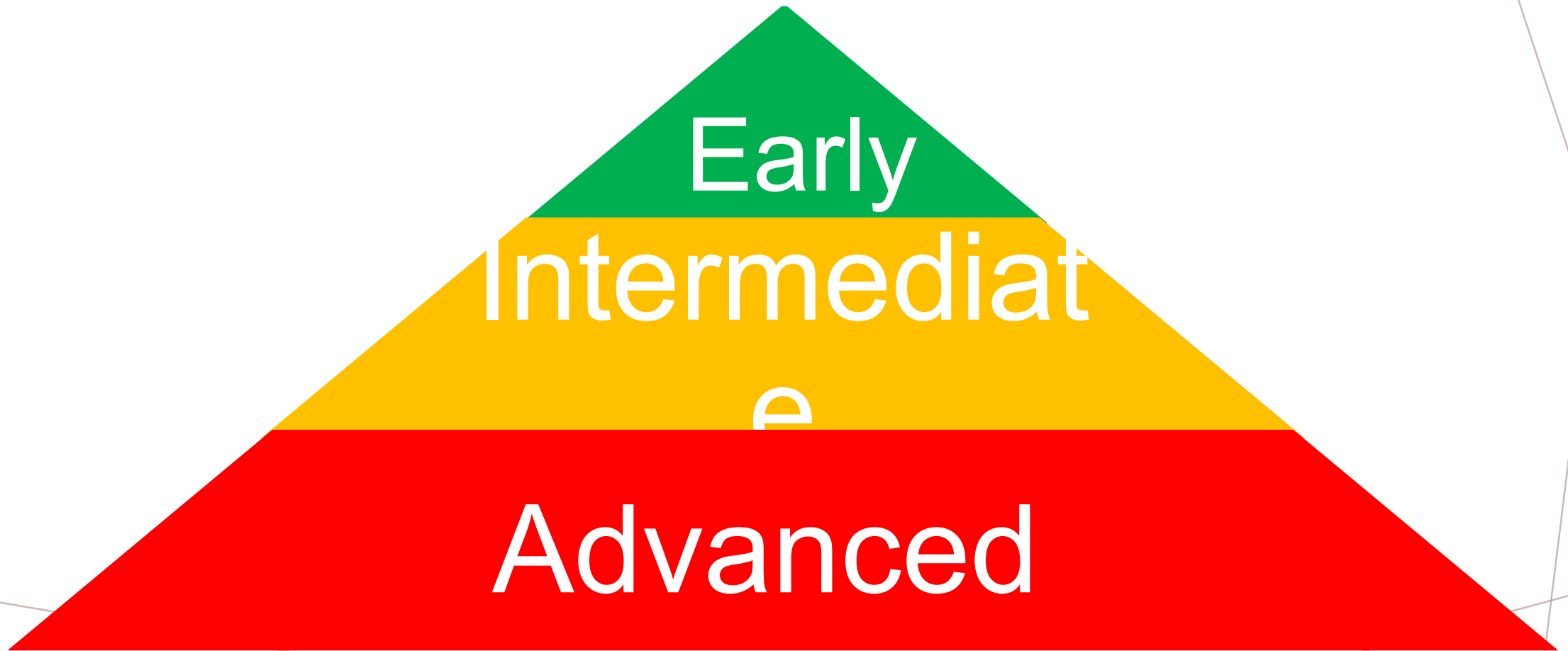


iRORA, cRORA and Other stuff

Khaled Aboushousha
CertRCOphth

AMD Classification

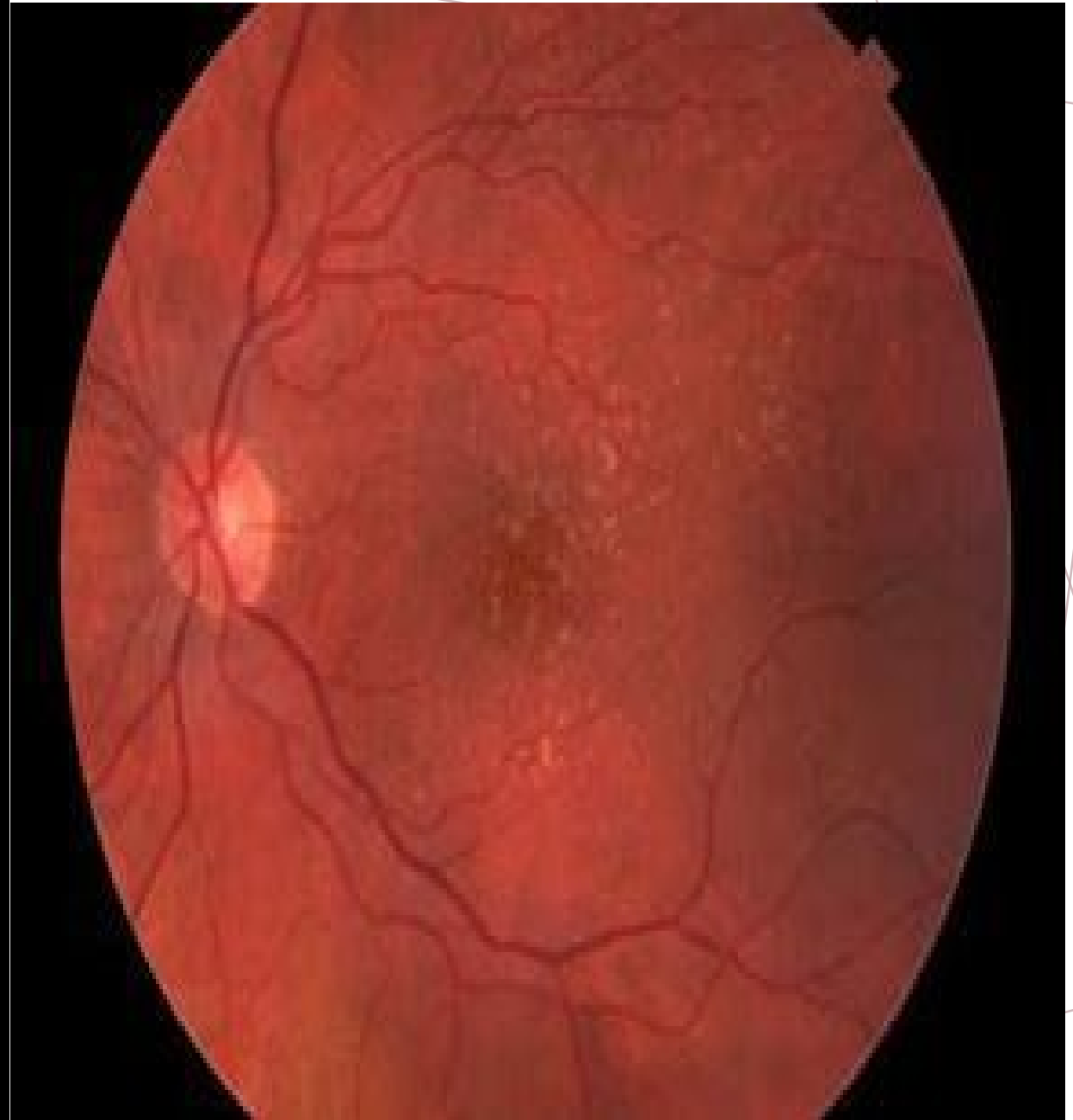


Early AMD

Drusen that are :

Multiple Small (less than 63 microns)

Few Intermediate (from 63 to 125 microns)



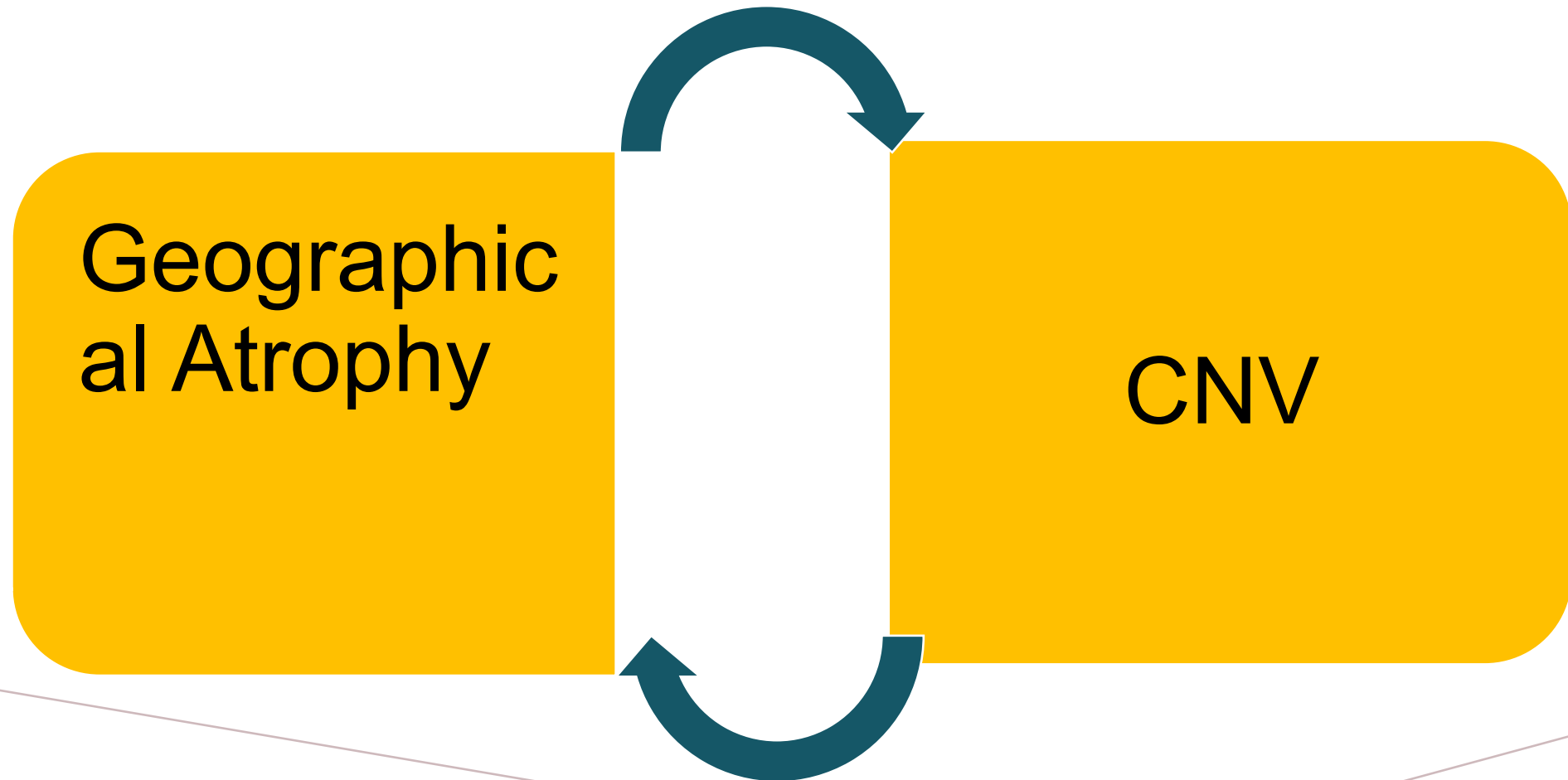
Intermediate AMD

extensive
intermediate
size

Any drusen
of large size
(≥ 125
microns)

