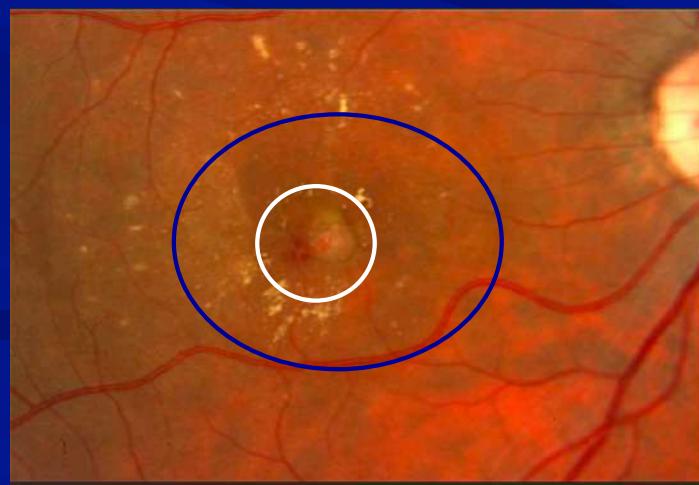
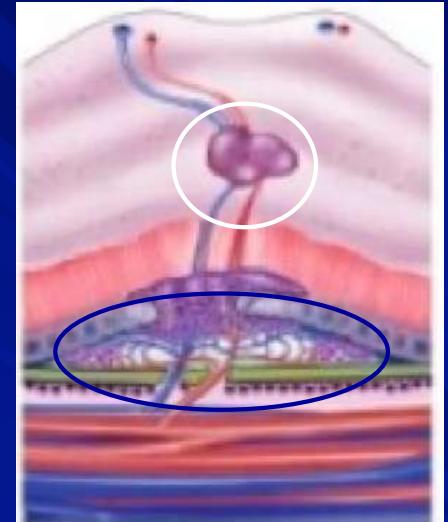
Serous pigment epithelial
detachment/ neurosensory
detachment

Stage 2





Stage 3



<http://imagebank.asrs.org/file/26943/retinal-angiomaticus-proliferation>

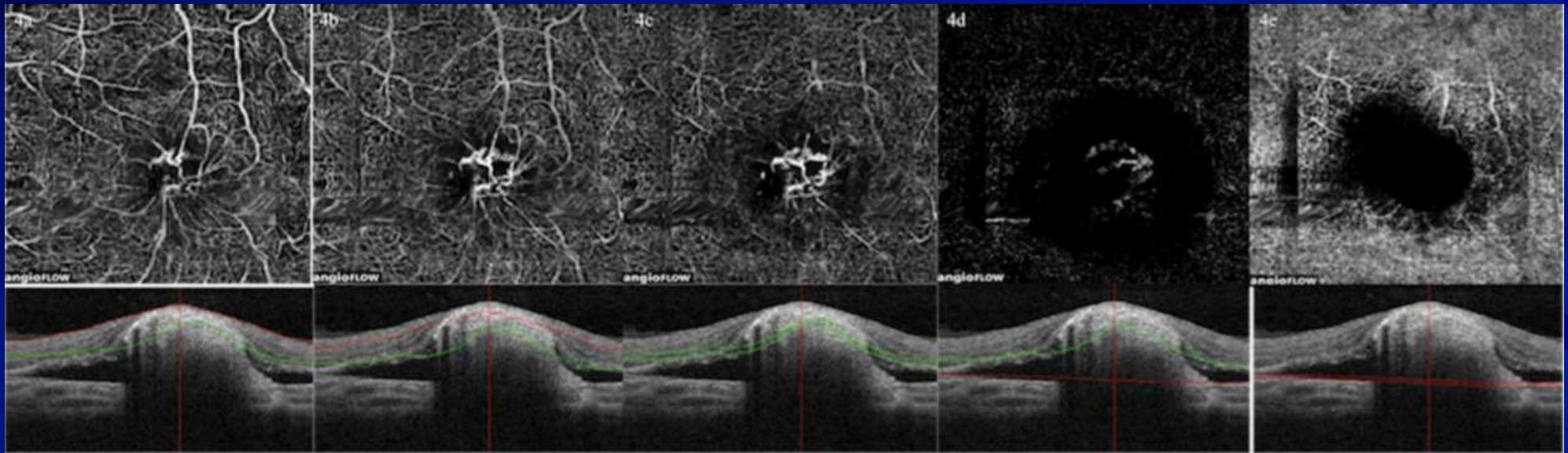
<https://www.ncbi-nlm-nih.gov.ezproxylocal.library.nova.edu/pubmed/29019795>

What about the OCTA?

OCT angiography demonstrates retinal angiomatic proliferation and chorioretinal anastomosis of type 3 neovascularization

Reema Bansal · Varshitha Hemanth · Samyak Mukutkar · Ramandeep Singh ·
Vishali Gupta · Mangat R. Dogra · Amod Gupta

Type 3 CNV: Intraretinal Anastomosis: THROUGH RPE



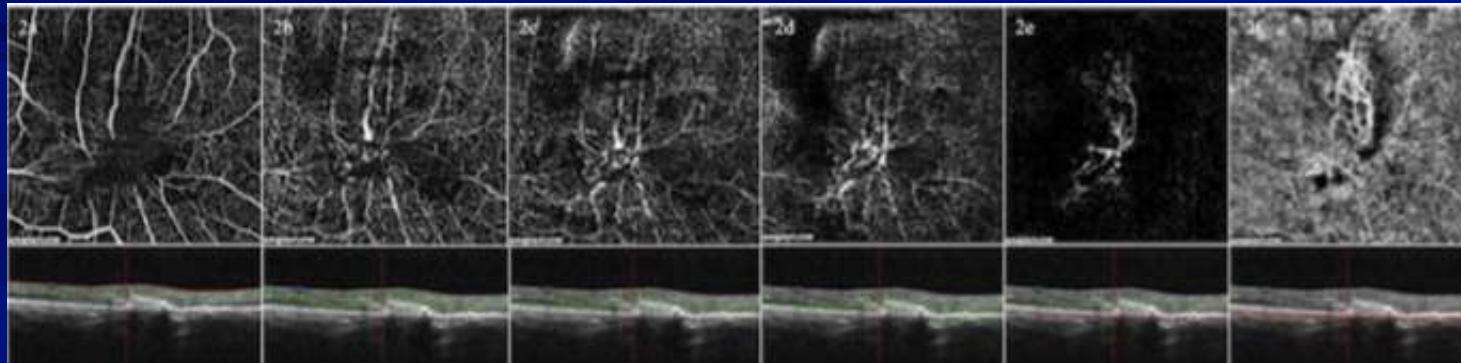
Inner retina (SCP+DCP) to Outer retina (Avascular/choriocapillaris)

What about the OCTA?

OCT angiography demonstrates retinal angiomatic proliferation and chorioretinal anastomosis of type 3 neovascularization

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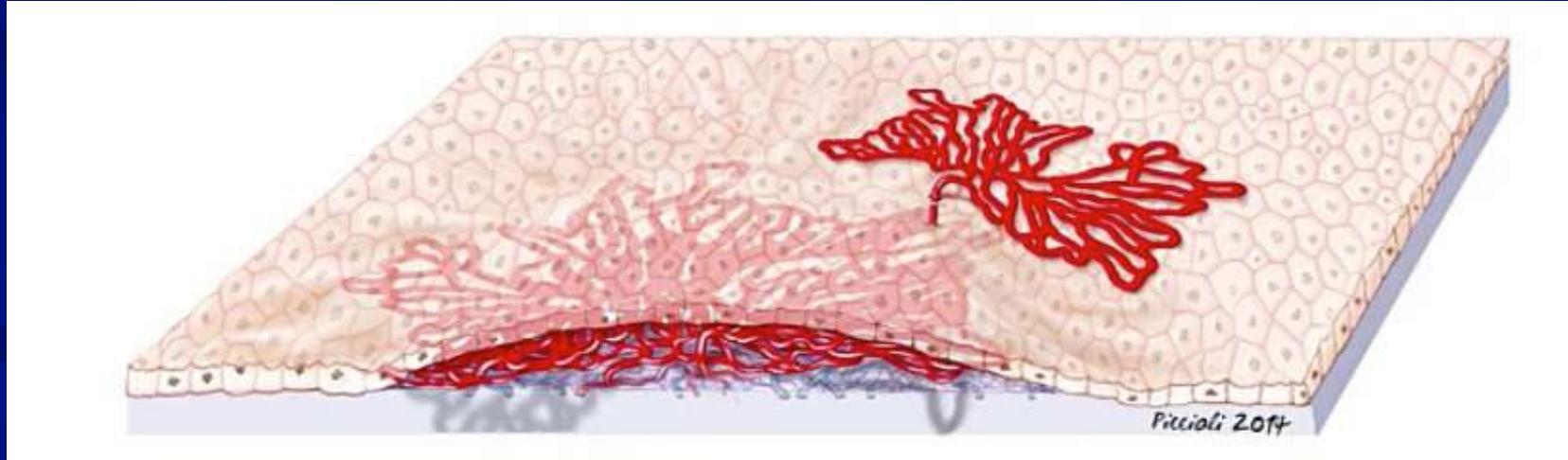
Type 3 CNV: Retinal/Choroidal Anastomosis: INTO CHOROID



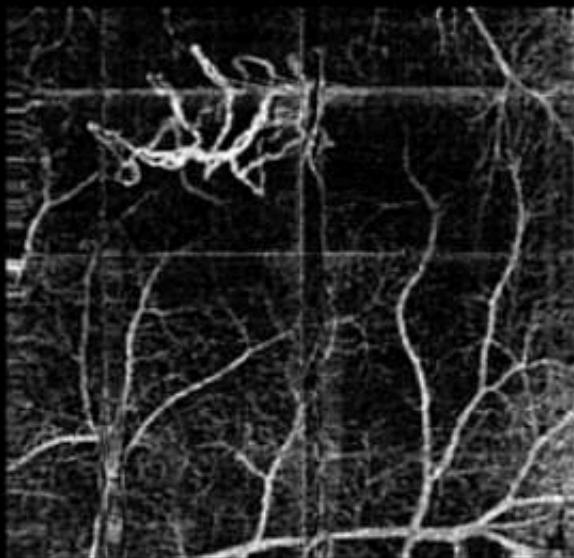
Inner retina (SCP+DCP) to Outer retina (Avascular/choriocapillaris)

Type 4 “Mixed”- Subretinal and Sub-RPE

- ~ Two or more CNV layers
 - * One above the RPE, one below the RPE
- ~ High flow lesions



