

DMLA: une vue d'ensemble

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Disclosures

Consultant for:

- Allergan
- Bayer
- Novartis
- Roche
- Thea

En théorie

- Maculopathie liée à l'âge
- Atrophie géographique
- DMLA exsudative

Maculopathie liée à l'âge

Généralités: épidémiologie, physiopathologie
Description clinique des formes de début
Examens complémentaires
Pronostic
Diagnostic différentiel
Traitement

EPIDÉMIOLOGIE-PHYSIOPATHOLOGIE

Prévalence majeure

1/3 population > 75 ans ?

Augmentation prévisible de la prévalence

Principal problème ophtalmologique de santé publique
dans les pays développés

Facteurs De Risque Génétiques

Différence de prévalence / ethnies

Etudes de corrélation familiale

Etudes de jumeaux

Etudes de gènes candidats :

- ABCR
- ARMD 1
- Allèles de l'Apo E

Antécédents familiaux = FDR reconnus

FDR GENETIQUES

Gène du facteur H du complément (CFH) : Variant Y402H:

- OR 2-3 pour hétérozygotes
- OR 5-6 pour homozygotes

Gènes ARMS2/HTRA1/PLEKHA1

- OR 2-3 pour hétérozygotes
- OR 7-8 pour homozygotes

Variants génétiques du facteur B et des composants C2 et C3 du complément

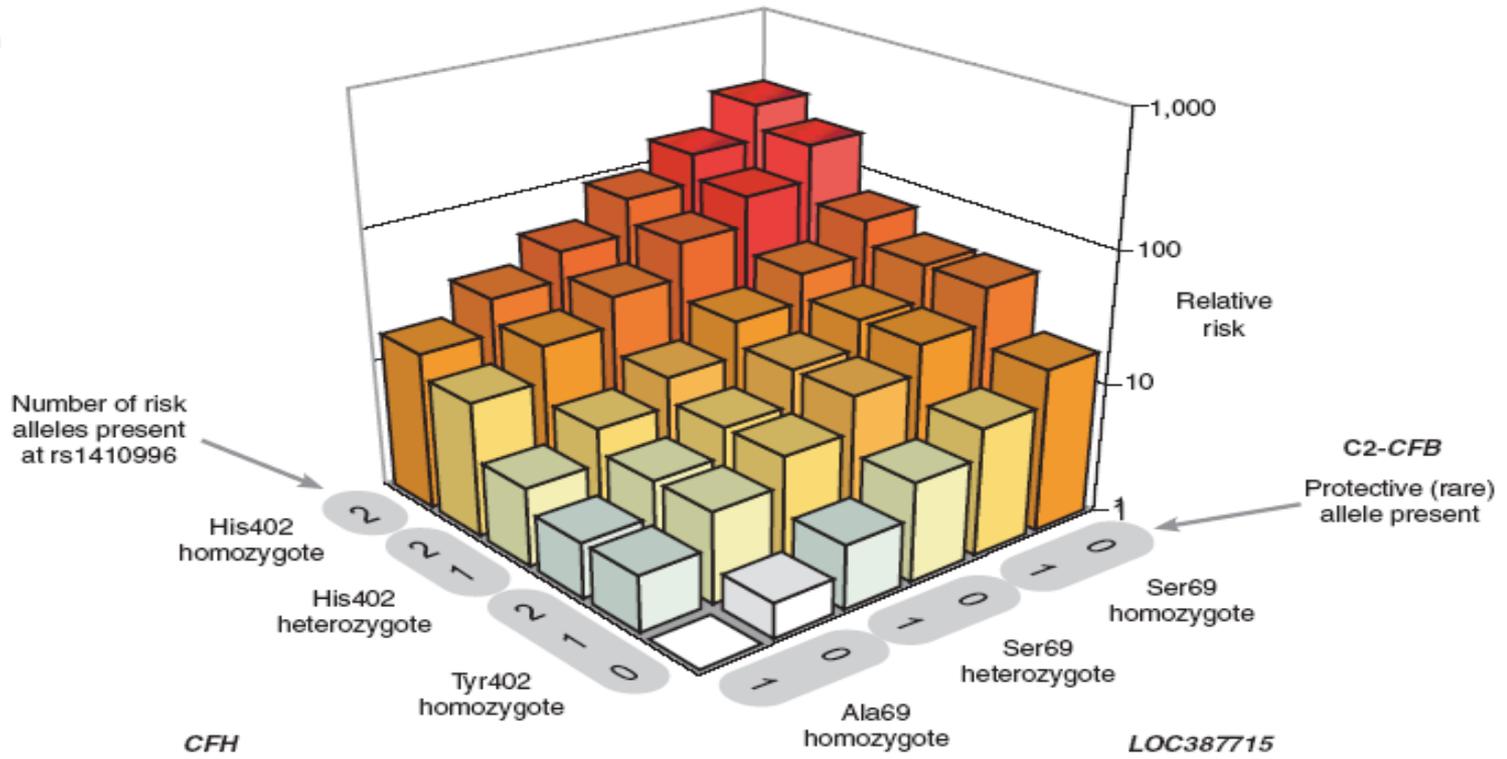


Figure 1 Relative risk plotted as a function of the genetic load of the five variants that influence risk of AMD. Two variants are in the *CFH* gene on chromosome 1: Y402H and rs1410996. Another common variant (A69S) is in hypothetical gene *LOC387715* on chromosome 10. Two relatively rare variants are observed in the *C2* and *BF* genes on chromosome 6. We find no evidence for interaction between any of these variants, suggesting an independent mode of action. (See also **Supplementary Table 4.**)

Common Variants

CFH - Y402H

LIPC

TNFRSF10A

CFH – rs1410996

CETP

IER3/DDR1

CFB

ABCA1

SLC16A8

C2

TIMP3/SYN3

RAD51B

C3

VEGFA

ADAMTS9

CFI

COL10A1

B3GALTL

ARMS2/HTRA1

COL8A1

TGFBRI

Rare Variants

CFH - R1210C

C3 - K155Q

C9 - P167S

CFI- increased burden of disease with multiple variants

FDR GENETIQUES

- > 20 gènes identifiés dont les variants sont associés à un risque statistique de DMLA

Risque d'autant plus grand qu'il existe des FDR environnementaux

Interaction gènes - milieu

FDR GENETIQUES

Variants plus rares associés à des formes plus graves de la maladie

Analyse génétique en routine ?

Non recommandée en l'absence de prévention primaire efficace

FDR CONSTITUTIONNELS

Sexe Féminin ?

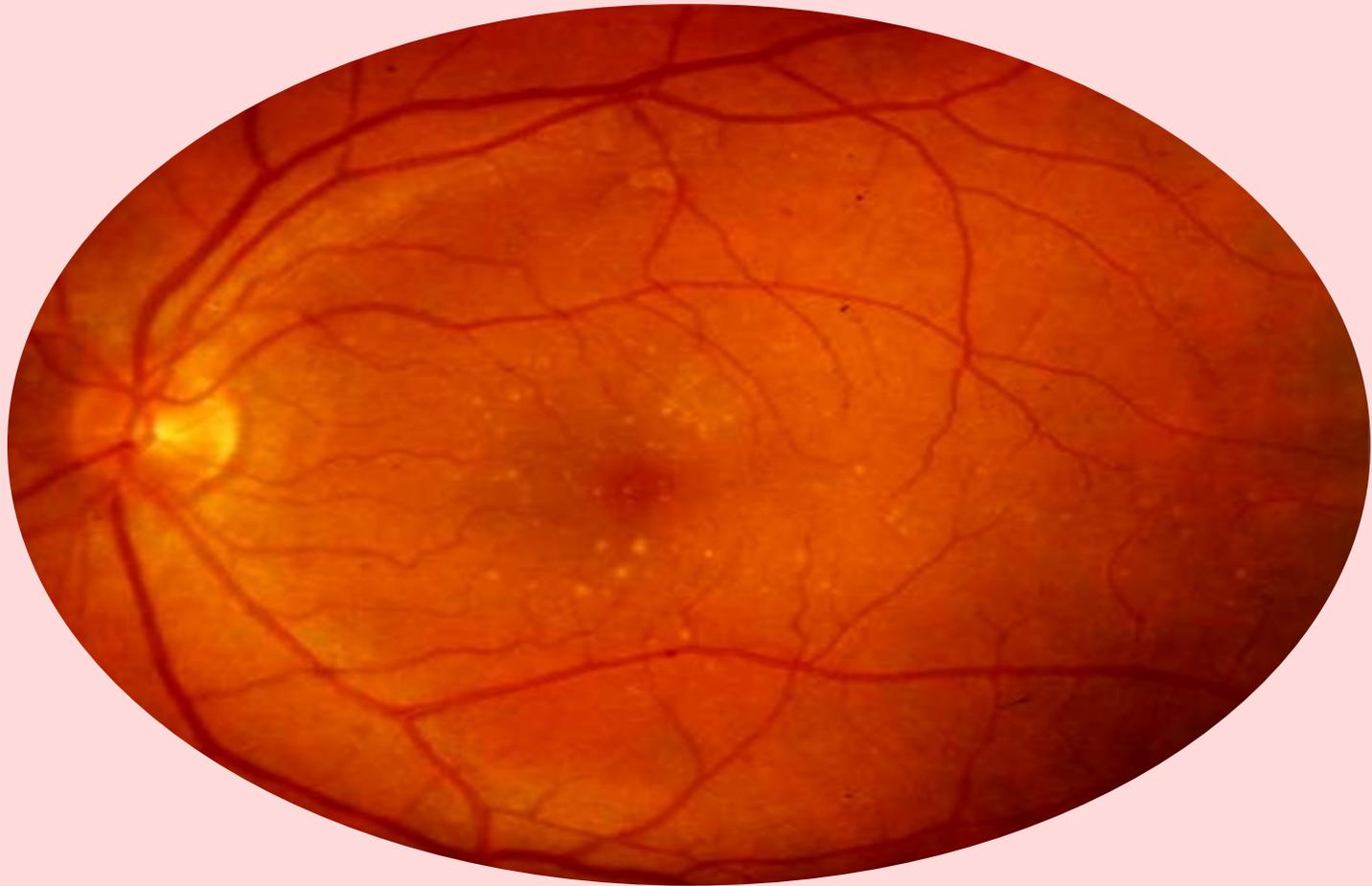
Yeux clairs ?

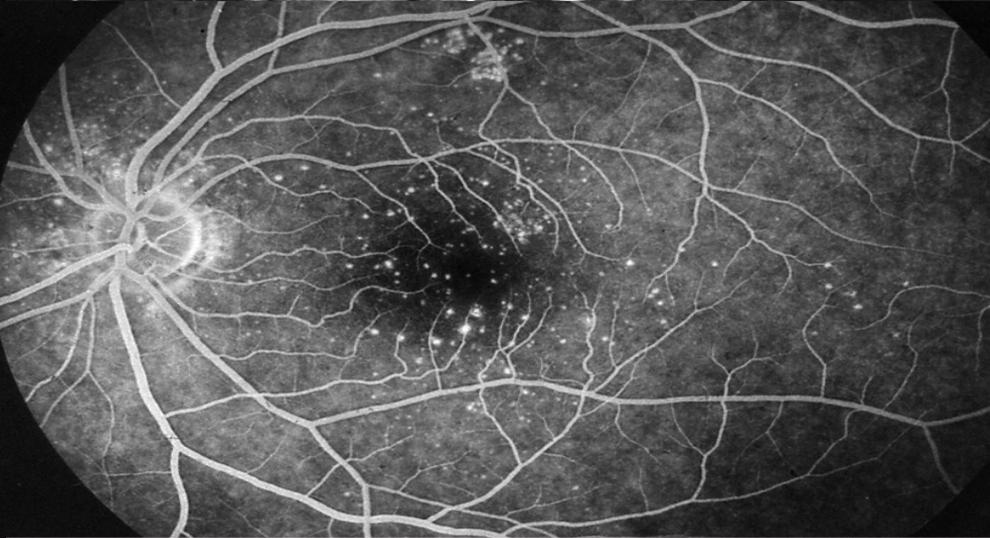
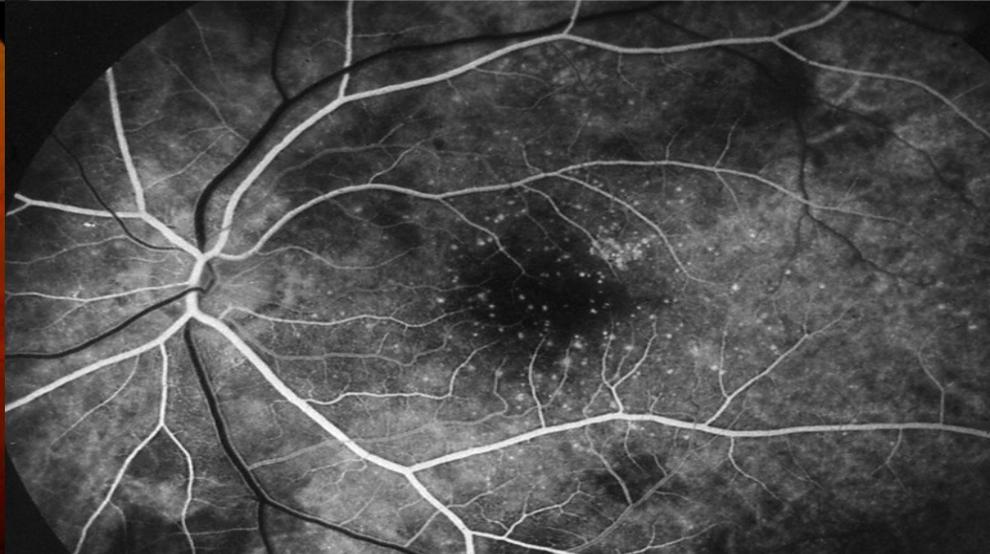
Artériosclérose ?

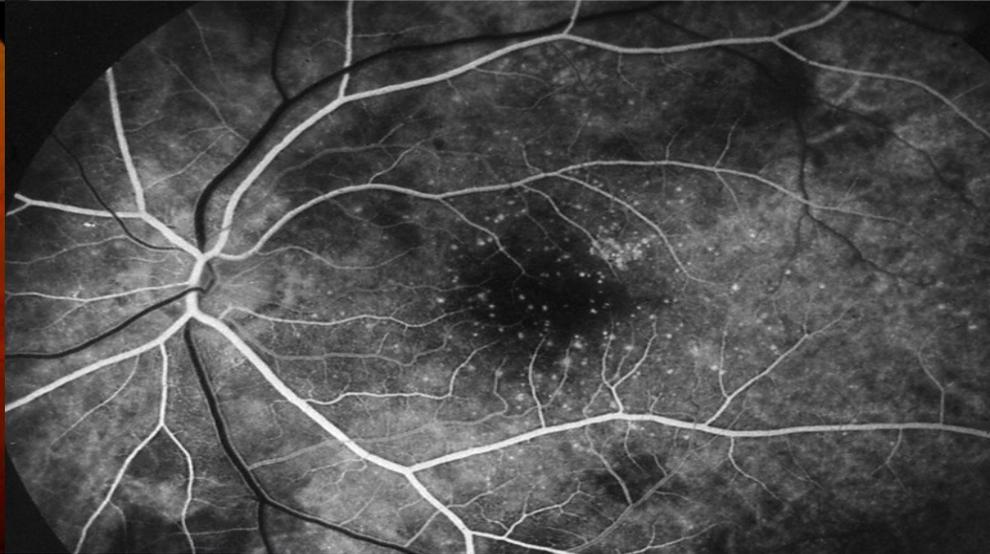
HTA ?

FDR ENVIRONNEMENTAUX

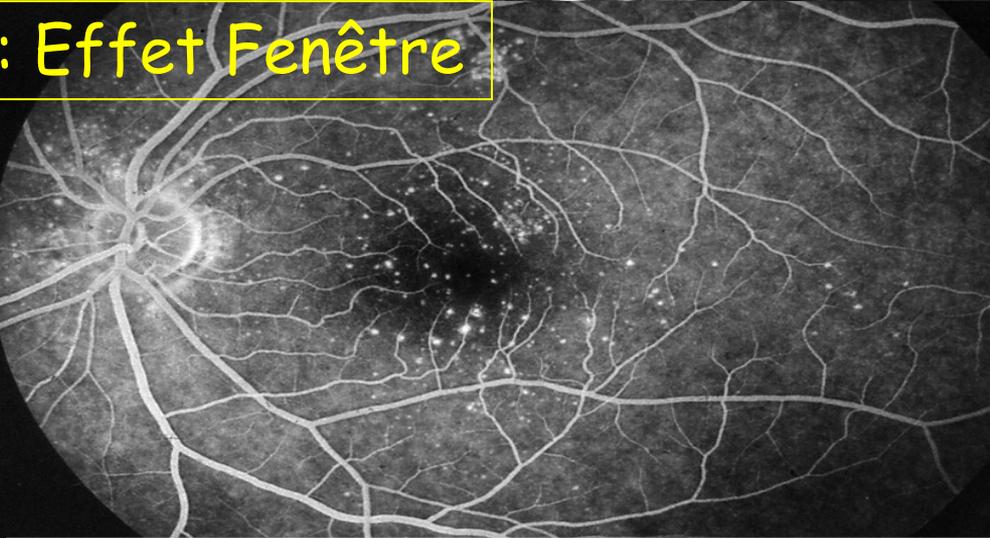
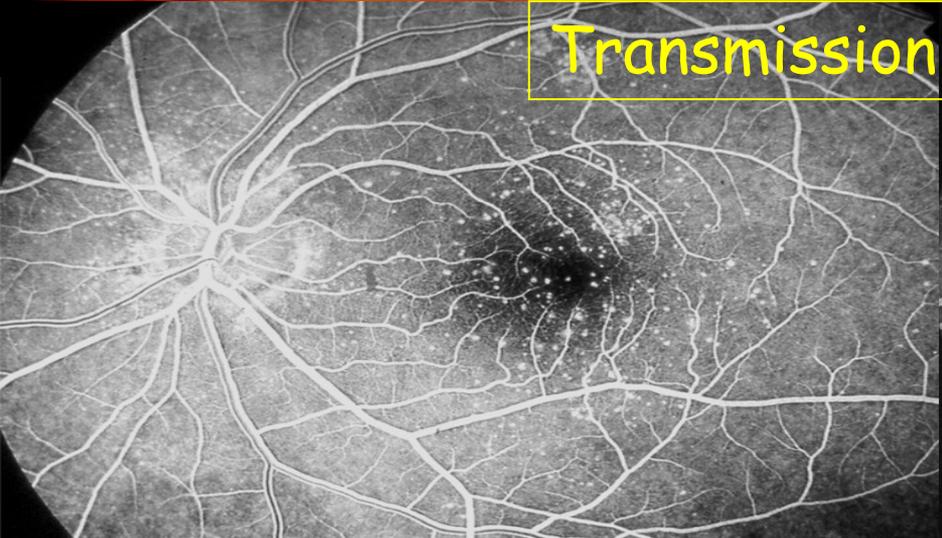
- Exposition à la lumière ?
- Carences en oligo-éléments et en vitamines ?
- Tabagisme
- Alimentation « occidentale »

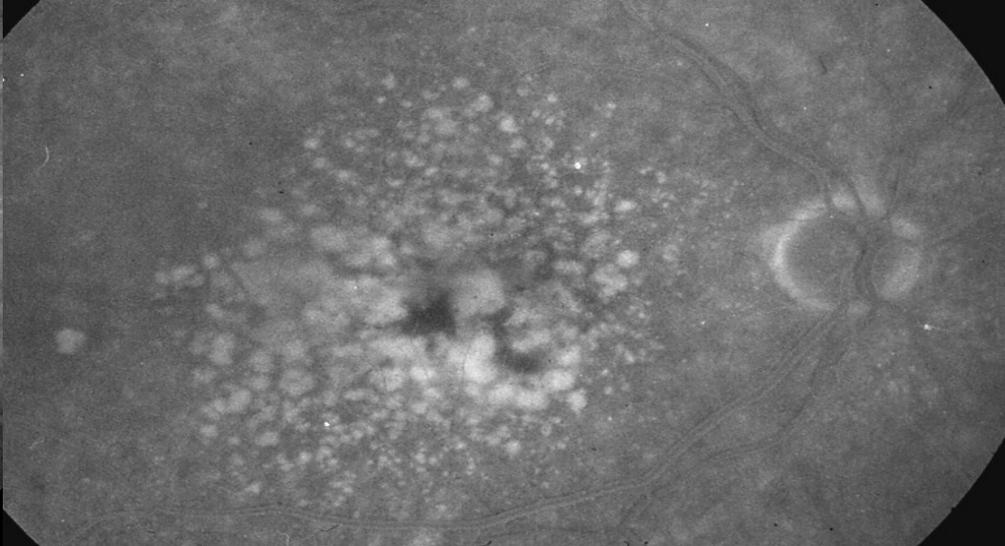
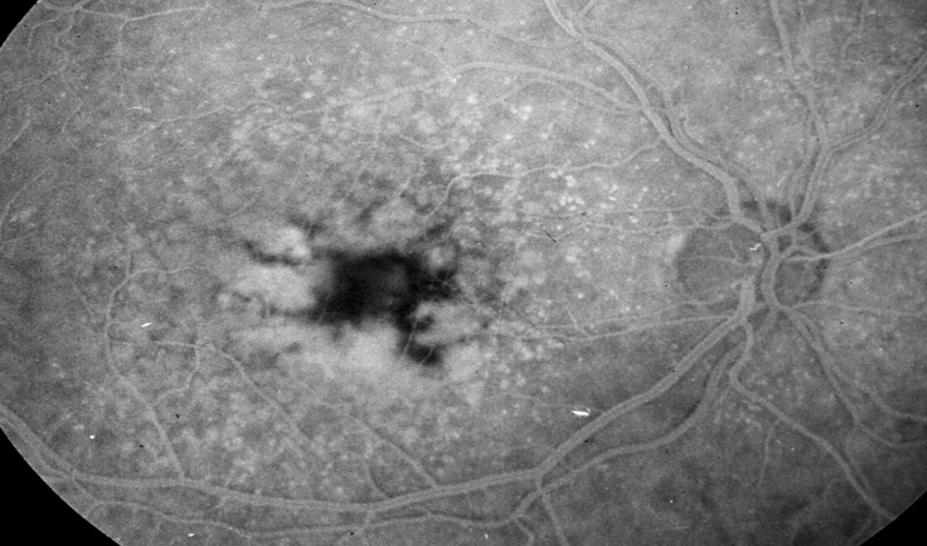
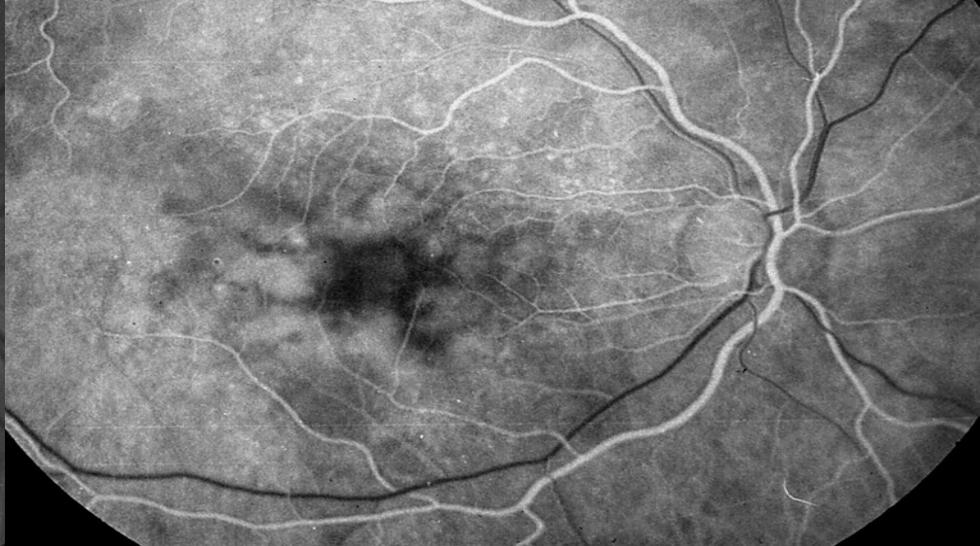
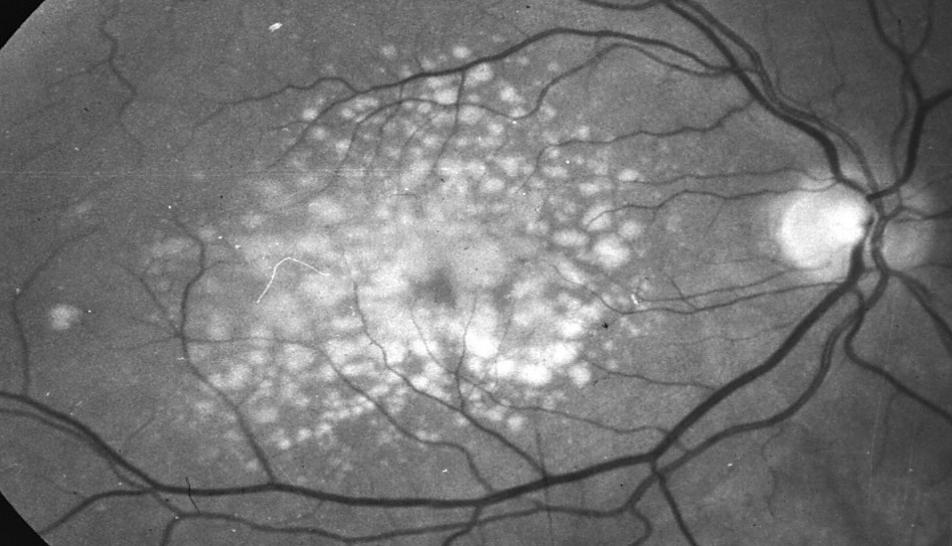


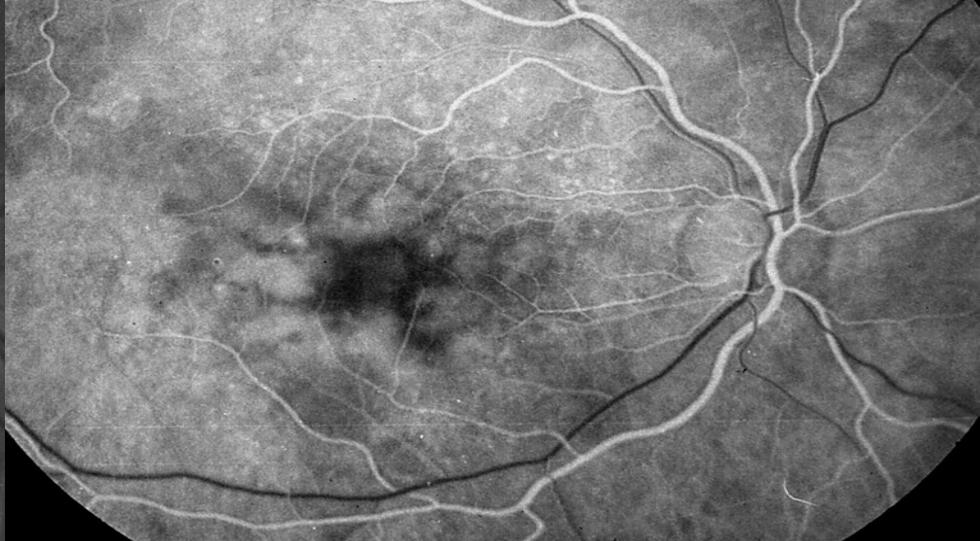
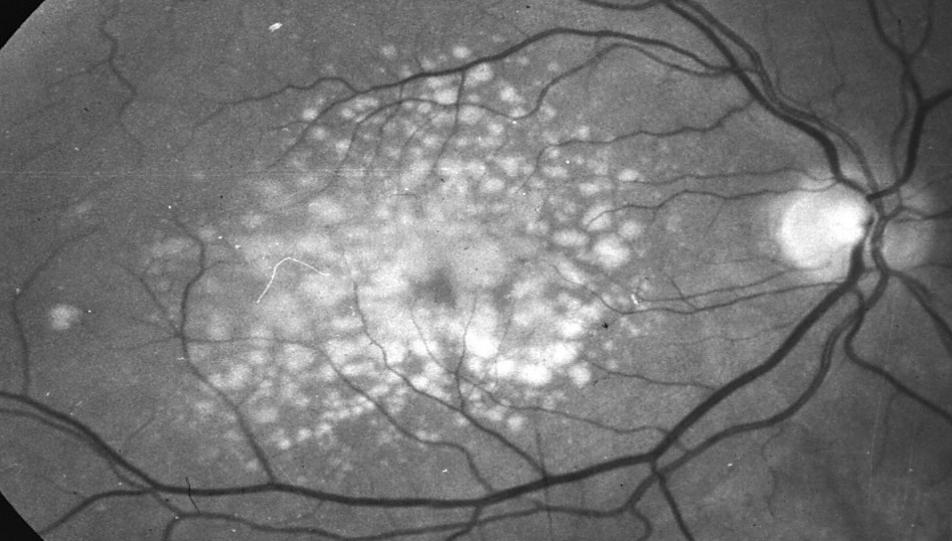




