Diagnostic Imaging in AMD

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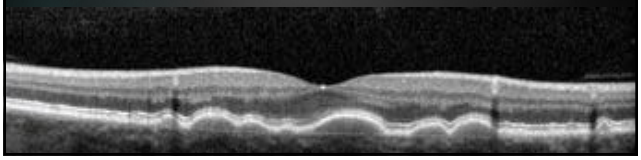

Financial Disclosures

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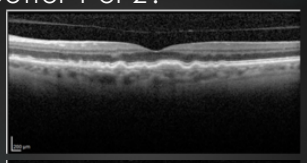
- Consultant, paid speaker for Notal Vision
- Paid speaker for Heidelberg Engineering
- Editorial board for Review of Optometry
- All relevant relationships have been mitigated.

Which is better 1 or 2?

1



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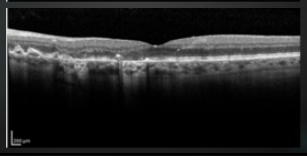


What is Age Related Macular Degeneration?

- Age-Related Macular Degeneration (AMD) is the leading cause of severe vision loss in adults over age 50. The Centers for Disease Control and Prevention estimate that 1.8 million people have AMD and another 7.3 million are at substantial risk for vision loss from AMD.
- This eye disease occurs when there are changes to the macula, a small portion of the retina that is located on the inside back layer of the eye. AMD is a loss of central vision that can occur in two forms: "dry" (atrophic) and "wet" (exudative).

https://www.aoa.org/patients-and-public/eye-and-vision-problems/glossary-of-eye-and-vision-conditions/macular-degeneration

What is Age Related Macular Degeneration?

- "Drusen, composed of acellular, polymorphous material, is considered the hallmark of early AMD"
- "…the accumulation of photo-oxidized debris within and under the RPE is considered the initiating cause of AMD.[5] The debris found within the RPE cells includes a yellow-brownish pigment granule called lipofuscin—a lipid-containing residue from lysosomal digestion with autofluorescent properties"

Rixon, Andrew OD, Richard Trevino OD, Roya Attar OD. "Arm Yourself for Dry AMD." *Review of Optometry.* January 2017.

What is Age Related Macular Degeneration?

- "AMD is a degenerative disorder affecting the macula. It is characterized by the presence of specific clinical findings including drusen and RPE changes as early features with no evidence the signs are secondary to another disorder"

Kanski, Jack J., and Brad Bowling. *Clinical Ophthalmology: a Systematic Approach*. Elsevier, 2012.

What is Age Related Macular Degeneration?

- "There is at present no universally accepted precise definition, including both initial diagnosis and staging, of the AMD phenotype for either clinical or research purposes."

-Ferris et al; Beckman Initiative for Macular Research Classification Committee

Ferris FL, Wilkinson CP, Bird A, et al. Clinical Classification of Age-related Macular Degeneration. *Ophthalmology*. 2013;120(4):844-851.

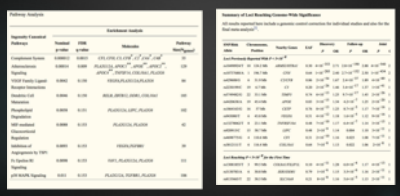
What is Age Related Macular Degeneration?

- As currently used, the term AMD is likely to have different causes leading to a final common pathway. More detailed phenotype information will be necessary for most research purposes. Because of this, as noted above, this discussion is limited to the phenotype of AMD that is widely recognized as evolving from small to large drusen with subsequent pigmentary abnormalities and eventual development of late AMD. As a first step, phenotype characteristics also are limited to those that can be identified by common ophthalmology office equipment, including an ophthalmoscope and a slit lamp with accessory lenses, to enhance its widespread applicability around the world. Although this proposed classification system is intended for clinical phenotyping, more detailed classification schemes based on new imaging technologies, genetic testing, and visual function evaluation are important to refine and expand the phenotypes of both early and late stages of AMD, and there are efforts underway to validate their usage in a more sophisticated classification system

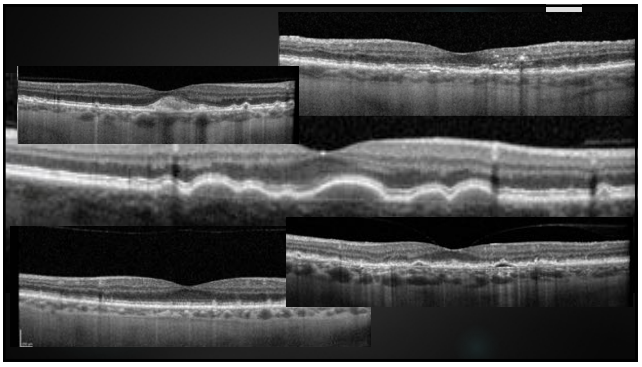
-Ferris et al.

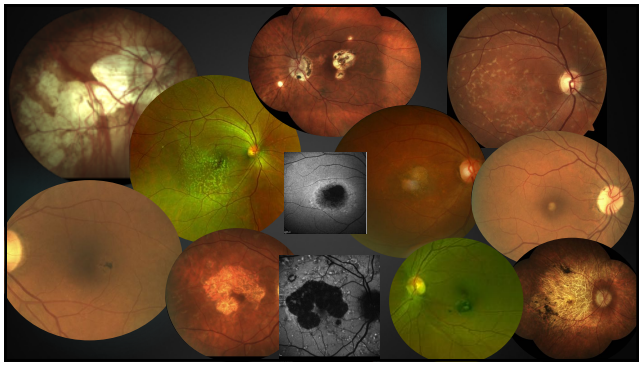
What is Age Related Macular Degeneration?

- AMD is a highly heritable progressive neurodegenerative disease that leads to loss of central vision through death of photoreceptors.

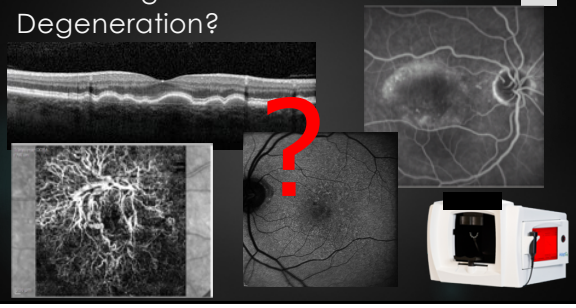


Fritsche LG, Chen W, Schu M, et al. Seven new loci associated with age-related macular degeneration. *Nat Genet*. 2013;45(4):433-439.





What is Age Related Macular Degeneration?



What is Age Related Macular Degeneration?

- You can't test positive for AMD
  - How do you know you have it?
  - How do you know you don't have something else?
  - How do you know if it's exudative or non-exudative?
  - How do you know who is most likely to suffer vision loss from advanced AMD?
  - How do we make a difference in the visual outcomes of our AMD patients?
- Multimodal imaging and visual function testing paints a more complete picture

Technology We Will Cover

- Fundus evaluation
- Fluorescein angiography
- Optical coherence tomography
- Fundus autofluorescence
- OCT-angiography
- Dark adaptation
- Home monitoring (ForeseeHome System)

- All modalities show unique aspects of AMD
- Pros/Cons
- Multimodal imaging tells more complete story
- Staying up to date is crucial as knowledge of the disease continues to expand

The Fundus Examination

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. Huisingh, MPH; Mark E. Clark, BS; Gerald McGwin Jr, PhD; Cynthia Owsley, PhD

1288 eyes from 644 people
- Mean age of 69.4
- 36% male
- 64% female

✓ **25%** of normal patients had findings consistent with AMD
✓ **30%** of missed AMD eyes had large drusen (Intermediate AMD)
✓ MDs and ODs miss AMD diagnosis equally

Reference: Neely DC, Bray KJ, Huisingh 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.

ARMD Classification in AREDS I

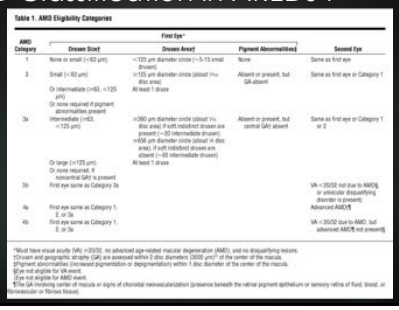
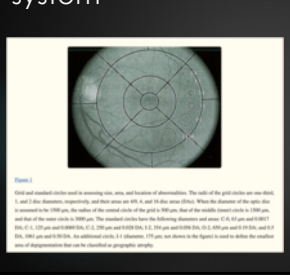


Table 1. AMD Eligibility Categories

AMD Category	First Eye* Drusen Size†	Drusen Area‡	Pigment Abnormalities§	Second Eye
1	None or small (<63 µm)	<125 µm diameter circle (~5-15 small drusen)	None	Same as first eye
2	Small (≥ 63 µm) Or intermediate (≥63, <125 µm) Or none required if pigment abnormalities present	<125 µm diameter circle (about ⅓ disc area) At least 1 druse	Absent or present, but GA absent	Same as first eye or Category 1
3a	Intermediate (≥63, <125 µm)	>360 µm diameter circle (about ⅓ disc area) if soft indistinct drusen are present (~20 intermediate drusen) >656 µm diameter circle (about ½ disc area), if soft indistinct drusen are absent (~65 intermediate drusen) At least 1 druse	Absent or present, but central GA‖ absent	Same as first eye or Category 1 or 3
3b	Or large (≥125 µm) Or none required, if noncentral GA‖ is present in first eye same as Category 3a			VA <20/32 not due to AMD¶, or vascular disqualifying disorder is present# Advanced AMD¶
4a	First eye same as Category 1, 2, or 3a			VA <20/32 due to AMD, but advanced AMD¶ not present¶
4b	First eye same as Category 1, 2, or 3a			

*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)[2] 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).