Type 4 CNV : Initially Located Below the RPE, NV Spreads into the Outer Retina



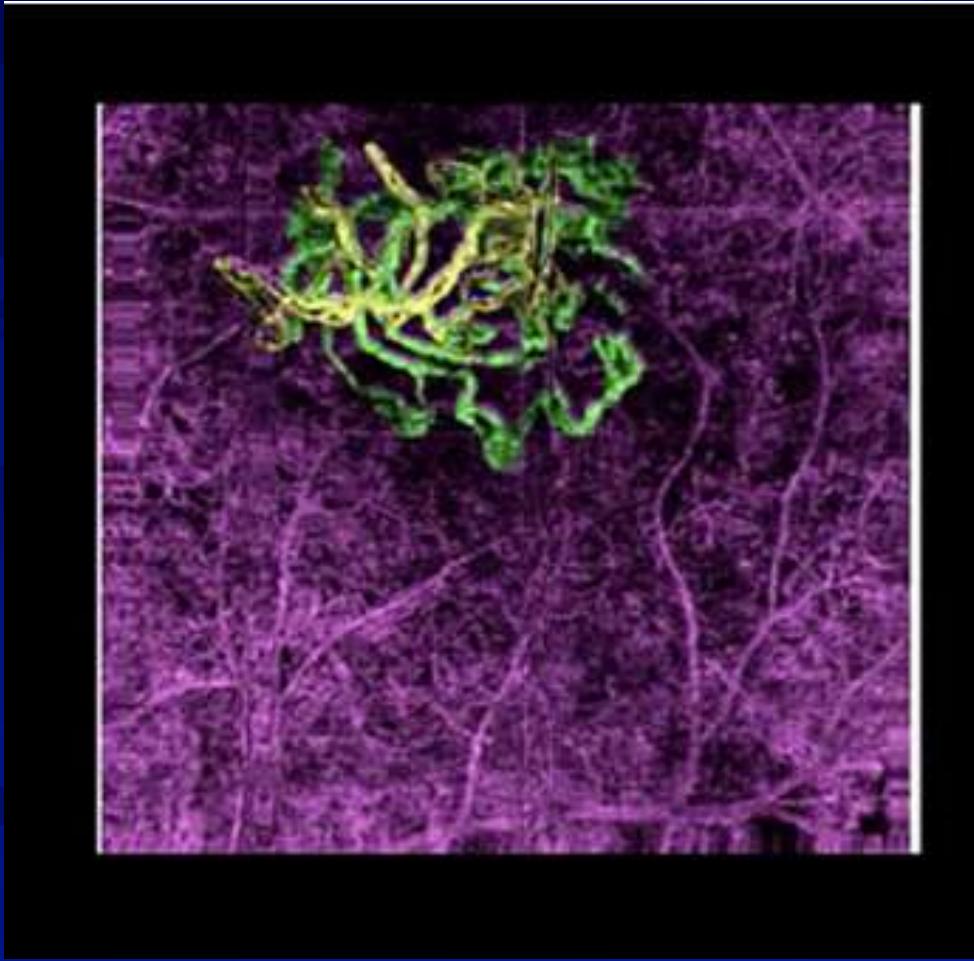
Angio - Deep



Angio - Outer Retina



Angio - Choroid Capillary

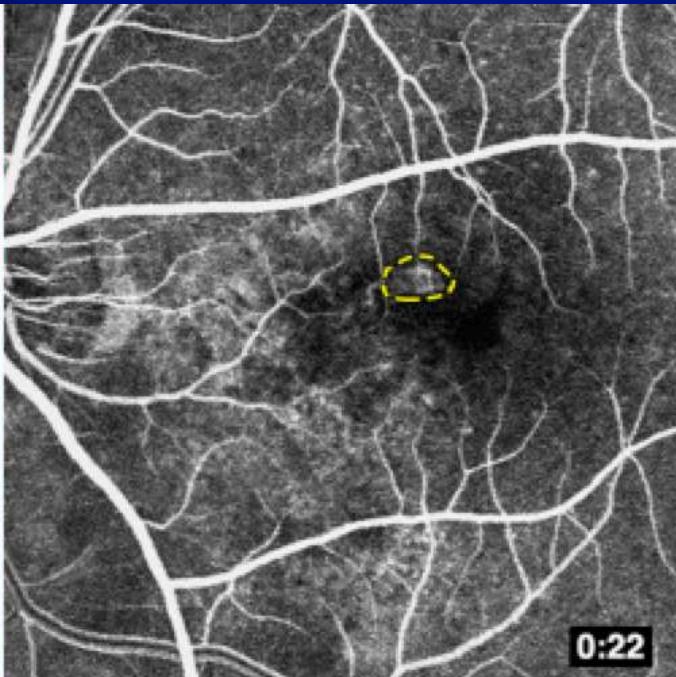


Green: Type 1 (Sub RPE)
Yellow: Type 2 (Subretinal)

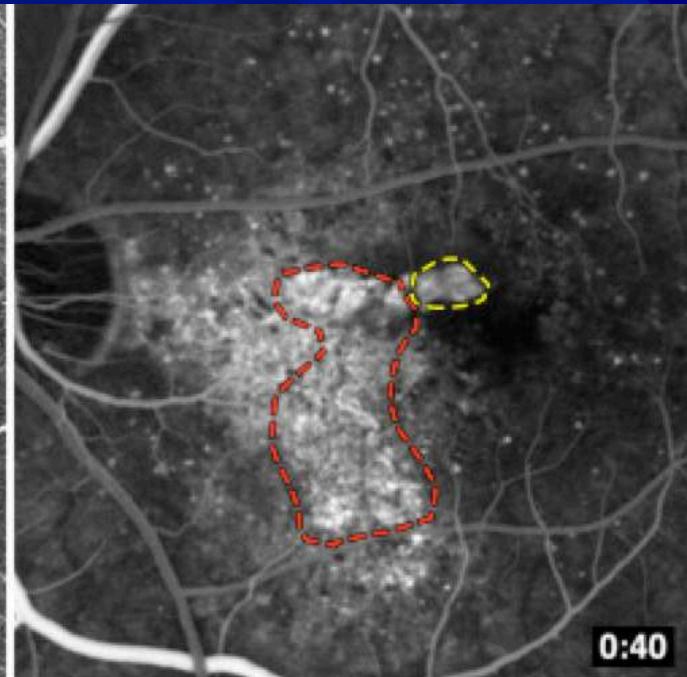
Case Example: Multimodal imaging of 66 y/o Caucasian male



Fundus image
and Occult

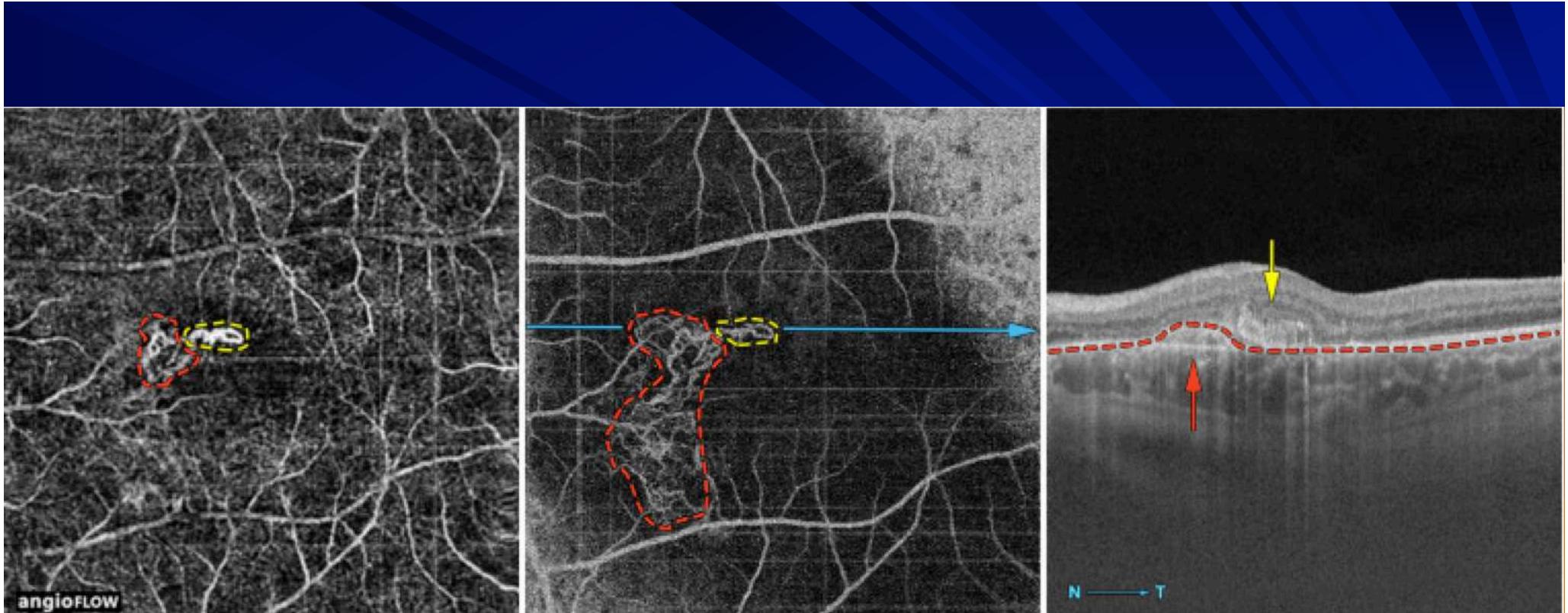


FFA: Early; Classic component



FFA: Late; Classic

Courtesy of Novais et al.



Choriocapillaris

Red: Occult;

Yellow: Classic

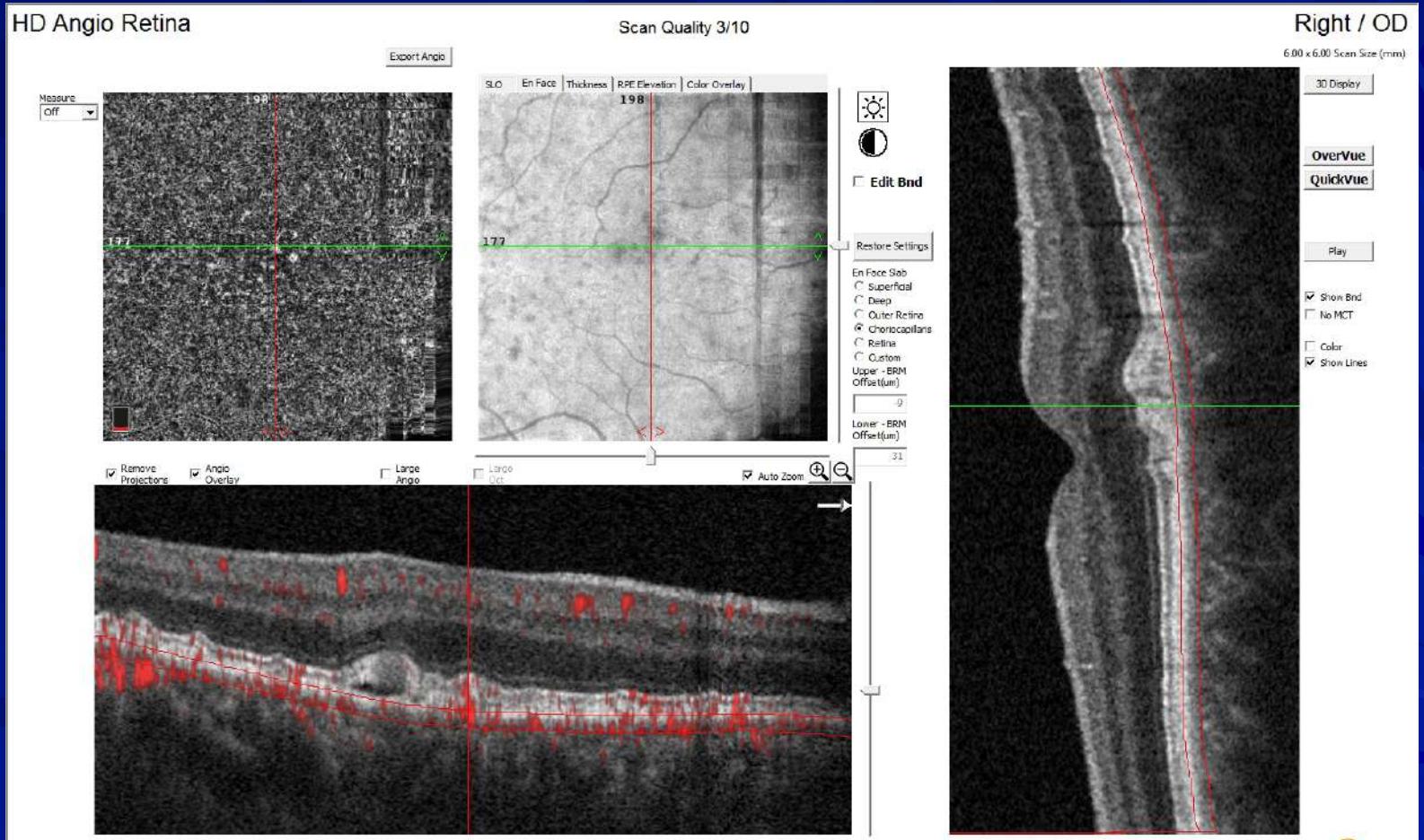
Courtesy of Novais et al.

