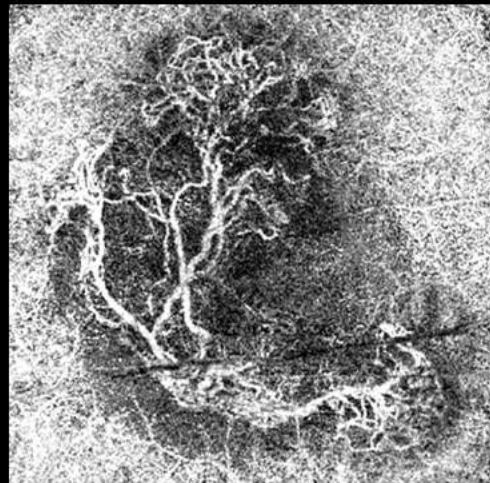
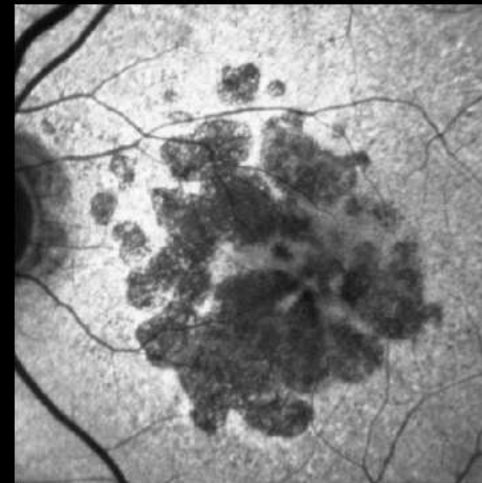
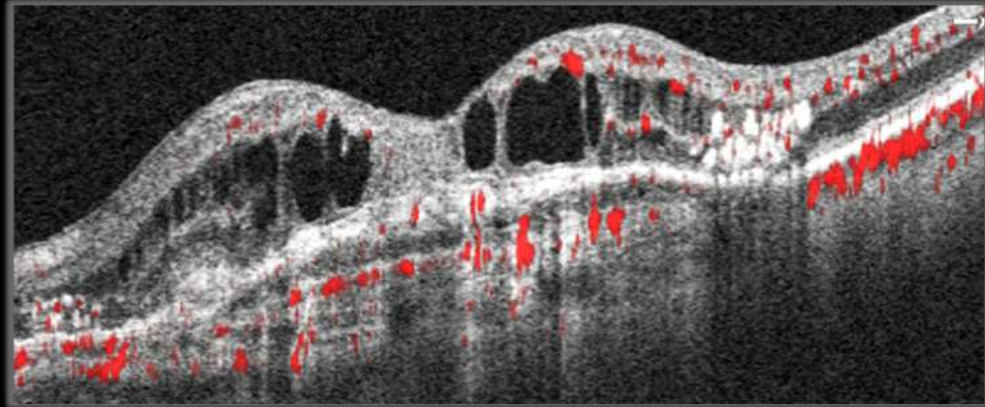


21ST CENTURY AMD RETINAL IMAGING AND DIAGNOSTICS



Carolyn Majcher, OD, FAAO, FORS
Oklahoma College of Optometry

Handout: www.octangio.org



Contact:

- majcher@nsuok.edu
- 918-444-4155

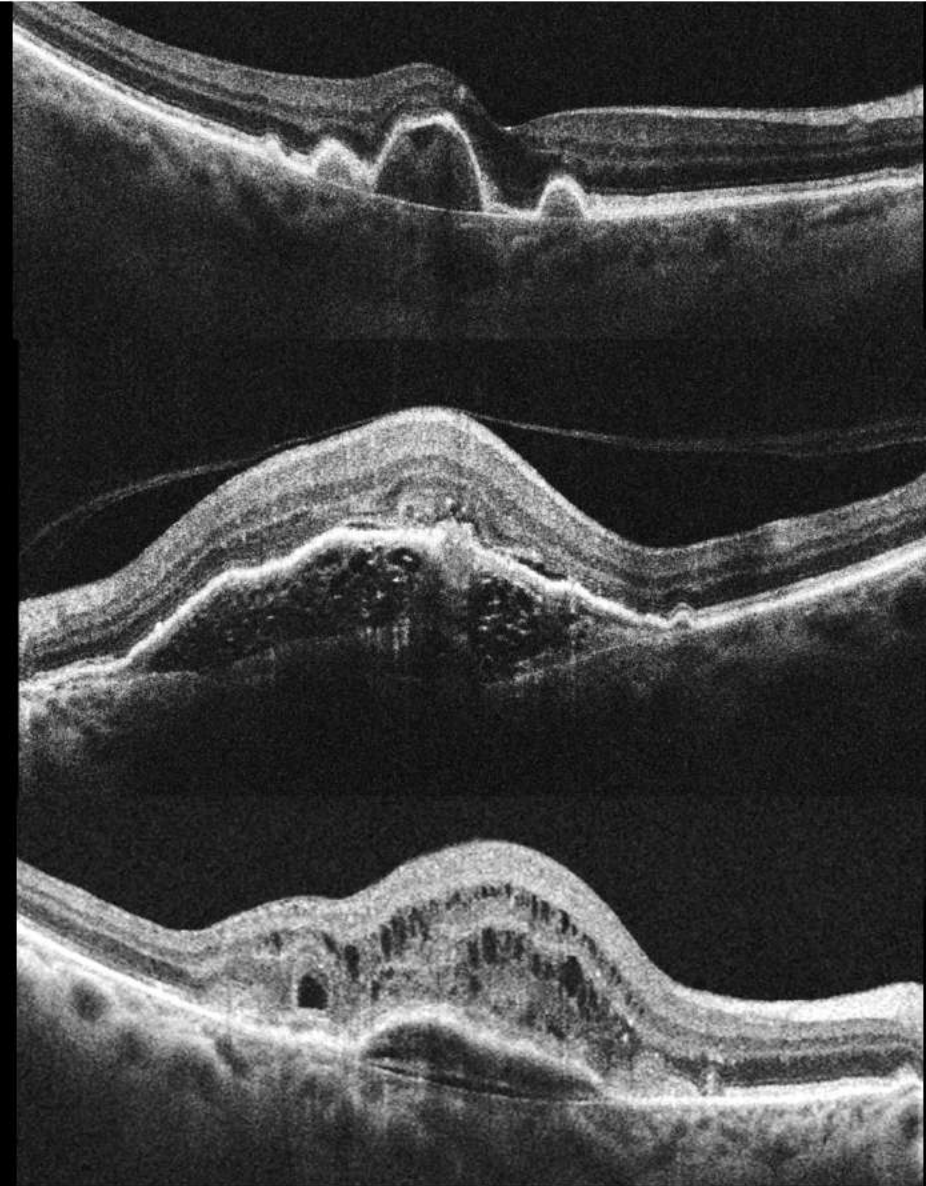
Disclosures:

- Paid consultant/speaker for:
 - Carl Zeiss Meditec
 - Iveric Bio
 - Regeneron Pharmaceuticals
 - Optomed
- Paid advisory board member for Apellis Pharmaceuticals, LENZ Therapeutics, Notal Vision, Ocuterra
- Non-financial support (writing assistance) from Roche



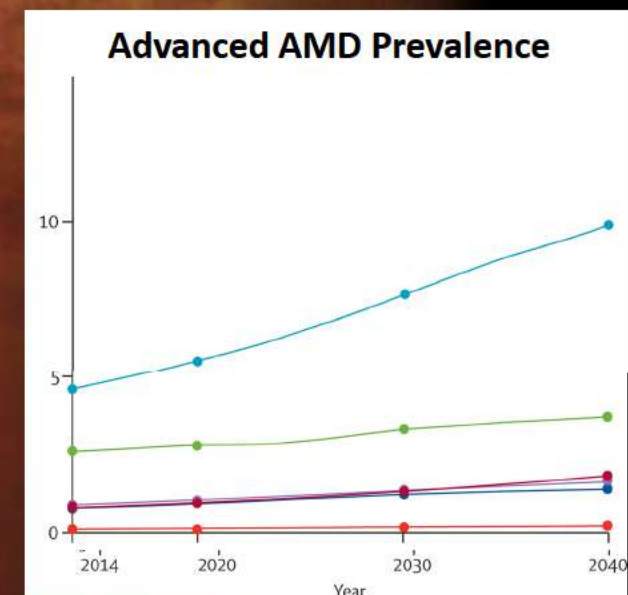
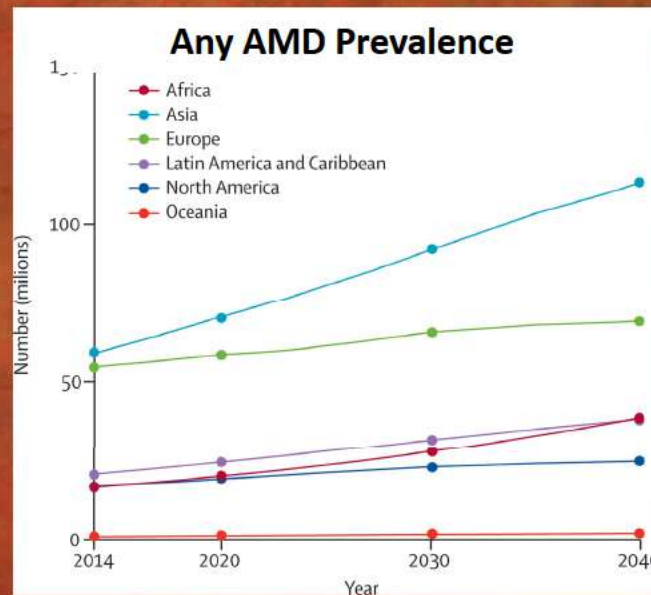
ROAD MAP

- Intro to AMD
- AMD staging/classification
- Retinal multimodal imaging technologies
- Utility of multimodal imaging in AMD
 - Nonexudative
 - Drusen subtypes
 - GA
 - High risk biomarkers for progression to advanced AMD
 - Neovascular & exudative AMD
- Home monitoring strategies to detect early conversion



AGE RELATED MACULAR DEGENERATION

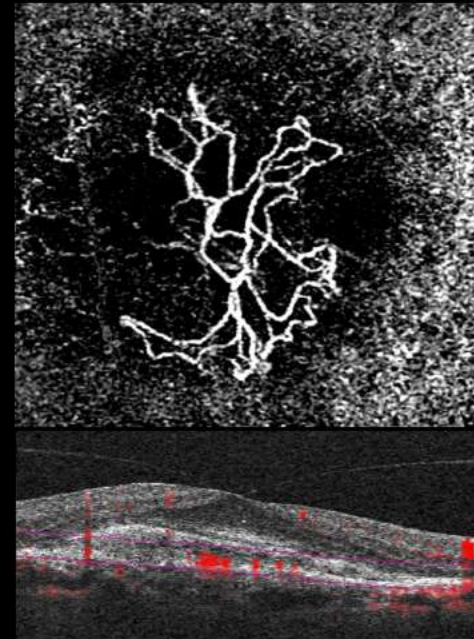
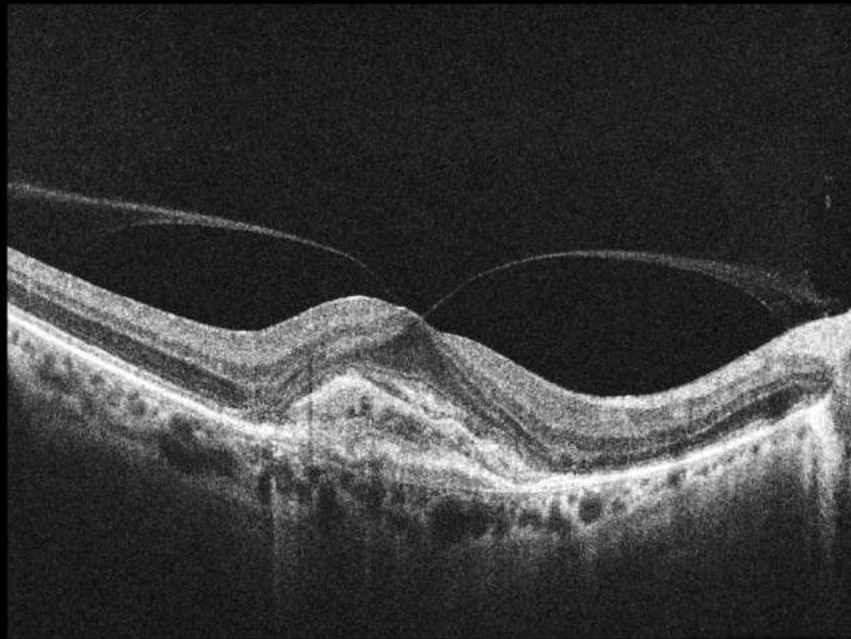
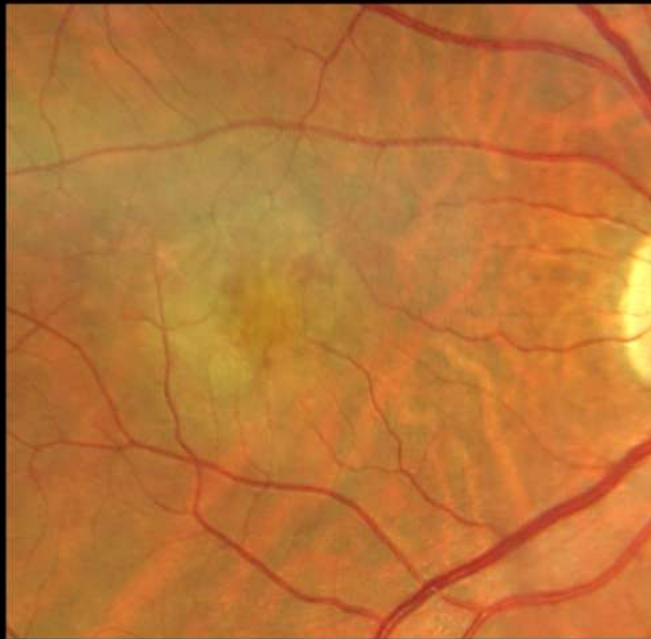
- Leading cause of blindness in the developed world in persons >50yo
 - Characterized by drusen, RPE abnormalities, geographic atrophy (GA), choroidal neovascularization (CNV)
- Prevalence of AMD is expected to ↑ to 22 million by the year 2050
 - # of cases of advanced AMD is expected to ↑ from 1.7 million in 2010 to 3.8 million in 2050



Global prevalence of AMD and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. The Lancet Global Health 2014.

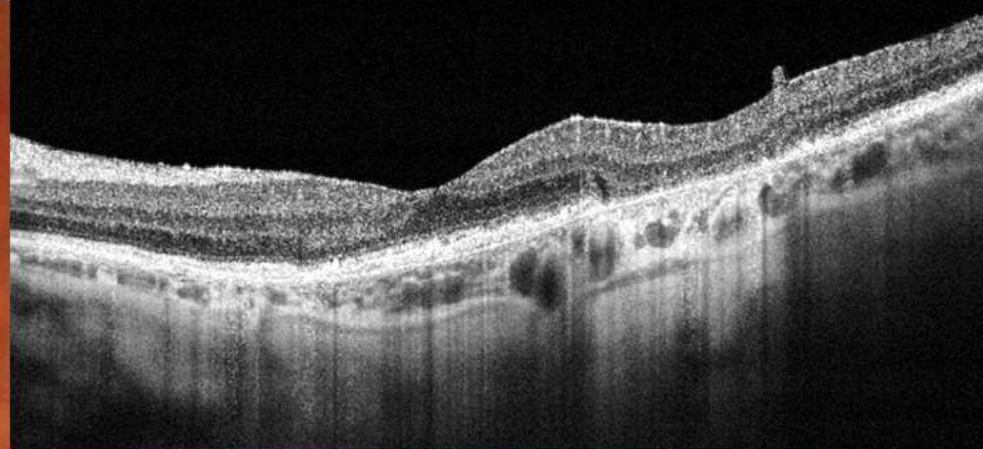
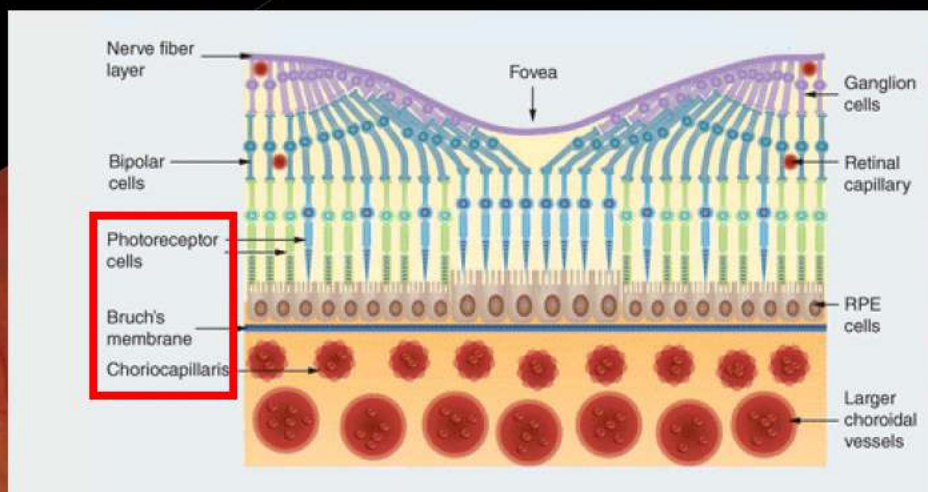
AGE-RELATED MACULAR DEGENERATION

- Of all AMD, approx. 80% nonexudative/20% exudative
 - **Neovascular exudative AMD accounts for 90% of severe central VA loss**



EARLY DETECTION AND PROMPT TREATMENT OF EXUDATIVE AMD IS CRITICAL TO MAXIMIZE VISUAL OUTCOMES!!!

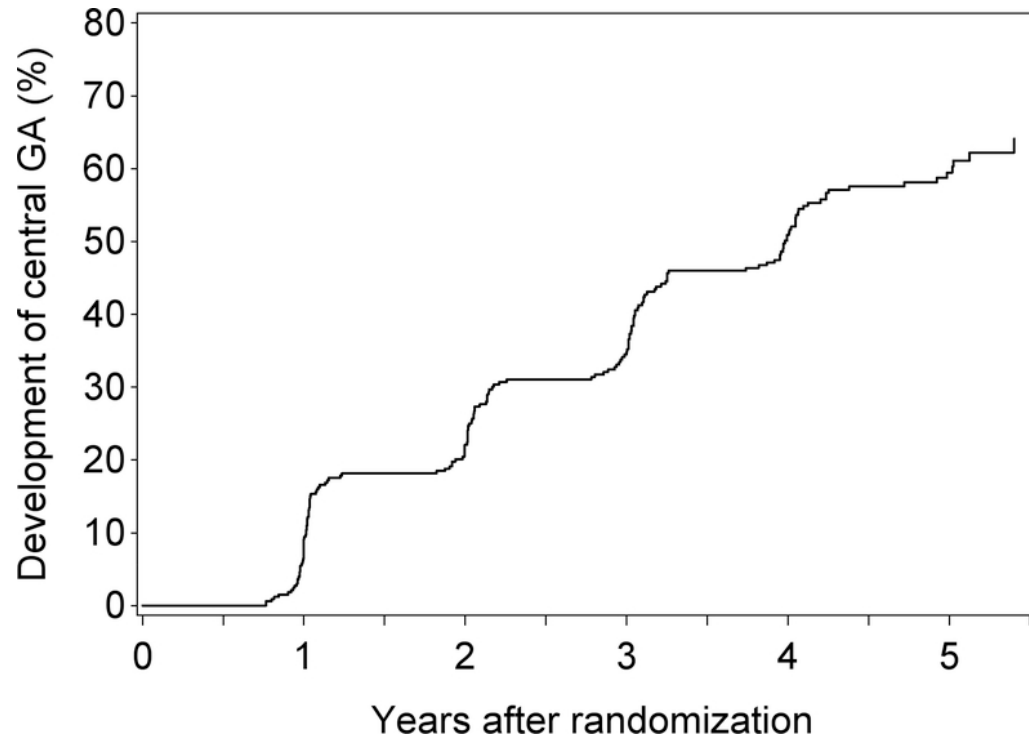
GEOGRAPHIC ATROPHY (GA)



- Advanced/late form of dry AMD
- **Irreversible atrophy of the RPE, photoreceptors & choriocapillaris (in the absence of neovascularization)**
 - Atrophy = tissue loss/attenuation
- Affects > 8 million worldwide (**~20% of ppl with AMD**)
- Accounts for 10-20% of legal blindness from AMD

AREDS Research Group. Change in area of GA in the AREDS: AREDS report number 26. *Arch Ophthalmol* 2009
Keenan TD, et al. AREDS2 Research Group. Progression of GA in ARMD: AREDS2 Report #16. *Ophthalmology* 2018

AREDS 2 Development of Central GA in Eyes Where Non-central GA was Present at Baseline (Kaplan-Meier plot)



GA enlargement is “RELENTLESS and often results in rapid central vision loss!”

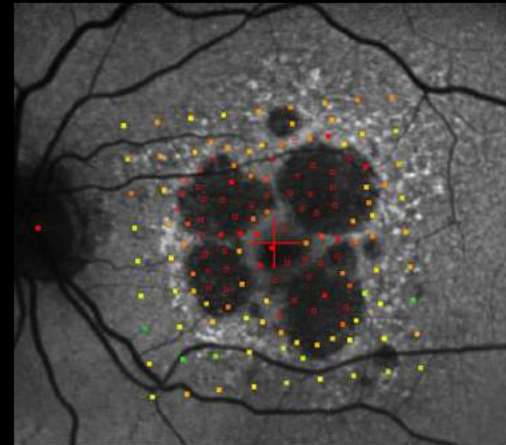
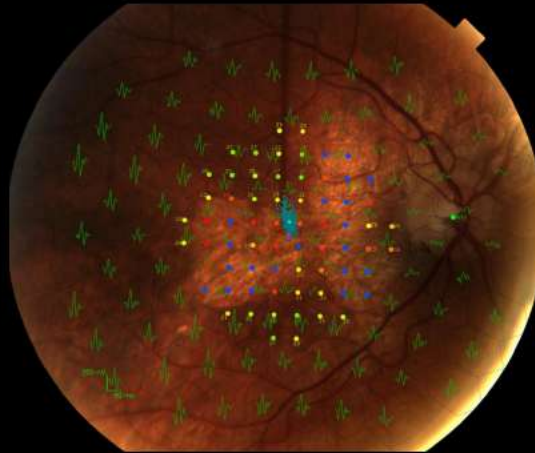
In eyes with incident non-central GA, 4-year risk of central involvement was 57%.

In the original AREDS study, the median time from any GA diagnosis to foveal involvement was 2.5 yrs

Keenan TD, et al. AREDS2 Research Group. Progression of GA in ARMD: AREDS2 Report #16. Ophthalmology 2018

THE FUNCTIONAL & MENTAL HEALTH IMPACTS OF AMD

- Areas of GA correspond to dense scotomas (areas of missing vision)
 - Even non-central GA can cause sig **difficulties with reading, facial recognition, mobility, driving, & independence**
 - Leads to **social isolation, ↑ risk of falls**
- **↑ risk for mental health problems in individuals with visual impairment from AMD (depression, anxiety)**
 - Older adults with visual impairment are **2xs more likely to have depression**
 - **↑ rates of mortality** & suicide among the visually impaired

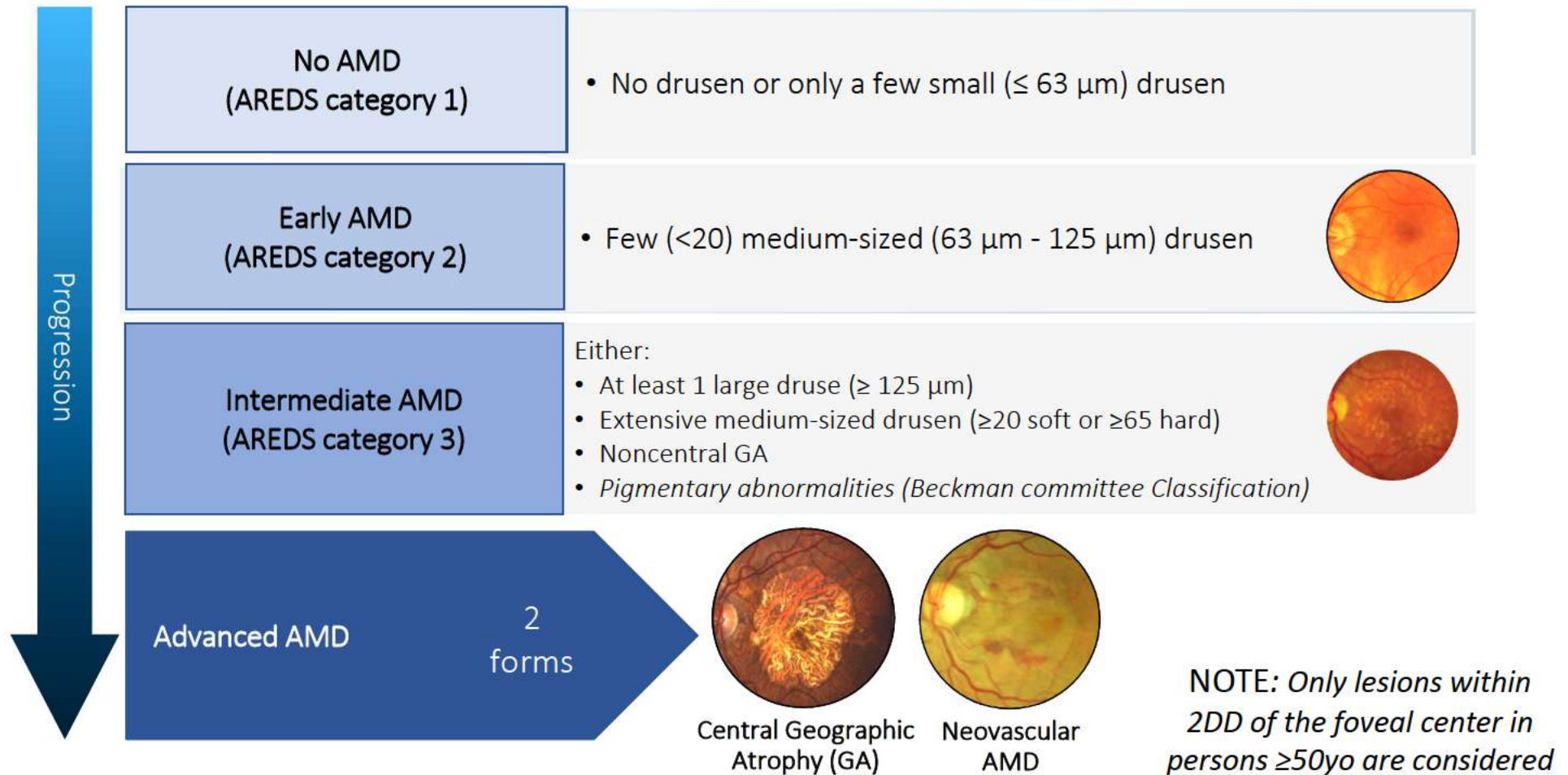


Burmedi D, et al. Emotional and social consequences of age-related low vision. *Vis Impair Res* 2002

McCarty CA, et al. Vision impairment predicts 5 year mortality. *Br J Ophthalmol* 2001

Pilotto E, et al. FAF and microperimetry in progressing GA secondary to ARMD. *British Journal of Ophthal* 2012

AMD STAGING/CLASSIFICATION



AMD STAGING/CLASSIFICATION

Intermediate non-exudative AMD (AREDS category 3): Either:

At least one large drusen
($\geq 125 \mu\text{m}$, ~ width of retinal
vein at disc margin)

Extensive medium-sized drusen
(≥ 20 soft; ≥ 65 hard)

Noncentral GA

Pigmentary abnormalities
(*Beckman committee
Classification*)

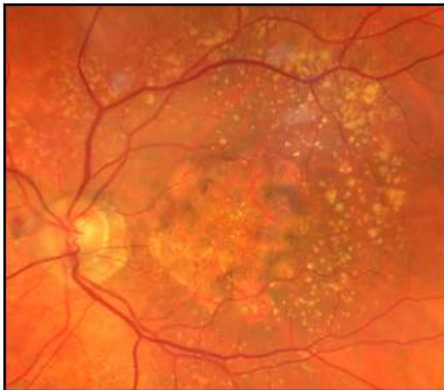


Risk for conversion to advanced AMD is ~ 18% within 5 years
(\uparrow to 26% if multiple large-sized drusen are present OU)

AMD STAGING/CLASSIFICATION

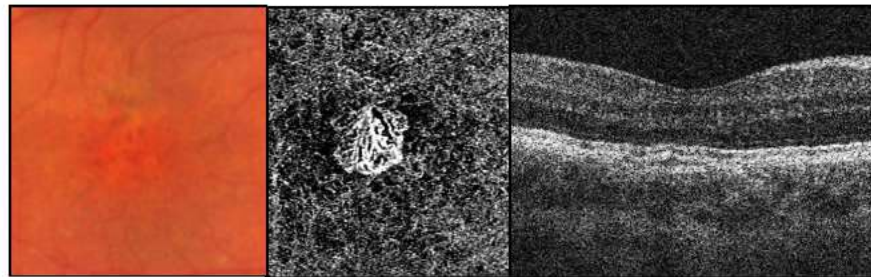
Advanced AMD (AREDS category 4): 2 forms

1) Central GA



2) Neovascularization

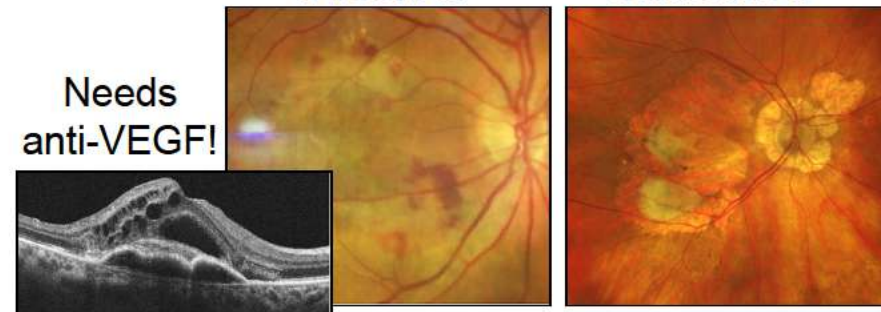
Non-exudative



Exudative

Active

Inactive



Needs
anti-VEGF!

Among pts that already have neovascular AMD in one eye, the risk for neo in the fellow non-exudative eye is ~ 42% at 5 yrs!!!

AREDS AMD Staging/Categories

First Eye [*]				
AMD Category	Drusen Size [†]	Drusen Area [†]	Pigment Abnormalities [‡]	Second Eye
1	None or small (<63 μm)	<125 μm diameter circle (≈5–15 drusen) small	None	Same as first eye
2	Small (<63 μm)	≥125 μm diameter circle (about 1/150 disc area)	Absent or present, but GA absent	Same as first eye or Category 1
	Or intermediate (≥63, <125 μm)	At least 1 druse		
	Or none required if pigment abnormalities present			
3a	Intermediate (≥63, <125 μm)	≥360 μm diameter circle (about 1/16 disc area) if soft indistinct drusen are present (≈20 intermediate drusen) ≥656 μm diameter circle (about 1/5 disc area), if soft indistinct drusen are absent (≈65 intermediate drusen)	Absent or present, but central GA [‡] absent	Same as first eye or Category 1 or 2
	Or large (≥125 μm)	At least 1 druse		
	Or none required, if noncentral GA [‡] is present			
3b	First eye same as Category 3a			VA <20/32 not due to AMD [§] , or unocular disqualifying disorder is present
4a	First eye same as Category 1, 2, or 3a			Advanced AMD [¶]
4b	First eye same as Category 1, 2, or 3a			VA <20/32 due to AMD, but advanced AMD [¶] not present [§]

^{*}Must have visual acuity (VA) ≥20/32, no advanced age-related macular degeneration (AMD), and no disqualifying lesions.

[†]Drusen and geographic atrophy (GA) are assessed within 2 disc diameters (3000 μm)³² of the center of the macula.

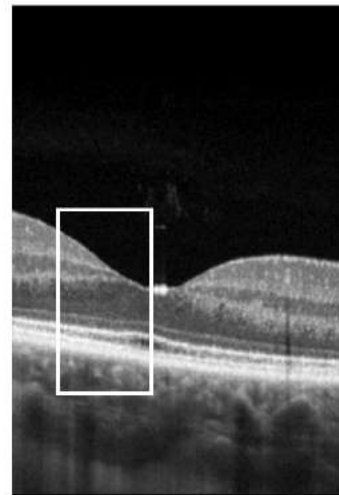
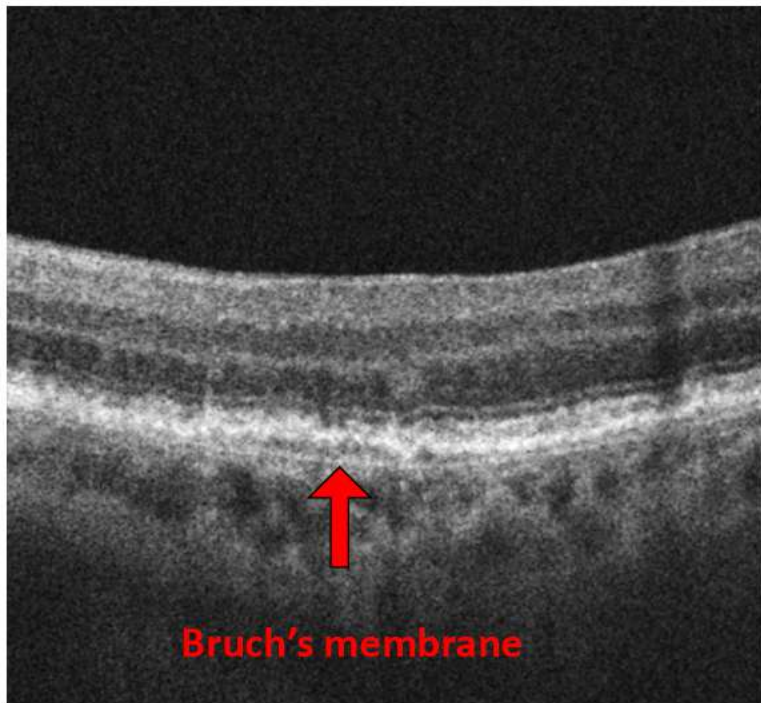
[‡]Pigment abnormalities (increased pigmentation or depigmentation) within 1 disc diameter of the center of the macula.

[§]Eye not eligible for VA event.

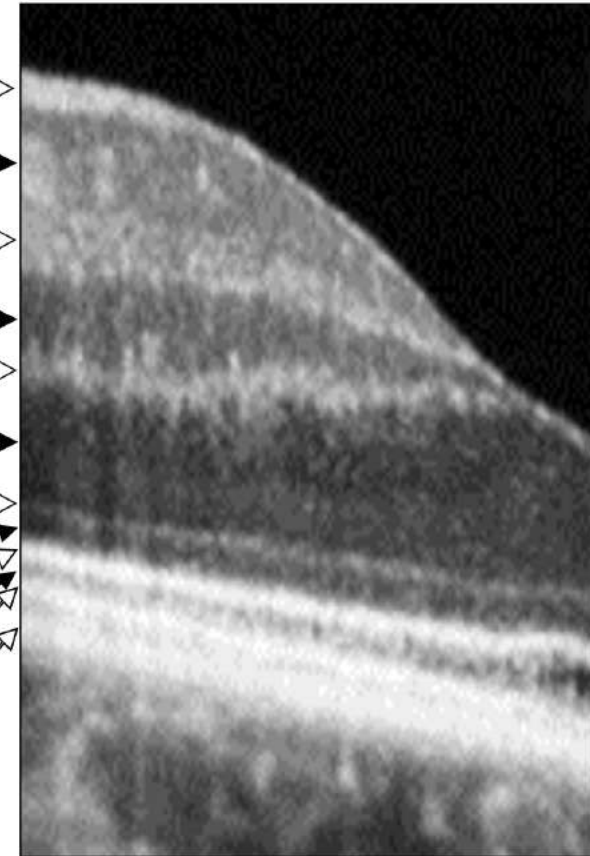
^{||}Eye not eligible for AMD event.

[¶]The GA involving center of macula or signs of choroidal neovascularization (presence beneath the retinal pigment epithelium or sensory retina of fluid, blood, or fibrovascular or fibrous tissue).

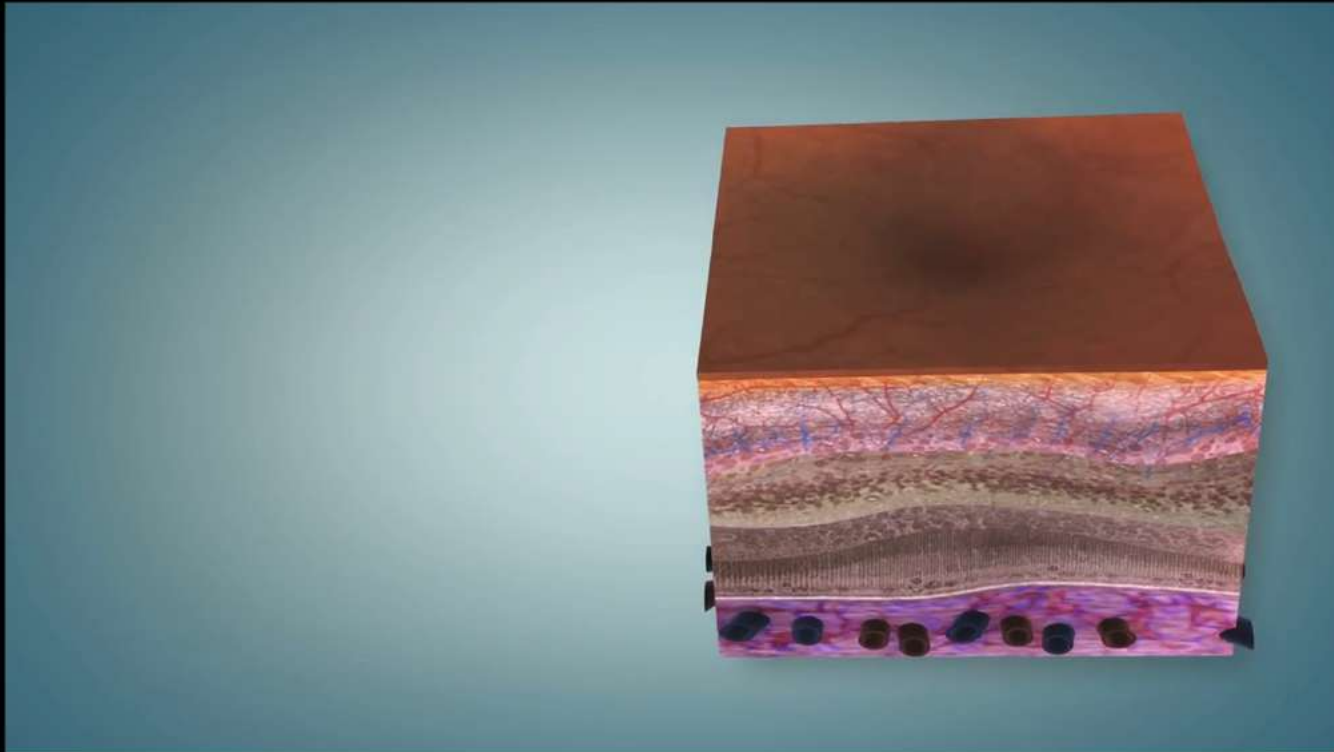
OCT RETINAL ANATOMY



- NFL →
- GCL →
- IPL →
- INL →
- OPL →
- ONL →
- ELM →
- PR myeloid zone →
- PR ellipsoid zone →
- PR outer segments →
- Interdigitation zone/COST →
- RPE/bruch's membrane complex →



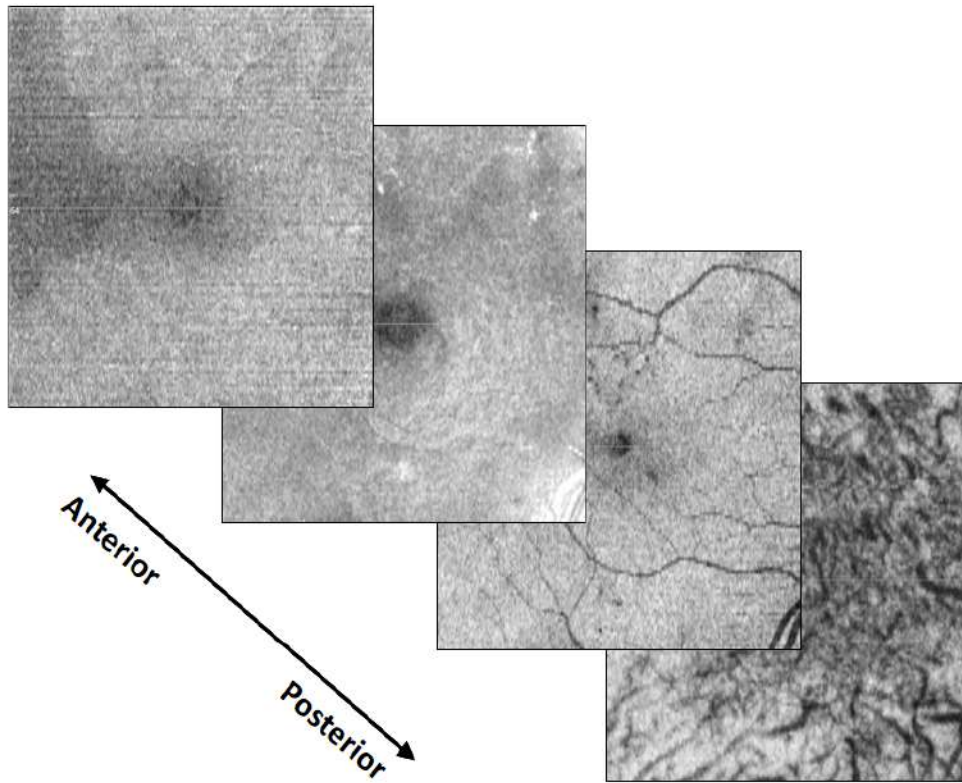
En-Face ANALYSIS



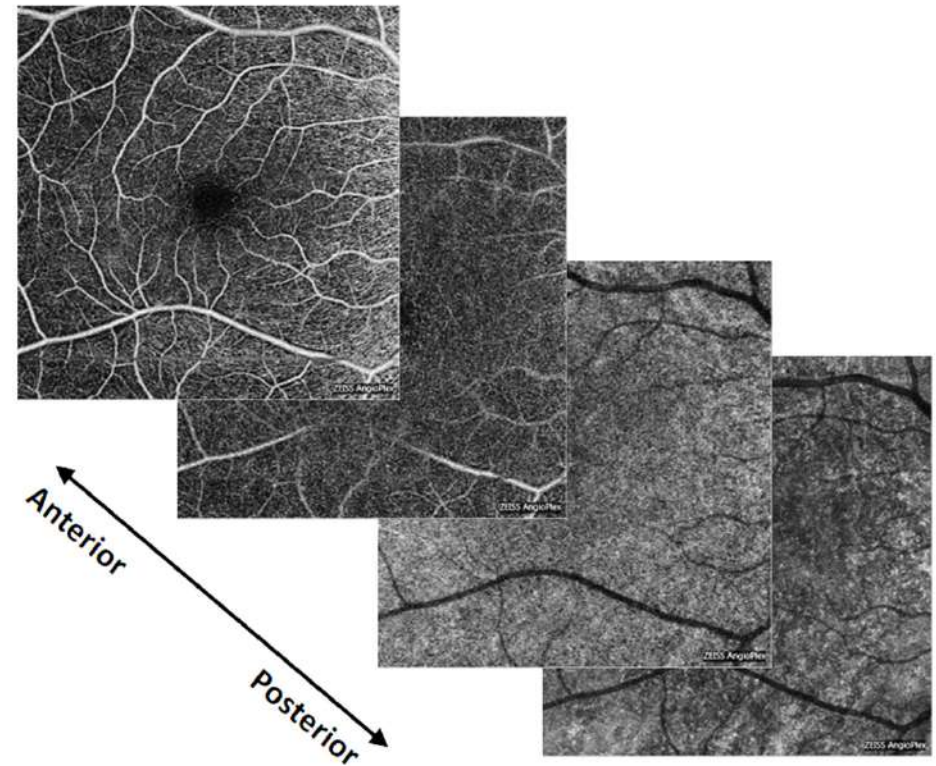
An en face image represents a slab of several retinal layers compressed into a 2D plane

En-Face ANALYSIS

Structural

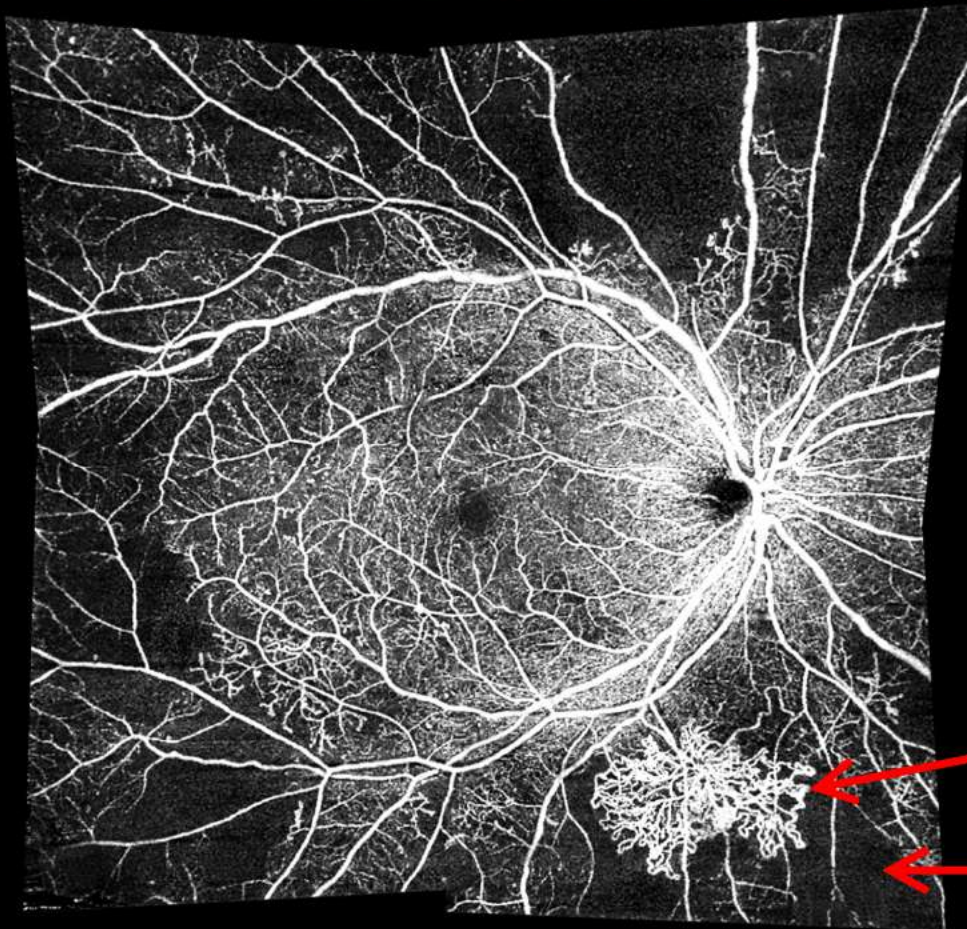


Vascular (OCTA)