AREDS Report 17: 9 step AMD system



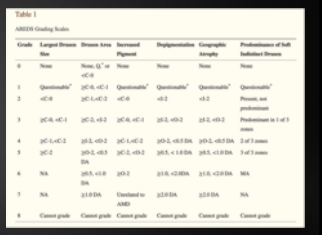


Table 1
AREDS Grading Scales

Grade	Largest Drusen Size	Drusen Area	Increased Pigment	Depigmentation	Geographic Atrophy	Predominance of Soft Indistinct Drusen
0	None	None, Q_1^* or <C-0	None	None	None	None
1	Questionable†	≥C-0, <C-1	Questionable†	Questionable†	Questionable†	Questionable†
2	<C-0	≥C-1, <C-2	<C-0	<3-2	<3-2	Present, not predominant
3	≥C-0, <C-1	≥C-2, <3-2	≥C-0, <C-1	≥3-2, <5-2	≥3-2, <5-2	Predominant in 1 of 3 zones
4	≥C-1, <C-2	≥3-2, <5-2	≥C-1, <C-2	≥5-2, <0.5 DA	≥5-2, <0.5 DA	2 of 3 zones
5	≥C-2	≥5-2, <0.5 DA	≥C-2, <5-2	≥0.5, < 1.0 DA	≥0.5, <1.0 DA	3 of 3 zones
6	NA	≥0.5, <1.0 DA	≥5-2	≥1.0, <2.0DA	≥1.0, <2.0 DA	MA
7	NA	≥1.0 DA	Unrelated to AMD	≥2.0 DA	≥2.0 DA	NA
8	Cannot grade	Cannot grade	Cannot grade	Cannot grade	Cannot grade	Cannot grade

Age Related Macular Degeneration

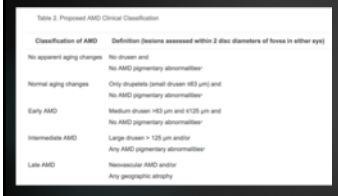
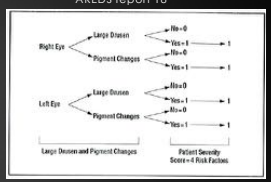


Table 2. Proposed AMD Clinical Classification

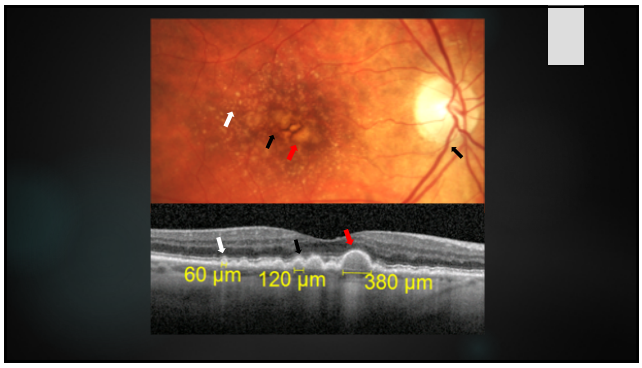
Classification of AMD	Definition (lesions assessed within 2 disc diameters of fovea in either eye)
No apparent aging changes	No drusen and No AMD pigmentary abnormalities*
Normal aging changes	Only drupelets (small drusen <63 µm) and No AMD pigmentary abnormalities*
Early AMD	Medium drusen ≥63 µm and <125 µm and No AMD pigmentary abnormalities*
Intermediate AMD	Large drusen ≥ 125 µm and/or Any AMD pigmentary abnormalities*
Late AMD	Neovascular AMD and/or Any geographic atrophy

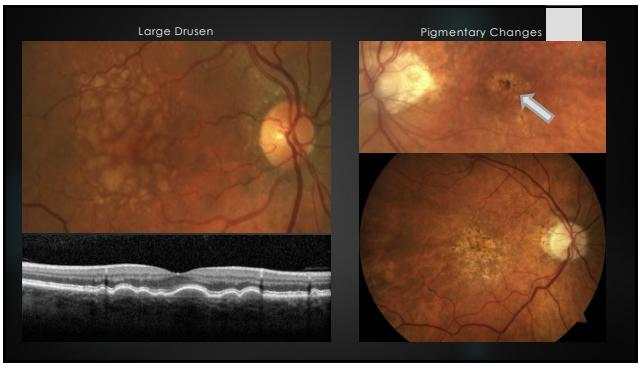
Ferris FL, Wilkinson CP, Bird A, et al. Clinical classification of age related macular degeneration. Ophthalmol. 2013;120(4):844-51.

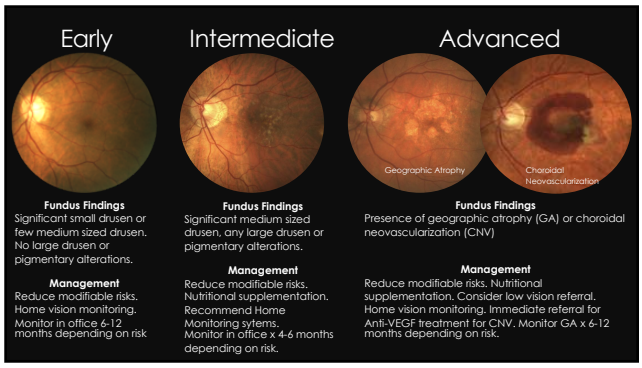
AREDS report 18

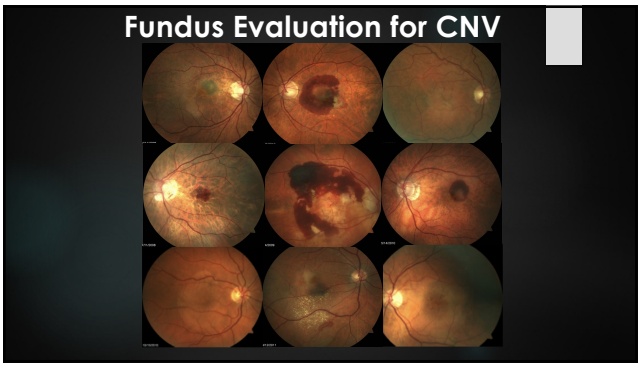


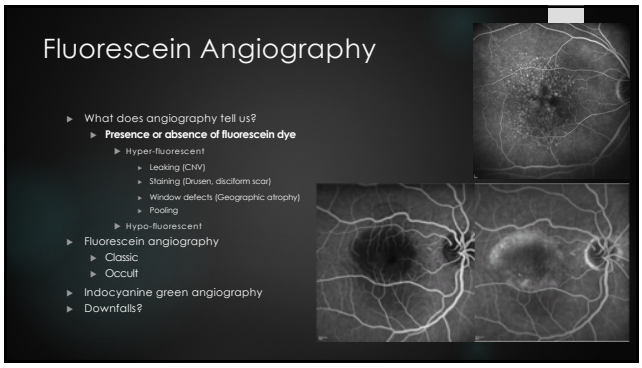
0 point=0.5%
1 point=3%
2 points=12%
3 points=25%
4 points=50%

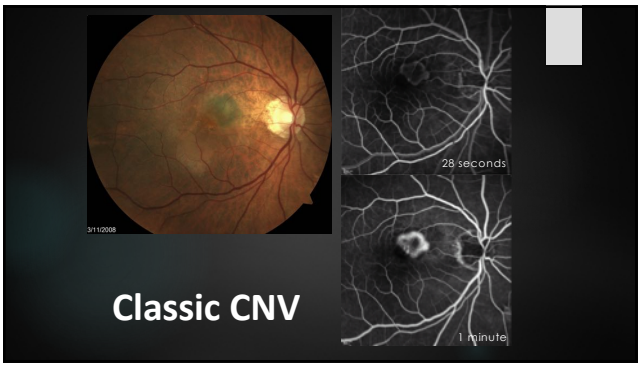

60 µm
120 µm
380 µm


Large Drusen
Pigmentary Changes

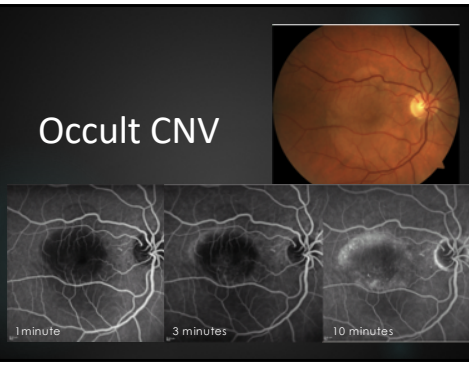

Early
Intermediate
Advanced
Geographic Atrophy
Choroidal Neovascularization
Fundus Findings
Significant small drusen or few medium sized drusen. No large drusen or pigmentary alterations.
Management
Reduce modifiable risks. Home vision monitoring. Monitor in office 6-12 months depending on risk
Fundus Findings
Significant medium sized drusen, any large drusen or pigmentary alterations.
Management
Reduce modifiable risks. Nutritional supplementation. Recommend Home Monitoring sytems. Monitor in office x 4-6 months depending on risk.
Fundus Findings
Presence of geographic atrophy (GA) or choroidal neovascularization (CNV)
Management
Reduce modifiable risks. Nutritional supplementation. Consider low vision referral. Home vision monitoring. Immediate referral for Anti-VEGF treatment for CNV. Monitor GA x 6-12 months depending on risk.

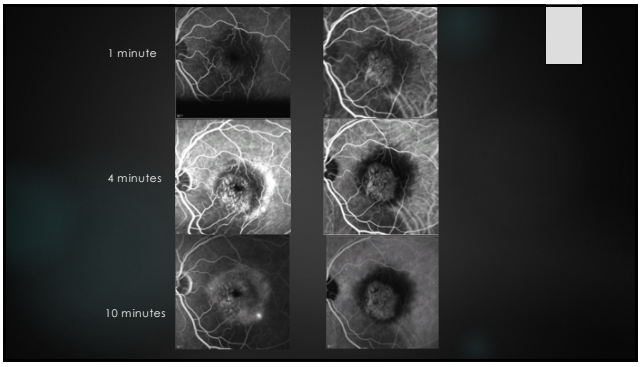

Fundus Evaluation for CNV


Fluorescein Angiography
What does angiography tell us?
Presence or absence of fluorescein dye
Hyper-fluorescent
Leaking (CNV)
Staining (Drusen, disciform scar)
Window defects (Geographic atrophy)
Pooling
Hypo-fluorescent
Fluorescein angiography
Classic
Occult
Indocyanine green angiography
Downfalls?