OCT Angiography

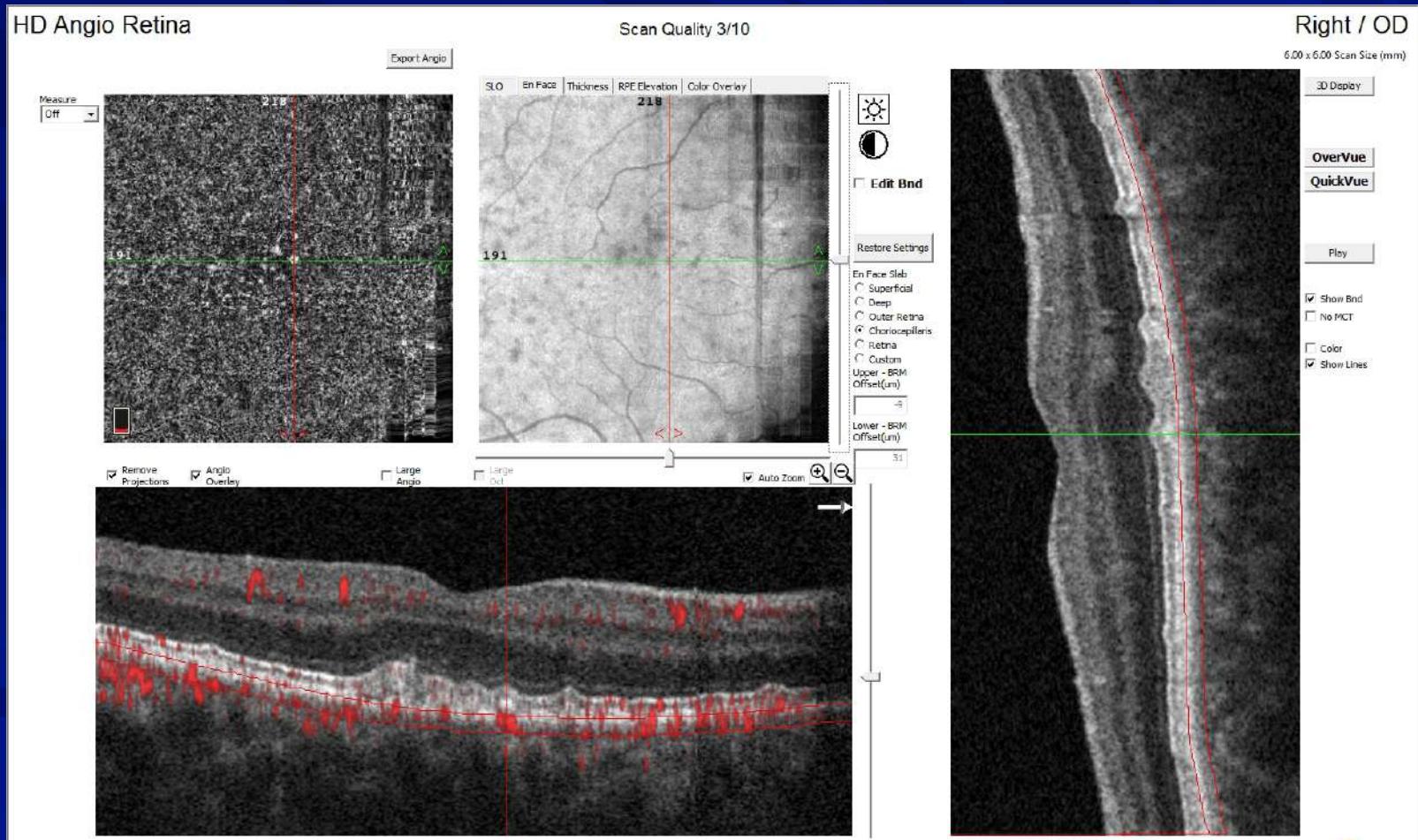
Subclinical CNV or “Occult non-exudative CNV”

Risk of exudation at 12 months is 15.2 times greater compared to eyes without subclinical CNV

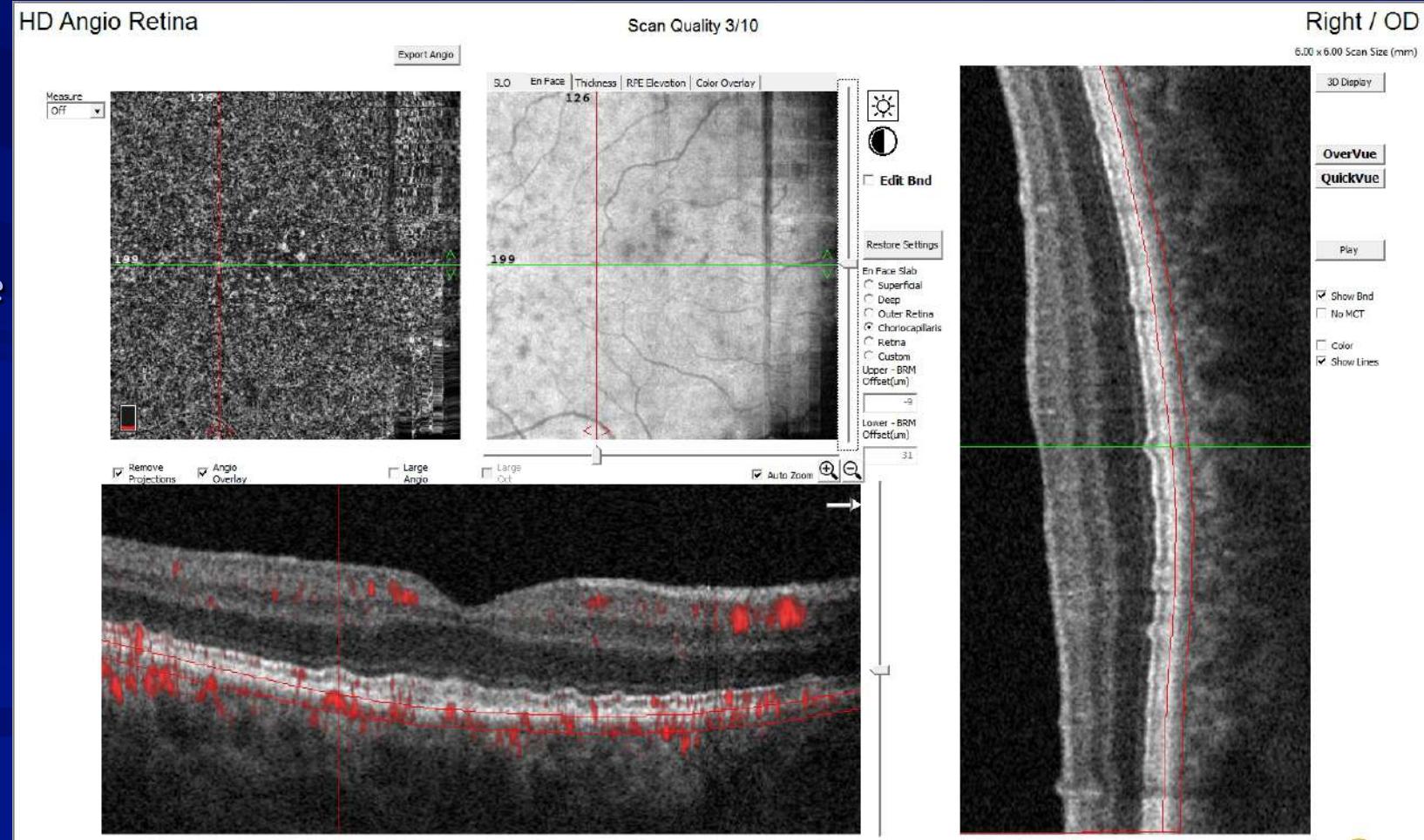
Occult Non-Exudative CNV Patient A



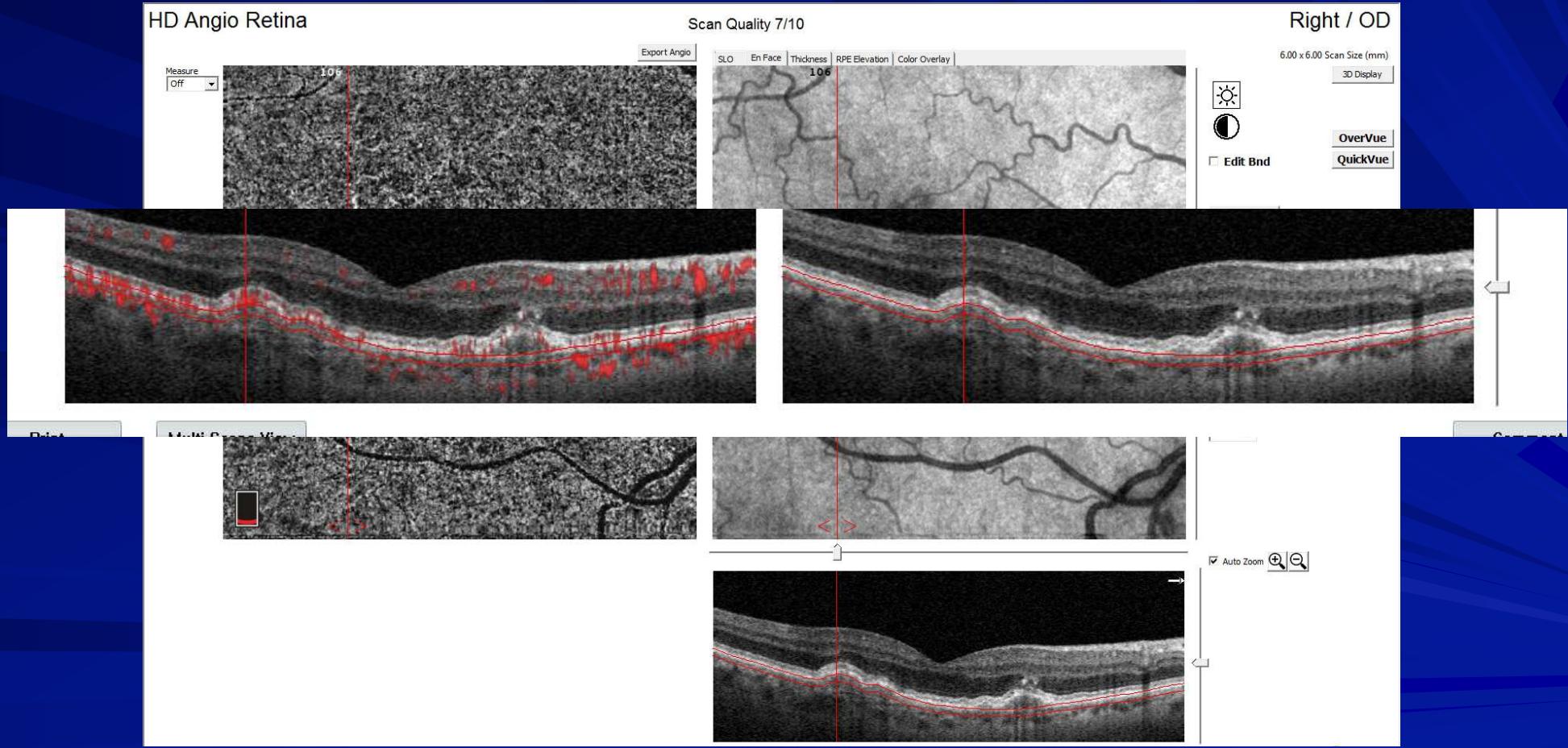
Occult Non-Exudative CNV Patient A



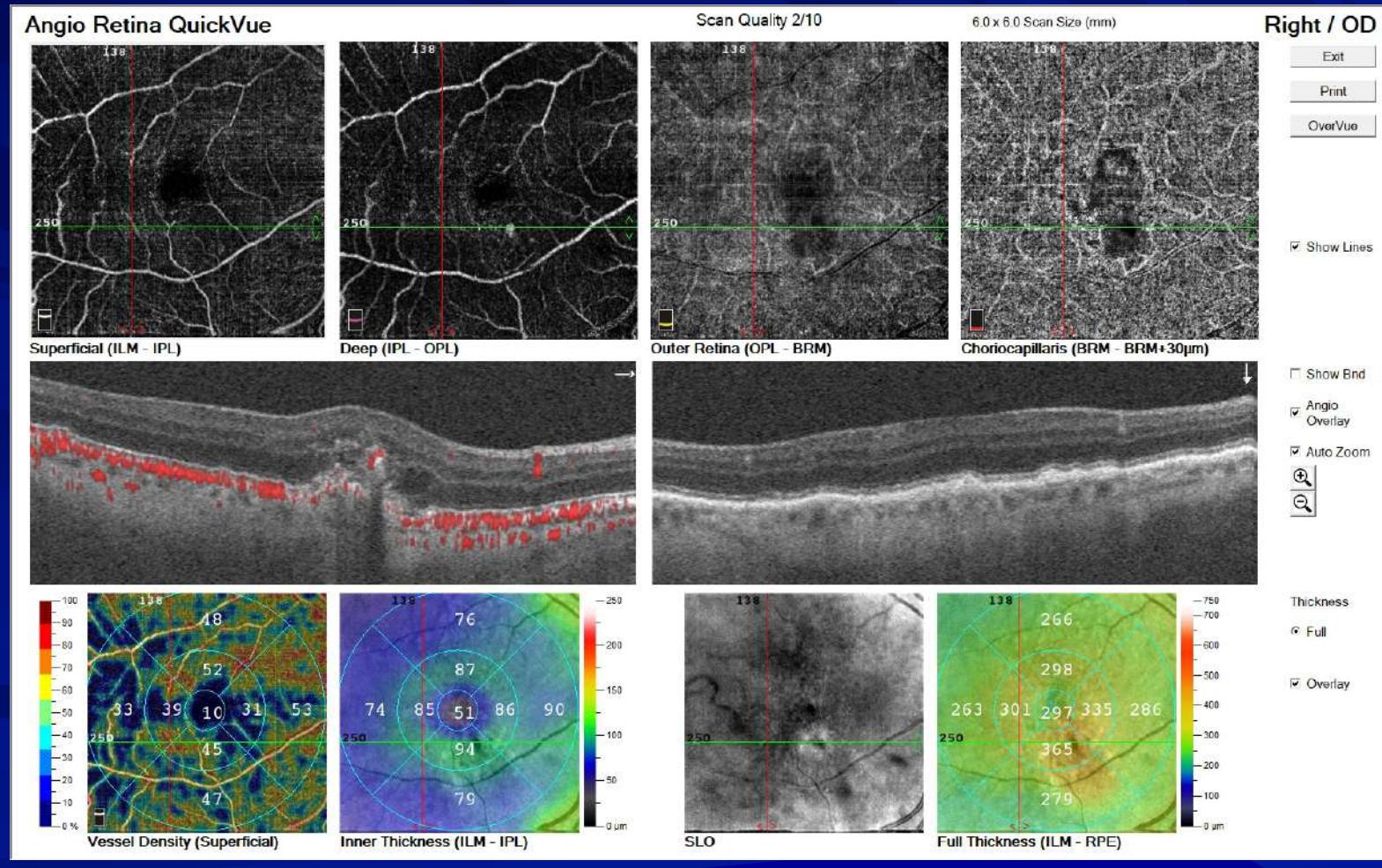
Occult Non-Exudative CNV Patient A



Which is More Suspicious?