OCT ANGIOGRAPHY (OCTA)

- Non-invasive “flow” imaging (**NO DYE INJECTION REQUIRED**)

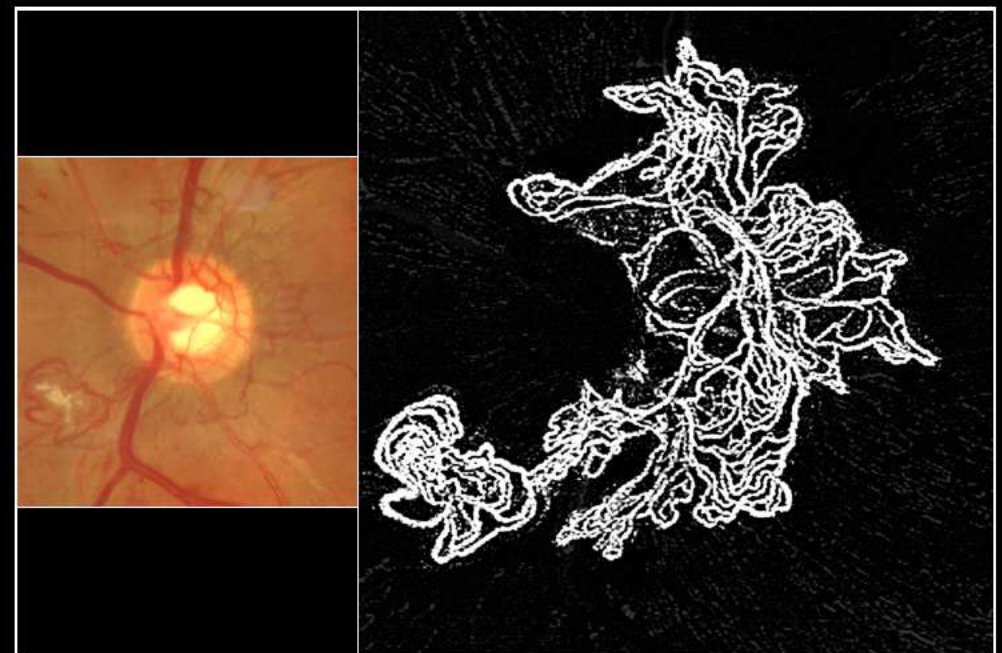
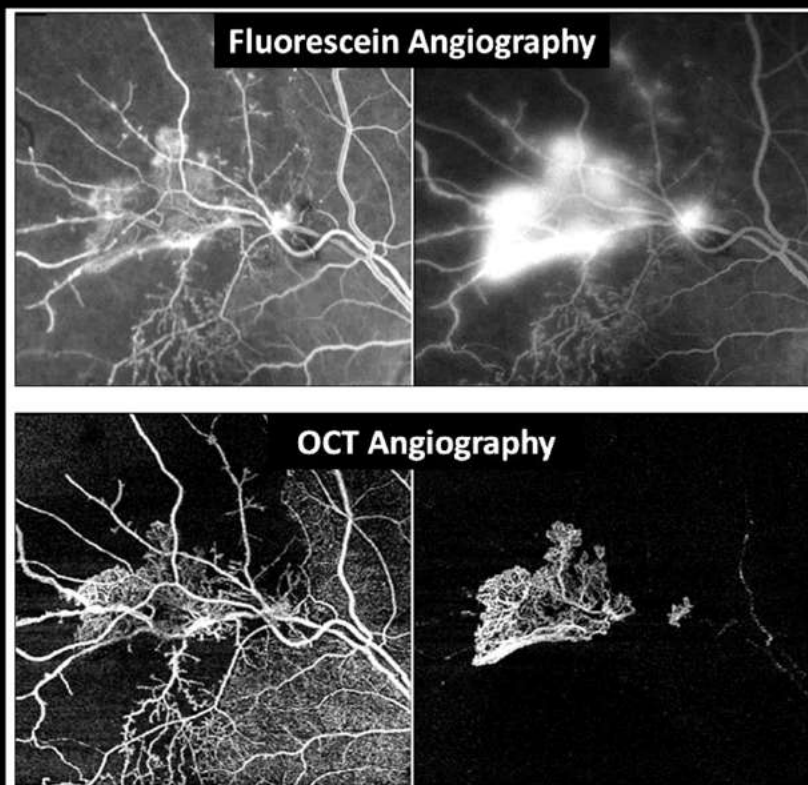


Bright → blood flow

Dark → no flow or too slow to detect

OCT ANGIOGRAPHY: THE BASICS

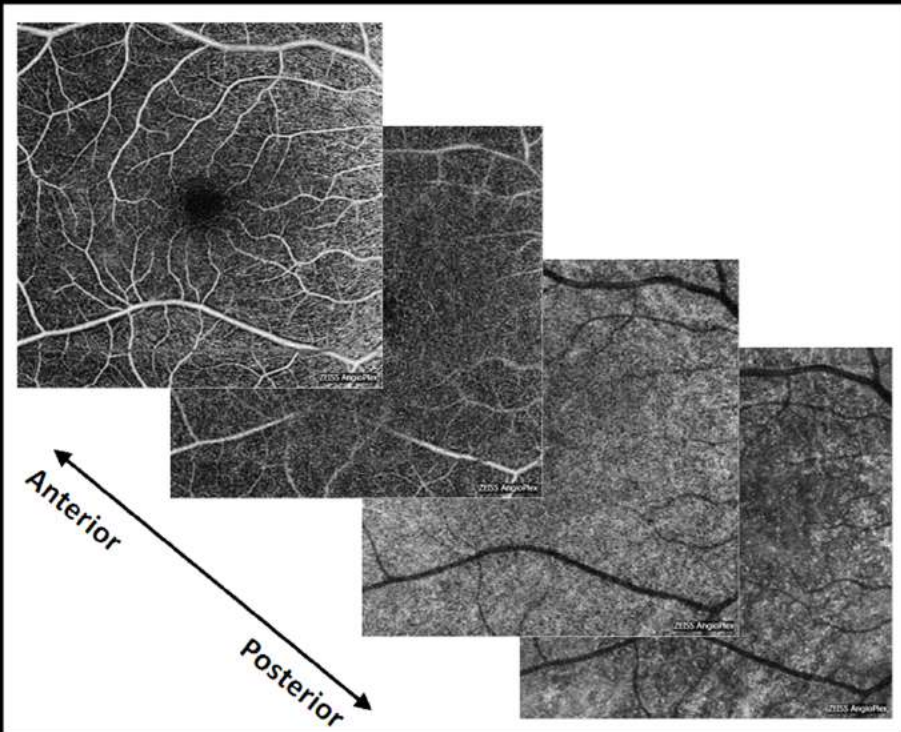
- Absence of late stage hyperfluorescence patterns (aka leakage)
= Precise delineation/measurement of neo



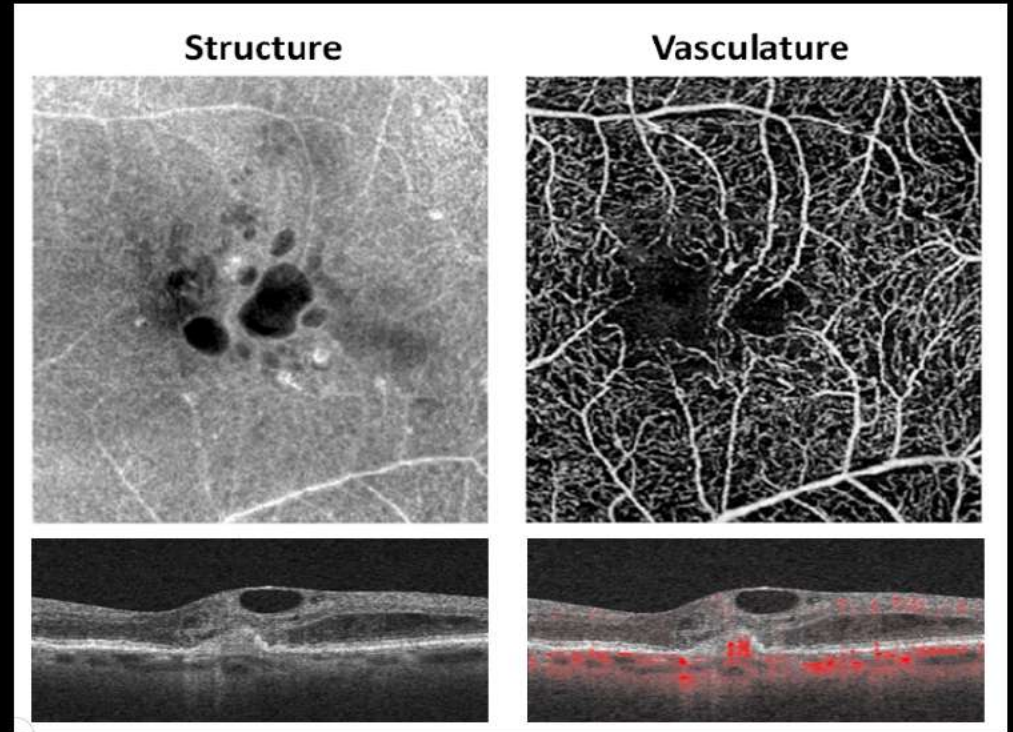
**HIGH RESOLUTION IMAGING OF NEOVASCULAR
MEMBRANES = MEASURE SIZE & CLASSIFY
MORPHOLOGY PATTERNS**

OCT ANGIOGRAPHY: THE BASICS

- 3D volumetric data

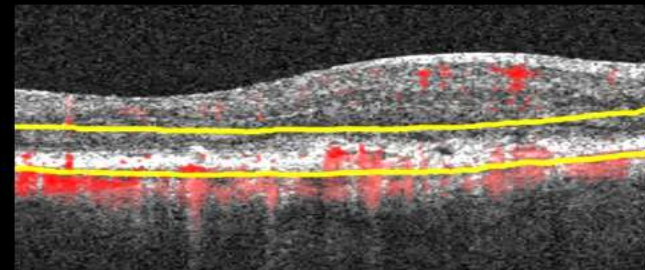
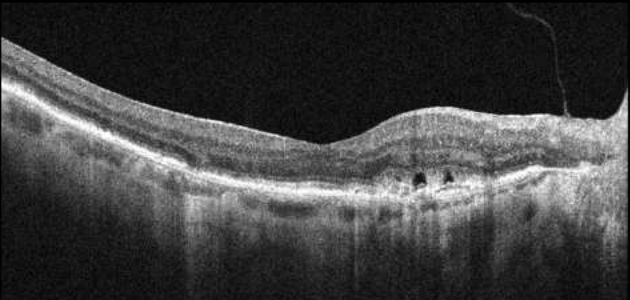
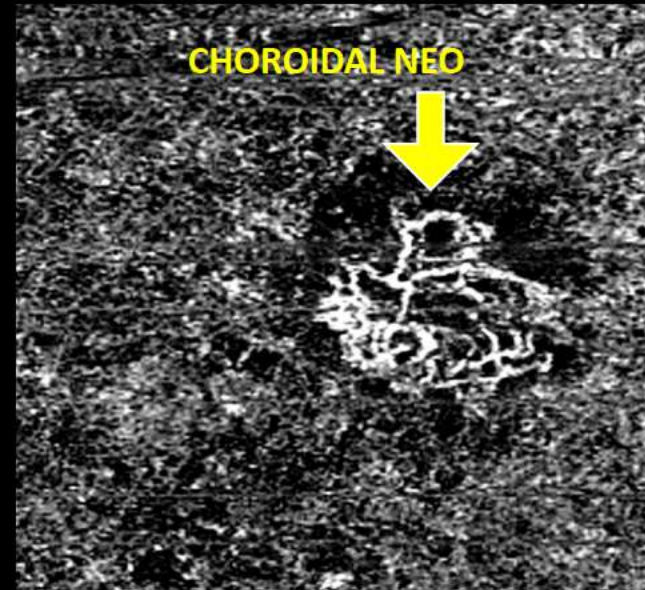
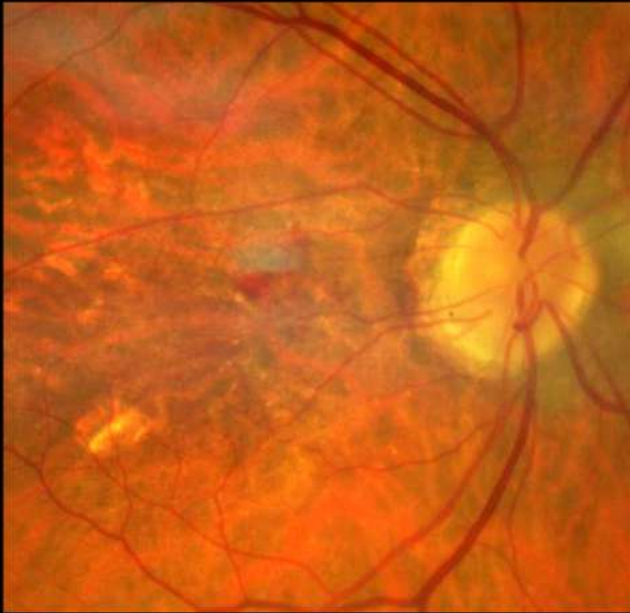


- Structure/ vasculature in tandem



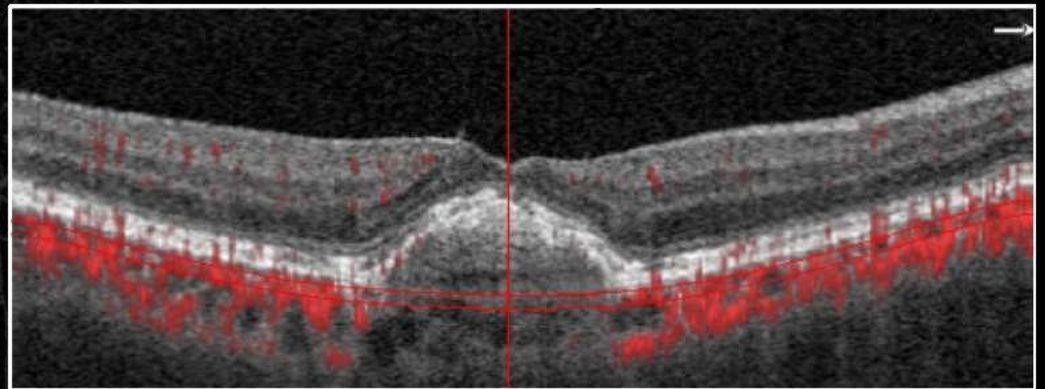
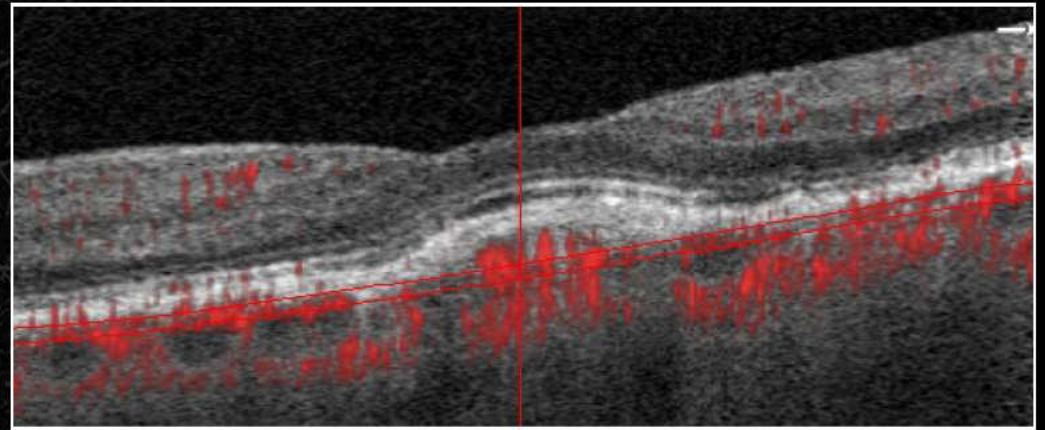
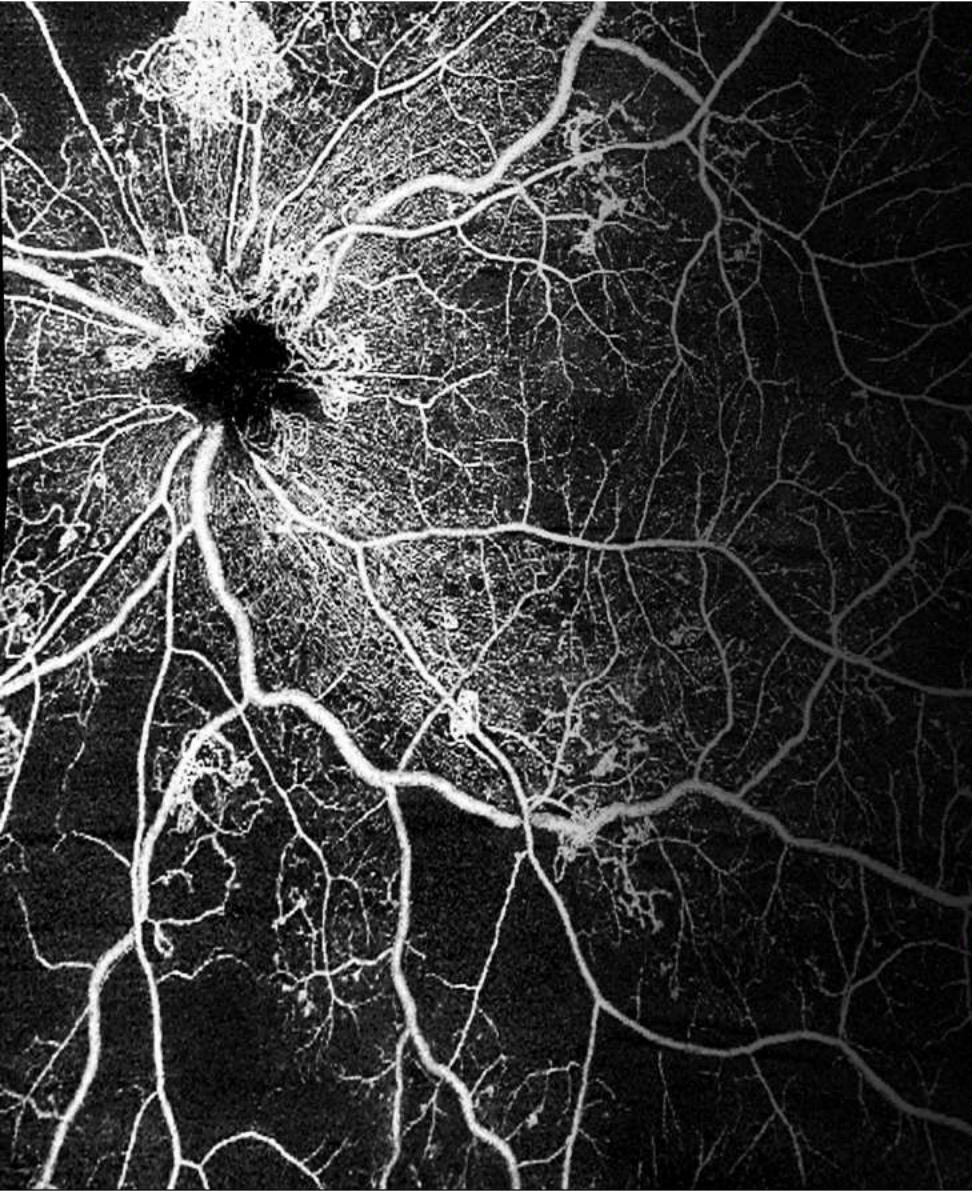
OCT ANGIOGRAPHY

Outer Retina Choriocapillaris (ORCC)

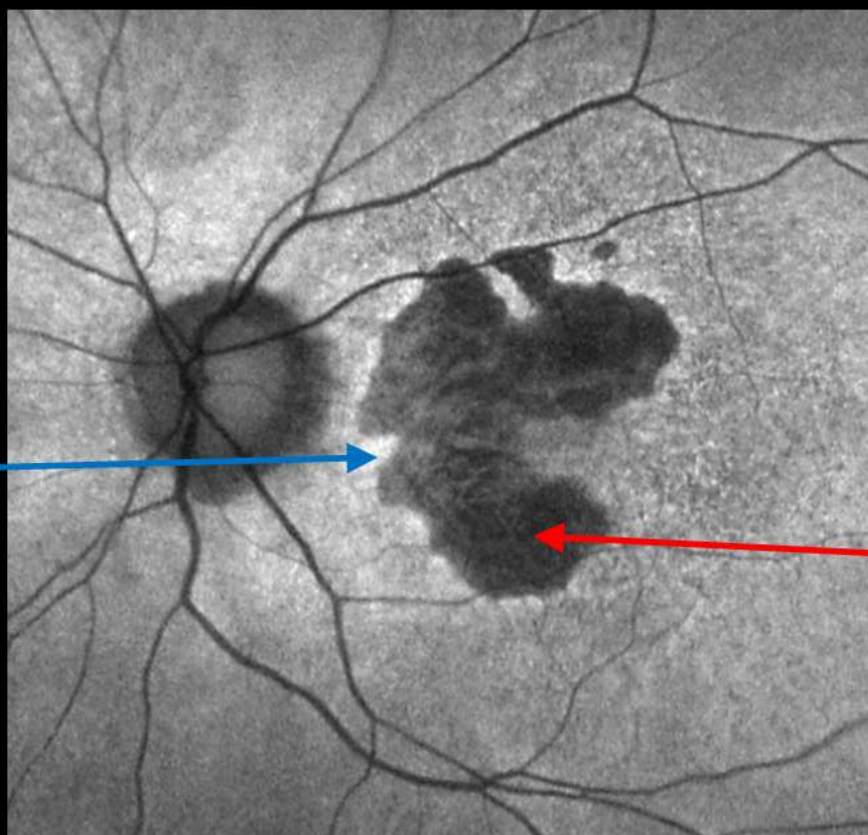


DISPLAY- B Scan Overlay

Which PED is vascularized?

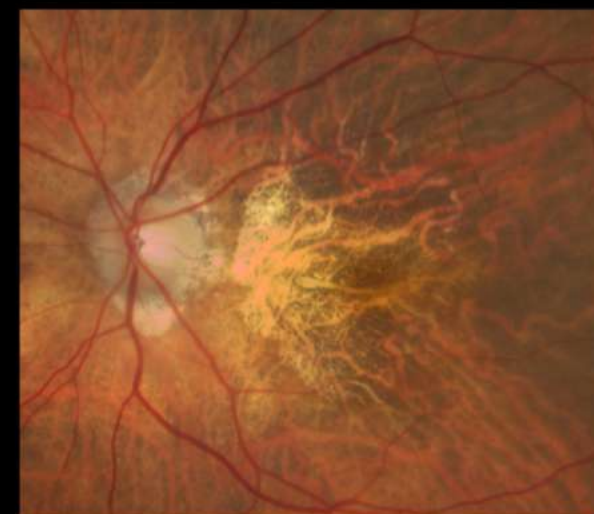


FUNDUS AUTOFLUORESCENCE (FAF)



Hyperfluorescence

- Impending RPE damage
- Advancing zones of degeneration
- Lipofuscin deposition



Hypofluorescence

- Disruption/loss of the RPE and/or photoreceptors
- Blockage

UTILITY OF IMAGING IN AMD

Color Fundus Photography (CFP)/ophthalmoscopy

- Detecting hemorrhage

OCT

- Detect new or recurrent neovascular disease activity (esp fluid!)
- Guides anti-VEGF therapy
- Subclassification of CNVM types
- Identify and monitor progression of GA
- Drusen subclassification
- Identify high risk biomarkers for progression to advanced AMD

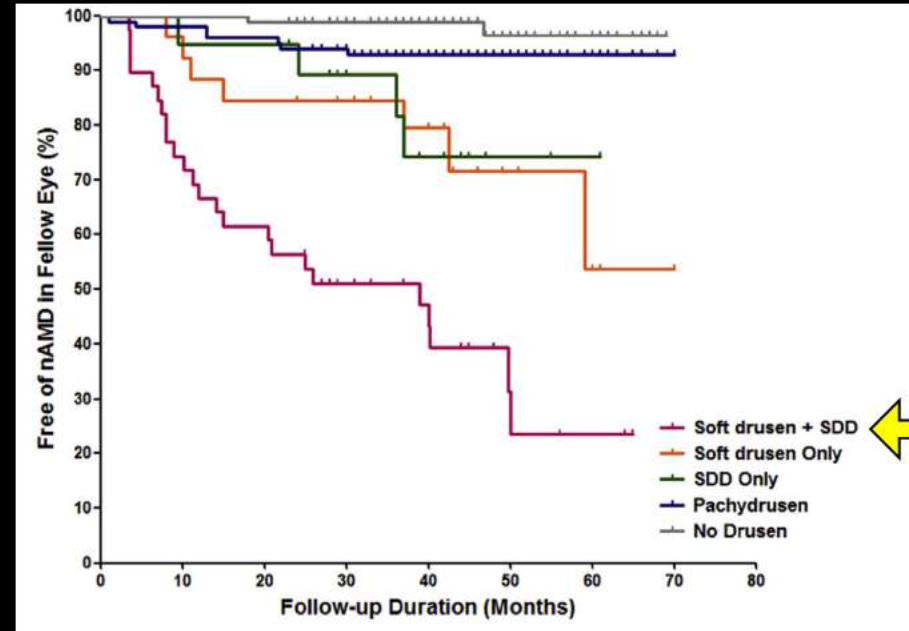
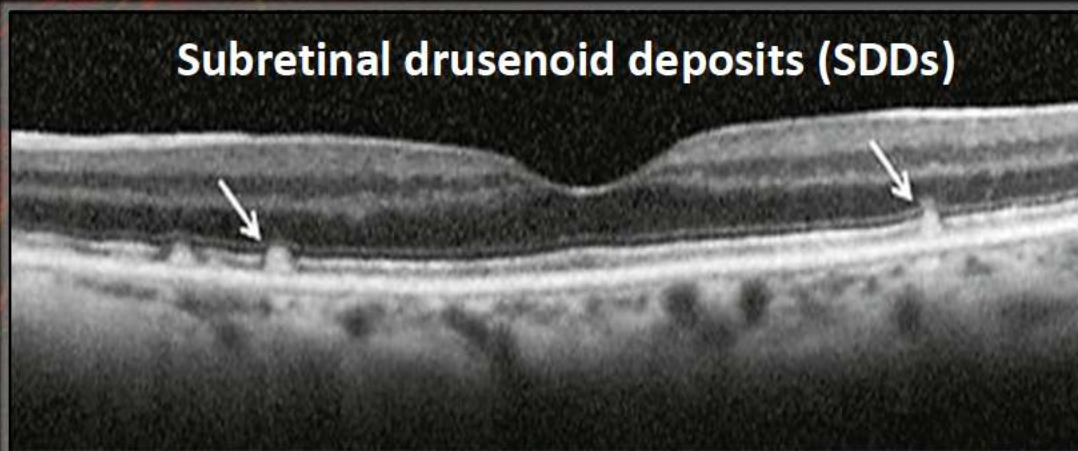
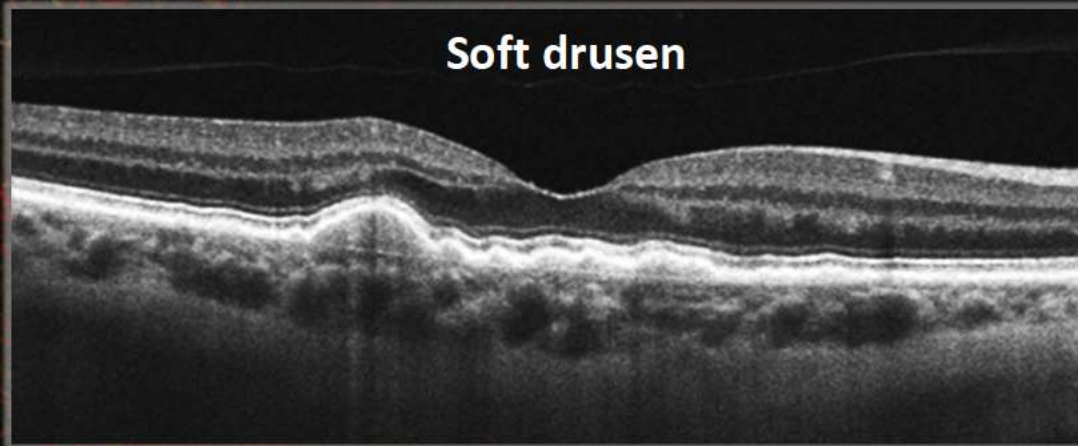
OCTA

- Detecting and morphologically characterizing CNVMs
- Detecting/monitoring nonexudative CNVMs
- Determining whether PED is vascularized

FAF

- Detection of early GA
- Monitoring GA area
- Predicting GA expansion
- Visualization of reticular pseudodrusen/subretinal drusenoid deposits (SDDs)

OCT DRUSEN SUBTYPES— PROGNOSTIC VALUE

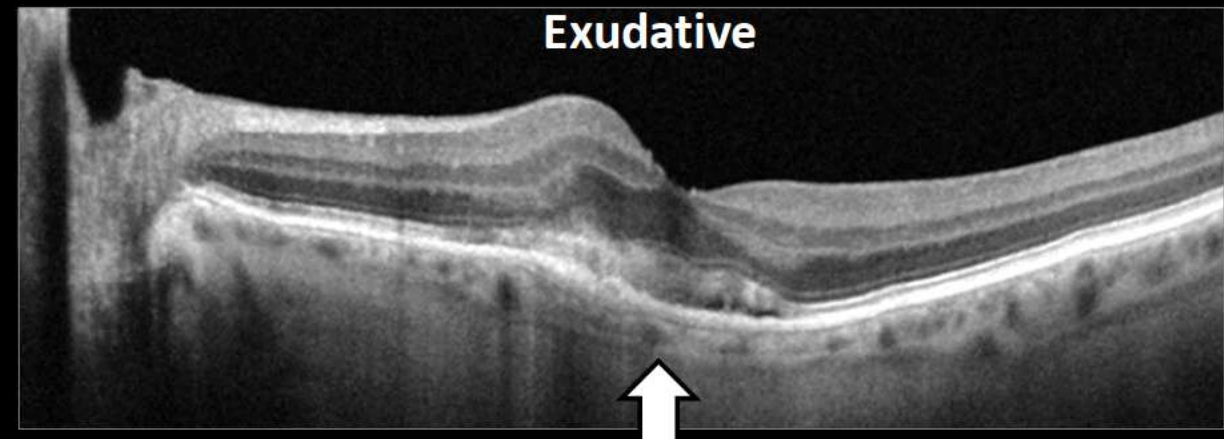


THE COMBINATION OF SOFT DRUSEN AND SDDs POSES THE GREATEST RISK FOR EXUDATIVE CONVERSION!!!

Lee J, et al. Neovascularization in Fellow Eye of Unilateral Neovascular AMD According to Different Drusen Types. Am J Ophthalmol. 2019

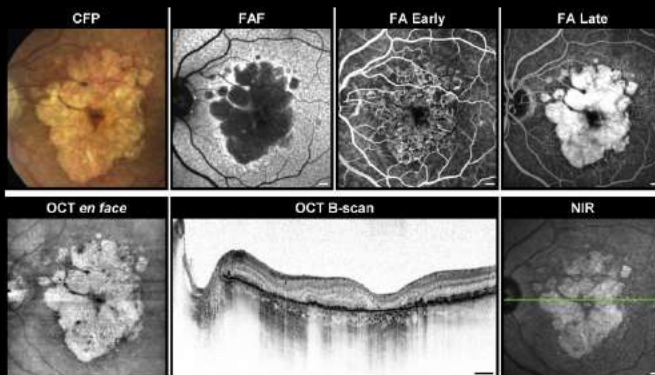
CHOROIDAL THICKNESS (CT) IN AMD

- Enhanced Depth Imaging (EDI)-OCT shows **choroidal thinning** in nonexudative and exudative AMD
- Progression of nonexudative AMD/GA is associated with ↓ subfoveal CT
- **CT may help differentiate AMD from pachychoroid spectrum diseases** (PCV, CSCR)



GA IMAGING MODALITIES

- Color fundus photography (CFP)
- **Fundus autofluorescence (FAF)**
- Near-infrared reflectance (NIR)
- **OCT**
 - **Cross sectional B-scan (AKA raster)**
 - **En-face**
 - OCT Angiography (OCTA)



Classification of Atrophy Meetings (CAM) Group

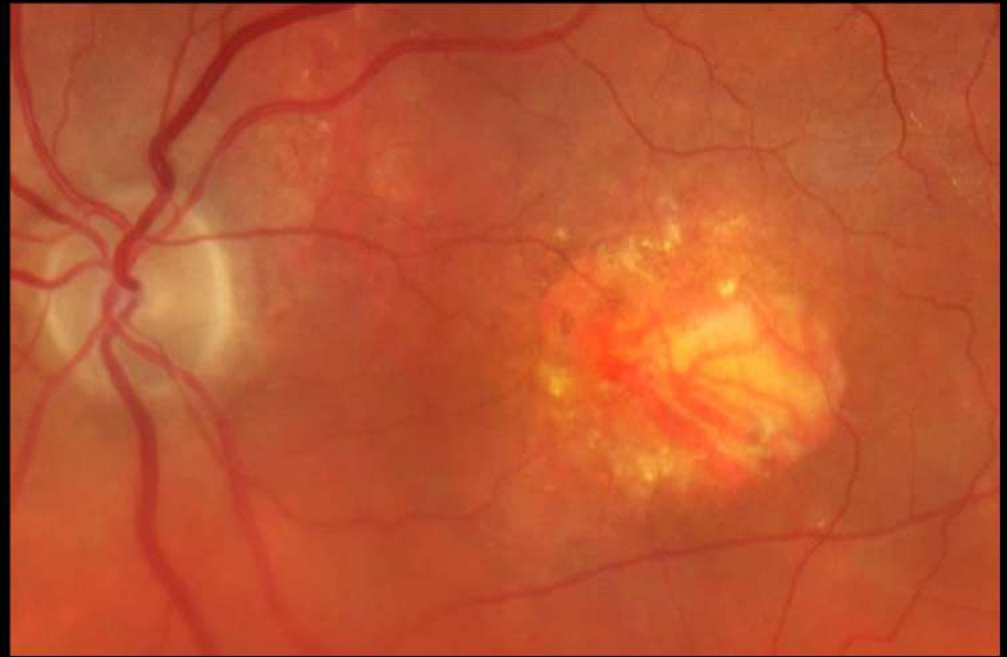
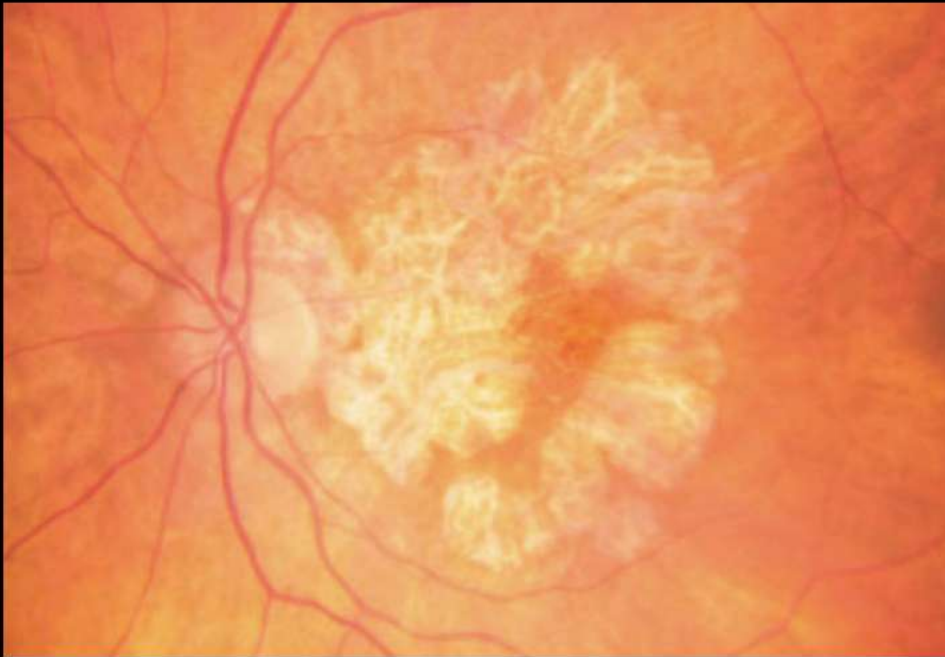


"It seems reasonable (and rather jolly marvelous) to incorporate information from multiple imaging sources to confirm the presence of GA"

A MULTIMODAL IMAGING APPROACH IS OPTIMAL
for detection and measurement of GA and its
associated features

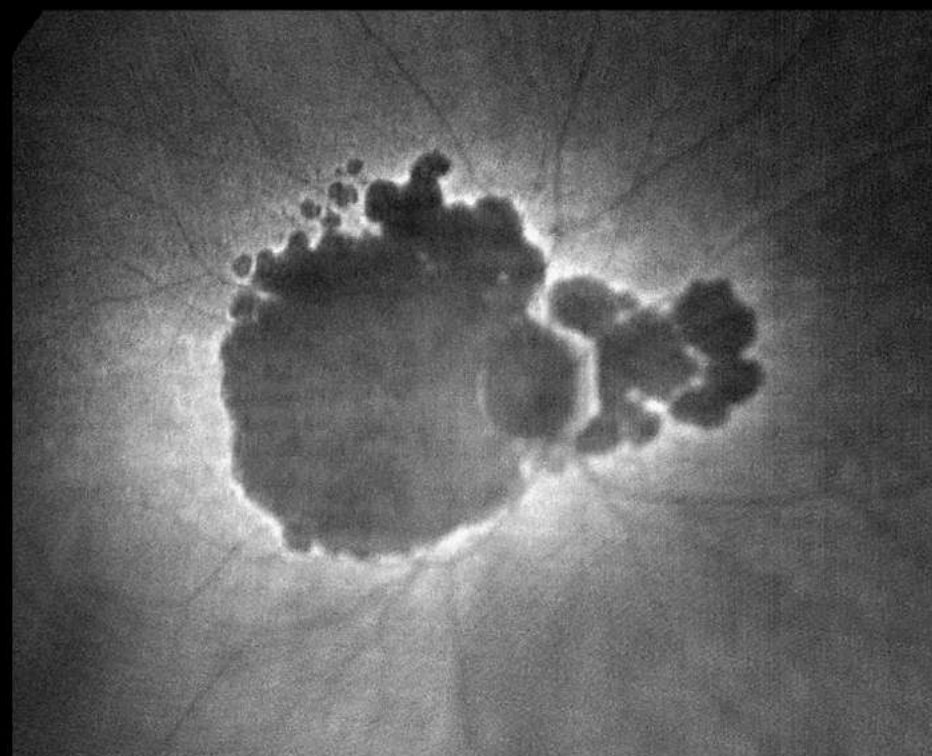
GA IMAGING- COLOR FUNDUS PHOTOGRAPHY (CFP)

- A sharply demarcated, usually circular zone of partial or complete RPE depigmentation, typically with exposure of underlying large choroidal blood vessels
- **Ineffective in detecting early GA** and NOT an ideal way track its enlargement over time



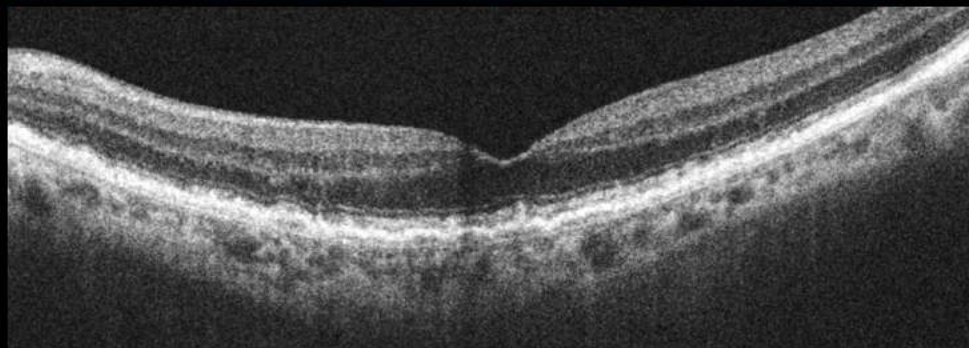
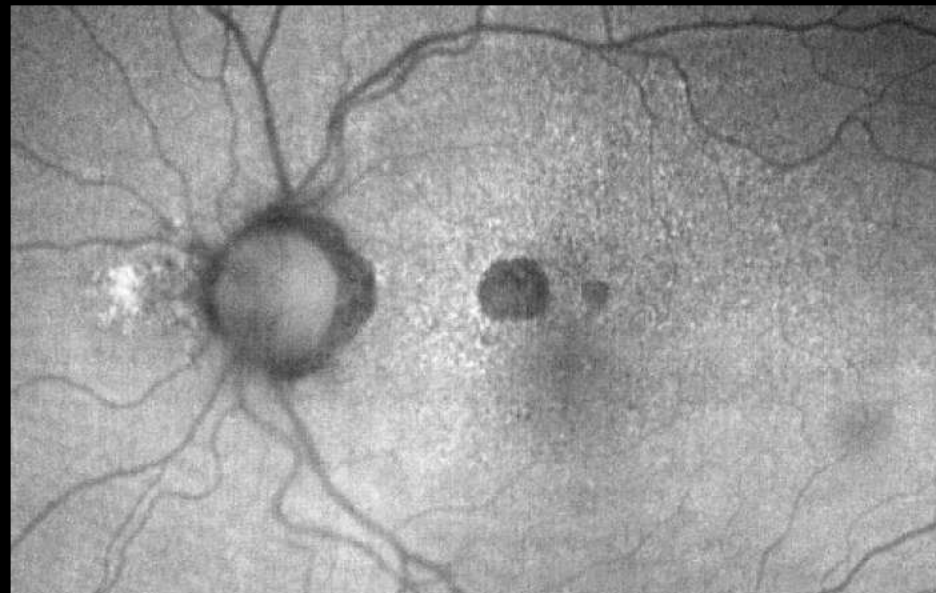
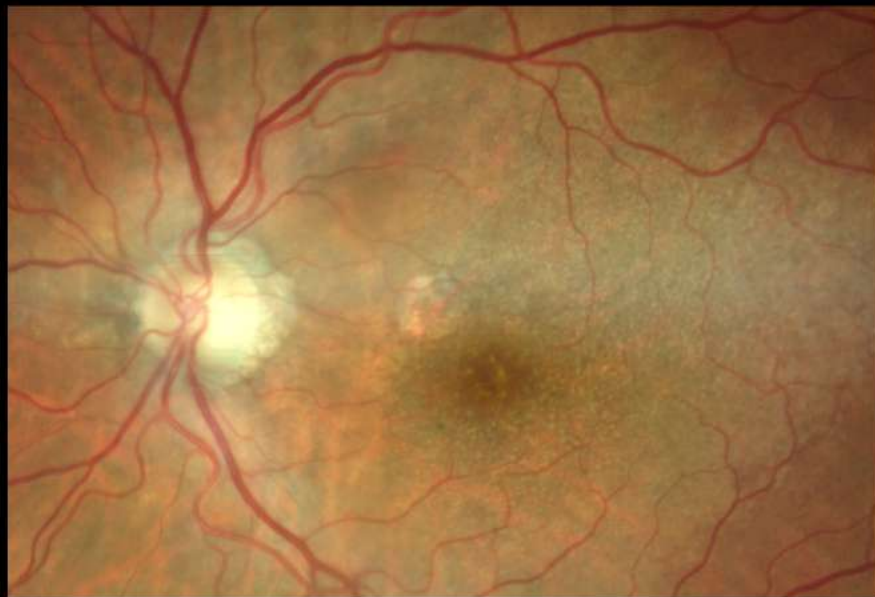
GA IMAGING - FUNDUS AUTOFLUORESCENCE (FAF)

**ONE OF THE PRIMARY METHODS USED TO DETECT,
MONITOR, AND QUANTIFY GA LESIONS!!!**



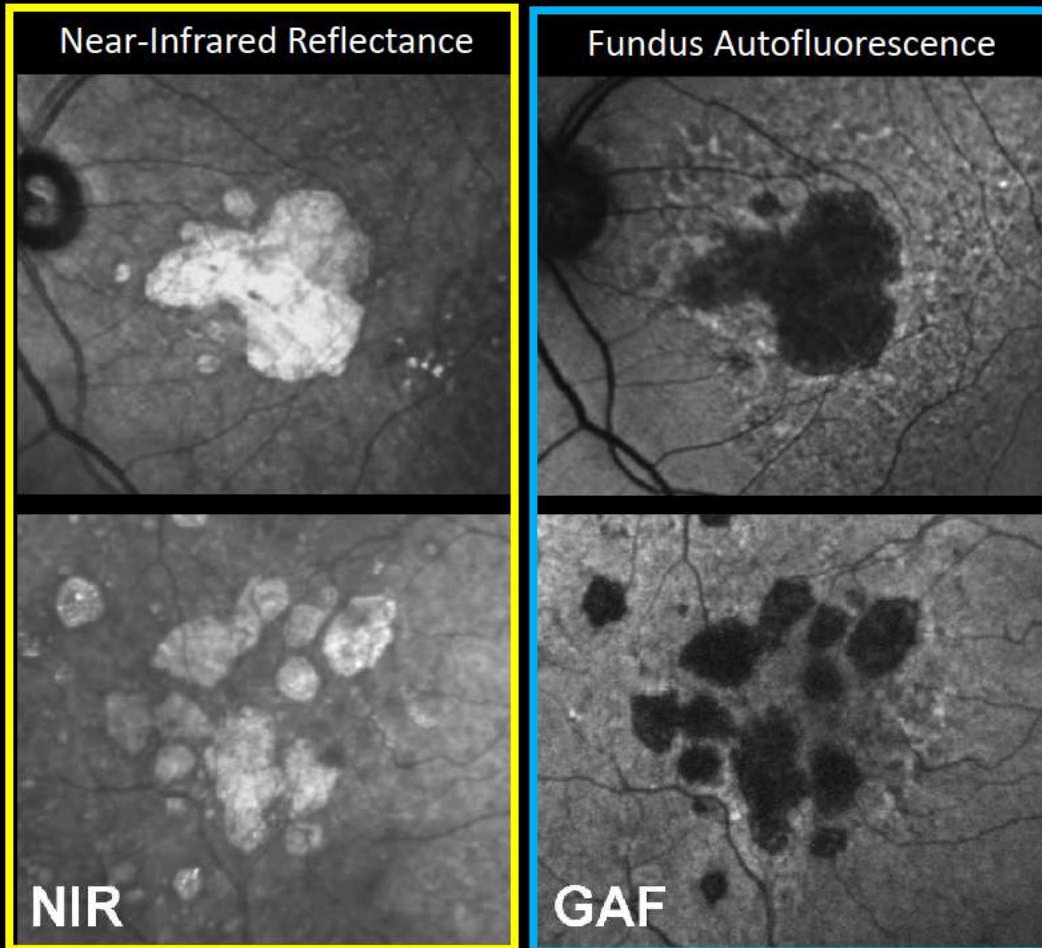
GA IMAGING - FUNDUS AUTOFLUORESCENCE (FAF)