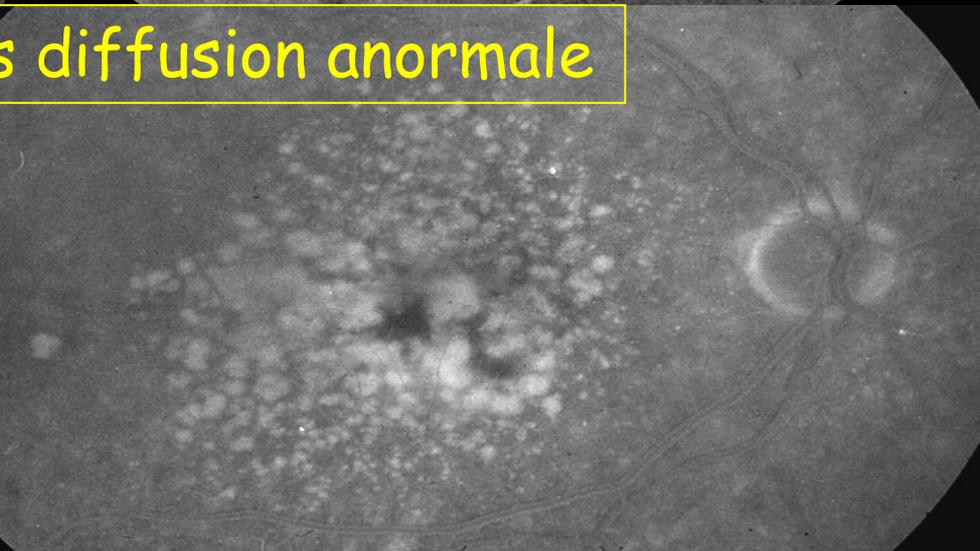
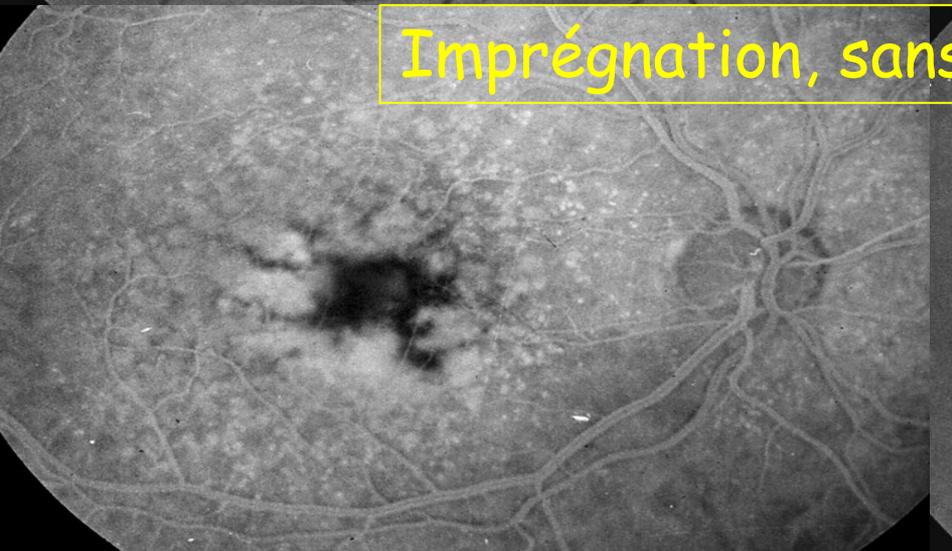
Transmission: Effet Fenêtre





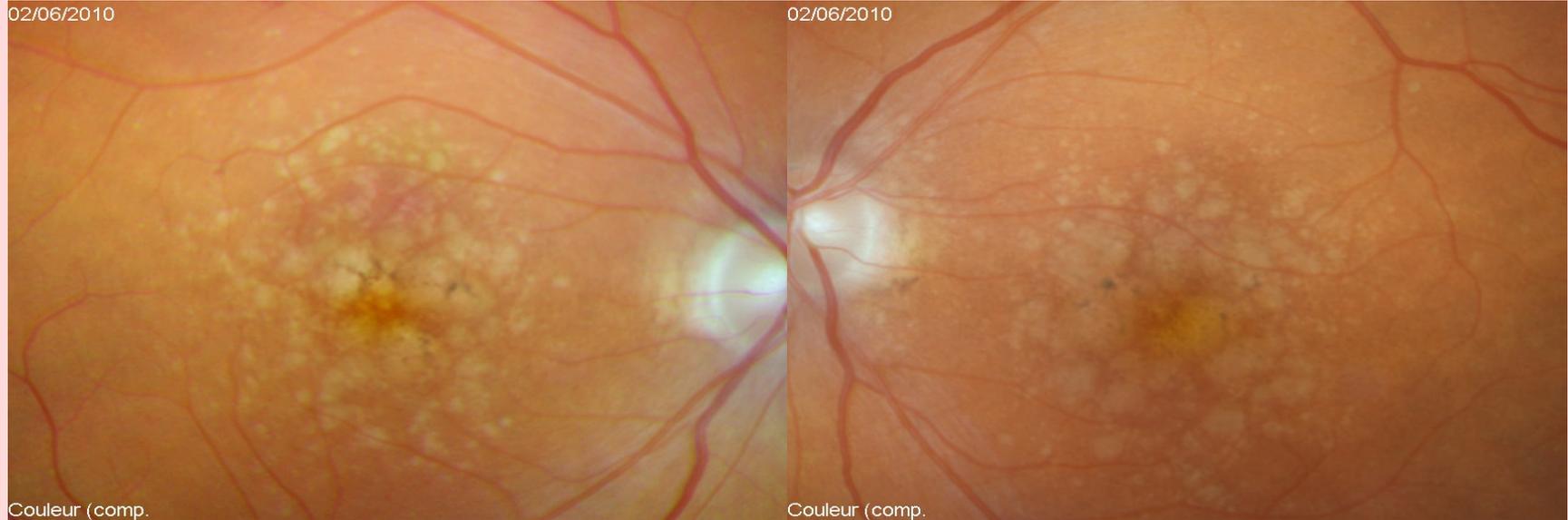


Imprégnation, sans diffusion anormale



02/06/2010

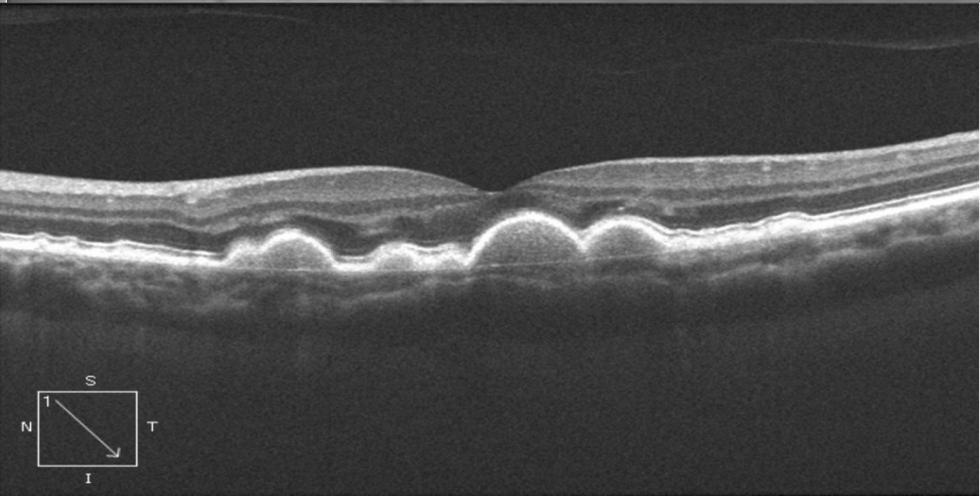
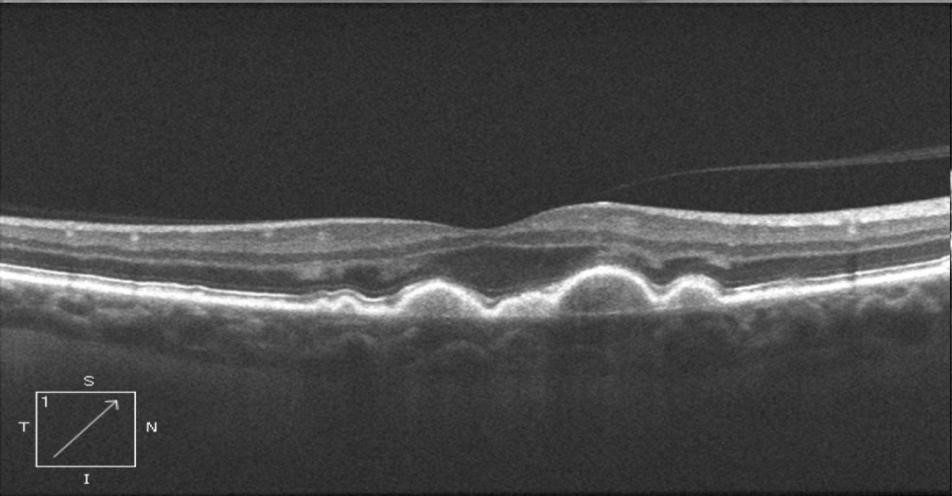
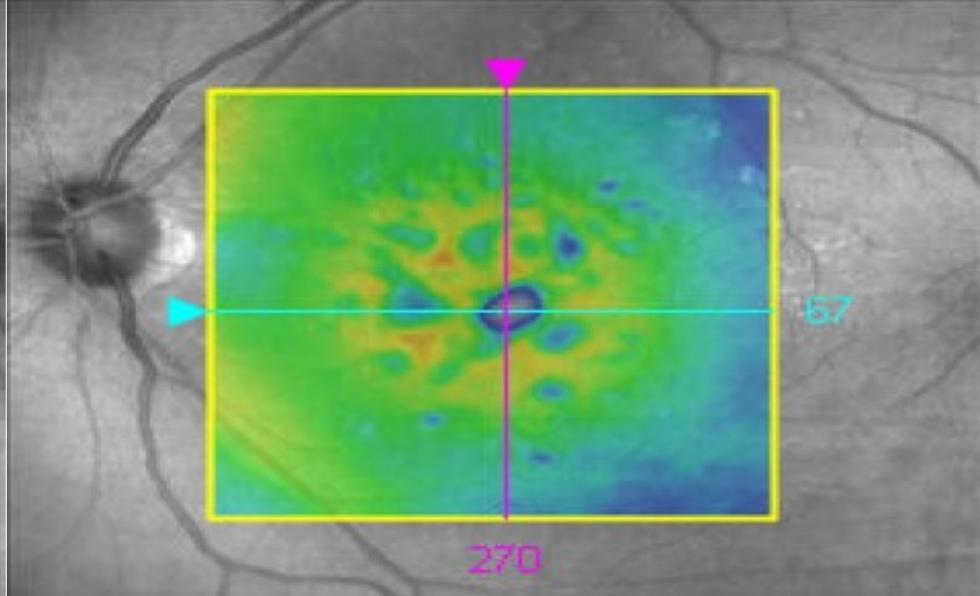
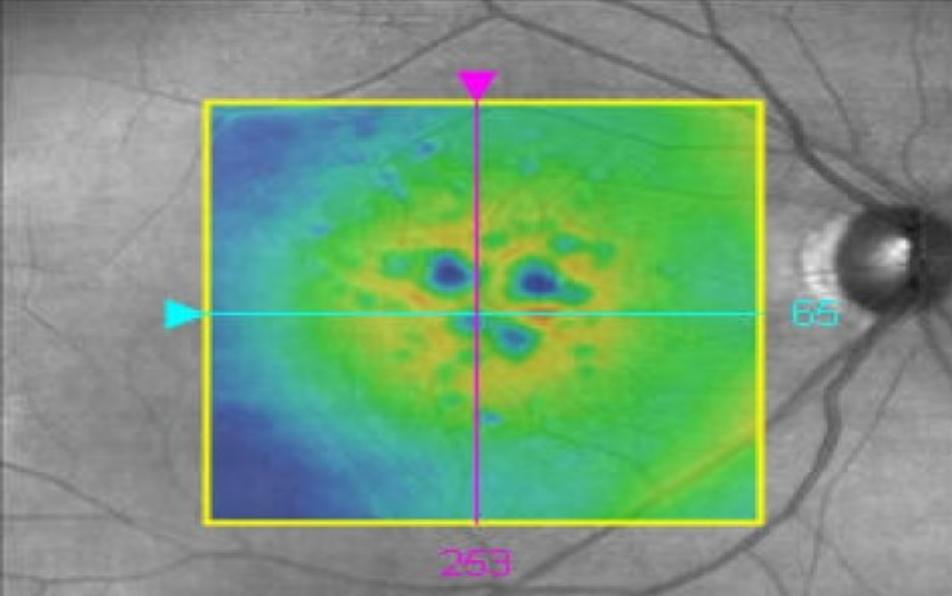
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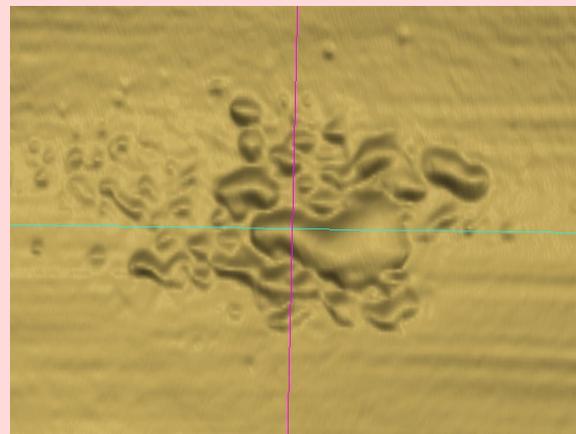
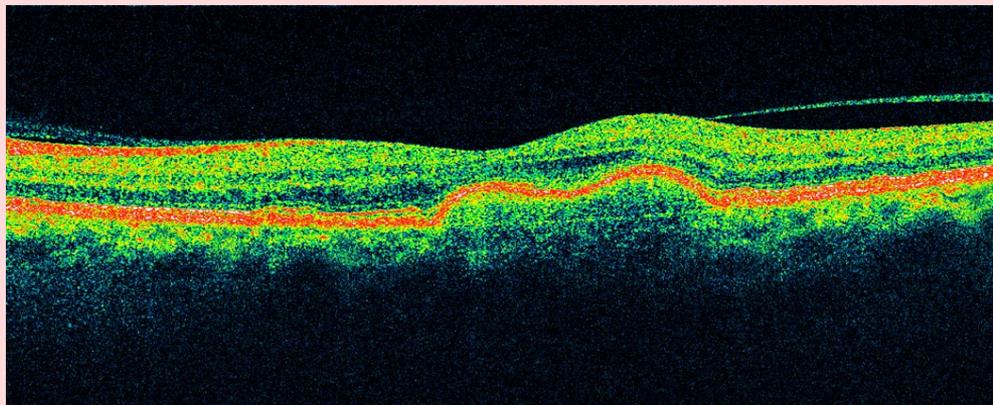
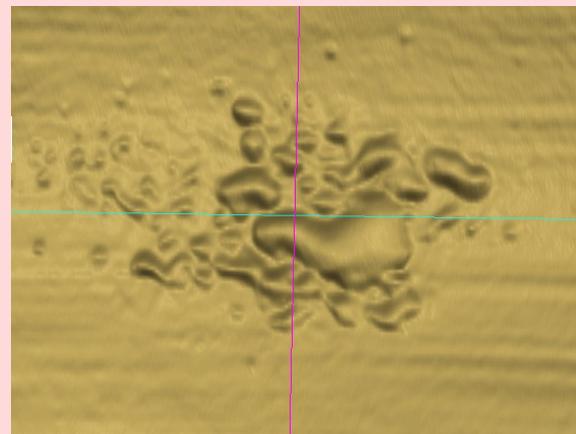
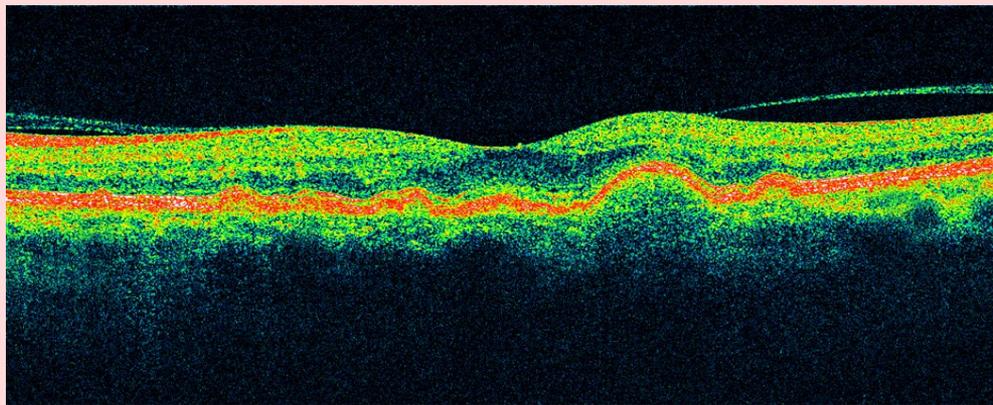


Couleur (comp.)

Couleur (comp.)

L'angiographie n'est plus indiquée dans les drusen
Rétinographie, Autofluorescence, OCT





13/06/2007



2007

Couleur (comp.
12/10/2009

13/05/2009



2008

Couleur (comp.
24/03/2011



2010

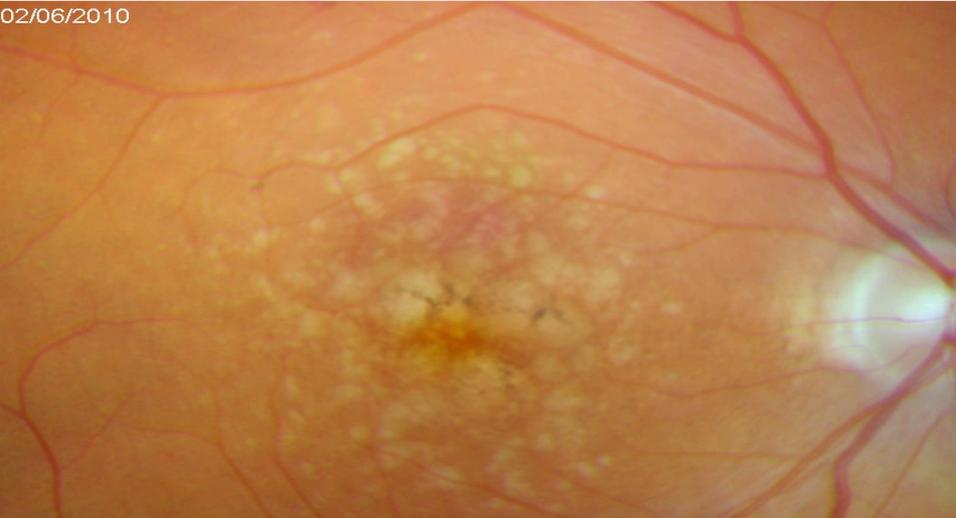
Couleur (comp.



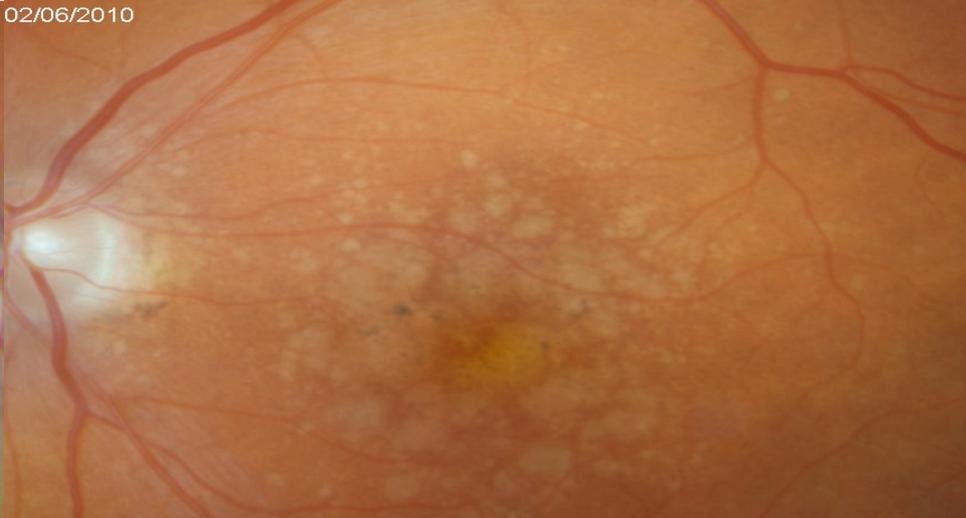
Couleur (comp.

2011

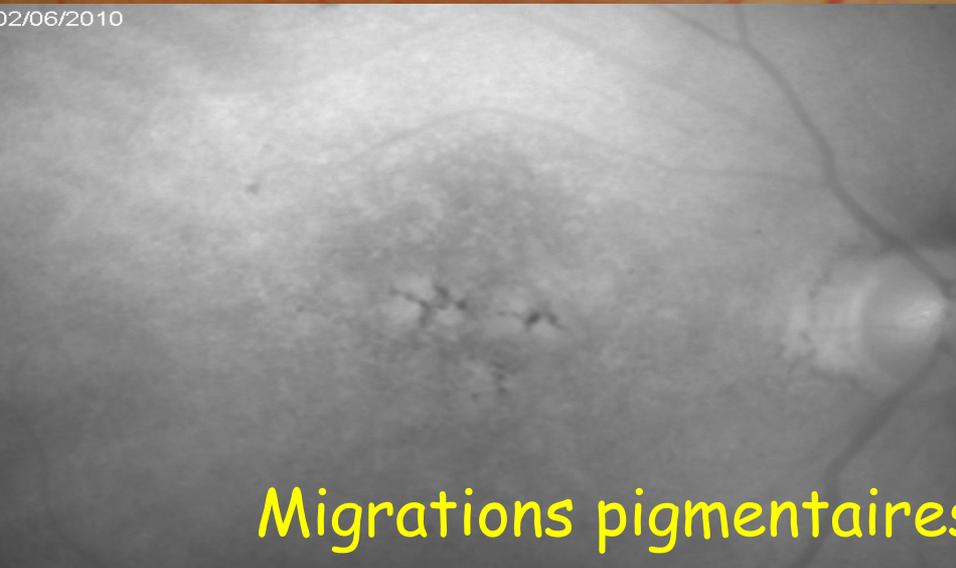
02/06/2010



02/06/2010



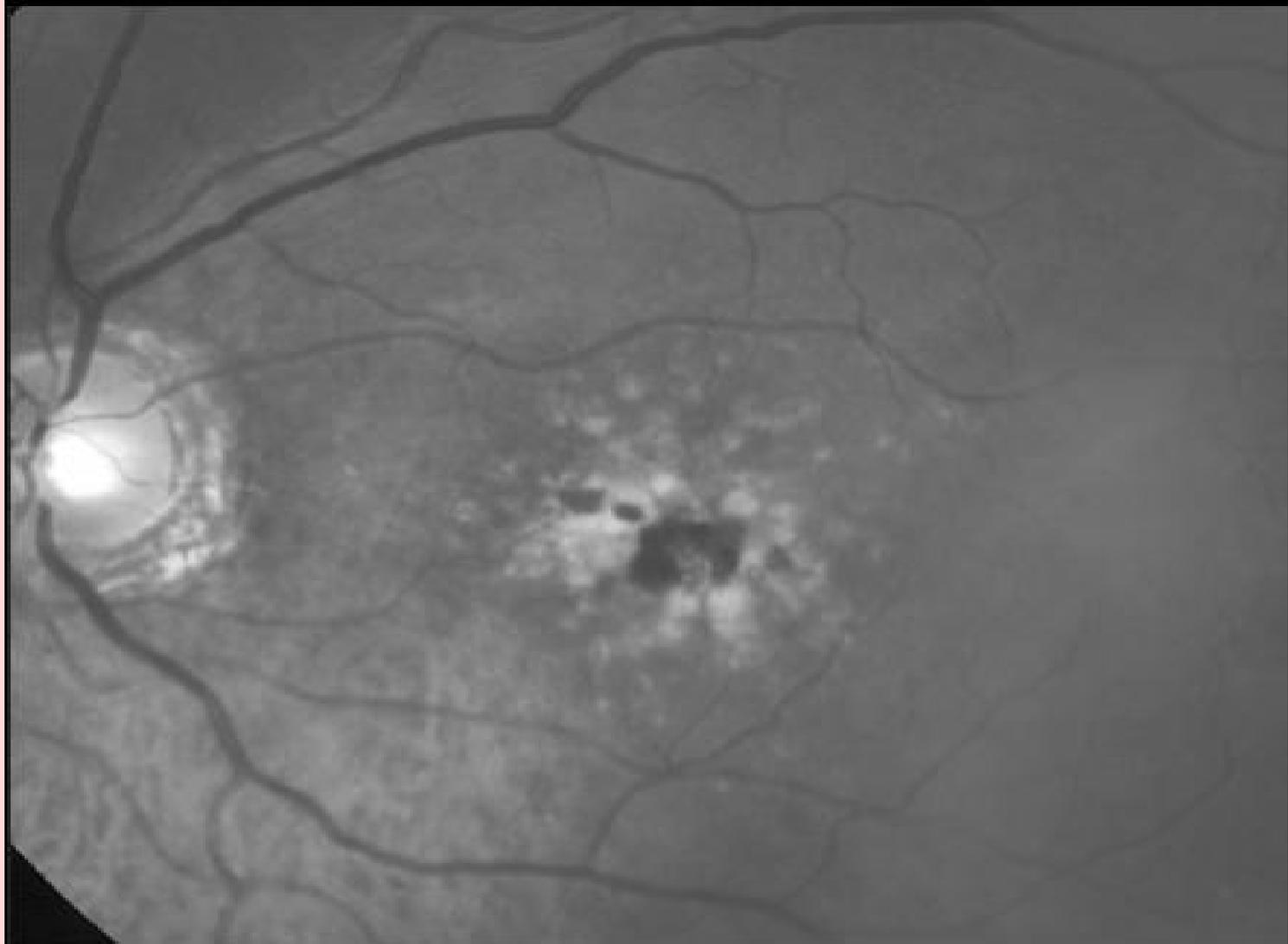
02/06/2010

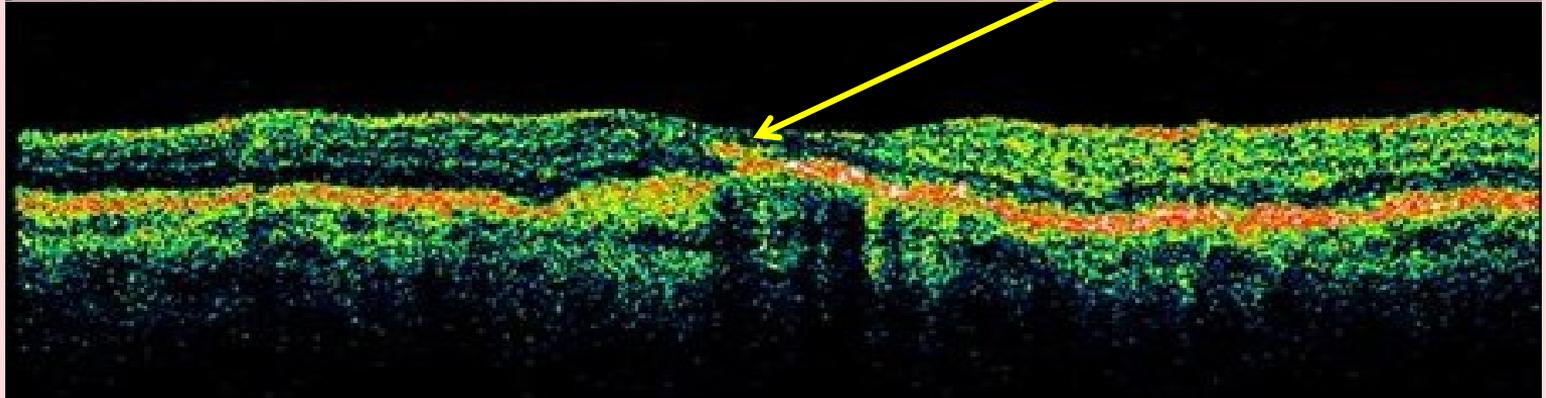
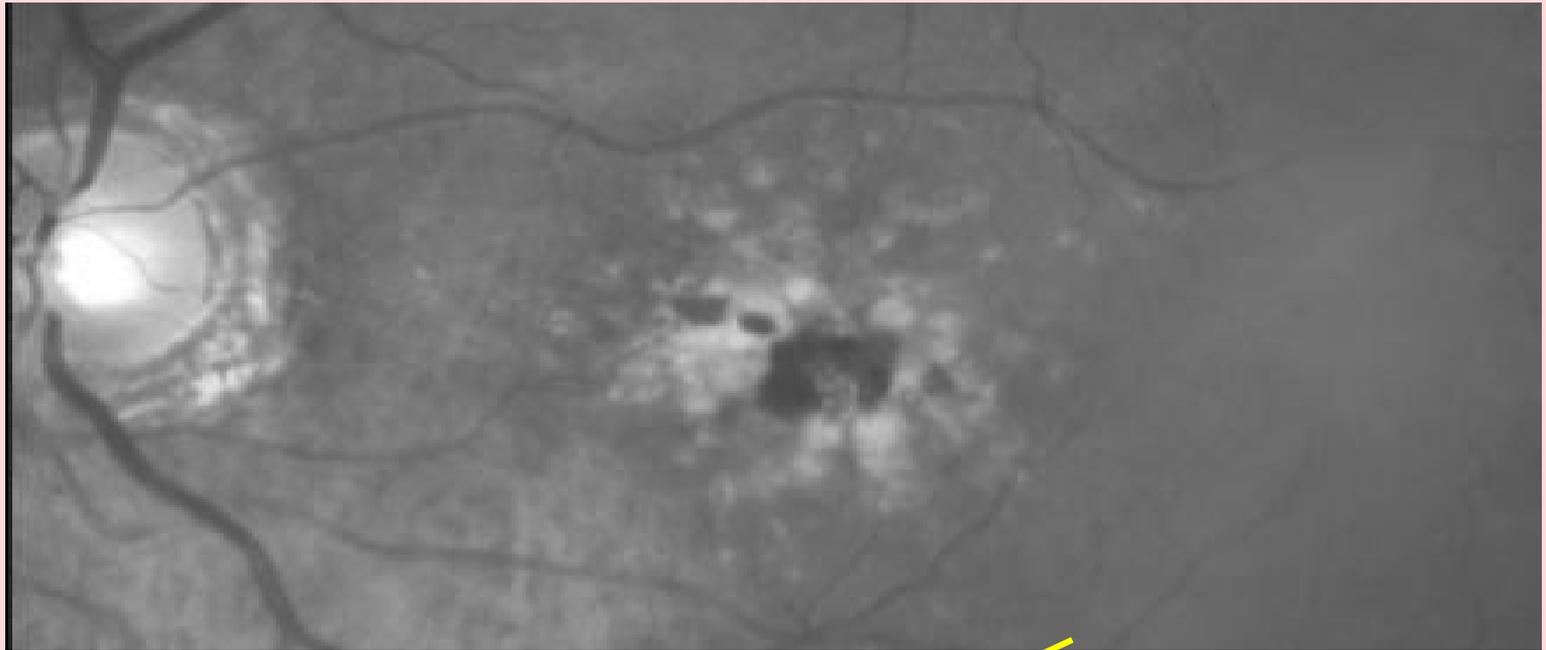