3/11/2008
28 seconds
1 minute
Classic CNV

Occult CNV





Optical Coherence Tomography

- What does OCT tell us??
  - **REFLECTIVITY!**
- Drusen
  - Drusen size
  - Drusen Volume
  - Regression
  - Reticular Pseudodrusen
  - Drusen structure
- Pigment mottling (hyper-reflective foci)
- Sub-RPE Hyper-reflective columns
- Choroidal Neovascular Membranes
  - Type 1 versus Type 2
  - Development
  - Monitoring response to treatment
- Geographic Atrophy (Nascent GA or incomplete retinal pigment epithelium and outer retinal atrophy)
- Choroidal thickness

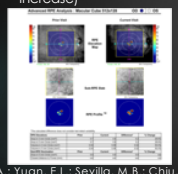
#1

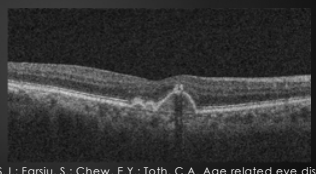
Drusen Size

Small Drusen : <63 microns
Intermediate Drusen : 63-125 microns
Large Drusen : >125 microns

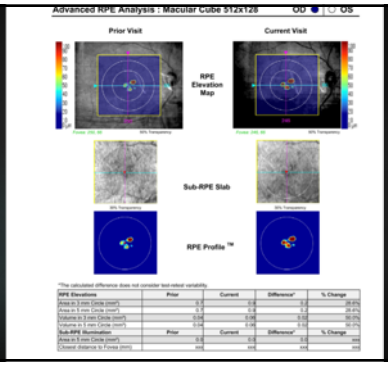
Drusen Volume

- 1.31 risk of progression to nAMD (for each 0.1 mm^3 of drusen volume increase)

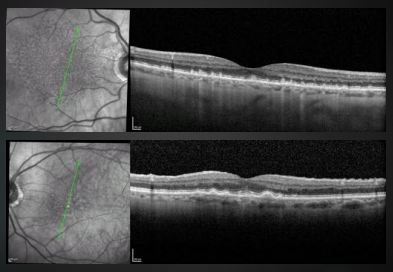




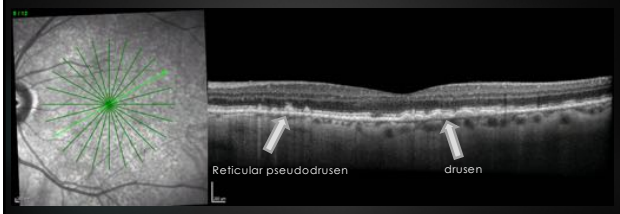
Folgar, F.A.; Yuan, E.L.; Sevilla, M.B.; Chiu, S.J.; Farsiu, S.; Chew, E.Y.; Toth, C.A. Age related eye disease study 2 ancillary spectral-domain optical coherence tomography study. G. drusen volume and retinal pigment epithelium abnormal thinning volume predict 2-year progression of age-related macular degeneration. Ophthalmology 2016, 123, 39–50 e31



Reticular Pseudodrusen



Reticular Pseudodrusen



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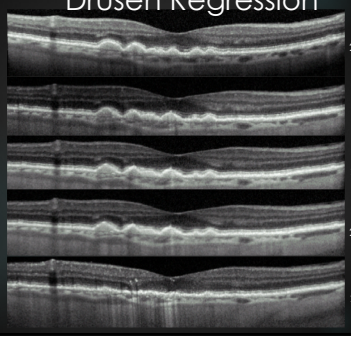
RPD and Cardiovascular Disease

Subretinal drusenoid deposits are strongly associated with coexistent high-risk vascular diseases

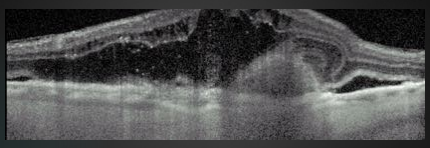
Abstract

Ledesma-Gil G, Otero-Marquez O, Alauddin S, et al. Subretinal drusenoid deposits are strongly associated with coexistent high-risk vascular diseases. *BMJ Open Ophthalmol*. 2022;7(1):e001154.

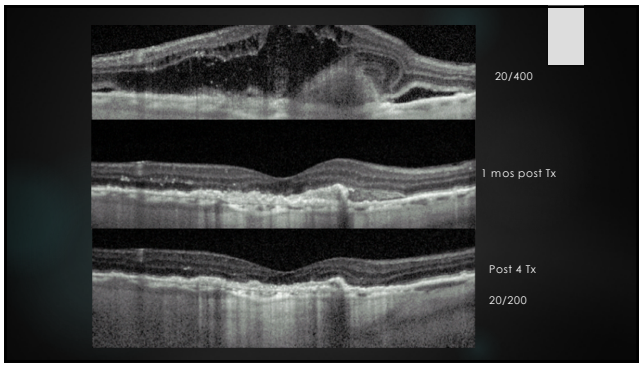
Drusen Regression



2016



Choroidal Neovascularization



Drusen Regression

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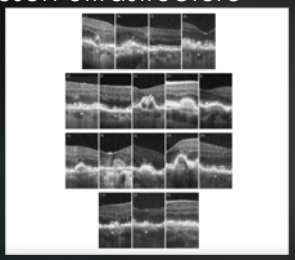
Drusen Ultrastructure



Shape
- Convex, concave, saw tooth

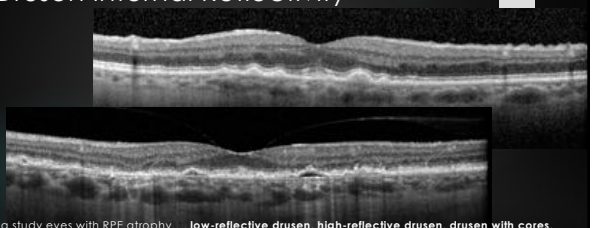
Internal reflectance
- low, medium, high

Homogeneity
- Homogeneous
- Non-homogeneous with cores
- Non-homogeneous without cores

Hyper-reflective foci
- Presence
- Absence

Khanifar AA, Koreishi AF, Izatt JA, Toth CA. Drusen Ultrastructure Imaging with Spectral Domain Optical Coherence Tomography in Age-related Macular Degeneration. *Ophthalmology*. 2008;115(11).

Drusen Internal Reflectivity



"Among study eyes with RPE atrophy…, **low-reflective drusen, high-reflective drusen, drusen with cores, and focal high reflectivity above drusen** were significantly more prevalent than in eyes without RPE atrophy…"

Leuschen JN, Schuman SG, Winter KP, et al. Spectral-domain optical coherence tomography characteristics of intermediate age-related macular degeneration. *Ophthalmology*. 2013;120(1):140-150.

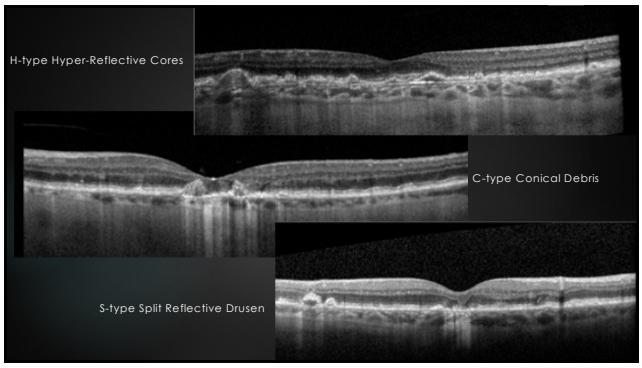
Drusen Cores

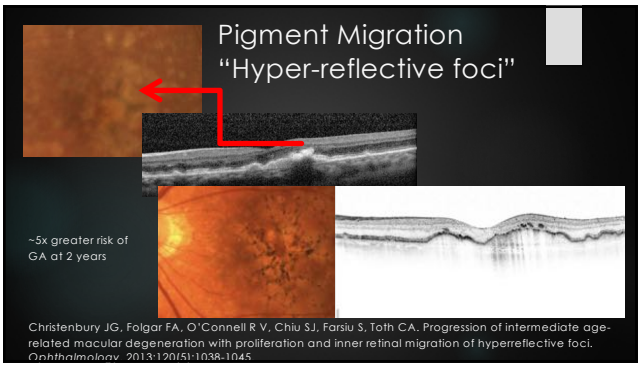
Table 1
Optical Coherence Tomography Reflective Drusen Substructures Grading Criteria

ORDS Type	Grading Criteria	SD-OCT Image
L-type Low-reflective cores	Consists of a focal, well-circumscribed subvolume of distinct reflectivity (i.e., a "core") within the drusen (<1000 μm in diameter) Not contiguous with Bruch's or RPE Cores are each ≥2 pixels on a single B-scan Hyporeflective relative to surrounding drusen material	
H-type High-reflective cores	Consists of a focal, well-circumscribed subvolume of distinct reflectivity (i.e., a "core") within the drusen (<1000 μm in diameter) Not contiguous with Bruch's or RPE ≥2 pixels on a single B-scan Hyperreflective relative to surrounding drusen material	
C-type Conical debris	Drusen (<1000 μm in diameter) has a conical shape Apex of drusen is not contiguous with RPE Cores are not contiguous with Bruch's or RPE Cores are each ≥2 pixels on a single B-scan Cores are hyperreflective relative to surrounding drusen material	
S-type Split-reflective drusen	Entire drusen (<1000 μm in diameter) is split into 2 subvolumes (in any proportion) of distinct levels of reflectivity (low and high) Each subvolume is ≥2 pixels on a single B-scan	
None	Drusen (<1000 μm in diameter) of homogeneous reflectivity	

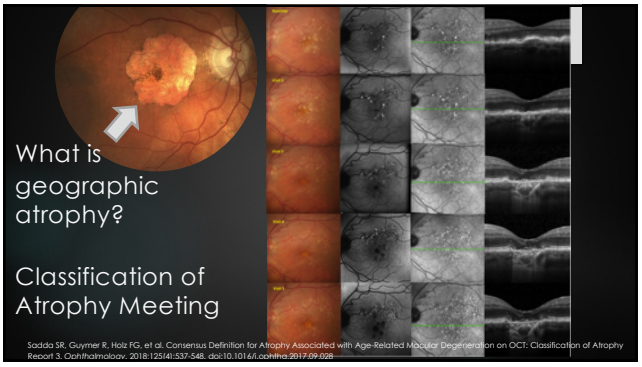
ORDS = optical coherence tomography–reflective drusen substructures; RPE = retinal pigment epithelium; SD-OCT = spectral-domain optical coherence tomography.