Reticular Pseudodrusen (subretinal drusenoid deposits) & early noncentral GA

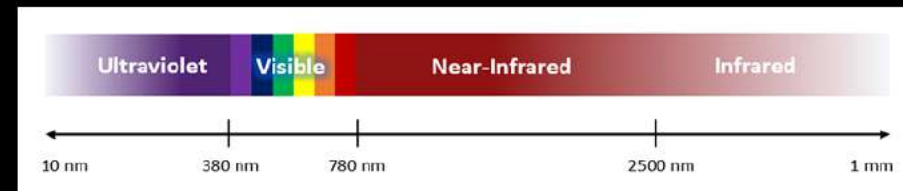


**FAF IS MORE SENSITIVE FOR GA
DETECTION THAN COLOR FUNDUS
PHOTOGRAPHY!!!**

GA IMAGING: NEAR-INFRARED (NIR) REFLECTANCE

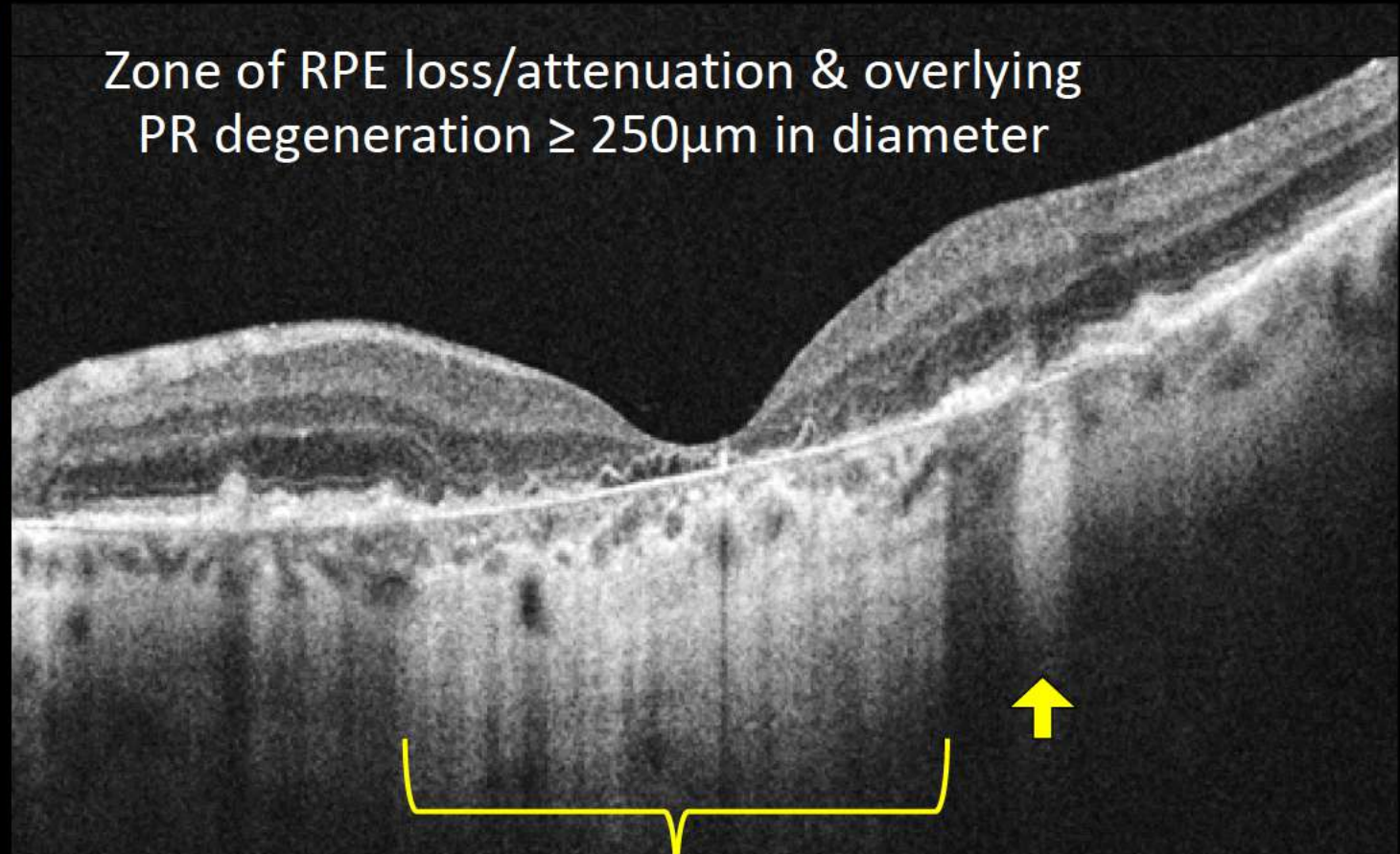
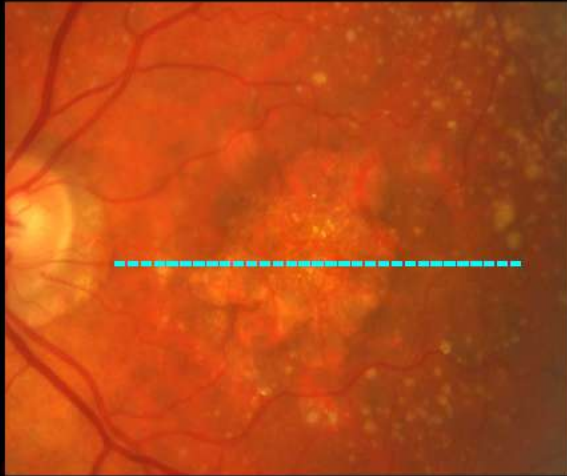


- On NIR GA is bright (hyperreflective)
- On FAF GA is dark (hypo-autofluorescent)



M. Pfau et al. Green-Light Autofluorescence Versus Combined Blue-Light Autofluorescence and Near-Infrared Reflectance Imaging in GA Secondary to AMD. IOVS 2017

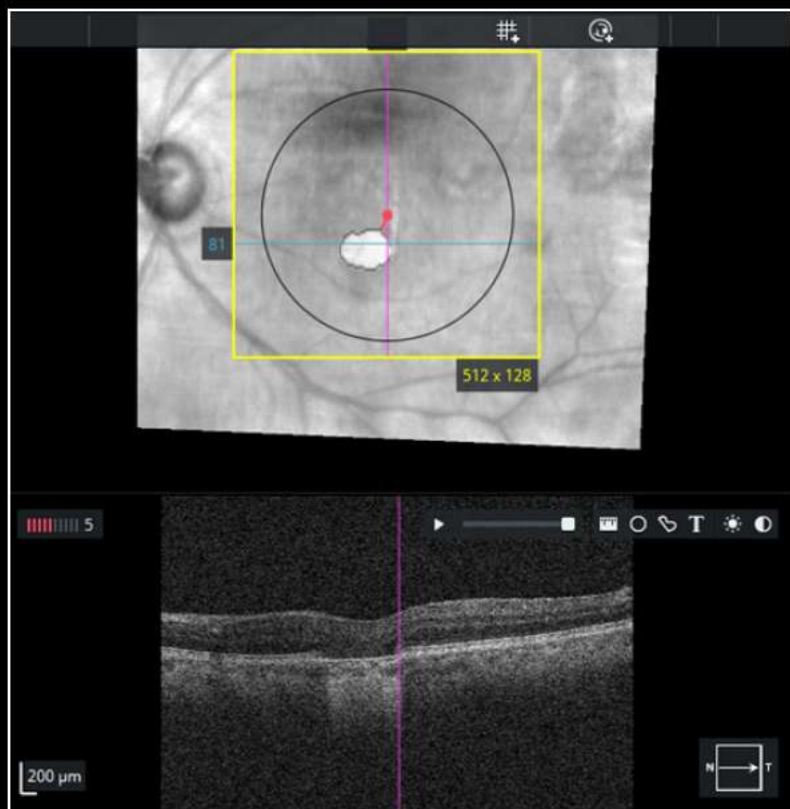
Geographic Atrophy Features on OCT



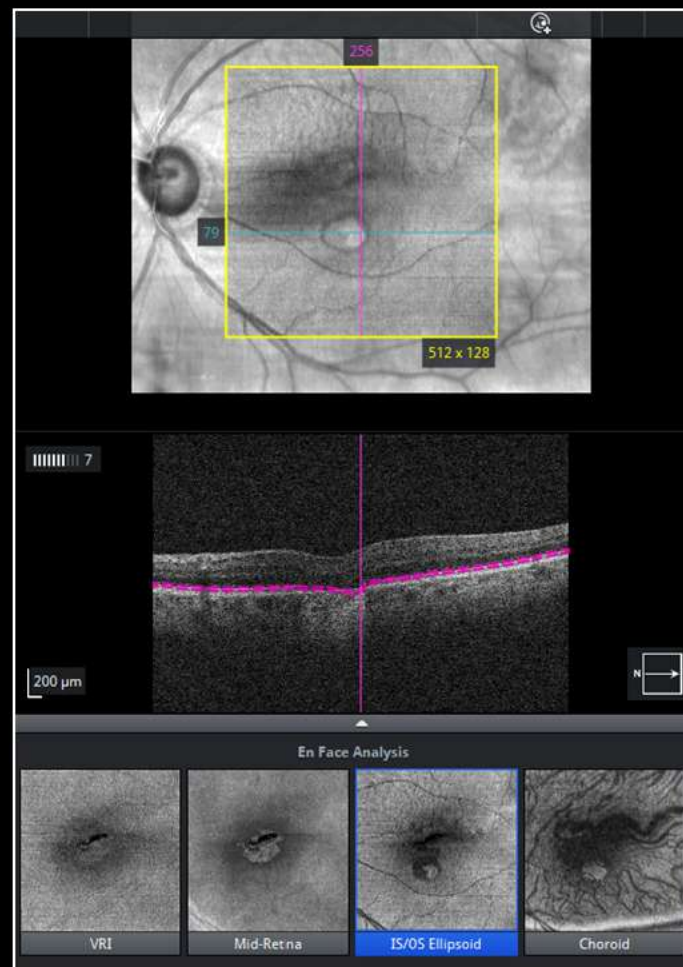
Homogenous choroidal hyper-transmission

En-Face ANALYSIS - GA

Sub-RPE slab
(choroidal hyper-transmission)

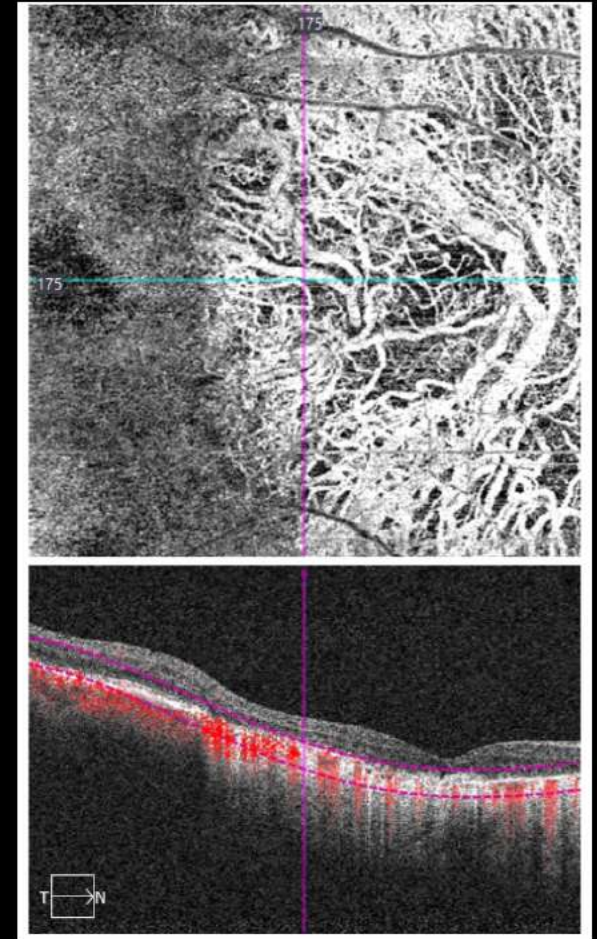
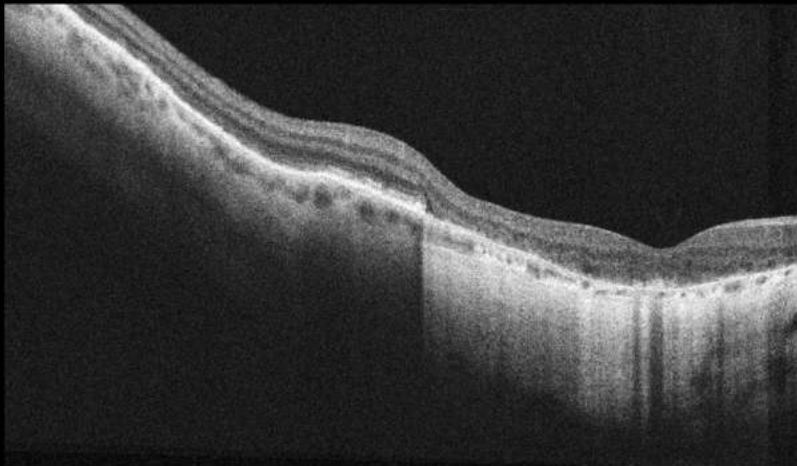
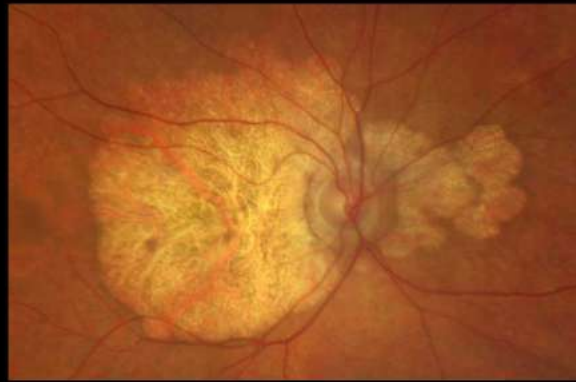


Ellipsoid Zone (EZ)

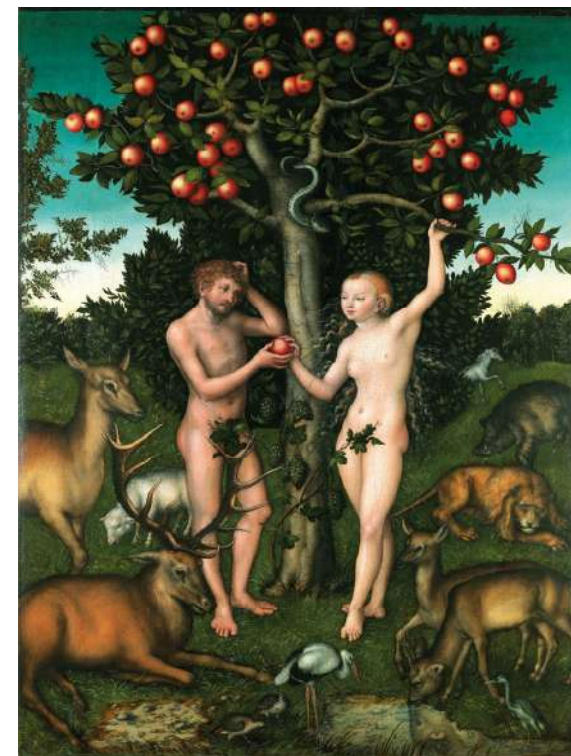
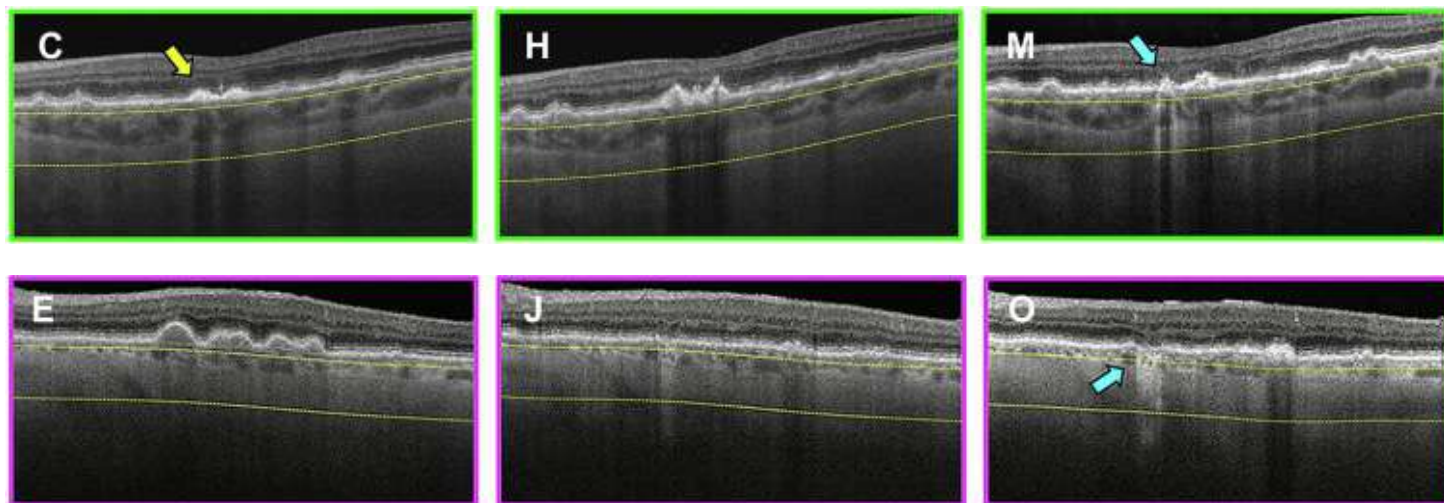
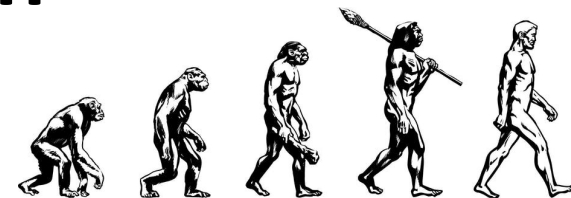


GA IMAGING - OCT ANGIOGRAPHY (OCTA) IMAGING OF GA

Highlights loss of the choriocapillaris!!! (allows for visualization of the deep/larger choroidal vessels)



More than 1 OCT-Defined Pathway Exists Leading to GA Formation



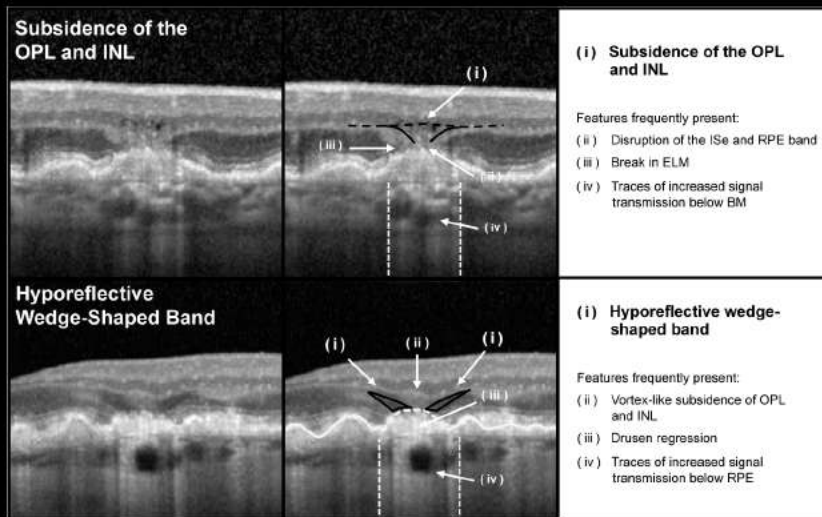
Relationship Between Presumptive INL Thickness and GA Progression in ARMD. IOVS 2016

NASCENT GA vs cRORA

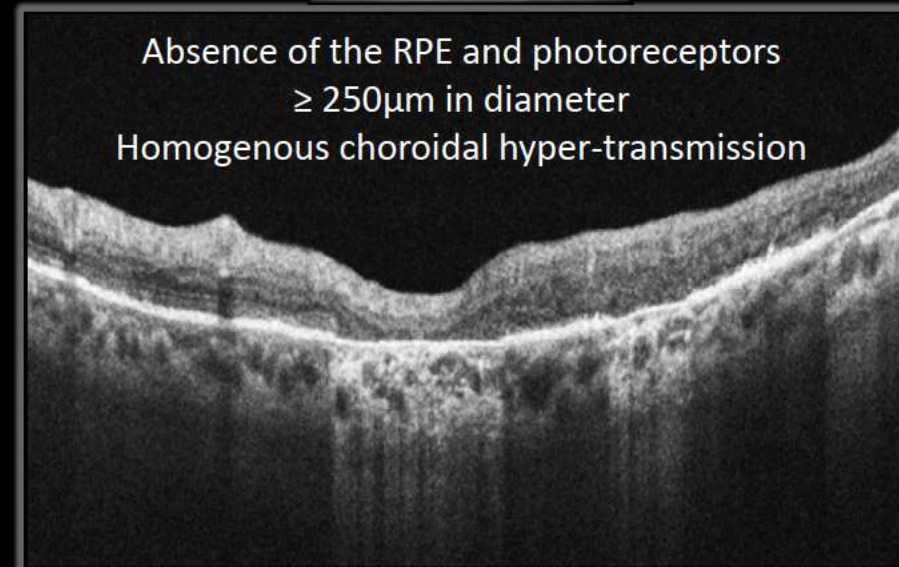
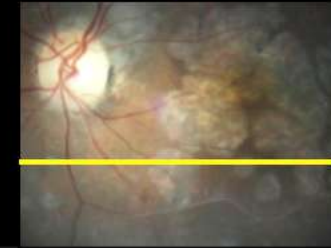
Nascent GA

AKA *Incomplete RPE and Outer Retinal Atrophy (iRORA)*

- “Impending GA”
- Subsidence of the OPL & INL and a hypo-reflective wedge
- Signal hypertransmission into the choroid with corresponding attenuation/disruption of the RPE



Complete RPE and Outer Retinal Atrophy (cRORA) = GA w/o neo



Sadda R, et al. Consensus definition for atrophy associated with ARMD on OCT: classification of atrophy report 3. *Ophthalmology* 2019

Wu Z, et al. Prospective Longitudinal Evaluation of Nascent GA in ARMD. *Ophthalmol Retina* 2020

Wu, Z. et al. Retina Microperimetry of Nascent GA in ARMD. *IOVS* 2014

OCT BIOMARKERS PREDICTING GA DEVELOPMENT

- Subsidence of inner nuclear layer (INL) and outer plexiform layer (OPL)
- External limiting membrane (ELM) descent
- ELM and/or photoreceptor ellipsoid zone (EZ) loss
- Hyporeflective wedges
- Intraretinal hyperreflective foci
- Drusen with hyporeflective cores
- Refractile drusen & hyperreflective crystalline deposits
- Drusenoid pigment epithelial detachment (PED) collapse

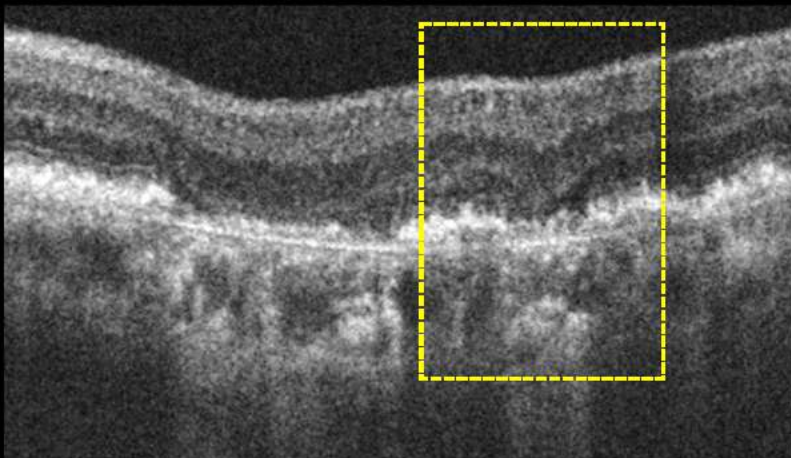
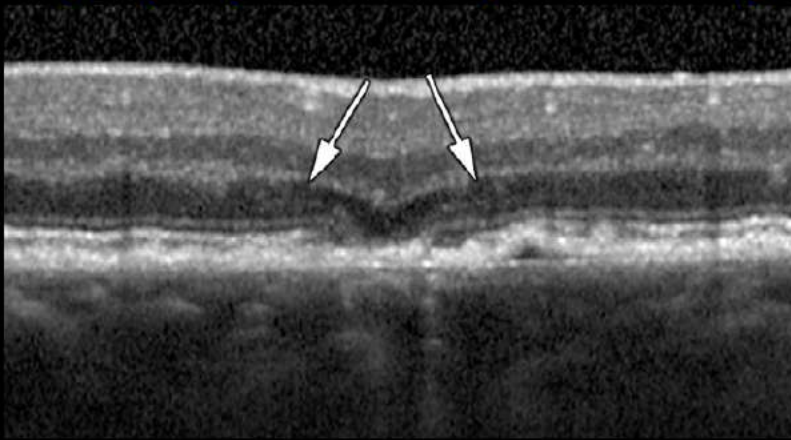


HIGH RISK OCT FEATURES THAT PREDISPOSE TO FUTURE GA DEVELOPMENT

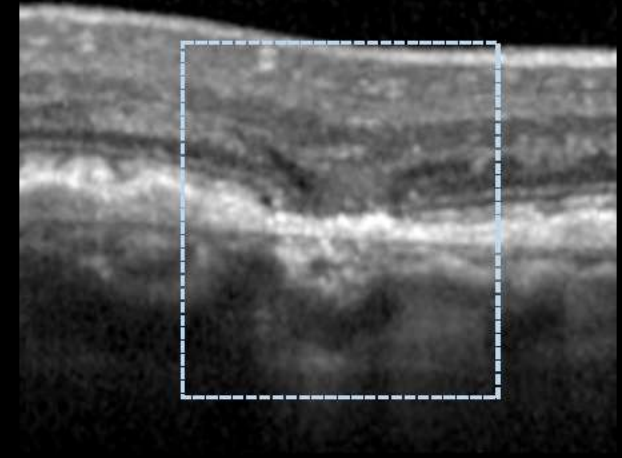
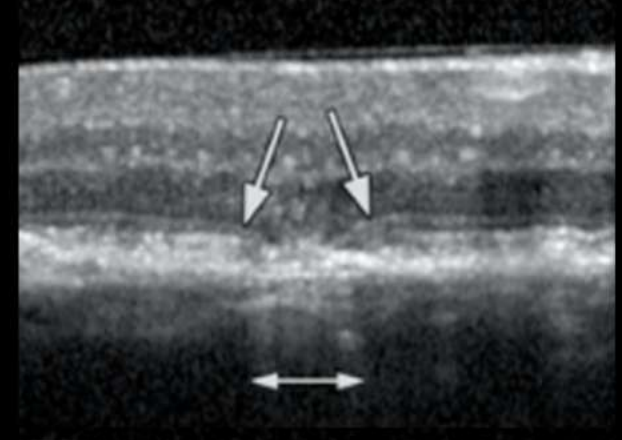
Jaffe GJ, et al. Imaging Features Associated with Progression to GA in ARMD: Classification of Atrophy Meeting Report 5. Ophthalmol Retina. 2021
Angelica Ly, et al. Developing prognostic biomarkers in intermediate ARMD: their clinical use in predicting progression. Clin Exp Optom 2018

OCT BIOMARKERS PREDICTING GA DEVELOPMENT

Subsidence (sinking) of the inner nuclear layer (INL) and outer plexiform layer (OPL)

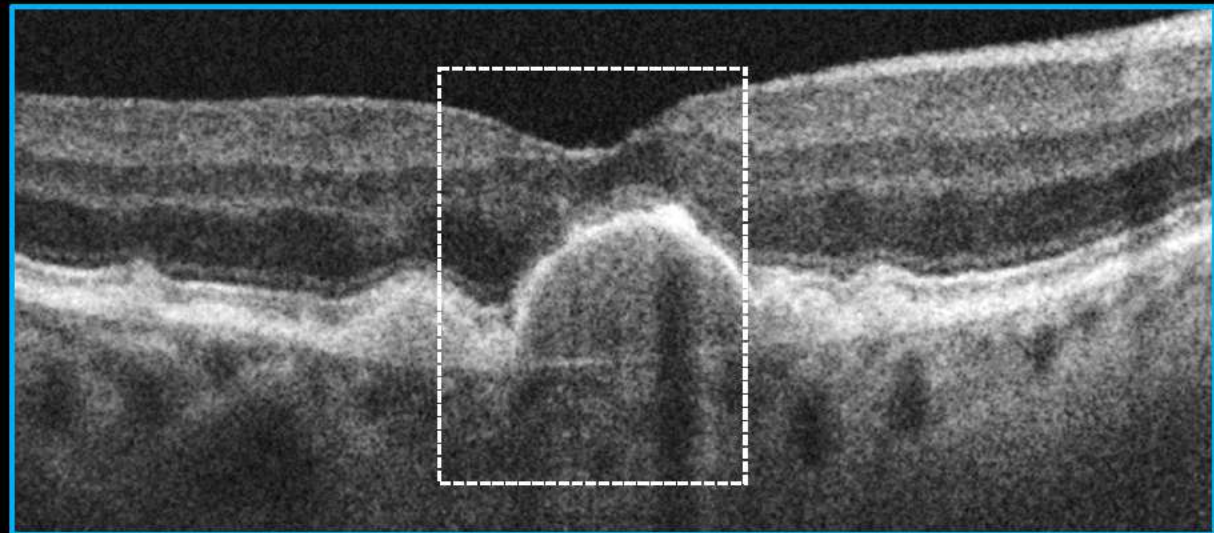
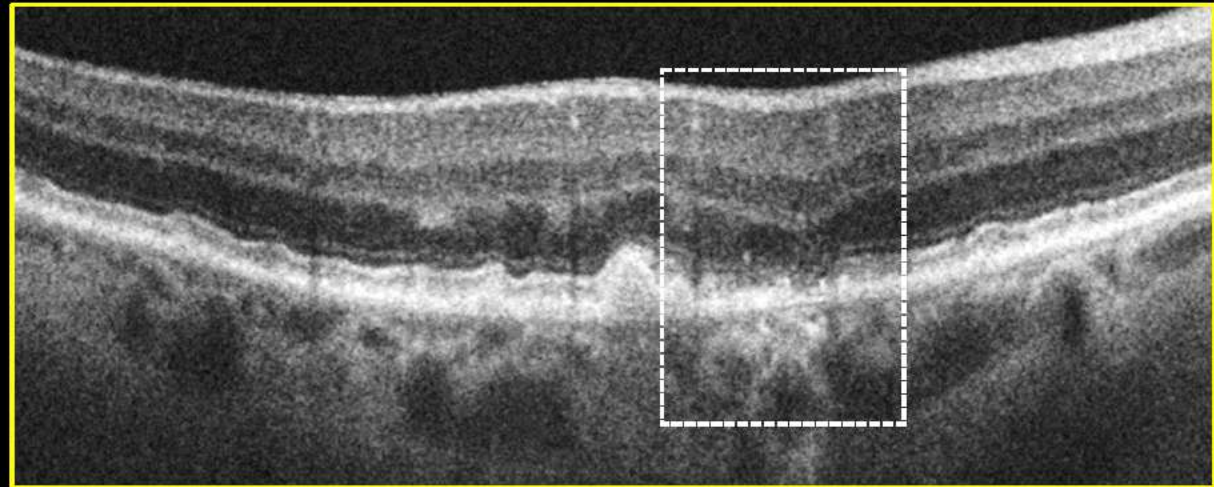
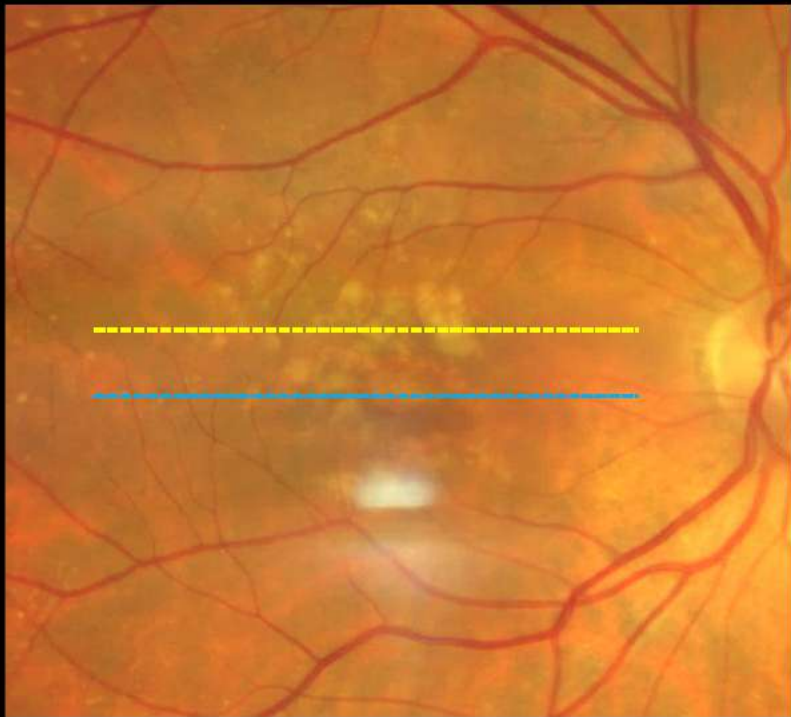


External limiting membrane (ELM) descent



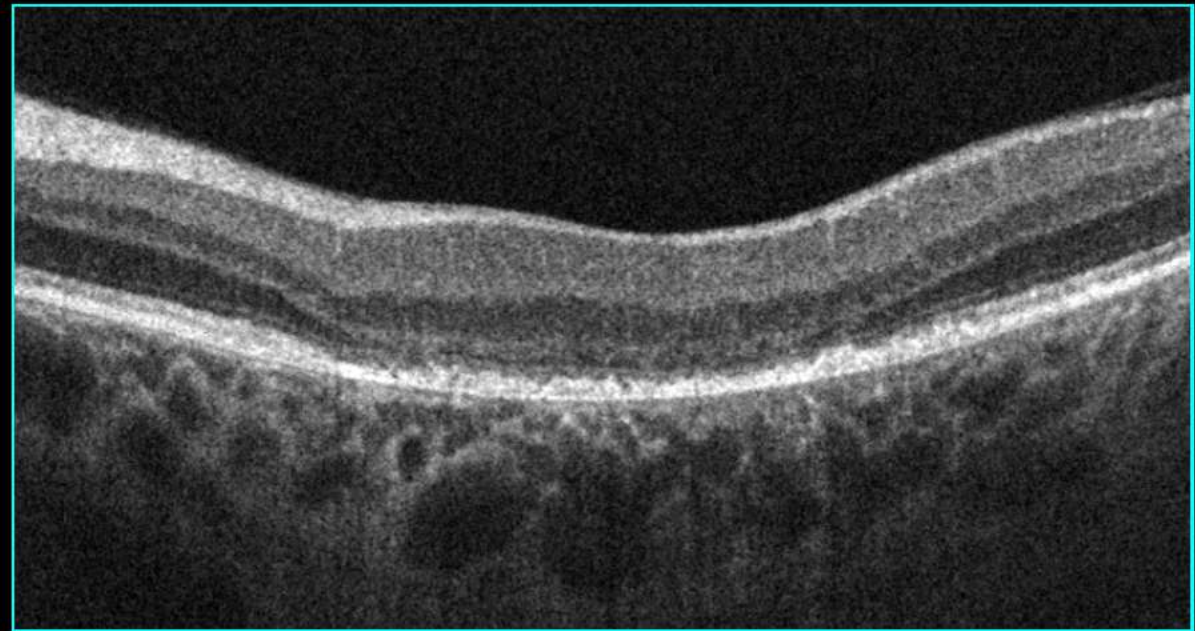
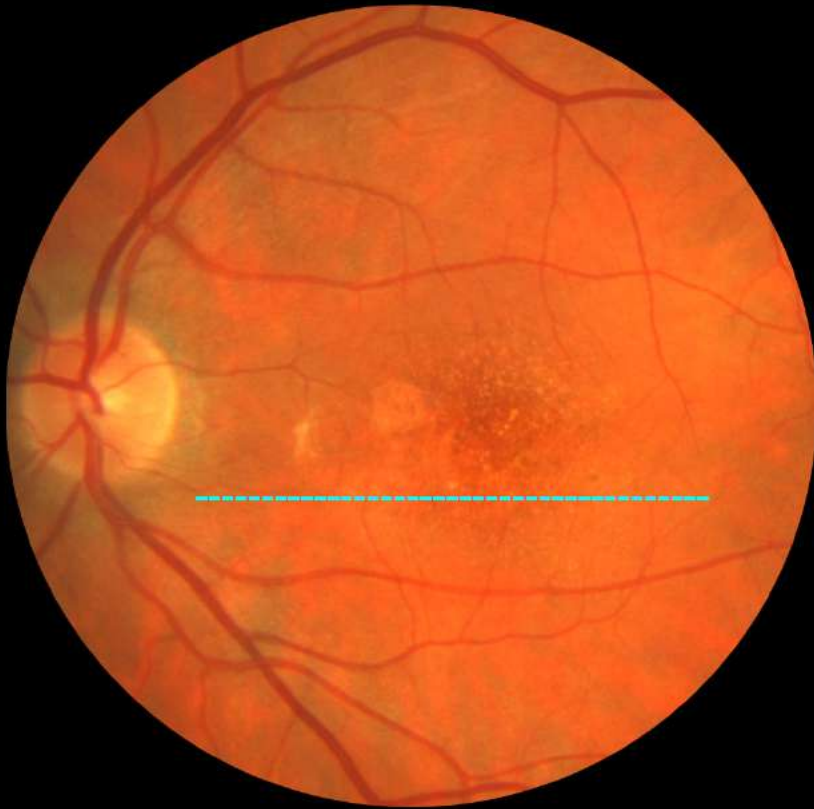
OCT BIOMARKERS PREDICTING GA DEVELOPMENT

ELM and/or EZ loss



OCT BIOMARKERS PREDICTING GA DEVELOPMENT

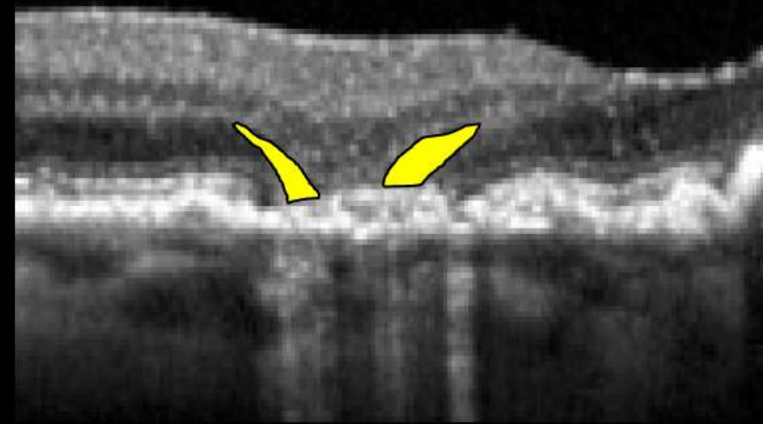
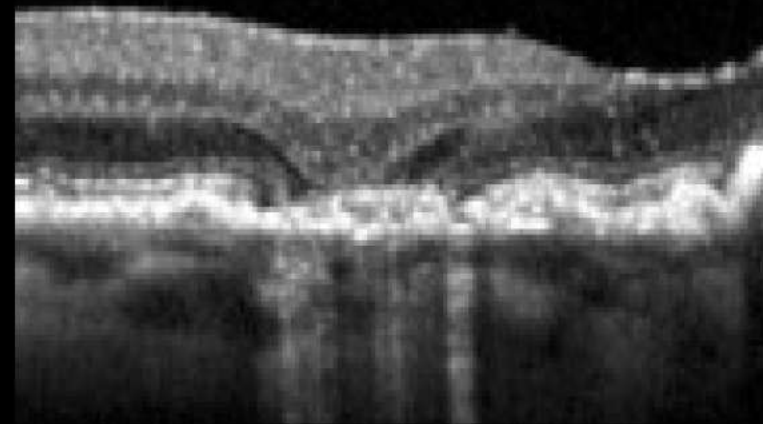
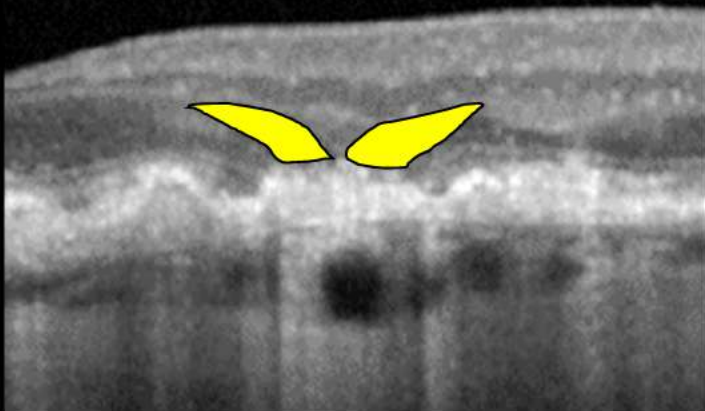
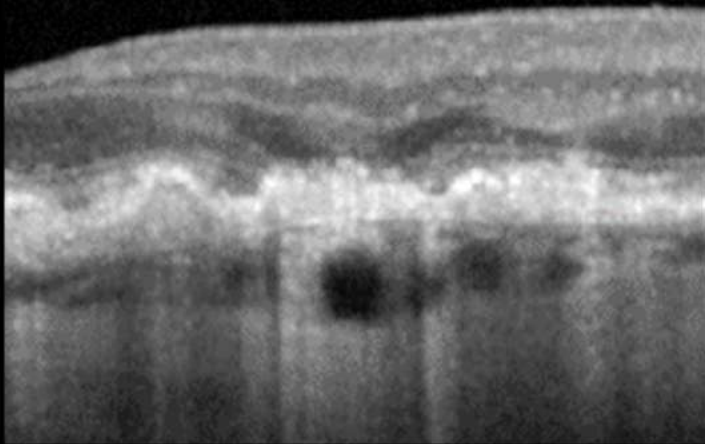
Photoreceptor Ellipsoid Zone (EZ) loss



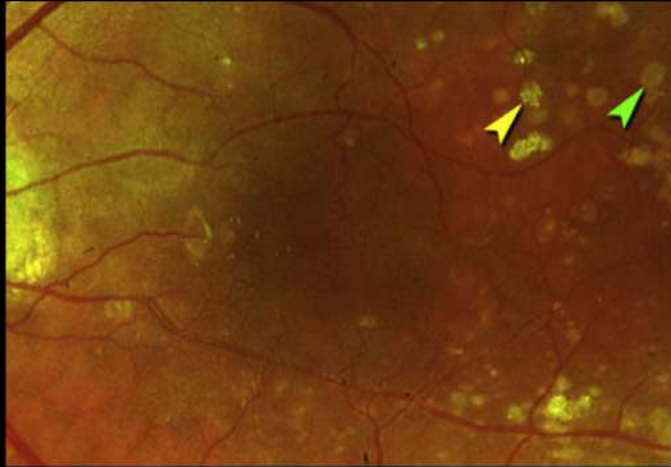
complete Outer Retinal Atrophy (cORA)

OCT BIOMARKERS PREDICTING GA DEVELOPMENT

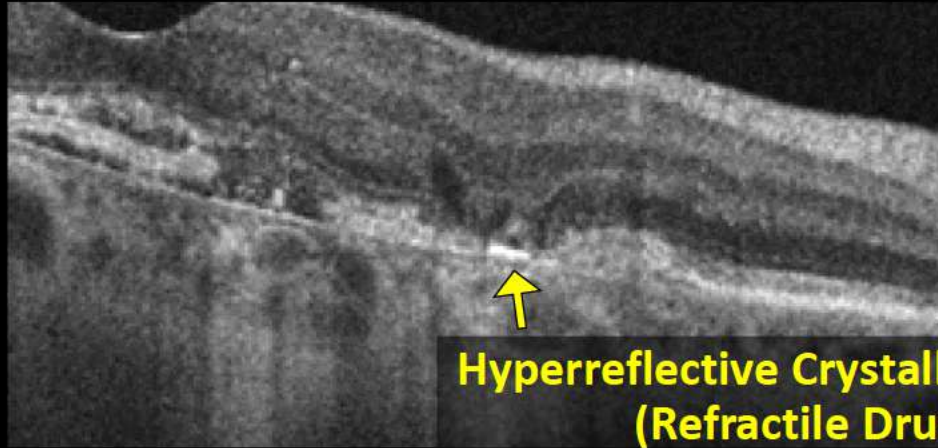
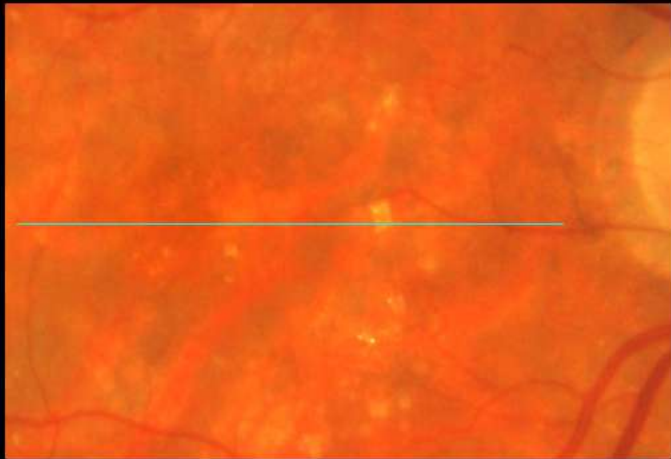
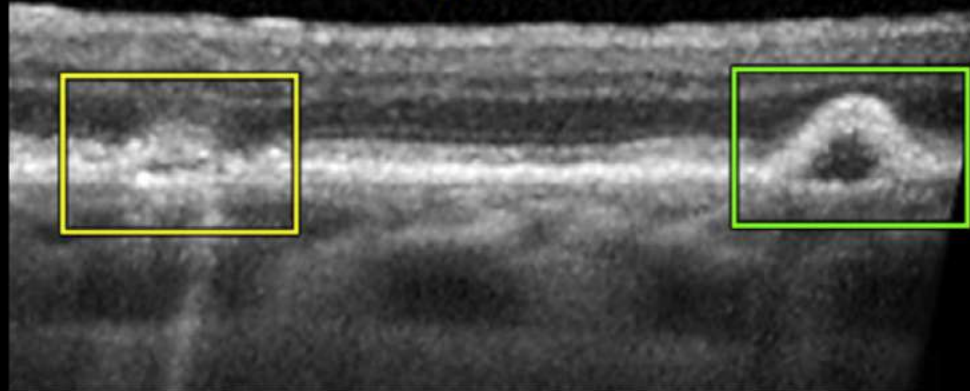
Hyporeflective wedges



OCT BIOMARKERS PREDICTING GA DEVELOPMENT



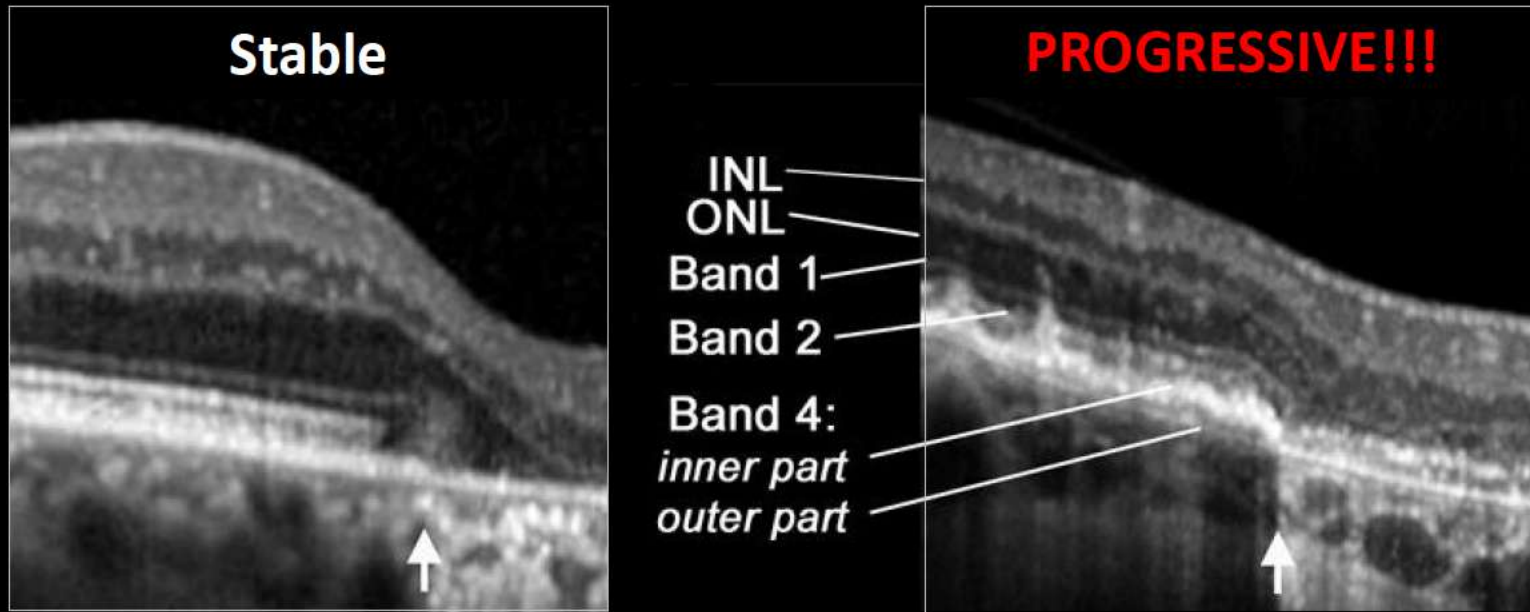
Drusen with hyporeflective cores



**Hyperreflective Crystalline Deposits
(Refractile Drusen)**

OCT FEATURES PREDICTING GA PROGRESSION

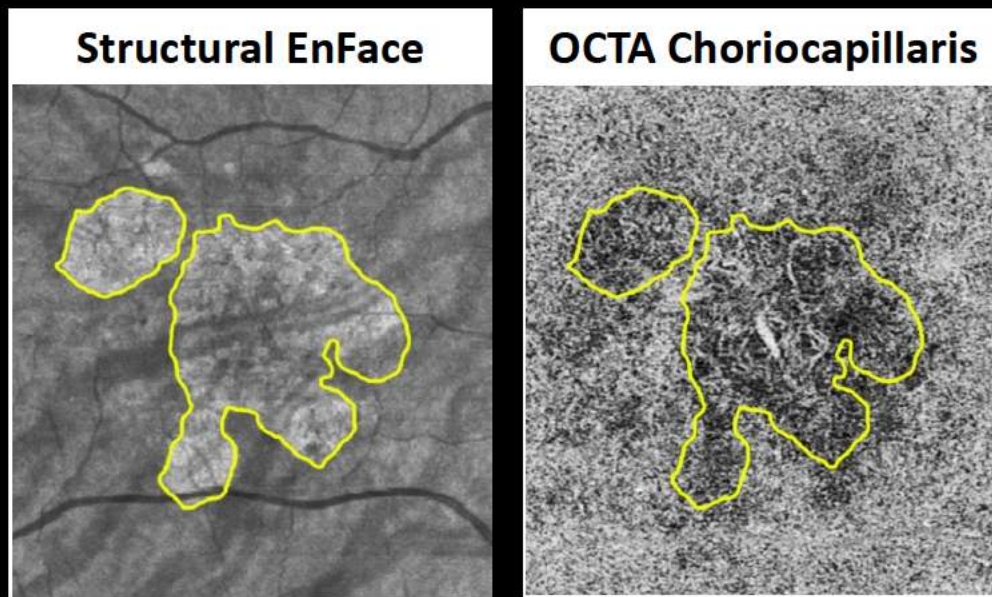
RPE/Bruch's membrane complex (band 4) splitting



Fleckenstein M, et al. FAF and SD-OCT characteristics in a rapidly progressing form of GA. Invest Ophthalmol Vis Sci. 2011.