02/06/2010



Migrations pigmentaires: facteur de gravité





Risque de Progression

Bien apprécié par les études AREDS

Œil droit	Drusen >125 μ m	Non =0 Oui =1
	Migrations pigmentaires	Non =0 Oui =1
Œil gauche	Drusen >125 μ m	Non =0 Oui =1
	Migrations pigmentaires	Non =0 Oui =1
	Total	De 0 à 4

Score proposé par Ferris dans le rapport 18 de l'étude AREDS

Risque de Progression à 10 ans

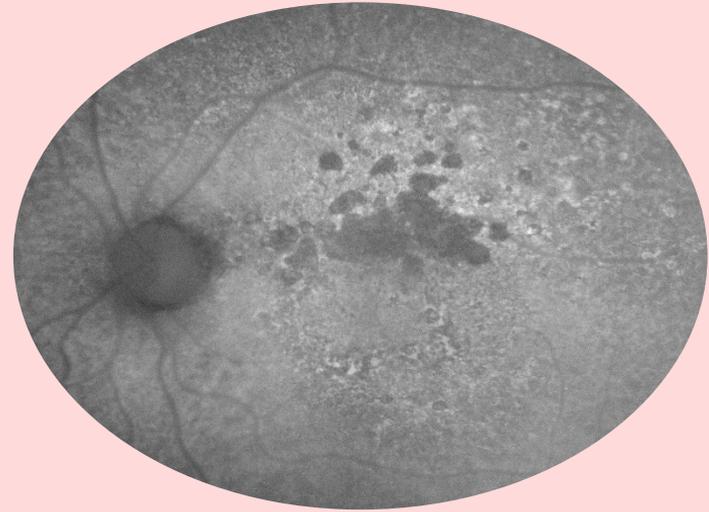
OD \ OG	0	1	2
0	0,5 %	8%	22%
1	8%	22%	49%
2	22%	49%	66%

Drusen séreux et/ou altérations pigmentaires constituent les lésions fondamentales de la DMLA débutante (ou MLA)

Mais il y a d'autres types de drusen:

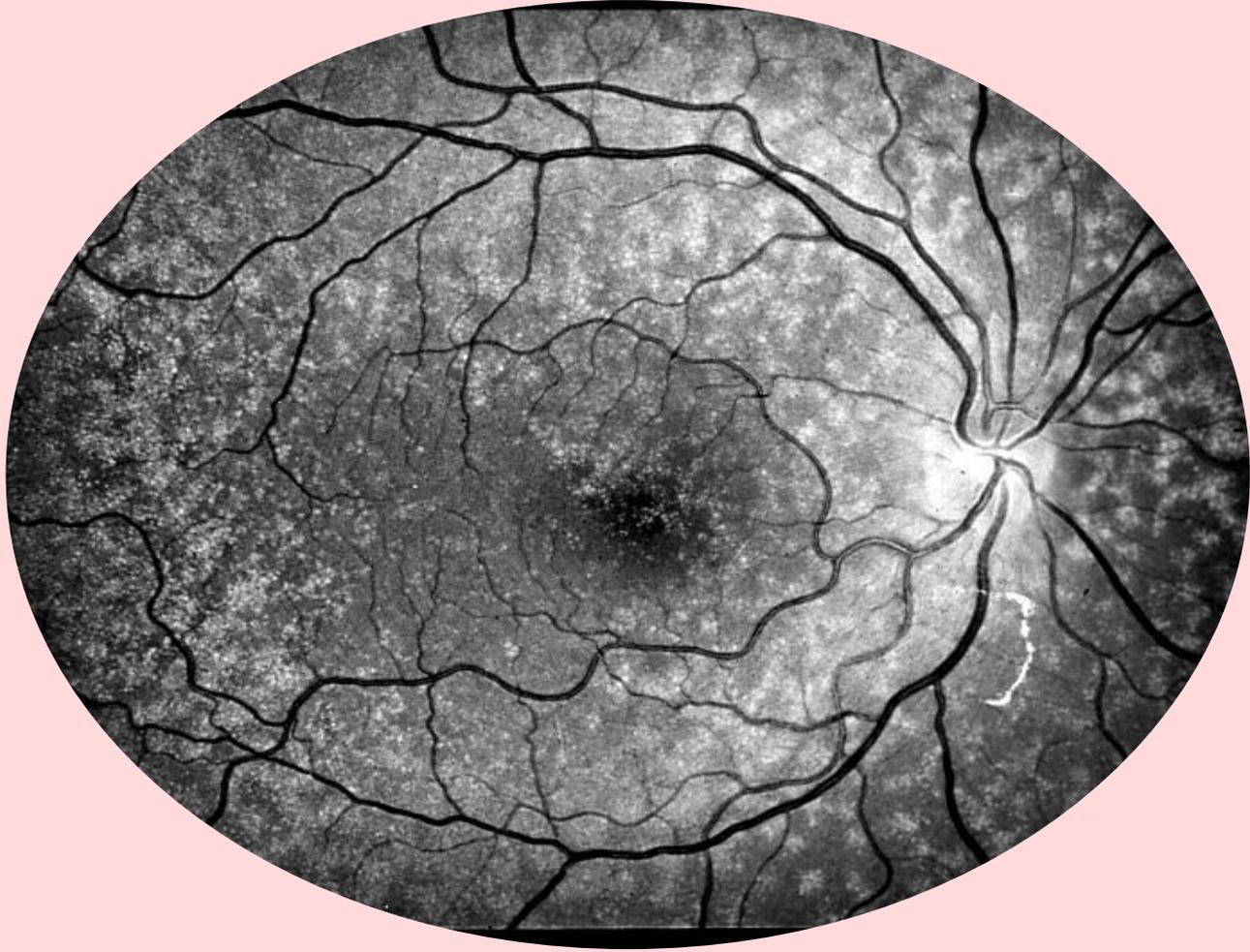
- Drusen calcifiés
- Drusen cuticulaires
- Pseudodrusen réticulés

Drusen calcifiés = drusen séreux + atrophie

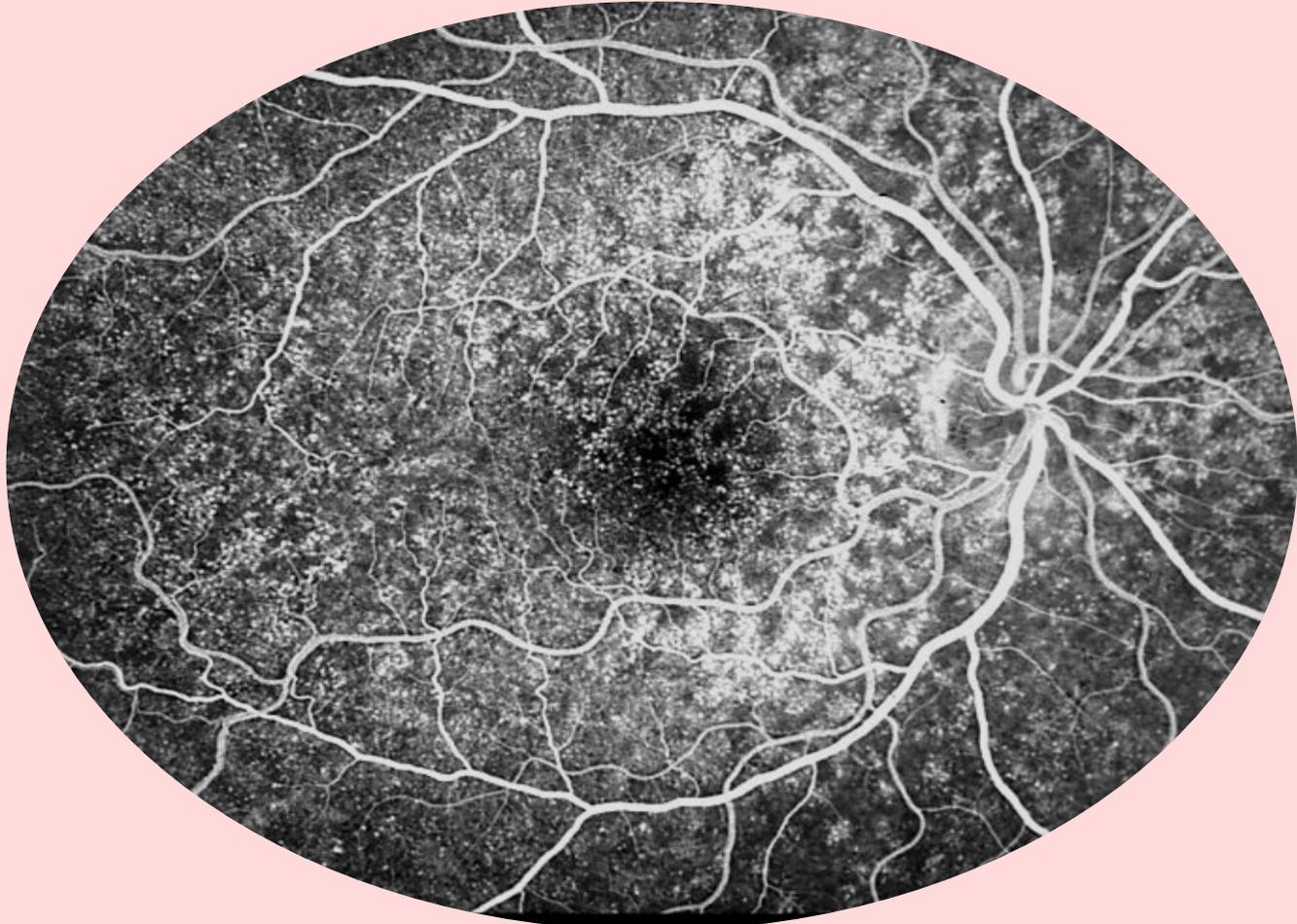


Les drusen séreux peuvent se calcifier et sont alors associés à l'atrophie géographique

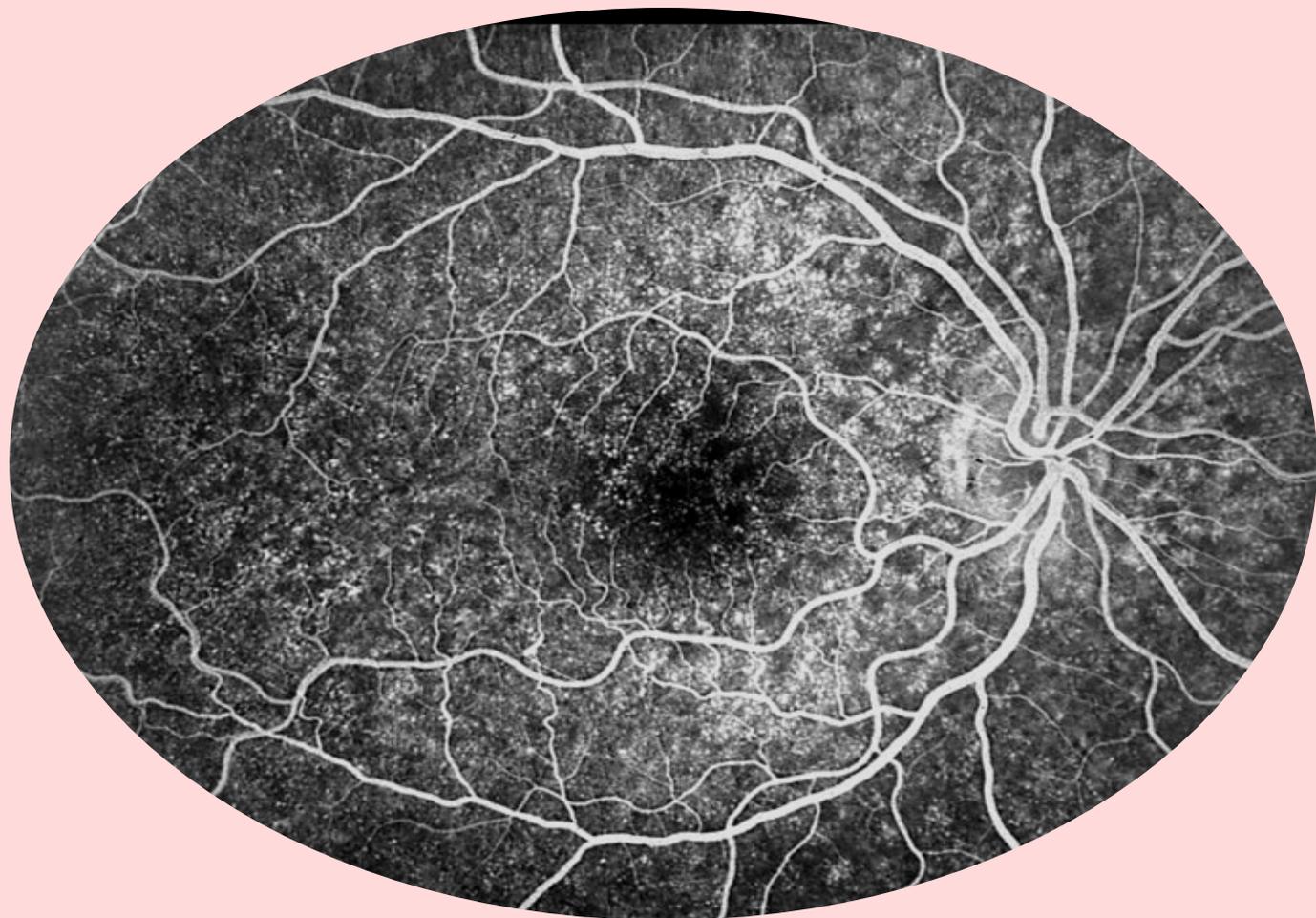
Drusen cuticulaires

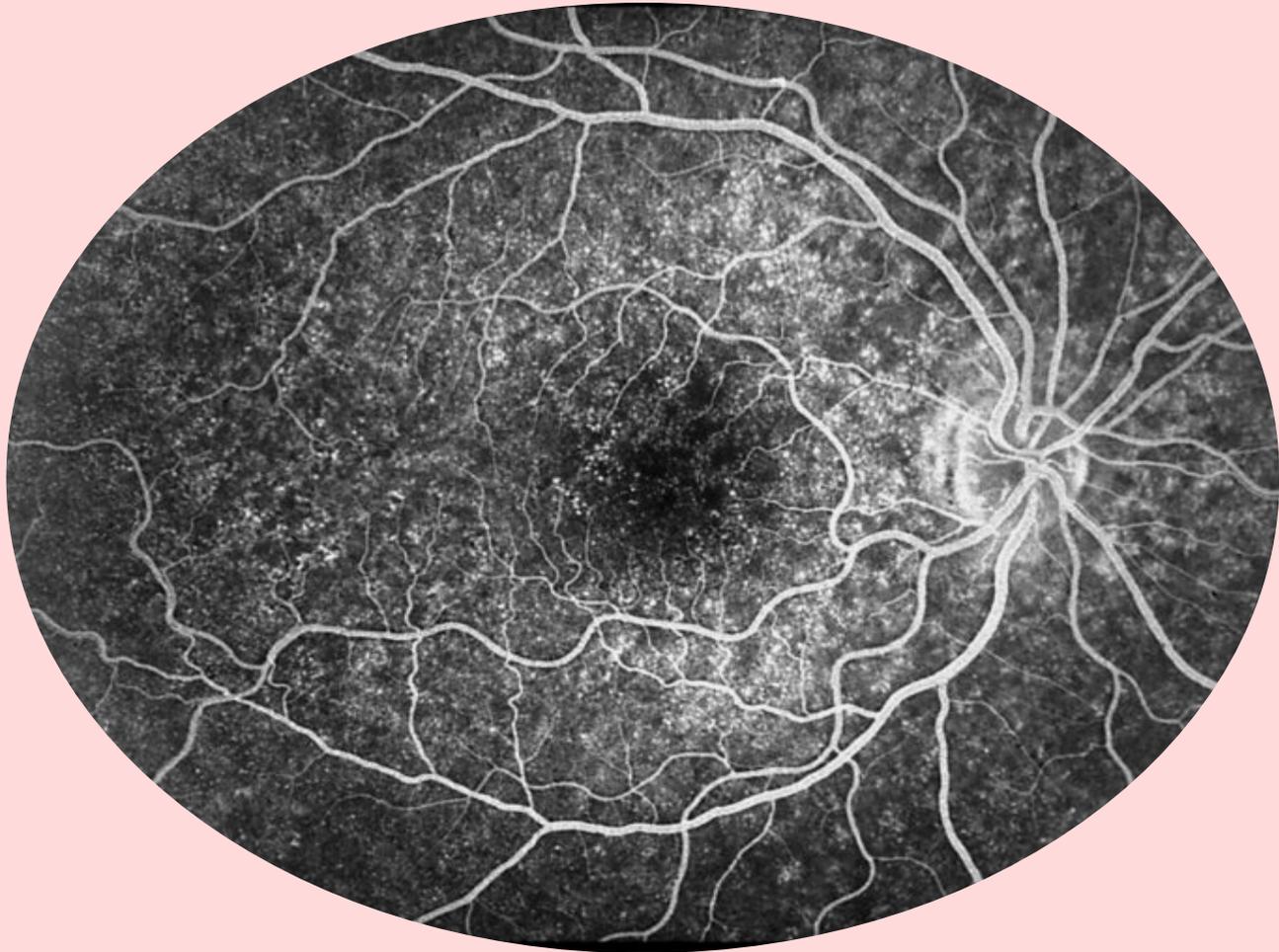


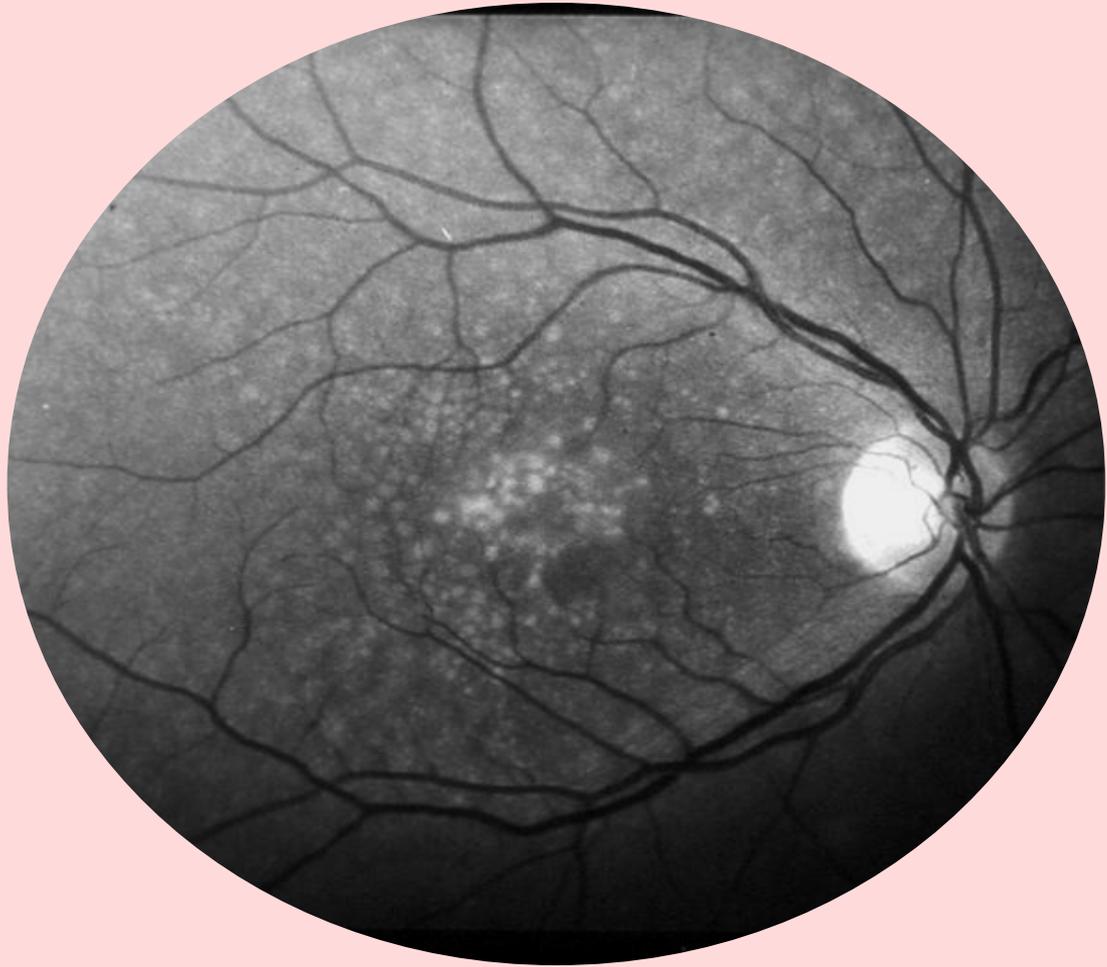




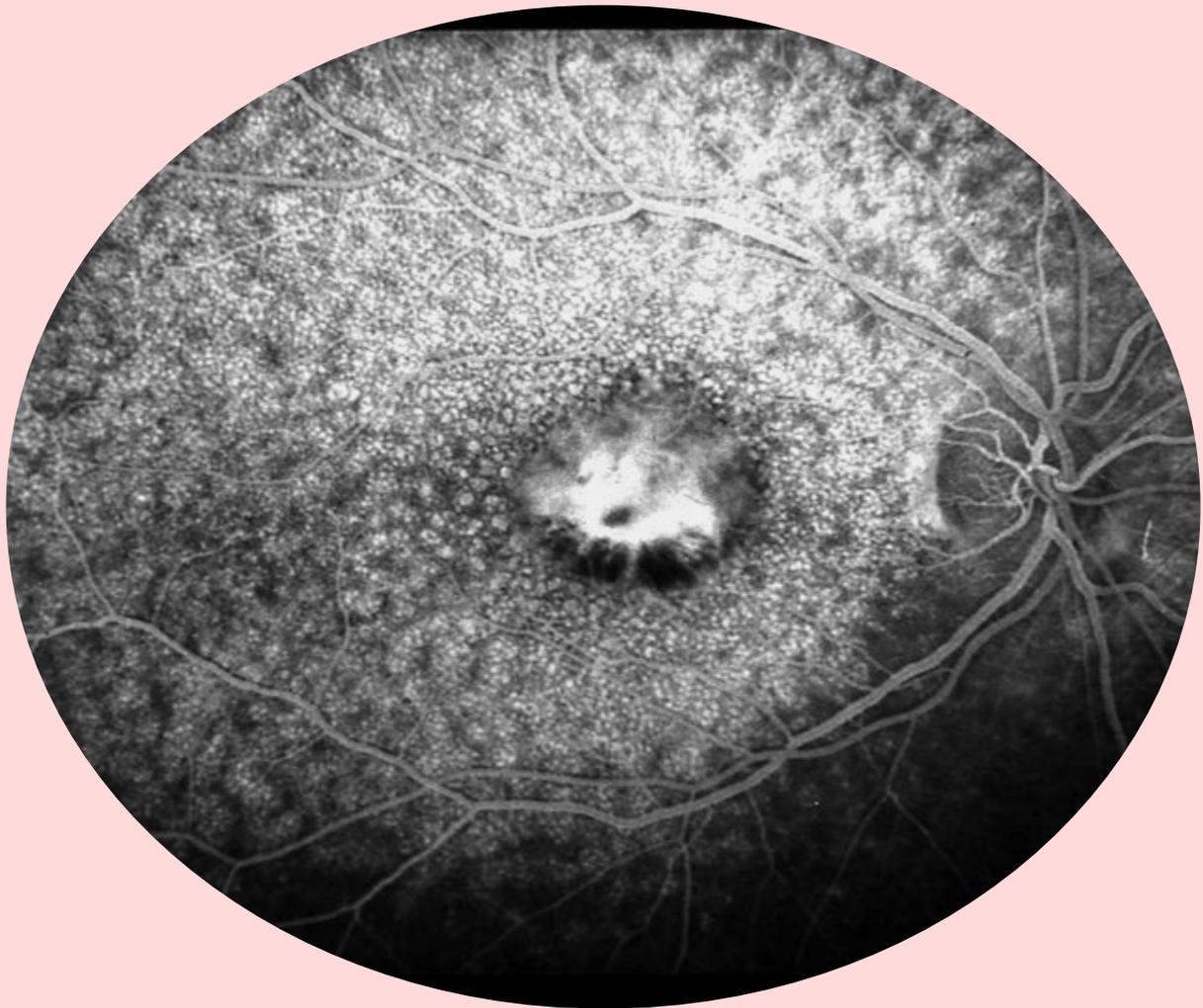
« Milky way » ou « Stars in the sky » pattern