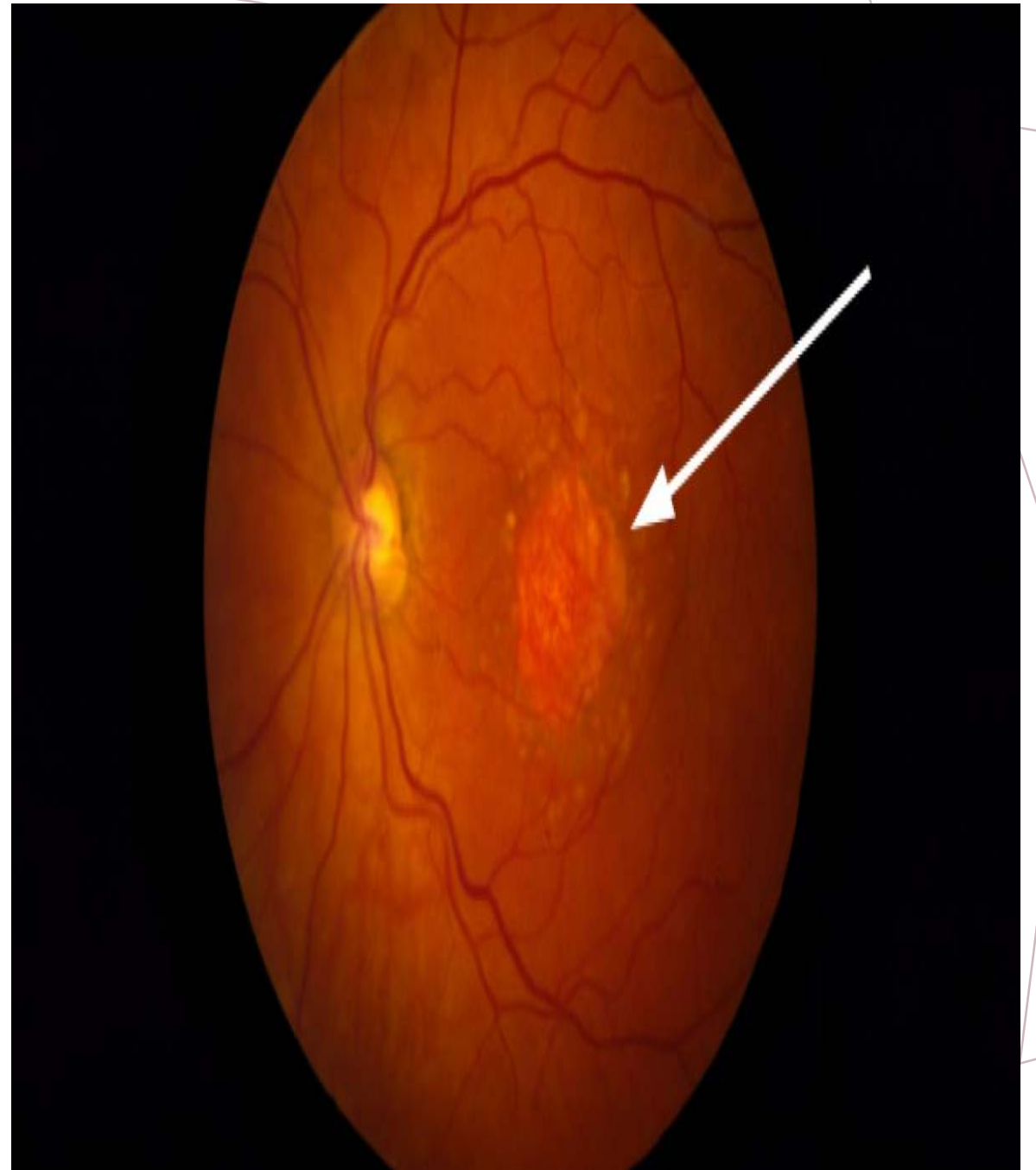


Advanced AMD



Geographical Atrophy

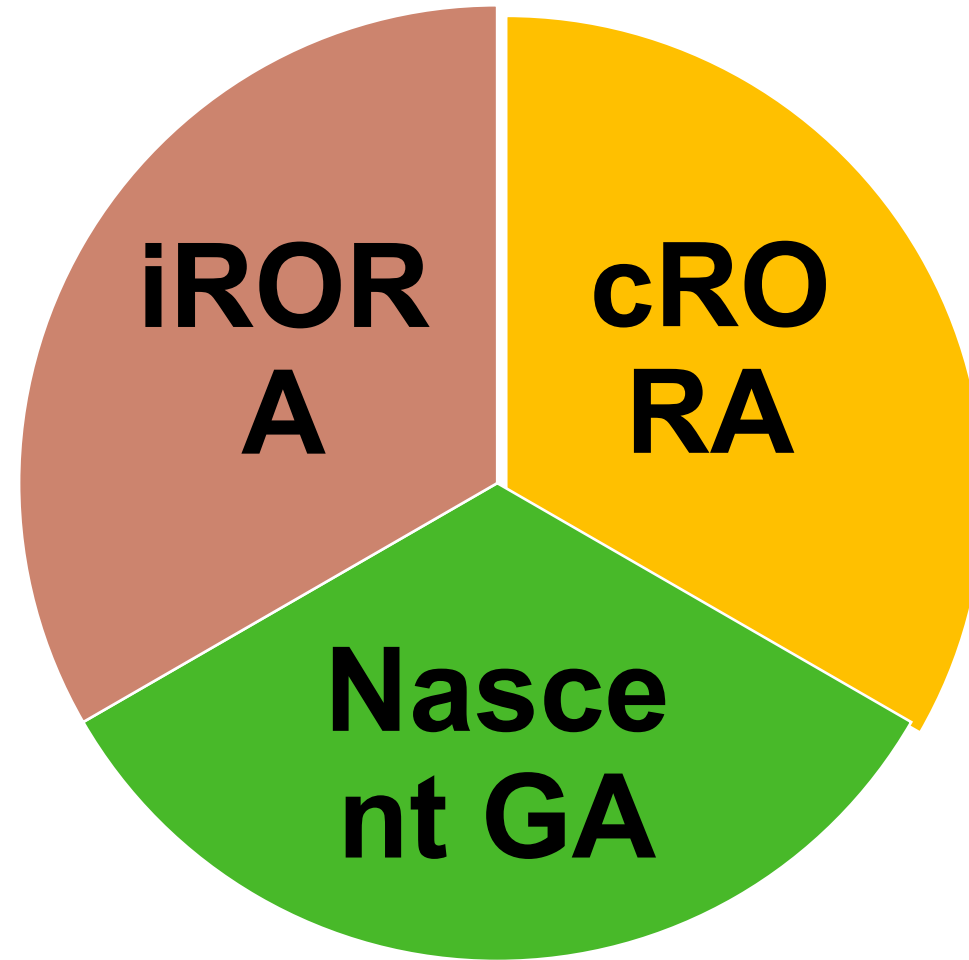
*GA has traditionally been defined on **color fundus photographs** (CFP) as a sharply delineated circular or oval area of hypopigmentation or depigmentation at least **175 μm** in diameter through which choroidal vessels are visible.*



Atrophy on OCT

Incomplete Retinal Pigment Epithelial and Outer Retinal Atrophy (iRORA) in Age-related Macular Degeneration: CAM Report 4

[Robyn H Guymer](#)¹, [Philip J Rosenfeld](#)², [Christine A Curcio](#)³, [Frank G Holz](#)⁴, [Giovanni Staurenghi](#)⁵, [K Bailey](#)
[Freund](#)⁶, [Steffen Schmitz-Valckenberg](#)⁴, [Janet Sparrow](#)⁷, [Richard F Spaide](#)⁶, [Adnan Tufail](#)⁸, [Usha Chakravarthy](#)
⁹, [Glenn J Jaffe](#)¹⁰, [Karl Csaky](#)¹¹, [David Sarraf](#)¹², [Jordi M Monés](#)¹³, [Ramin Tadayoni](#)¹⁴, [Juan Grunwald](#)¹⁵,
[Ferdinando Bottoni](#)⁵, [Sandra Liakopoulos](#)¹⁷, [Daniel Pauleikhoff](#)¹⁸, [Sergio Pagliarini](#)¹⁹, [Emily Y Chew](#)²⁰,
[Francesco Viola](#)¹⁶, [Monika Fleckenstein](#)⁴, [Barbara A Blodi](#)²¹, [Tock Han Lim](#)²², [Victor Chong](#)²³, [Jerry Luttj](#)²⁴, [Alan](#)
[C Bird](#)⁸, [Srinivas R Sadda](#)²⁵



cRORA criteria

An area of at least **250 um** on a **single horizontal** b-scan showing the following:

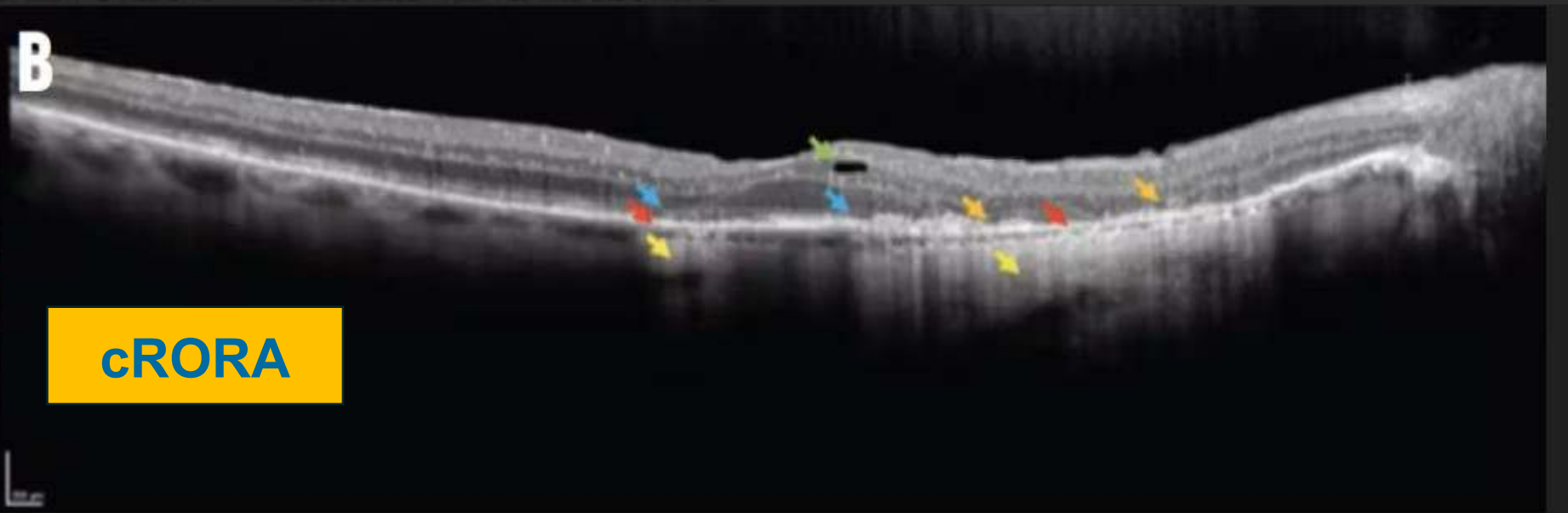
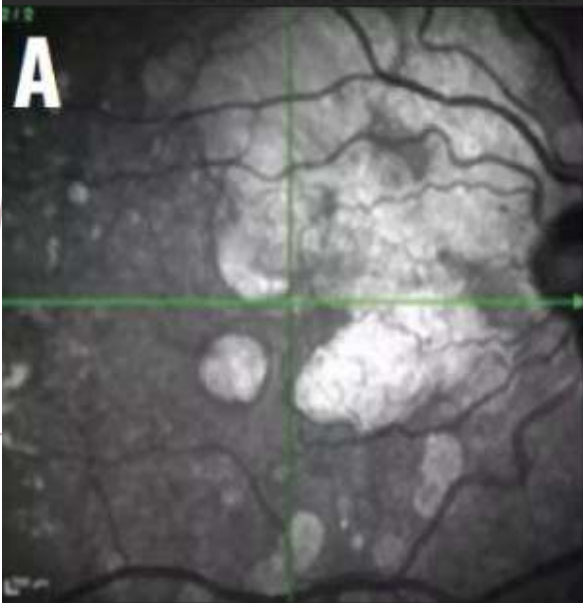
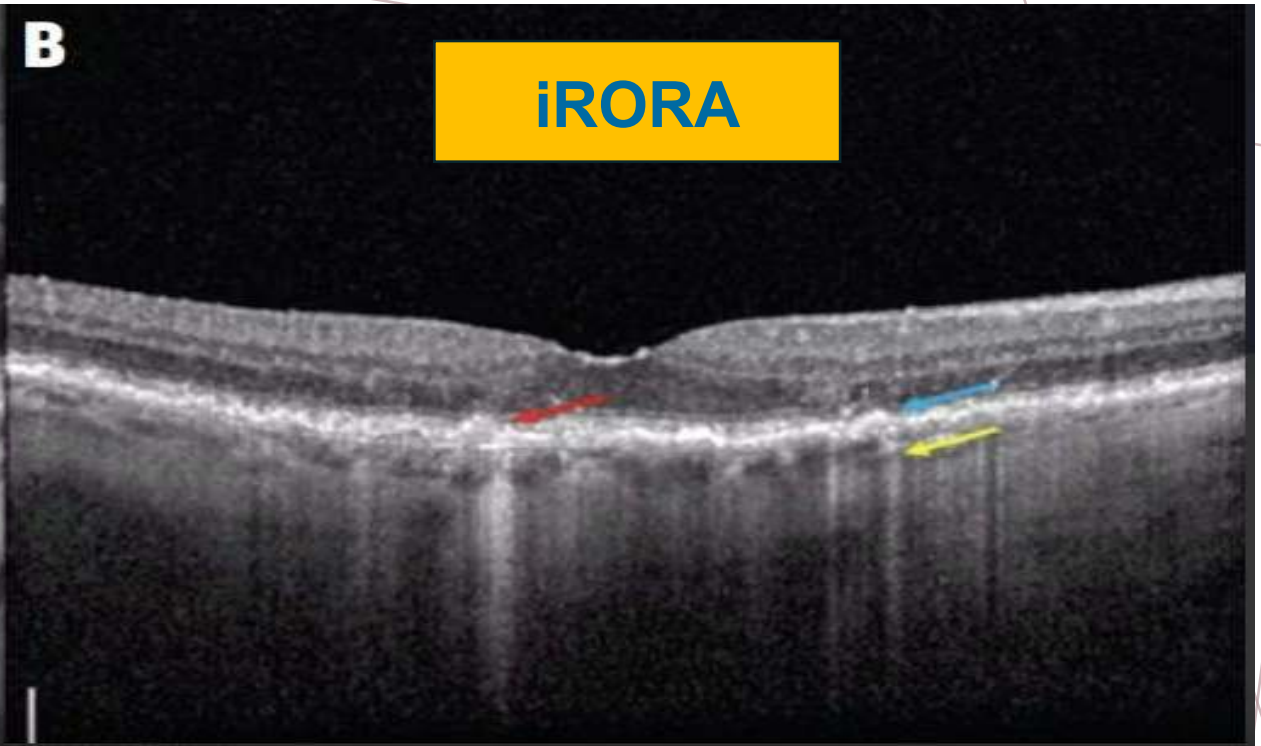
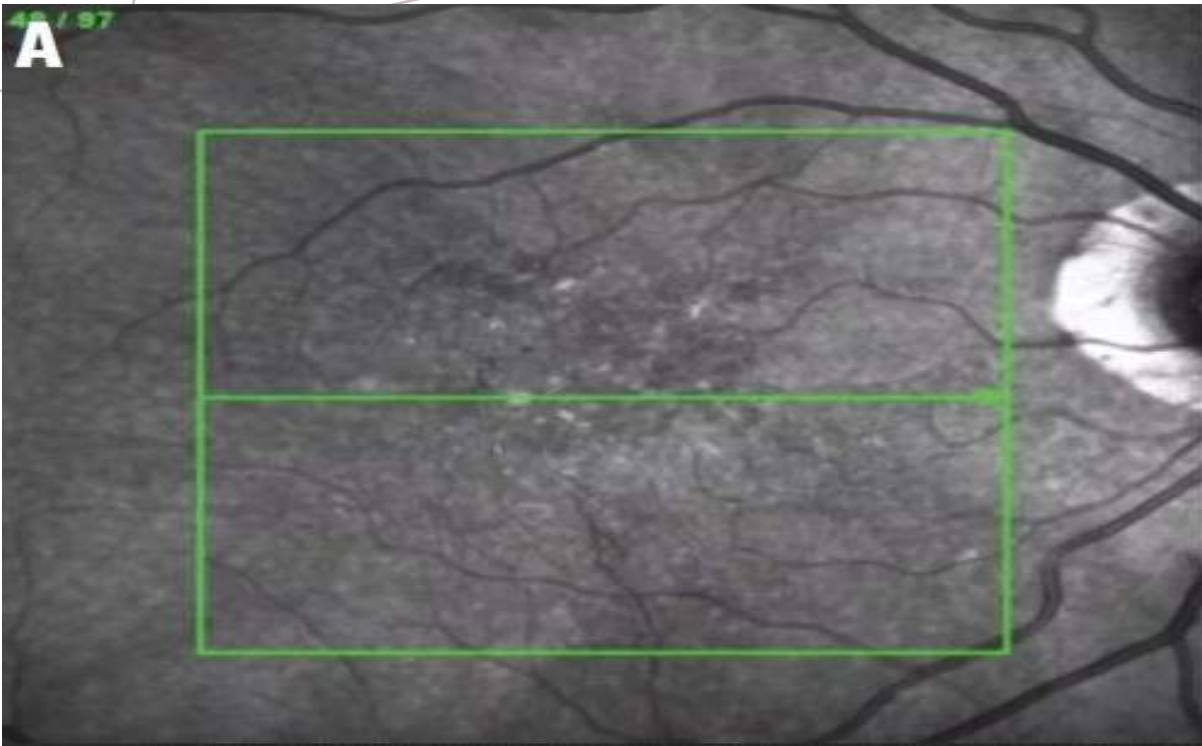
Attenuation or complete loss of the RPE

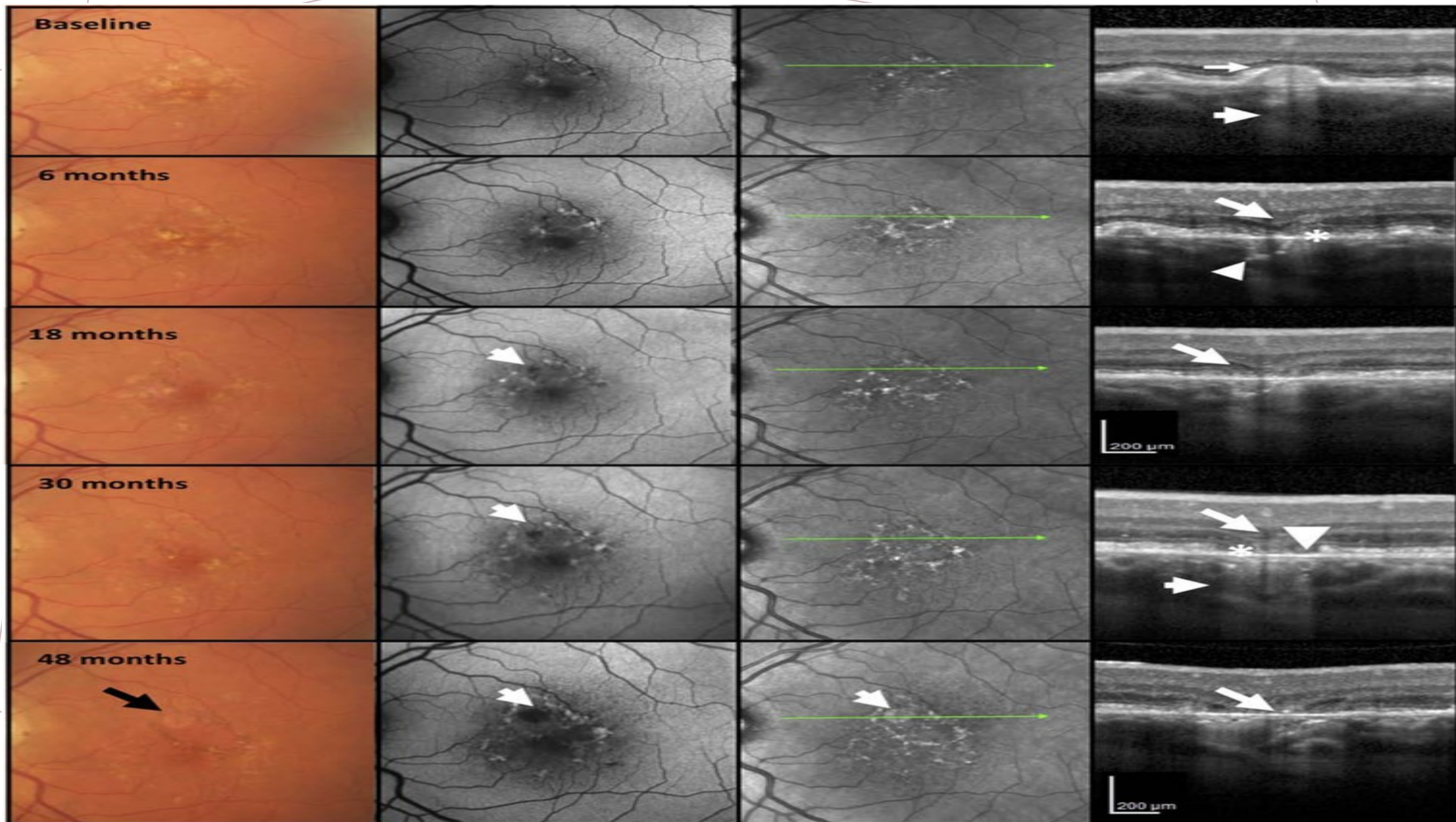
A corresponding hyper-transmission defect (hyperTD) through the area of RPE change,