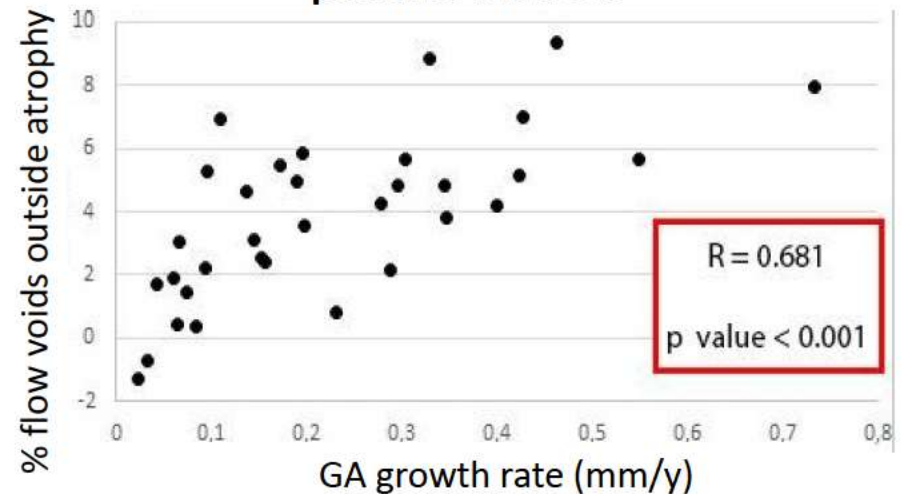
OCTA FEATURES PREDICTING GA PROGRESSION

- Impairment of choriocapillaris flow is present immediately surrounding GA lesions
- **↑ degree of choriocapillaris flow impairment = faster GA enlargement!!**



Nassisi M, et al. Choriocapillaris impairment around the atrophic lesions in patients with GA: a SS-OCTA study. Br J Oph. 2018.

Correlation between CC flow impairment around atrophic lesions and yearly growth rate in patients with GA

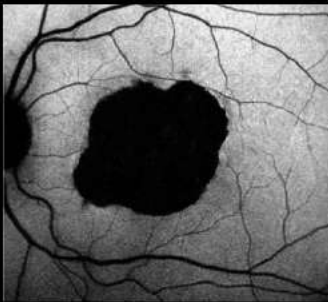


Nassisi M, et al. Choriocapillaris flow impairment surrounding GA correlates with disease progression. PLoS One 2019.

PROGNOSTIC VALUE OF GA PHENOTYPIC FAF PATTERNS

Slow Progression

No abnormality (0.38 mm²/yr)



Focal (0.81 mm²/yr)

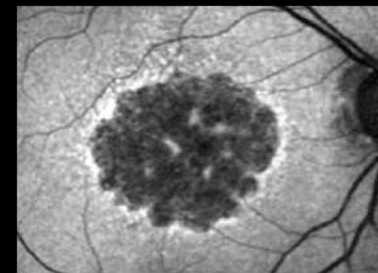
Single or individual small spots of ↑ FAF adjacent directly to margin of GA



Rapid Progression

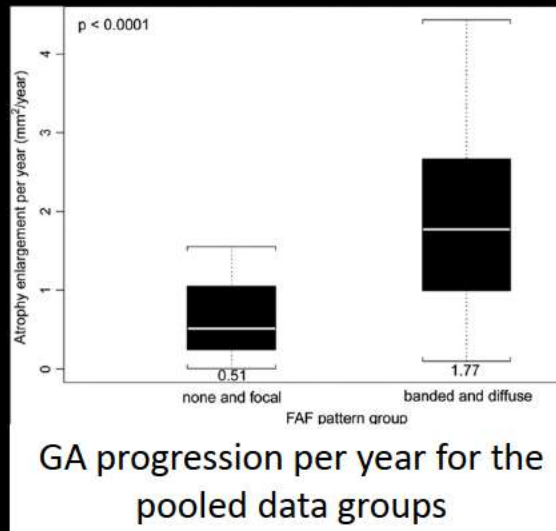
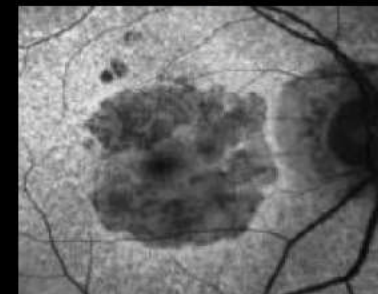
Banded (1.81 mm²/yr)

↑ FAF adjacent directly to margin of GA in an almost continuous ring shape



Diffuse (1.77 mm²/yr)

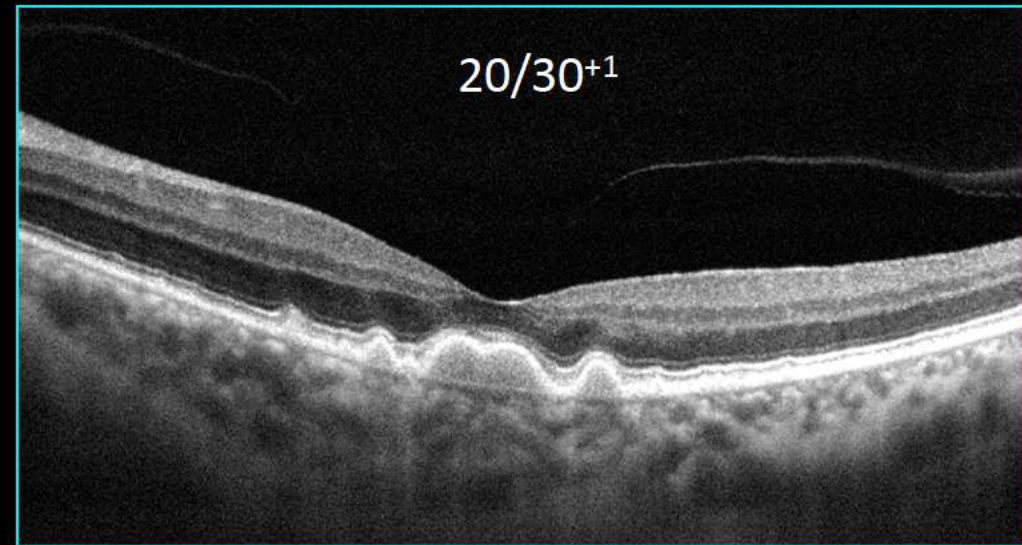
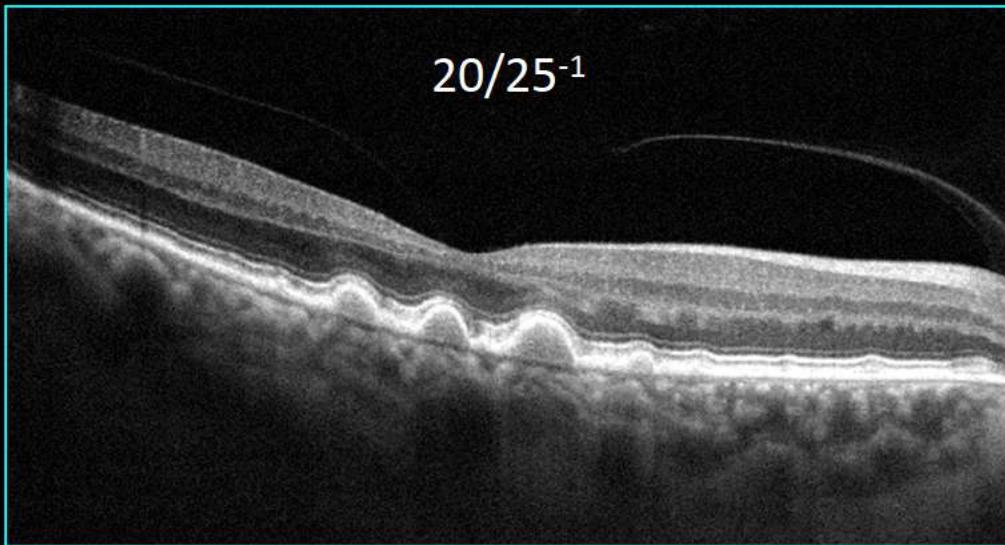
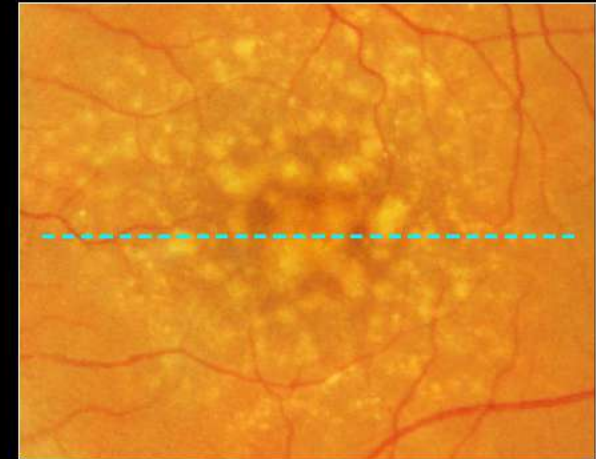
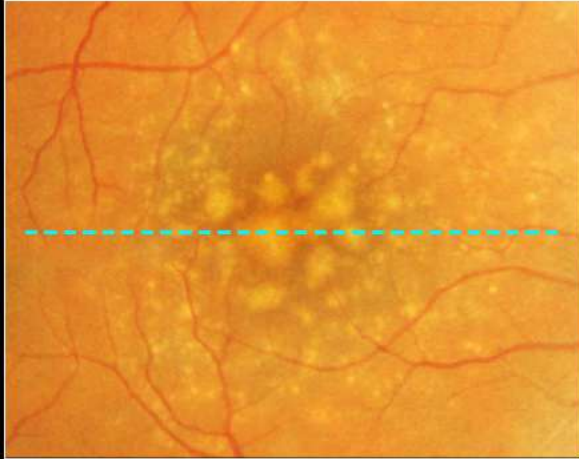
↑ FAF at the margin and elsewhere



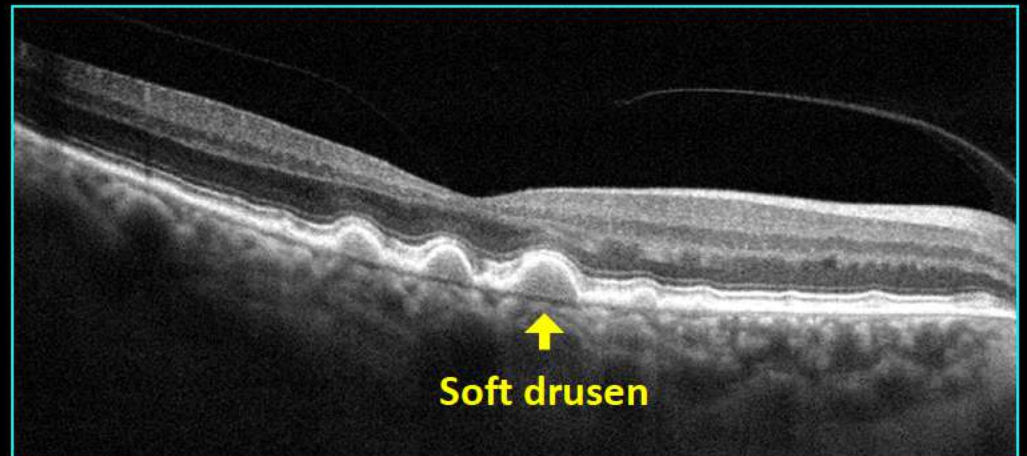
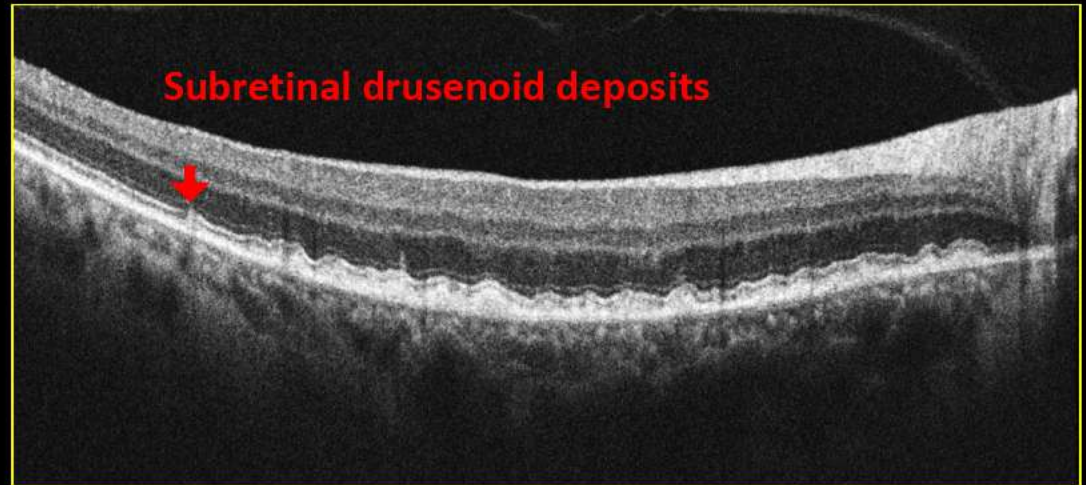
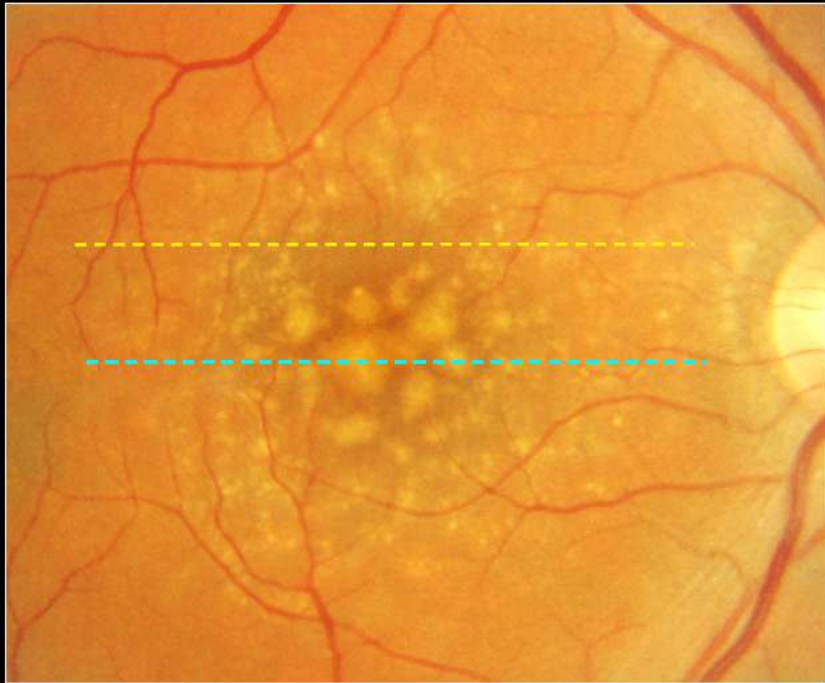
The GAIN Study. Am J Ophthalmol. 2015;160: 345–353.e5.

Holz FG, et al (FAM-Study Group). Progression of GA and impact of FAF patterns in ARMD. Am J Ophthalmol. 2007 Mar;143(3):463-72.

CASE IN POINT – 60yo Female



CASE IN POINT

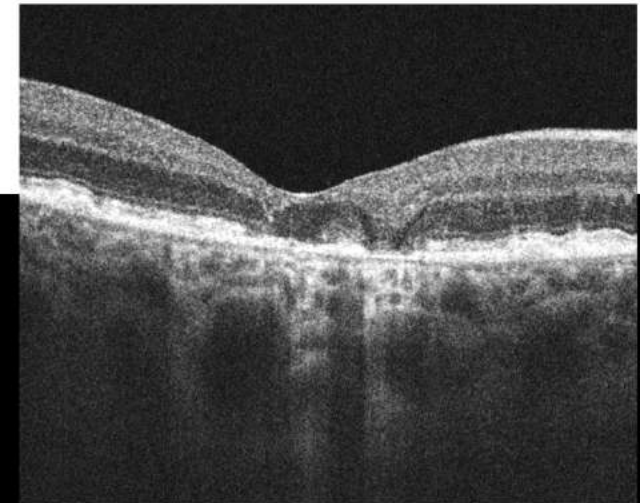
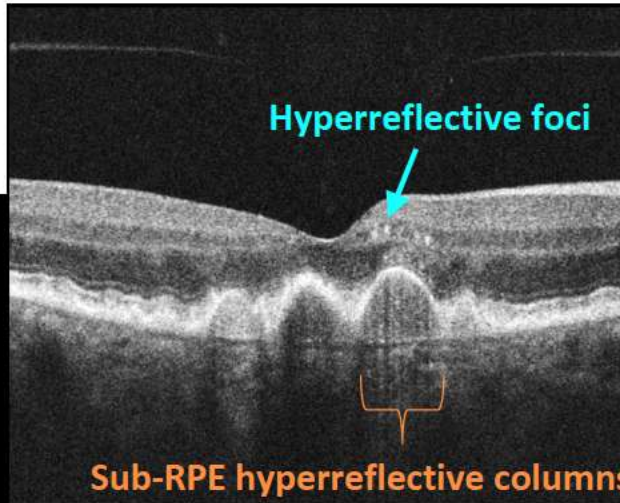
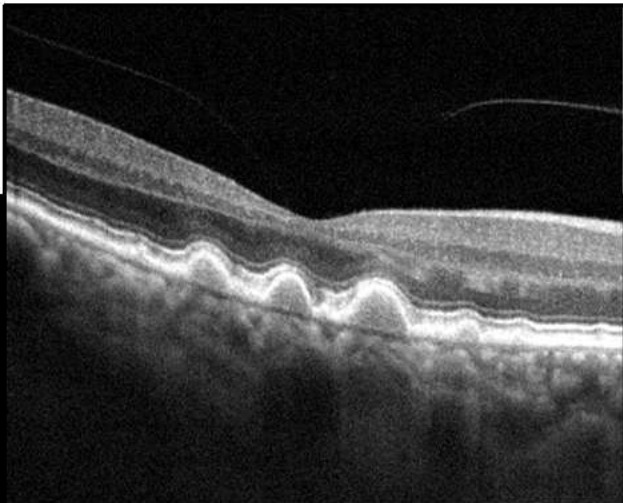
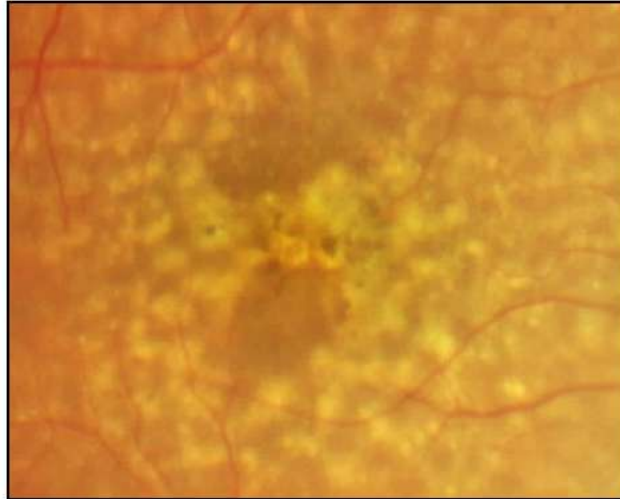


Right Eye

BASELINE

4 YEARS

5 1/2 YEARS

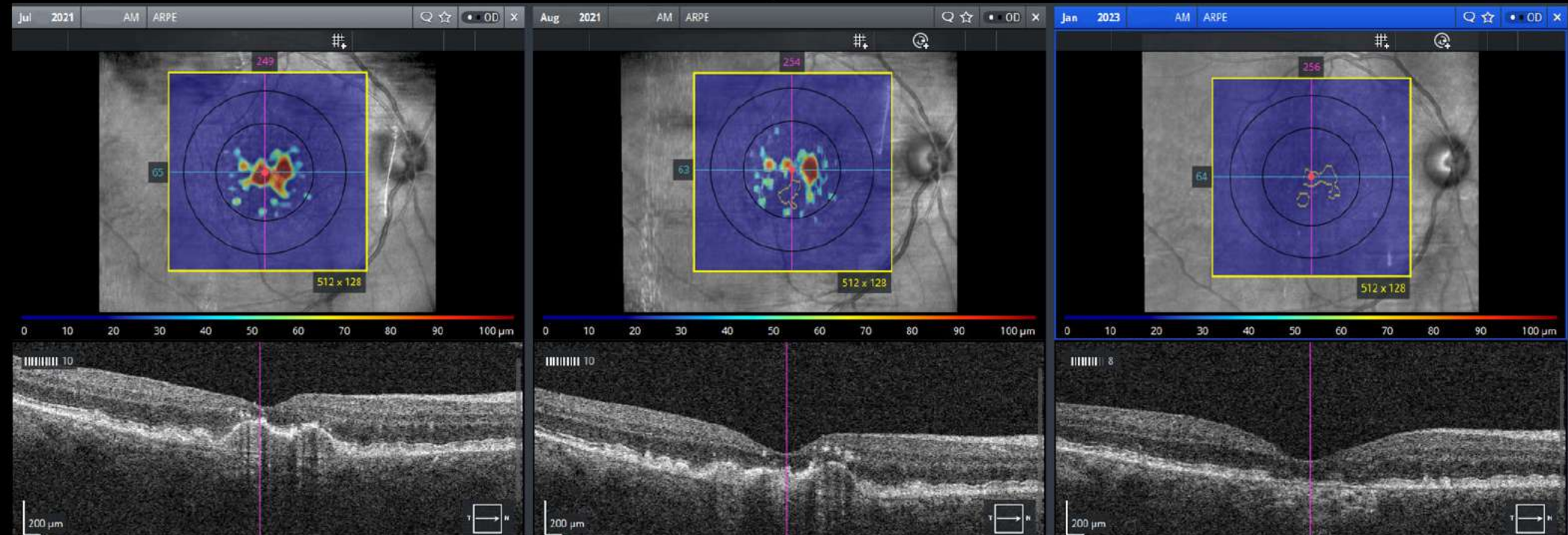


RPE Elevation

Jul 2021

Aug 2021

Jan 2023



Sub RPE Slab & Trend Analysis

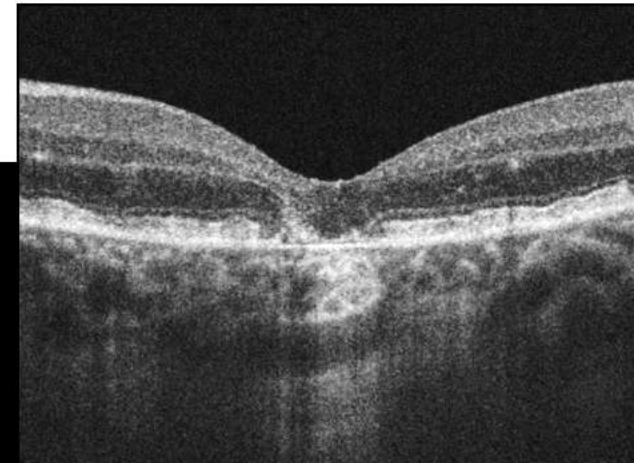
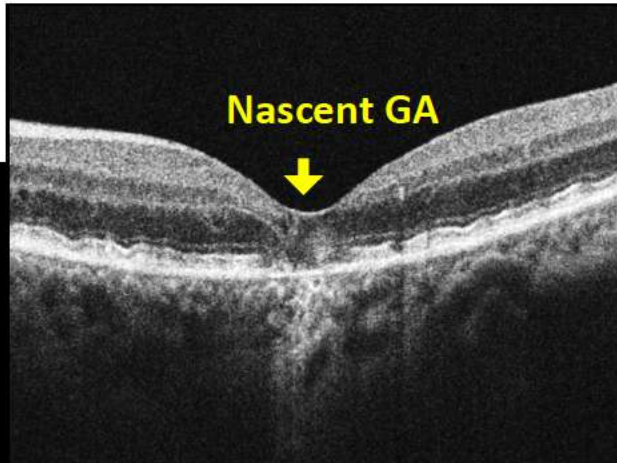
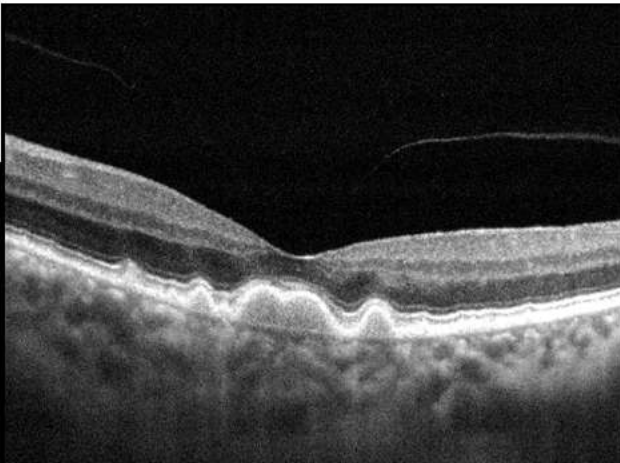
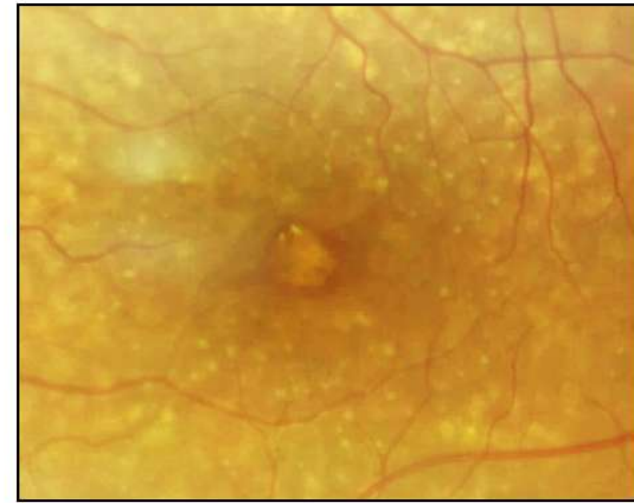
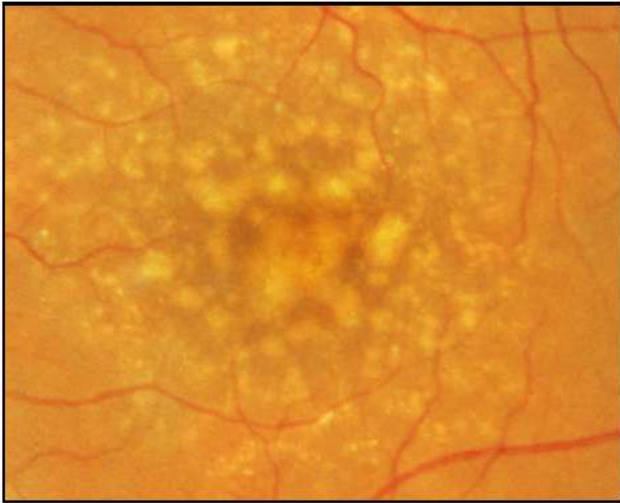


BASELINE

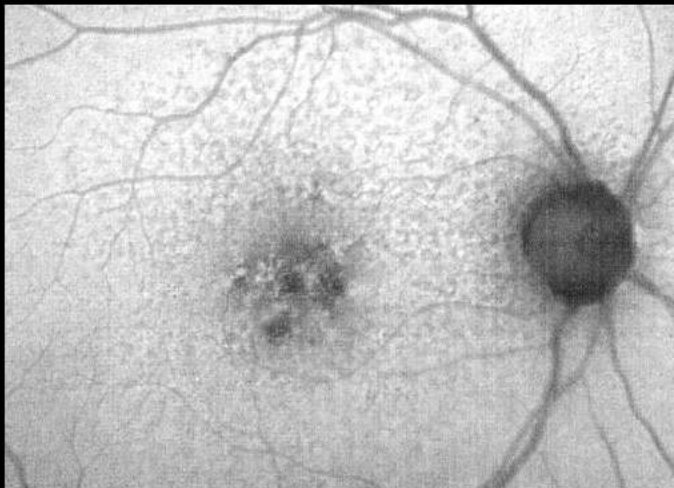
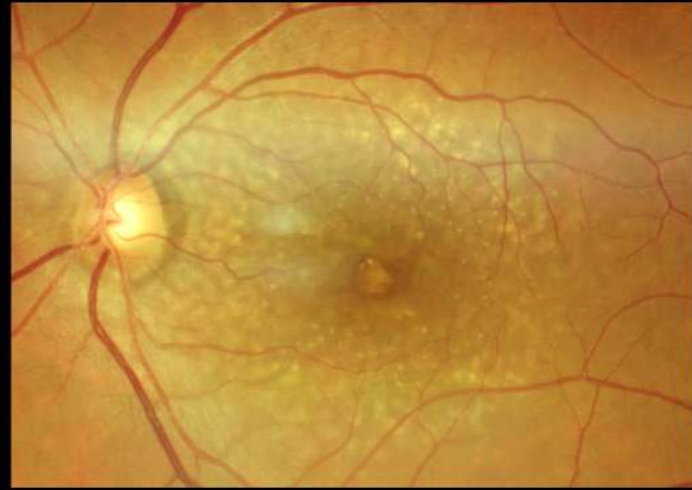
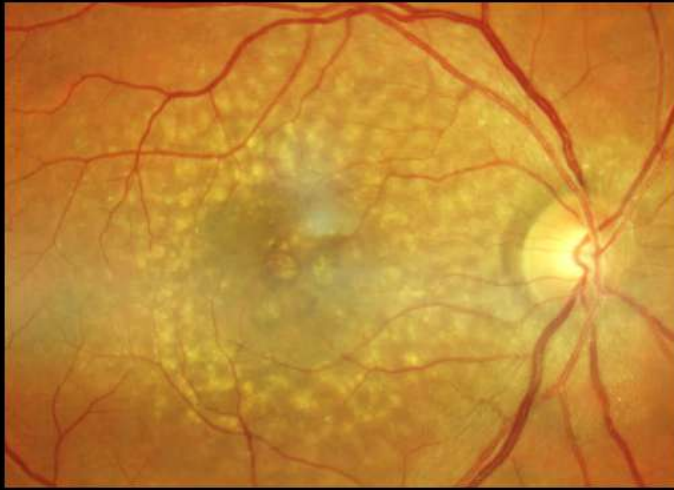
4 YEARS

5 1/2 YEARS

Left Eye

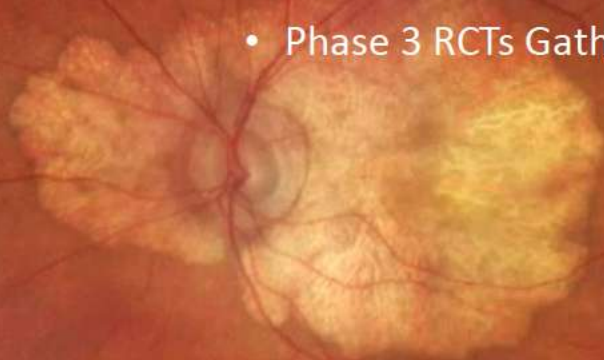


5 1/2 YEAR FU FUNDUS AUTOFLUORESCENCE (FAF)



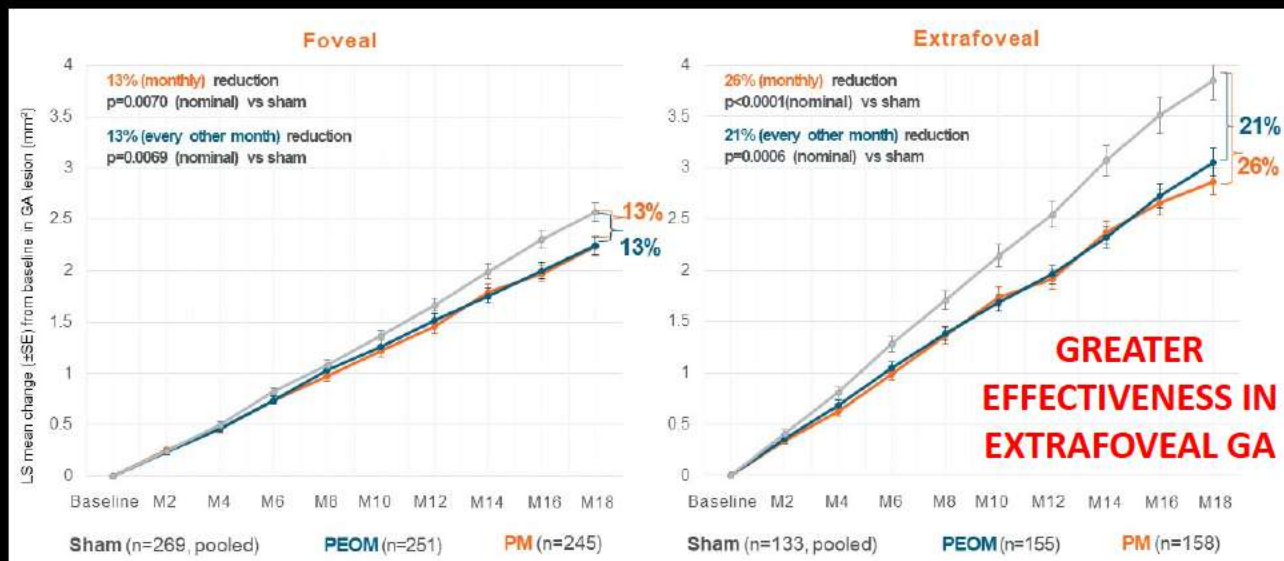
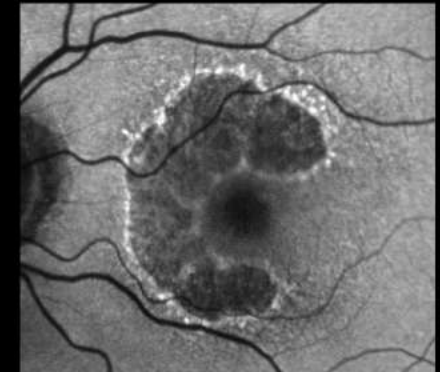
EMERGING TREATMENTS FOR GA

- Treatment **slows progression**, does not halt GA enlargement
- Administered via **INTRAVITREAL INJECTION** monthly or every other month
- Complement inhibitors
 - Pegcetacoplan (SYFOVRE®) – C3 Inhibitor- FDA approved Feb 2023
 - Phase 3 RCTs DERBY & OAKS
 - Avacincaptad Pegol (Zimura?) – C5 Inhibitor- PDUFA data pending Aug 2023
 - Phase 3 RCTs Gather I & Gather II



EMERGING TREATMENTS FOR GEOGRAPHIC ATROPHY (GA)

- Pegcetacoplan (SYFOVRE®): 18 month combined results from phase 3 studies DERBY & OAKS
 - Inclusion:
 - BCVA 20/320 or better, **no neo or exudation in study eye**
 - Total GA area between 2.5 - 17.5 mm² (**1 - 7 disc areas**) via FAF
 - Any pattern of **FAF hyperautoFL in the junctional zone** of GA
 - Primary endpoint: Change in total GA lesion area on FAF



<https://investors.apellis.com/news-releases/news-release-details/apellis-announces-detailed-18-month-results-phase-3-derby-and>

Rates of Progression to CNV

OAKS and DERBY Combined

New-onset investigator-determined neovascular AMD, ^a n (%) patients	Pegcetacoplan Monthly (n = 419)	Pegcetacoplan EOM (n = 420) ^b	Sham Pooled (n = 417)
12 months	25 (6.0%)	17 (4.1%)	10 (2.4%)
24 months – cumulative	51 (12.2%)	28 (6.7%)	13 (3.1%)
24 months – confirmed by reading center At time of investigator-reported neovascular AMD, 100% of patients had available SD-OCT and 82% had available FA for reading center evaluation	37 (8.8%)	23 (5.5%)	11 (2.6%)

- Vast majority of CNV lesions were classified as occult
- Patients who developed neovascular AMD continued treatment with study drug and received anti-VEGF therapy per investigator discretion
- No patients in the pegcetacoplan study arms discontinued the studies due to neovascular AMD

CONTINUE TO VIGILANTLY MONITOR PATIENTS UNDERGOING GA TREATMENT (AND EDU PTS TO SELF MONITOR AT HOME) FOR EXUDATIVE CONVERSION!!!

- Need for intravitreal anti-VEGF therapy in addition to complement inhibition

Which patients with GA should you refer?

Those most **likely** to benefit:

- Extrafoveal GA esp those demonstrating progression over time (or with surrounding FAF hyperautoFL) or those with central involving GA in the fellow eye
- Pts motivated to undergo intravitreal injection at least every other month
- Pts that have enough life left to live to experience a benefit from treatment



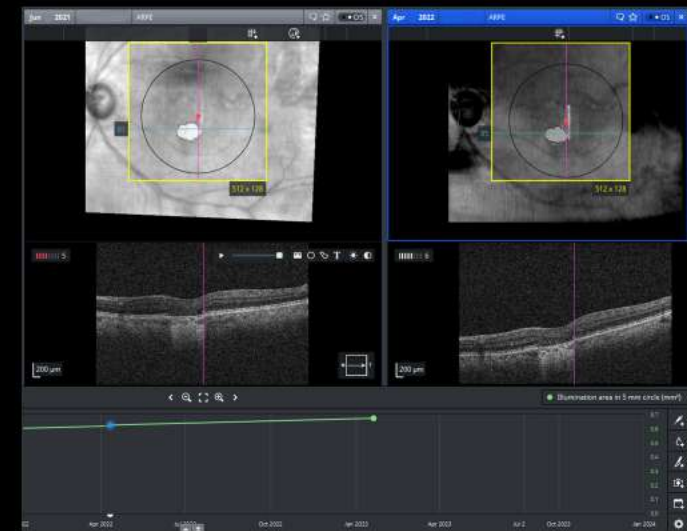
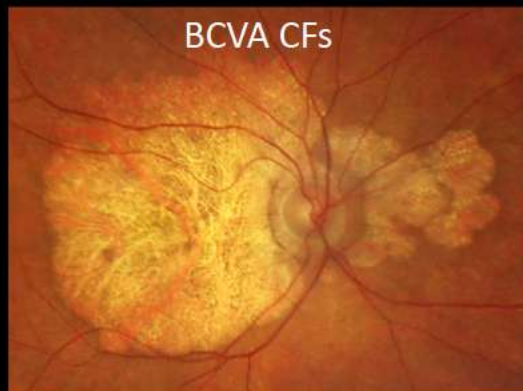
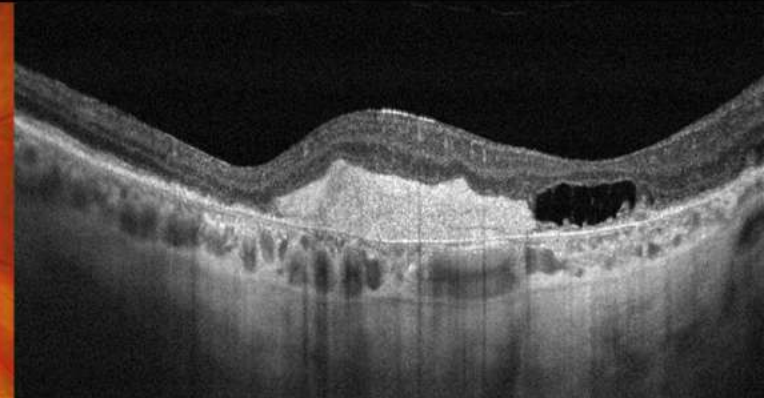
**IF YOU HAVE DOCUMENTATION OF PROGRESSION
SEND IT TO THE RETINAL SPECIALIST WHEN YOU REFER**

Disclaimer* These are my own personal opinions/thoughts

Which patients with GA should you **NOT** refer?