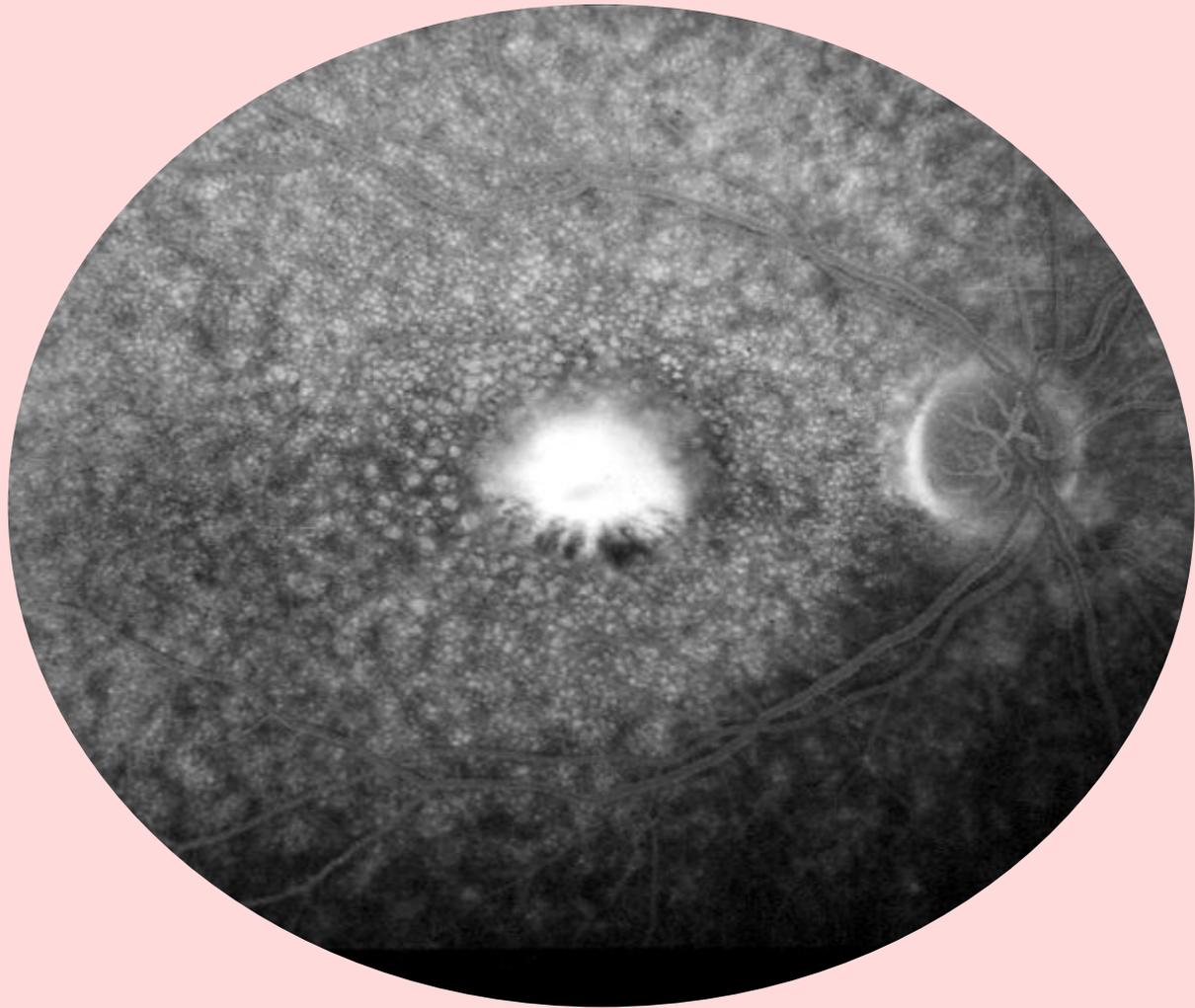


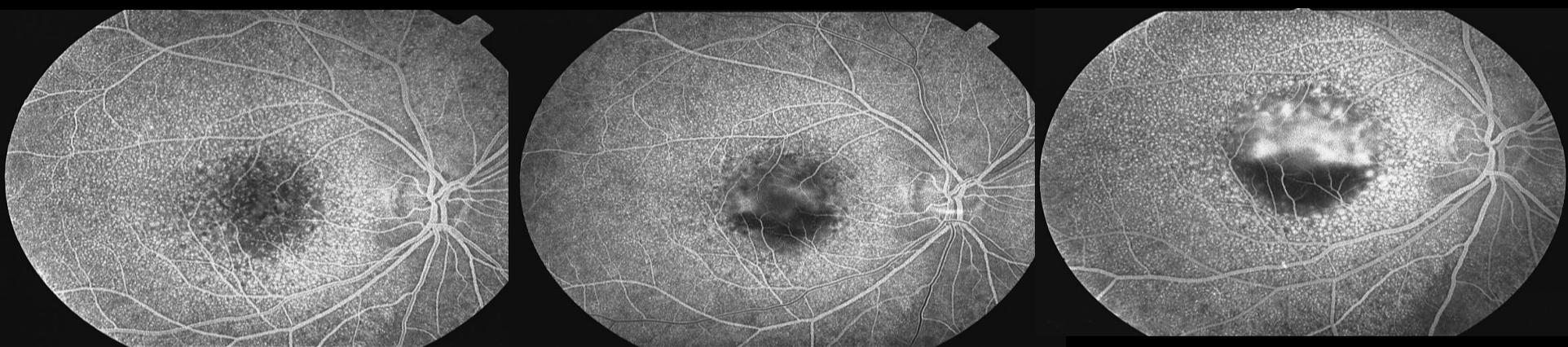




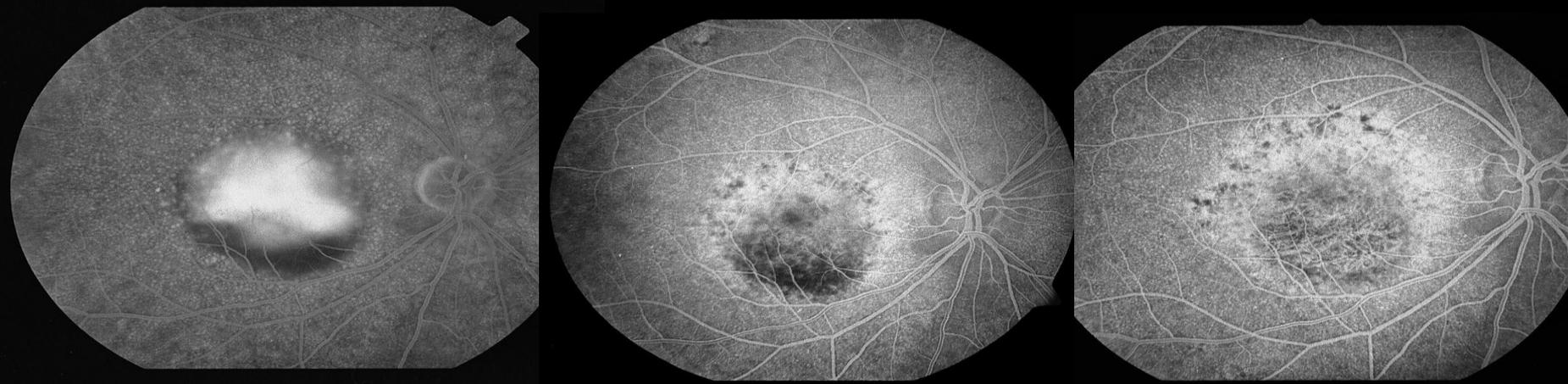




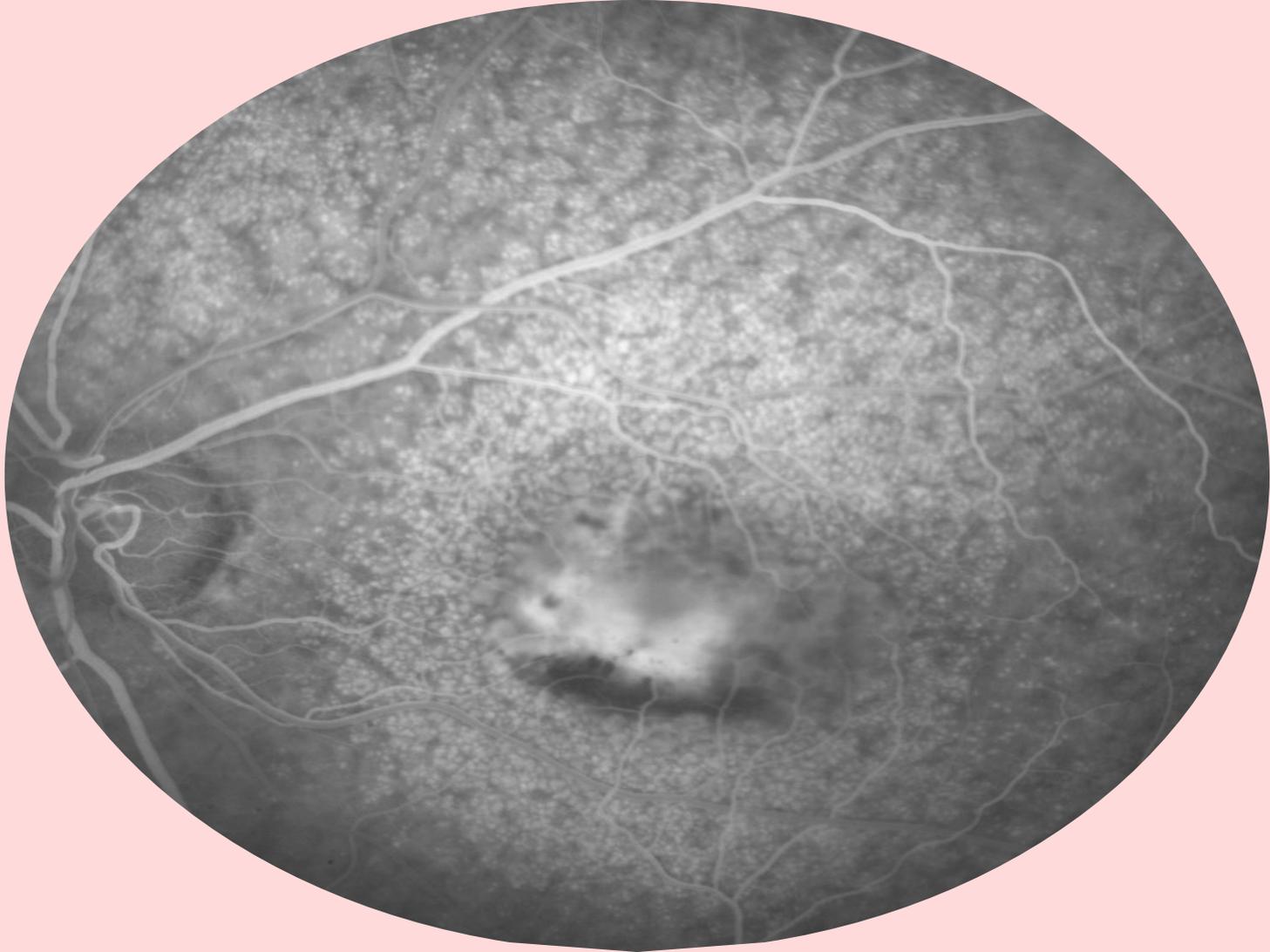


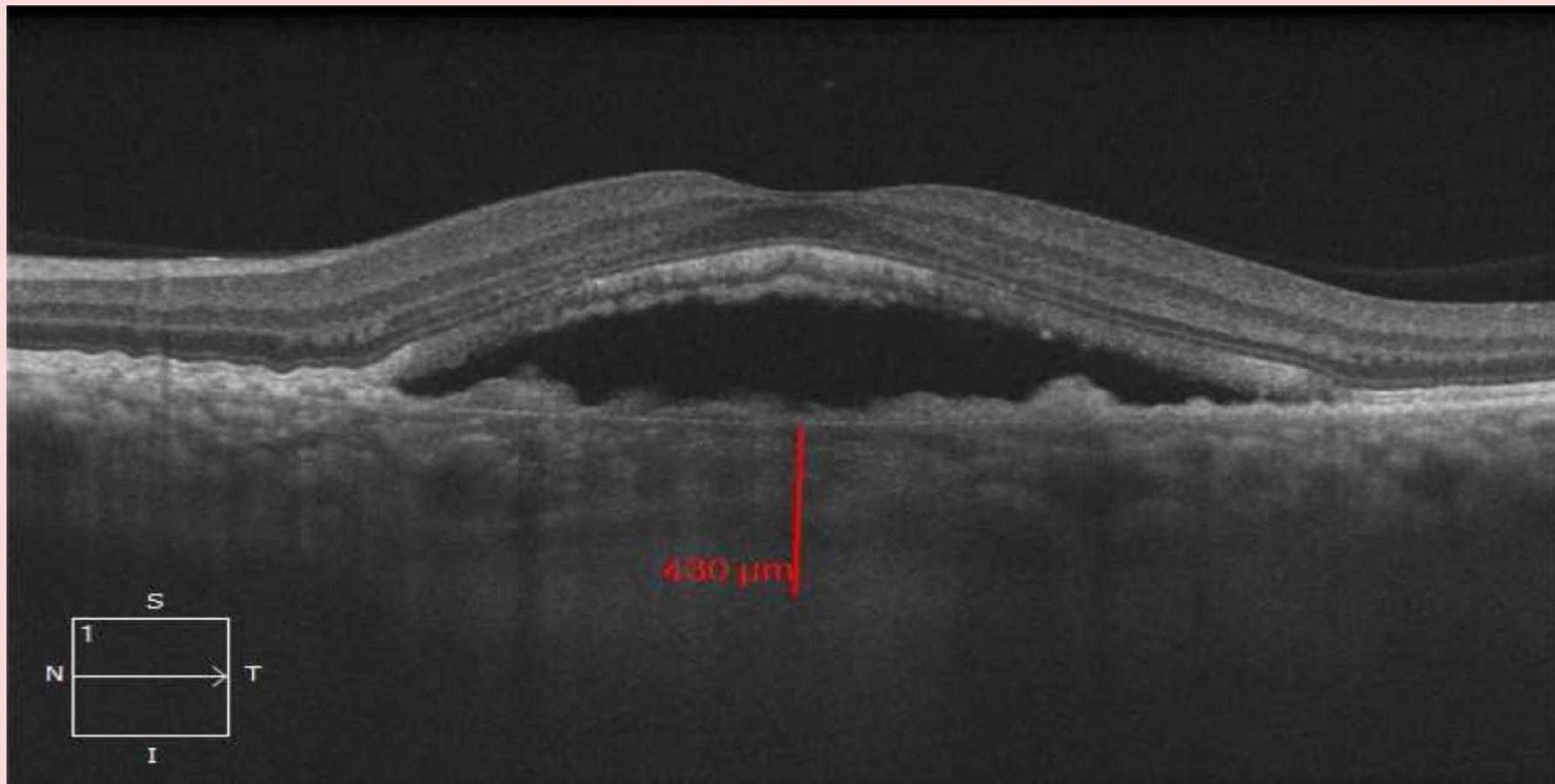


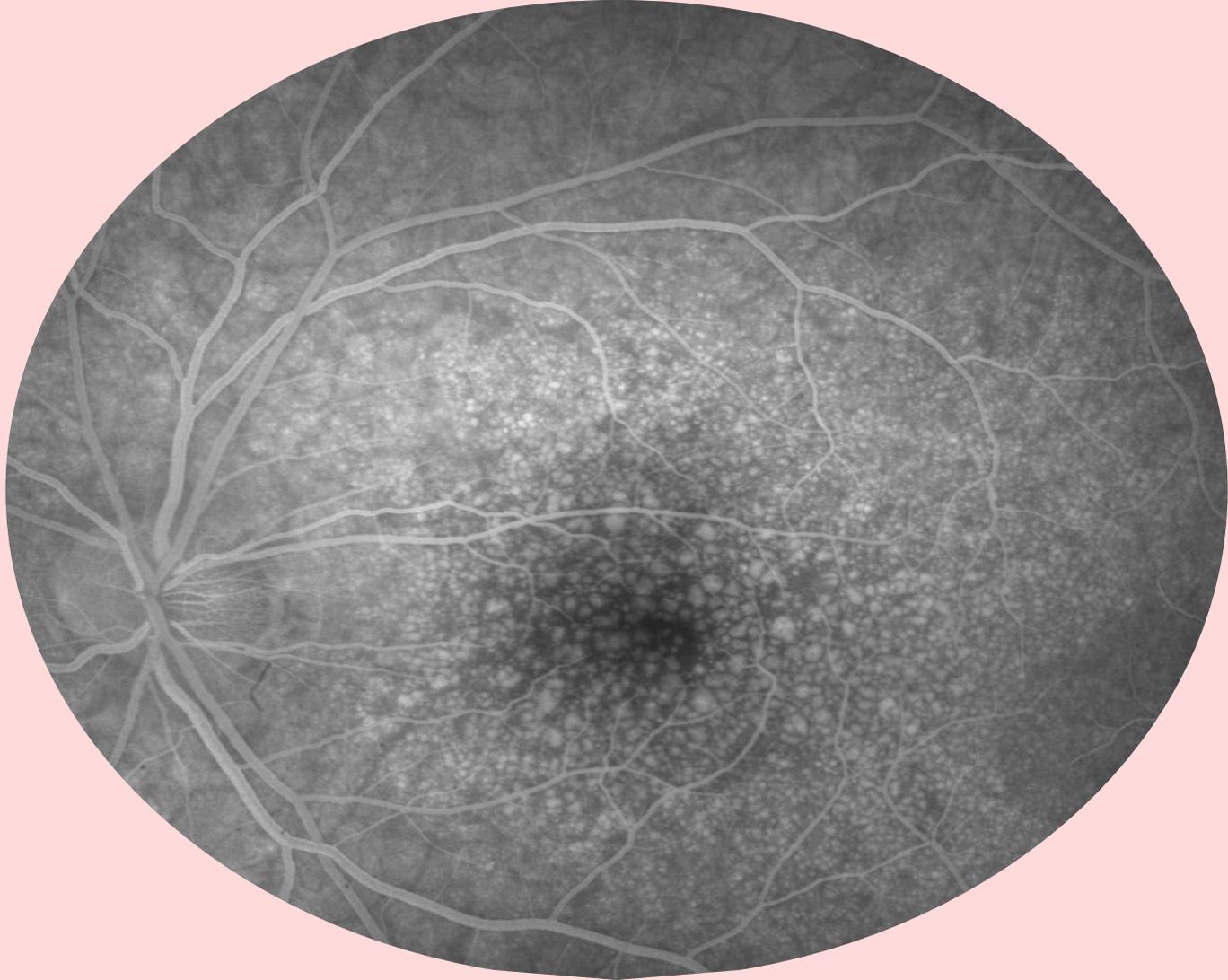
Five-year evolution of basal laminar drusen

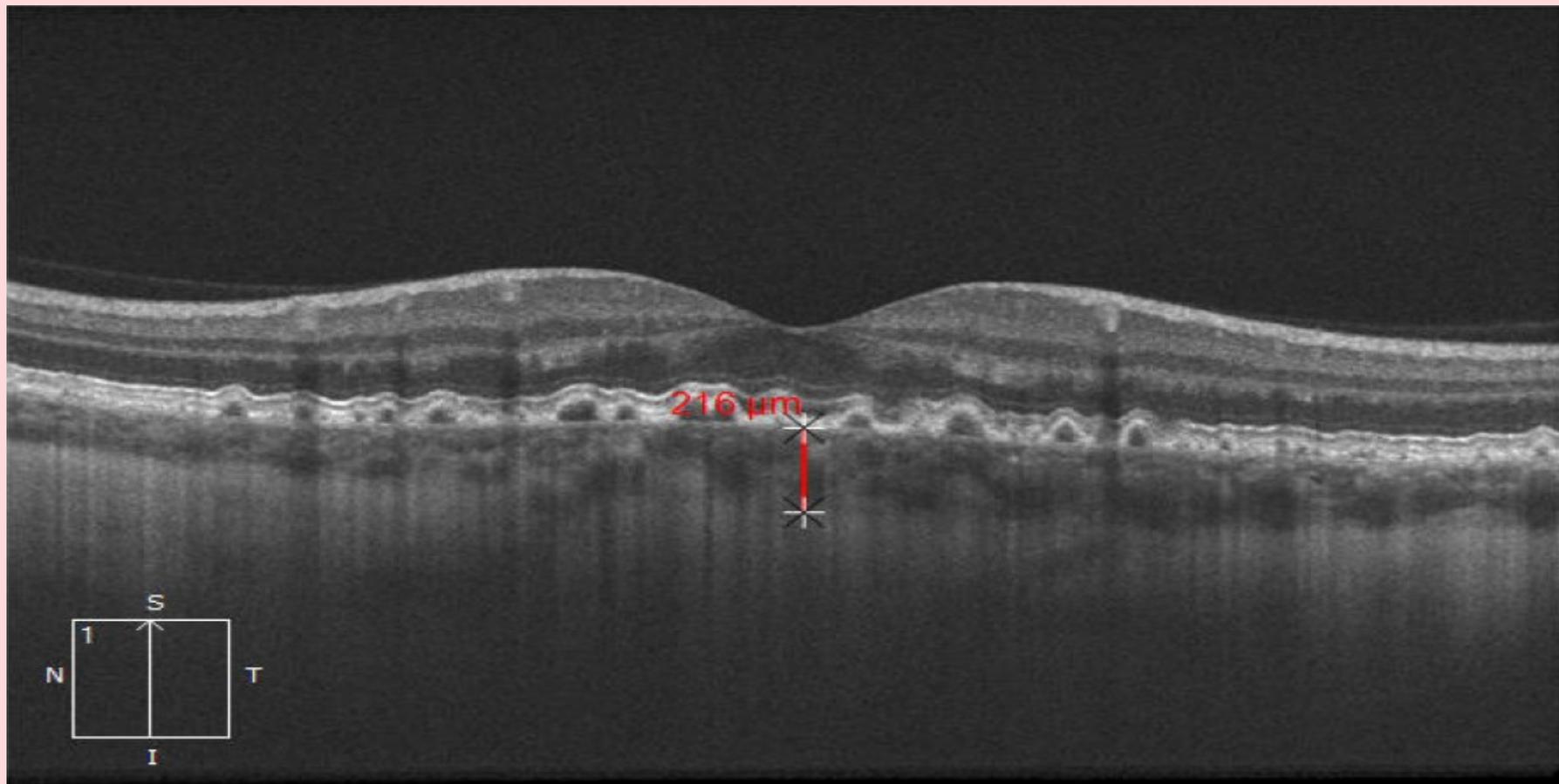








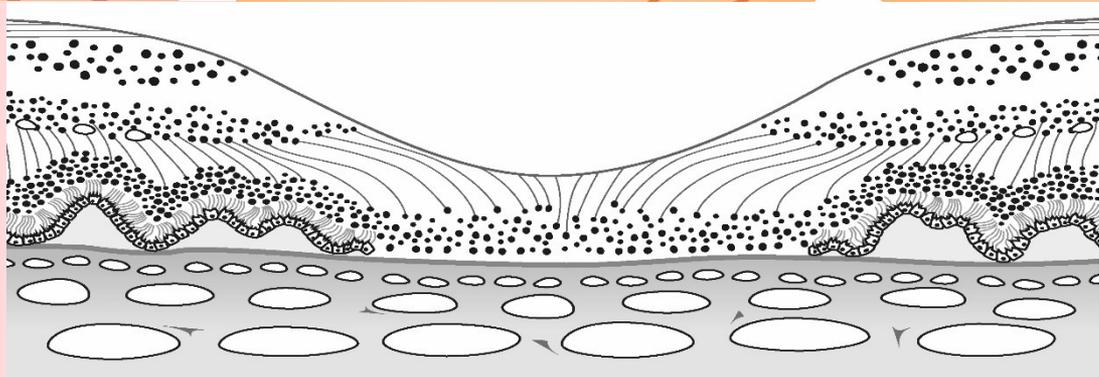
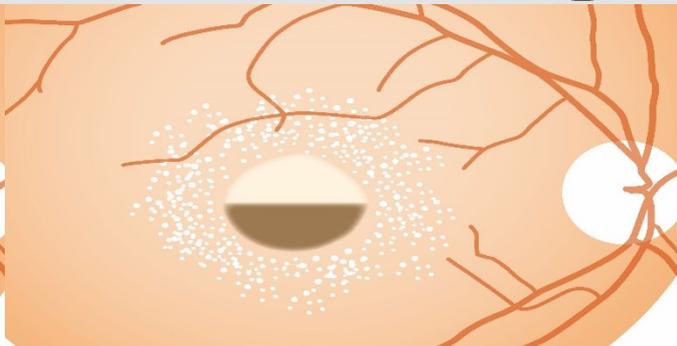
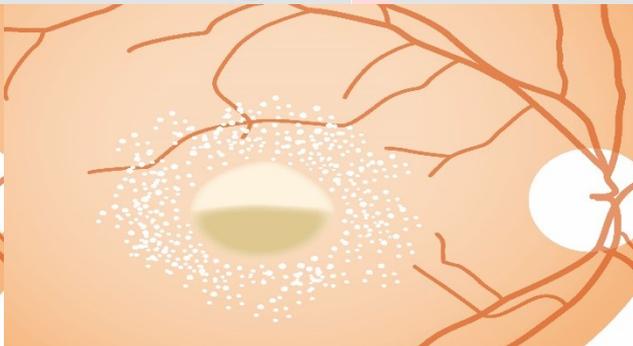
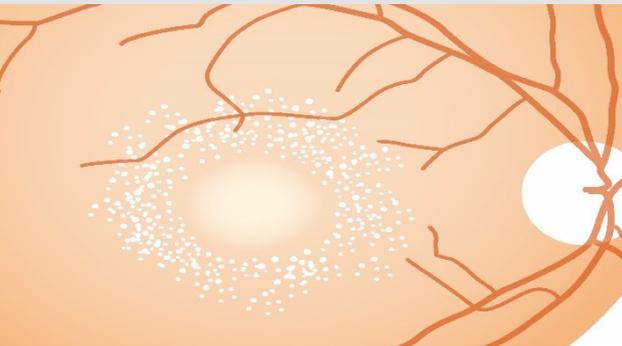
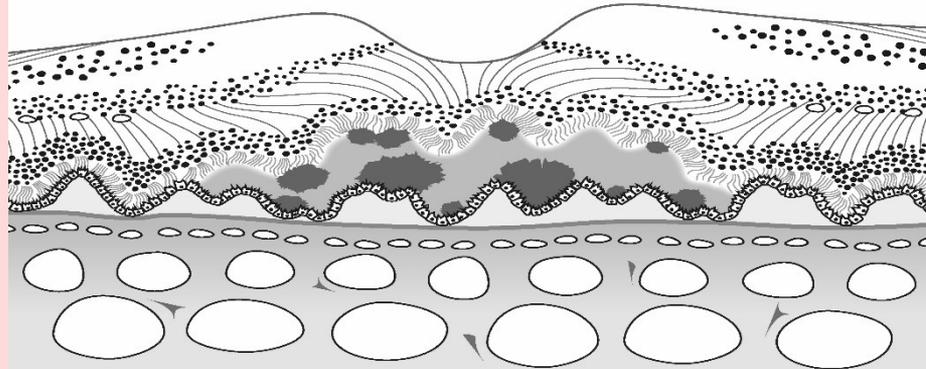
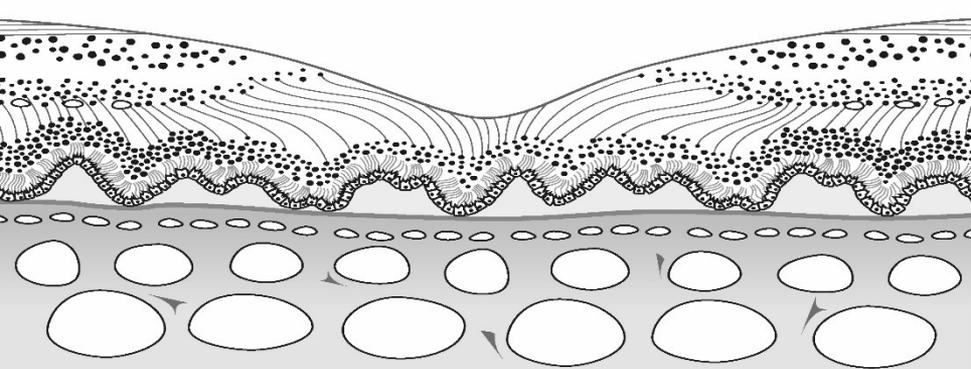


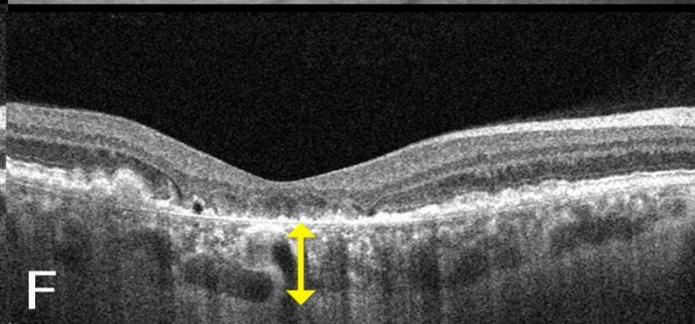
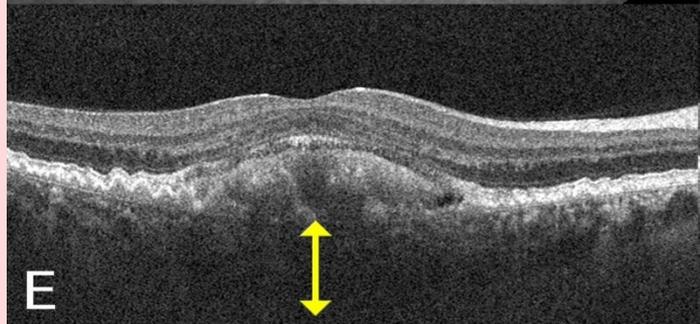
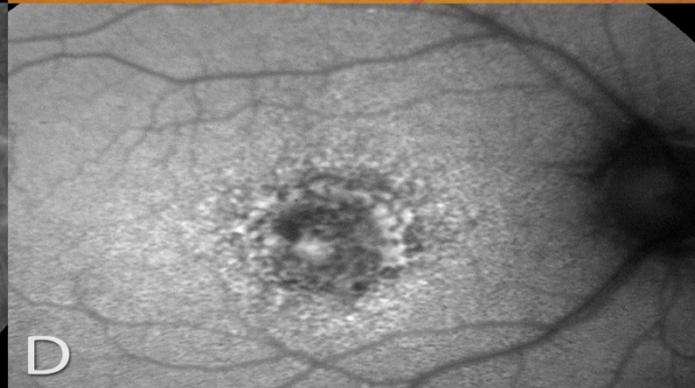
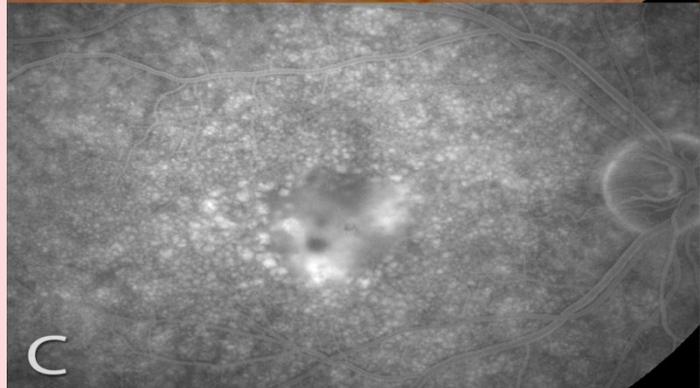


	12 eyes <u>without</u> vitelliform detachment	12 eyes <u>with</u> vitelliform detachment	
Subfoveal thickness	266± 58 μm	369±96 μm	P = 0,006

Mrejen-Uretsky S, Ayrault S, Nghiem-Buffer S, Quentel G, Cohen SY.