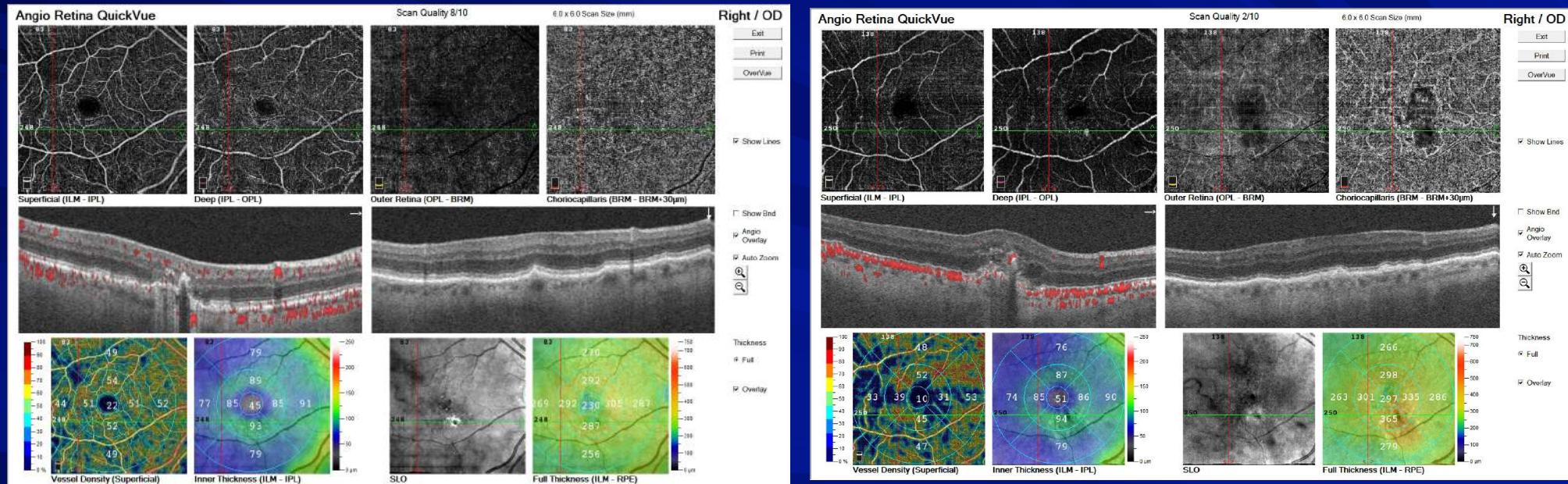


OCT Angiography Evaluation AMD



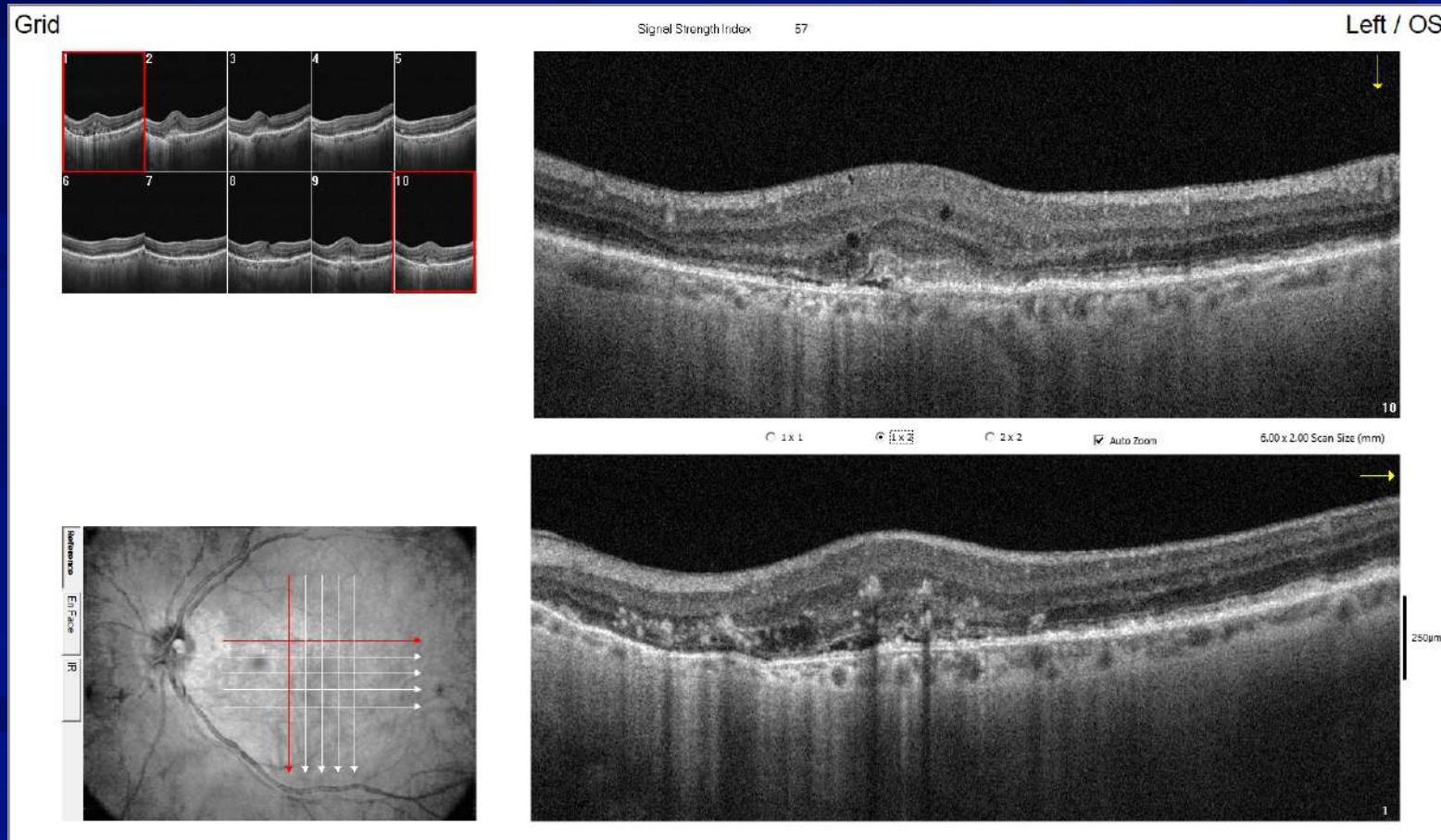
OCT Angiography Evaluation AMD

After and Before Bevacizumab (Avastin)

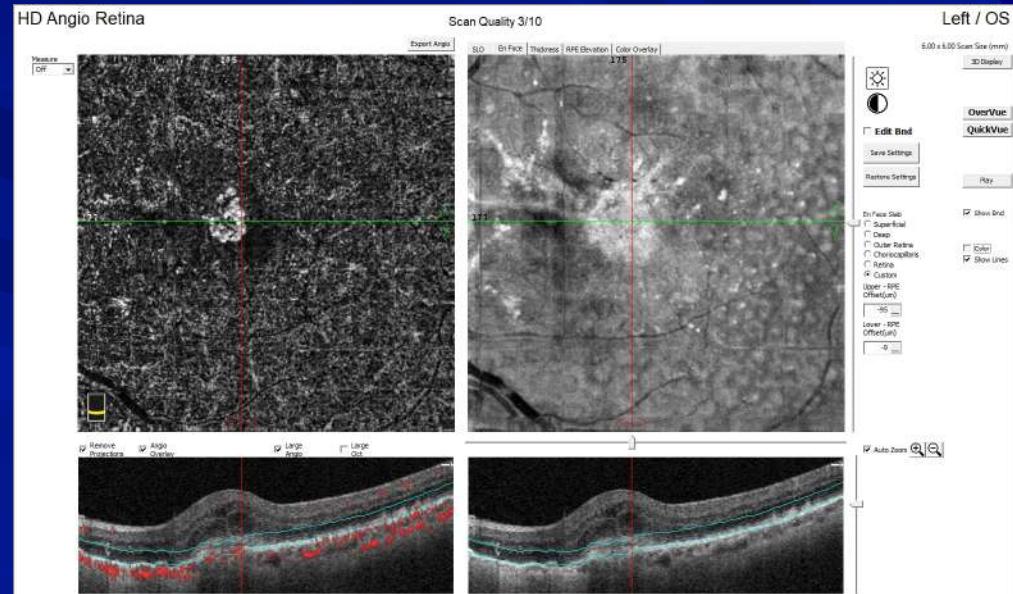
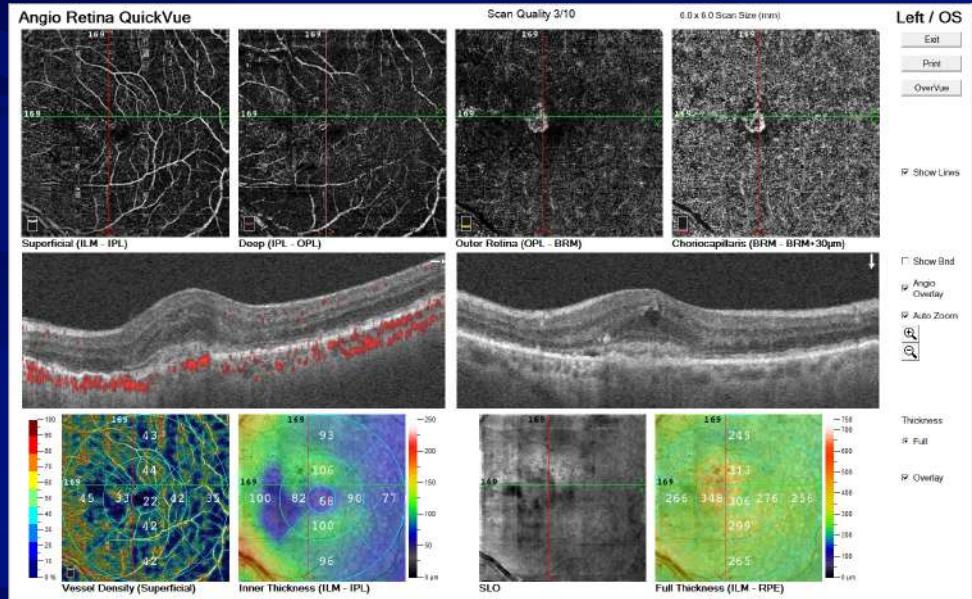