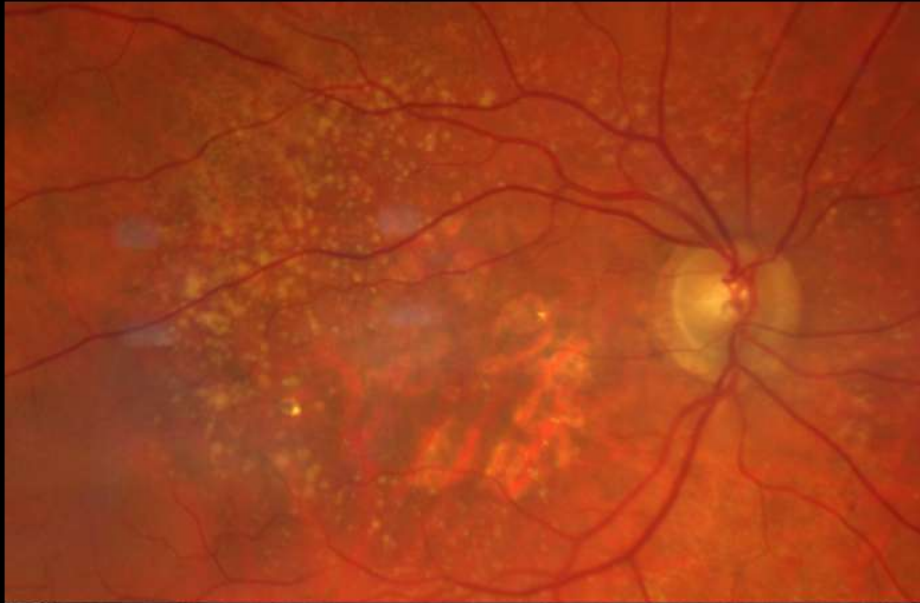
Those **unlikely** to benefit:

- Neovascular/exudative AMD or hx of anti-VEGF treatment in the affected eye (fellow eye OK)
- Disciform macular scars
- Extensive central-involving GA with poor acuity
- Stable GA lesions (no surrounding FAF hyperautoFL)
- RPE atrophy from other cause (POHS, AOFVD, IRD, etc.)
- Presence of other confounding disease limiting BCVA (end stage glaucoma, etc.)

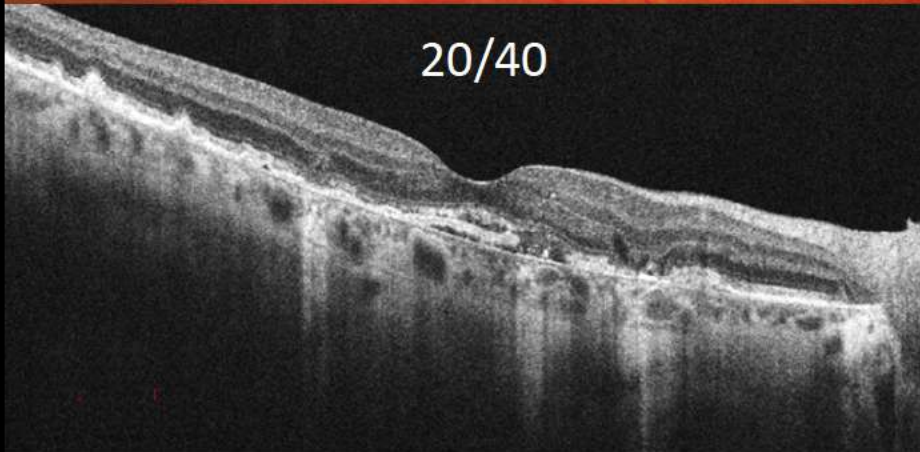


Disclaimer* These are my own personal opinions/thoughts

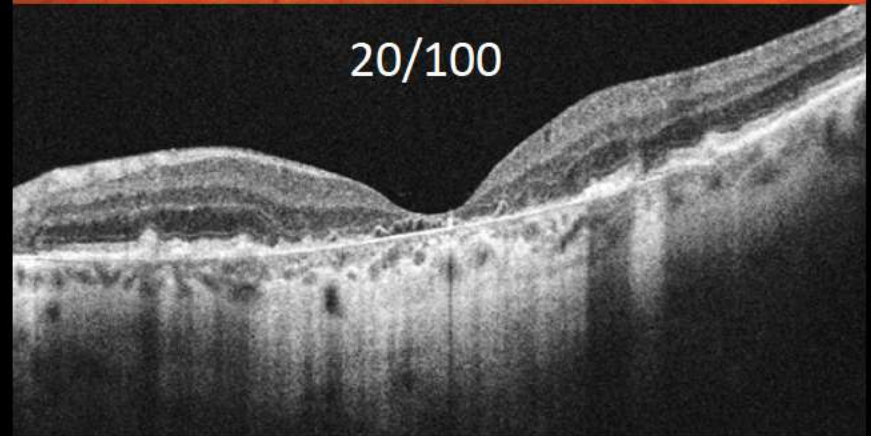
81yo female – complaining of progressive decrease in vision OS > OD



20/40



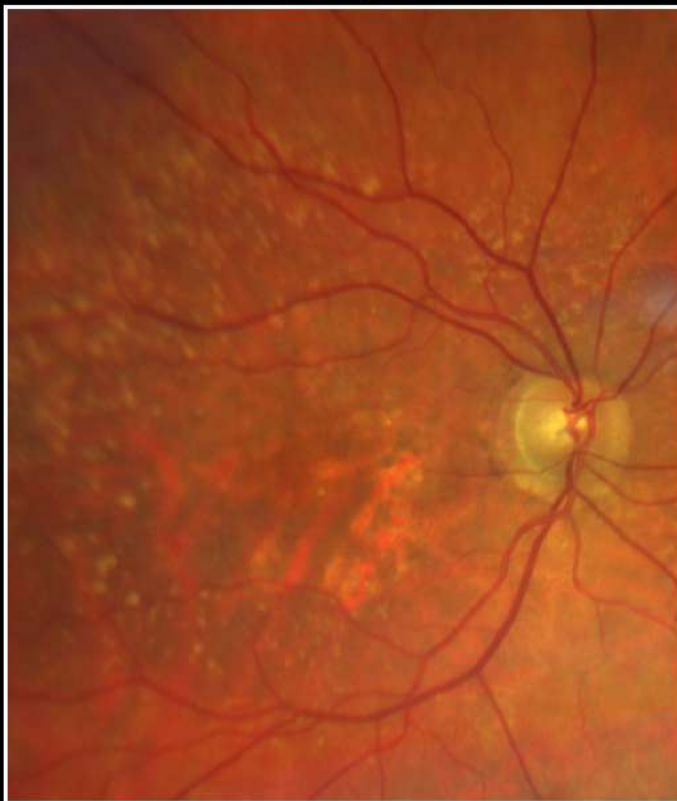
20/100



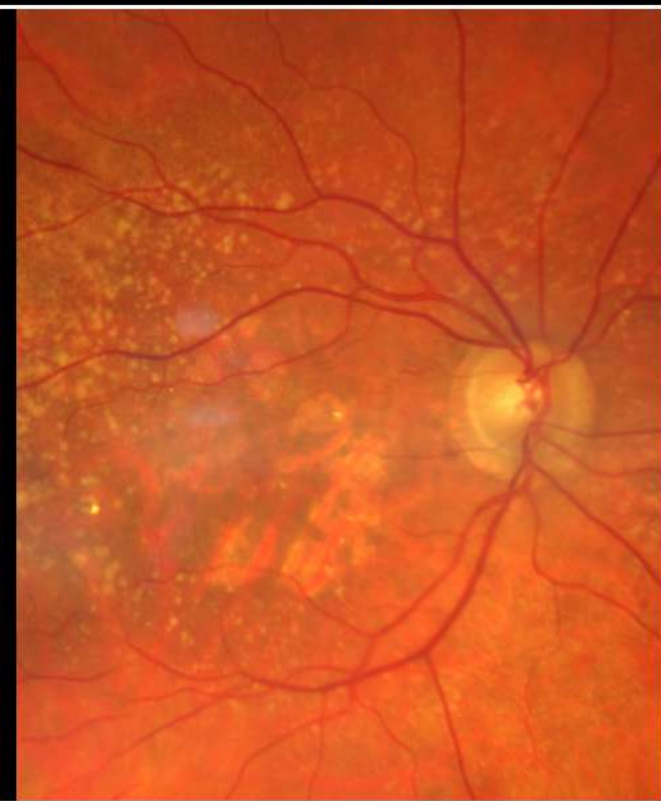
Baseline



1.5 yrs



2.5 yrs

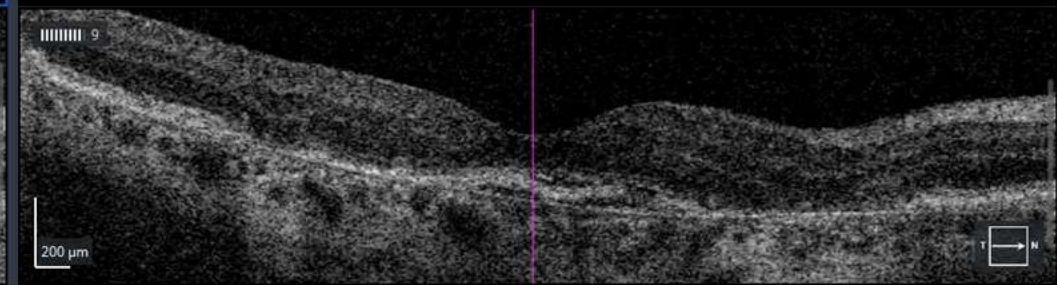
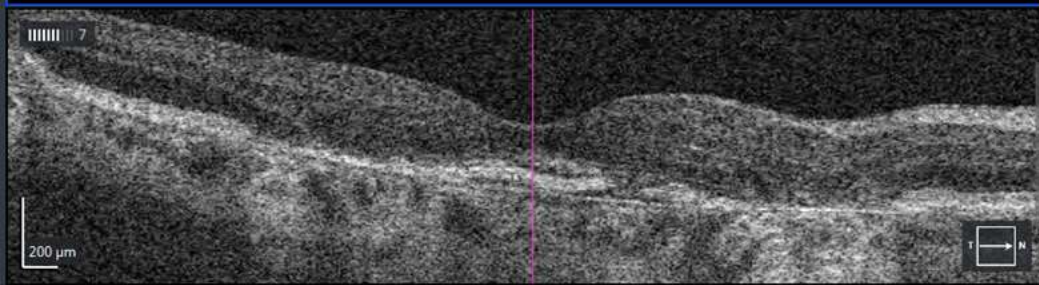
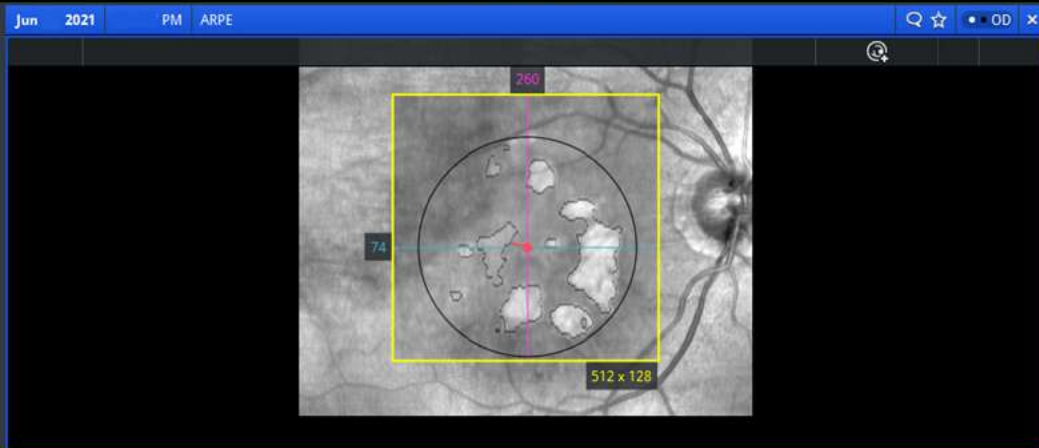


VA remains 20/40 throughout 2.5yrs FU

Exams 1 yr apart

Jun 2021

July 2022

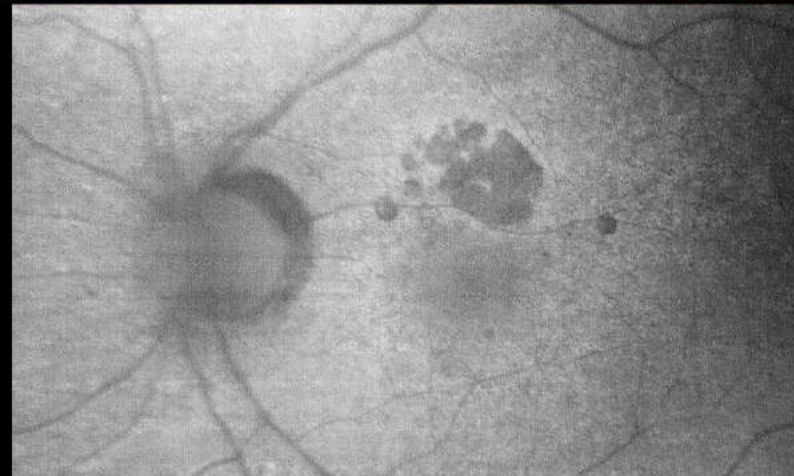
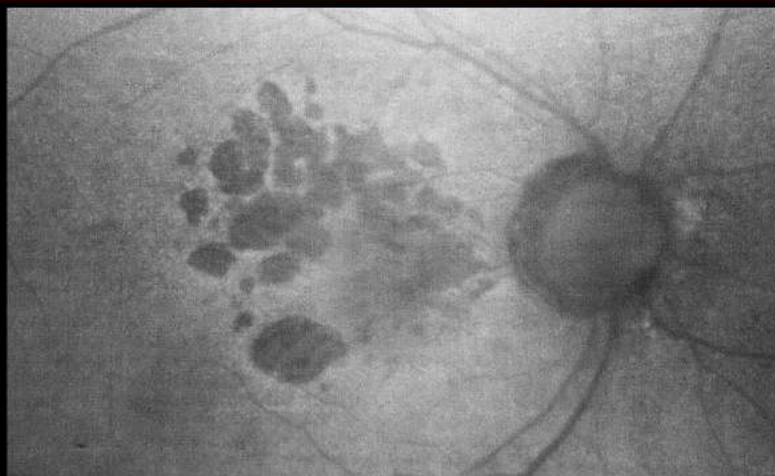


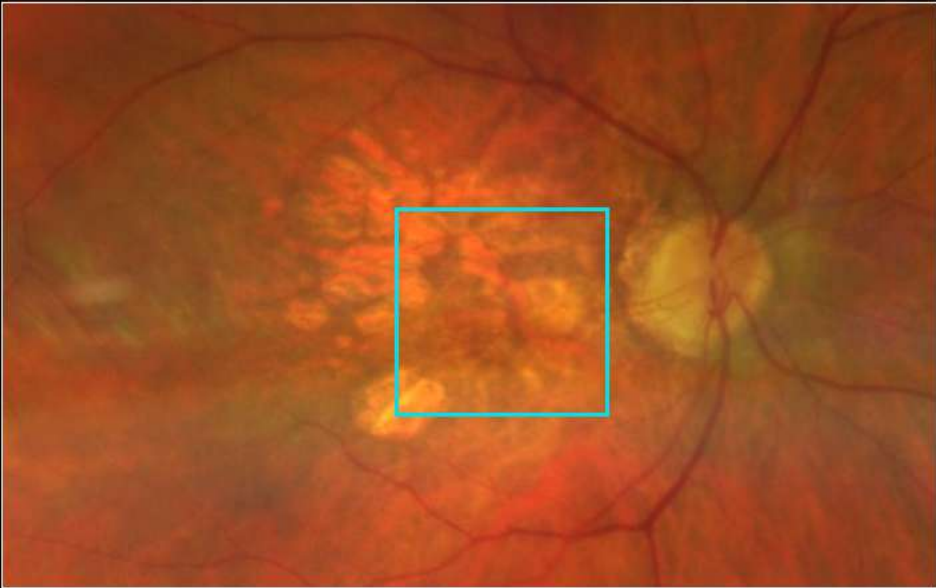
80yo male- currently undergoing anti-VEGF tx OD

20/50

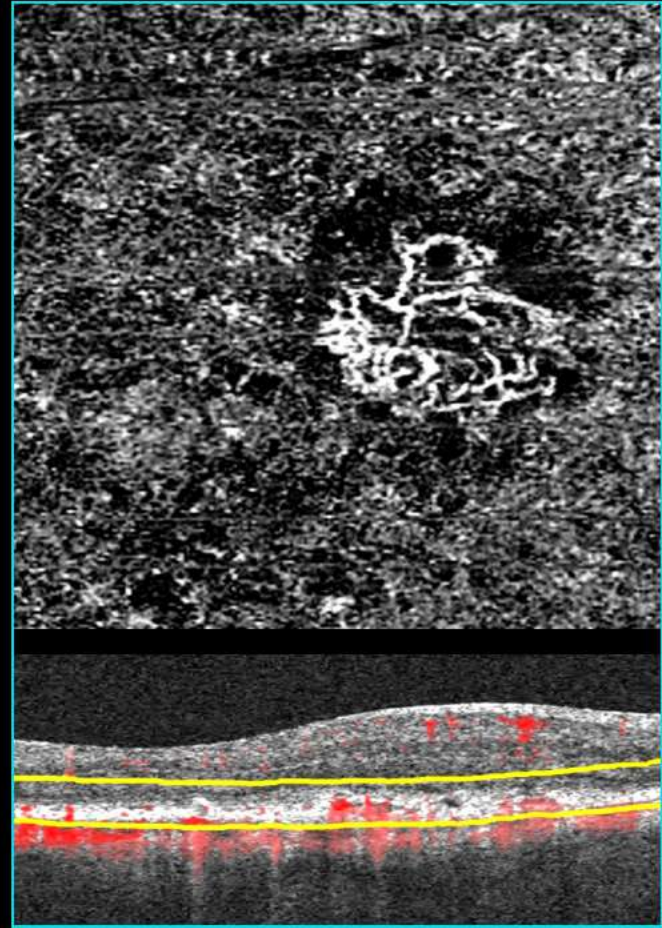


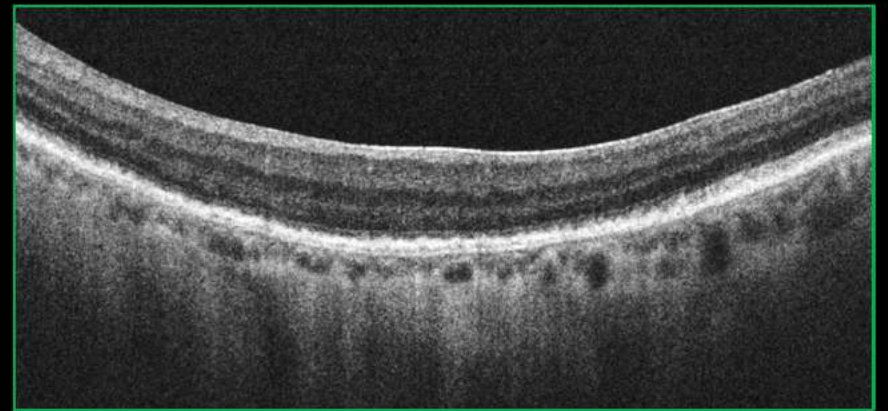
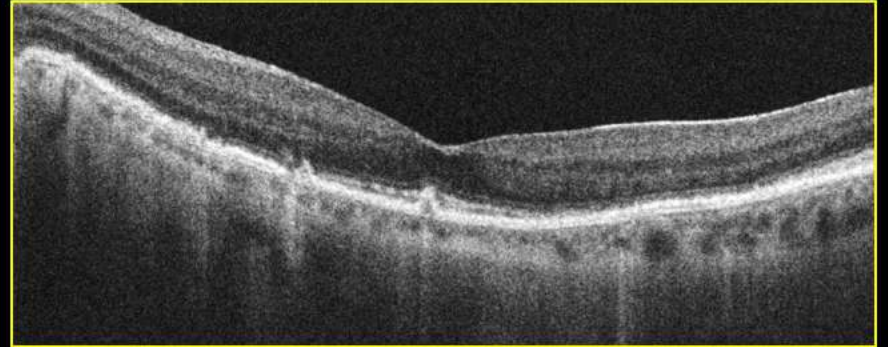
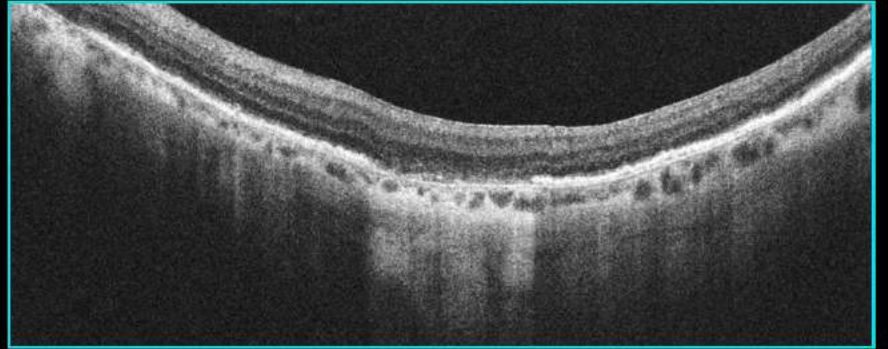
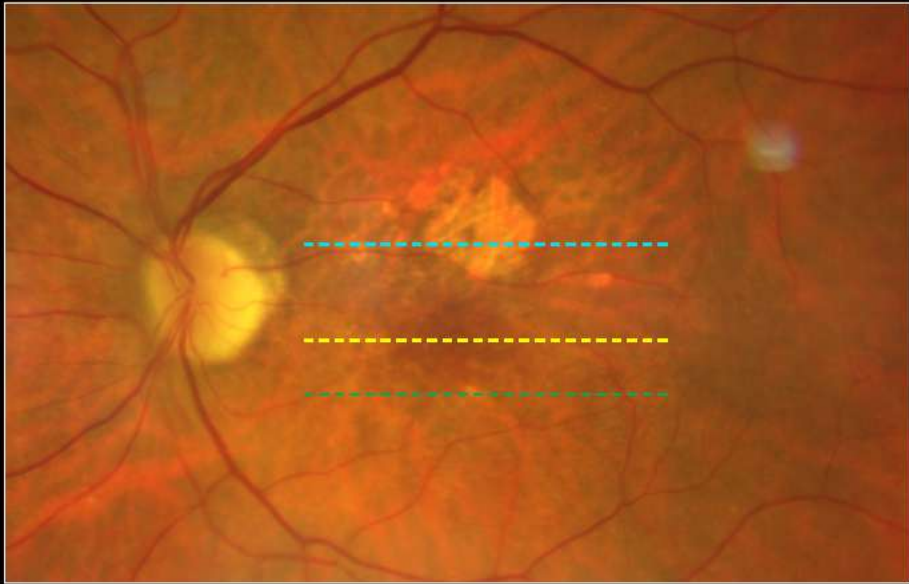
20/30





Outer Retina Choriocapillaris

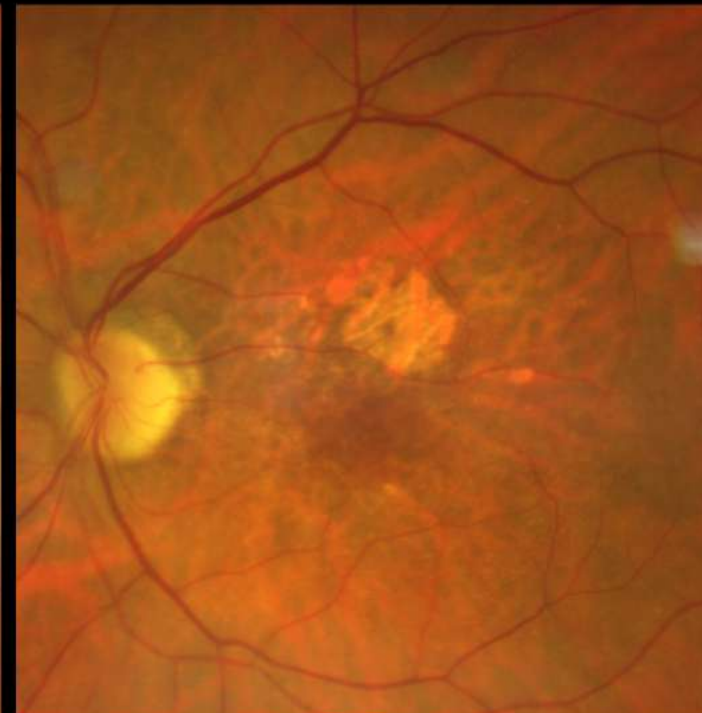




May 2021 (20/25⁻²)

Nov 2022

Feb 2023 (20/30)

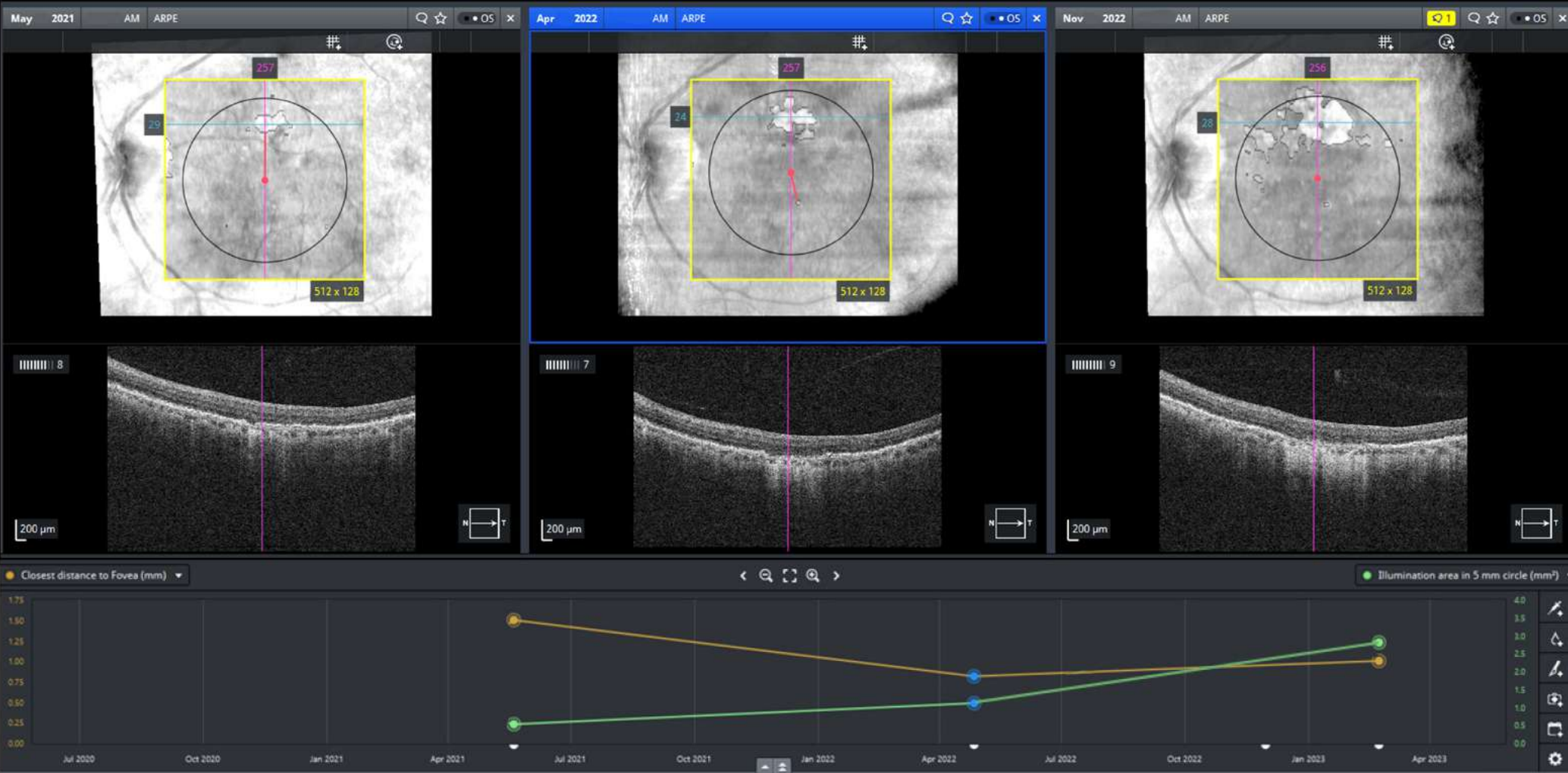


1.5 yr span

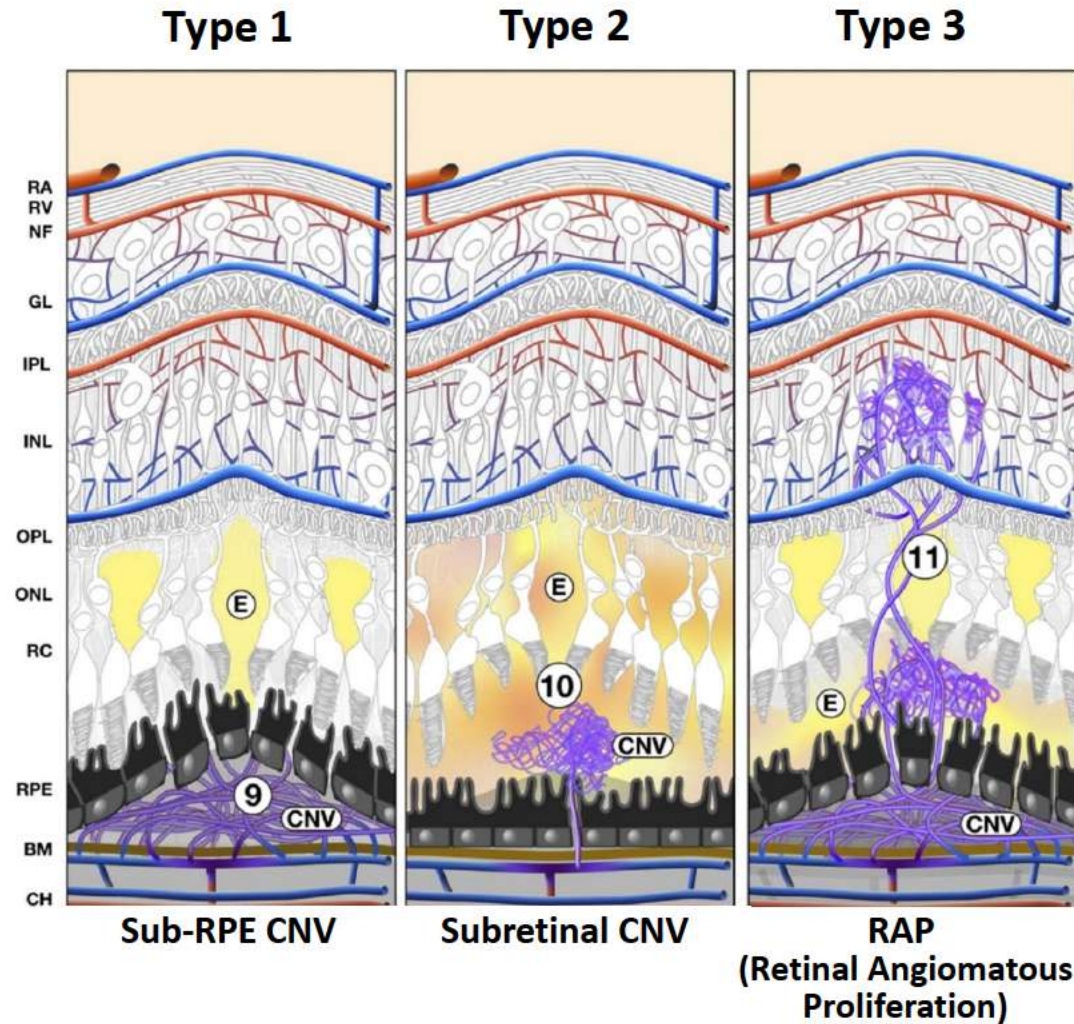
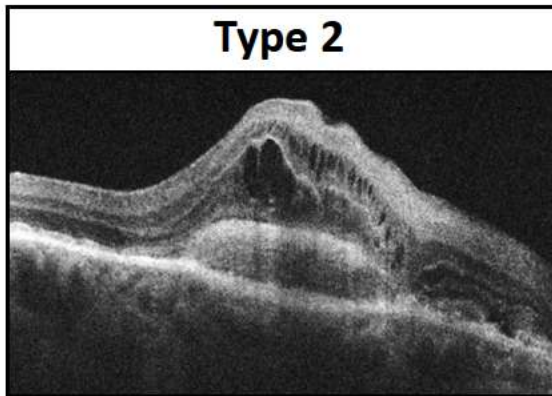
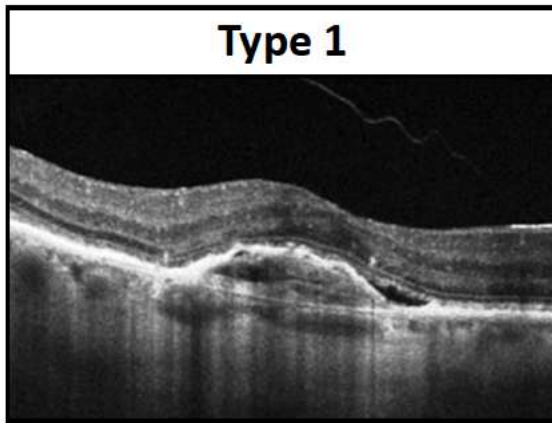
May 2021

April 2022

Nov 2022



TYPES OF CHOROIDAL NEOVASCULARIZATION IN AMD

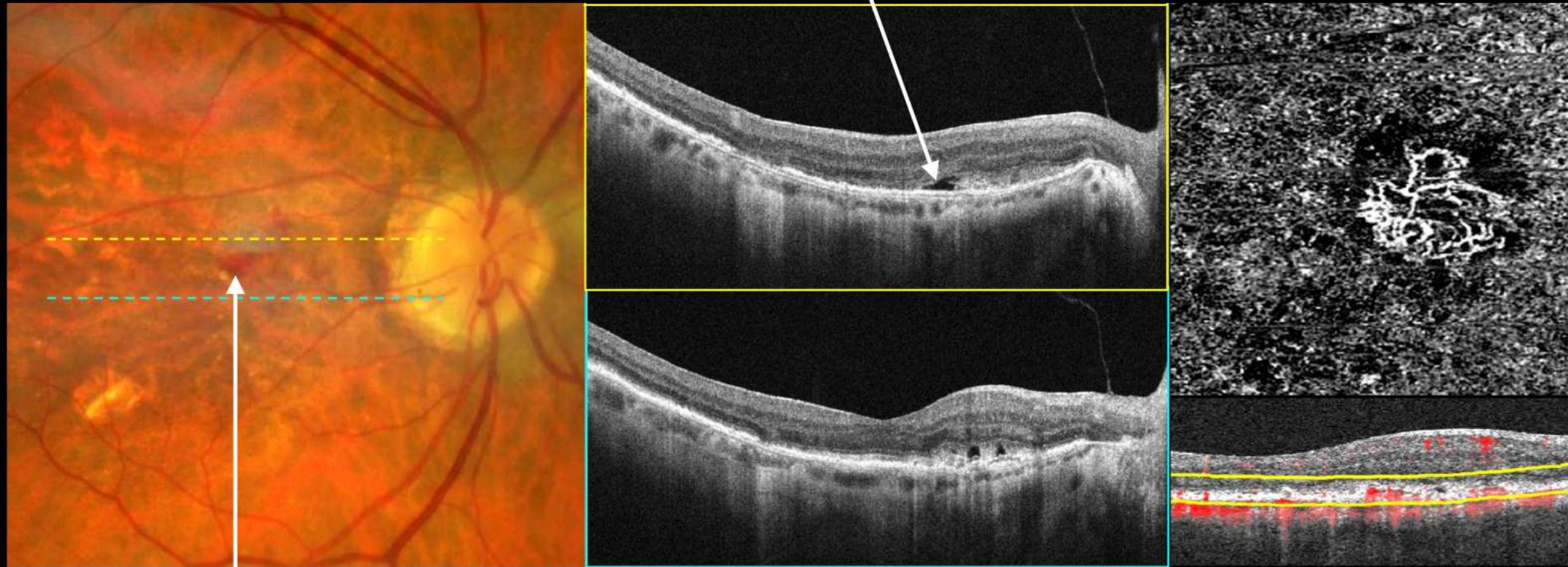




Exudative & Neovascular AMD Features

Hemorrhage, fluid, exudate, PED, OCTA membranes

SRF



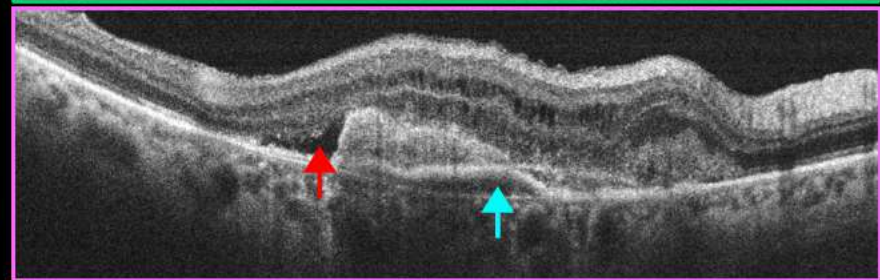
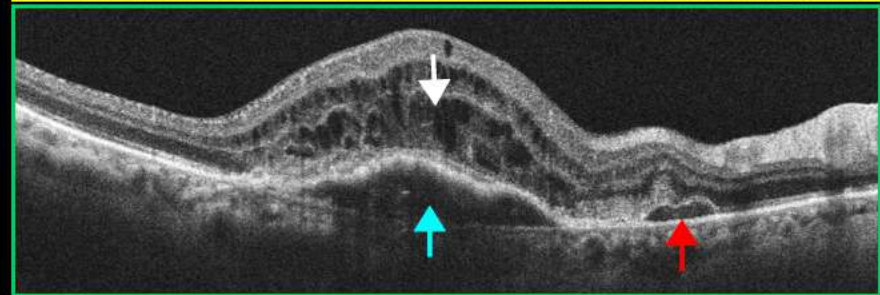
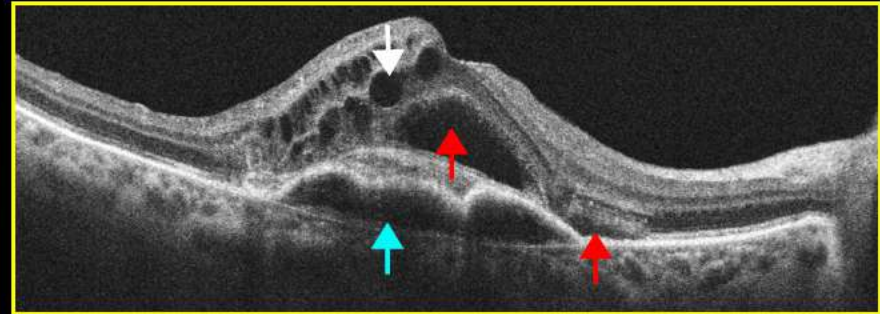
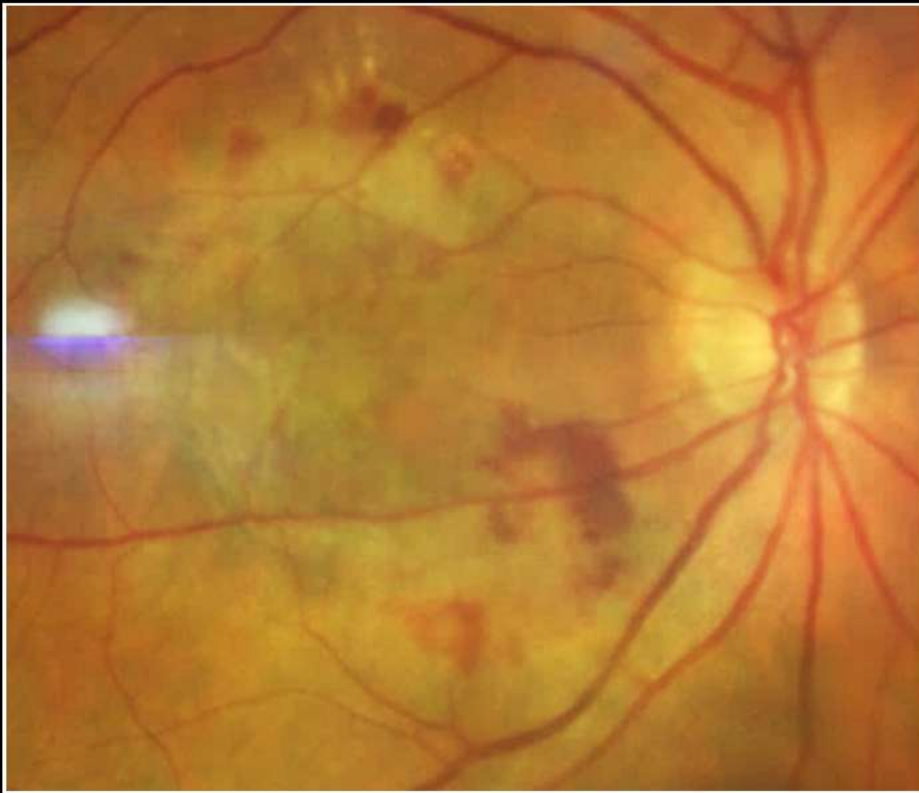
Hemorrhage

EARLY DETECTION AND PROMPT TREATMENT OF EXUDATION IS CRITICAL TO MAXIMIZE VISUAL OUTCOMES!!!



Exudative AMD OCT Features

FLUID AT ANY LEVEL (intraretinal, **subretinal**, **subRPE**)

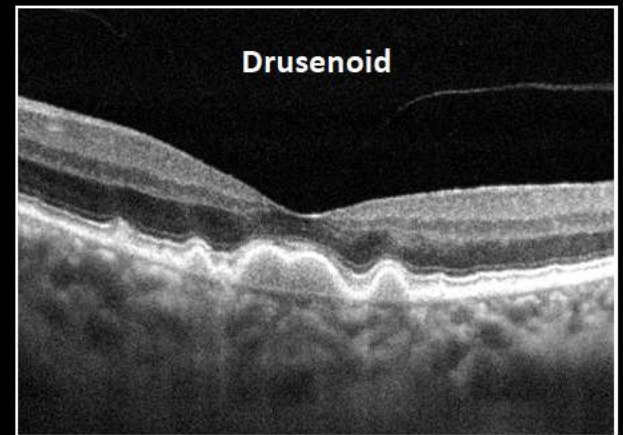
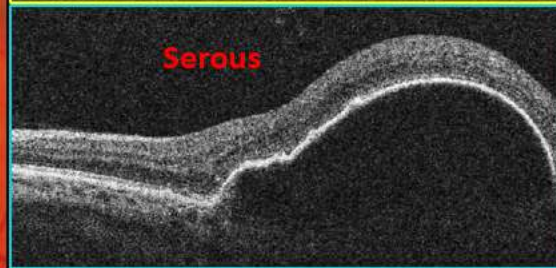
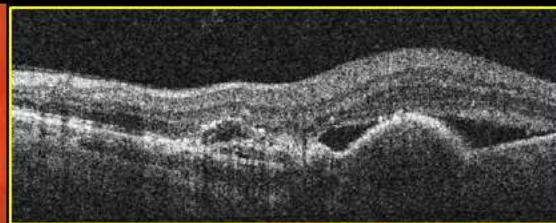
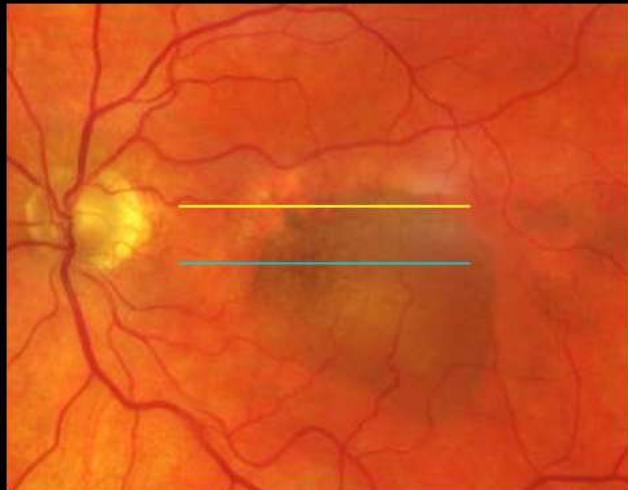
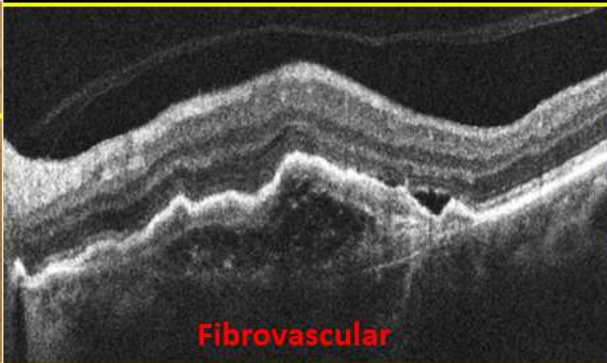
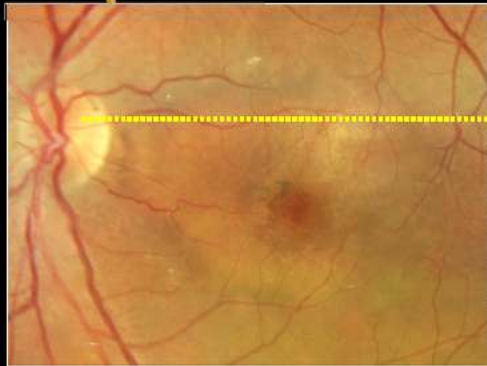


EARLY DETECTION AND PROMPT TREATMENT OF EXUDATION IS CRITICAL TO MAXIMIZE VISUAL OUTCOMES!!!