Choroidal thickening in patients with cuticular drusen combined with vitelliform macular detachment. *Retina*. 2016 Jun;36(6):1111-8.





8° Les pseudo-drusen en lumière bleue

Chez certains patients, apparaissent des lésions un peu particulières, notées par l'un de nous (G. Soubrane), surtout visibles sur le cliché

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

**DÉGÉNÉRESCENCES
MACULAIRES ACQUISES
LIÉES À L'ÂGE
ET NÉOVAISSEAUX SOUS-RÉTINIENS**

G.COSCAS

AVEC LA PARTICIPATION DE

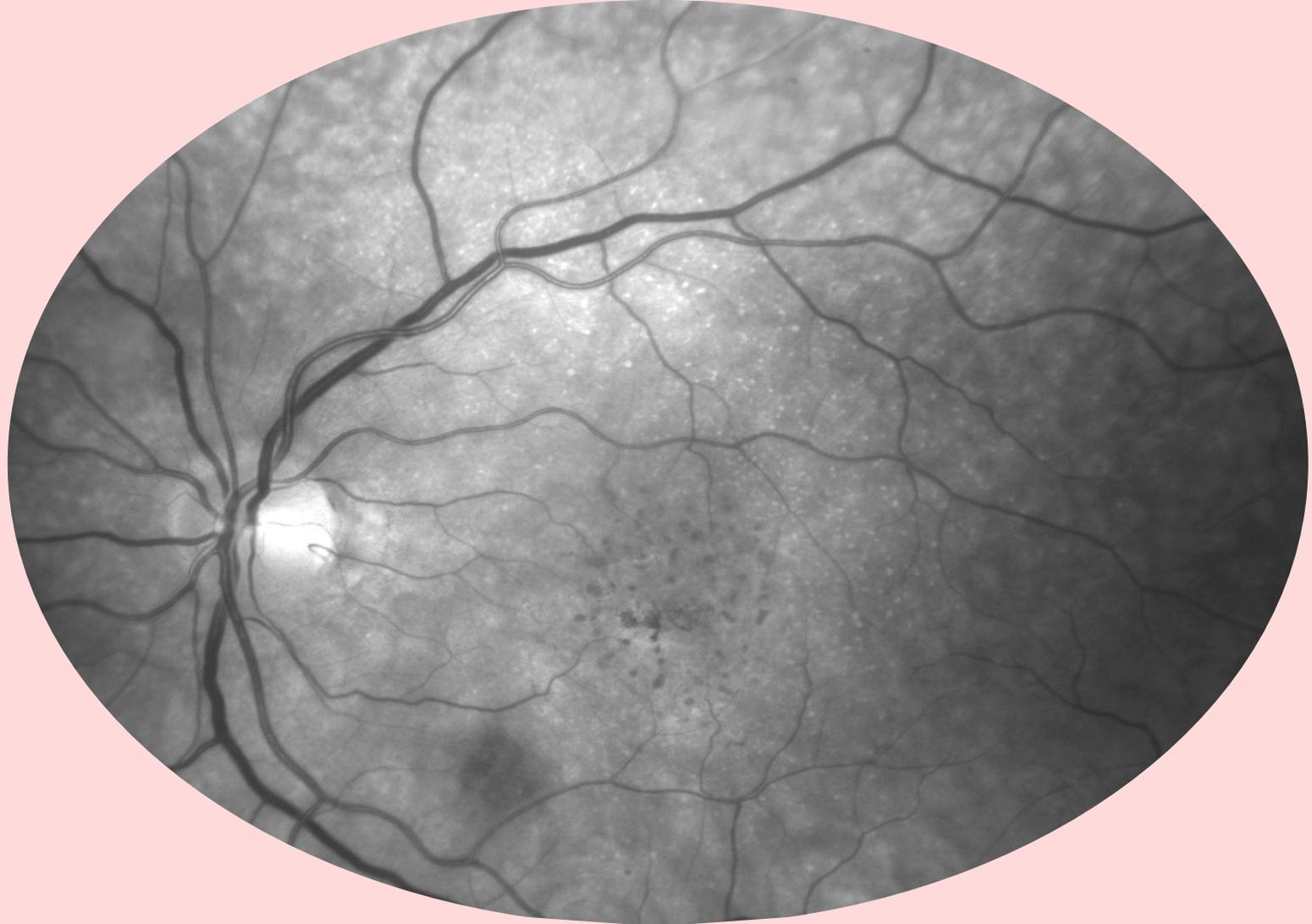
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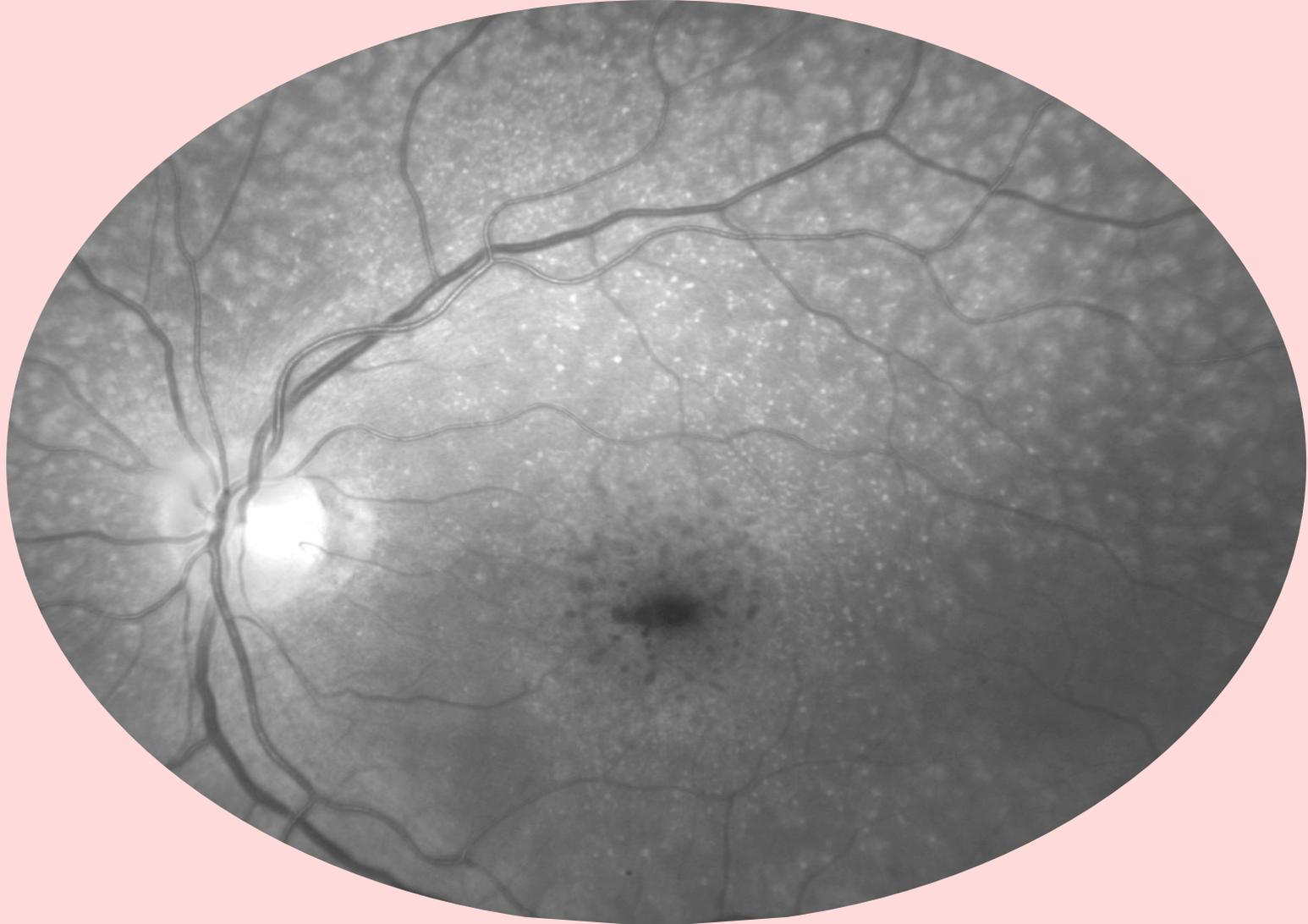
ET DE

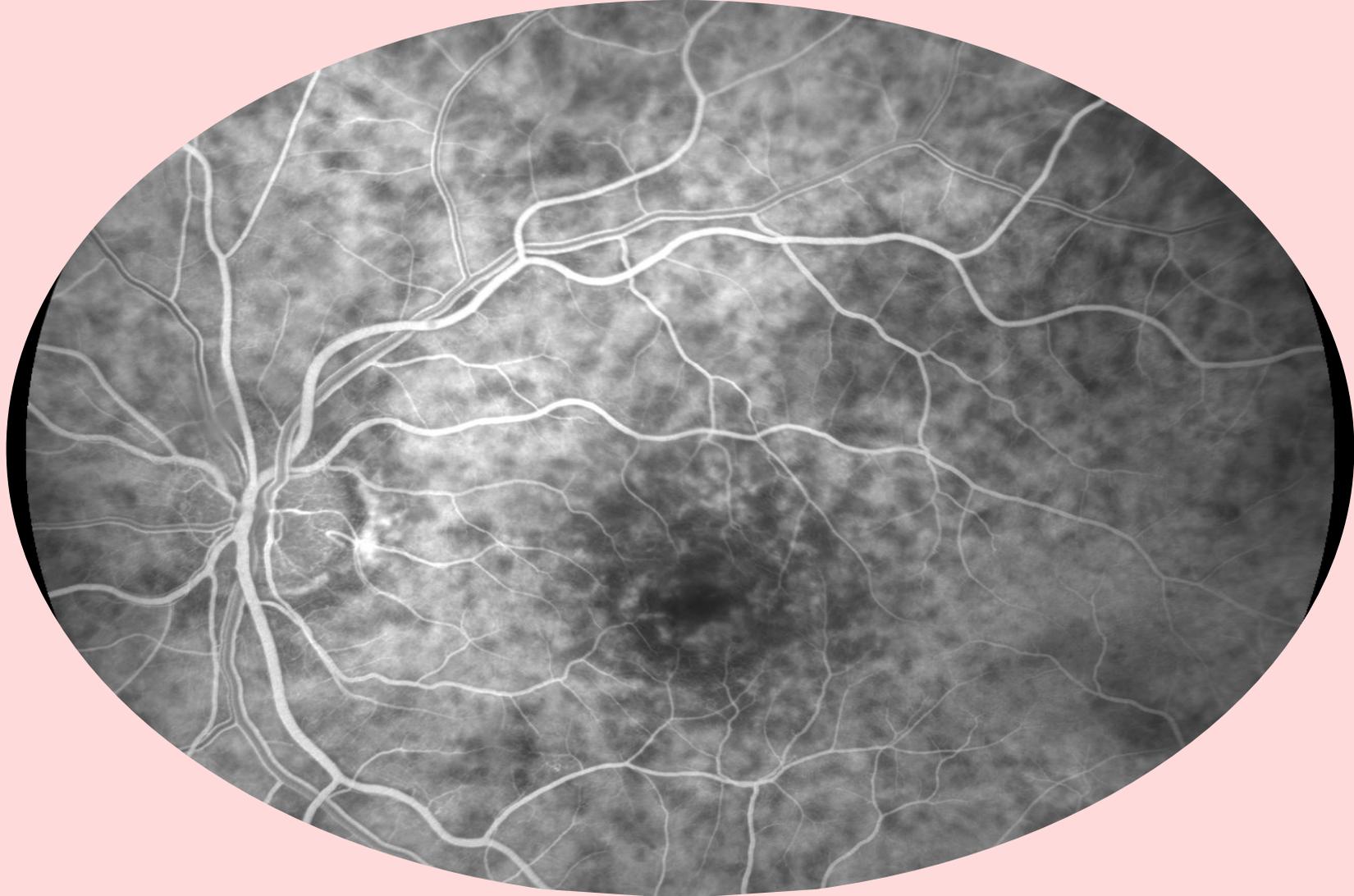
P.AMALRIC J.SAHEL J.SUNNESS

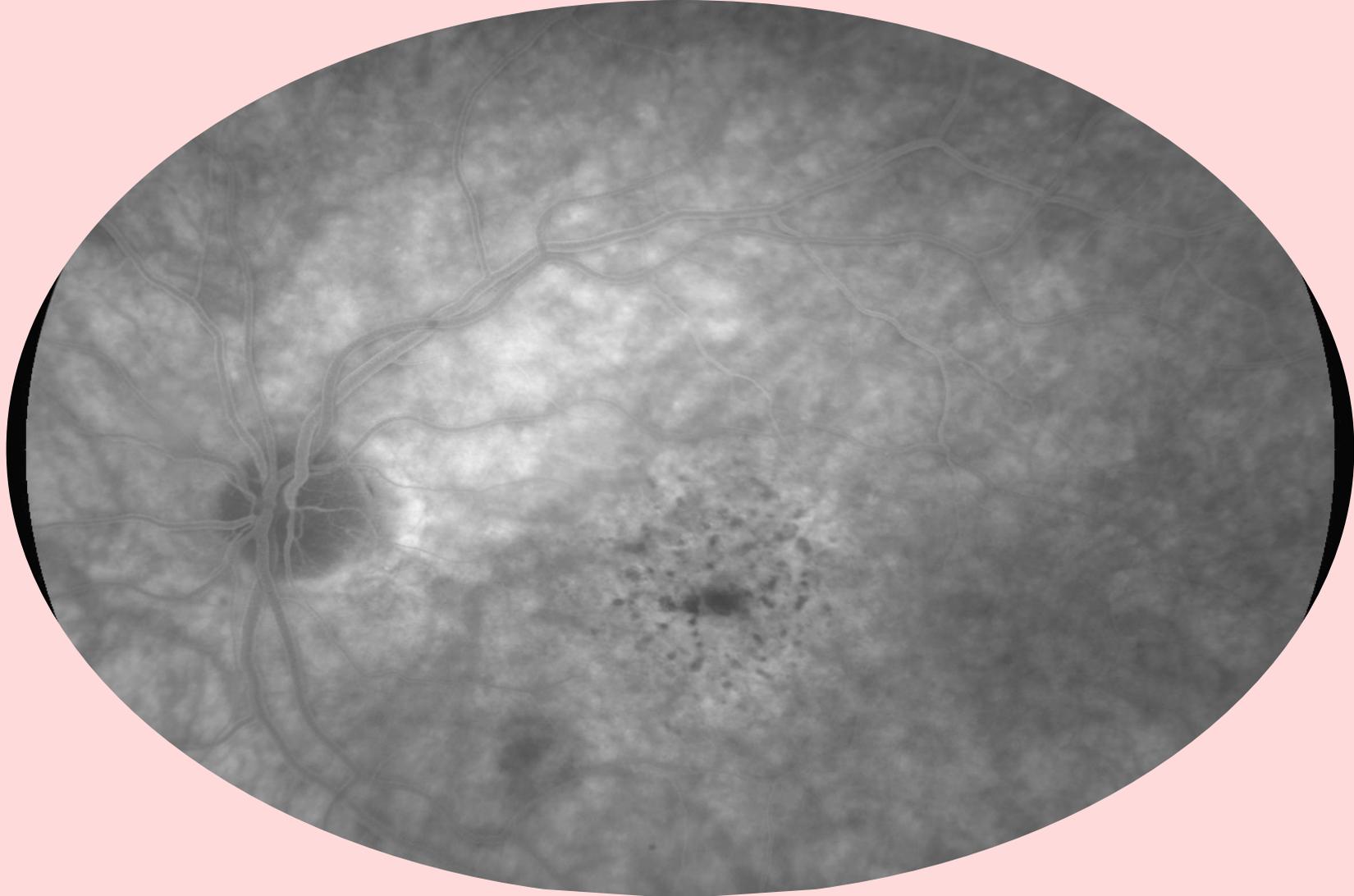
ET L'AIDE DE SES COLLABORATEURS DE CRÉTEIL







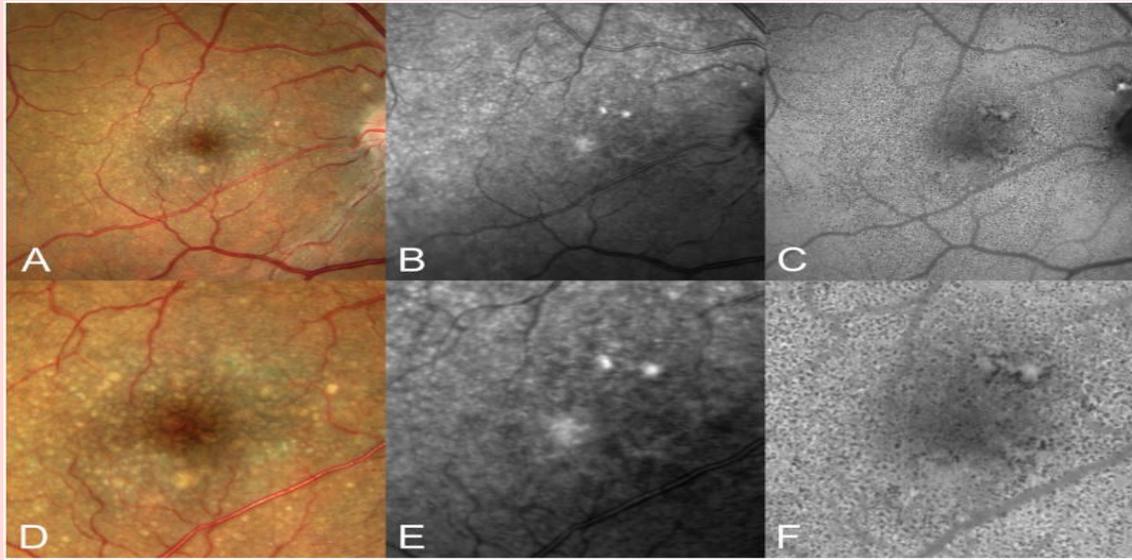


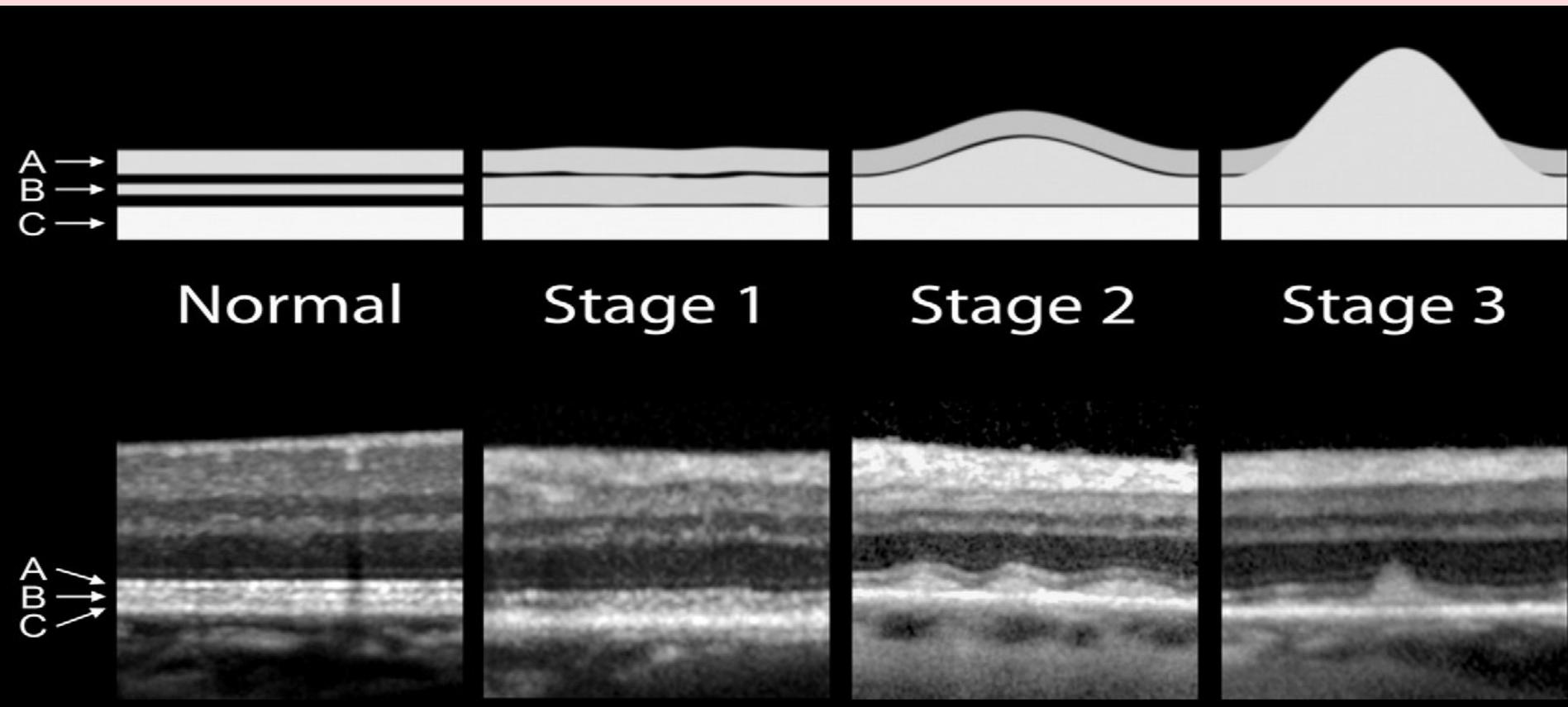


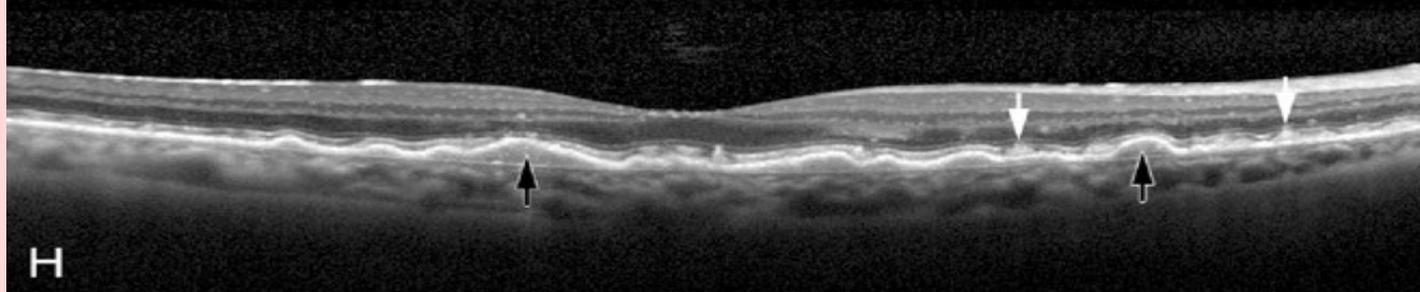
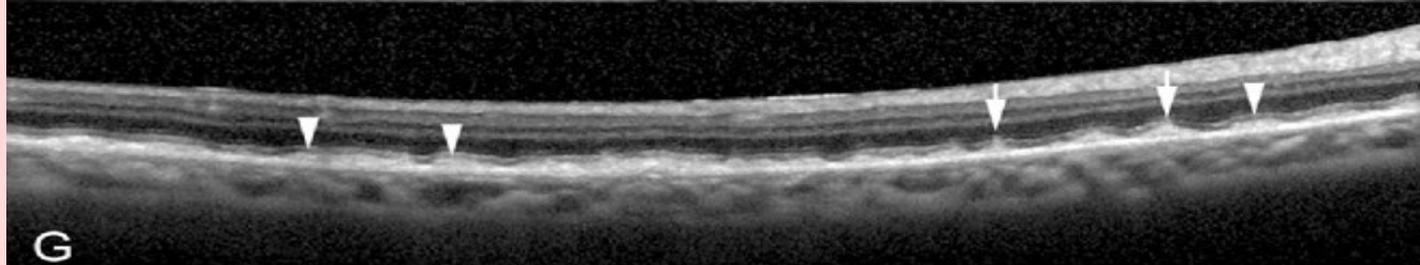
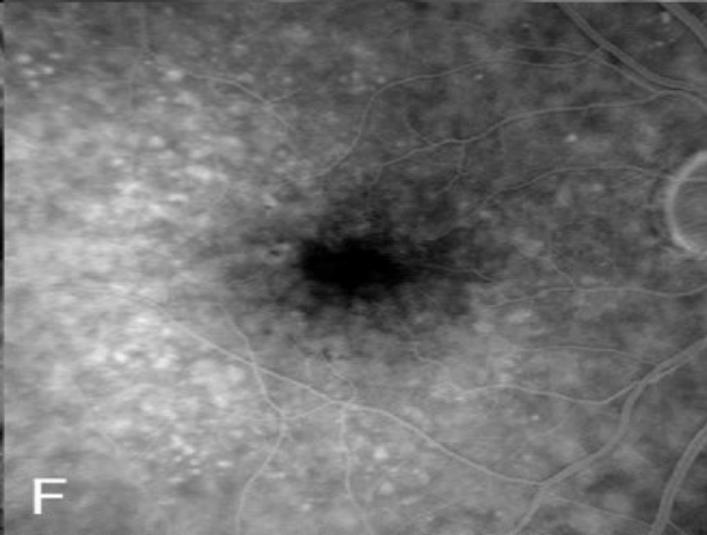
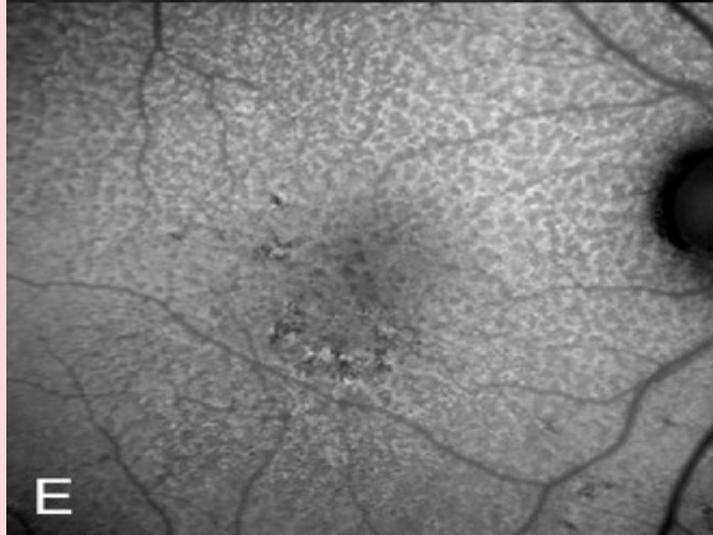
Données plus récentes

Les pseudodrusen sont des dépôts drusenoïdes sous-rétiniens (et non sous-épithéliaux)

Zweifel SA, Spaide RF, Curcio CA, Malek G, Imamura Y. Reticular pseudodrusen are subretinal drusenoid deposits. *Ophthalmology*. 2010 Feb;117(2):303-12



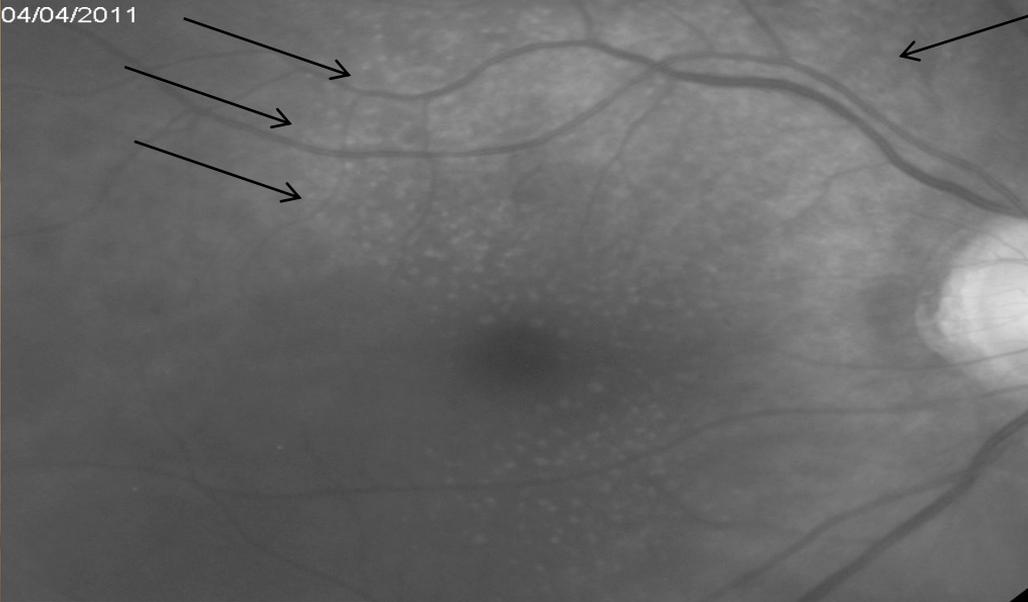




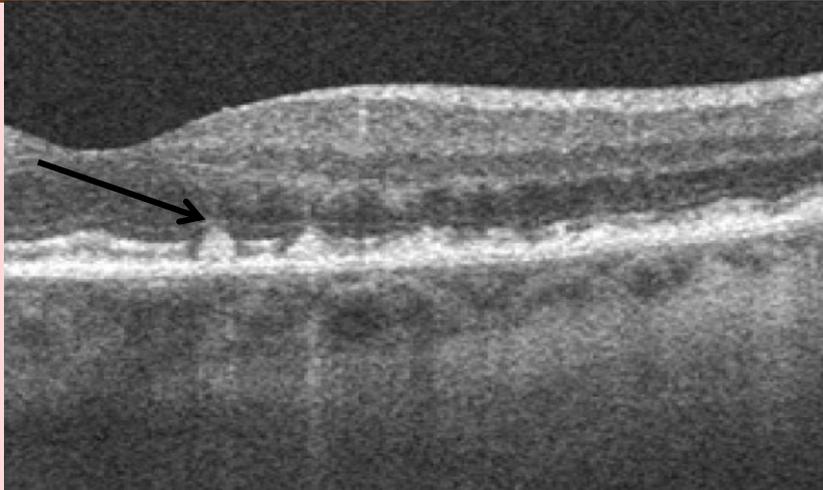
04/04/2011



04/04/2011



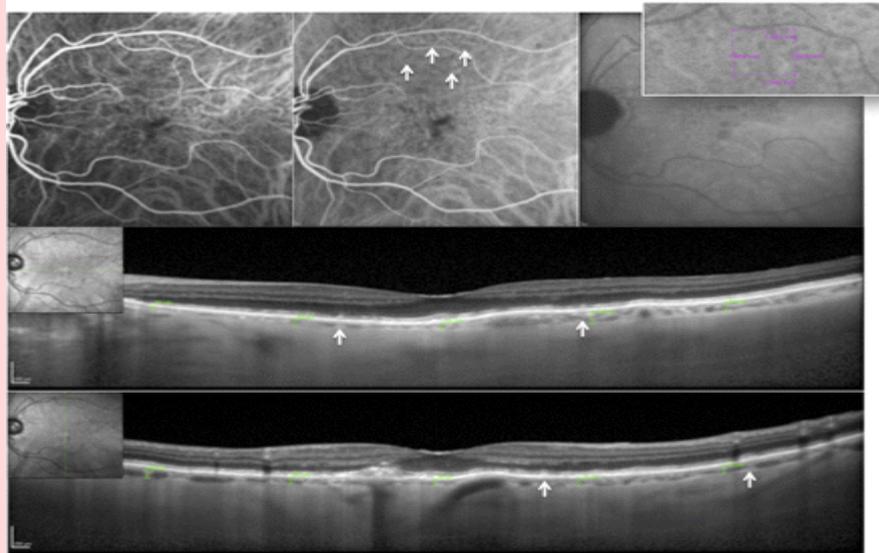
Couleur (comp.