signs of photoreceptors degeneration

**In the
absence
of RPE
tear**

***iRORA** refers to a horizontal b-scan area that has some, **but not all,** of the features of cRORA*





Nascent GA

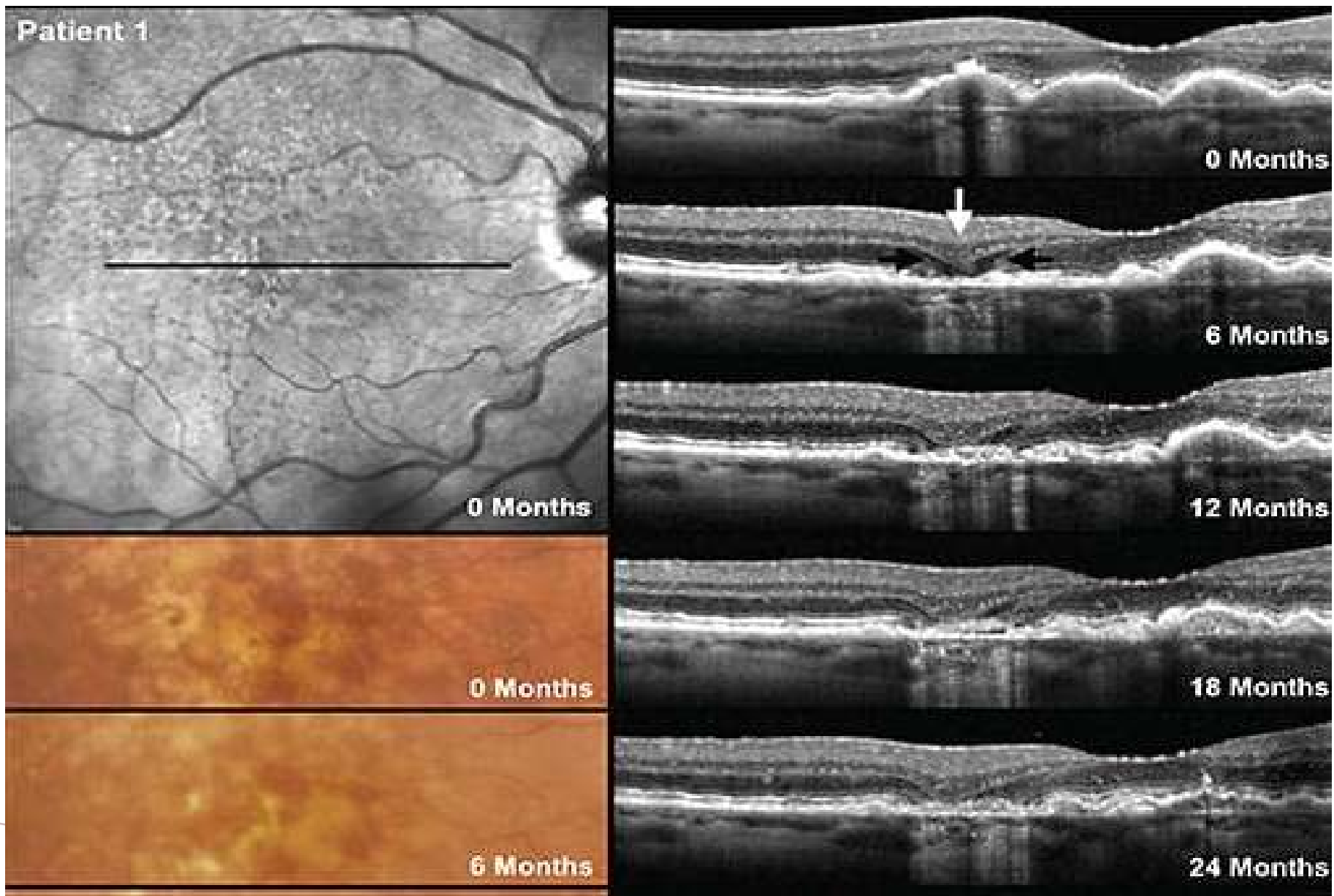
- Having a hyporeflective wedge in the Henle fiber layer +/- subsidence of the INL and outer plexiform layer with or without RPE disruption or hyperTD

Attenuation or complete loss of the RPE

A corresponding hyper-transmission defect (hyperTD) through the area of RPE change,

signs of photoreceptors degeneration





Nascent GA

GA

Watching your enemy , how can OCT see GA coming?



shutterstock.com · 253078696

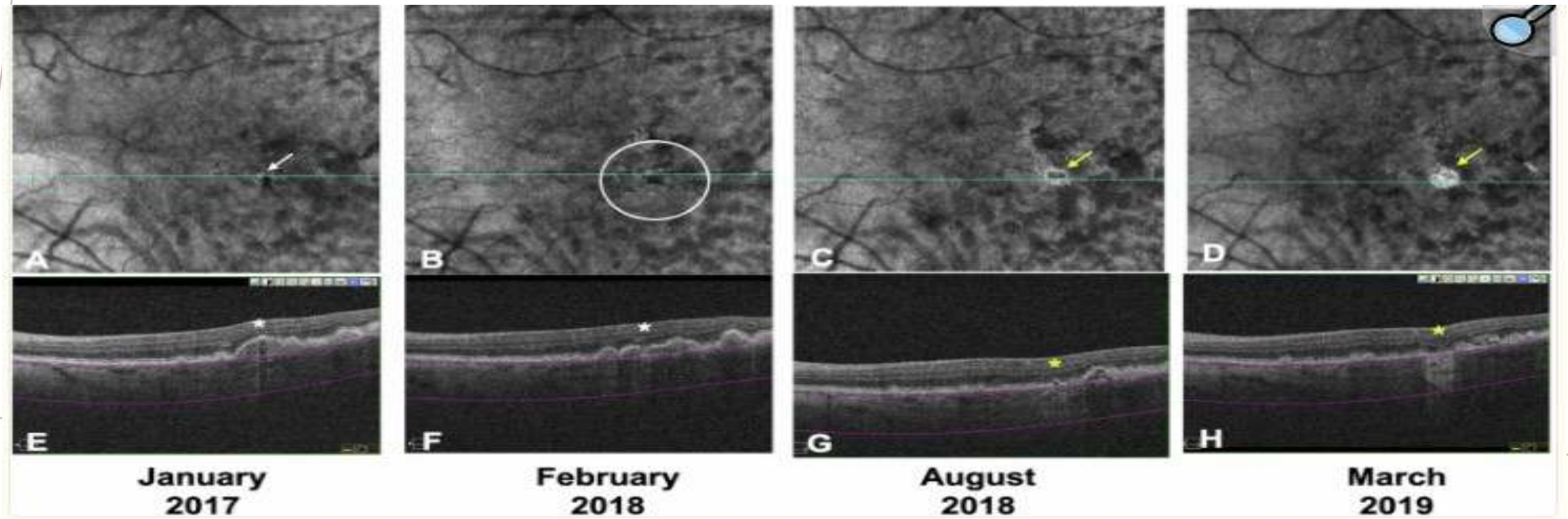
HYPERTRANSMISSION DEFECT



► Eye (Lond). 2024 Sep 15;38(18):3488–3494. doi: [10.1038/s41433-024-03338-0](https://doi.org/10.1038/s41433-024-03338-0) 

Relationship between hypertransmission defect size and progression in eyes with intermediate age-related macular degeneration

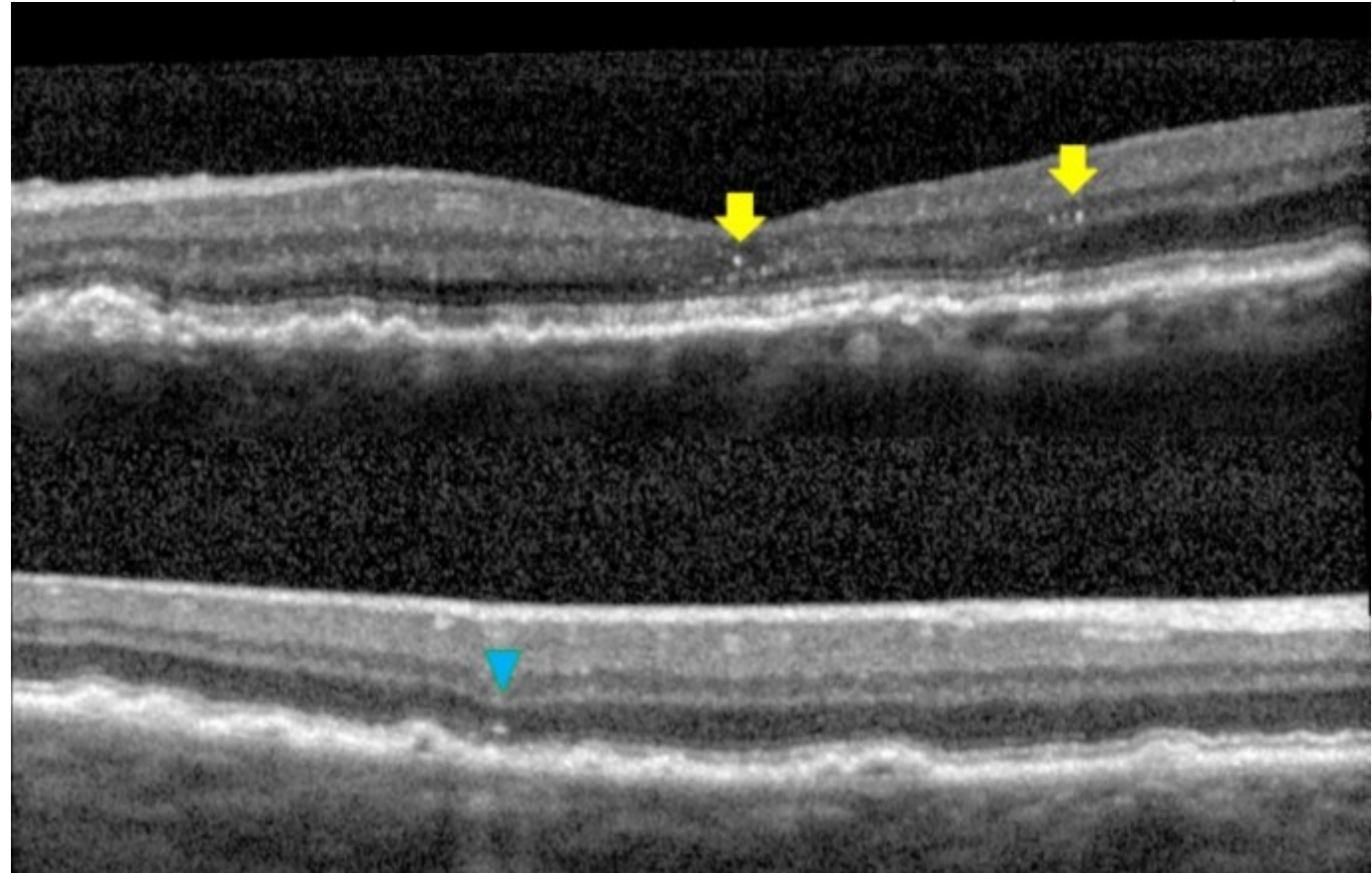
while most of the iAMD eyes **without hyperTDs** at baseline are likely to remain **stable** over two years, eyes with **hyperTDs of any size**, are at substantially higher risks for **progression** to iRORA, cRORA, and/or nAMD. Thus, hyperTDs may be useful for risk stratification and selection of high-risk patients for early intervention clinical trials for iAMD.