Subtypes of RPE Detachments (PEDs)

fibrovascular, hemorrhagic, serous, drusenoid

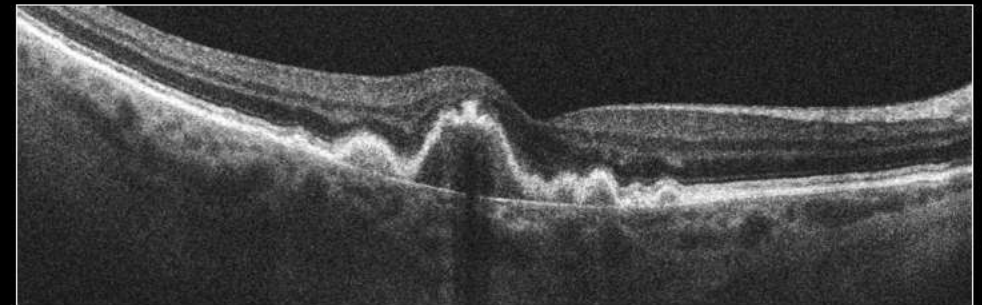
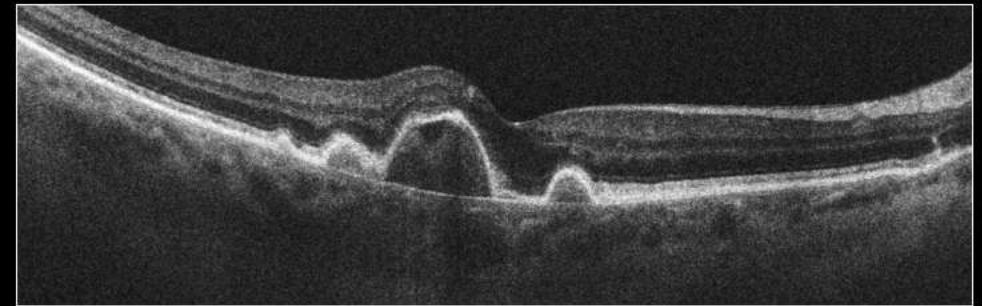
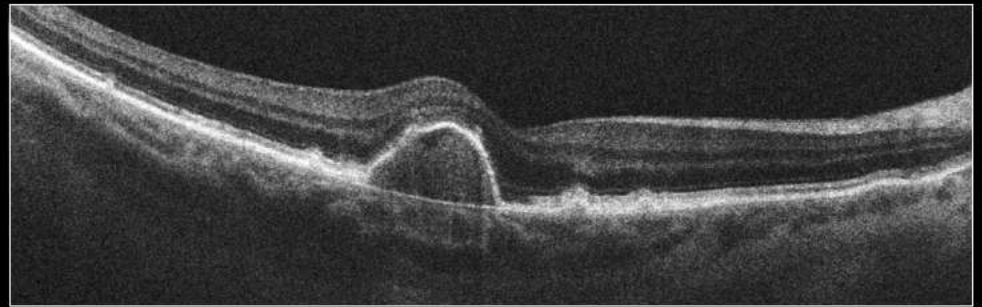




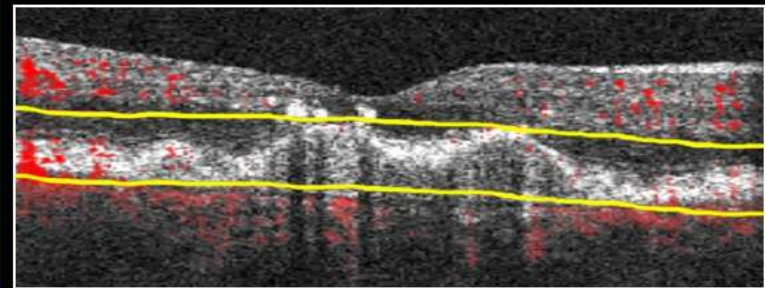
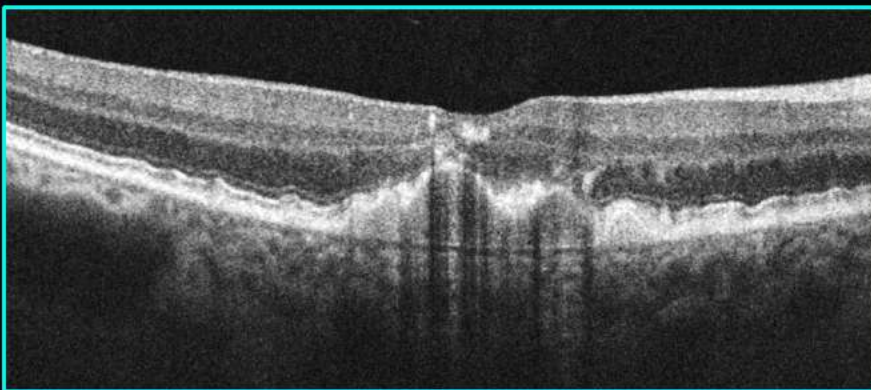
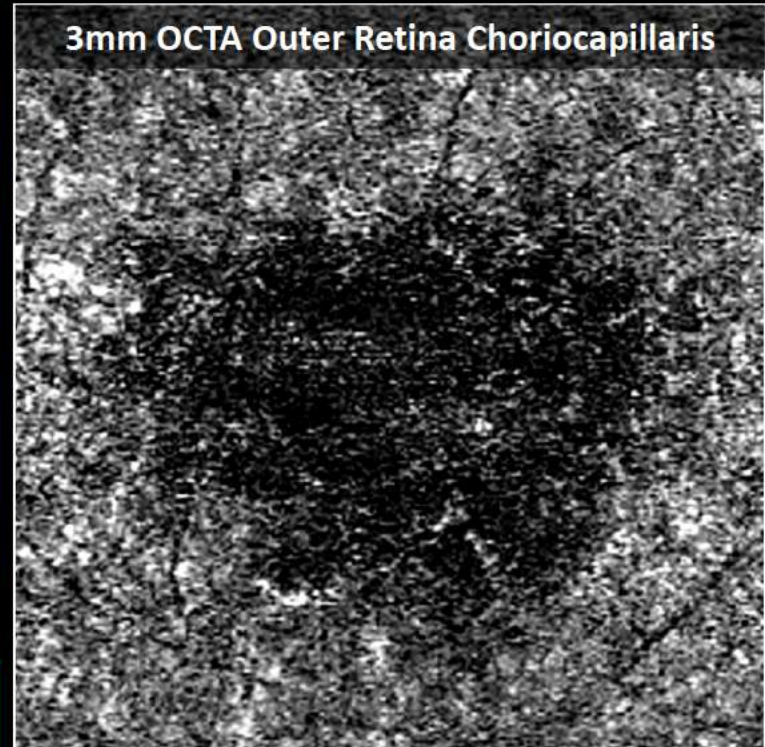
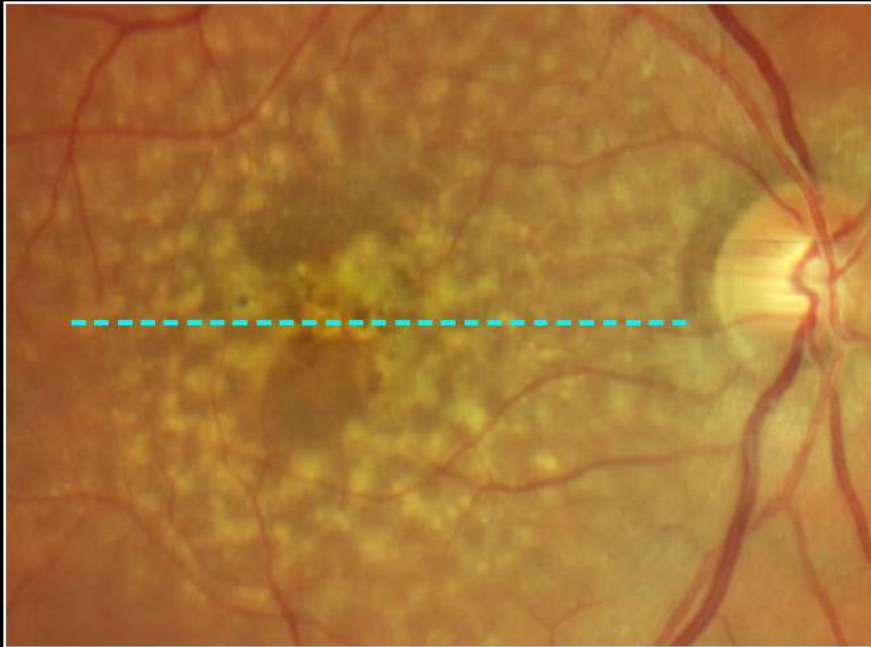
Subtypes of RPE Detachments (PEDs)

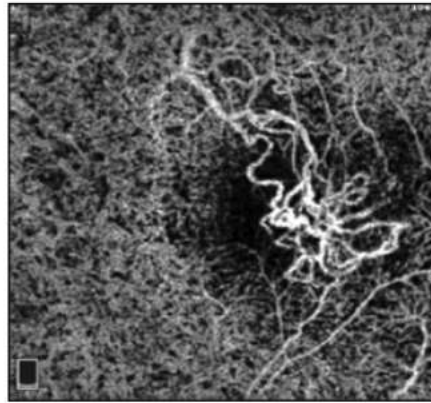
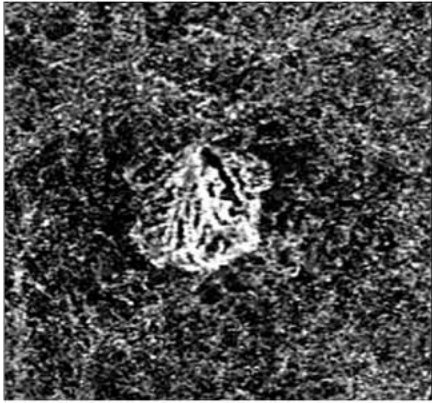
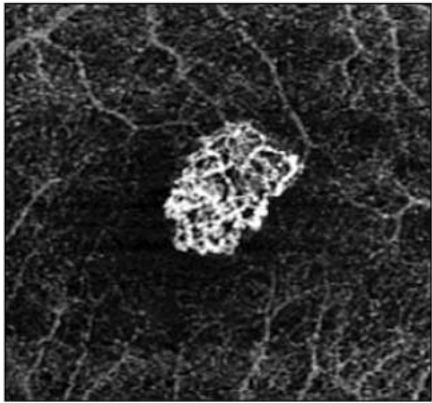
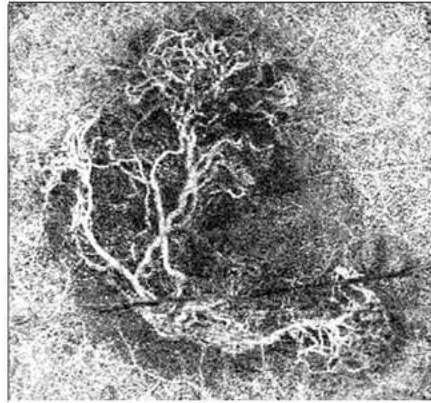
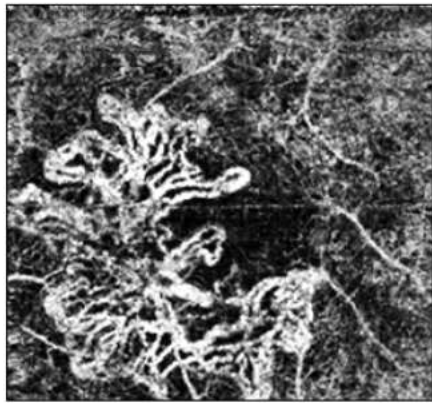
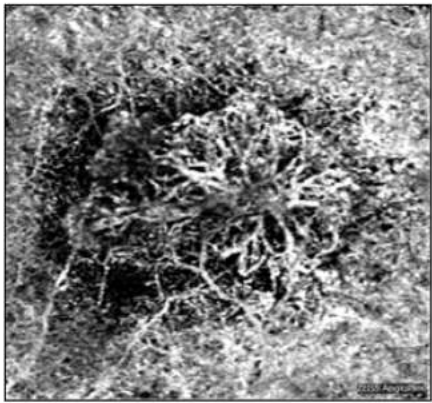


BEWARE of presumed drusenoid PEDs with non-homogenous (or non-uniform) variable internal reflectivity!



USING OCTA TO CONFIRM THAT DRUSENOID PED IS **AVASCULAR**!



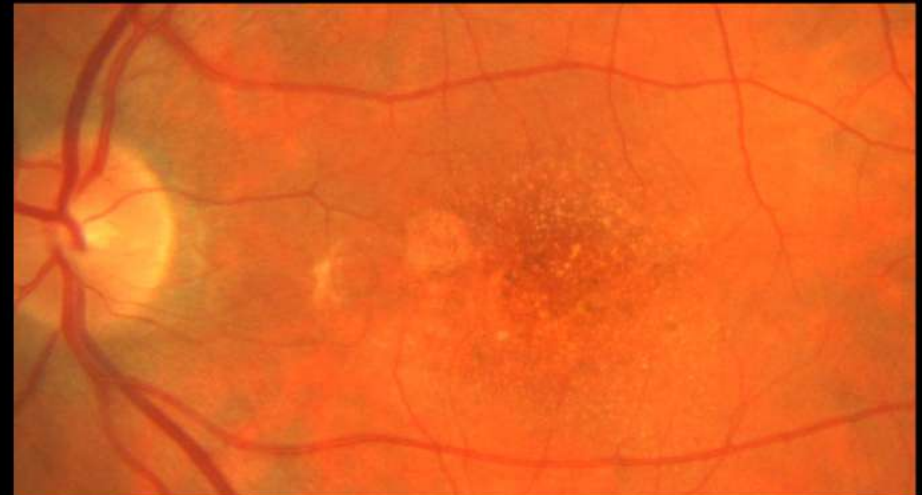
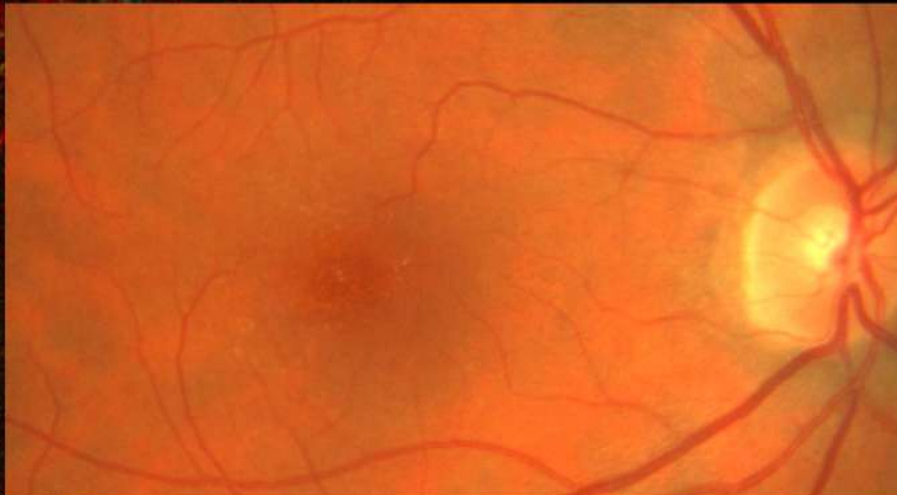


The Many Faces of Neovascular AMD via OCTA!

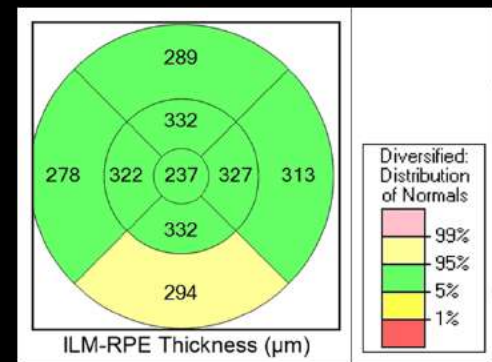
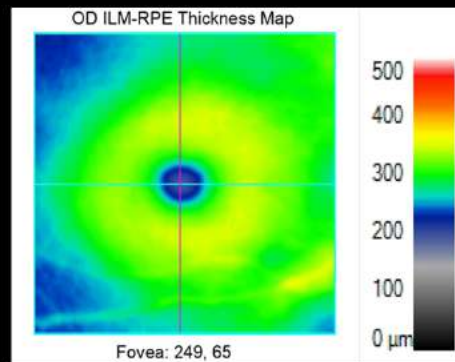
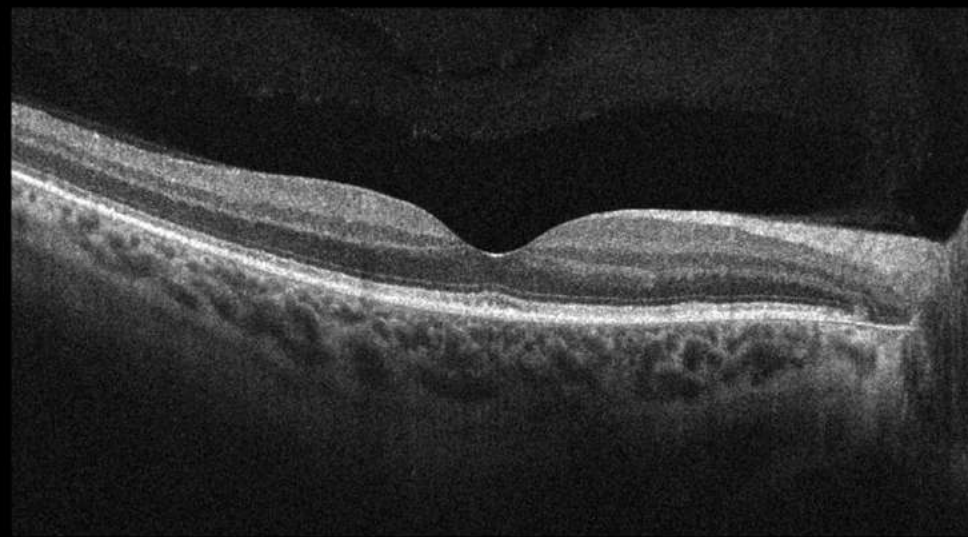
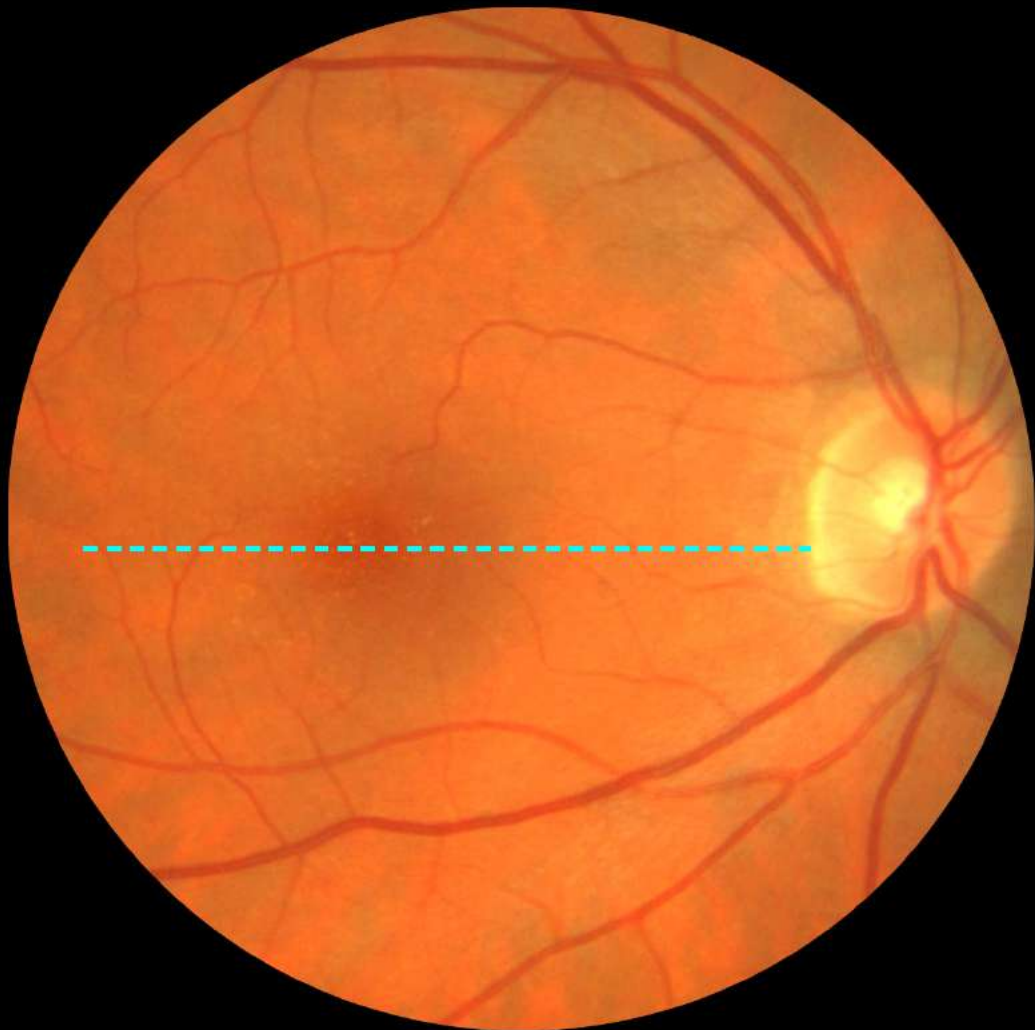
DON'T WAKE THE SLEEPING DRAGON

68yo male

- CC: **Routine exam**, no visual complaints
- Oc Hx:
 - **Dry AMD x 5 years OU**, taking AREDS 2
 - Cataract NS 1+ OU
- Med Hx:
 - HTN, Type 2 DM
 - Never smoker
- Vision: BCVAs @dist
 - OD 20/20
 - **OS 20/40+1**



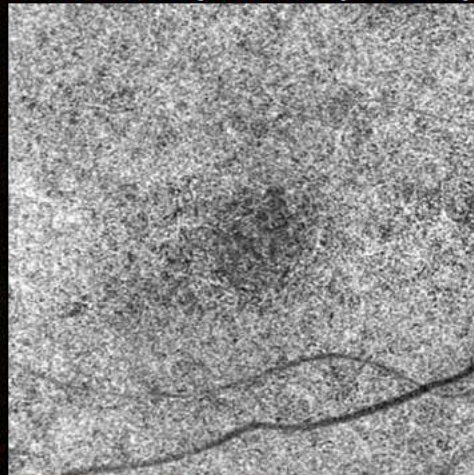
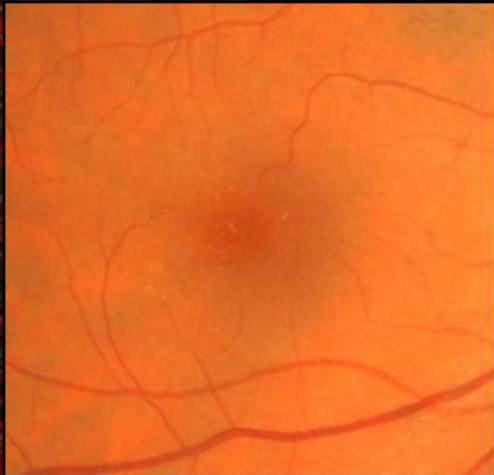
DON'T WAKE THE SLEEPING DRAGON



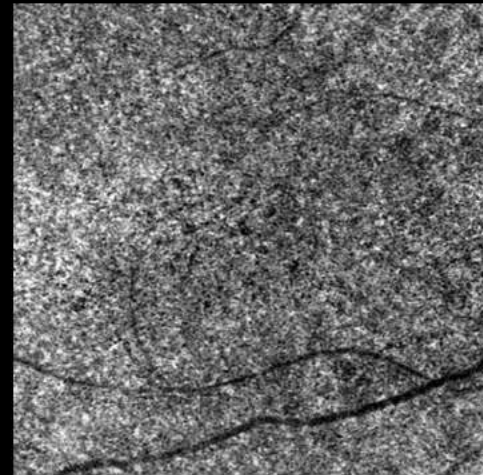
DON'T WAKE THE SLEEPING DRAGON

OCT Angiography 6mm Macula OD

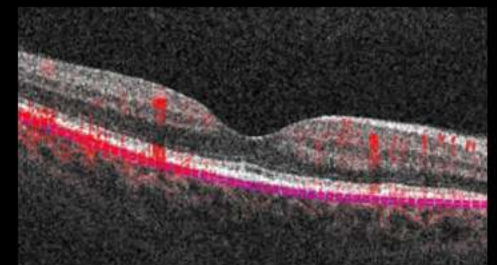
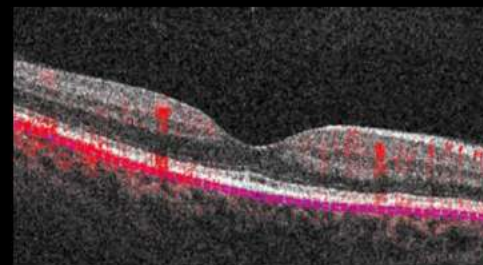
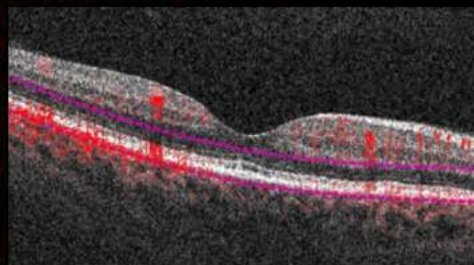
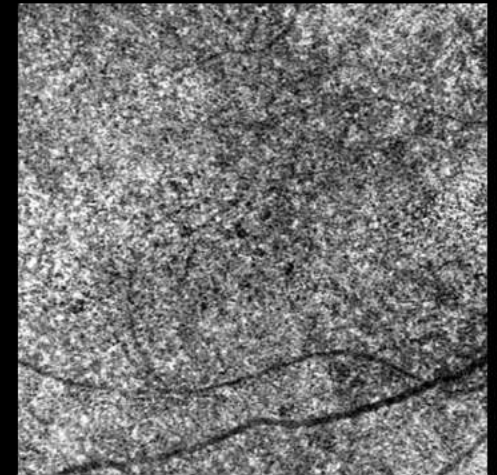
Outer Retina
Choriocapillaris (ORCC)



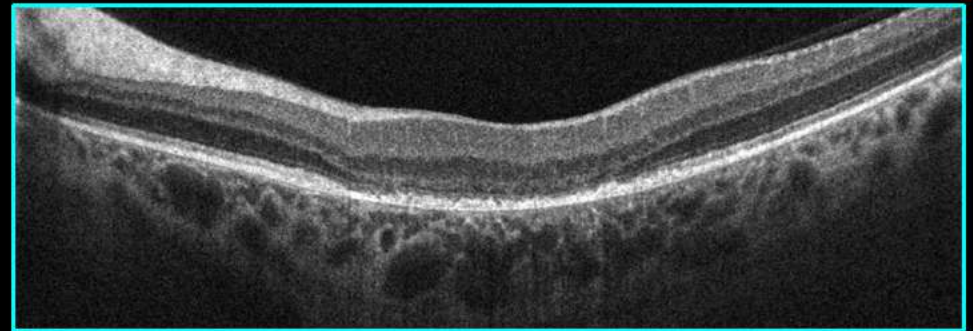
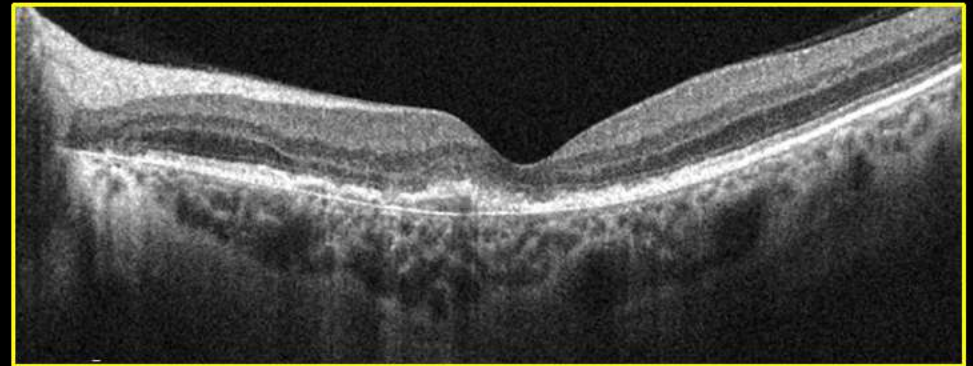
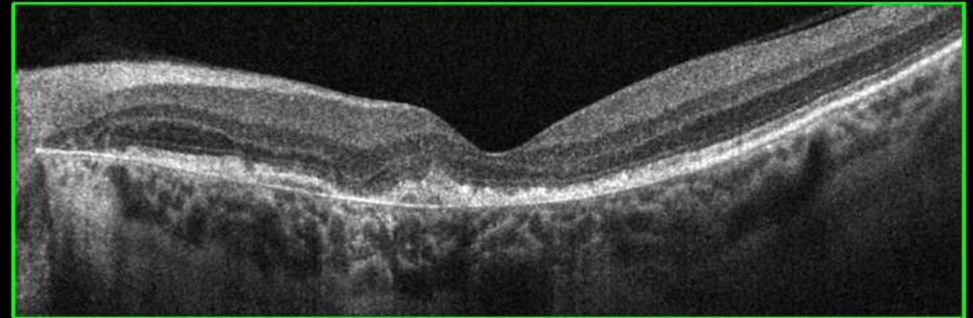
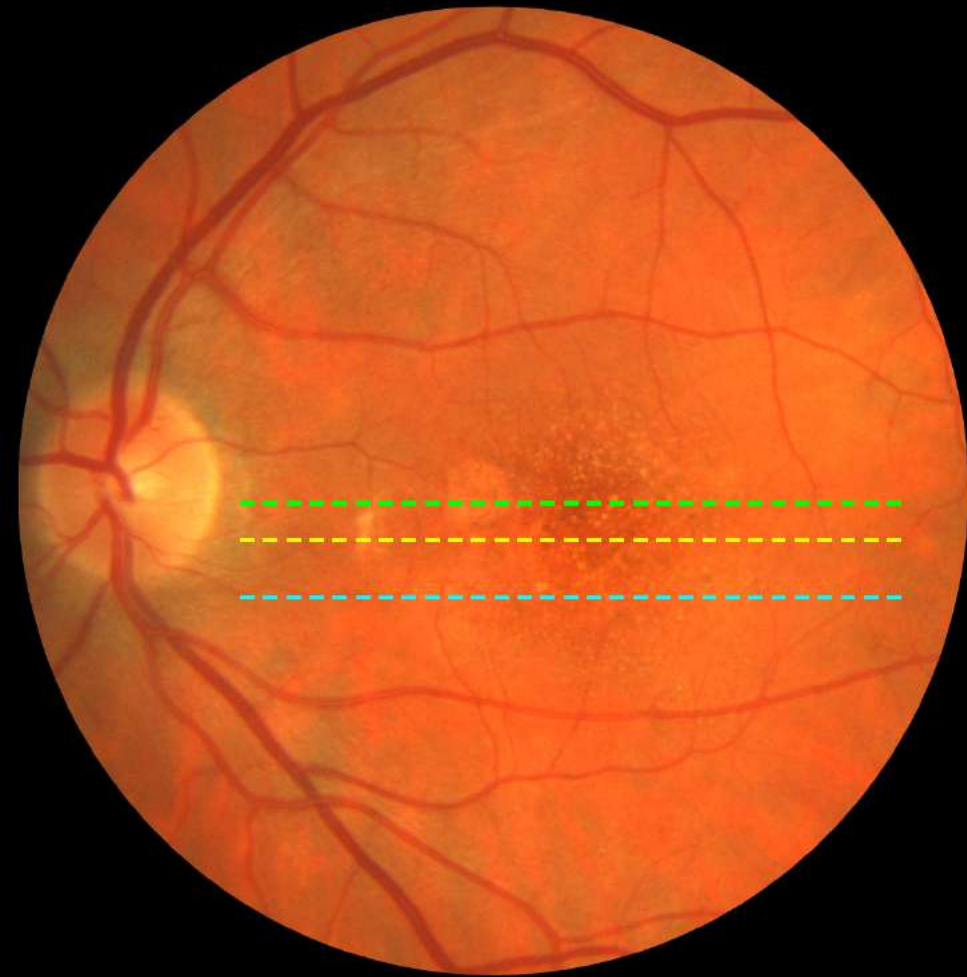
Sub RPE



Choriocapillaris



DON'T WAKE THE SLEEPING DRAGON

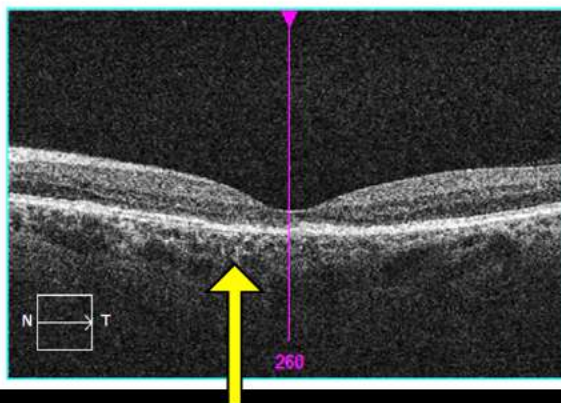
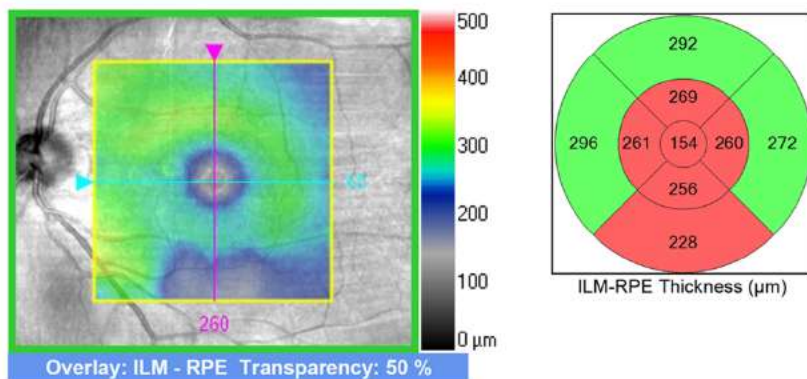


DON'T WAKE THE SLEEPING DRAGON

Last exam 1 year ago

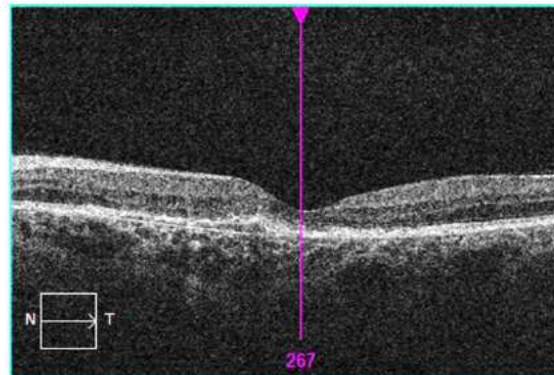
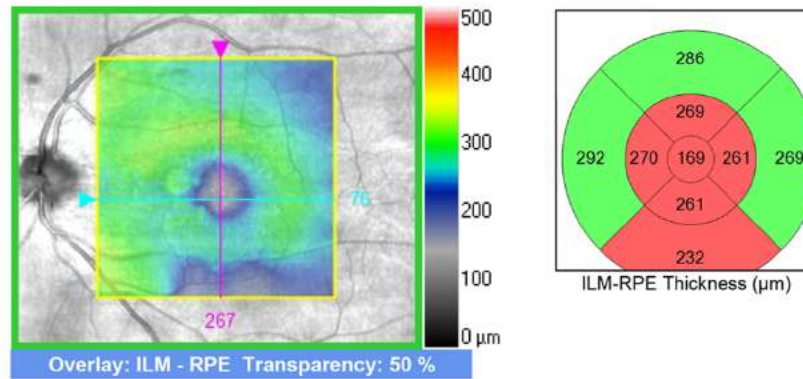
Present exam

Macula Thickness : Macular Cube 512x128



No PED

Macula Thickness : Macular Cube 512x128

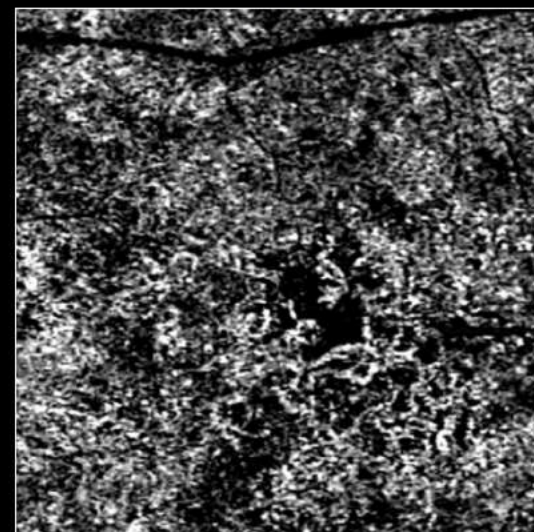
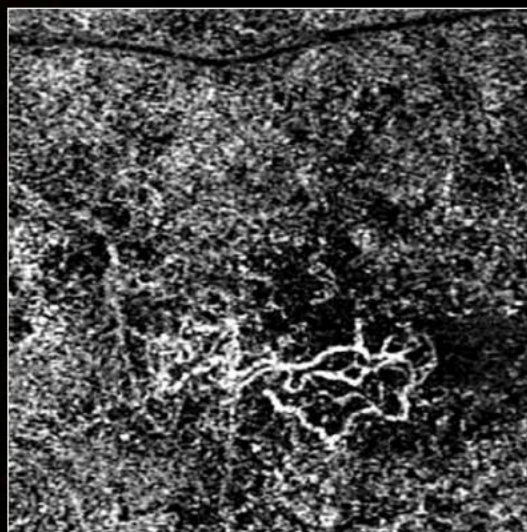
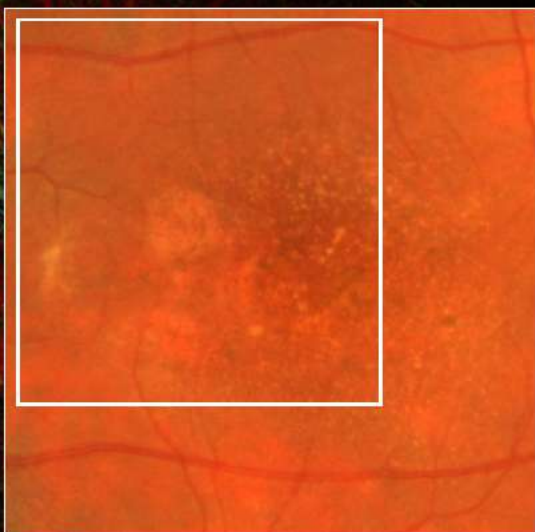


DON'T WAKE THE SLEEPING DRAGON

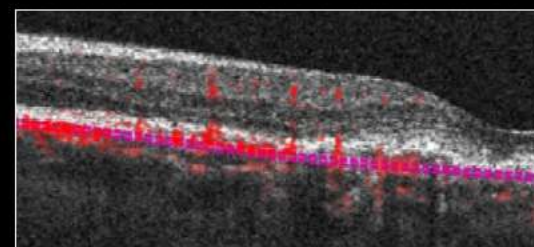
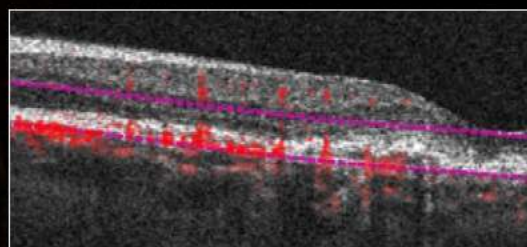
OCT Angiography 3mm Macula OS

Outer Retina
Choriocapillaris (ORCC)

Choriocapillaris



- OS Non-exudative but **neovascular AMD**
- Amsler, FU in 3 months



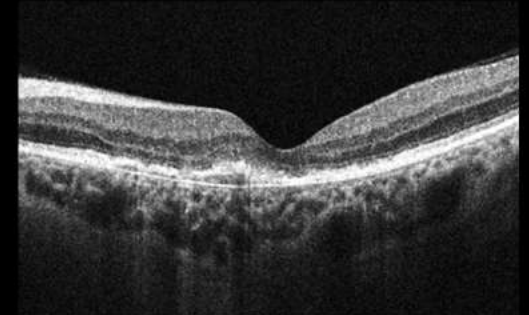
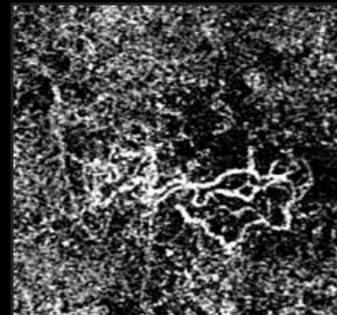
DON'T WAKE THE SLEEPING DRAGON

Assessment

- OD Early stage non-exudative AMD
- OS Non-exudative AMD with probably quiescent CNV

Management

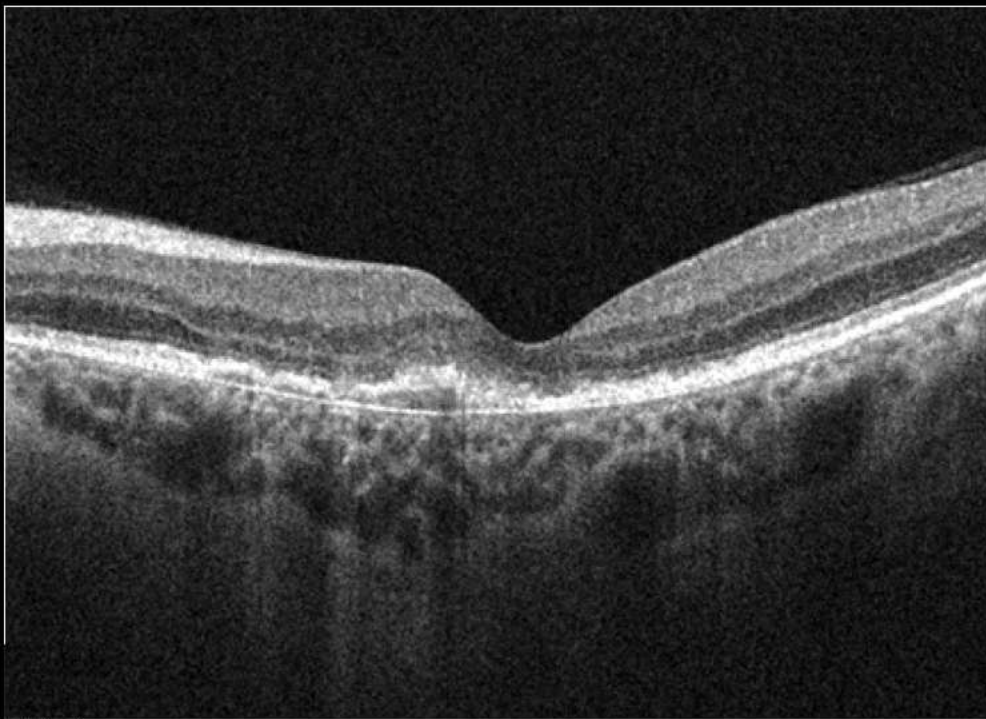
- FU 3 months
- Cont. amsler & AREDS 2



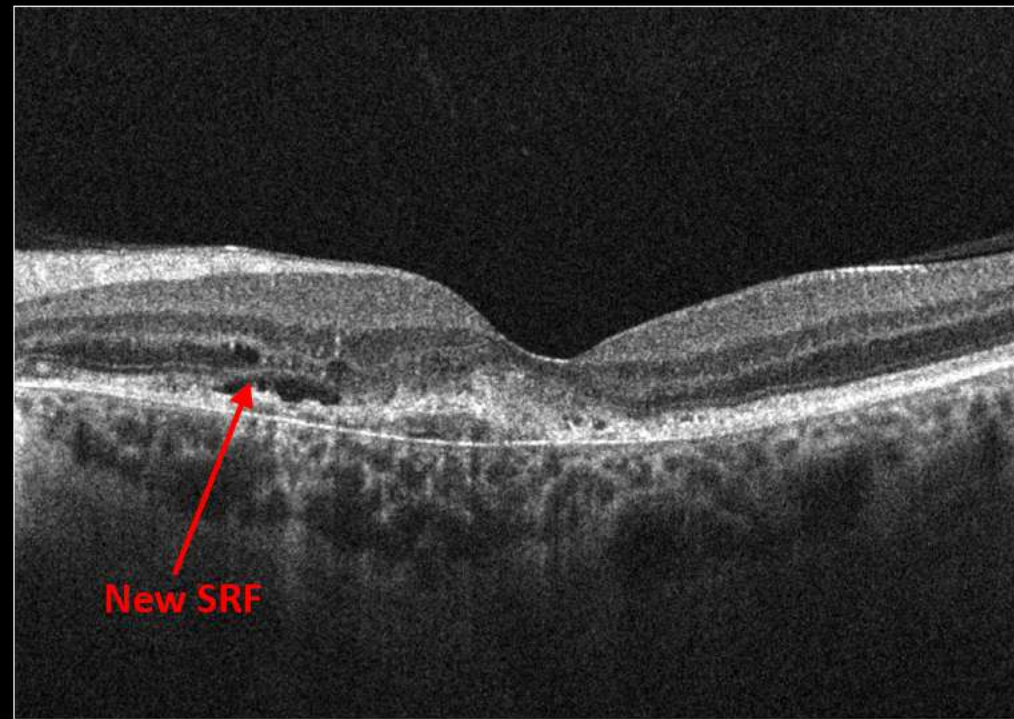
DON'T WAKE THE SLEEPING DRAGON

No shows 3 month FU appt, **returns 6 months later** (no complaints and stable VA)

Baseline



6 Month FU

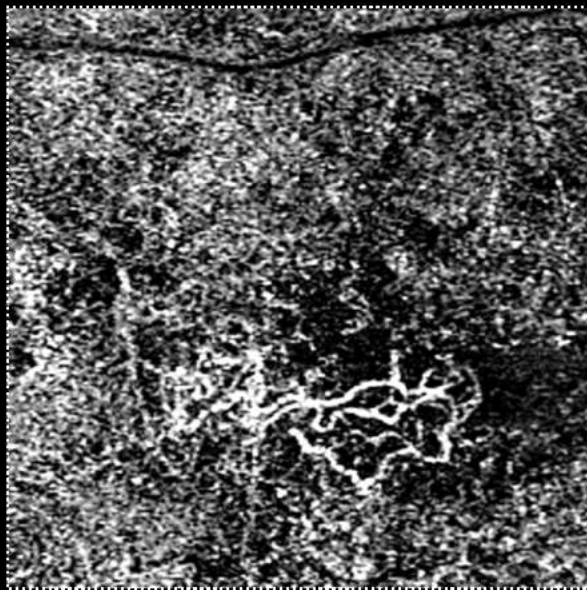


OS EXUDATIVE AMD!!!! Refer to retina for anti-VEGF

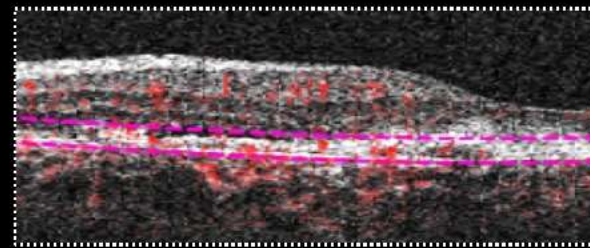
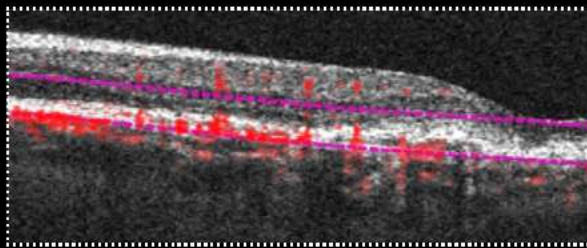
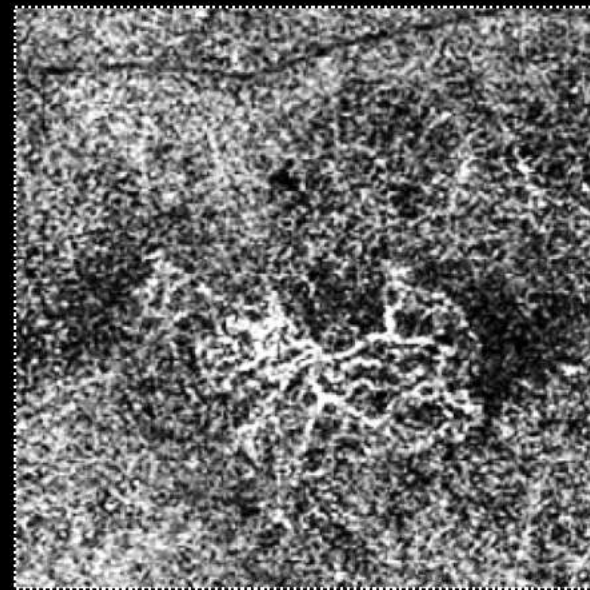
DON'T WAKE THE SLEEPING DRAGON