Données plus récentes

Les pseudodrusen sont associés à un amincissement choroidien

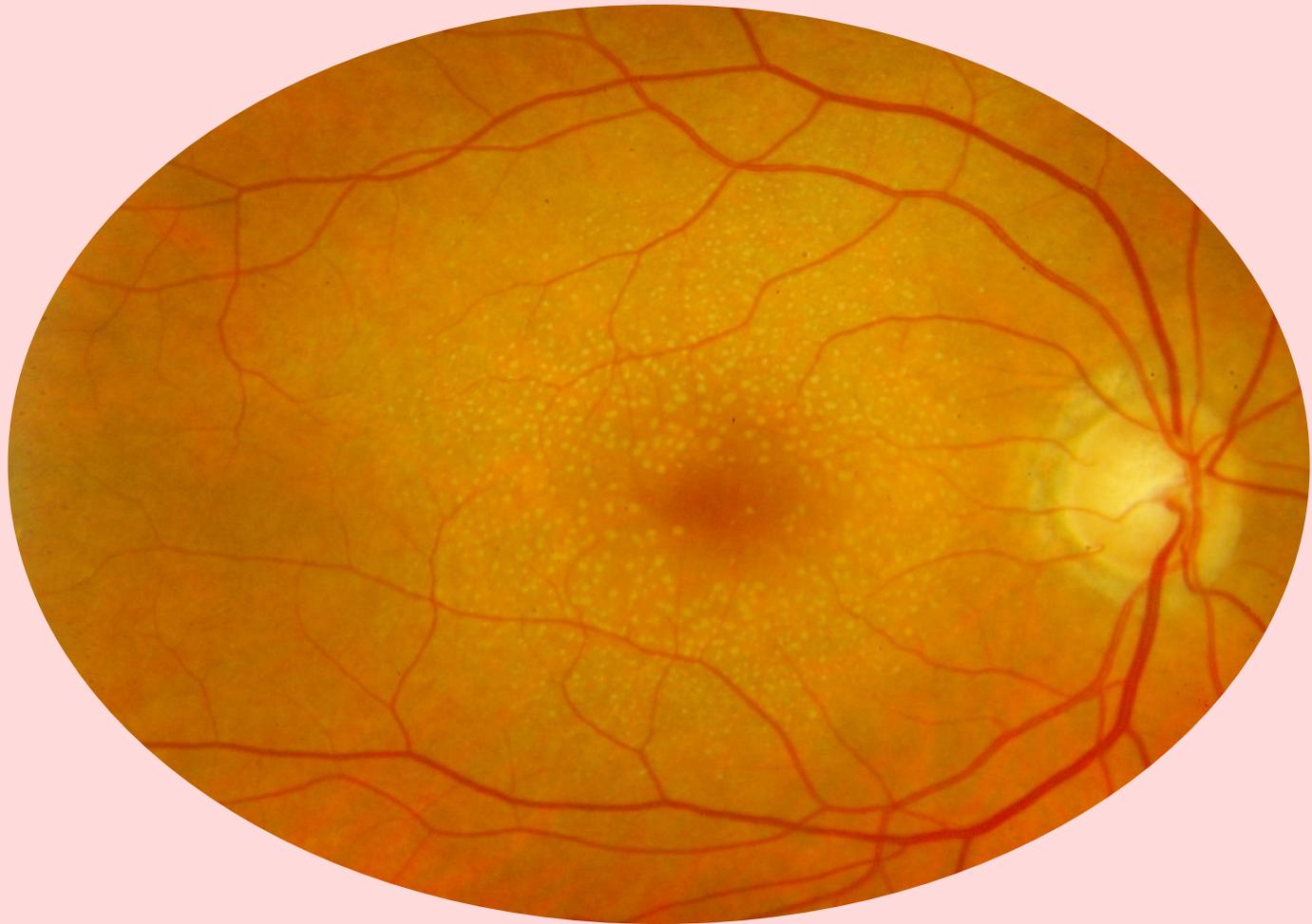
Querques G, Querques L, Forte R, Massamba N, Coscas F, Souied EH. Choroidal changes associated with reticular pseudodrusen. Invest Ophthalmol Vis Sci. 2012 Mar 9;53(3):1258-63

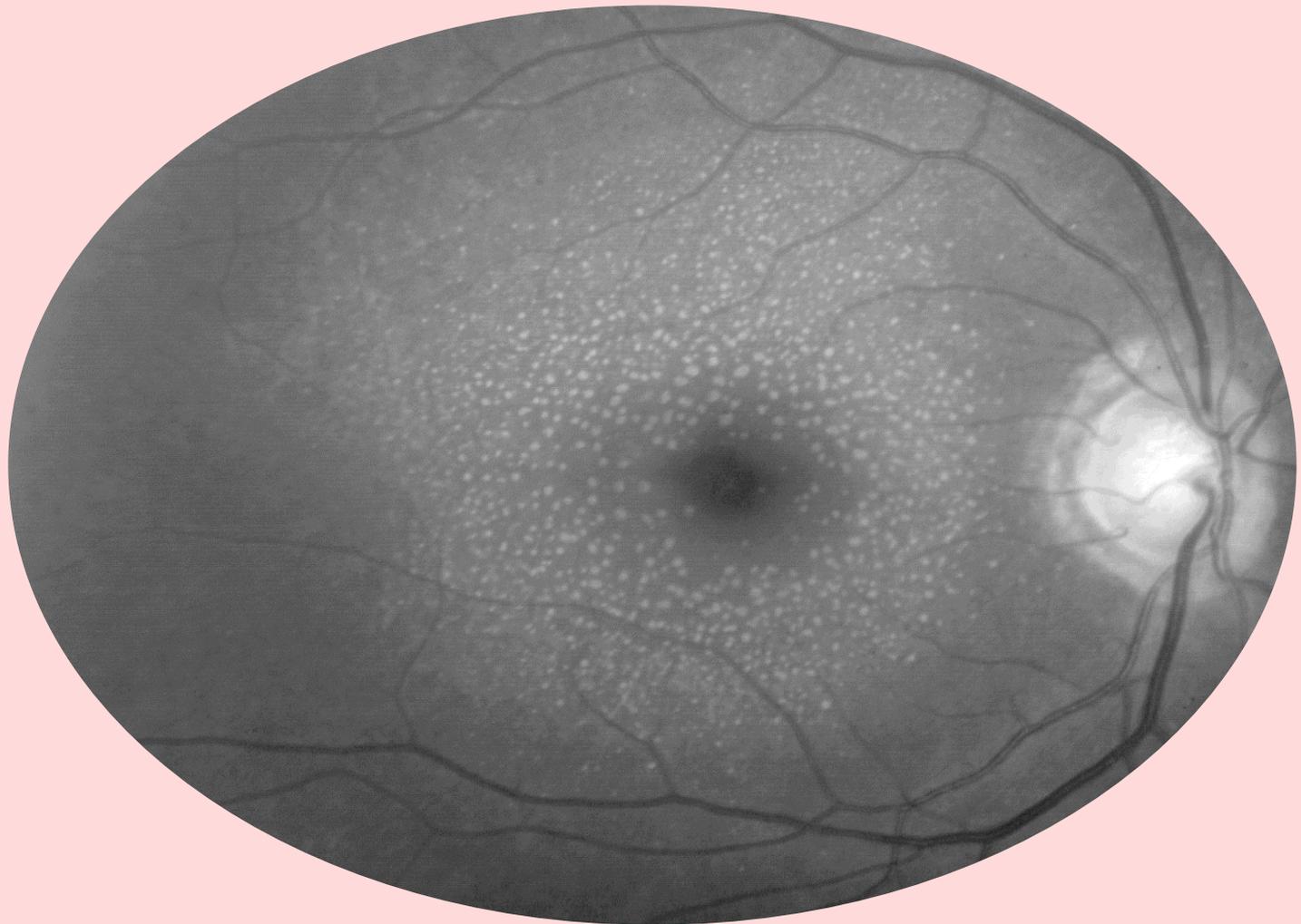


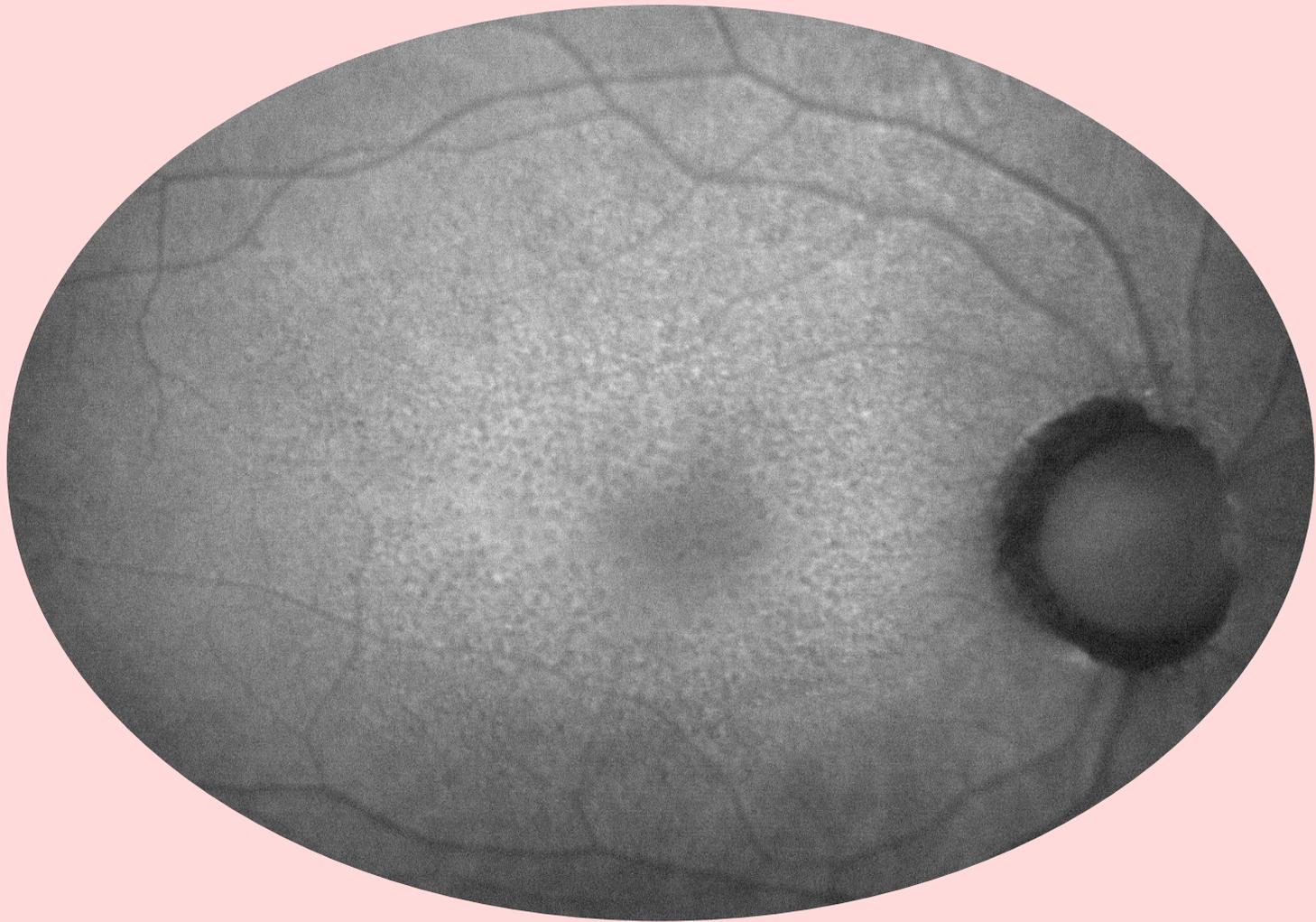
OUTER RETINAL ATROPHY AFTER REGRESSION OF SUBRETINAL DRUSENOID DEPOSITS AS A NEWLY RECOGNIZED FORM OF LATE AGERELATED MACULAR DEGENERATION

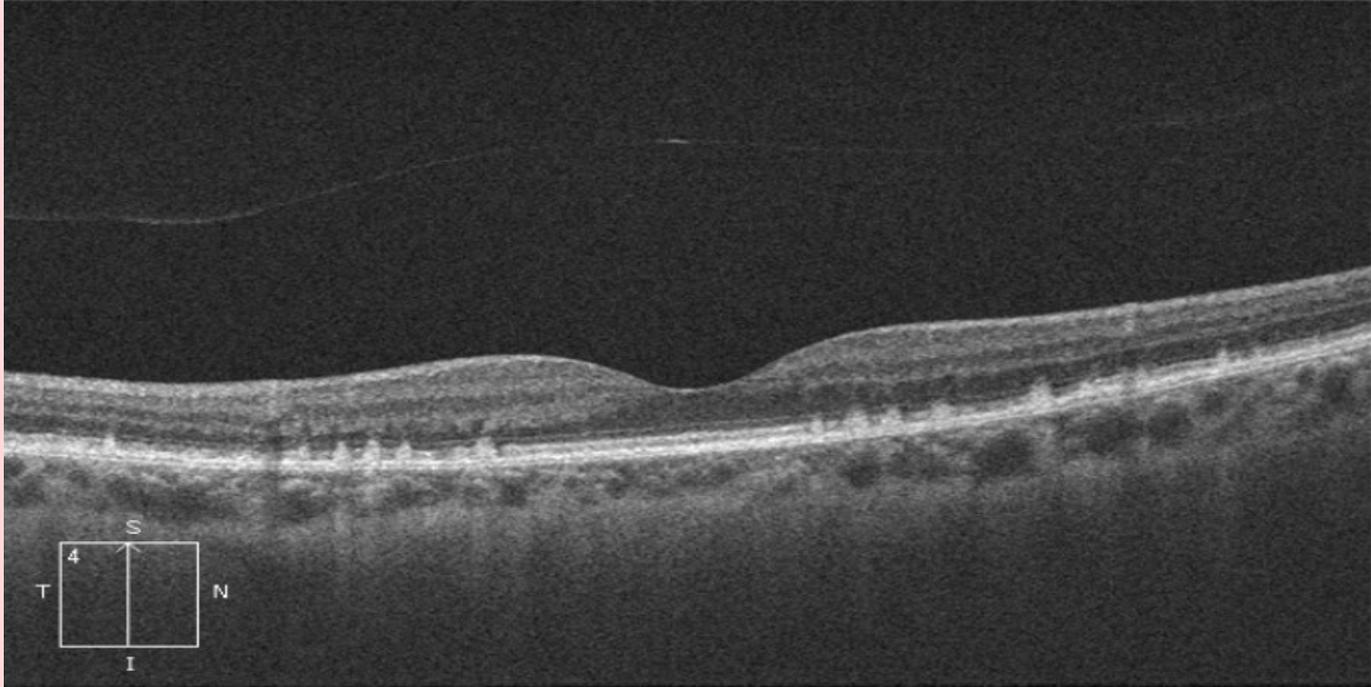
RICHARD F. SPAIDE, MD
RETINA 33:1800-1808, 2013

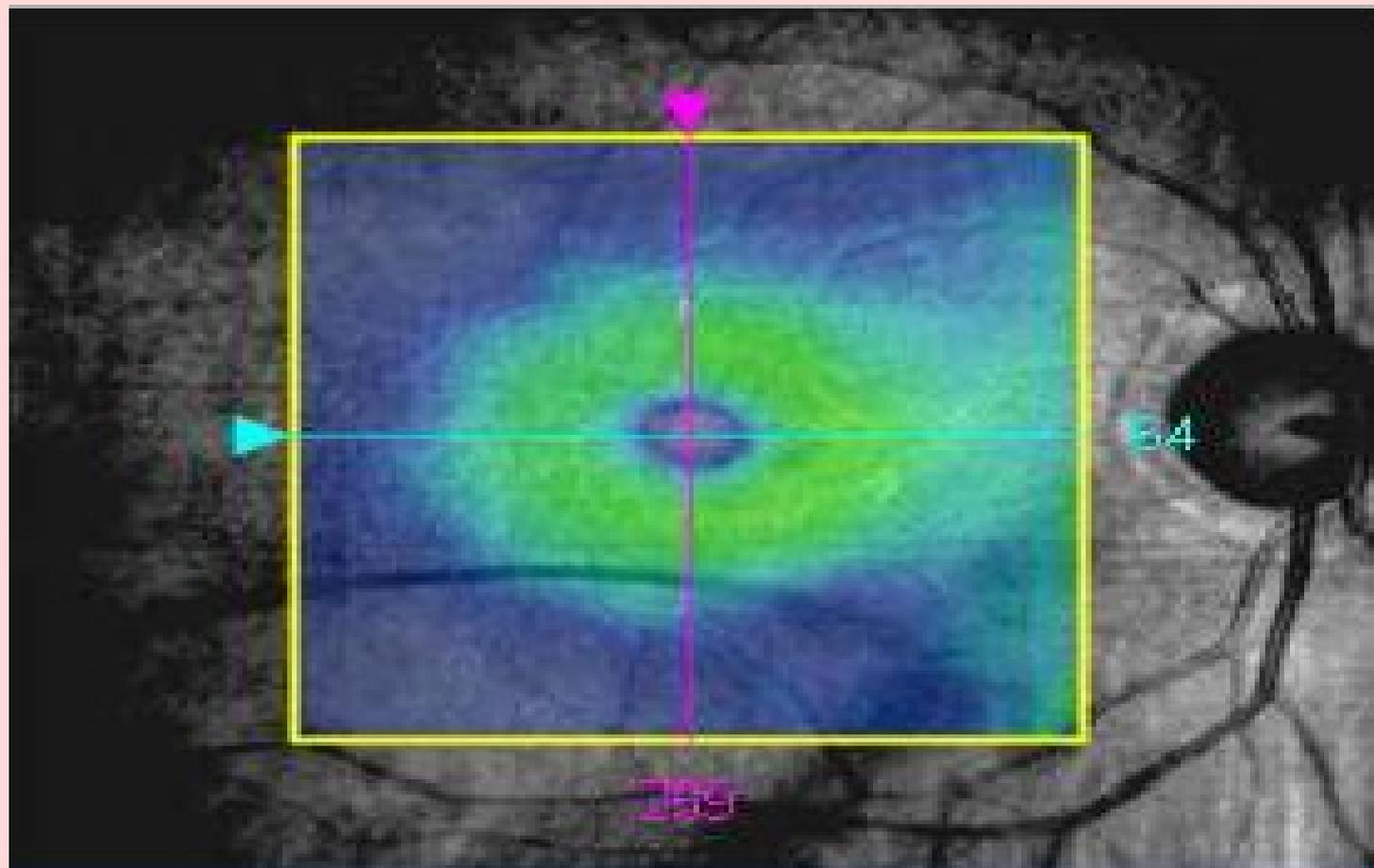
Eyes with regression of subretinal drusenoid deposits develop outer retinal atrophy and loss of the underlying choroidal thickness