Hyperreflective Foci

five-fold increased risk of developing **GA** within 2 years in eyes with HRF compared with eyes without baseline HRF .

~**Christenbury et al**



Reticular Pseudodrusen

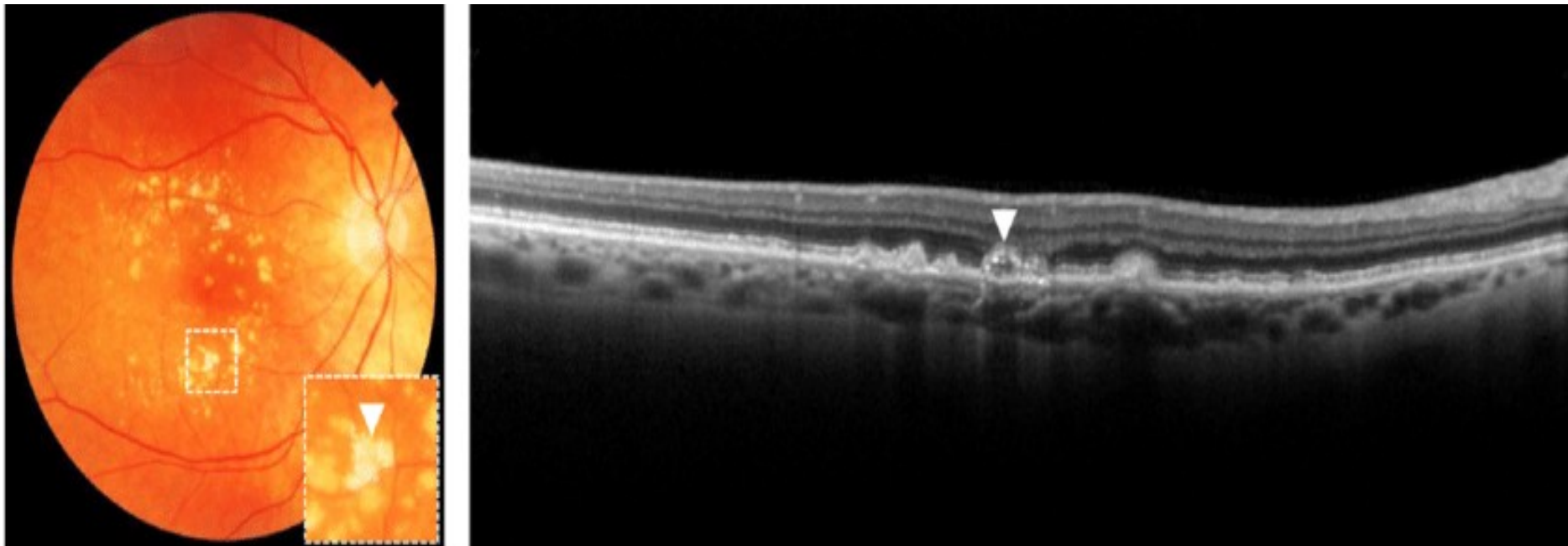
presence of RPD was associated with a nearly **three-fold** increased risk of progression **to late AMD**

~ **Zweifel et al**



Calcified Drusen

Heterogeneous internal reflectivity within drusen was present in 45% of eyes with iAMD and was associated with the development of **late AMD** within **1 year** ~ **Tan et al**



DRUSEN OOZE

SPRINGER NATURE Link

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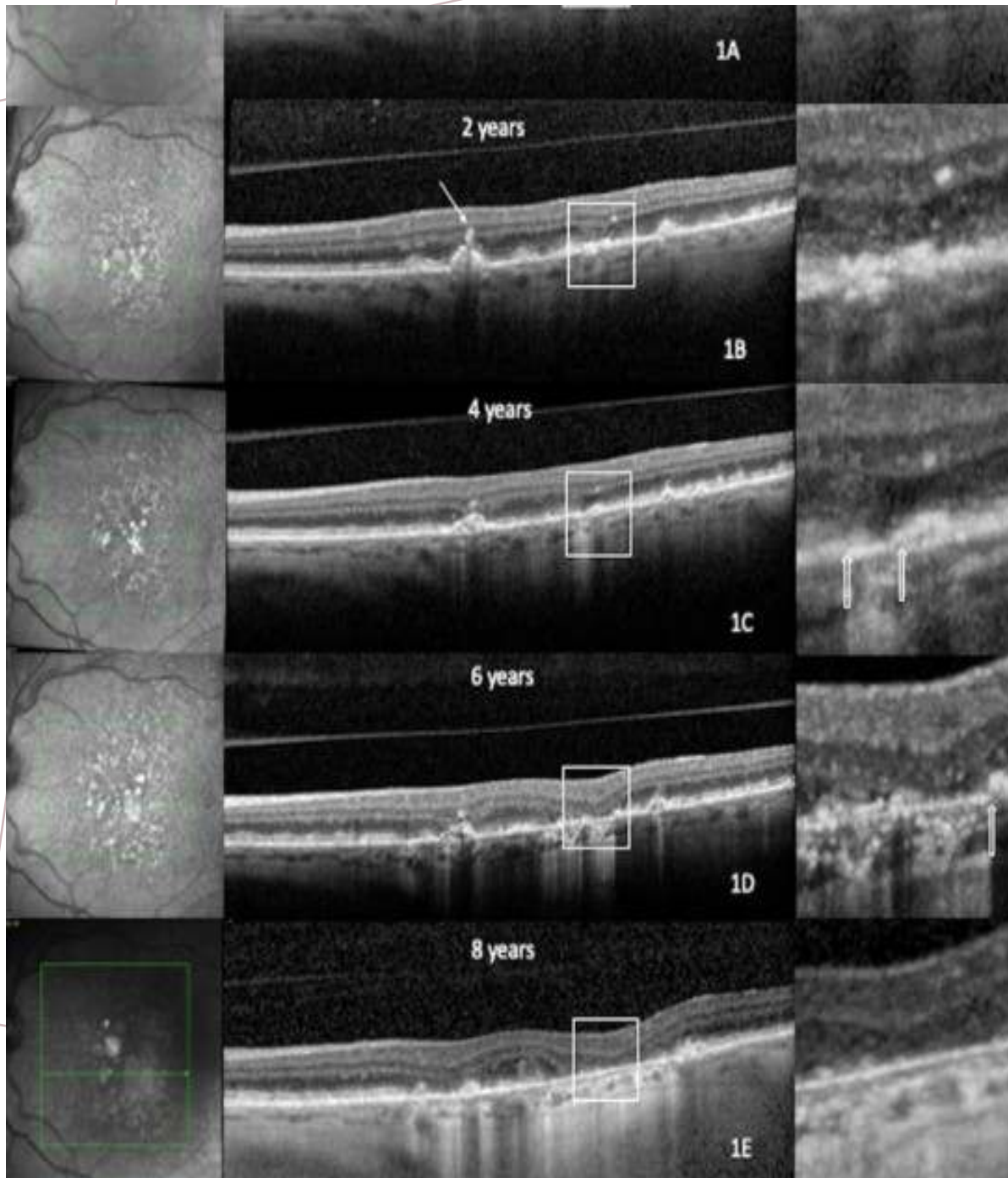
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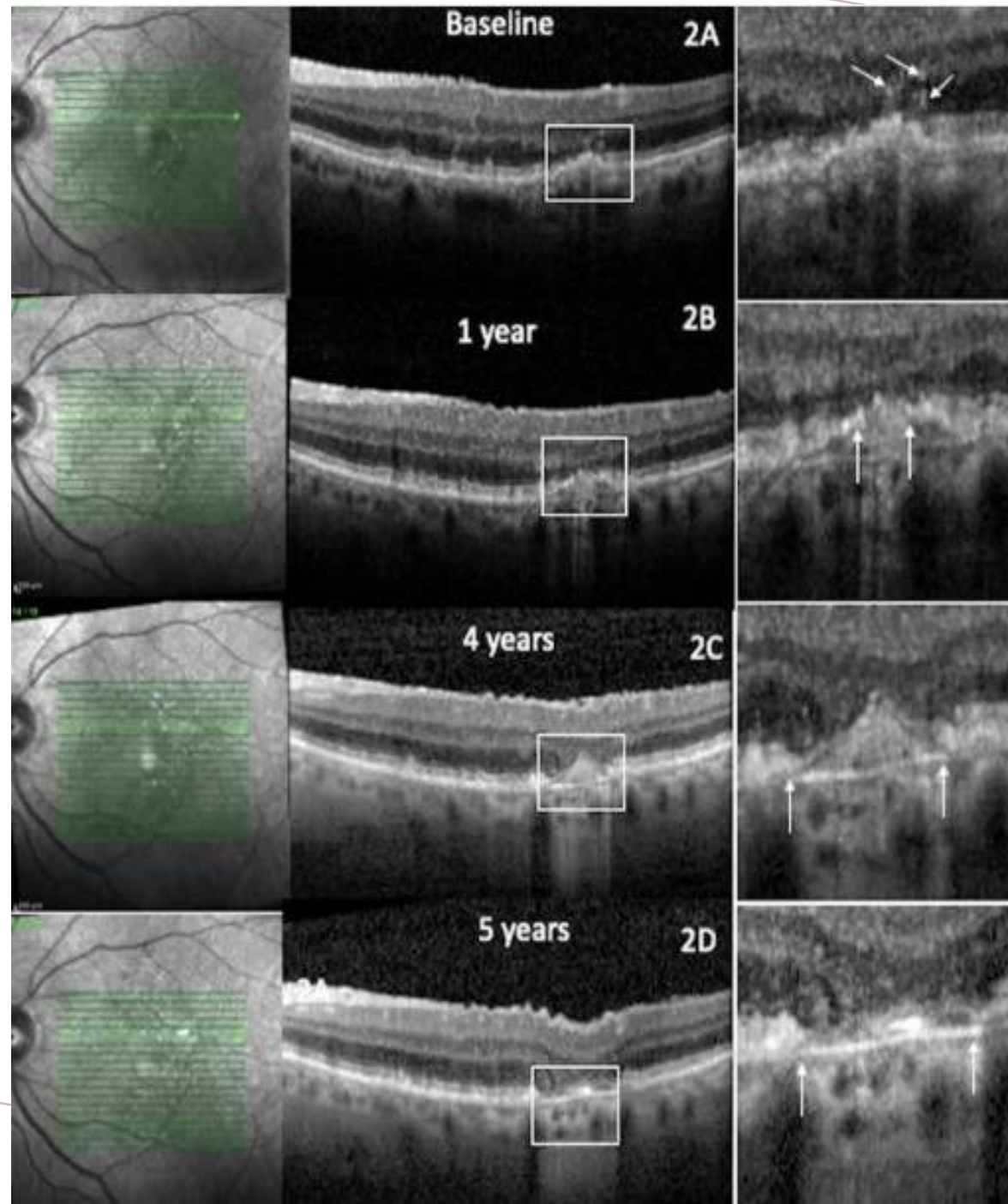
Drusen ooze: Predictor for progression of dry age-related macular degeneration