OCT Angiography 3mm Outer Retina Choriocapillaris OS

Baseline



6 Month FU (6mm)



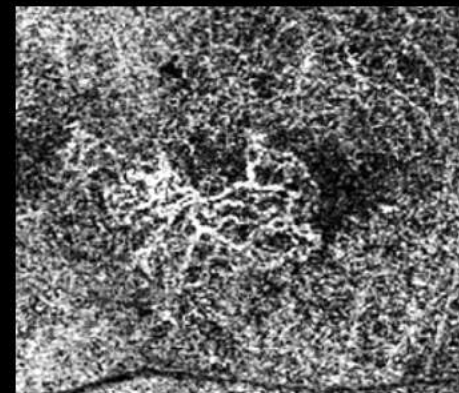
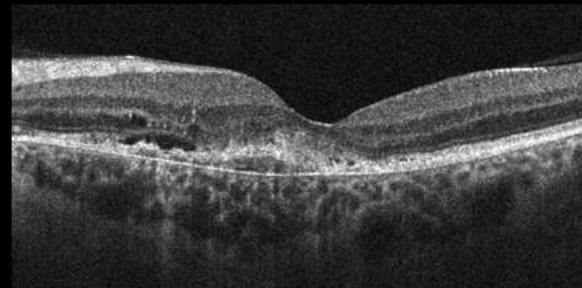
DON'T WAKE THE SLEEPING DRAGON

Assessment

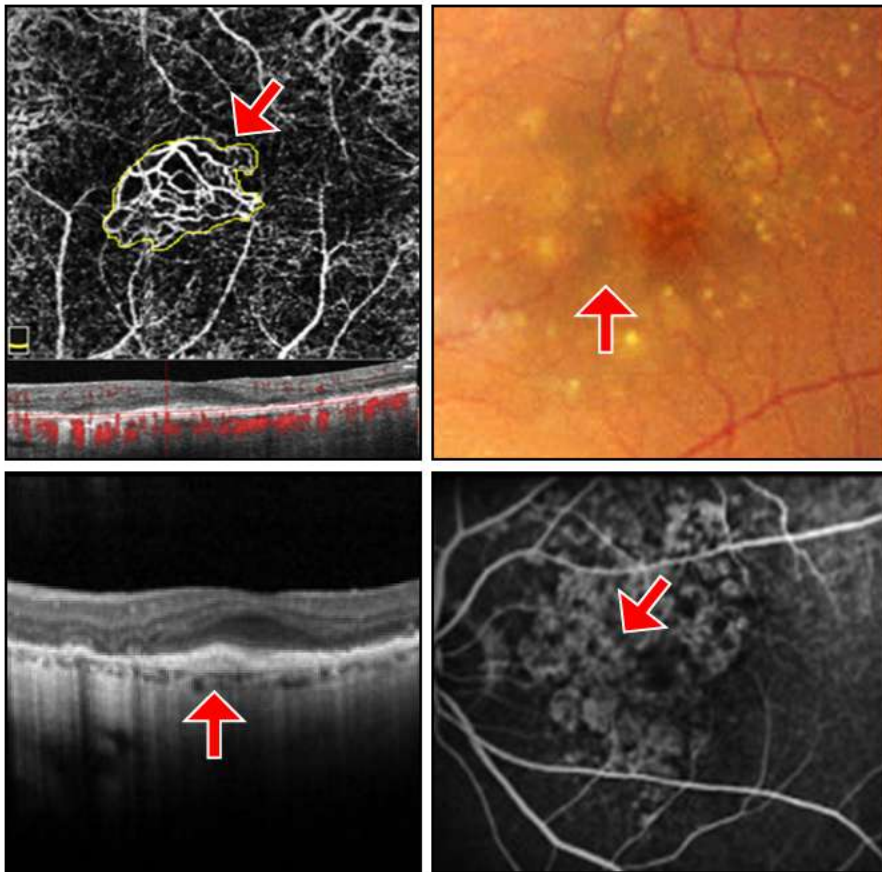
- OD Early stage non-exudative AMD
- OS **EXUDATIVE** AMD

Management

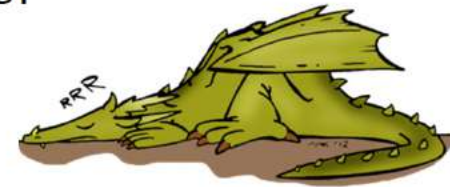
- Refer to retina for intravitreal anti-VEGF



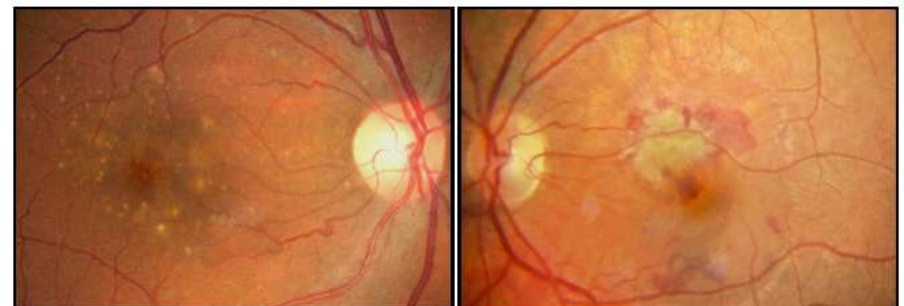
NONEXUDATIVE CNV



1. Well-defined neovascular complex via OCTA
2. No signs of exudation via ophthalmoscopy such as exudate or blood
3. No fluid via structural OCT
4. No leakage with IVFA



Present in approx. 10% of high risk AMD eyes (intermediate AMD, exudative fellow eye)



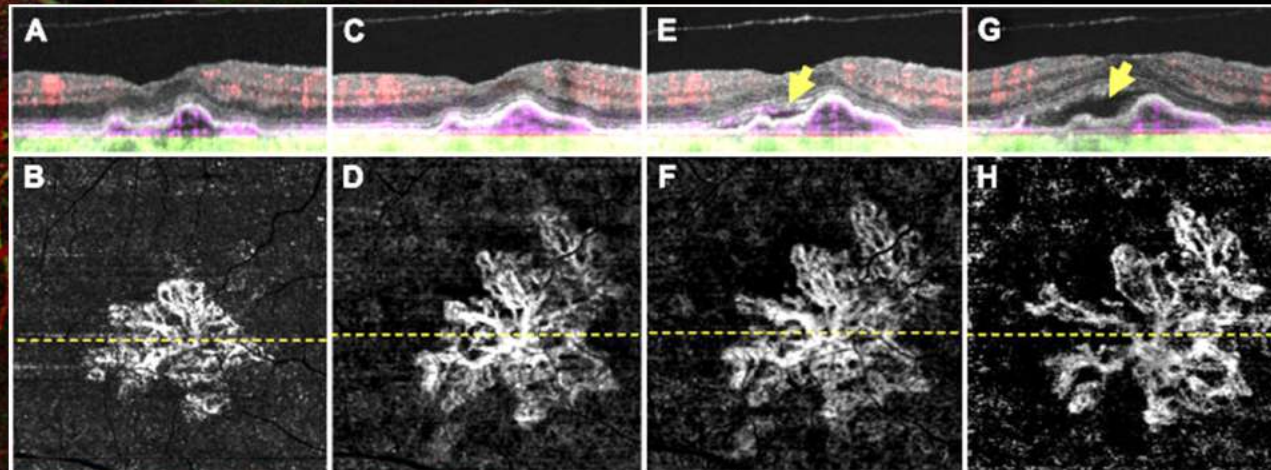
Carnevali A, et al. OCTA: A Useful Tool for Diagnosis of Treatment-Naïve Quiescent CNV. Am J Ophth. 2016.

Or C, et al. Incidence of Vascularized Drusen in Non-Exudative ARMD using SD-OCTA. ARVO 2018.

NONEXUDATIVE CNV

Prognosis

- Rate of future exudation, eyes with nonexudative CNV vs eyes without nonexudative CNV
 - **Bailey S ARVO 2017.** 60% vs 4% (5 months)
 - **De Oliveira Dias J Ophthal 2018.** 21% vs 4% (12 months)
 - 15x greater risk of exudation after detection of nonexudative CNV



**EYES WITH
NONEXUDATIVE CNV
ARE AT HIGH RISK FOR
EXUDATIVE
CONVERSION!**

Bailey S et al. Early detection of CNV with OCTA. ARVO 2017.

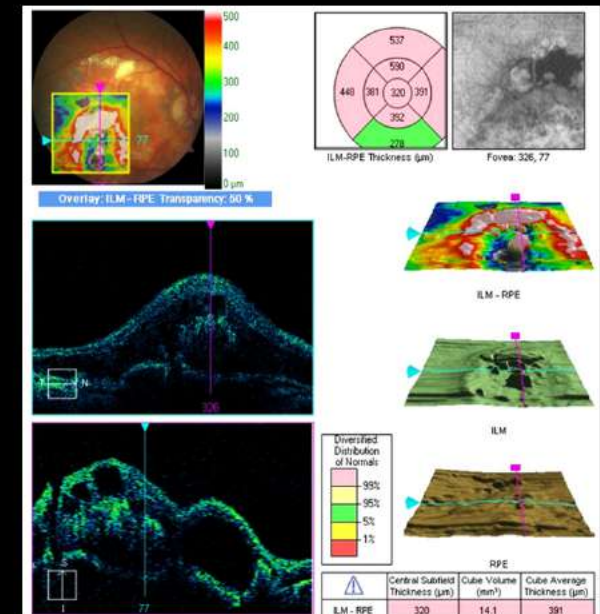
De Oliveira Dias JR, et al. Natural History of Subclinical Neovascularization in Nonexudative ARMD Using SS-OCTA. Ophthalmol 2018.

CASE IN POINT!

87yo Hispanic female

- History of exudative AMD OD S/P 12 Lucentis injections-wants a second opinion of whether or not she should continue injections OD
- Med HX remarkable for DM type 2
- VAs OD HM, OS 20/40

Right Eye

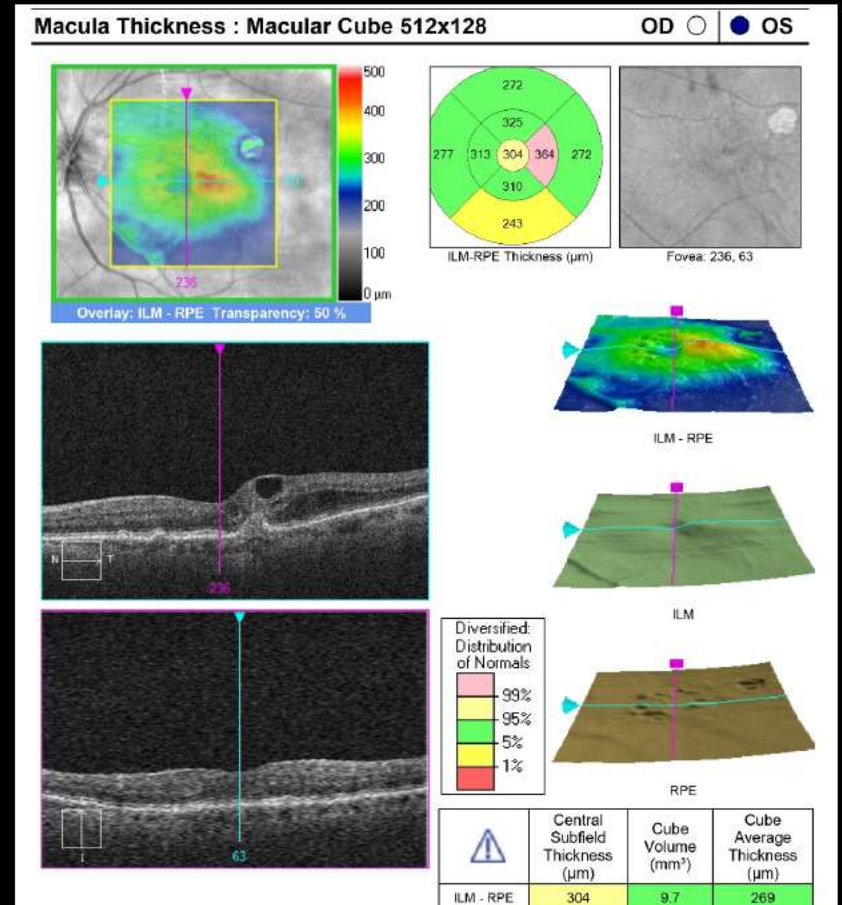


Left eye = 20/40



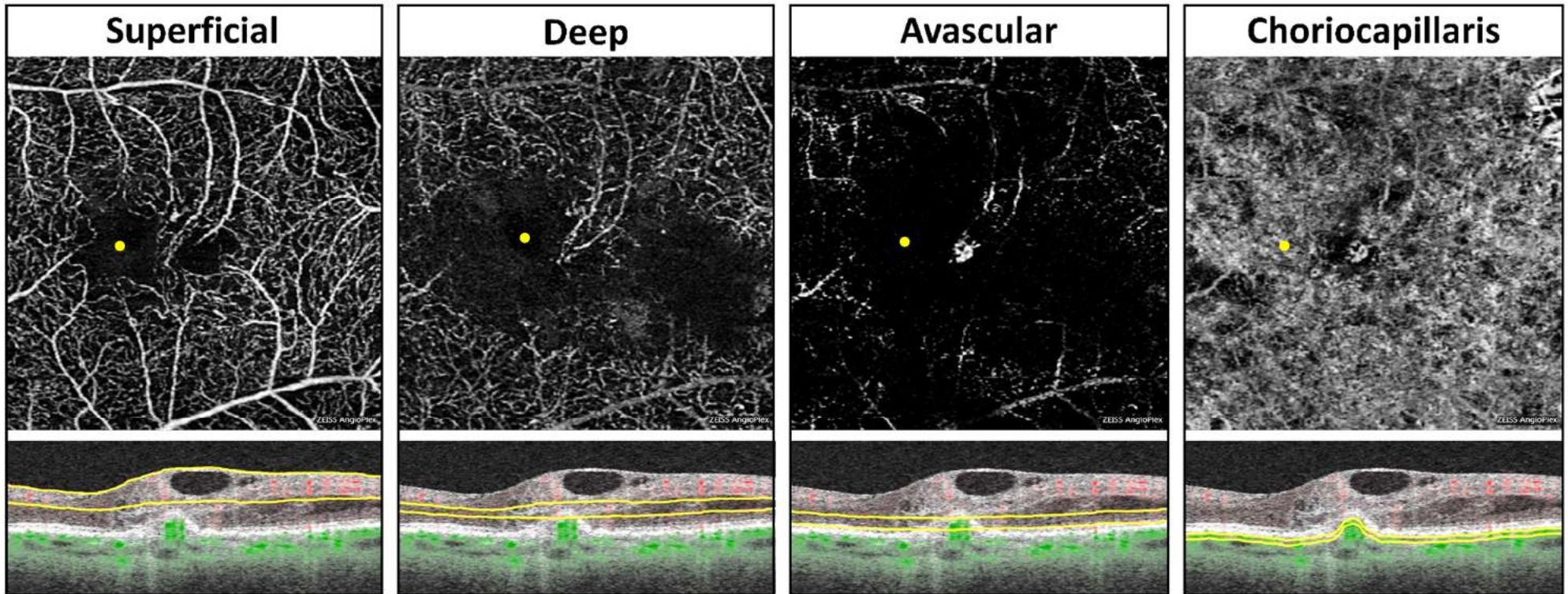
**What classification/
stage of AMD is
present OS?**

Small solid PED temporal fovea with overlying/adjacent intraretinal fluid



CHOROIDAL NEOVASCULARIZATION

AMD- Type 3 RAP (Retinal Angiomatous Proliferation)



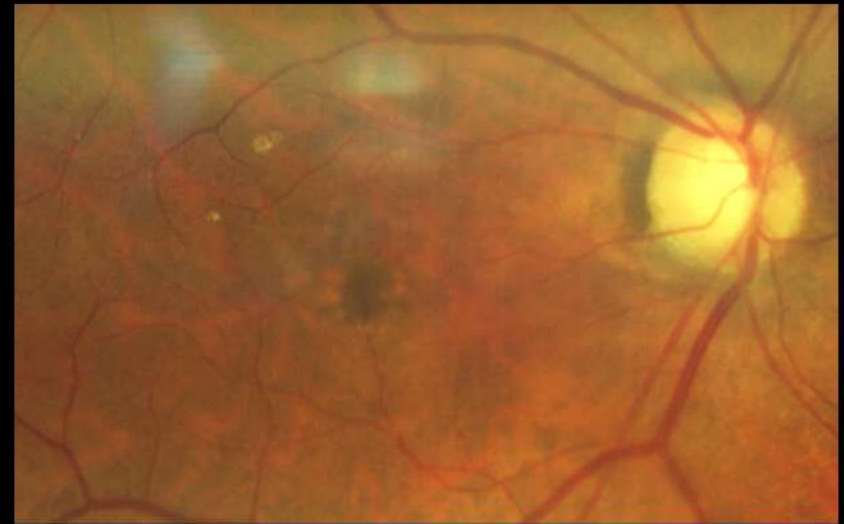
CHOROIDAL NEOVASCULARIZATION

AMD- Type 3 RAP (Retinal Angiomatous Proliferation)

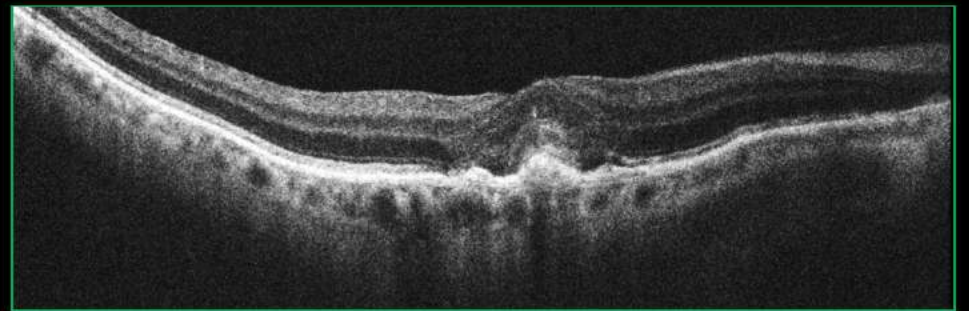
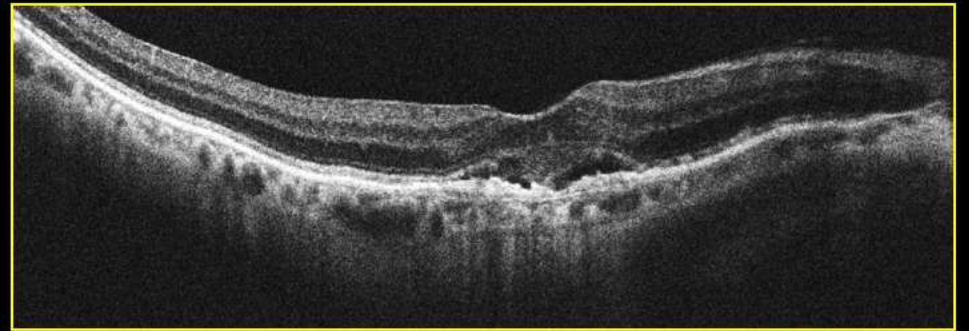
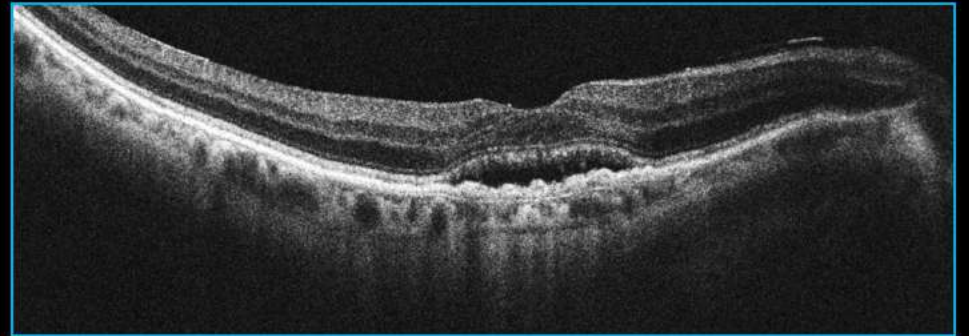
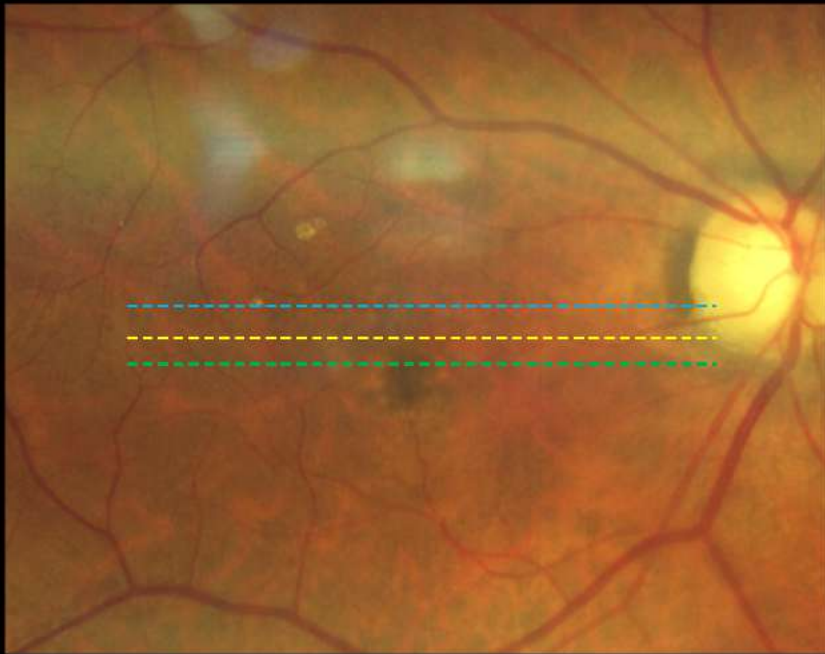
IT'S THE LITTLE THINGS THAT MATTER MOST

80yo female

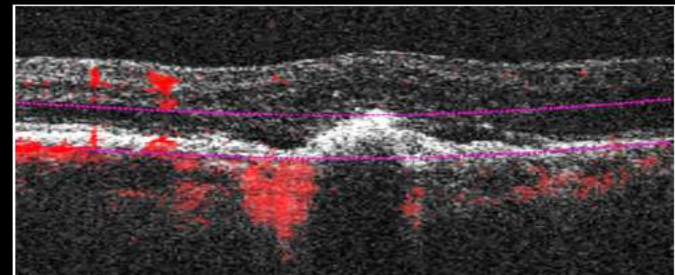
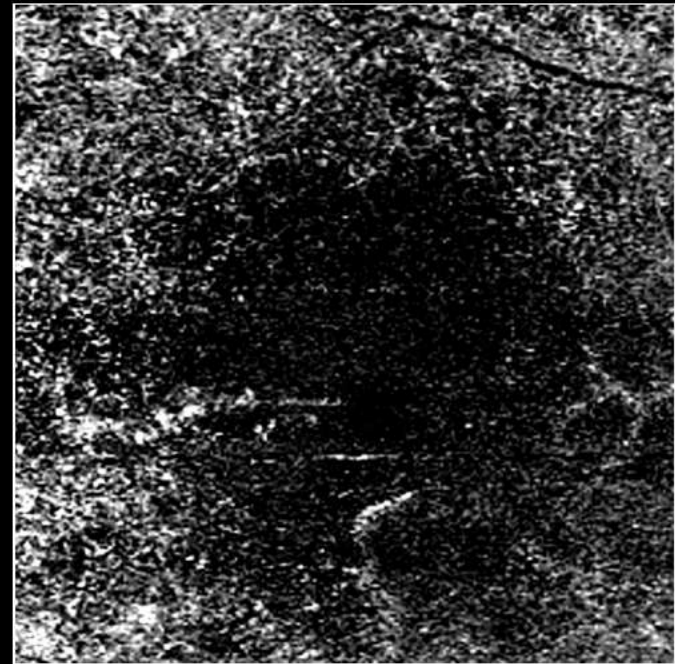
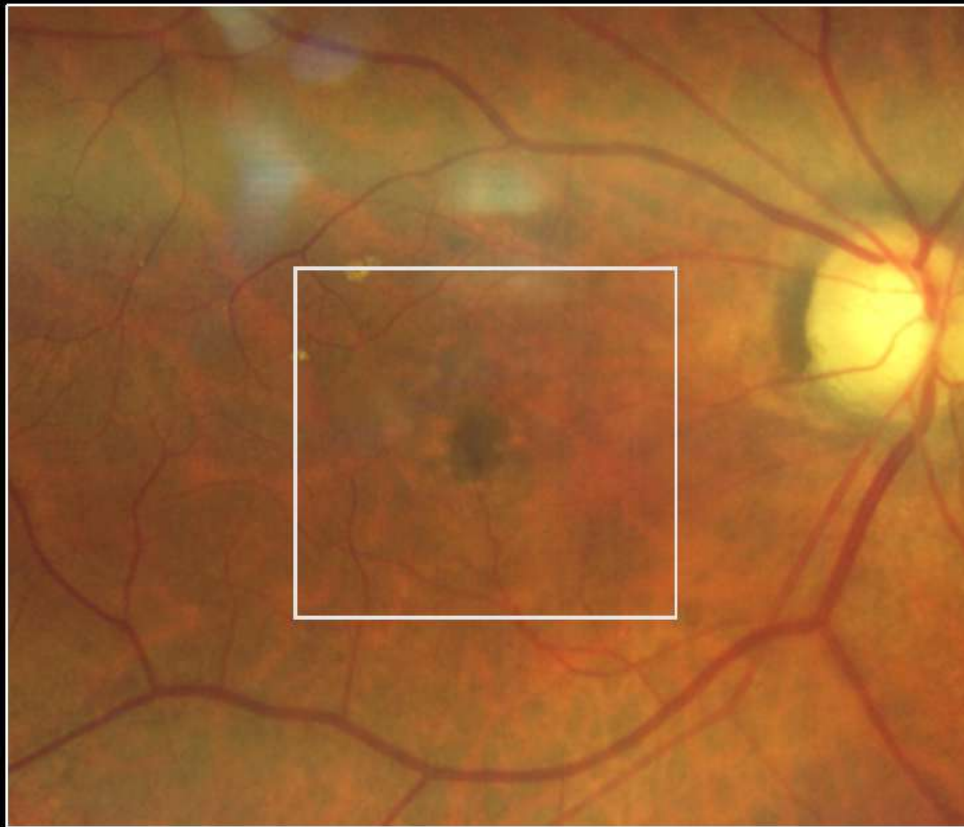
- CC: No visual complaints
- Oc Hx:
 - **Dry AMD OU**, taking AREDS 2
 - **CSCR OD x 1 yr** – followed by retinal specialist, no tx done thus far
 - **FTMH repair OS 20+ yrs ago**
 - Cat surg OS
- Med Hx:
 - HTN, Type 2 DM, chol
 - Former light smoker
- Vision: BCVAs @dist
 - **OD 20/50+2**
 - **OS 20/70+1**



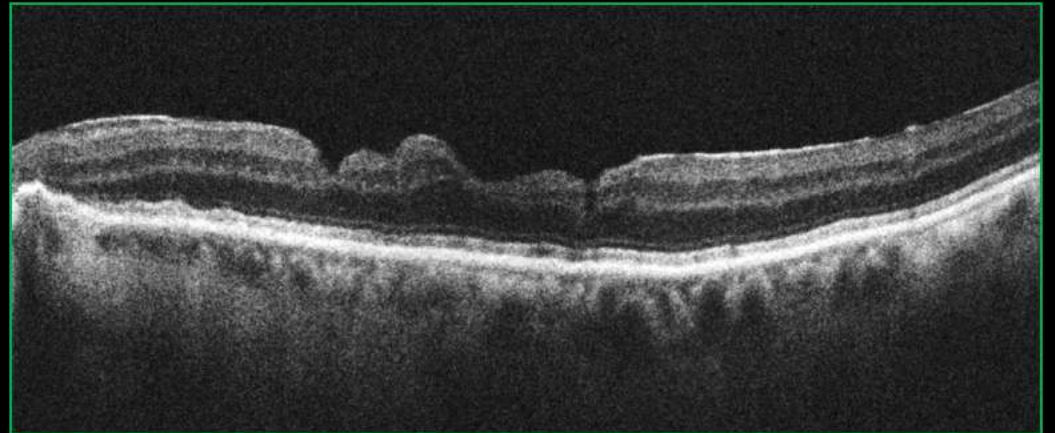
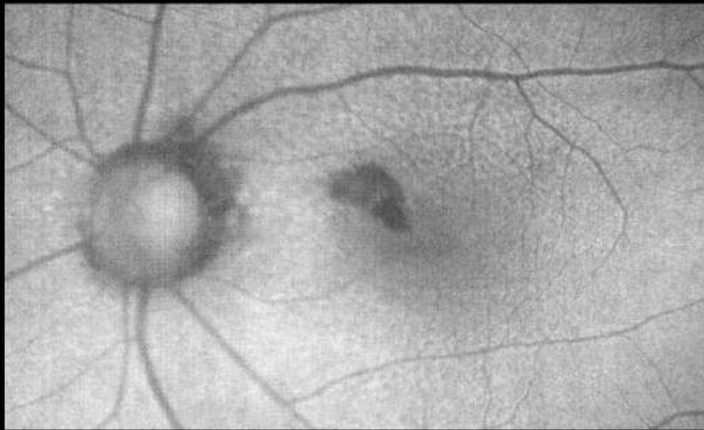
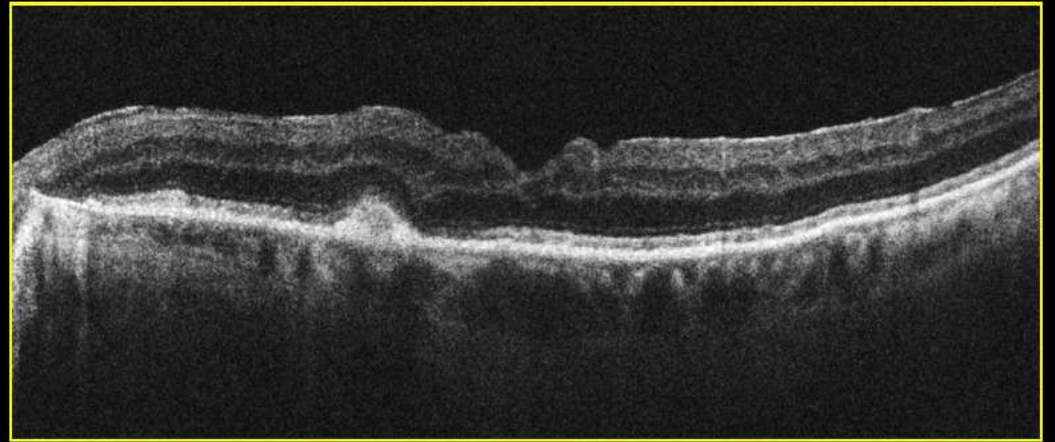
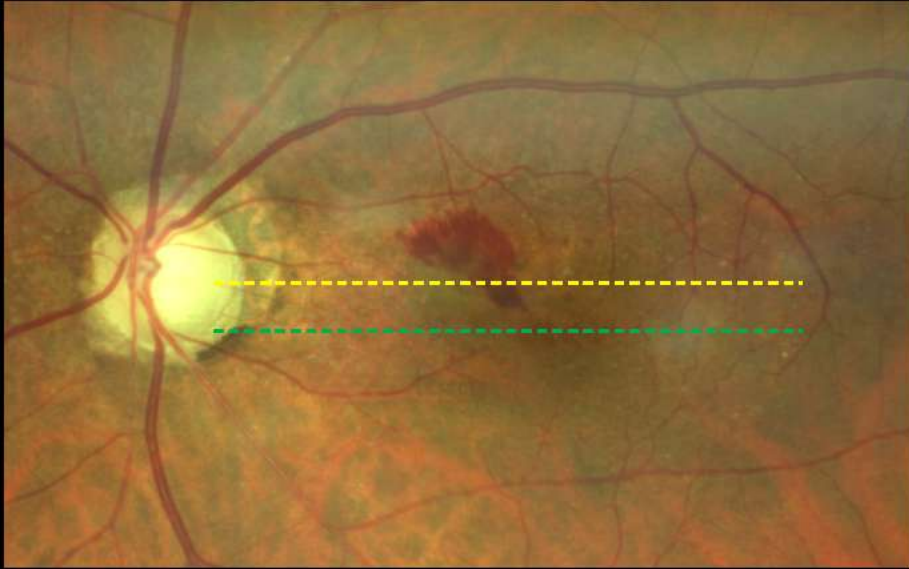
IT'S THE LITTLE THINGS THAT MATTER MOST



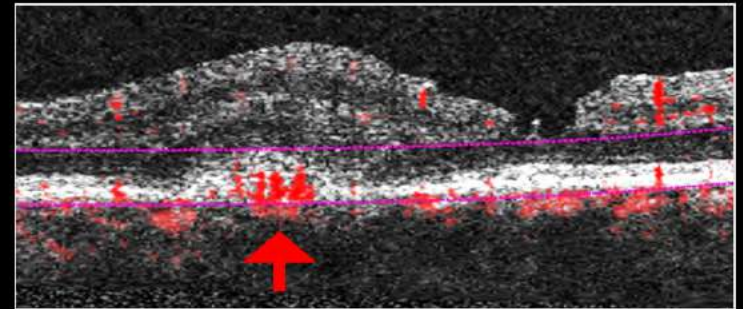
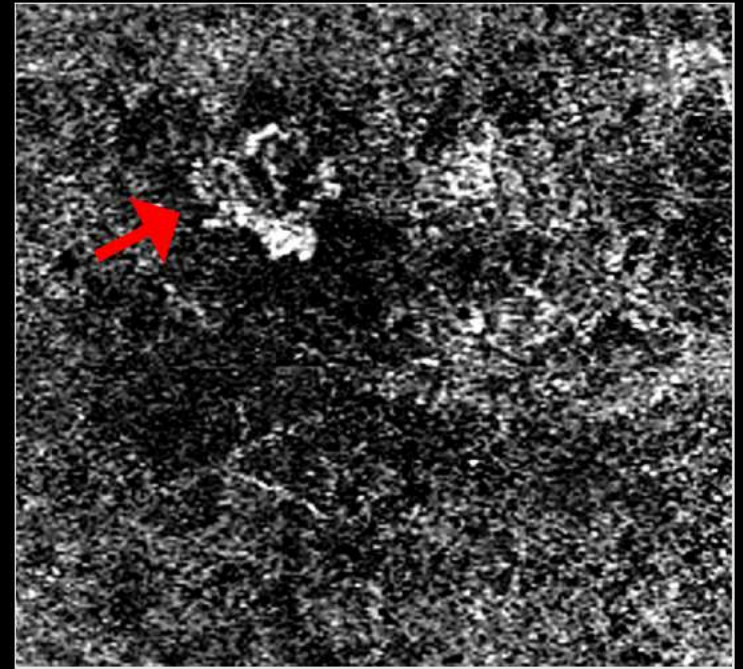
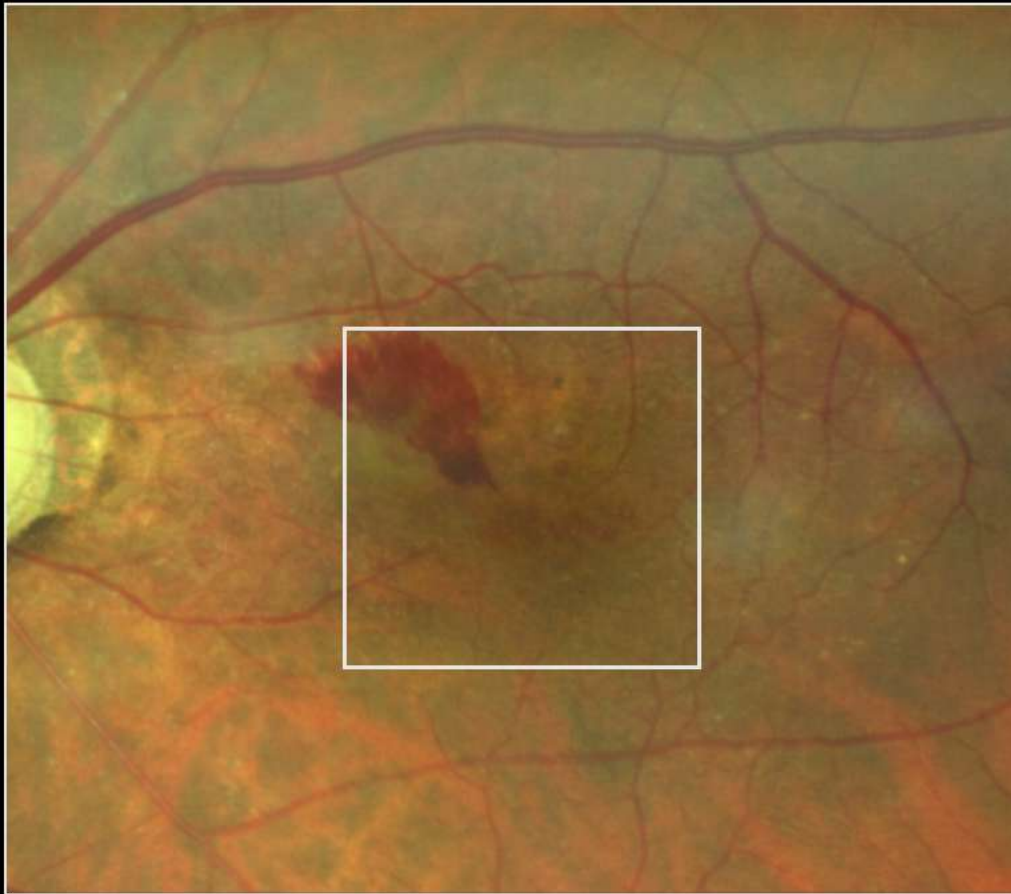
IT'S THE LITTLE THINGS THAT MATTER MOST



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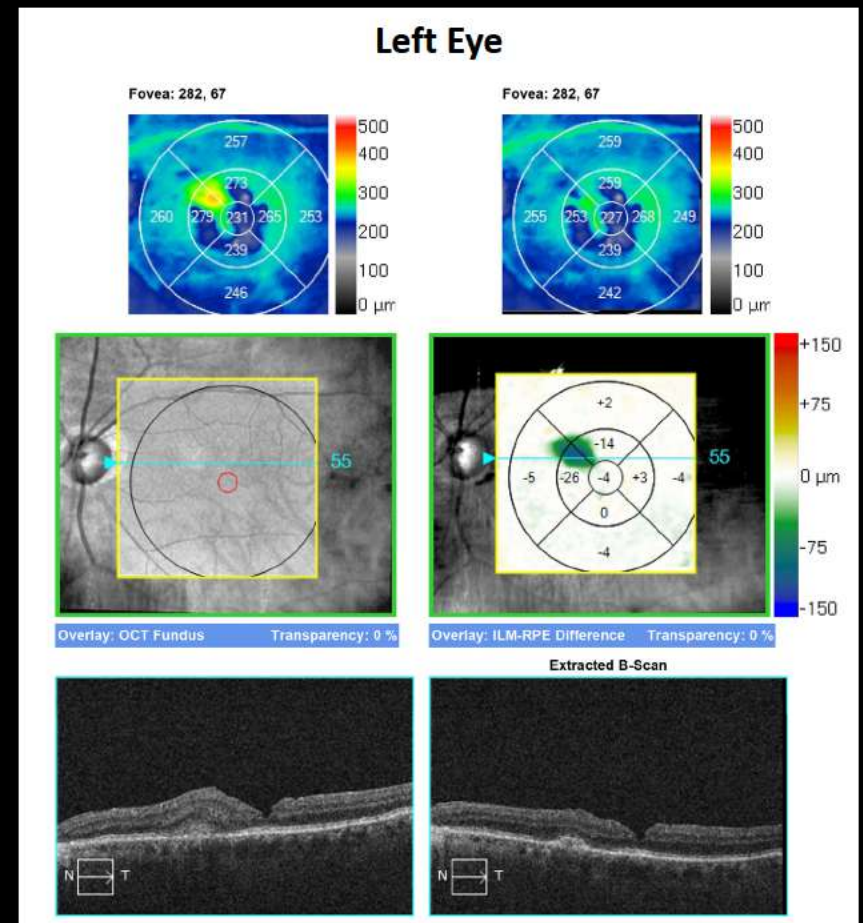
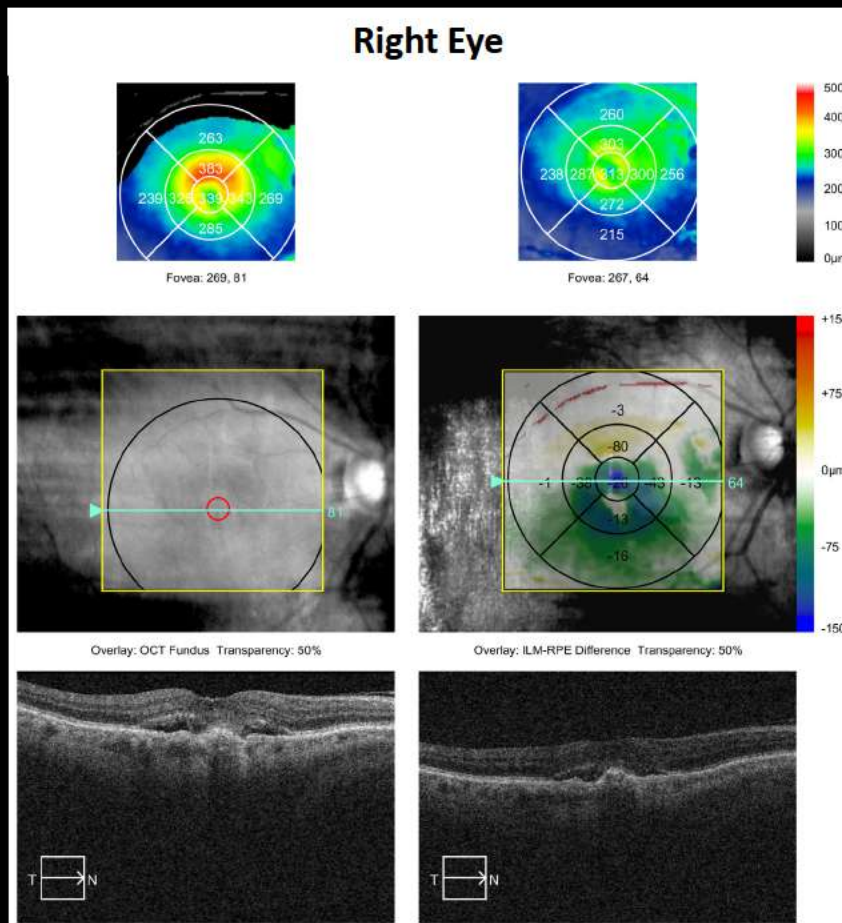


IT'S THE LITTLE THINGS THAT MATTER MOST



IT'S THE LITTLE THINGS THAT MATTER MOST

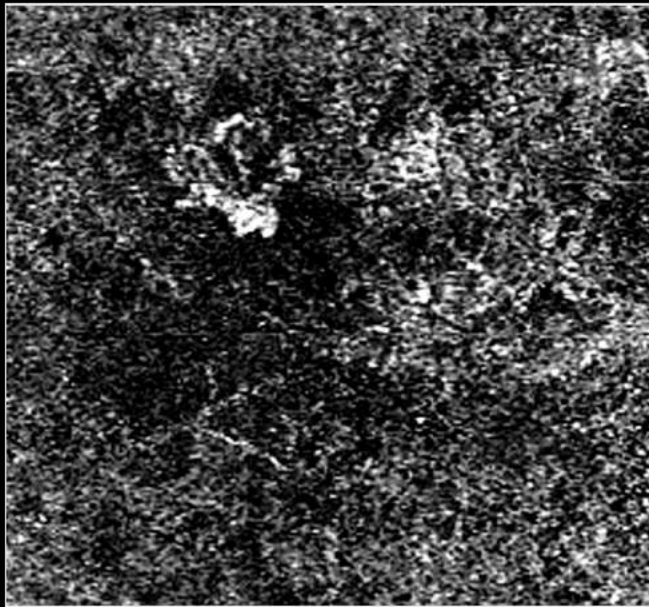
Macular change analysis before & after 3 bevacizumab injections OU



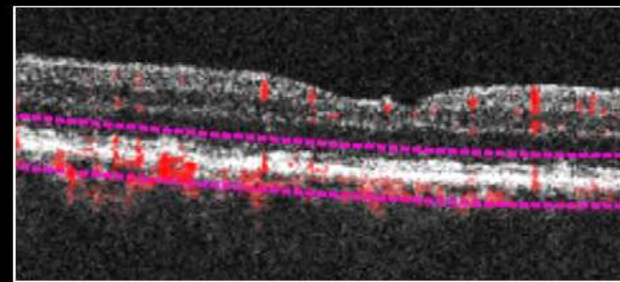
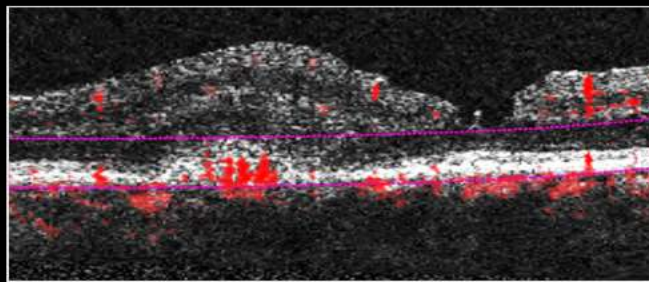
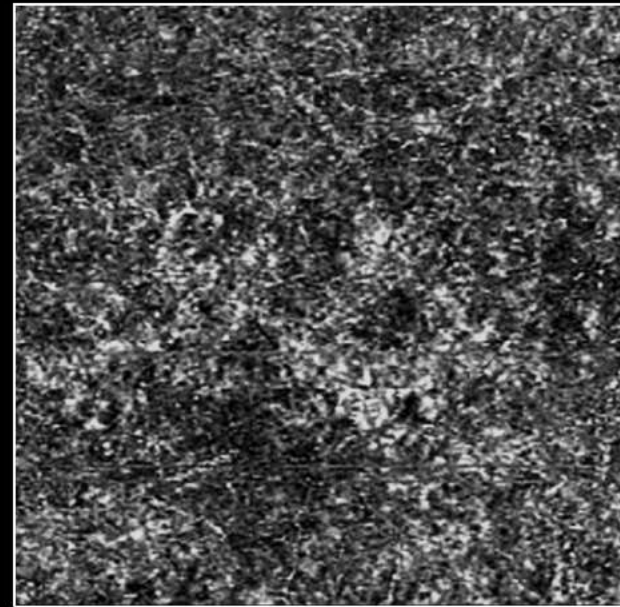
IT'S THE LITTLE THINGS THAT MATTER MOST