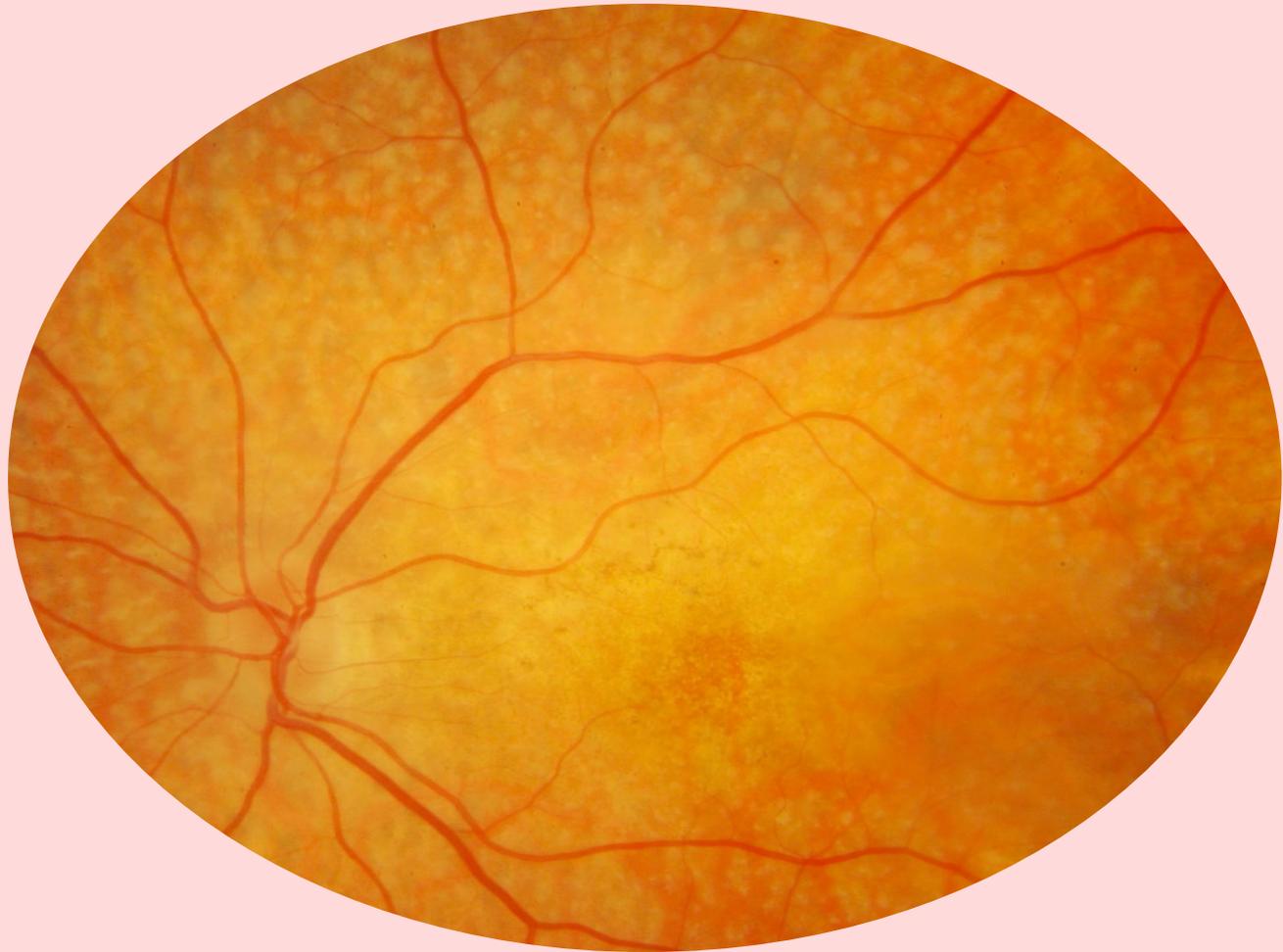


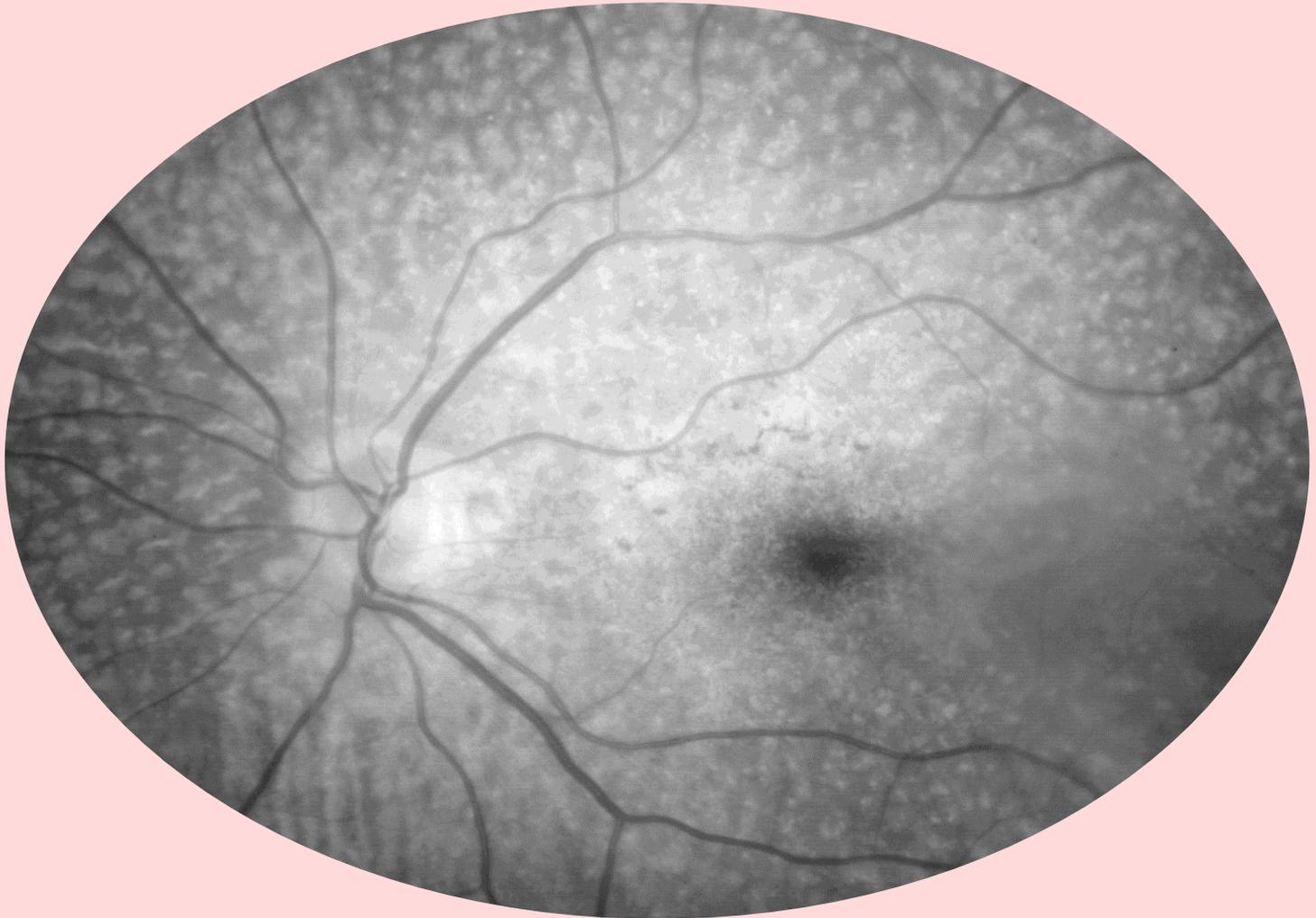


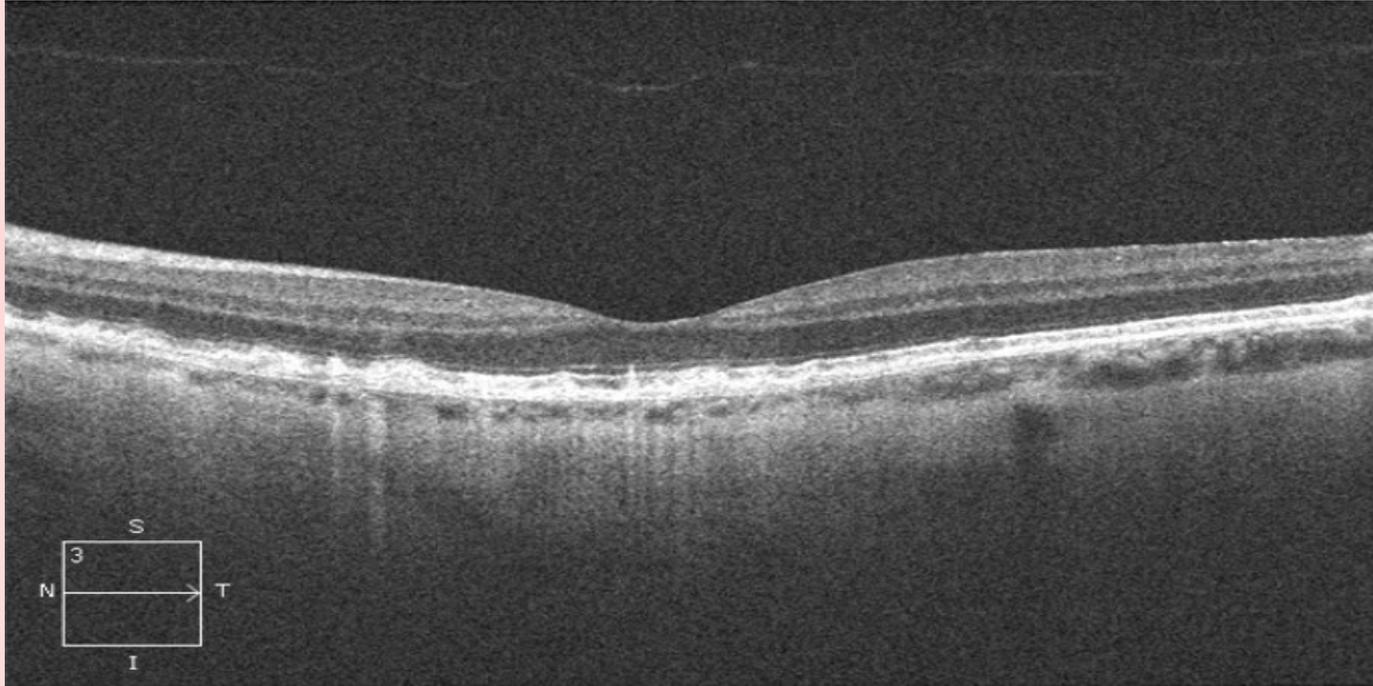


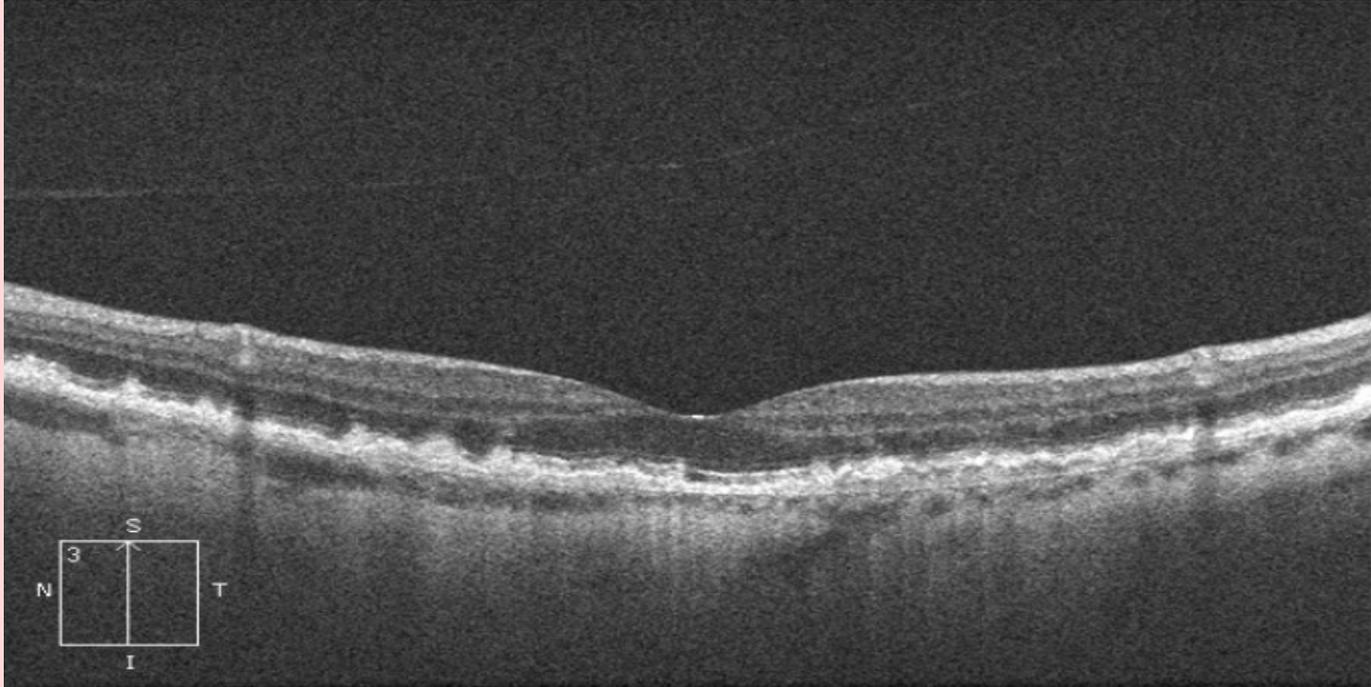












Incidence and Risk Factors of Reticular Pseudodrusen Using Multimodal Imaging

Cyril Duthel, MD; Mélanie Le Goff, MSc; Audrey Cougnard-Grégoire, PhD; Sarra Gattoussi, MD, PhD;
Jean-François Korobelnik, MD; Marie-Bénédicte Rougier, MD, PhD; Cédric Schweitzer, MD, PhD;
Cécile Delcourt, PhD; Marie-Noëlle Delyfer, MD, PhD

JAMA, 2020 May 14

Reticular Pseudodrusen: the Third Macular Risk Feature for Progression to Late Age-related Macular Degeneration

Authors

Elvira Agrón, MA¹, Amitha Domalpally, MD, PhD², Catherine A. Cukras, MD, PhD¹, Traci E. Clemons, PhD³, Emily Y. Chew, MD¹, and Tiarnan D. L. Keenan, BM BCh, PhD¹, for the AREDS and AREDS2 Research Groups⁴

Ophthalmology, May 2022

RPD represent an important anatomical risk factor for progression to late AMD, particularly GA. However, the added risk associated with RPD varies markedly by severity level. It carries highly increased risk at lower/moderate levels and less increased risk at higher levels. RPD status should be included in updated AMD classification systems, risk calculators, and clinical trials.

Ophthalmology, May 2022

Formes à faible risque:

- Drusen miliaires

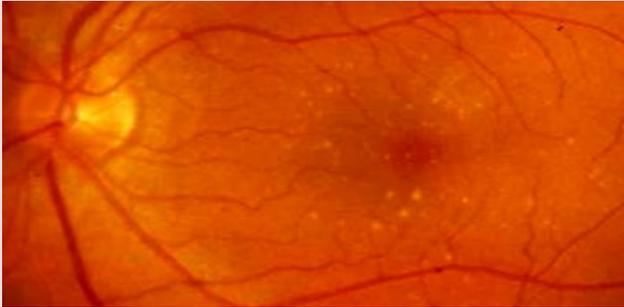
Formes à haut risque:

- Drusen séreux (de grande taille, confluents)
- Migrations pigmentaires
- Pseudodrusen réticulés
= dépôts drusenoïdes sous-rétiniens

Formes à faible risque

Ex: Drusen miliaires

Documentation ?
- Photo couleur

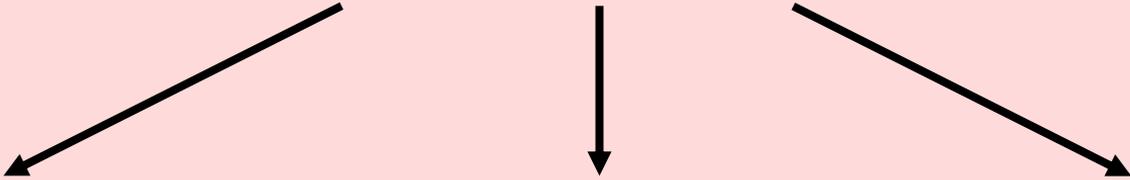


Discours :
- Vieillissement
Autosurveillance

Prescription ?
- Antiox +Zn
- Lutéine
- Omega 3
- Rien ?

Formes de début

Drusen Séreux



Documentation ?

- Photo couleur
 - OCT spectral
- domain comme à tout patient

Discours :

- DMLA
- Autosurveillance
- Contrôles du FO
- Tabac
- Lumière
- Alimentation

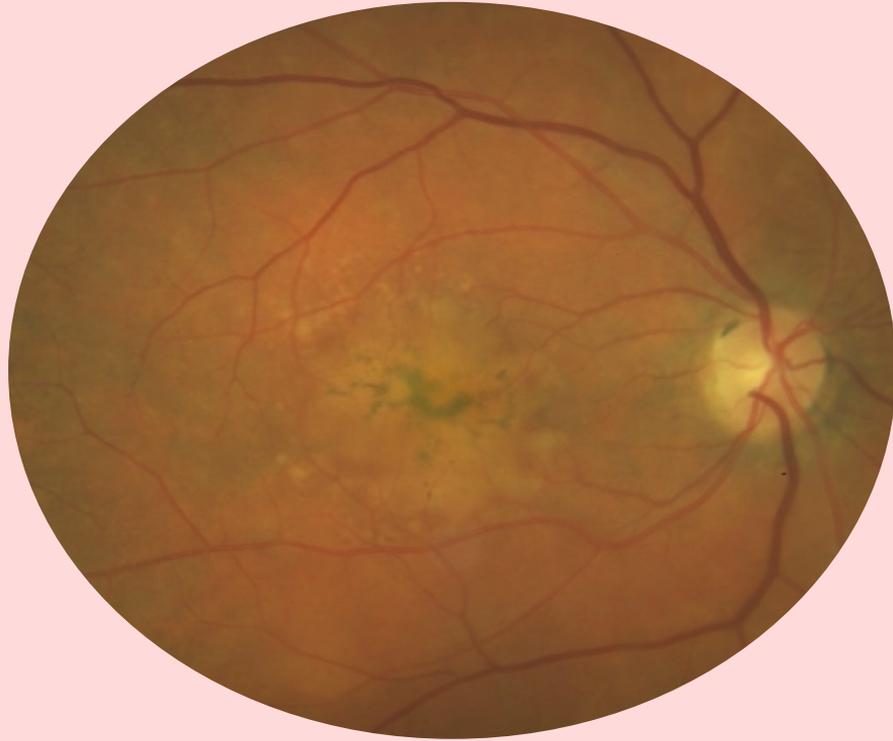
Prescription ?

- Antiox + Zinc
- Lutéine ?
- Omega 3 ?
- Surcorrections
- Eclairage
- Filtres ?

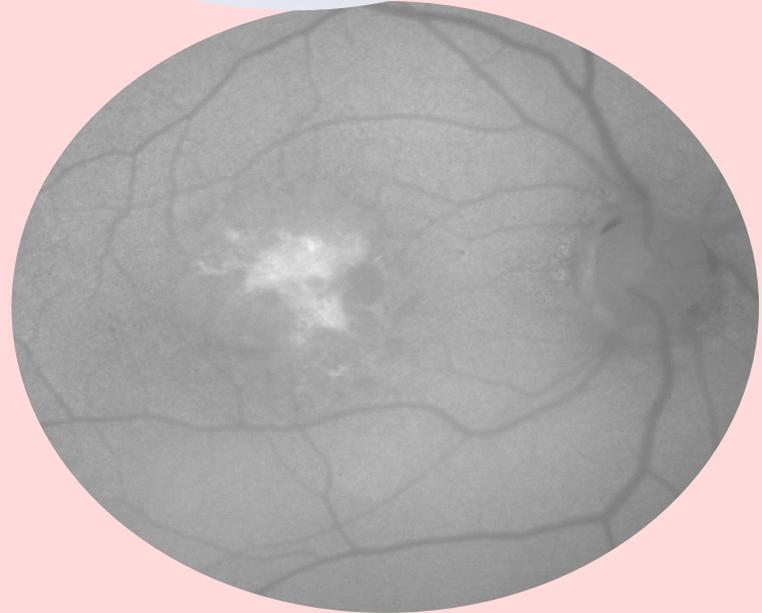
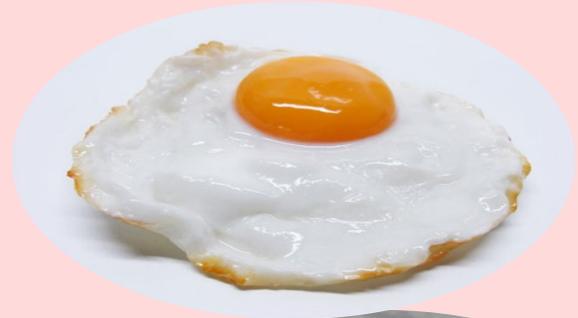
Non-exudative ARM

- Pseudo-exudations observed in:
 - Confluents soft drusen
 - Avascular PED

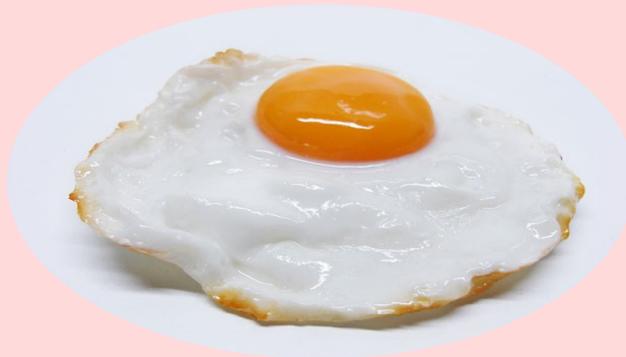
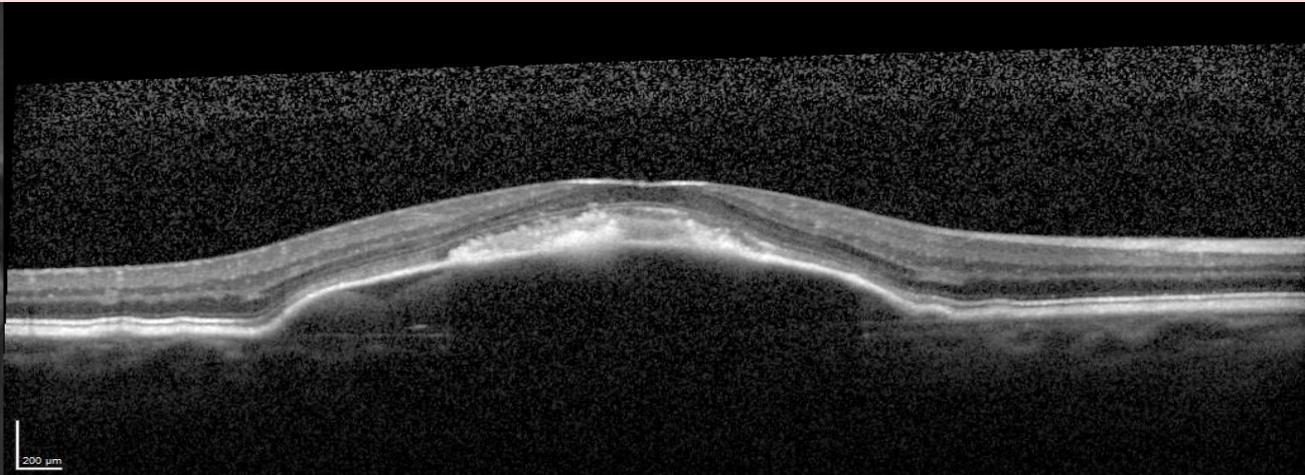
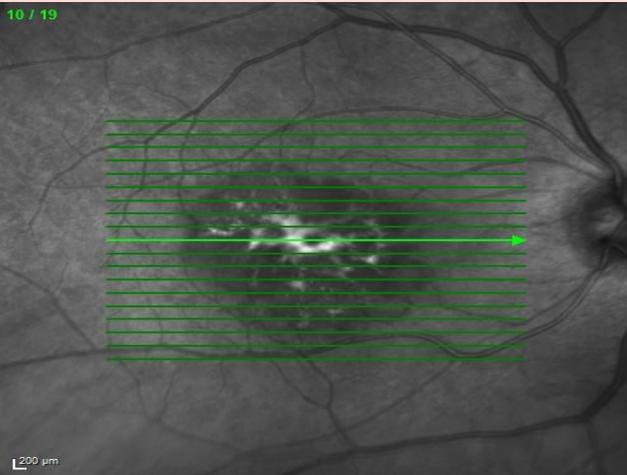
Drusenoid PEDs and vitelliform lesions



The "sunny-side up"...

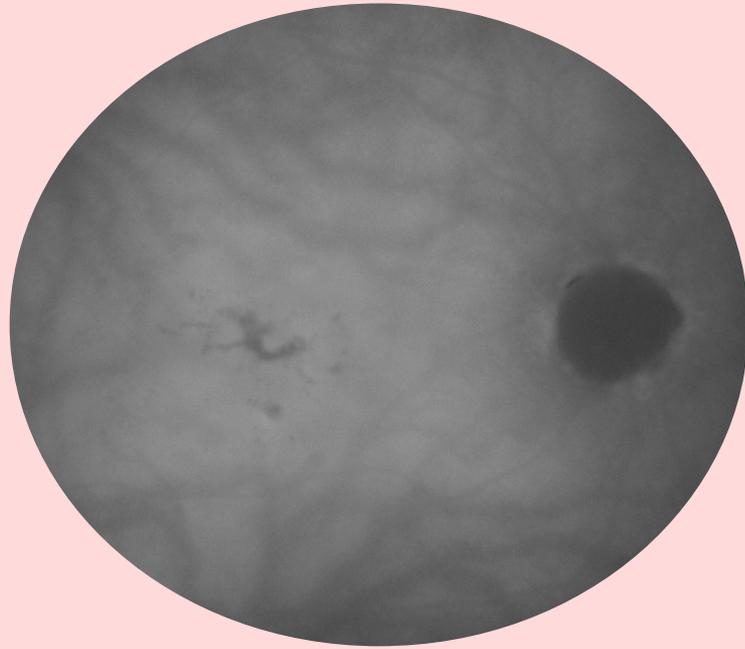


Drusenoid PEDs and vitelliform lesions



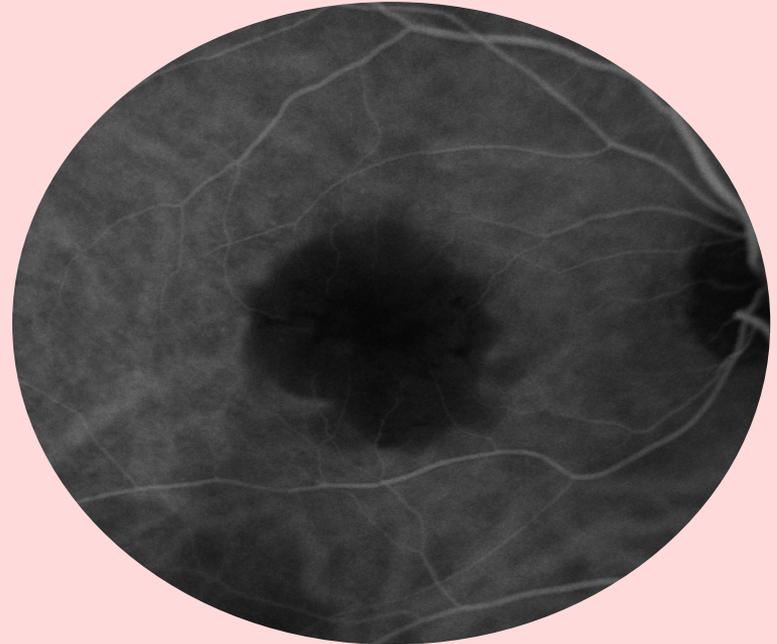
The "sunny-side up"

Drusenoid PEDs
ICGA

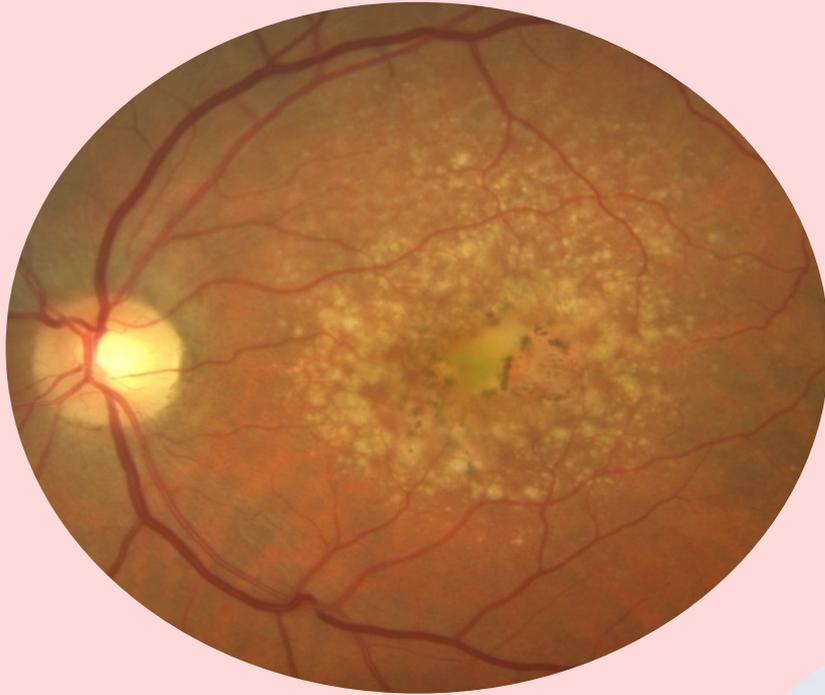


Fundus camera

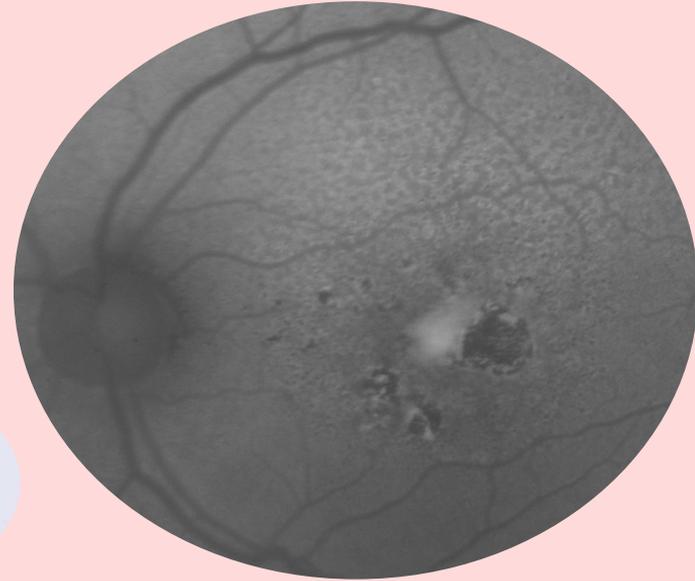
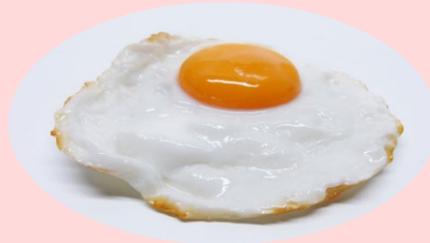
SLO



Drusenoid PEDs and vitelliform lesions

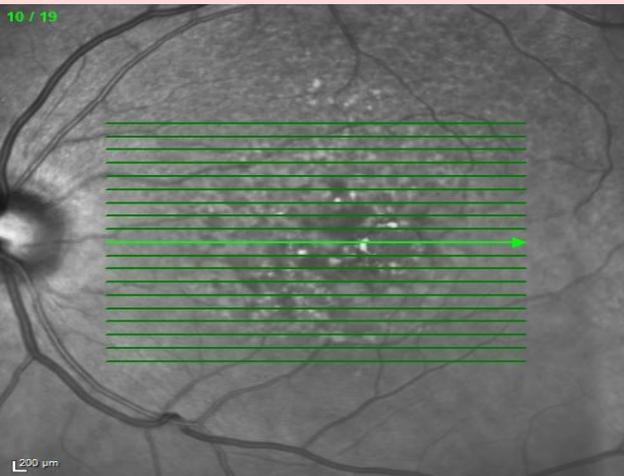
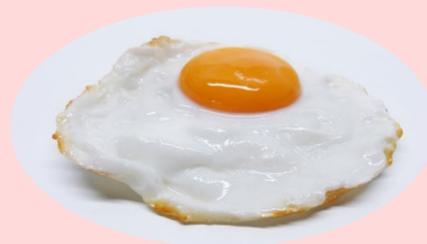
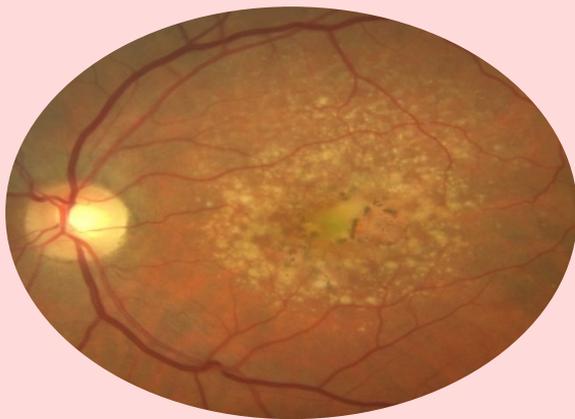


The "sunny-side up"

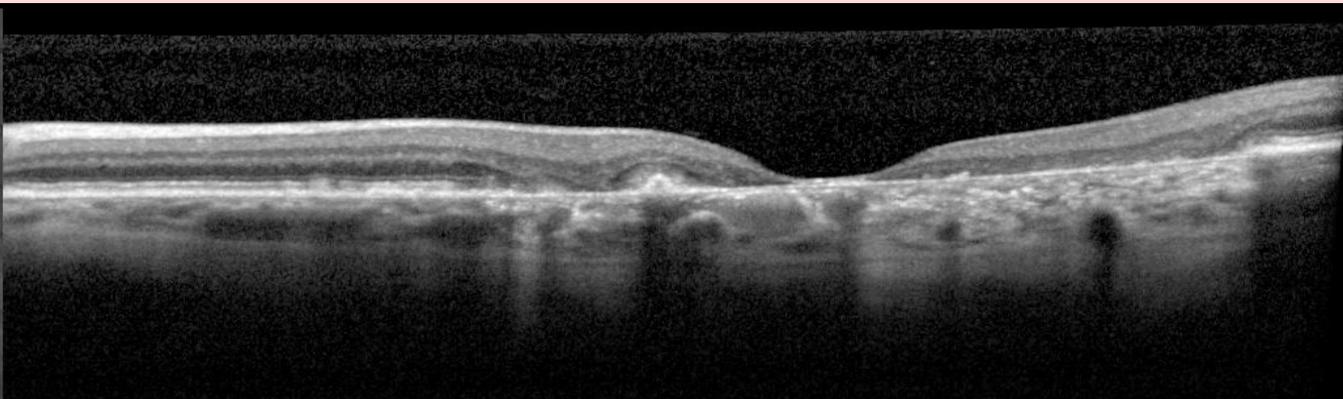
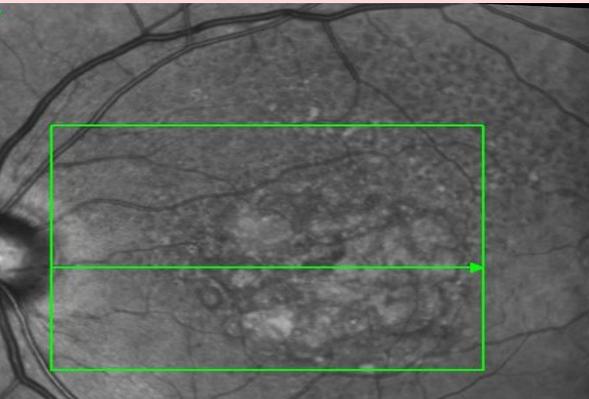


Freund KB et al. AVL Unresponsive to Anti-VEGF. OSLI. 2010 Nov 1;41(6):S81-4.