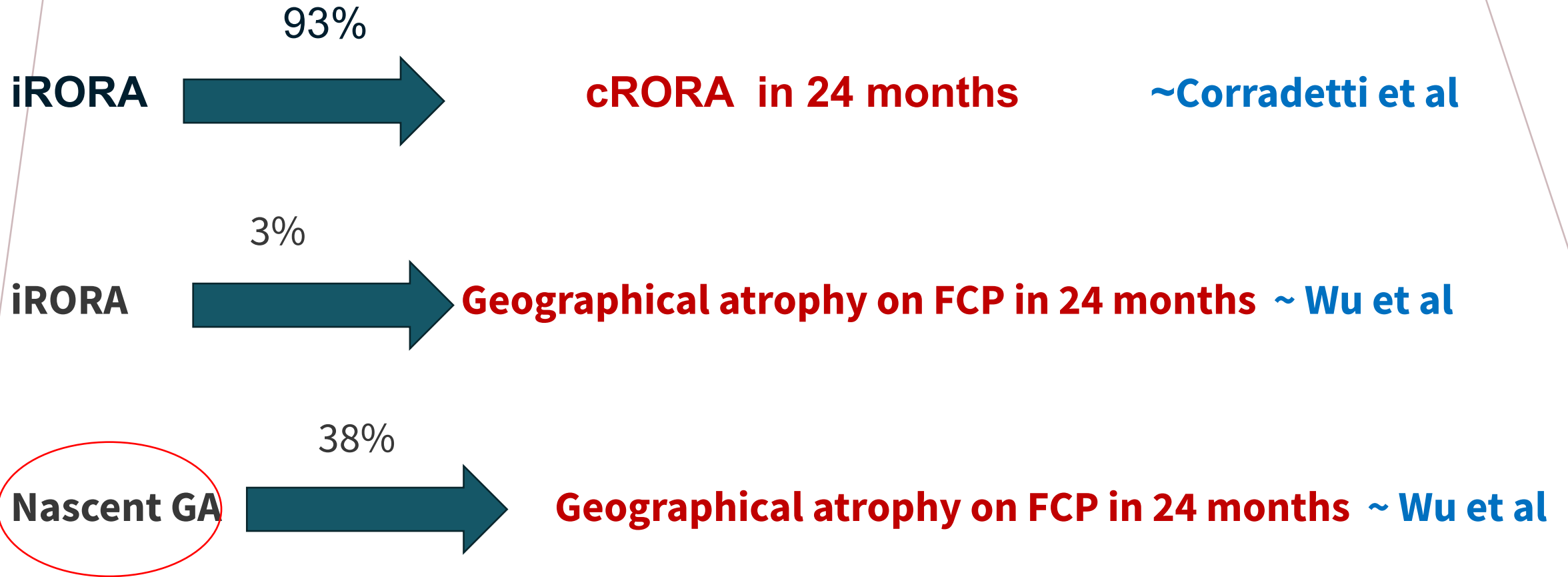
Retinal Disorders | Published: 12 March 2021

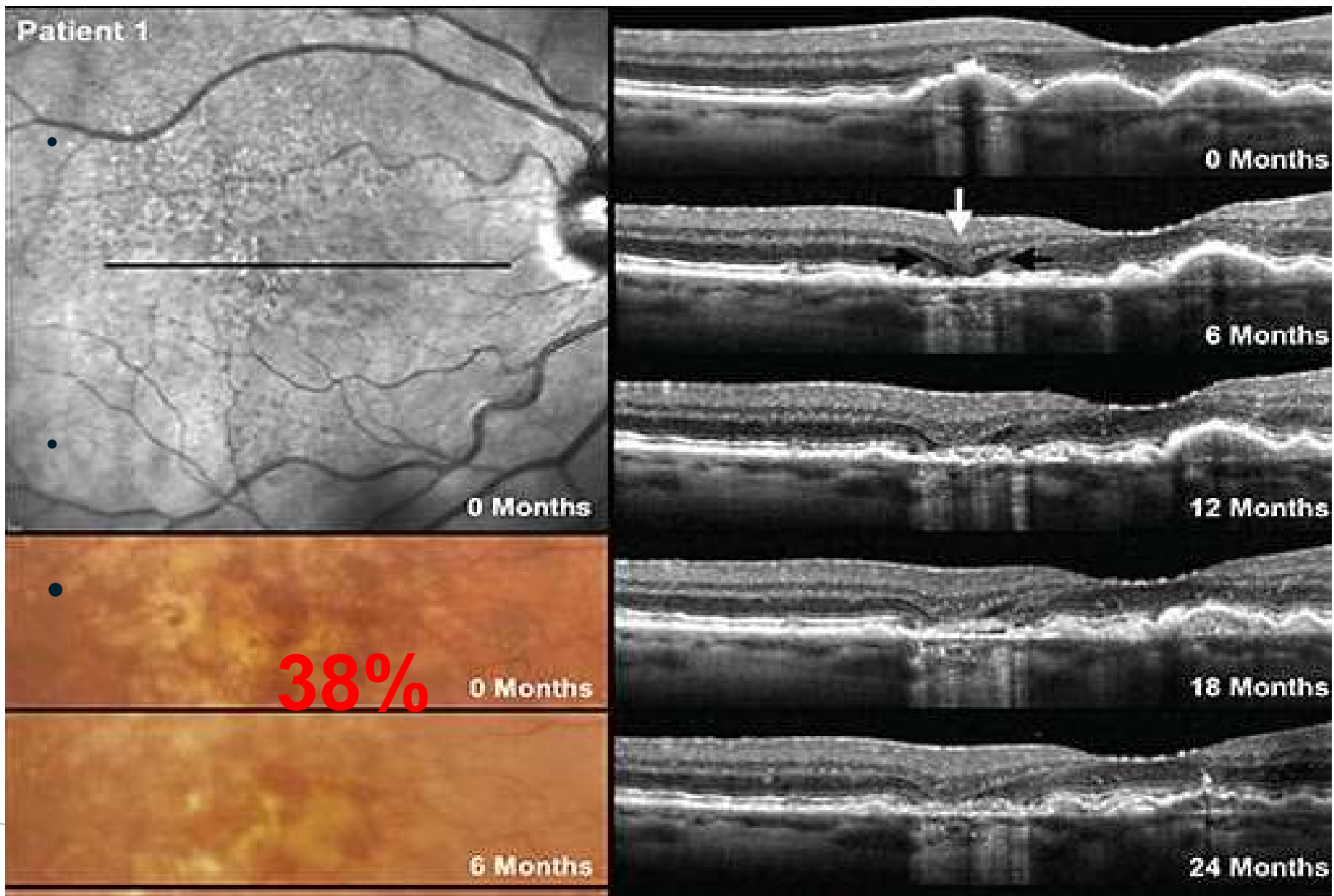
Volume 259, pages 2687–2694, (2021) [Cite this article](#)



Drusen ooze is highly prevalent in eyes with dry AMD and has a higher risk of developing iRORA and cRORA. poor correlation of drusen ooze with neovascular conversion. Drusen ooze could be considered as a predictor for dry AMD progression.







Nascent GA



GA

SECOND EYE INVOLVEMENT

European Journal of Ophthalmology

Mary Ann
Liebert

Impact Factor: 1.4 / 5-Year Impact Factor: 1.7



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| Research article

| First published online October 3, 2023

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Bilateral evolution of OCT biomarkers in dry AMD: Long-term follow up study