Veerappan M, El-Hage-Sleiman AKM, Tai V, et al. Optical Coherence Tomography Reflective Drusen Substructures Predict Progression to Geographic Atrophy in Age-related Macular Degeneration. *Ophthalmology*. 2016;123(12):2554-2570.





OCT and Geographic Atrophy



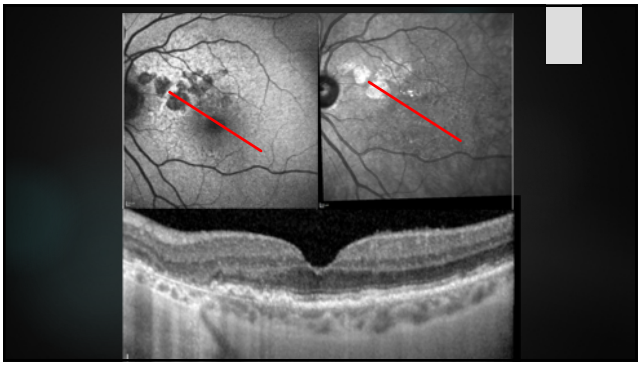
Complete RPE and Outer Retinal Atrophy

Table 2. Criteria for Diagnosis of Complete Retinal Pigment Epithelium and Outer Retinal Atrophy on Optical Coherence Tomography and Confirmatory Findings on Other Imaging Methods

Optical Coherence Tomography	Fundus Autofluorescence	Near-Infrared Reflectance	Color/Multicolor
Zone of hypertransmission of ≥250 μm Zone of attenuation or disruption of RPE band of ≥250 μm	Sharply demarcated borders Hypoautofluorescent: black level similar to optic nerve head or retinal blood vessels*	Sharply demarcated borders Hyperreflective	Sharply demarcated borders Hypopigmentation
Evidence of overlying photoreceptor degeneration whose features include: ONL thinning, ELM loss, and EZ or IZ loss	Diameter, ≥250 μm (area, 0.05 mm²)	Diameter, ≥250 μm (area, 0.05 mm²)	Increased visibility of choroidal vessels
Exclude: scrolled RPE or other signs of RPE tear	Exclude: macular pigment or other artifact	Exclude: artifact	Diameter, ≥250 μm (area, 0.05 mm²)

ELM = external limiting membrane; EZ = ellipsoid zone; IZ = interdigitation zone; ONL = outer nuclear layer; RPE = retinal pigment epithelium.
*If trickling junctional autofluorescence pattern is present or refractile drusen deposits or residual debris are present in bed of atrophy, lesion can appear grey rather than black.

Sadda SR, Guymer R, Holz FG, et al. Consensus Definition for Atrophy Associated with Age-Related Macular Degeneration on OCT: Classification of Atrophy Report 3. *Ophthalmology*. 2018;125(4):537-548. doi:10.1016/j.ophtha.2017.09.028



Incomplete RPE and Outer Retinal Atrophy

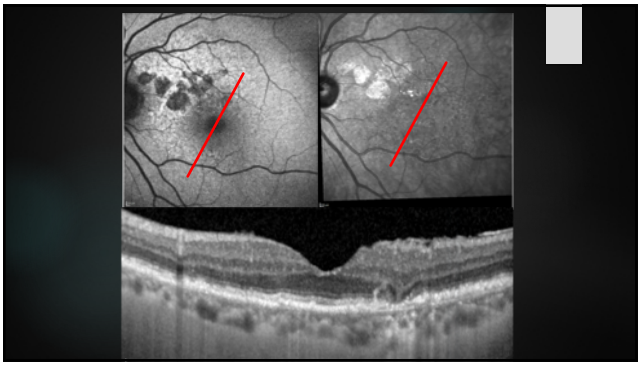
(1) A region of signal hypertransmission into the choroid and
(2) A corresponding zone of attenuation or disruption of the RPE, with or without persistence of basal laminar deposits (BLamD), and
(3) evidence of overlying photoreceptor degeneration, i.e., subsidence of the inner nuclear layer (INL) and outer plexiform (OPL), presence of a hyporeflective wedge in the Henle fiber layer (HFL), thinning of the outer nuclear layer (ONL), disruption of the external limiting membrane (ELM), or disintegrity of the ellipsoid zone (EZ), and when these criteria do not meet the definition of cRORA.

The term iRORA should not be used in the presence of an RPE tear. Corroborating signs on CFP, FAF, and NIR are not required as they are not always evident

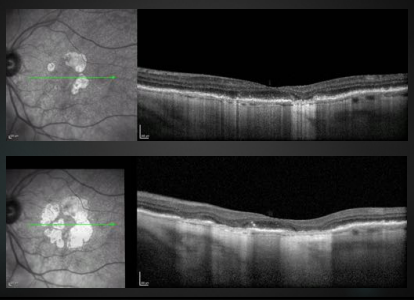
Sadda SR, Guymer R, Holz FG, et al. Consensus Definition for Atrophy Associated with Age-Related Macular Degeneration on OCT: Classification of Atrophy Report 3. *Ophthalmology*. 2018;125(4):537-548. doi:10.1016/j.ophtha.2017.09.028

· 5.2 risk of progression to central GA

· Wu, Z.; Luu, C.D.; Ayton, L.N.; Goh, J.K.; Lucci, L.M.; Hubbard, W.C.; Hageman, J.L.; Hageman, G.S.; Guymer, R.H. Optical coher- ence tomography-defined changes preceding the development of drusen-associated atrophy in age-related macular degeneration. Ophthalmology 2014, 121, 2415–2422



Geographic Atrophy



February 3, 2022

Association of Pegcetacoplan With Progression of Incomplete Retinal Pigment Epithelium and Outer Retinal Atrophy in Age-Related Macular Degeneration

A Post Hoc Analysis of the FILLY Randomized Clinical Trial

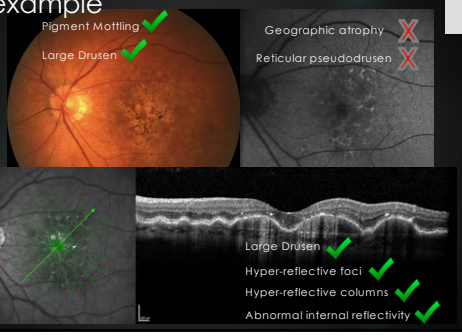
Muneeswar Gupta Nittala, MPH[1]; Ravi Mettapally, PhD[2]; Michael Ip, MD[3]; et al

> Author Affiliations

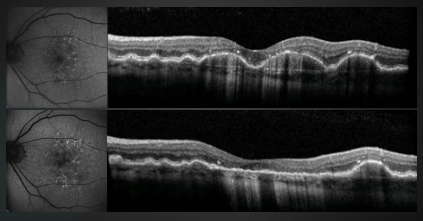
JAMA Ophthalmol. 2022;140(3):243-249. doi:10.1001/jamaophthalmol.2021.6067

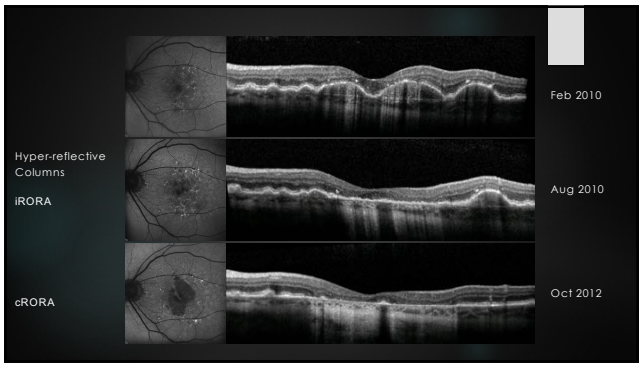
"This post hoc analysis of a phase 2 randomized clinical trial of 167 patients with GA secondary to AMD who received pegcetacoplan monthly (n = 41) or every other month (n = 56) or a sham injection (n = 70) suggested that rates of progression from iRORA to complete RPE and outer retina atrophy were lower in eyes treated with intravitreal pegcetacoplan monthly or every other month vs sham, after excluding participants who developed exudative AMD or had missing data."