Evaluation AMD Patients for Neovascularization

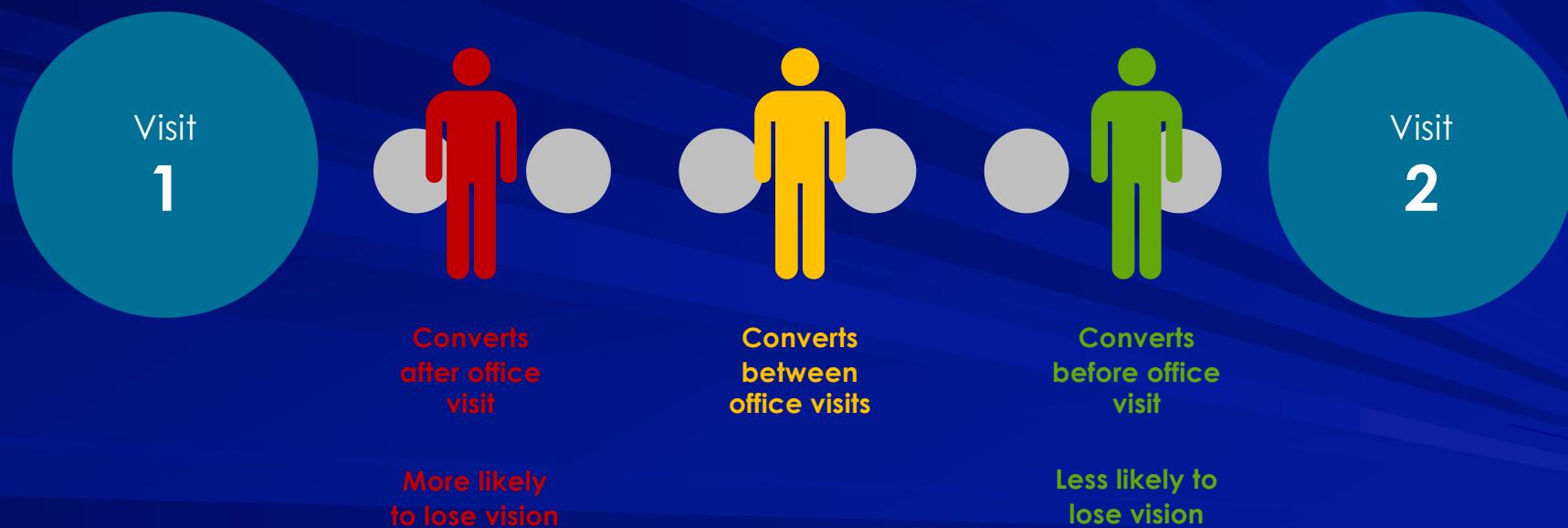
OCT Grid



Evaluation AMD Patients for Neovascularization Using OCT Angiography



At-risk Patients May Convert to Wet AMD at Any Point Between Follow-up Visits



Reference: Rauch R, et al. *Retina*. 2012;32(7):1260-1264.

Notal Vision - ForeseeHome® product overview



Reference: Data on File.

Readjusting our point of view to preventable vision loss



1. Chow EY, Clemons TE, Bressler SB, et al; Ophthalmology. 2014;121:535-544. 2. Rao P, Lum F, Wood K, et al. Ophthalmology. 2016;125(4):522-528. 3. Ho AC, Albini TA, Brown DM, Boyer DS, Regillo CD, Heier JS. JAMA Ophthalmol. 2017;135(3):268-273.

Notal Vision- PERIMETRY: The ForeseeHome Test

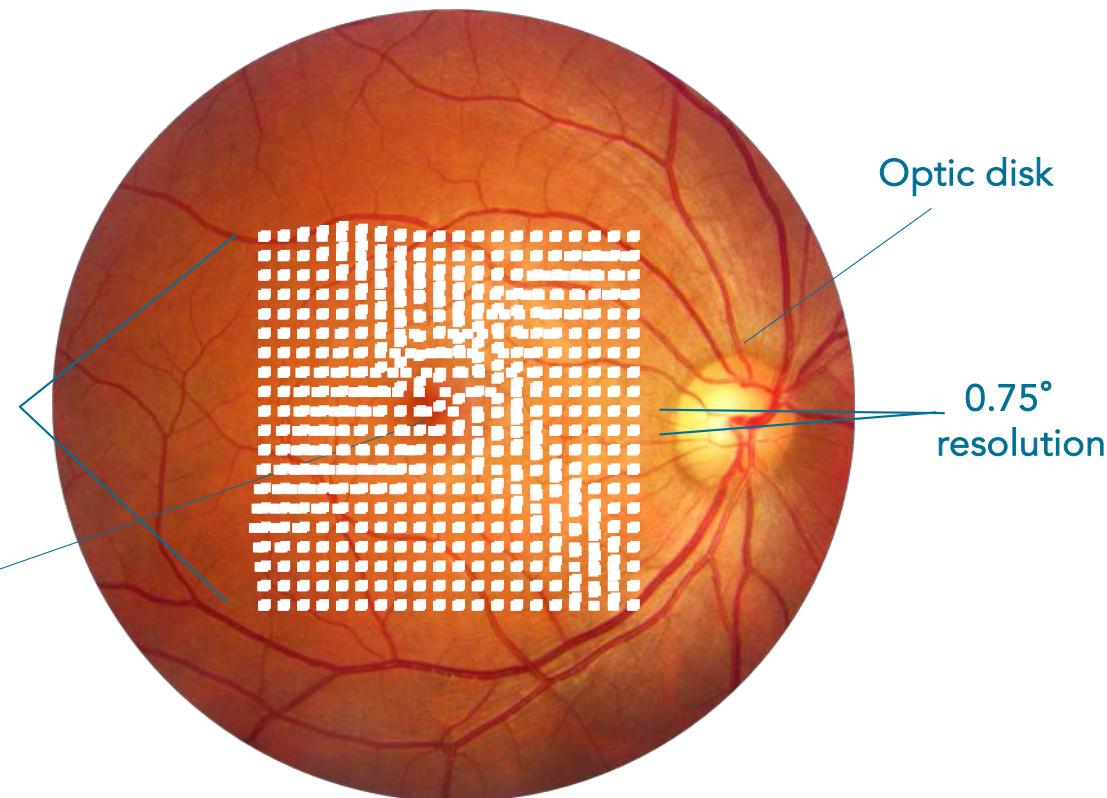
Total of 500 data points
tested 3 to 5 times each

Stimuli are presented
on screen for 160 ms

Visual field – central 14°
(4200 microns)

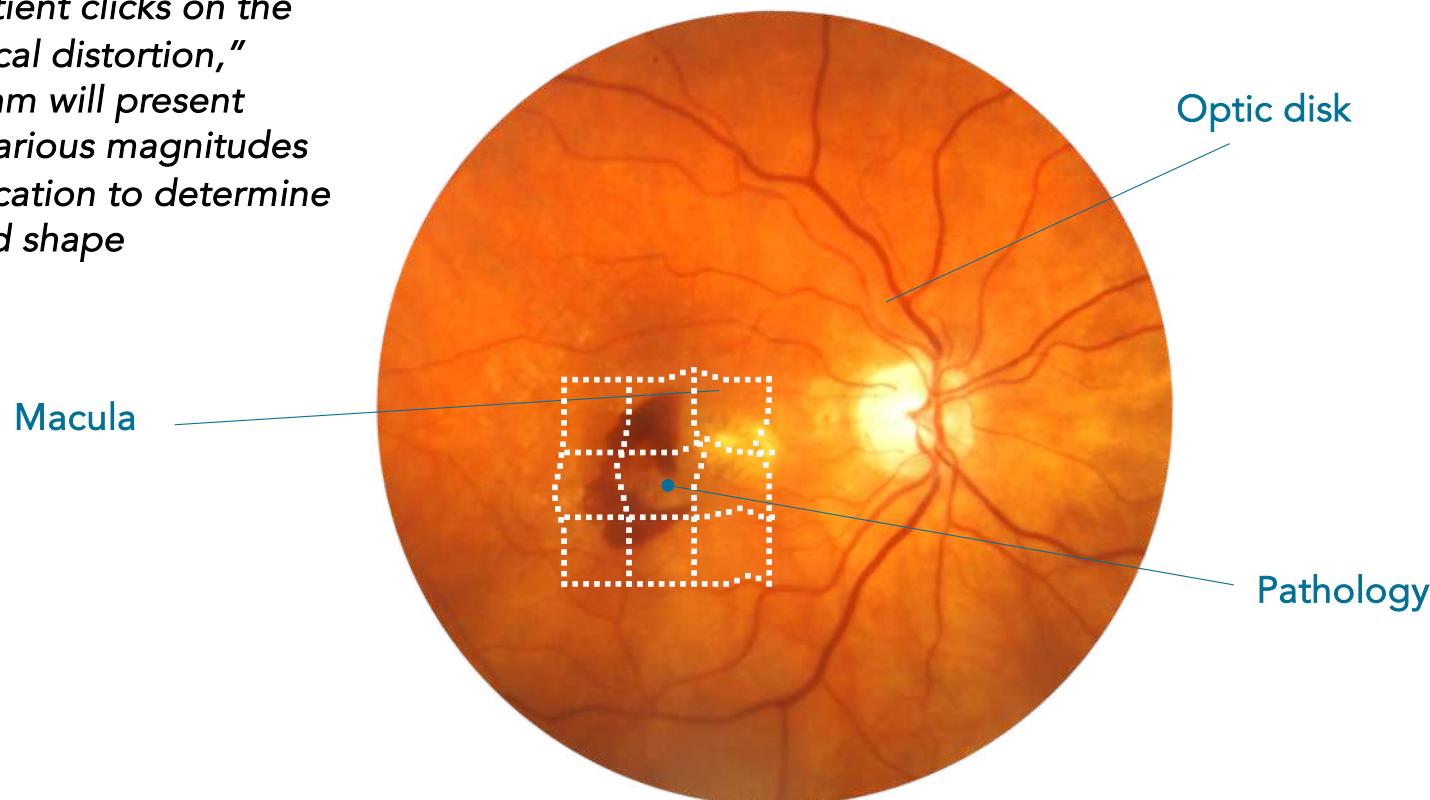
Macula

Optic disk
 0.75°
resolution



Once pathology is suspected, the area is bracketed to localize and quantify pathology

When a patient clicks on the “pathological distortion,” the algorithm will present stimuli of various magnitudes over the location to determine the size and shape

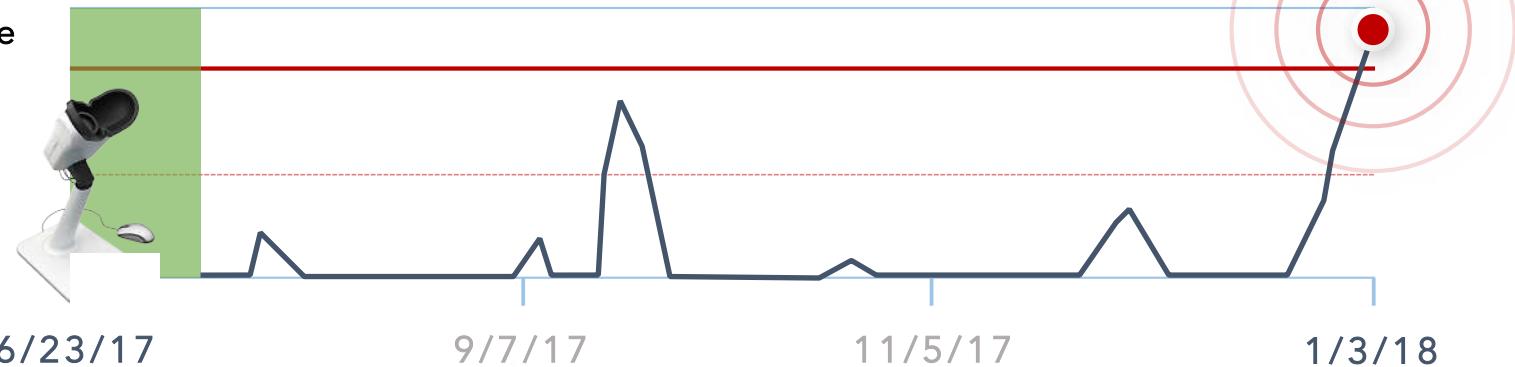




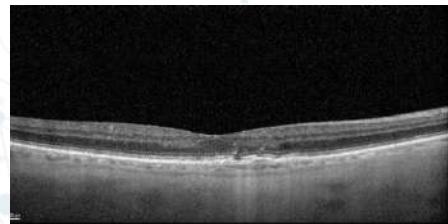
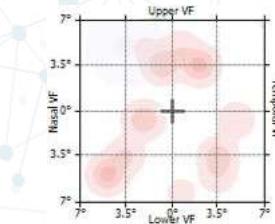
CASE 1 →

86 y/o Male | Baseline Vision: 20/30 OU

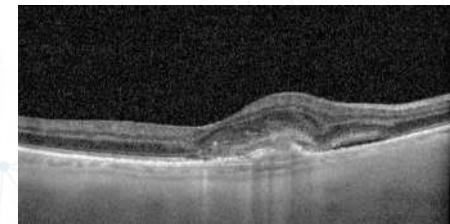
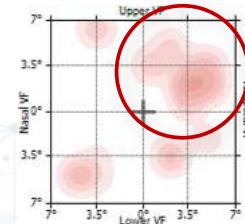
Trend Score