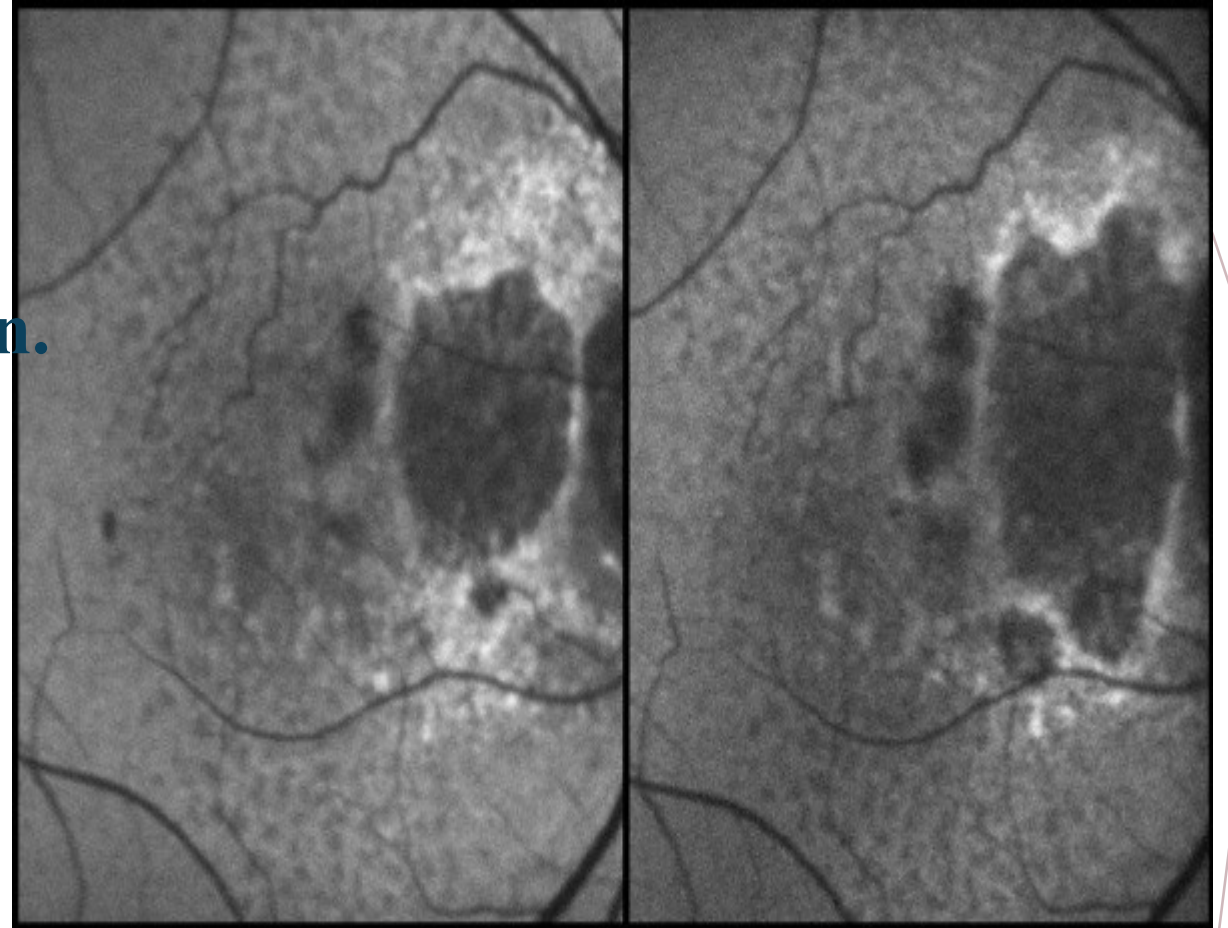
[Anindya Samanta](#) , [Supriya Arora](#), [...], and [Jay Chhablani](#) [View all authors and affiliations](#)

[Volume 34, Issue 3](#) | <https://doi.org/10.1177/11206721231204383>

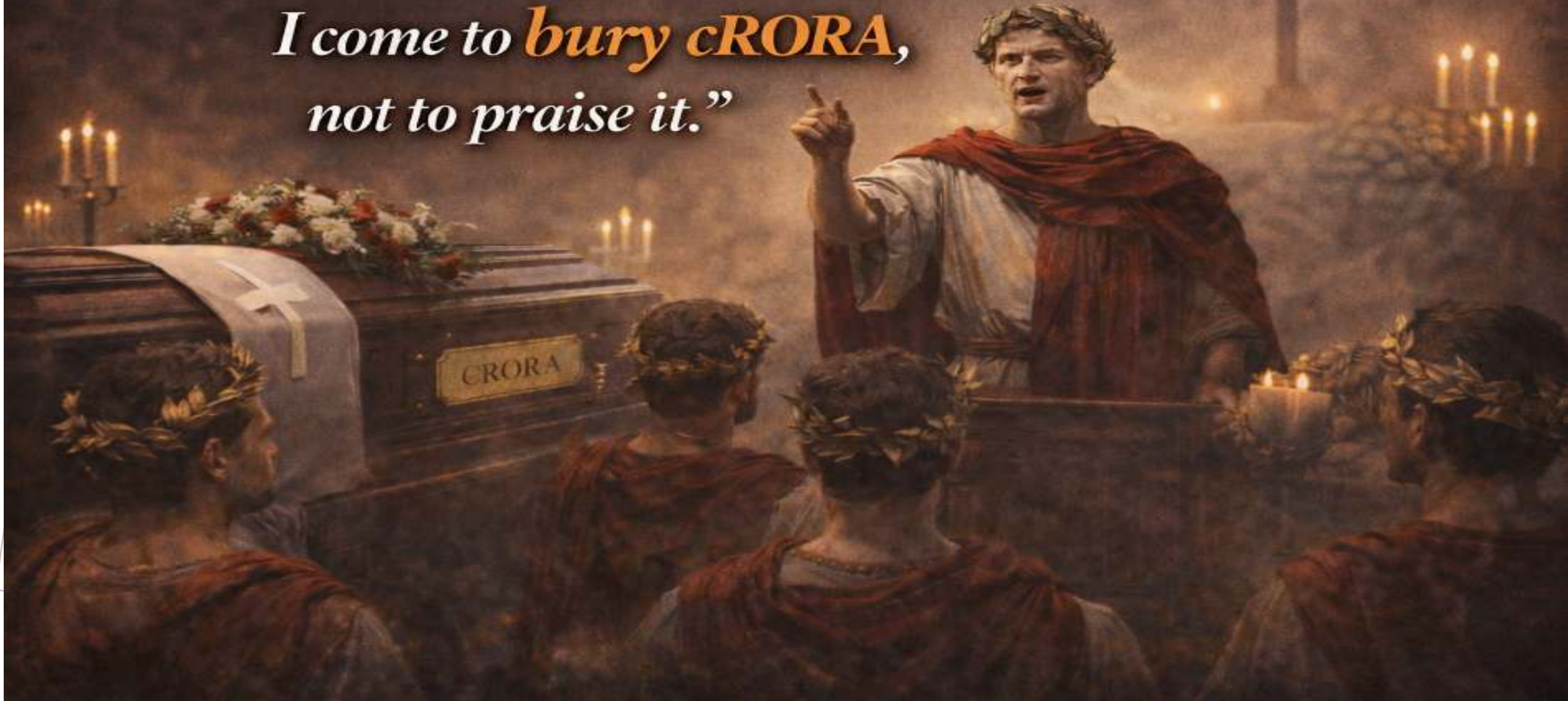
Late-stage OCT biomarkers are seen bilaterally at 21.9% at baseline and at 56.3% at 5.8 years follow-up. Once present in one eye, cRORA had the shortest mean interval (1-2 years) before appearance in the other eye.

FAF

**Besides helping quantify the
hypoautofluorescent atrophic lesion.
The amount of
hyperautofluorescence correlates
well with the rate of GA
progression.**



*“Friends, Romans, countrymen —
I come to **bury cRORA**,
not to praise it.”*





ORIGINAL ARTICLE · Volume 4, Issue 2, 100425, March-April, 2024 · [Open Access](#)

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Functional Evaluation of Retinal Pigment Epithelium and Outer Retinal Atrophy by High-Density Targeted Microperimetry Testing

[Zhichao Wu, BAppSc\(Optom\), PhD](#) ^{1,2}   · [Emily K. Glover, OD](#) ¹ · [Erin E. Gee, BAppSc\(MedRad\)](#) ¹ · [Lauren A.B. Hodgson, MPH](#) ¹ · [Robyn H. Guymer, MBBS, PhD](#) ^{1,2}

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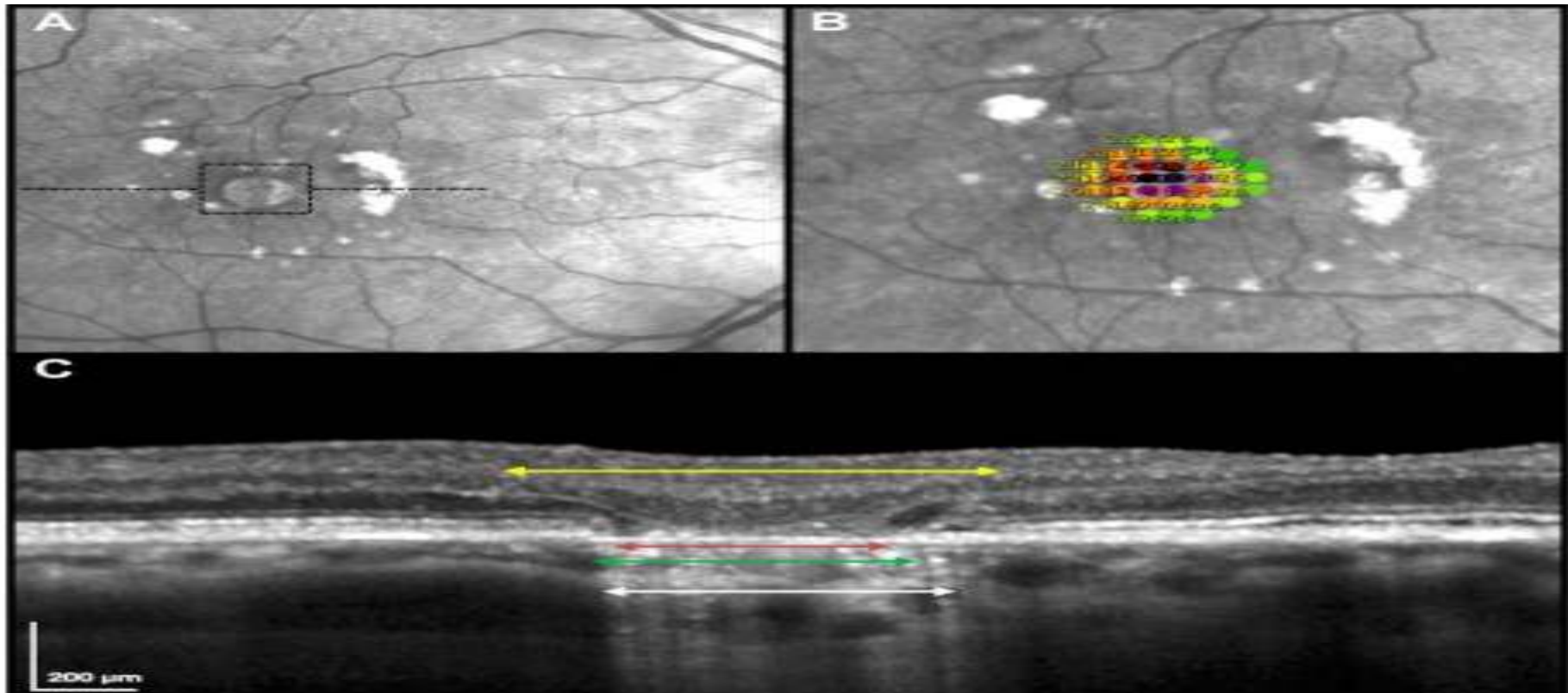