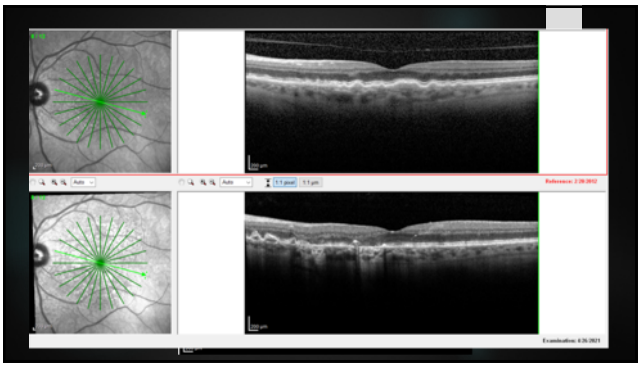
Case example



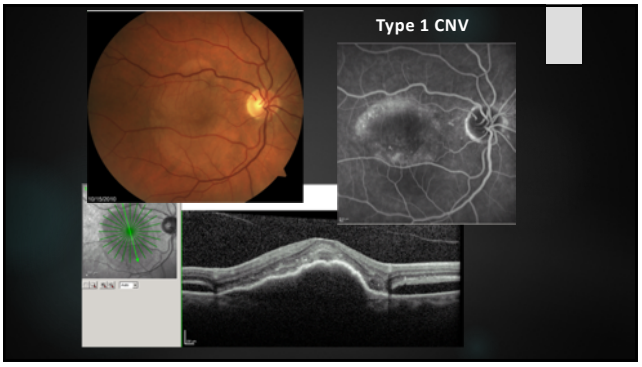
6 months later: my vision is getting worse!! Straight lines look wavy

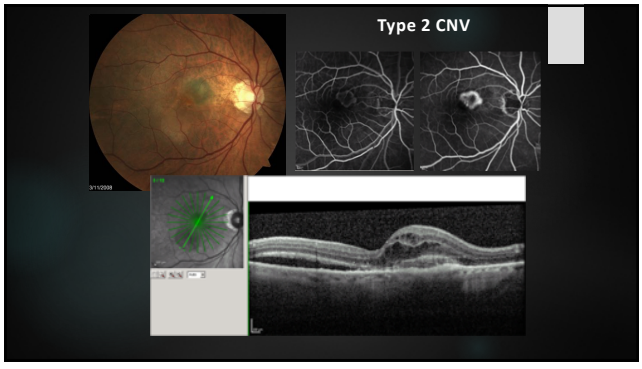


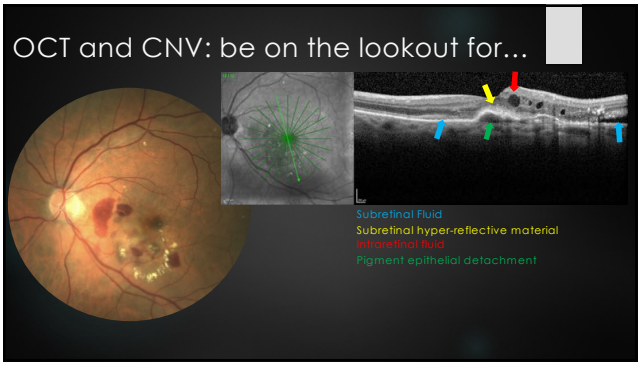

Hyper-reflective Columns
iRORA
cRORA
Feb 2010
Aug 2010
Oct 2012



OCT and CNV

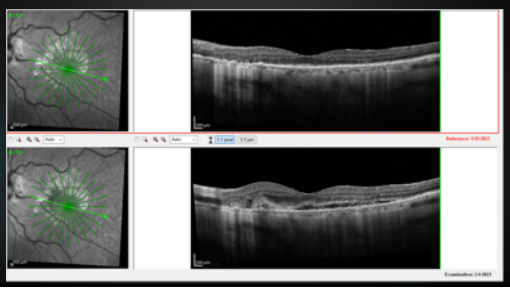

Type 1 CNV


Type 2 CNV


OCT and CNV: be on the lookout for...
Subretinal Fluid
Subretinal hyper-reflective material
Intraretinal fluid
Pigment epithelial detachment

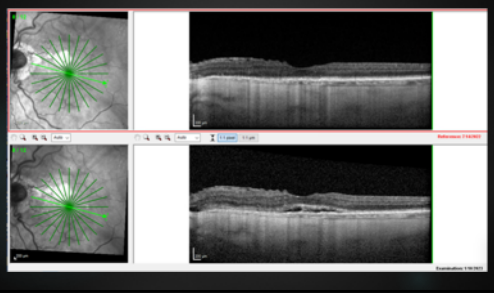
OCT and Early CNV Detection

CNV Conversion: 2.5 weeks later



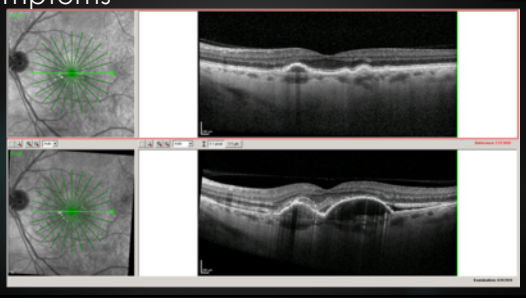
20/25

CNV Conversion: 6 mos follow up



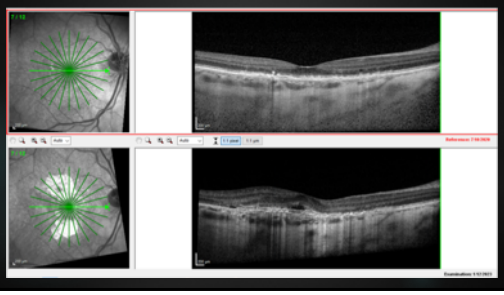
20/25

CNV Conversion: Patient reports symptoms



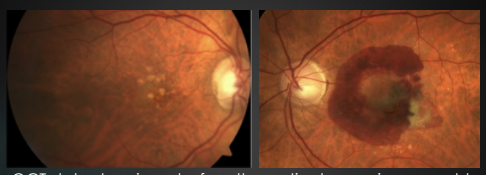
20/50

CNV Conversion: 2.5 years later…



20/200

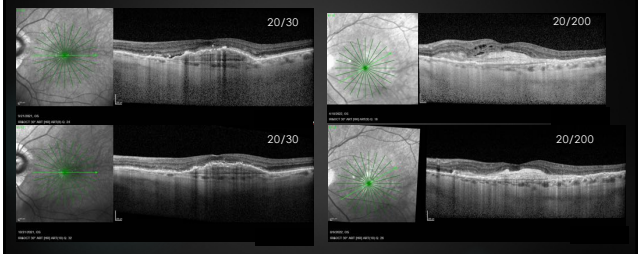
Early Detection of CNV



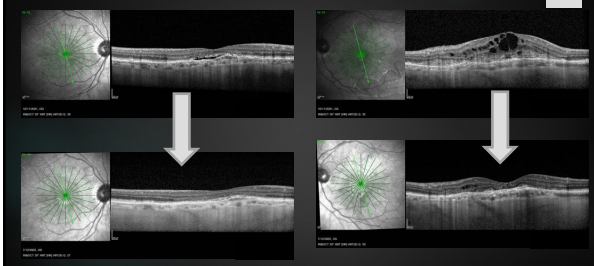
Can OCT detect an issue before the patient perceives a problem?
Can OCT detect an issue before you perceive a problem?

"…SD-OCT also provided additional information that was not obtained from CFP. Subfoveal RPE atrophy or absence was observed in 2.5% of eyes identified as category 3 AMD by CFP… Additionally, 27.4% of eyes contained 1 SD-OCT characteristics suggestive of CNV and/or intra- or subretinal fluid… All of these eyes were originally graded nonadvanced based on CFP."
--Leuchen et al

Distribution of fluid: CNV response

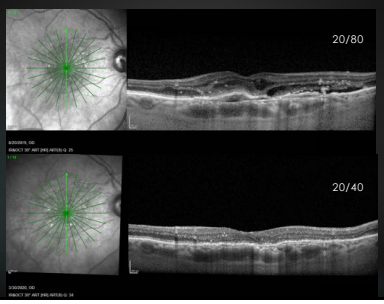


Distribution of fluid: CNV response

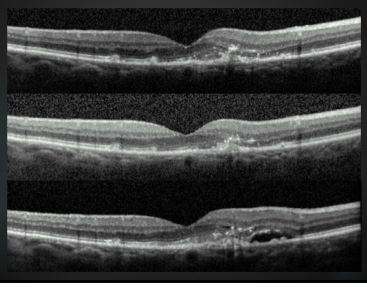


Subretinal Hyper-reflective Material

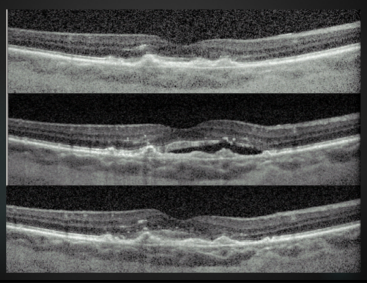
Weakness of OCT Biomarkers in AMD?