OCTA before & after 3 bevacizumab injections OS

Baseline



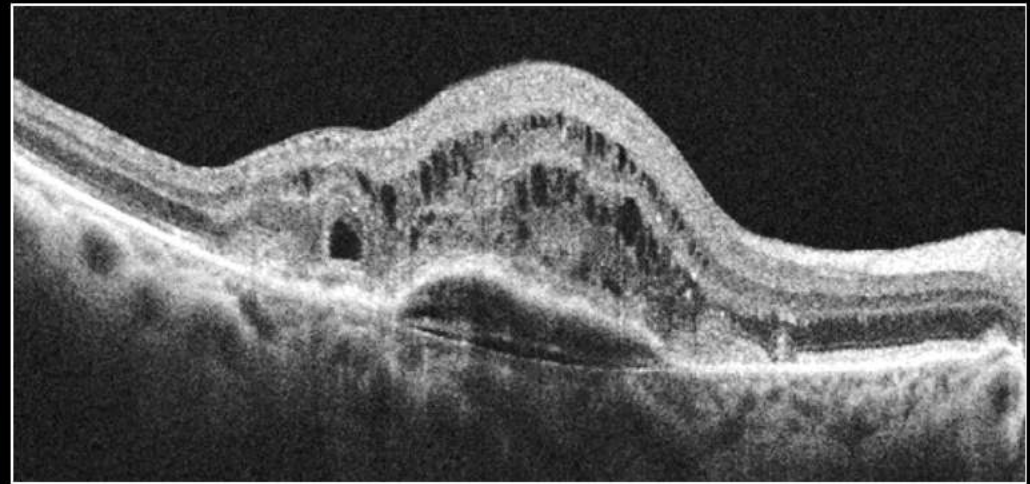
S/P bevacizumab



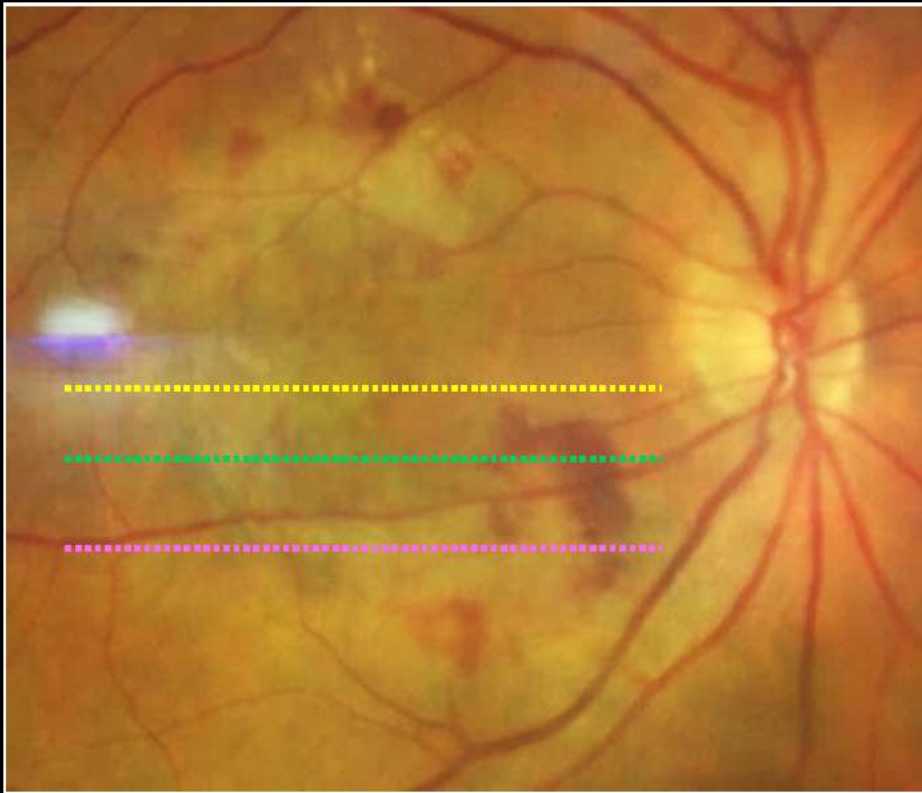
COVID CASUALTY

73yo Native American female

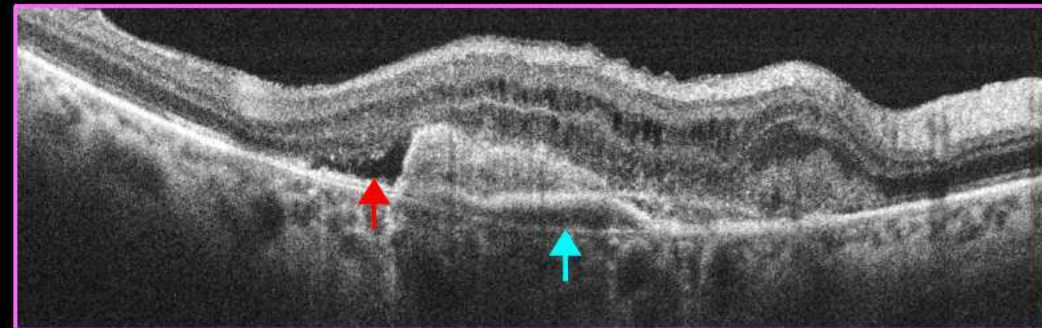
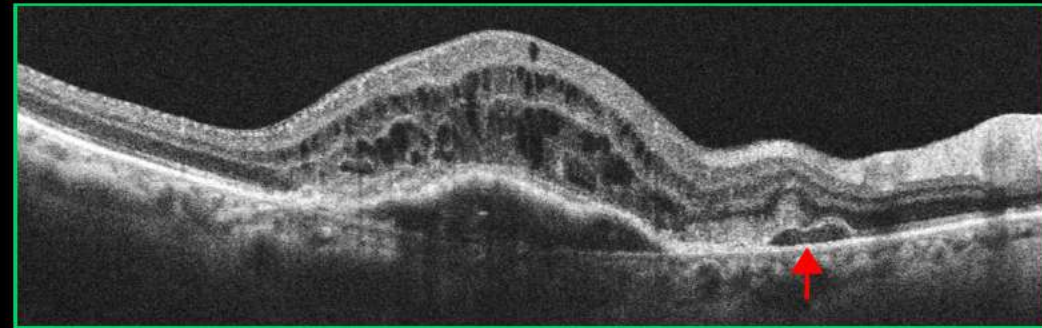
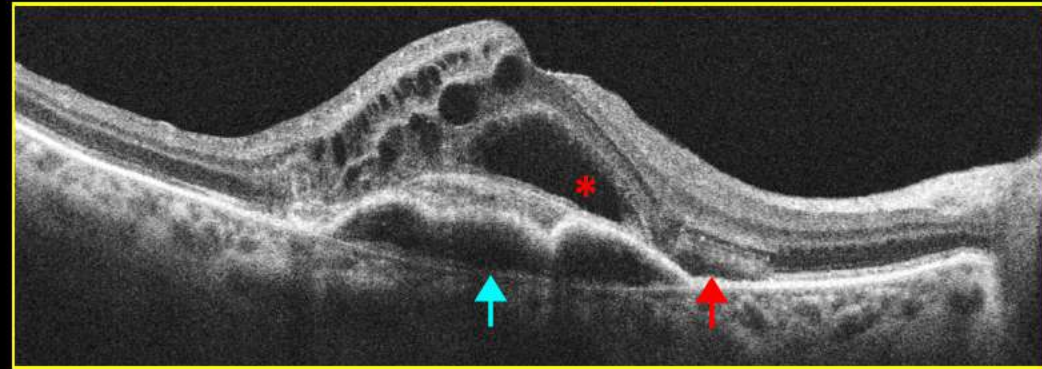
- **Decreased vision OD x 6 months**, dark spots and grayish vision esp when reading
- **Dry AMD x 7 yrs taking AREDS 2**
- LEE approx. 15 months ago
- VA OD: **20/100 PHNI** (was 20/20 15 months ago)



**OCT FLUID AT ANY LEVEL =
SUSPECT EXUDATIVE AMD!!**

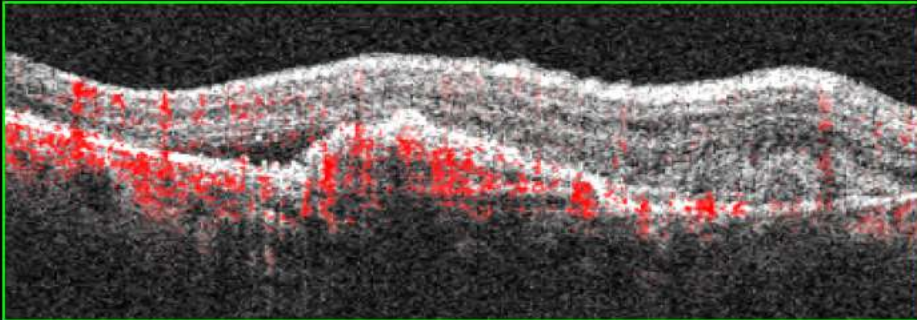
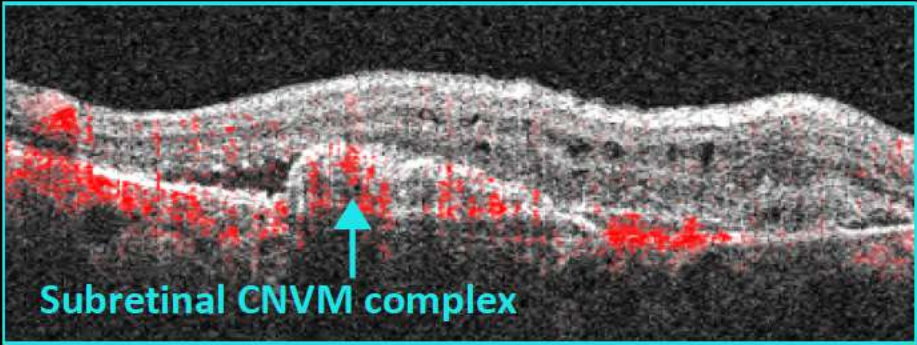
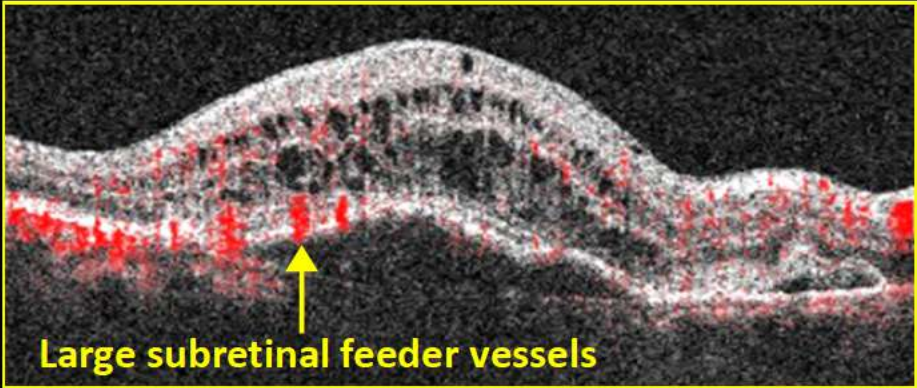
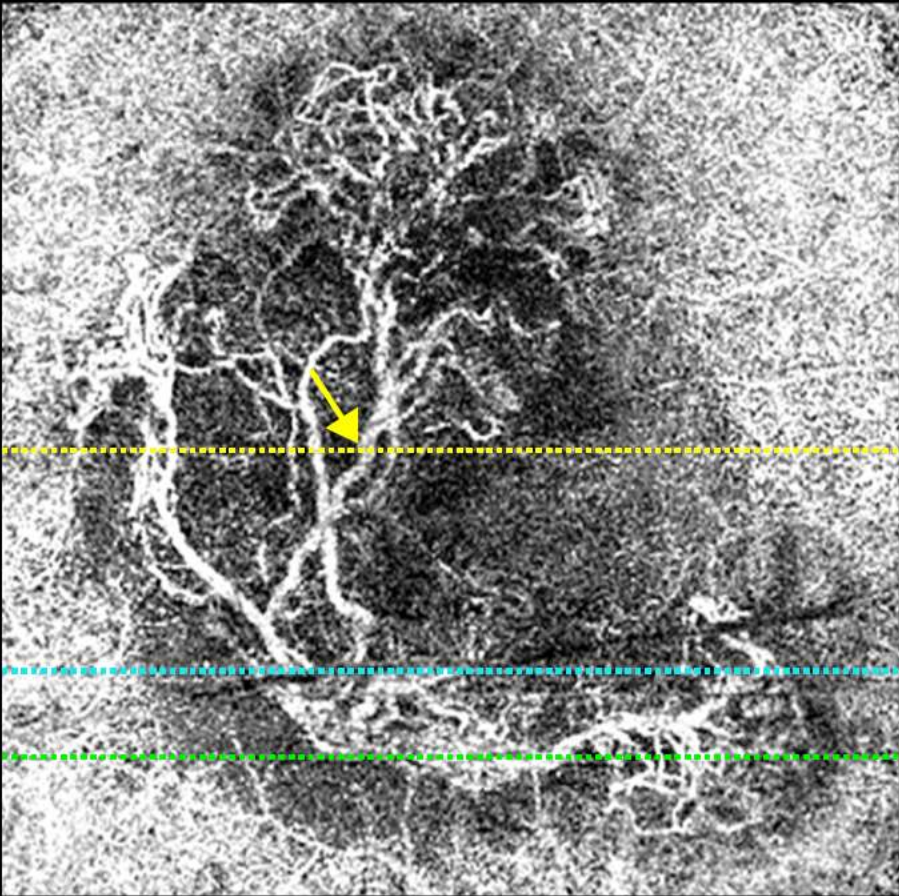


Intraretinal, Subretinal, SubRPE fluid



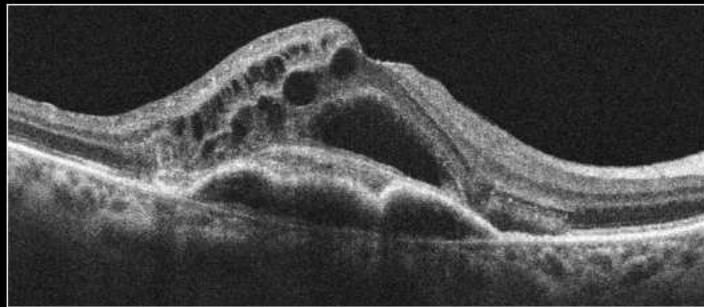
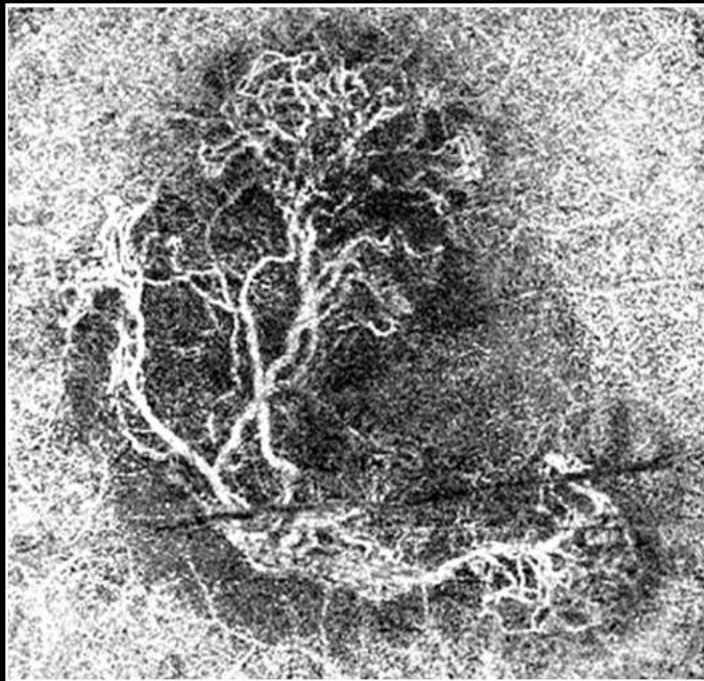
COVID CASUALTY

OCTA 6mm ORCC

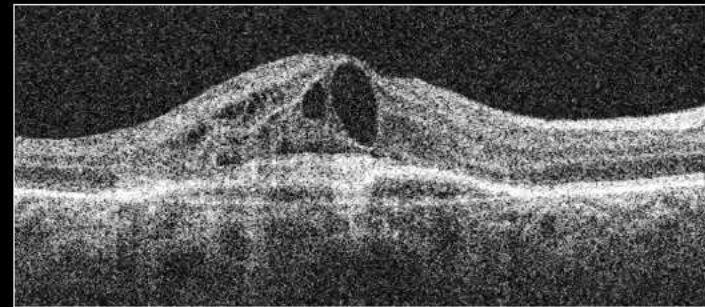
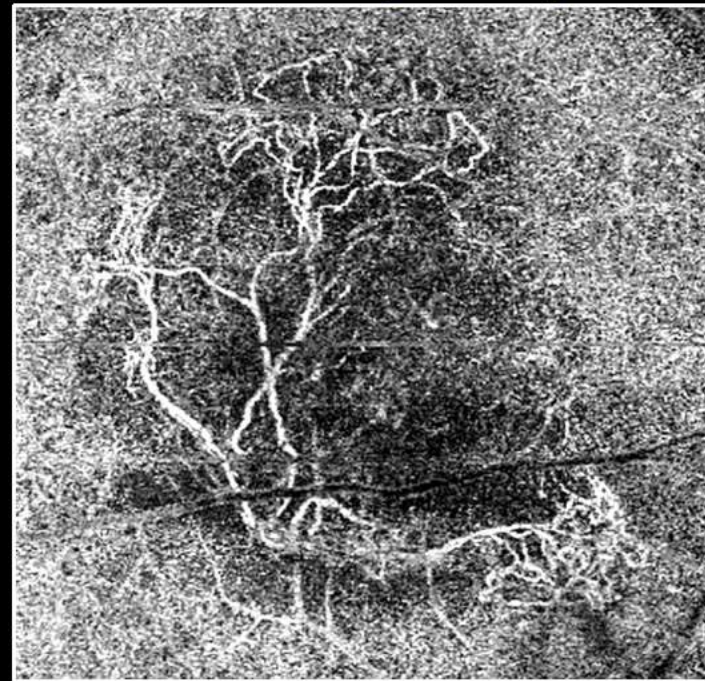


COVID CASUALTY

Baseline (20/100)

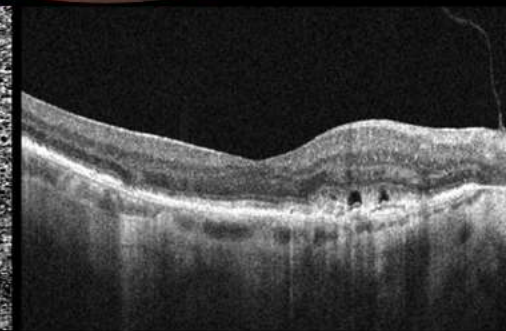
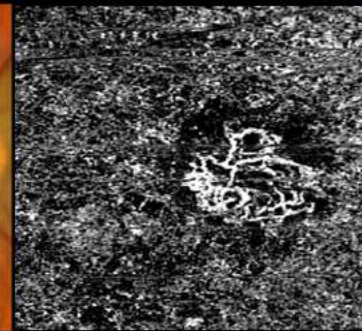
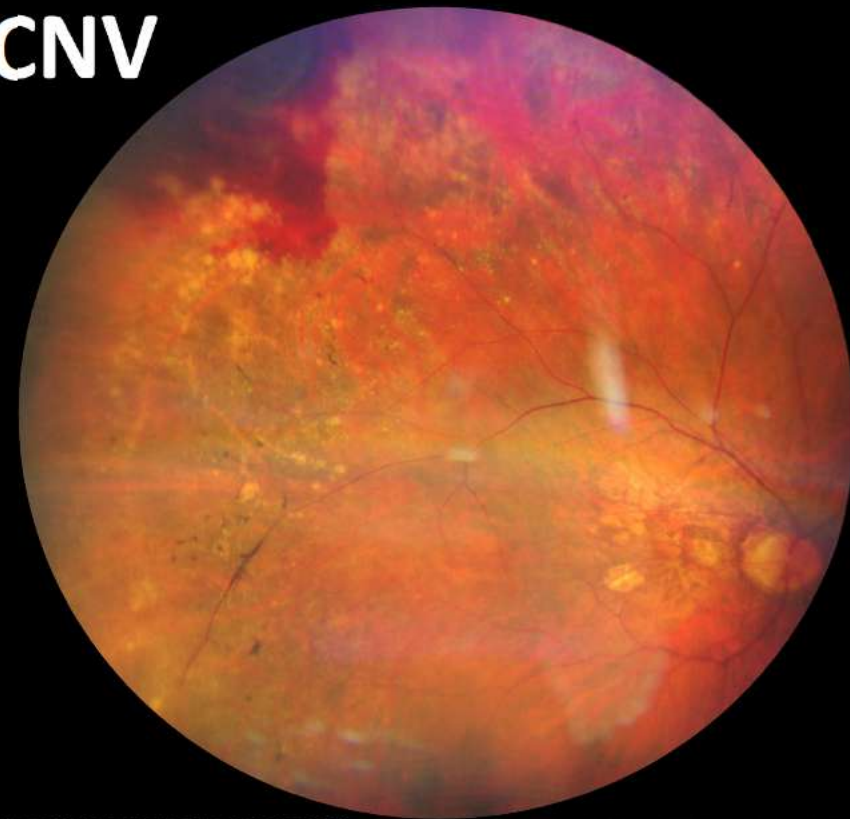


1 Year FU (20/200)

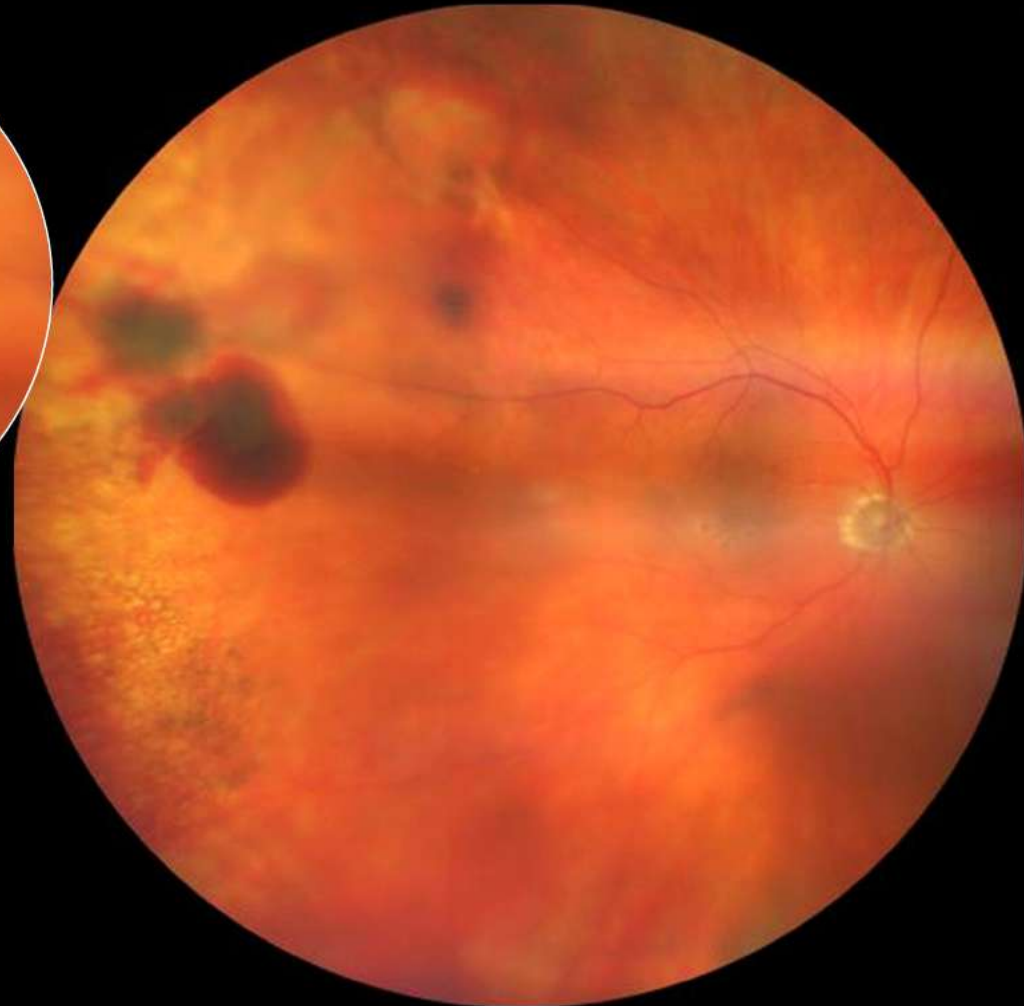
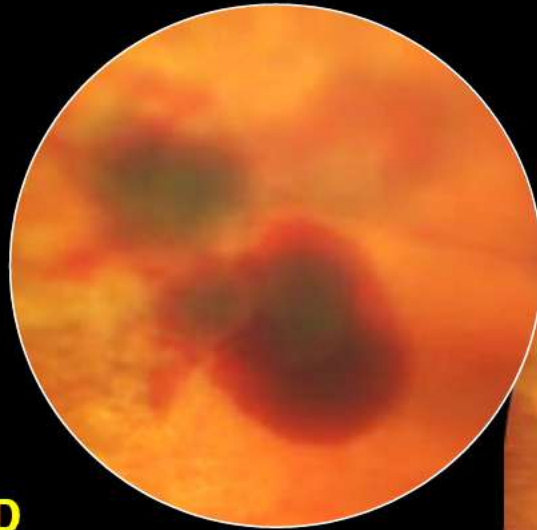


PERIPHERAL CNV

- AKA: **Peripheral exudative hemorrhagic chorioretinopathy (PEHCR)**
- Uncommon peripheral degeneration causing **peripheral exudative mass** (subretinal or subRPE hemorrhage & fluid, exudates, vit heme possible)
 - Usually **temporal**, 30% bilateral
- **Older Caucasian females** (mean 77-83 yrs)
- Systemic assoc: **HTN ~ 50%**, systemic anticoagulation or anti-platelet tx
- Ocular Assoc: **ARMD ~ 23-70%, macular CNV 8%**
- ~ 90% stabilize or regress without tx
- Consider anti-VEGF and/or laser photocoag if macular involvement
- **R/O macular CNV and choroidal melanoma!!!**



PERIPHERAL CNV

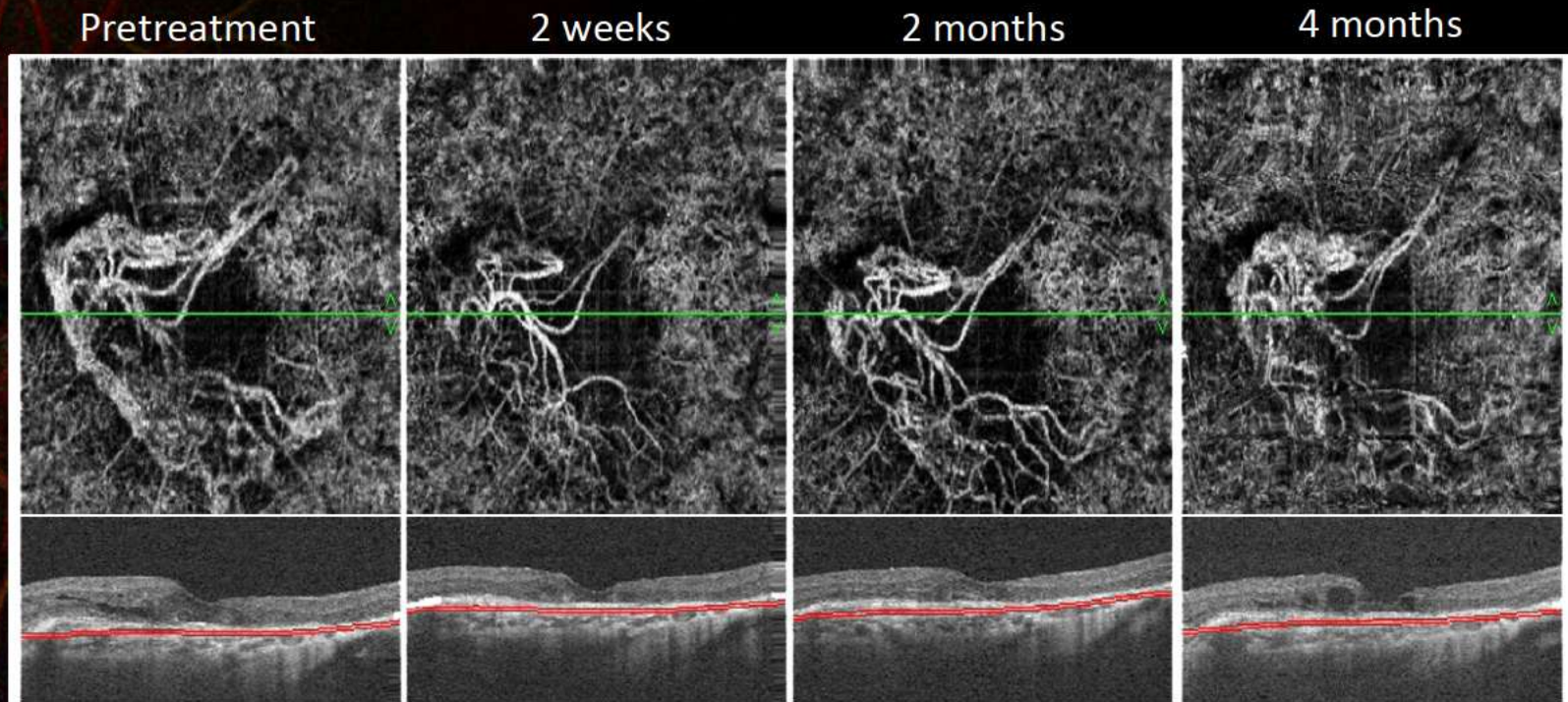


82yo white male

- CC: **Vision loss OD**
- Med Hx: **HTN**, hyperchol
- Oc Hx: Cat surg OU
- **VA OD 20/30⁻²**
- Externals/ant seg SLE: all WNLs
- **1+ vitreous hemorrhage OD**

Case courtesy of Dr. Riley Laster (Fayetteville, AR VAMC)

OCTA Morphologic CNV Features Associated with Disease Activity



When to retreat?

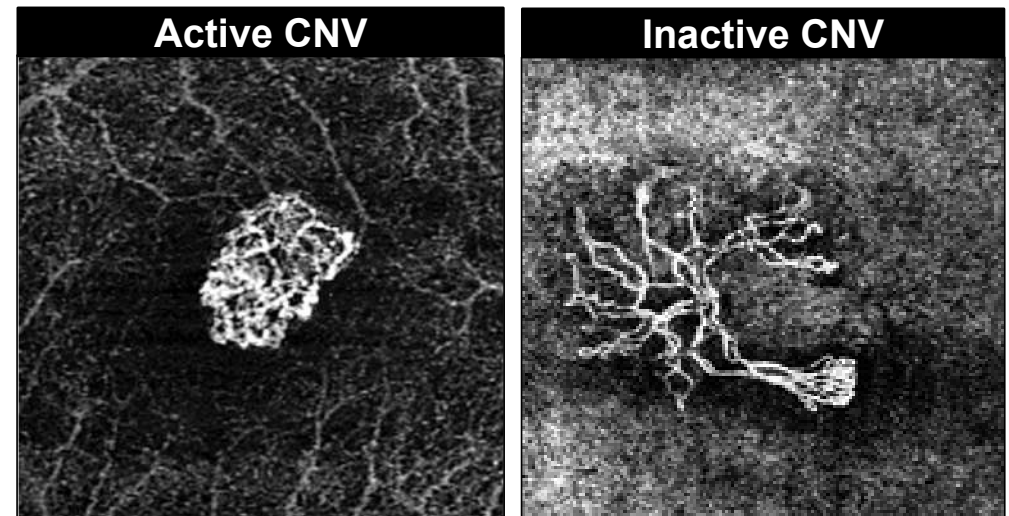
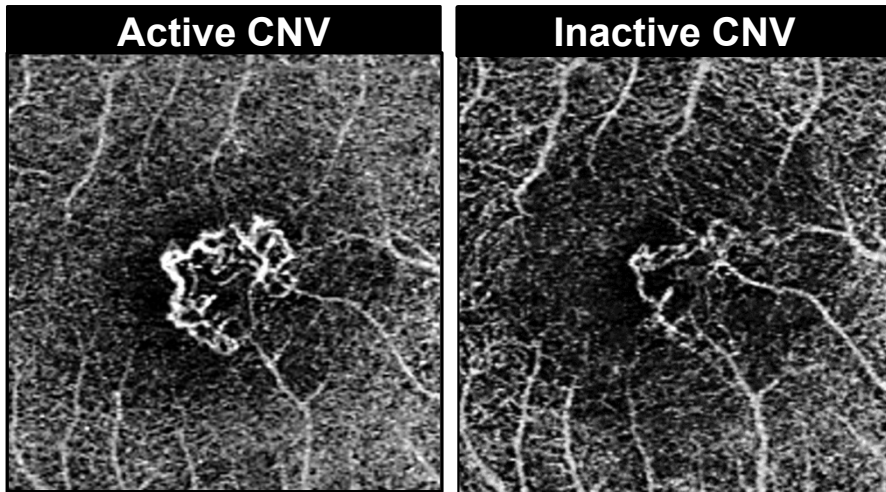
NEOVASCULAR ACTIVITY

OCTA morphologic CNV features associated with disease activity

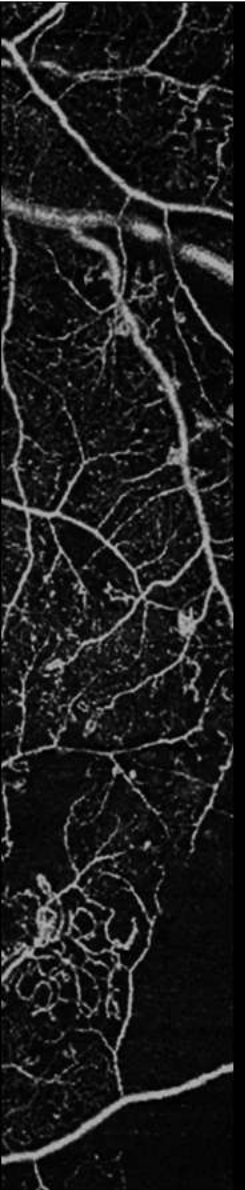
- Peripheral arcade of anastomosing capillaries vs dead tree



- “Lacy wheel” vs long filamentous linear vessels
- Numerous tiny capillaries vs large mature vessels



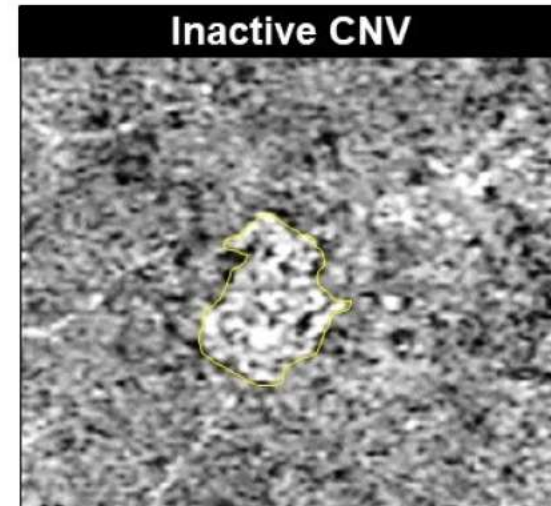
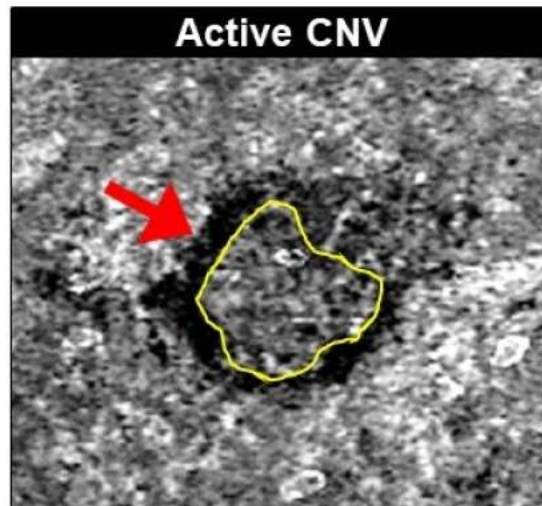
Coscas GJ. OCTA vs traditional multimodal imaging in assessing the activity of exudative ARMD: A new diagnostic challenge. Retina 2015.



NEOVASCULAR ACTIVITY

OCTA morphologic CNV features associated with disease activity

- Perilesional hypointense halo



Coscas GJ. OCTA vs traditional multimodal imaging in assessing the activity of exudative ARMD: A new diagnostic challenge. Retina 2015.

AMD HOME MONITORING SYSTEMS

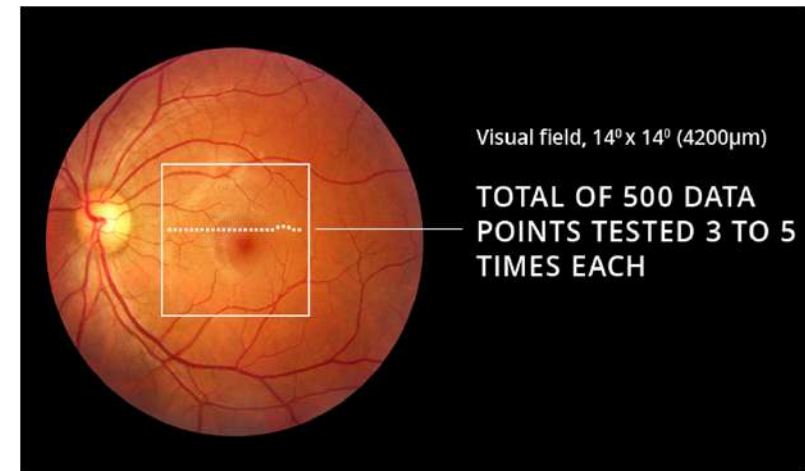
Why was it developed?

- AMD is the leading cause of blindness in the developed world in persons >50yo
- Neo accounts for 90% of severe central VA loss from AMD
- Early detection and prompt treatment of neo improves the visual outcomes
- **Need for home monitoring between routine office visits to detect early conversion** from intermediate nonexudative to neovascular AMD

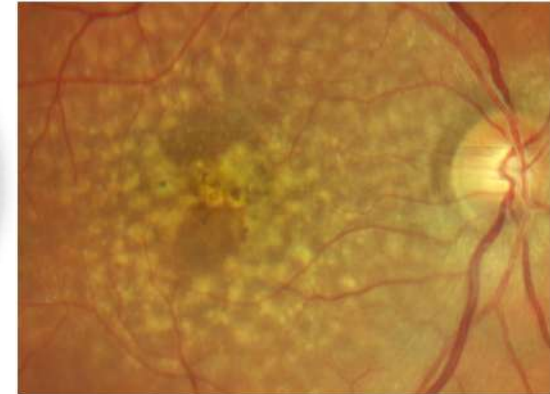


What is it?

- **FDA approved home preferential hyperacuity perimeter (PHP)** that *augments* in-office exams
 - Detects and characterizes central and paracentral metamorphopsia
 - Only available by physician order
 - The Notal Vision Monitoring Center- provides pt training, compliance reminders, & communicates with prescribing eyecare provider



AMD HOME MONITORING SYSTEMS



Who should use it?

- Patients with **intermediate nonexudative AMD in at least one eye**
 - **BCVA 20/60 or better** (stable vision and fixation)
- Covered by Medicare and some private insurances

What is the test like?

- Pt clicks where a wave or bump appears in a dotted line
 - Takes ~ 3 min per eye
 - Daily testing recommended

How is early conversion detected?

- Each test result is compared to a normative database and the pt's personal baseline
- Clinician is alerted if sig change

Common intermediate dry AMD patient types			
Intermediate dry AMD with 1 large drusen ($\geq 125 \mu\text{m}$)	Intermediate dry AMD with multiple medium drusen (63 - 124 μm) in both eyes	Intermediate dry AMD with drusen and hyperpigmentation	Intermediate dry AMD in one eye, wet AMD or central GA in the fellow eye
Patients must have:			
OD (right eye) H 35.31 1 2 (dry intermediate, right eye) BCVA 20/60 or better	or	OS (left eye) H 35.31 2 2 (dry intermediate, left eye) BCVA 20/60 or better	or
H 35.31 3 2 (dry intermediate, bilateral)			

AMD HOME MONITORING SYSTEMS

DOES RESEARCH SUPPORT ITS USE?

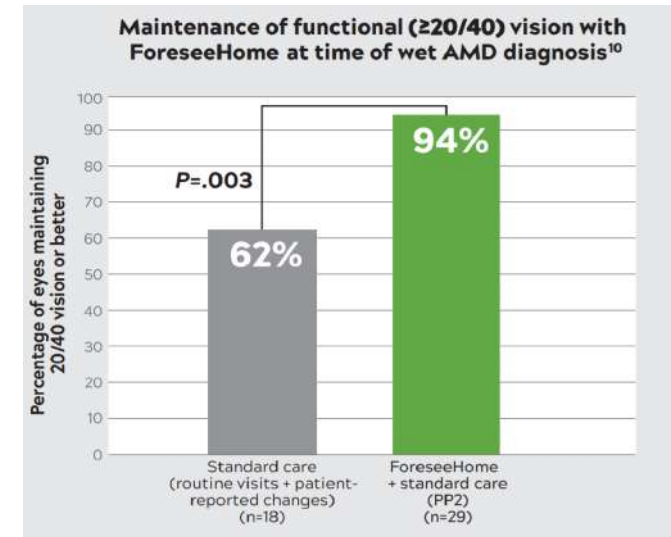
AREDS 2 HOME Study

- Foresee Home identified 64% of converters
 - **Functional vision ($\geq 20/40$) at conversion was maintained in 94% of patients using Foresee Home** vs 62% without

ALOFT Study (Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring)

- Large retrospective review of clinical data from 2010 to 2020 (3334 eyes)
- 52% of conversions detected by system alert
- Median acuity measures of converters at:
 - Baseline 20/30
 - Initial conversion 20/39
 - **Final follow-up 20/32**
- 82% of eyes that converted had functional vision ($\geq 20/40$) at final follow up

Chew EY, et al. Randomized Trial of the Foreseehome Device for Early Detection of nARMD. Home Study Report Number 1. Contemp Clin Trials 2014.
Ho AC, et al. Real-World Performance of a Self-Operated Home Monitoring System for Early Detection of nARMD. *J Clin Med* 2021.
Mathai M, et al. Analysis of the Long-term visual Outcomes of ForeseeHome Remote Telemonitoring - The ALOFT study. *Ophthalmology Retina* 2022.



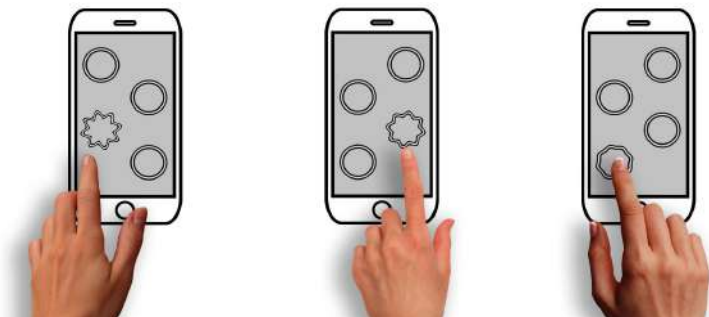
Home OCT device in development



AMD MOBILE MONITORING SYSTEMS

myVisionTrack (mVT®) app

- Smartphone and tablet-based app
- Based on shape discrimination hyperacuity testing
- Monitors progression of DME and AMD
- Prescription required
- Clinician is alerted if significant change in test results

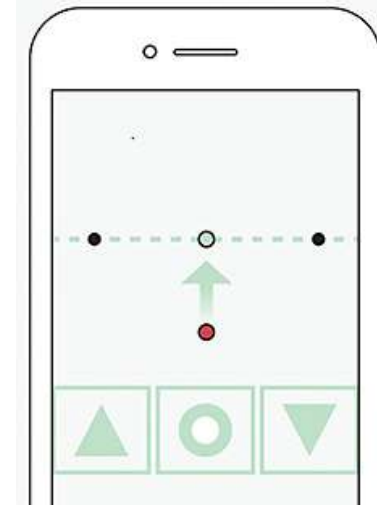


MaculaTester app

- Electronic version of the Amsler grid
- Record areas of distortion by touching screen
- Does NOT automatically detect progression or communicate with doctor
- Can set up reminder notifications

Alleye app

- 2 different app versions:
 1. AlleyeOne: for those at increased risk of retinal disease
 2. Alleye: for those with existing retinal disease (AMD & DME)
- Assesses vernier acuity using an alignment task
- In studies, 52-66% of the pts who came to the clinic bc of a + test result received an intravitreal injection
- Register as a provider online (<https://alleye.io/provider>)





Take Home Message

- Be familiar with features suggestive of exudative AMD (blood, fluid, PED, etc)
- OCT/OCTA allows for earlier detection of neovascularization and exudation in AMD = Earlier treatment = Vision preservation!!!
- OCTA is the only method of detecting and monitoring growth of non-exudative CNV membranes
- Look (with FAF & OCT) and refer patients with GA that may benefit from newly approved therapies
- Recognize OCT biomarkers for conversion from intermediate nonexudative AMD to advanced AMD