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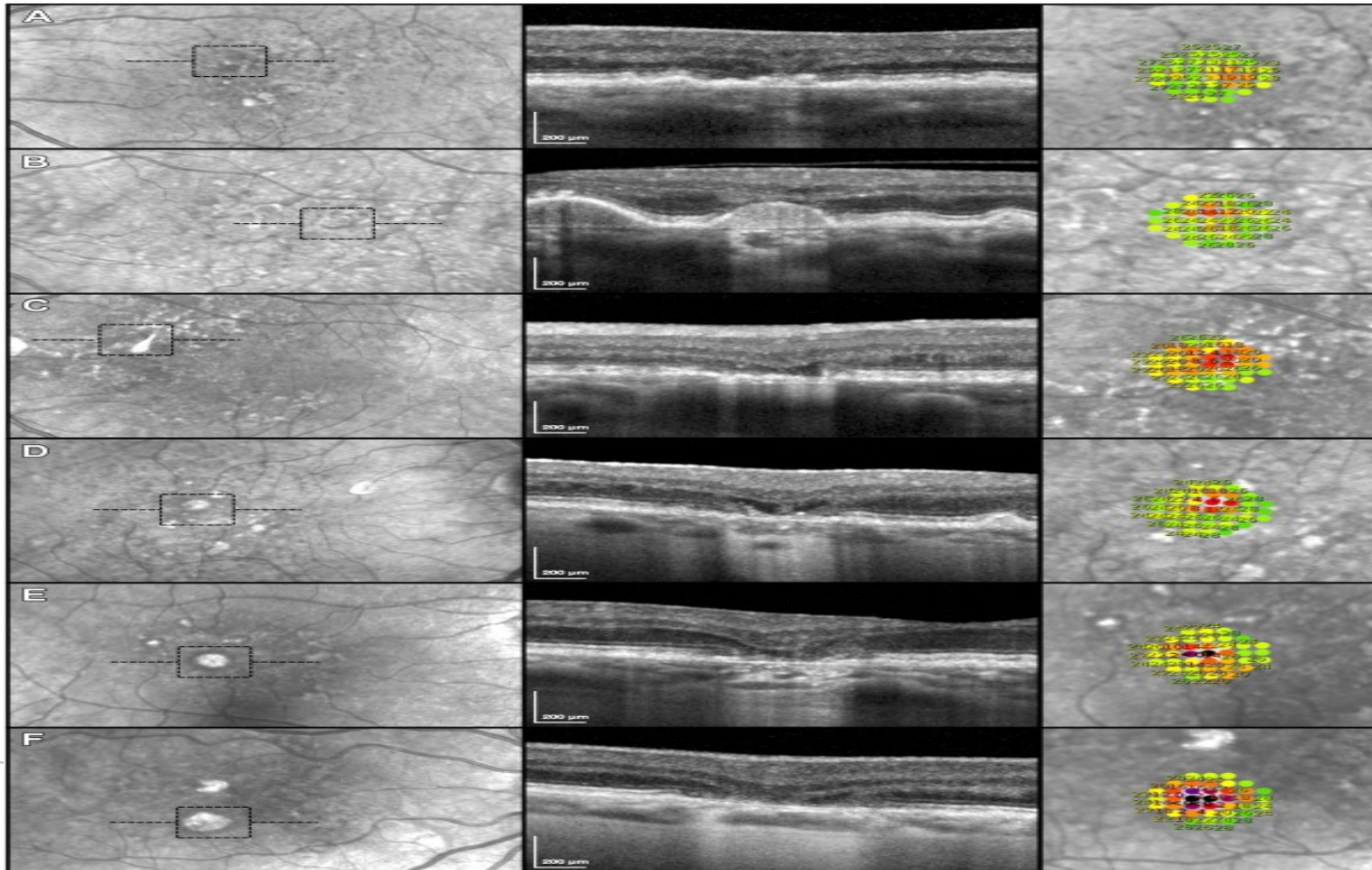
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Not all cRORA lesions exhibit a significant difference in the number of deep visual sensitivity defects, and only those with choroidal signal hypertransmission $\geq 500 \mu\text{m}$ and/or complete RPE loss $\geq 250 \mu\text{m}$ showed a significantly greater number of deep visual sensitivity defects.



**lesions with Nascent GA $\geq 500 \mu\text{m}$ in extent,
irrespective of hypertransmission $\geq 500 \mu\text{m}$ and
complete RPE loss $\geq 250 \mu\text{m}$, showed **a significantly
higher number of deep visual sensitivity defects ≤ 10
dB****





ORIGINAL ARTICLE · Volume 5, Issue 6, 100884, November-December, 2025 · [Open Access](#)

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OCT-Defined Atrophic Age-Related Macular Degeneration Changes Associated with Deep Visual Sensitivity Losses: A Multicenter Study

[Zhichao Wu, BAppSc\(Optom\), PhD](#)  ^{1,2}  · [Barbara A. Blodi, MD](#) ³ · [Frank G. Holz, MD](#) ⁴ · ... · [Leon von der Emde, MD](#) ⁴
· [Jordan Winkler, BSc](#) ³ · [Robyn H. Guymer, MBBS, PhD](#) ^{1,2} ... [Show more](#)

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FUNCTIONALLY RELEVANT CLINICAL ENDPOINTS OF END-STAGE ATROPHIC AMD TO FACILITATE PREVENTATIVE TREATMENT TRIALS.

cRORA



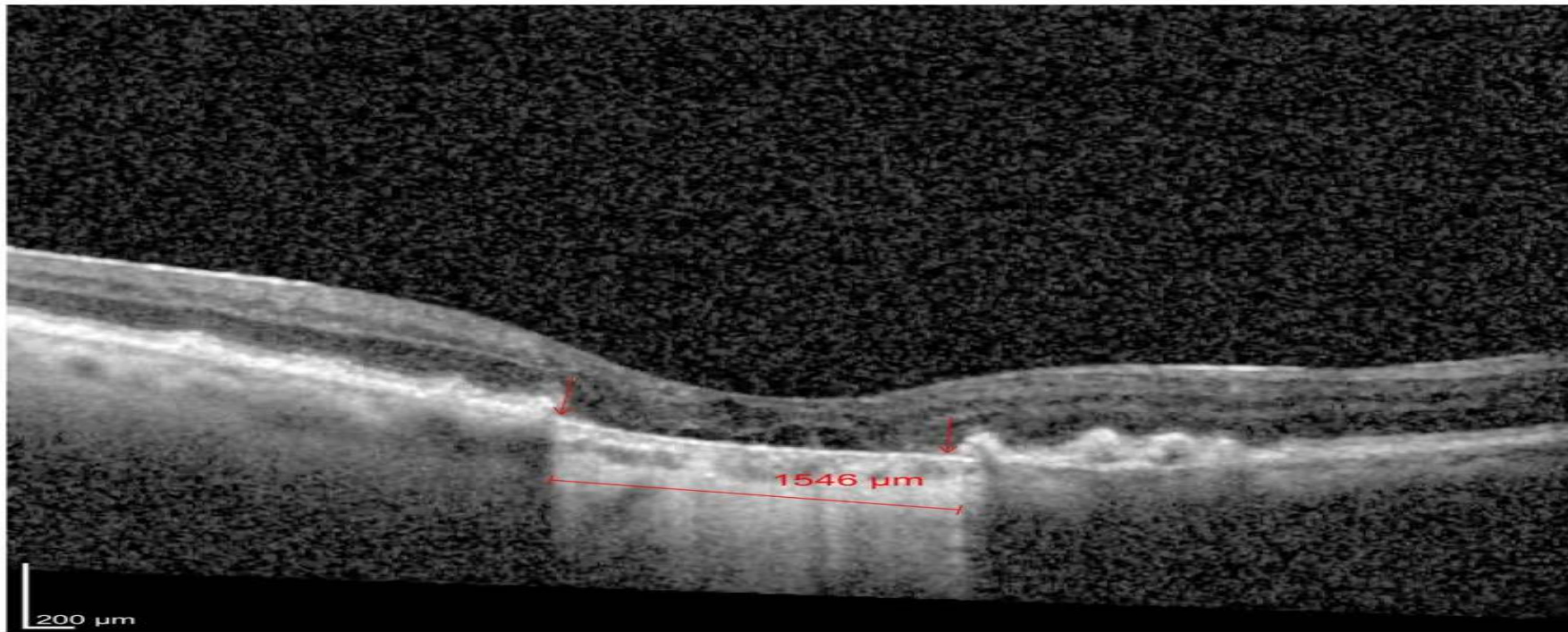
60% had a repeatable ≤ 10 dB defect.

- **HYPERTRANSMISSION DEFECT**
- **COMPLETE RPE LOSS ≥ 500 UM**
- **ANY SIZE OF PHOTORECEPTORS DEGENERATION**



between 92% and 98% had a repeatable ≤ 10 dB defect

cRORA identifies complete outer retinal and RPE atrophy structurally, but does not necessarily imply irreversible functional loss.



OAKS AND derby studies

pegcetacoplan



complement 3 inhibitor

reduced the rate of growth of GA lesions in 2 years compared to sham

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ARTICLES - Volume 402, Issue 10411, P1434-1448, October 21, 2023 [Download Full Issue](#)

Pegcetacoplan for the treatment of geographic atrophy secondary to age-related macular degeneration (OAKS and DERBY): two multicentre, randomised, double-masked, sham-controlled, phase 3 trials

[Jeffrey S Heier, MD ^{a,*}](#) - [Eleonora M Lad, MD ^{b,*}](#) - [Prof Frank G Holz, MD ^c](#) - [Prof Philip J Rosenfeld, MD ^d](#) - [Prof Robyn H Guymer, MBBS ^e](#) - [David Boyer, MD ^f](#) et al. [Show more](#)

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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

Eyes receiving *intravitreal pegcetacoplan* had *lower rates of progression from iRORA to cRORA* compared with controls, suggesting a potential role for pegcetacoplan therapy *earlier* in the progression of AMD prior to the development of GA.

GATHER study

Avacincaptad pegol



complement 5 inhibitor

Over this 18-month study, ACP 2 mg and 4 mg showed continued reductions in the progression of GA growth compared to sham and continued to be generally well tolerated.

Clinical Trial > Eye (Lond). 2023 Dec;37(17):3551-3557. doi: 10.1038/s41433-023-02497-w.
Epub 2023 Mar 24.

Avacincaptad pegol for geographic atrophy secondary to age-related macular degeneration: 18-month findings from the GATHER1 trial

Sunil S Patel ¹, David R Lally ², Jason Hsu ³, Charles C Wykoff ⁴, David Eichenbaum ⁵ ⁶,
Jeffrey S Heier ⁷, Glenn J Jaffe ⁸, Keith Westby ⁹, Dhaval Desai ⁹, Liansheng Zhu ⁹,
Arshad M Khanani ¹⁰

Take Home message :

- *OCT biomarkers and classifications are important tools for early slowing and maybe preventing GA in the future .**
- *Structural loss doesn't always mean irreversible functional loss .**

*Thank
you*

The background is a solid light beige color. It is decorated with various small, faint elements: circular floral patterns made of small dots, small white five-petaled flowers, and small colored dots in green, yellow, and pink. Two dark green leafy branches are positioned on either side of the text, one extending from the top right and the other from the bottom left.