Monitoring CNV Treatment



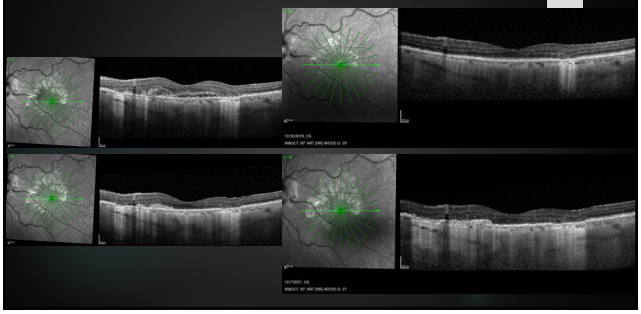
Monitoring CNV Treatment



9 years later
20 injections later

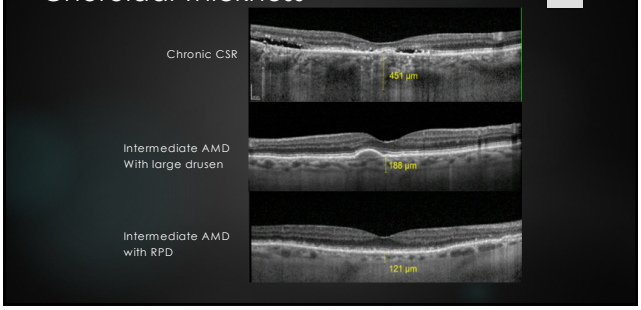
20/40

Anti-VEGF Does Not Treat AMD

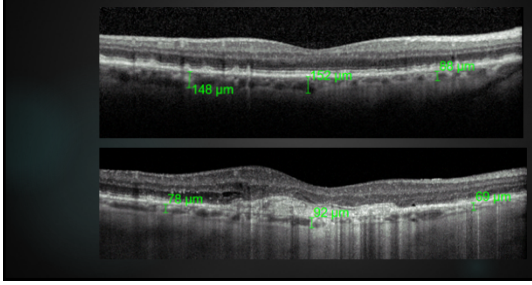


Don't Forget the Choroid

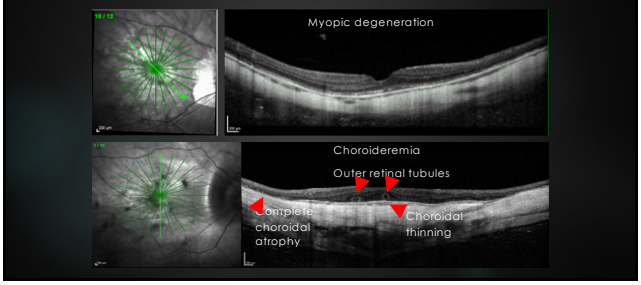
Choroidal Thickness



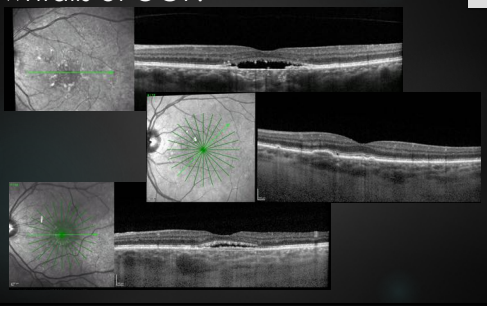
Choroidal Thickness



Thin Choroid = AMD?



Downfalls of OCT?

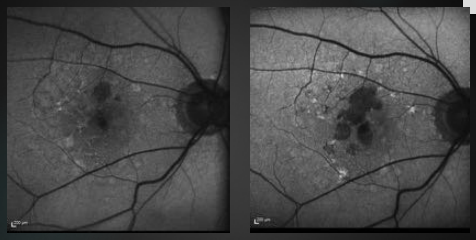


Fundus autofluorescence

- What does FAF tell us??
  - Lipofuscin map
- Geographic atrophy
  - Early detection
  - Monitoring progression
- Patient Education
- Reticular Pseudodrusen
- Extent/pattern of RPE disruption and lipofuscin accumulation
- Ruling out masqueradors

Early Detection of Geographic Atrophy

GA Progression

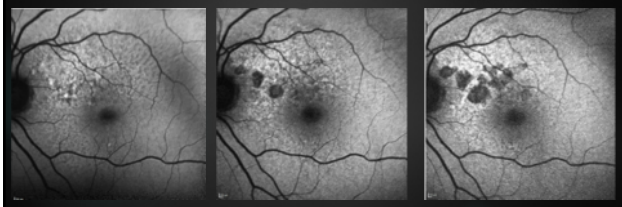


20/20 VA

20/20 VA, but I can't see as well!

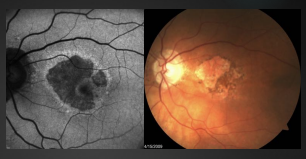
2 years apart

FAF: Putting it all together



Patient Education

"Mom can see 20/20, I don't know what she is complaining about?"



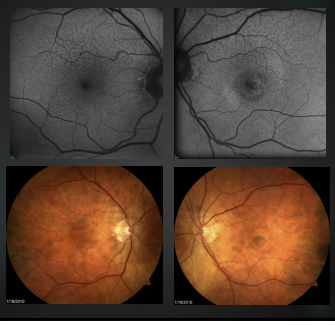
2009

"My vision is getting worse! I don't understand"

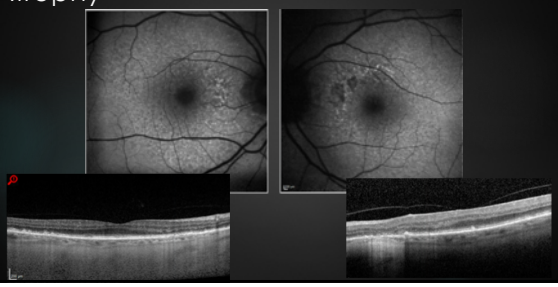
--Still 20/30

2012

Reticular Pseudodrusen



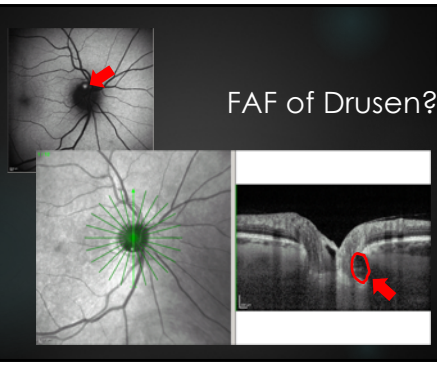
Reticular Pseudodrusen/Geographic Atrophy



FAF of drusen

- What do drusen look like on FAF??

FAF of Drusen?



FAF Drusen

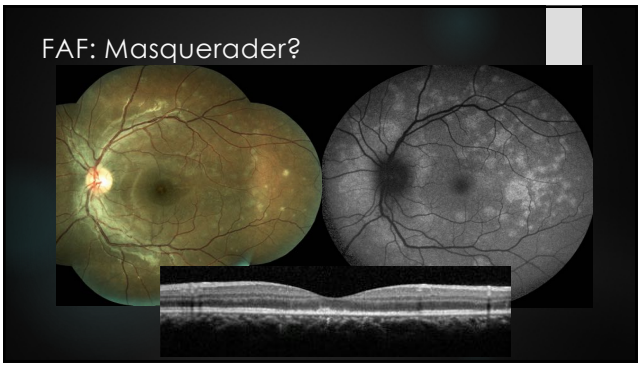
	Small drusen Hard drusen	Large drusen Soft drusen	Subretinal deposit Reticular pseudodrusen
Colour fundus photography (CFP)	Small (<63 μm) discrete yellow-white deposits with distinct edges. Found in macula and peripheral retina.	Larger (usually >125 μm) less discrete deposits found only in the posterior pole (more frequent in central macula, superior and temporal quadrants). Yellow appearance; central part may be whiter.	Variable diameter (≥ 100 μm); may be dot-like or reticular. Found preferentially in the perifovea (often more predominant superiorly). Whiter and more irregular than conventional drusen. Near infrared CSLO reflectance imaging is more sensitive than CFP.
Short wavelength auto-fluorescence	Foci of reduced AF sometimes surrounded by increased AF	Moderate hyperautofluorescence. Larger drusen may show heterogenous AF signal.	Reticular pattern, hypoautofluorescent. A minority may be atypically hyperautofluorescent.

Khan KN, Mahroo OA, Khan RS, et al. Differentiating drusen: Drusen and drusen-like appearances associated with ageing, age-related macular degeneration, inherited eye disease and other pathological processes. *Prog Retin Eye Res*. 2016;53:70-106.

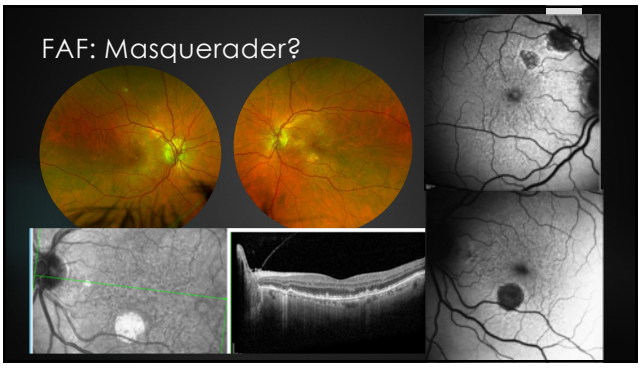
FAF in AMD

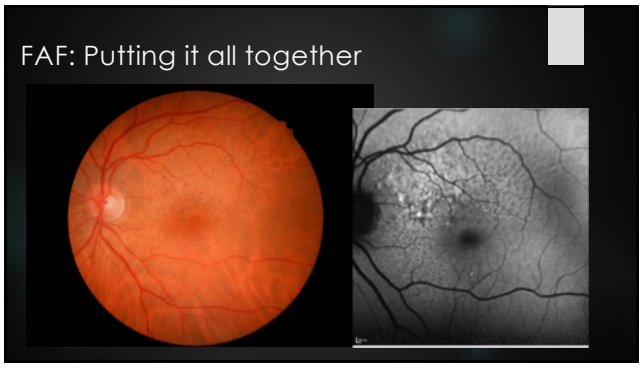
FAF in AMD

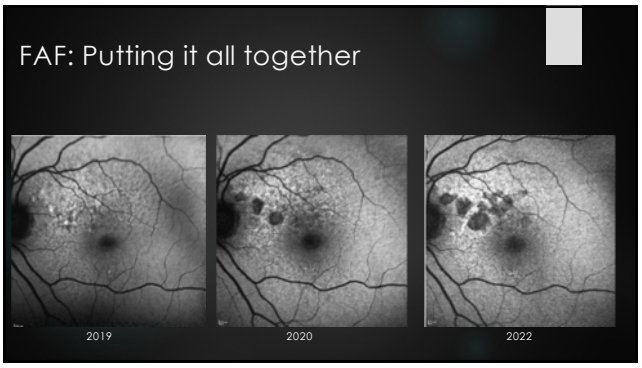

FAF in AMD


FAF: Masquerader?


FAF: Masquerader?


FAF: Masquerader?