STARTED TESTING



ALERTED
20/60 OD and asymptomatic

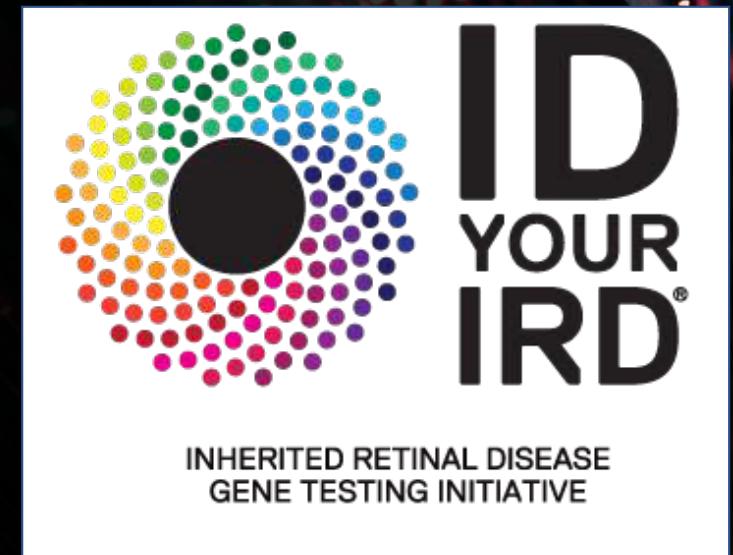


Ocular Genetic Testing

Generalized Ocular Testing

Inherited Retinal Disease and Spark Therapeutics

- Panel tests for mutations in approximately 300 genes associated with inherited retinal disease (IRD)
 - More commonly tested for:
 - *Retinitis pigmentosa*
 - *Leber congenital amaurosis*
 - *Stargardt disease*
 - Commonly associated symptoms
 - Nyctalopia
 - Central and/or peripheral field loss
 - Color vision deterioration and/or loss
 - Severe photophobia



****ID your IRD does NOT currently test for genes associated with AMD****

Generalized Ocular Testing

Inherited Retinal Disease and Spark Therapeutics



ID YOUR IRD® Testing Panel

The only way to confirm that your patient has an inherited retinal disease (IRD) is with a genetic test. Through the **ID YOUR IRD gene testing Initiative**, Spark Therapeutics supports people living with certain IRDs by providing genetic information that can empower their decisions. The ID YOUR IRD panel tests for mutations in approximately **300 genes** associated with IRDs.

Visit IDYOURIRD.com for more information or to order Irid® test kits.



BRUNSWICK BOSTON, INC.

Visit [IDYOURIRD.com](#) for more information or to order free test kits.

MANUFACTURER'S COPY OF CURRENT AND RECENT PUBLICATIONS RECEIVED
IN LIBRARIES LISTED IN *LIBRARY SYSTEMS* (LSS). RECEIVED SEPTEMBER 7, 2008. E-MAIL
SUBSCRIPTIONS: <http://www.libarts.ubc.ca/~systems/>

WATSON, L. Cooper, G.R. COOPER, C.G. McLELLAN, D.J. MULHOLLAND, "Medical Interventions in Hospitalized Traumatic Brain Injury Patients," *Journal of Clinical Neuroscience*, Volume 19, Number 10, October 2012, pp. 1350-1354.

Бюджет 2020

Spark

spark NLP

Здрав, Юрий Георгиевич! Ваша книга «БИОГРАФИЯ СЛОВА» – это необычный и интересный труд, я рекомендую ее всем, кто интересуется этим вопросом.

Digitized by srujanika@gmail.com

Age-Related Degeneration Genetic Testing

Peer-Reviewed Published Studies

Prospective assessment of genetic effects on progression to different stages of age-related macular degeneration using multistate Markov models. *IOVS* 53.3 (2012): 1548-1556.

CFH and ARMS2 genetic polymorphisms predict response to antioxidants and zinc in patients with age-related macular degeneration. *Ophthalmology* 120.11 (2013): 2317-2323.

Validation of a prediction algorithm for progression to advanced macular degeneration subtypes. *JAMA ophthalmology* 131.4 (2013): 448-455.

Treatment response to antioxidants and zinc based on CFH and ARMS2 genetic risk allele number in the Age-Related Eye Disease Study. *Ophthalmology* 122.1 (2015): 162-169.

Response to AREDS supplements according to genetic factors: survival analysis approach using the eye as the unit of analysis. *British Journal of Ophthalmology* 100.12 (2016): 1731-1737.

CFH and ARMS2 genetic risk determines progression to nvAMD after antioxidant and zinc supplementation. *Proc National Academy of Sciences* 115.4 (2018): E696-E704.

Age-Related Degeneration Testing

Arctic Medical Laboratories (<https://arcticdx.com>)



Vita Risk® is a DNA test measuring the two main genetic variations (three genetic variations in two genes) that interact with common vitamin/mineral supplements containing zinc. People in one genetic group have increased risk of progression of age-related macular degeneration, to wet AMD.

Does my patient carry the genetic variations associated with vision loss when using chronic supplements such as AREDS?

*****Patients positive for VitaRisk are advised to avoid long-term AREDS/AREDS2 supplements***

Age-Related Degeneration Testing

Arctic Medical Laboratories (<https://arcticdx.com>)



Macula Risk® is a DNA test combining many of the genes (15 genetic variations in 12 genes) associated with the progression of age-related macular degeneration (AMD). The genetic result is integrated into a formula developed from research at Tufts Medical Center and includes a patient's age, AMD disease status, height, weight, sex, age, and smoking history, which provides a basis for progression risk.

What is the likelihood of my patient progressing to advanced AMD?

Should my patient avoid chronic zinc supplementation?

*****Predictive algorithm touts 89% accuracy @ 2, 5 and 10-year time points***

Treatments for AMD

☞ Early detection and meaningful treatments with significant value, do not cure, but have been shown to slow or halt progression. Not limited to early stages but all stages of AMD

★ Prescribe smoking cessation programs

□ Smoking and AMD

- Depletes serum antioxidants
- Decreases pigmentary density
- Increases risk to advanced AMD

★ Lifestyle changes

□ Diet

□ Exercise

★ Systemic disease management

□ Cardiovascular disease, DM, obesity, high cholesterol

Risk Alleles

↵ Ancestry

↵ 23 and me

↵ Lot's of marketing once we they have the allele

Treatment for AMD

↳ Nutritional supplements

★ Sub-clinical/sub-structural or early disease

- Controversy flourishes
 - No definitive guideline exists
 - Despite consensus evidence suggests using supplements

★ Intermediate – advance disease

- No controversy on advocating for supplements

★ AREDS 1

- Contains Beta-carotene and no lutein or zeaxanthin, no longer recommended
- Investigated early AMD, no statistically significant benefit

★ AREDS 2

- Recommended for intermediate and advanced AMD, study protocol

★ The Practical Guide for the Treatment of AMD - 3 primary options

- Macular pigment supplement
 - Carotenoids: lutein, zeaxanthin, meso-zeaxanthin
- Carotenoids, antioxidants, zinc, and vitamins C & E
 - AREDS 2
- Carotenoid macular supplement in subclinical and early AMD. Carotenoid and antioxidant is intermediate and AMD that is progressing

Treatment for AMD

❖ Retinal light protection

- ★ Sun exposure

❖ Closer follow up

- ★ 12 months is currently accepted as being too long to detect progression
- ★ 6 months or sooner based on risk of CNV

❖ Low vision and rehabilitation consultation

Treating Half the Retina?



[Oxid Med Cell Longev.](#) 2019; 2019: 9783429.

Published online 2019 Feb 12. doi: [10.1155/2019/9783429](https://doi.org/10.1155/2019/9783429)

PMCID: PMC6390265

PMID: 30891116

Health Benefits of Polyphenols and Carotenoids in Age-Related Eye Diseases

Simona Bungau,¹ Mohamed M. Abdel-Daim,^{✉ 2, 3} Delia Mirela Tit,¹ Esraa Ghanem,^{✉ 4} Shimpei Sato,³ Maiko Maruyama-Inoue,³ Shin Yamane,³ and Kazuaki Kadonosono³

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Abstract

Go to:

Oxidative stress and inflammation play a critical role in the initiation and progression of age-related ocular abnormalities as cataract, glaucoma, diabetic retinopathy, and macular degeneration. Therefore, phytochemicals with proven antioxidant and anti-inflammatory activities, such as carotenoids and polyphenols, could be of benefit in these diseases. We searched PubMed and Web of Science databases for original studies investigating the benefits of different carotenoids and polyphenols in age-related ophthalmic diseases. Our results showed that several polyphenols (such as anthocyanins, *Ginkgo biloba*, quercetin, and resveratrol) and carotenoids (such as lutein, zeaxanthin, and mezoxanthin) have shown significant preventive and therapeutic benefits against the aforementioned conditions. The involved mechanisms in these findings include mitigating the production of reactive oxygen species, inhibiting the tumor necrosis factor- α and vascular endothelial growth factor pathways, suppressing p53-dependent apoptosis, and suppressing the production of inflammatory markers, such as interleukin- (IL-) 8, IL-6, IL-1a, and endothelial leucocyte adhesion molecule-1. Consumption of products containing these phytochemicals may be protective against these diseases; however, adequate human data are lacking. This review discusses the role and mechanisms of polyphenols and carotenoids and their possible synergistic effects on the prevention and treatment of age-related eye diseases that are induced or augmented by oxidative stress and inflammation.

Carotenoids and Polyphenols

www.oncotarget.com Oncotarget, 2018, Vol. 9, (No. 24), pp: 17181-17198
Review

Oxidative stress: role of physical exercise and antioxidant nutraceuticals in adulthood and aging

Carolina Simioni¹, Giorgio Zauli¹, Alberto M. Martelli², Marco Vitale^{3,4}, Gianni Sacchetti⁵, Arianna Gonelli¹ and Luca M. Neri¹

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³Department of Medicine and Surgery, University of Parma, Parma, Italy
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Keywords: exercise training; nutraceuticals; flavonoids intake; aging; antioxidant supplementation

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Resveratrol can be implied in anti-aging actions by influencing the mitochondrial environment and metabolic diseases, by regulating the levels of some inflammatory mediators and cytokines and by modulating lipolysis [125, 152, 153]. Mitochondrial dysfunction has been proved to be associated with aging and disease development [154], and it was seen

39

Oncotarget

Annu Rev Nutr. 2019;39:95-120. Downloaded from www.annualreviews.org

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Furthermore, resveratrol maintains the vascular fitness through its antioxidant and anticoagulant activities, and on the other hand is relevant in blocking the formation of new blood vessels, in inhibiting the VEGF release and attenuating Hypoxia-Inducible Factor (HIF-1α) in different tumor cells [163].

It is reported that also curcumin possesses anti-

ASSESSMENT OF CAROTENOIDS

Impact of Carotenoid Assessment

Because carotenoids appear to play a key role in retinal diseases, intensive research has resulted in a variety of innovative carotenoid assessment techniques. The breadth of possibilities for assessing retinal carotenoids is often confusing because methodologies, units of measurement, and the presentation of results vary widely. Accurate readings of carotenoid status are important in order to correctly advise individuals with regards to supplementation. Furthermore, in diseases such as macular telangiectasia type 2 (MacTel), the assessment of carotenoids may be crucial to the diagnosis, as reduced MP levels as well as abnormal distributions are among the first signs of the disease. Therefore, the measurement of carotenoids can impact clinical practice, and the evaluation of MP may eventually become an integral part of comprehensive ophthalmological care. The following sections describe and aim to give an organized overview of different MP assessment techniques.

A large variety of methods are used to assess carotenoid status in humans, most of which are focused on the eye, but carotenoids can also be measured in tissue outside of the eye, such as the skin, blood, and the brain. Measurements of ocular carotenoids can be distinguished between subjective (psychophysical) and objective (optical) methods used to assess the amount of MP. In subjective methods, a direct answer from the patient is required, whereas objective measurement methods typically require just enough cooperation to generate an image (73).