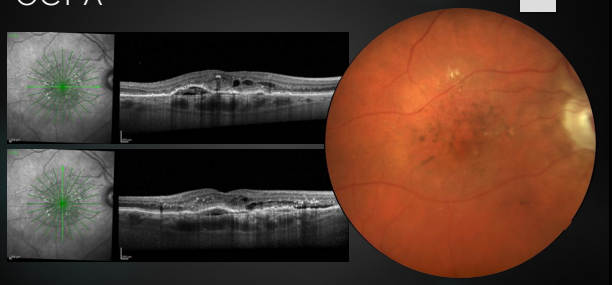

FAF: Putting it all together


FAF: Putting it all together
2019
2020
2022

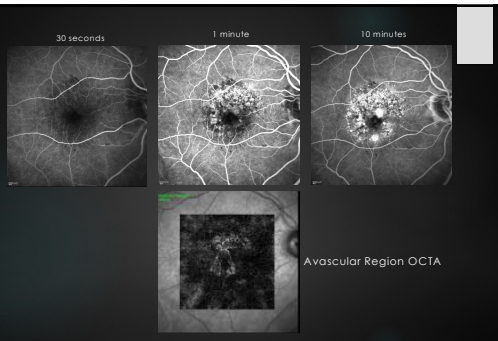
OCT-A

- What does OCT-A tell us??
- How does this differ from FA?
- What new classifications, insights, obstacles will this technology bring us?
  - Exudative vs. non-exudative CNV
  - Subclinical CNV
  - Segmentation errors, projection artifacts, distorted anatomy, accuracy of technology
  - To treat or not to treat?
  - To refer or not to refer?
  - Learning curve

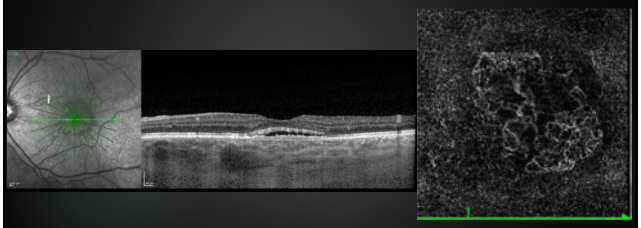
OCT-A



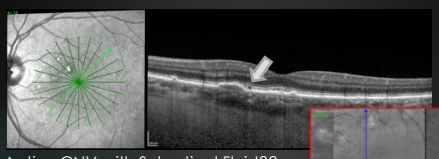
OCT-A

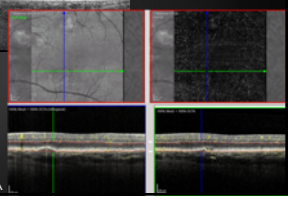


OCT-A

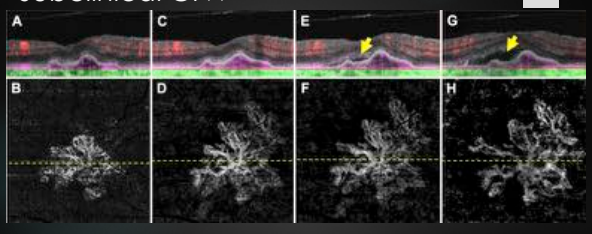


OCT-A


Active CNV with Subretinal Fluid??


No CNV present on OCTA

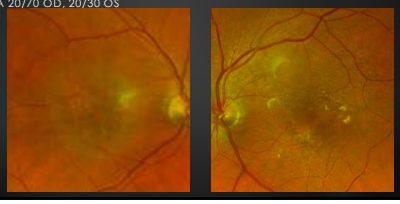
Subclinical CNV

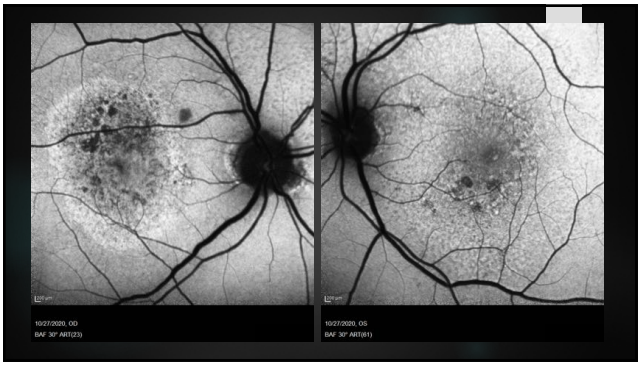


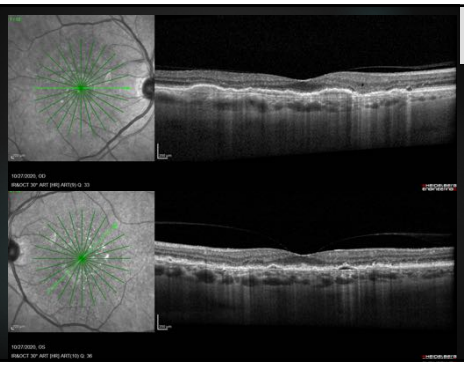
de Oliveira Dias JR, Zhang Q, Garcia JMB, et al. Natural History of Subclinical Neovascularization in Nonexudative Age-Related Macular Degeneration Using Swept-Source OCT Angiography. *Ophthalmology*. 2018;125(2):255-266.

OCTA example

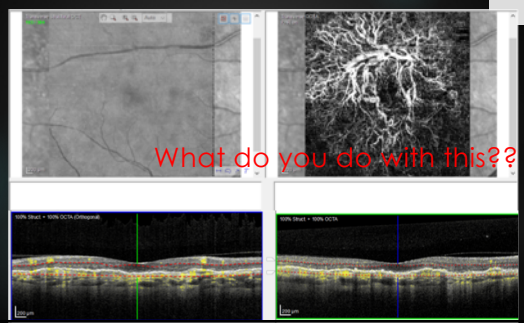
- 75 year old white male
  - Decreased vision over the last year OD
  - BCVA 20/70 OD, 20/30 OS



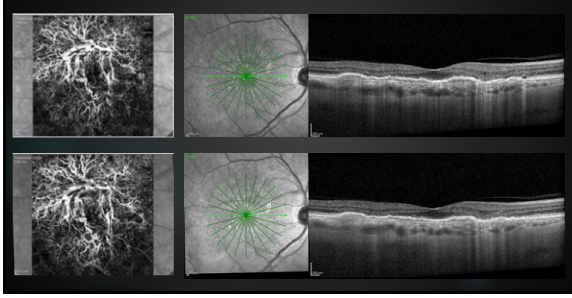




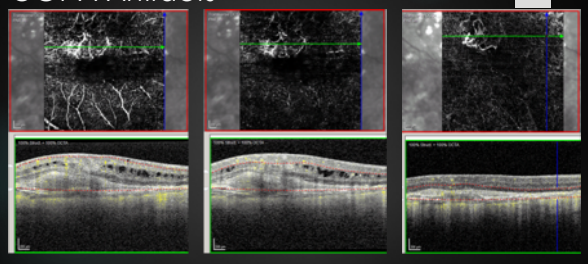
OCTA of avascular complex



What do you do with this??

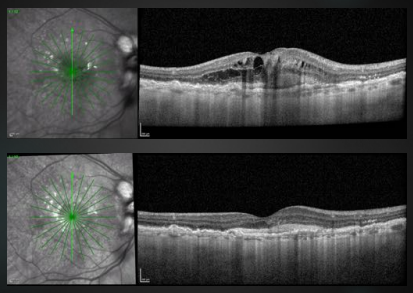


OCT-A Artifacts



Instrument segmentation | Manuel segmentation | Post treatment: instrument segmentation

OCT-A Artifacts



Dark Adaptation

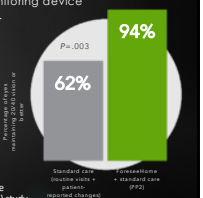
- What does dark adaptation tell us?
  - A test of visual **FUNCTION**
  - Real life applications
- What new insights does this bring us?
  - Reduced retinal function before clinical signs
  - Worsening dark adaptation with worsening clinical disease
    - Patients with RPD have worse dark adaptation
  - Patients have multiple diseases
    - AMD + Cataracts
  - 20/20 patient…"but doc, I can't see!"
- What obstacles exist?
  - Delayed dark adaptation is not exclusive to AMD
  - How does this change my patient management?

Dark Adaptation

- 90% sensitivity and specificity in detecting AMD
  - Jackson GR, Scott IU, Kim IK, Quillen DA, Iannaconne A, Edwards JG. Diagnostic Sensitivity and Specificity of Dark Adaptometry for Detection of Age-Related Macular Degeneration. Invest Ophthalmol Vis Sci. 2014;55:1427-1431
- Ability to detect AMD 3 years before clinical findings are present
  - Owsley, Cynthia, Gerald McGwin, Mark E. Clark, Gregory R. Jackson, Michael A. Callahan, Lanning B. Kline, C. Douglas Witherspoon, and Christine A. Curcio. "Delayed Rod-Mediated Dark Adaptation Is a Functional Biomarker for Incident Early Age-Related Macular Degeneration." Ophthalmology, October 30, 2015.

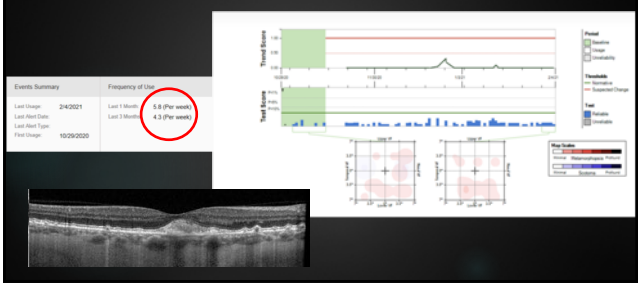
At Home Vision Monitoring

- What does this tell us?
  - FDA approved (for intermediate AMD) at home vision monitoring device using hyper-acuity to detect early conversion to wet AMD.
- Benefits
  - The biggest risk to vision remains conversion to wet AMD
  - Earlier detection = better visual outcomes!
  - Earlier detection than Amsler grid
- What obstacles exist?
  - Patient buy in
  - "Do I really need something like this at the stage I am in?"



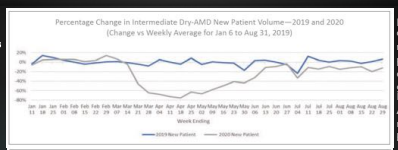
Chew EY, Clemons TE, Bressler SB, et al; AREDS2-HOME Study Research Group. Randomized trial of a home monitoring system for early detection of choroidal neovascularization home monitoring of the Eye (HOME) study. Ophthalmology. 2014;121(2):535-544.