Measuring Macular Pigment

☞ Retina macula biopsy

☞ Clinical Imaging

★ Subjective

□ ZeaVision MPSII

□ Guardion Mapcat SF

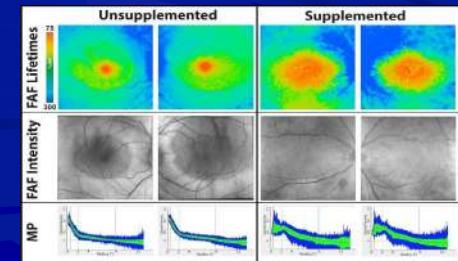
★ Clinical

□ ZeaVision MPR

□ Zeiss Visucam 200

□ Spectralis HRA+OCT

□ Spectralis MPOV



Thank you! Dr. Chris Putnam

Measuring Macular Pigment

Biophotonic Scanner

- ★ Measures carotenoids
- ★ Based on an optical method known as Resonant Raman Spectroscopy (RSS)

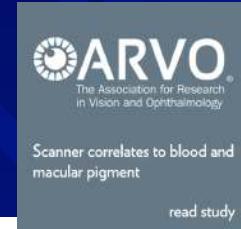
□ Used for many years in research laboratories

★ Skin RRS measurements

- Noninvasive
- Objective
- Reliable methods to assess carotenoid levels
 - Ocular
 - Systemic



Carotenoid Levels



Biomarker of health for diet and lifestyle

*Yale University

Phospholipid bi-layer

Carotenoids, flavonoids, and polyphenols



Clinical and Epidemiologic Research

Correlations Between Macular, Skin, and Serum Carotenoids

Christopher D. Conrady,¹ James P. Bell,¹ Brian M. Besch,¹ Aruna Gorusupudi,¹ Kelliann Farnsworth,¹ Igor Ermakov,² Mohsen Sharifzadeh,² Maia Ermakova,² Werner Gellermann,^{1,2} and Paul S. Bernstein¹

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Submitted: March 7, 2017

Accepted: June 18, 2017

Citation: Conrad CB, Bell JP, Besch BM, et al. Correlations between mac-

Liu, et al. Correlations between nail, skin, and serum carotenoids. *Invest Ophtalmol Vis Sci*. 2017;58:3616-3627. DOI:10.1167/ijon.17.31818.

PURPOSE. Ocular and systemic measurement and imaging of the macular carotenoids lutein and zeaxanthin have been employed extensively as potential biomarkers of AMD risk. In this study, we systematically compare dual wavelength retinal autofluorescence imaging (AFD) of macular pigment with skin resonance Raman spectroscopy (RRS) and serum carotenoid levels in a clinic-based population.

METHODS. Eighty-eight patients were recruited from retina and general ophthalmology practices from a tertiary referral center and excluded only if they did not have all three modalities tested, had a diagnosis of macular telangiectasia (MacTel) or Stargardt disease, or had poor AF1 image quality. Skin, macular, and serum carotenoid levels were measured by RRS, AFL and HPLC, respectively.

RESULTS. Skin RSE measurements and serum zeaxanthin concentrations correlated most strongly with AFA macular pigment volume under the curve (MPVUC) measurements up to 9° eccentricity relative to MPVUC, or rotationally averaged macular pigment optical density (MPOD) measurements at smaller eccentricities. These measurements were reproducible and not significantly affected by cataracts. We also found that these techniques could readily identify subjects taking oral carotenoid-containing supplements.

CONCLUSIONS. Larger macular pigment volume AFI and skin RRS measurements are noninvasive, objective, and reliable methods to assess ocular and systemic carotenoid levels. They are an attractive alternative to psychophysical and optical methods that measure MPOD at a limited number of eccentricities. Consequently, skin RRS and MPVUC at 9° are both reasonable biomarkers of macular carotenoid status that could be readily adapted to research and clinical settings.

Keywords: macular pigment, carotenoids, macula

Carotenoid Levels



- | Quick Test
(approx. 30 sec)
- | Portable
- | Cost Effective
- | Remeasure in 60 days
- | Reassurance to you and patient

Raman Spectroscopy



Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies

Susan T. Mayne ^{a,*}, Brenda Cartmel ^a, Stephanie Scarmo ^{a,b}, Lisa Jahns ^c, Igor V. Ermakov ^d, Werner Gellermann ^d



^a Yale School of Public Health and Yale Cancer Center, 60

^b Center for Science in the Public Interest, 1220 L Street

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Biomarker

ABSTRACT

Resonance Raman spectroscopy is a noninvasive method that has been developed to assess carotenoid status in human tissues including human skin *in vivo*. Skin carotenoid status has been suggested as a promising biomarker for human studies. This manuscript describes research done relevant to the development of this biomarker, including its reproducibility, validity, feasibility for use in field settings, and factors that affect the biomarker such as diet, smoking, and adiposity. Recent studies have evaluated the response of the biomarker to controlled carotenoid interventions, both supplement-based and dietary [e.g., provision of a high-carotenoid fruit and vegetable (F/V)-enriched diet], demonstrating consistent response to intervention. The totality of evidence supports the use of skin carotenoid status as an objective biomarker of F/V intake, although in the cross-sectional setting, diet explains only some of the variation in this biomarker. However, this limitation is also a strength in that skin carotenoids may effectively serve as an integrated biomarker of health, with higher status reflecting greater F/V intake, lack of smoking, and lack of adiposity. Thus, this biomarker holds promise as both a health biomarker and an objective indicator of F/V intake, supporting its further development and utilization for medical and public health purposes.

900 STUDIES

*Arch Biochem Biophys. PMC 2014 Nov 15.

ARVO STUDY

Interrelationships between Macula, Skin and Serum Carotenoids- Paul Bernstein,Werner Gellerman et al ARVO May 2016

Conclusions:

"Our results emphasize the importance of measuring the total amount of carotenoids in the macula region using an objective image based modality such as AFI w Spectralis rather than subjective MPOD."

Skin resonance Raman Spectroscopy of skin carotenoids is a reasonable biomarker of macula carotenoid status. and correlates better than than subjective MPOD tests.



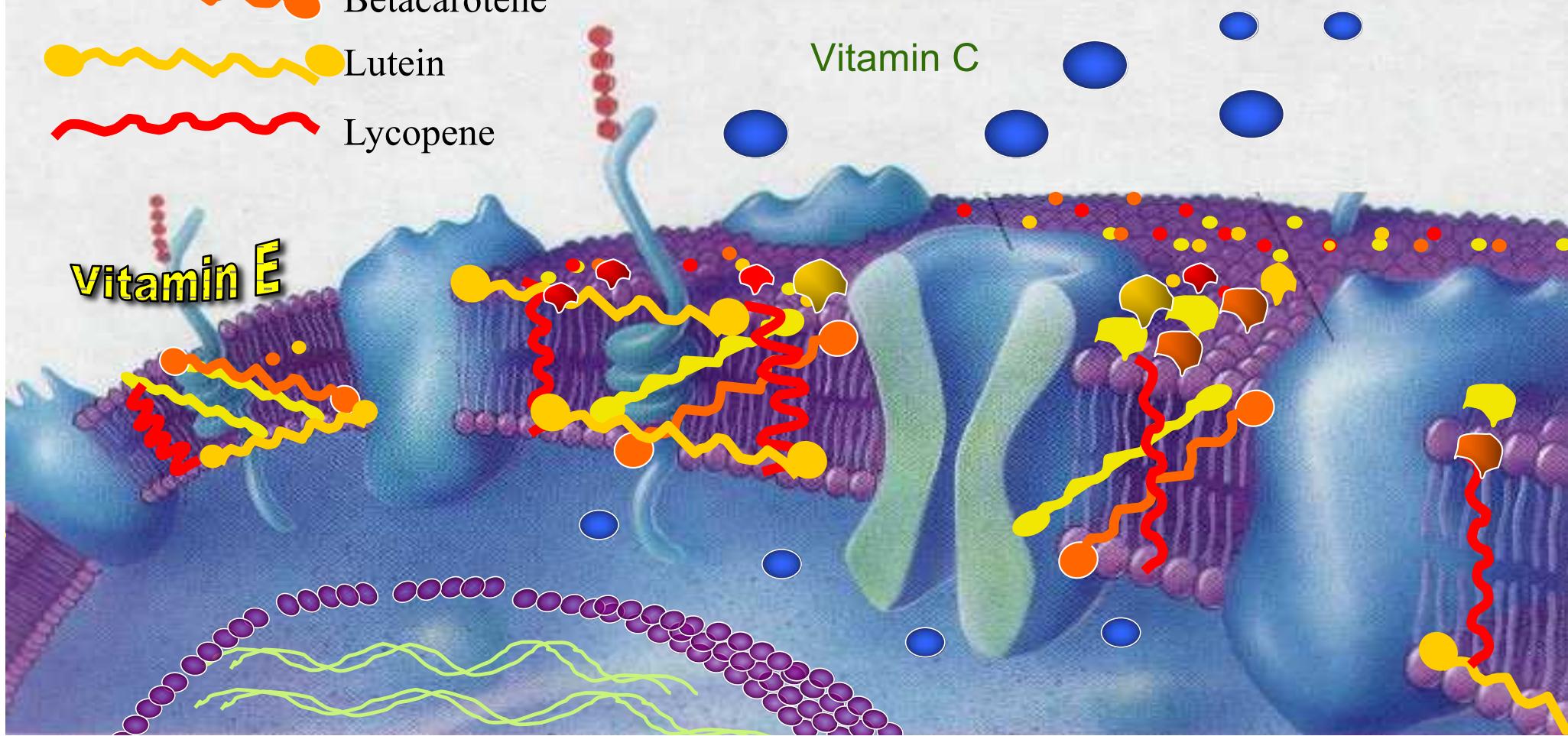
The objective hand scanner is better than the subjective Macuscope, QuantifEYE, and Densitometer for estimating macula pigment.

Vulnerable to Oxidation

Betacarotene
Lutein
Lycopene

Vitamin C

Vitamin E



53-year-old man

❖ Family history of AMD

- ★ Dad with 43 injections for AMD

❖ Pre-diabetic with borderline HbA1c

❖ Vision 20/20 OU

❖ DFE- retina clear

❖ OCT normal

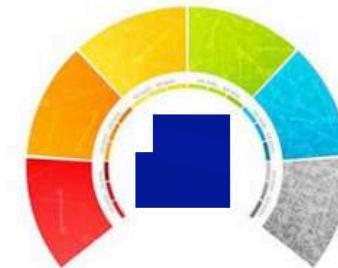
❖ Passes dark adaptation

**CONGRATULATIONS ON TAKING THE FIRST STEPS
TOWARDS OPTIMIZING YOUR SCS**

Dear [REDACTED]

Recently, on 12/15/2020, you met with me and I scanned the palm of your hand with the [REDACTED] BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 26000.

This score represents the current carotenoid level of your skin. The higher the score, the more carotenoids your body is receiving.



26000

Ingredients

Ingredients	Amount	% Daily Value
Serving Size: 1 Packet		
Vitamin A (83% as Beta Carotene (1875 mcg RAE) from <i>Blakeslea trispora</i> , and Vitamin A palmitate) (375 mcg RAE)	2250 mcg RAE	250%
Vitamin C (as Calcium Ascorbate)	200 mg	222%
Vitamin D (as Cholecalciferol)	5 mcg (200 IU)	25%
Vitamin E (as D-Alpha-Tocopheryl Acetate, D-Alpha Tocopherol, Tocotrienols)	50.3 mg	335%
Vitamin K (as Phytonadione)	20 mcg	17%
Thiamin (as Thiamine Mononitrate)	3.75 mg	313%
Riboflavin (as Riboflavin)	4.25 mg	327%
Niacin (as Niacinamide)	17.5 mg NE	109%
Vitamin B6 (as Pyridoxine Hydrochloride)	5 mg	294%
Folate	500 mcg DFE (300 mcg folic acid)	125%
Vitamin B12 (as Cyanocobalamin)	15 mcg	625%
Biotin (as Biotin)	75 mcg	250%
Pantothenic Acid (as D-Calcium Pantothenate)	15 mg	300%
Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%

Calcium (as Calcium Carbonate, Di-Calcium Malate, Calcium Ascorbate)	250 mg	19%
Iodine (as Potassium Iodide)	50 mcg	33%
Magnesium (as Magnesium Glycinate, Magnesium Oxide)	125 mg	30%
Zinc (as Zinc Bisglycinate)	7.5 mg	68%
Selenium (as L-Selenomethionine, Sodium Selenite)	70 mcg	127%
Copper (as Copper Bisglycinate)	0.5 mg	56%
Manganese (as Manganese Bisglycinate)	1 mg	43%
Chromium (as Chromium Nicotinate Glycinate)	100mcg	286%
Molybdenum (as Molybdenum Bisglycinate)	37.5 mcg	83%
Polyphenol and Flavonoid Blend	97.5 mg	*
Catechins (from <i>Camellia sinensis</i> Leaf Extract)	(45 mg)	*
Quercetin	(25 mg)	*
Grape Seed Extract (min. 95% Polyphenols)	(12.5 mg)	*
Citrus Bioflavonoids (from Citrus Fruits)	(12.5 mg)	*
Resveratrol (from <i>Polygonum cuspidatum</i> root extract)	(2.5 mg)	*
Mixed Tovopherols (Gamma, Delta & Beta Tocopherols)	53 mg	*
Alpha-Lipoic Acid	15 mg	*
Inositol (as Inositol)	5 mg	*
Carotenoid Blend	3.5 mg	*
Lycopene (as Lycopene)	(2.5 mg)	*
Lutein (from Marigold Flower Extract)	(1 mg)	*
Boron (as Boron Citrate)	1.5 mg	*
Vanadium (as Vanadyl Sulfate)	10 mcg	*

OTHER INGREDIENTS: Gelatin, Microcrystalline Cellulose, Crosmarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Titanium Dioxide.

CONTAINS: Fish (Cod, Pollack, Haddock, Hake, Cusk, Redfish, Sole, Flounder).

SUPPLEMENT FACTS**Supplement Facts**

Serving Size 2 Softgels	Servings Per Container 60	% DV
Amount Per Serving		
Total Calories	15	
Total Fat	1 g	1%*
Saturated Fat	0 g	0%
Trans Fat	0 g	
Vitamin D ₃ (as cholecalciferol)	12.5 mcg (500 IU)	63%
Vitamin K ₂ (as menaquinone-7)	20 mcg	17%
Ultra-pure fish oil concentrate:		
EPA (Eicosapentaenoic acid)	300 mg	**
DHA (Docosahexaenoic acid)	200 mg	**
Citrus Bioflavonoids (including hesperidin and naringin)	100 mg	**
Purple corn (<i>Zea mays L.</i>) cob extract including anthocyanins	66.67 mg	**
Alpha Lipoic Acid	50 mg	**
Quercetin (from <i>Quercus robur</i> fruit extract)	37.5 mg	**
D-Limonene (from <i>Citrus sinensis</i> peel)	25 mg	**
Rosemary (<i>Rosmarinus officinalis L.</i>) leaf extract including carnosic acid	18.75 mg	**
Resveratrol (from <i>Polygonum cuspidatum</i> root)	15 mg	**
Coenzyme Q10	15 mg	**
Lycopene	2.5 mg	**
Lutein (from marigold flower (<i>Tagetes erecta</i>))	2 mg	**
Astaxanthin (from <i>Haematococcus pluvialis</i> algae)	0.5 mg	**

* Percent Daily Values are based on a 2,000 Calorie Diet.

** Daily Value (DV) not established.

OTHER INGREDIENTS: Gelatin, Glycerin, Beeswax, Sunflower Lecithin, Vanillin.**CONTAINS:** Fish (anchovies, sardines, mackerel).

53-year-old man

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Dear [REDACTED]

Recently, on 12/27/2020, you met with me and I scanned the palm of your hand with the [REDACTED] BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 33000.

This score represents the current carotenoid level of your skin. The higher the score, the more carotenoids your body is receiving.



33000

CONGRATULATIONS ON TAKING THE FIRST STEPS TOWARDS OPTIMIZING YOUR SCS

Dear [REDACTED]

Recently, on 01/23/2021, you met with me and I scanned the palm of your hand with the [REDACTED] BioPhotonic Scanner. Your scan returned a Skin Carotenoid Score (SCS) of 47000.

This score represents the current carotenoid level of your skin. The higher the score, the more carotenoids your body is receiving.



47000

Measuring Macular Pigment

~~ Retina macula biopsy

~~ Clinical Imaging

* Subjective

□ ZeaVision MPSII

□ Guardion Mapcat SF

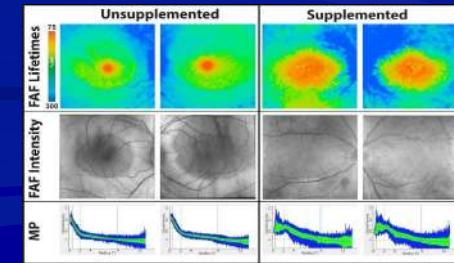
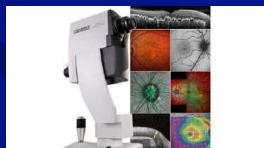
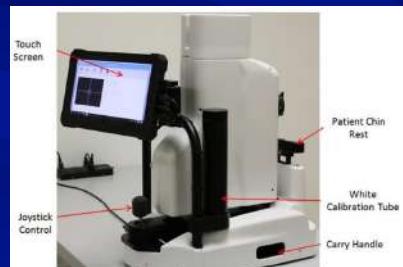
* Clinical

□ ZeaVision MPR

□ Zeiss Visucam 200

□ Spectralis HRA+OCT

□ Spectralis MPOV



Thank you! Dr. Chris Putnam

Treatments for Choroidal Neovascularization (CNV)

Current Anti-VEGF treatments

- ★ Bevacizumab (Avastin)
 - Humanized full length monoclonal antibody
 - AMD
- ★ Ranibizumab (Lucentis)
 - Humanized monoclonal antibody fragment
 - AMD, DME, DR, RVO
- ★ Aflibercept (Eylea)
 - Fusion protein
 - AMD, DME, DR
- ★ brolucizumab-dbll (Beovu)
 - Humanized single-chain antibody fragment
 - Up to 3 months dosing intervals, most are 4-6 weeks
 - 50% remained 3 months after 1 year
- ★ Pegaptanib (Macugen)
 - RNA aptamer
 - AMD

than going in. Tough call.

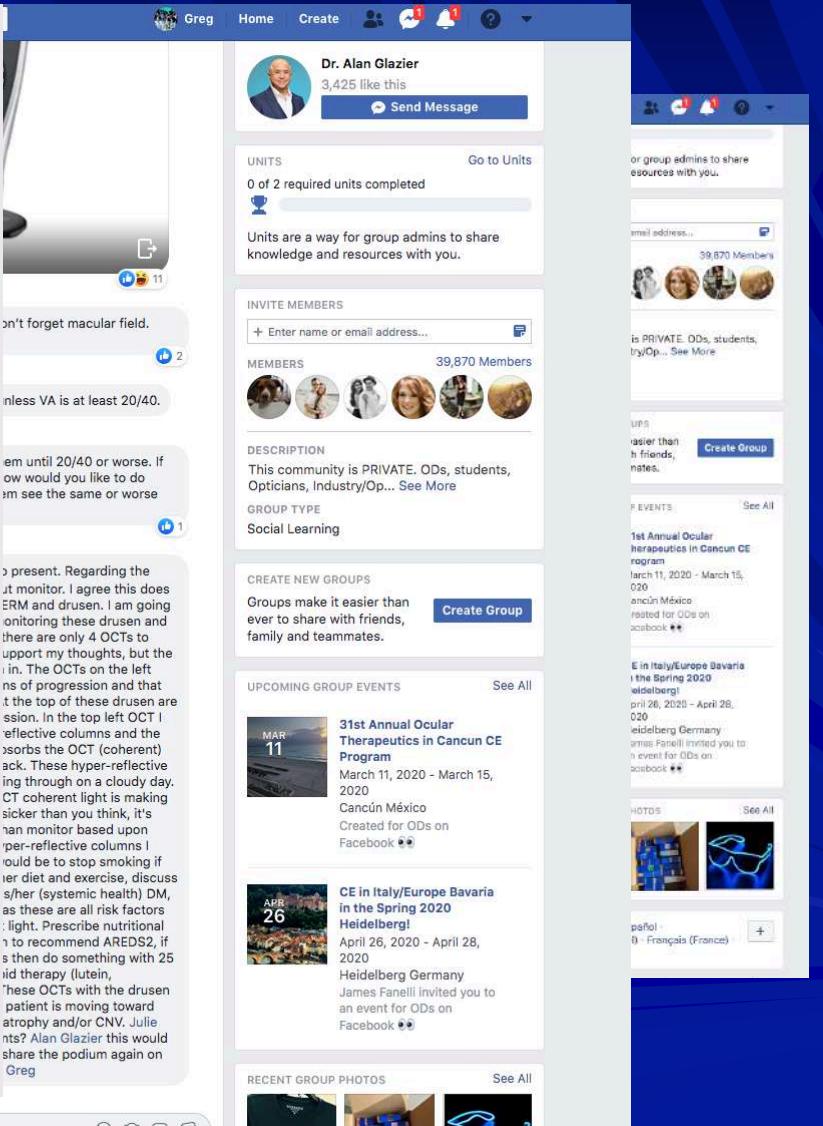
Like · Reply · 1d

Greg Caldwell  Chad F. December 11, 2019 · Loss of foveal p... may be vitelliform cataracts ou. W...

Chad, great case to present. Regarding the ERM I agree with my colleagues about monitor. I agree this does not need to see retina based on the ERM and drusen. I am going to respectfully disagree about just monitoring these drusen and this patient. I will start off by saying there are only 4 OCTs to review, looking at more would help support my thoughts, but the two here are enough for me to weigh in. The OCTs on the left side top and bottom are showing signs of progression and that the RPE is sicker than just monitor. At the top of these drusen are hyper-reflective foci a sign of progression. In the top left OCT I see two columns of sub-RPE hyper-reflective columns and the bottom left 5-6 columns. The RPE absorbs the OCT (coherent) light typically keeping the choroid black. These hyper-reflective columns are like rays of sunlight poking through on a cloudy day. The RPE is atrophied here and the OCT coherent light is making its way into the choroid. This RPE is sicker than you think, it's oxidized, inflamed, it's sick. Rather than monitor based upon hyper-reflective foci and sub-RPE hyper-reflective columns I would treat this patient. Treatment would be to stop smoking if the patient is a smoker, discuss his/her diet and exercise, discuss the best possible management for his/her (systemic health) DM, cholesterol, obesity, cardiovascular, as these are all risk factors in AMD. Sunglasses in any ultraviolet light. Prescribe nutritional supplements, this RPE is sick enough to recommend AREDS2, if you want to avoid the high zinc levels then do something with 25 mg of zinc, or at least triple carotenoid therapy (lutein, zeaxanthin, and meso-zeaxanthin). These OCTs with the drusen size, foci, and columns are signs the patient is moving toward advanced AMD which is geographic atrophy and/or CNV. Julie Friedman Rodman any other comments? Alan Glazier this would be a great case to present when we share the podium again on cases from ODs on FB. Respectfully, Greg

Like · Reply · 2m

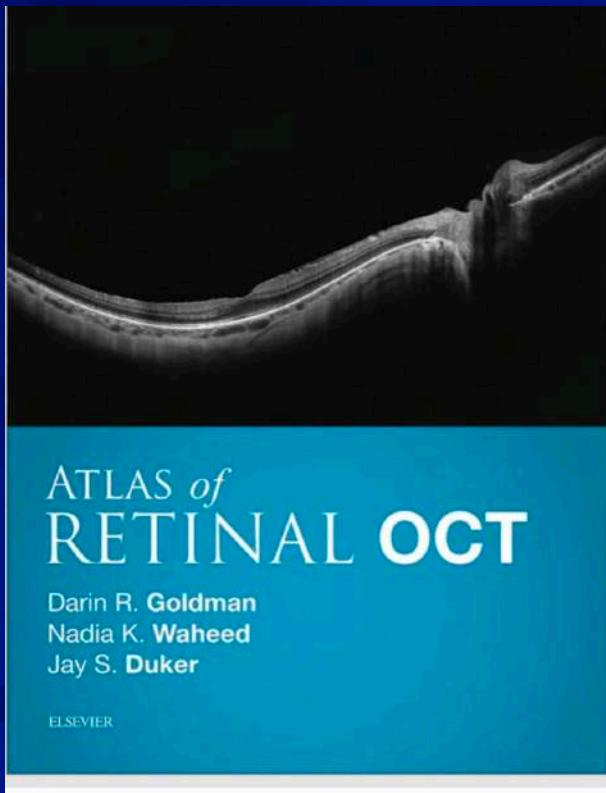
Write a comment...



Resource: OCT Community for OCT and OCT-A

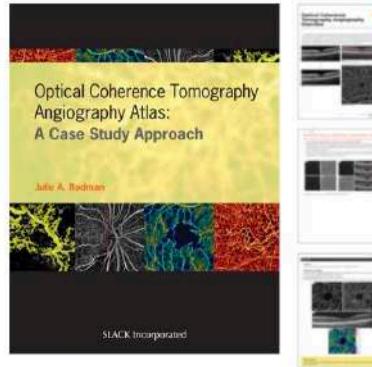


Book Resources



Optical Coherence Tomography Angiography Atlas: A Case Study Approach

Julie A Rodman, OD MSc FAAO



\$149.95

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AMD A-to-OCT-to-RI-to-Z

What You Need to Know

Thank You!!!

Hope You Enjoyed!

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