He Sees You When Your Testing….

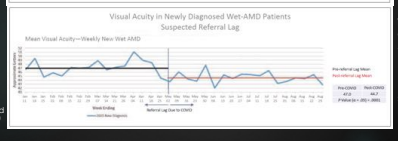


COVID Delays in AMD Management

New retina specialist patients



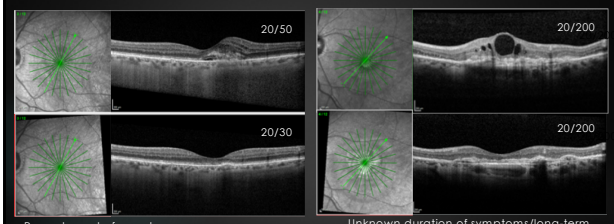
Drop in office visits during the initial months of the pandemic has created a significant gap in care. Intermediate dry AMD patient volume remains about 15% below 2019.



VA at wet AMD diagnosis dropped 2.3 letters ($P = < .0001$) due to delay in office visits. Finding is considered significant on a population basis.

Vestrum Health data published in *Retina Times*, October, 2020

Why Does Early Detection Matter?

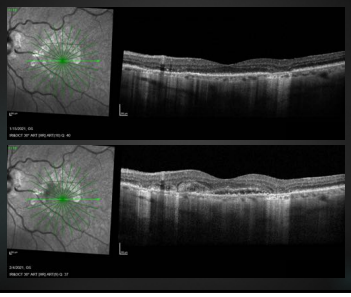


Recent onset of symptoms
Good VA at initiation of treatment

Unknown duration of symptoms/long-term symptoms
Poor VA at initiation of treatment

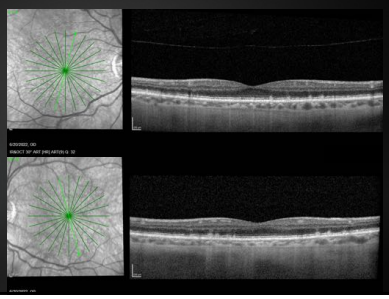
Anijeet DR, Hanson RJ, Bhagey J, Bates RA. National survey of the technique of intravitreal triamcinolone injection in the United Kingdom. Eye. 2007;21(4):480-486. doi:10.1038/sj.eye.6702232

Conversion Can Happen at Any Time

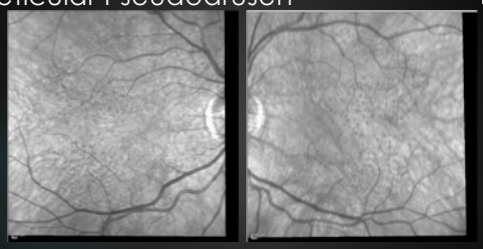


Case Example 1

- 81 YO WM
- 20/20 OD, OS



Reticular Pseudodrusen



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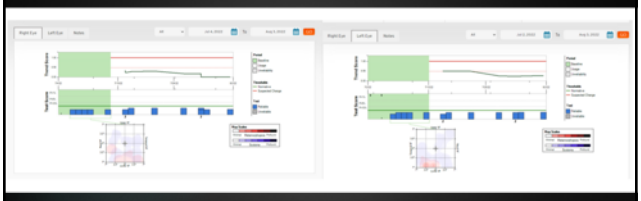
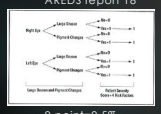


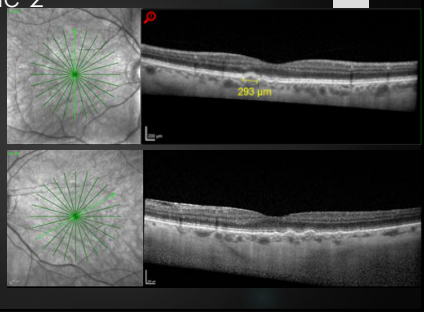
Case Example 2

- PT 72 YO WF Aug 2020
- BCVA 20/30 OD, 20/20 OS

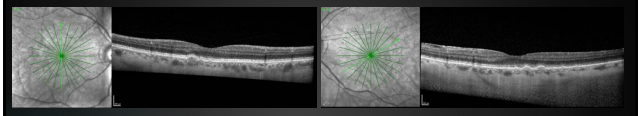
AREDS report 18



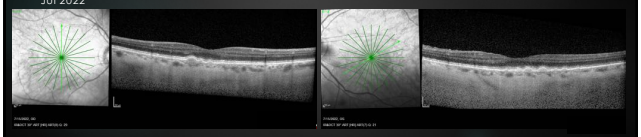
0 point=0.5%
1 point=3%
2 points=12%
3 points=25%
4 points=50%



Aug 2020



Jul 2022

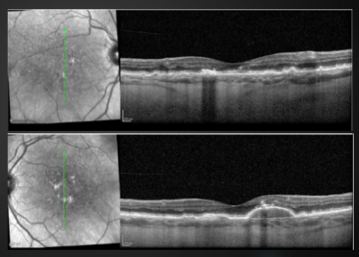


Case Example 3

- GS 73 YO WM Aug 2021
- BCVA 20/25 OD, 20/20 OS

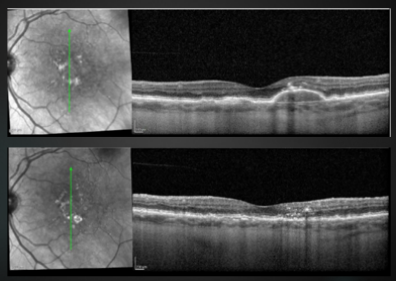
AREDS report 18

0 point=0.5%
1 point=3%
2 points=12%
3 points=25%
4 points=50%

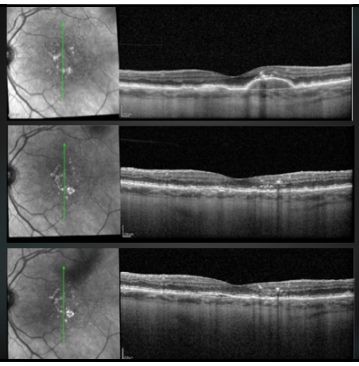


March 2022

- ALERT!!!



- Aug 2021
- March 2022
- Aug 2022



Drusen Regression

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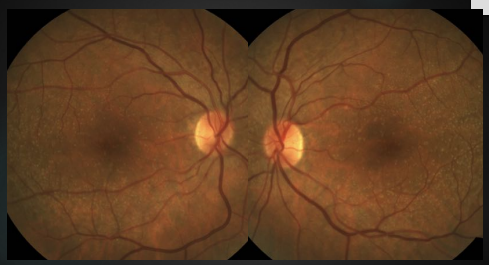
- Yehoshua Z, Wang F, Rosenfeld PJ, et al. Natural history of drusen morphology in age related macular degeneration using spectral domain optical coherence tomography. Ophthalmology. 2011;118(12):2434-41.
- Schlantz FG, Baumann B, Kundi M, et al. Drusen volume development over time and its relevance to the course of age-related macular degeneration. Br J Ophthalmol. April 4, 2016.
- Folgar FA, Yuan EL, Sevilla MB, et al. Drusen volume and retinal pigment epithelium abnormal thinning volume predict 2-year progression of age-related macular degeneration. Ophthalmology. 2016;123(1):39-50.

AMD Managements on the Horizon

- Beovu (brolucizumab)
  - 50% able to maintain q12 week injections
- Vabysomo (faricimab)
  - Inhibits VEGF and ang-2
  - 60% maintain 4 month injections (2 year data)
- Biosimilars
- Susvimo
  - Port delivery system: refilled x 6 mos
  - Recalled
- Future considerations
  - Gene therapy delivery
  - GA treatments
  - Light therapy
  - Oral medications/supplements
  - Topicals?

Final Case Example

CASE 1: 70 year old white male: 20/20 OU



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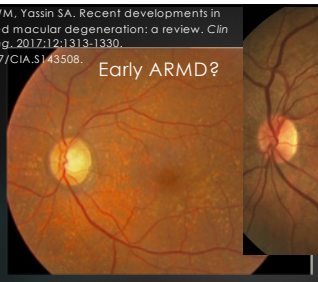
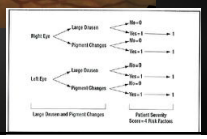
Early ARMD?

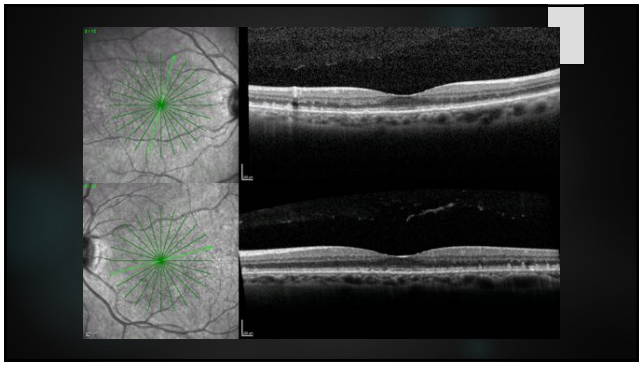




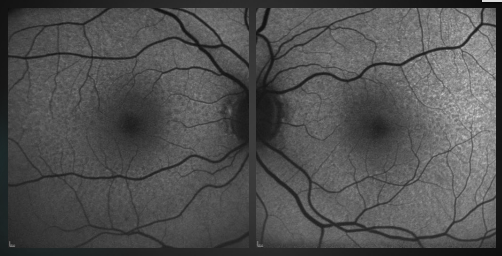
0 points: 0.5% five year risk of conversion to advanced AMD

"You just have a little AMD"

How could we have known???



Fundus Autofluorescence



Could we have done something different?

"Your detailed pictures show that you are at a higher risk of vision loss from your macular degeneration"

"While your vision is 20/20, your visual FUNCTION is ALREADY being affected by this disease"

"I am going to prescribe you a device to monitor your vision at home daily"

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