Drusenoid PEDs and vitelliform lesions



The "sunny-side up"



Non-exudative ARM/AMD

- Pseudo-exudations observed in:
 - Confluents soft drusen
 - Avascular PED

Avascular serous PEDs and exudation

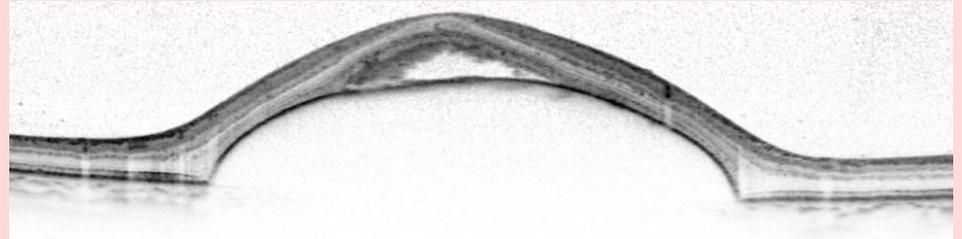
Clinical Findings of Acquired Vitelliform Lesions
Associated With Retinal Pigment Epithelial Detachments

MASAAKI SAITO, TOMOHIRO IIDA, K. BAILEY FREUND, MARIKO KANO, AND LAWRENCE A. YANNUZZI

32 eyes (24 patients)

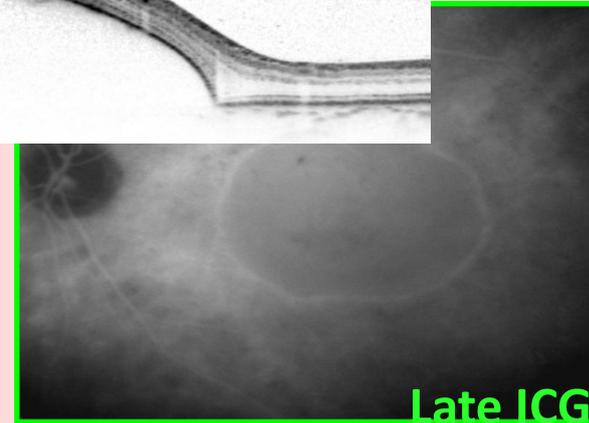
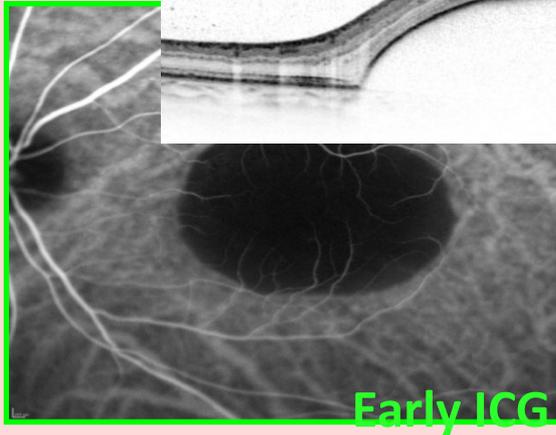
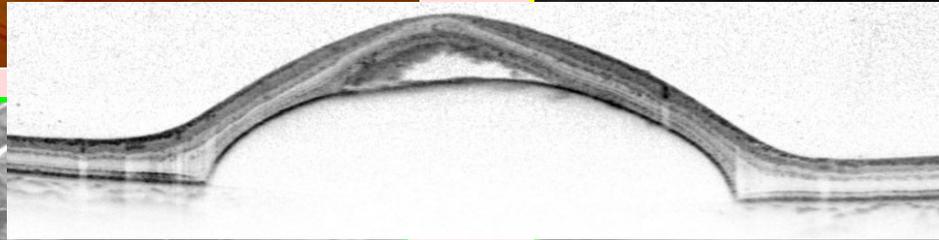
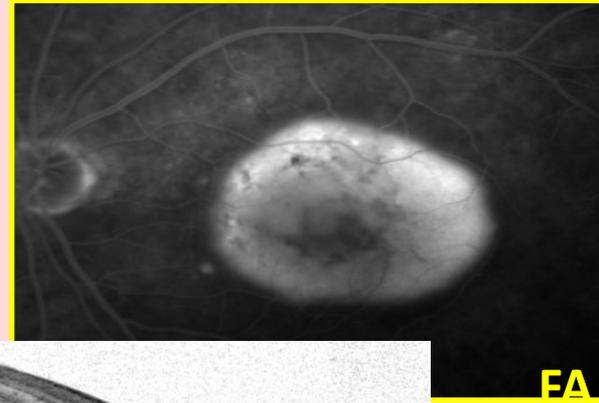
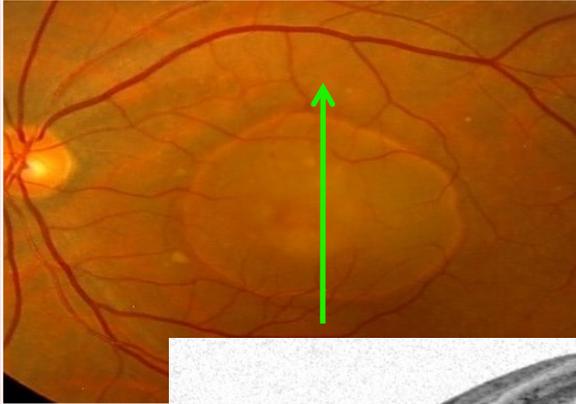
Serous PEDs with vitelliform lesions

7 eyes treated with anti-VEGF: no change



Avascular serous PEDs and exudation

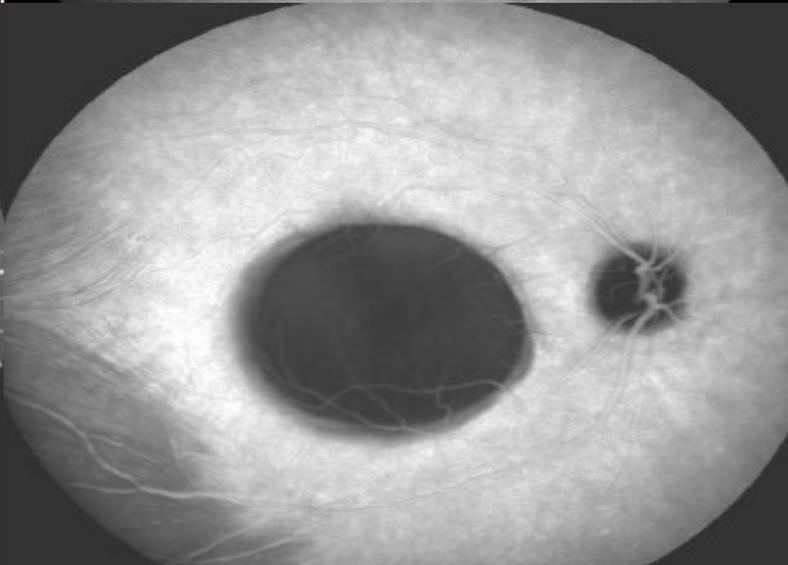
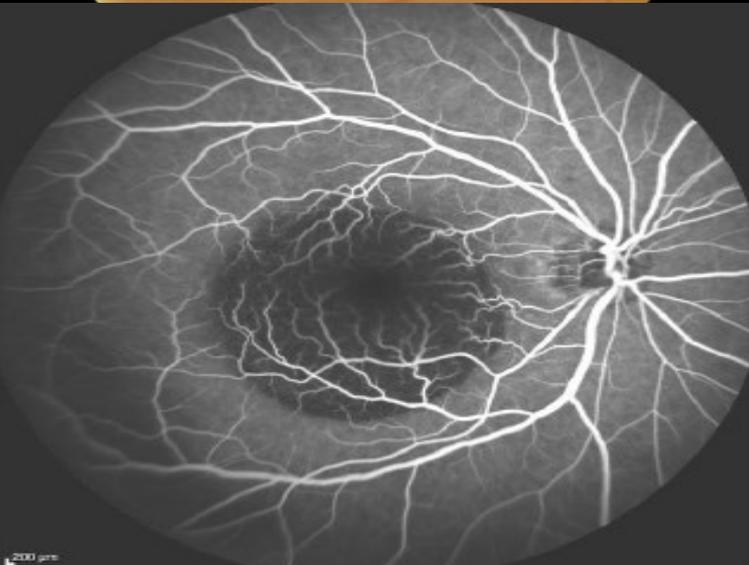
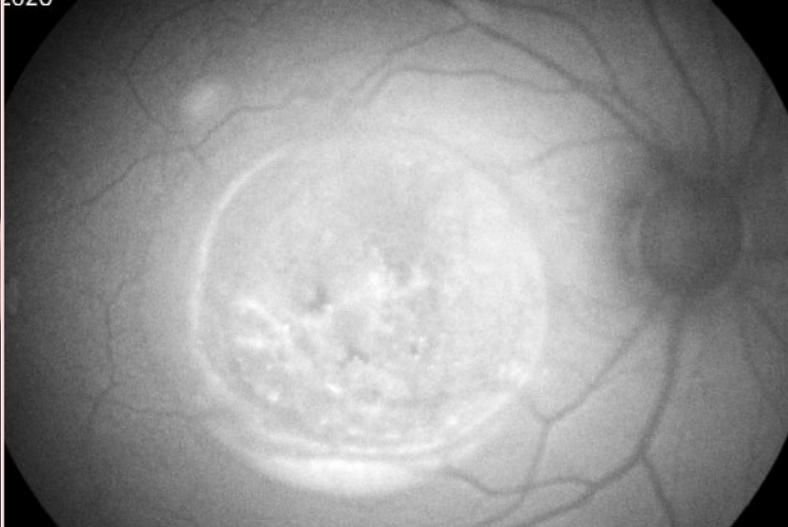
74 y/o male

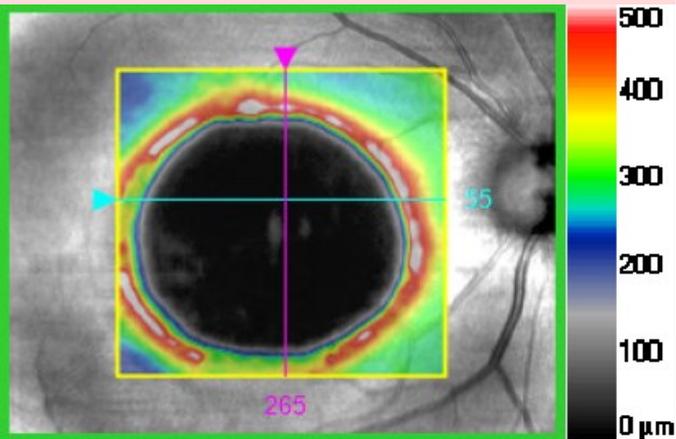


19/02/2020

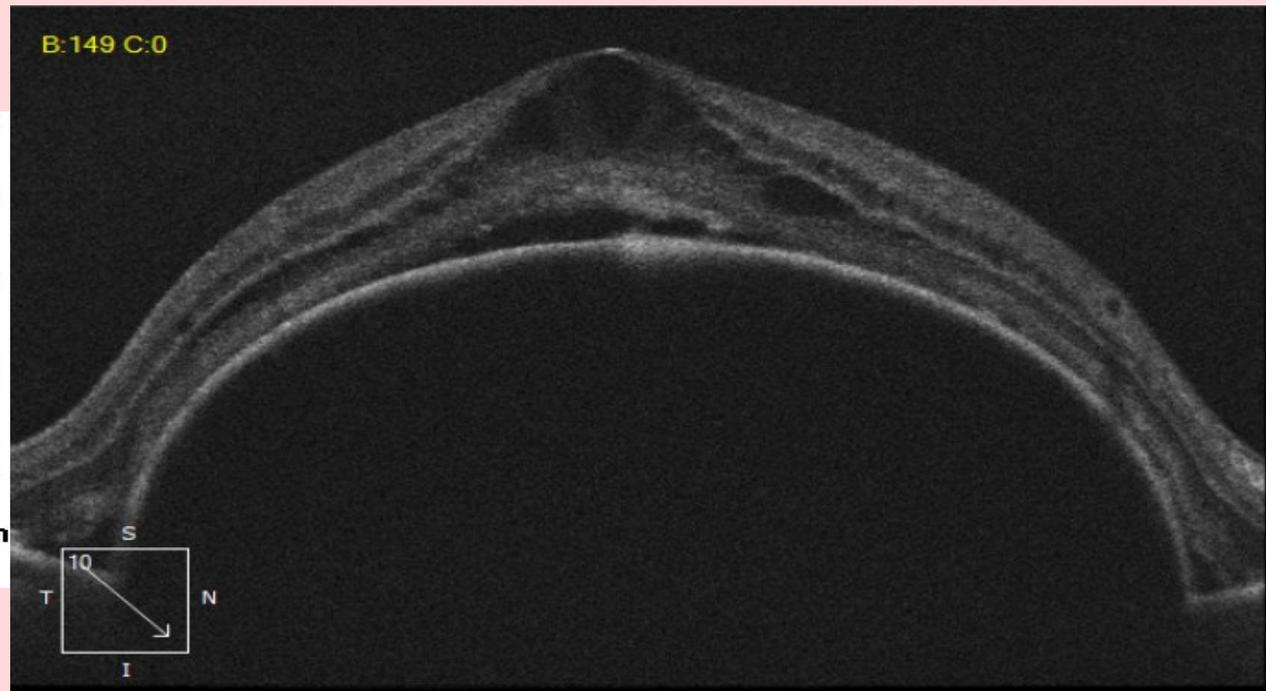


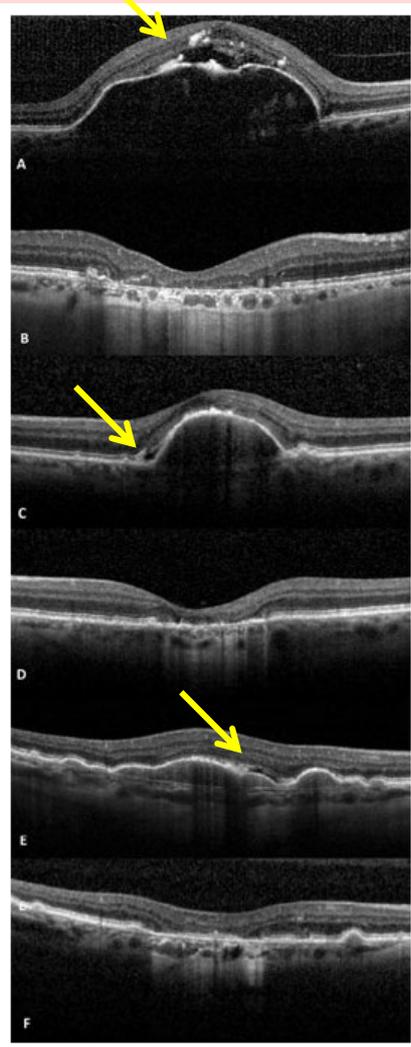
2020





Overlay: ILM - RPE Transparency: 50 %





Fluid located at the apex

Fluid located at the angle

Fluid located in a shallow drape

Hilely A, et al. Non-neovascular age-related macular degeneration with subretinal fluid. *Br J Ophthalmol.* 2021 Oct;105(10):1415-1420.

AREDS

- Randomisation en 4 groupes :
 - 1- Antioxydants (Vit C, E, β Carotène)
 - 2- Zinc (+ cuivre pour éviter l'anémie)
 - 3- Antioxydants + Zinc
 - 4- Placebo
- Risque de progression :
 - Néovaisseaux, atrophie centrale, DEP, hémorragies, fibrose.

AREDS

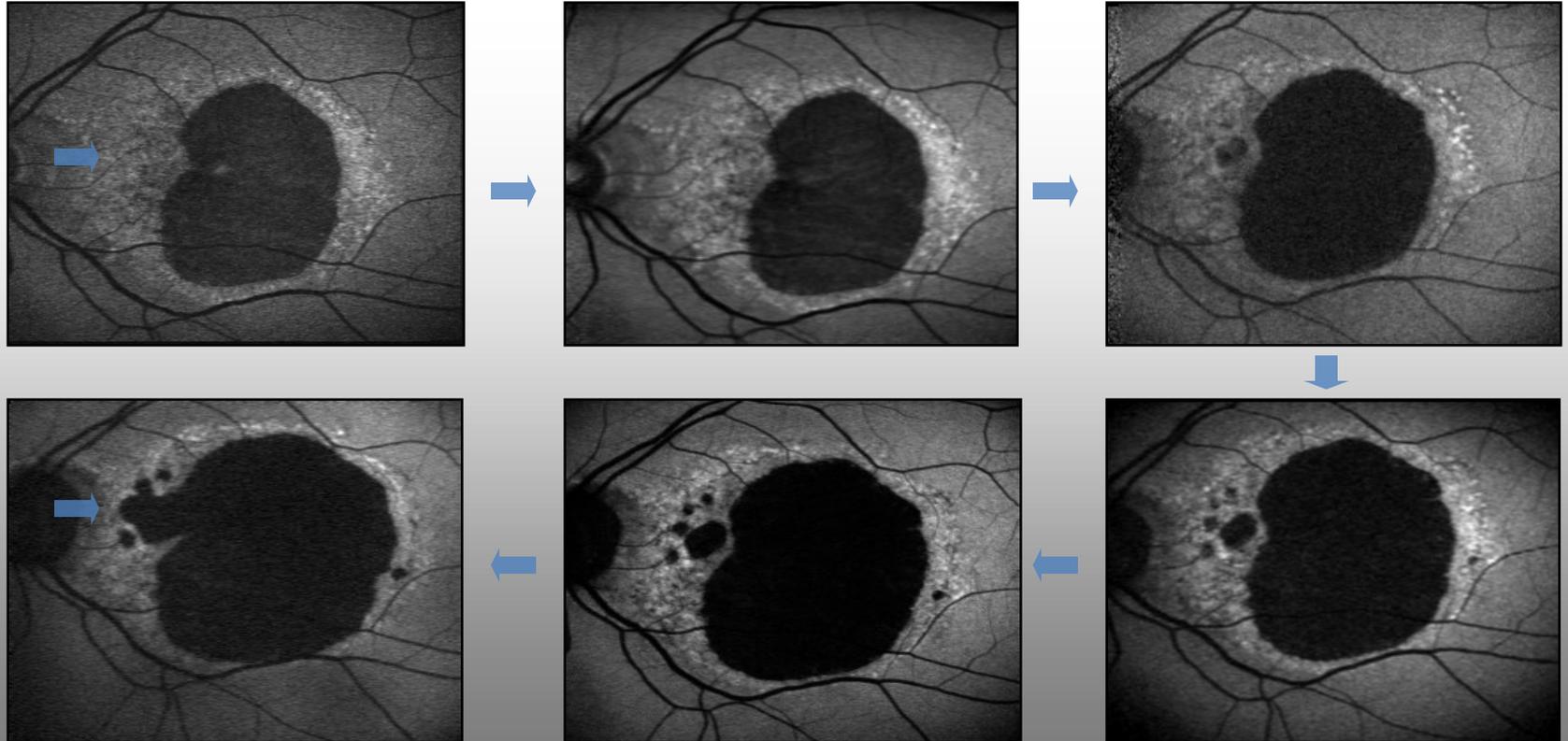
- Drusen < 125 µm ou AEP isolée :
Risque de progression faible = 1,3% à 5 ans
Pas d'effet du traitement
- Drusen > 125 µm ou surface de drusen > 1/5
surface papillaire ou atrophie ou DMLA
avancée unilatérale
Effet du traitement

AREDS

- Problèmes réels ou théoriques
- Vitamine A
 - Fumeurs
 - Evolution vers l'atrophie
- Cocktails sans vitamine A, remplacée par lutéine +/- zeaxanthine

AUTOFLUORESCENCE DU FOND D'ŒIL

Observation longitudinale: Valeur prédictive?



Holz FG, Bellmann C, Staudt S, et al. Fundus autofluorescence and development of geographic atrophy in age-related macular degeneration. Invest Ophthalmol Vis Sci 2001;42:1051-6

AREDS

- Problèmes réels ou théoriques
- Vitamine A
 - Fumeurs
 - Evolution vers l'atrophie
- Cocktails sans vitamine A, remplacée par lutéine +/- zeaxanthine

AREDS + ?

- Pigments maculaires:

Lutéine et Zéaxanthine ?

- Oméga-3:

EPA et DHA

Pigment et DMLA

Pigments et FDR de DMLA:

- Sexe: densité du PM plus faible chez la femme ($p < 0,05$).
- Couleur de l'iris: densité plus faible si iris clair ($p < 0,009$).
- Tabagisme: densité plus faible si consommation > 10 cigarettes par jour ($p < 0,034$). (Hammond, IOVS, 2000).

Pigments

- Absence d'étude randomisée et contrôlée sur l'efficacité d'un régime supplémenté en L et Z pour ralentir la DMLA
- Mais, faisceau cohérent d'arguments en faveur d'un rôle protecteur du PM

Omega-3

- Etudes anatomiques: le DHA est un constituant essentiel des membranes des photorécepteurs
- Arguments épidémiologiques
- Etude NAT-2
- Mais étude AREDS 2 non concluante

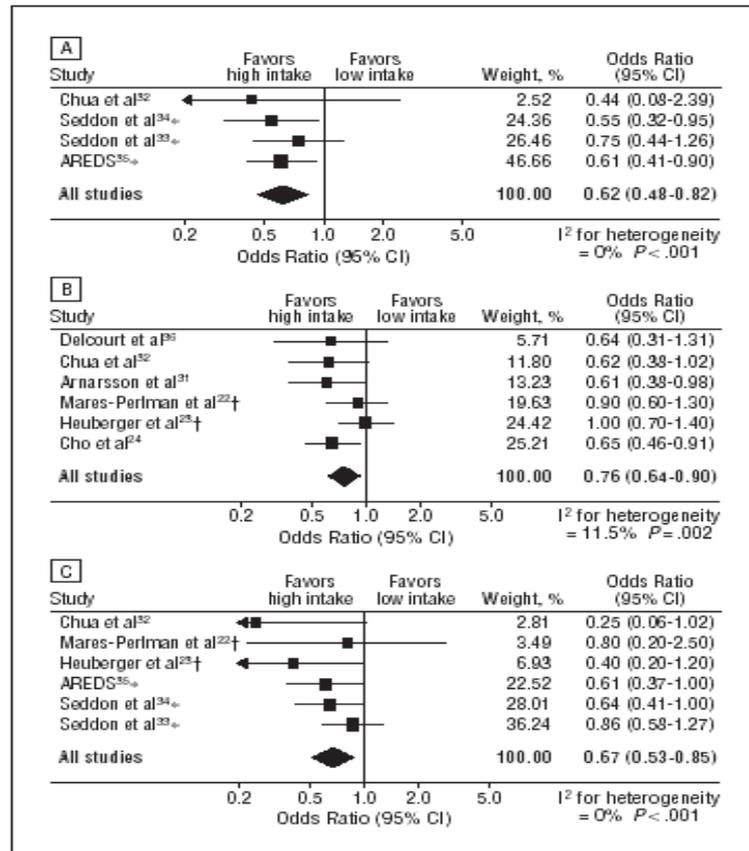
DMLA et consommation en poissons/omega-3

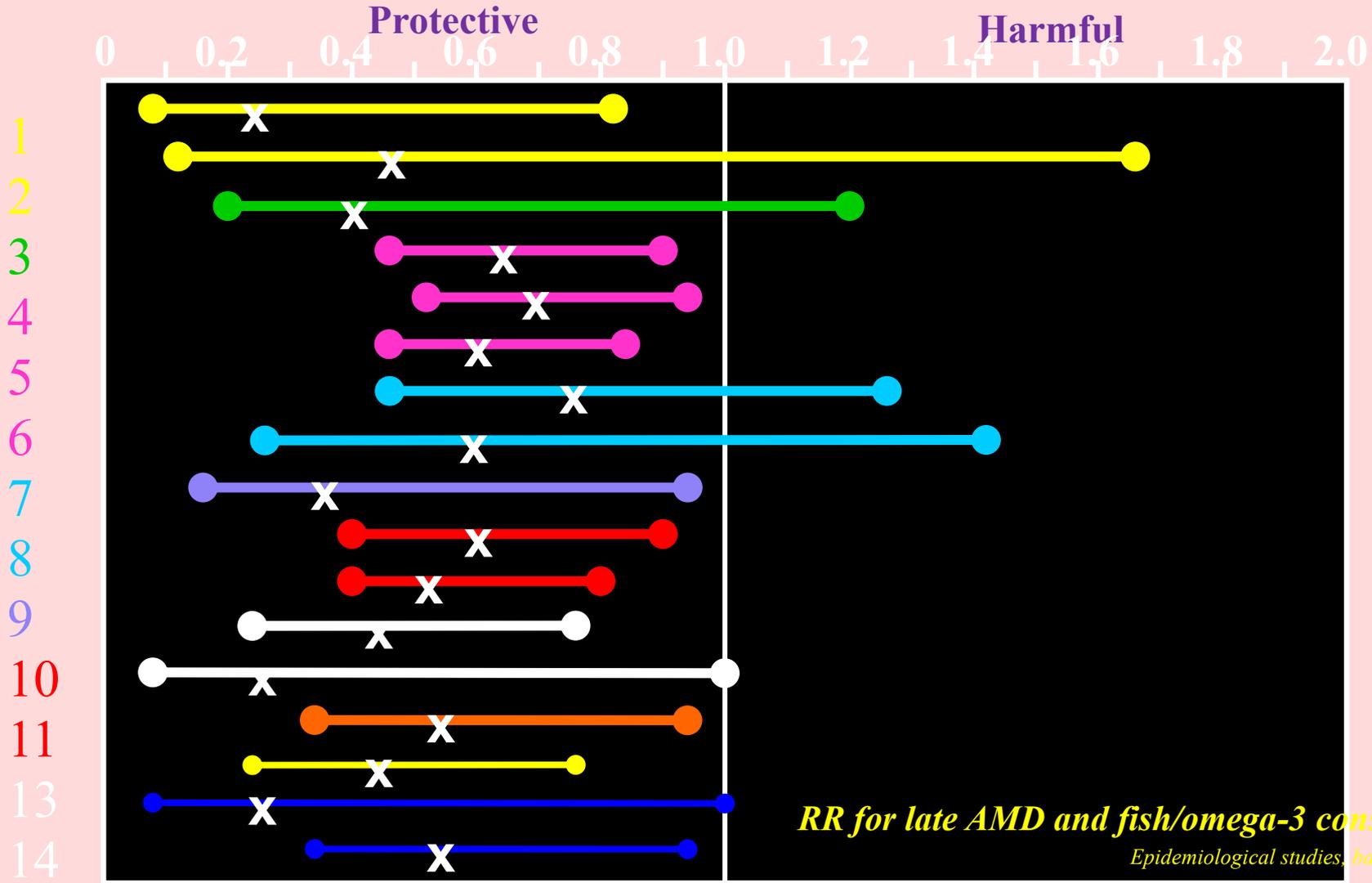
Etudes épidémiologiques basées sur questionnaires alimentaires

Chong, Arch Oph May 2008:

Meta-analyse:

- Omega3 et DMLA: OR: 0.62 [0.48-0.82]
- Poisson et MLA: OR: 0.76 [0.64-0.90]
- Poisson et DMLA: OR: 0.67 [0.53-0.85]





Cocktail idéal ?

- Vitamine C, Vitamine E (dose ?)
- Zinc (dose ?)
- Pas de Vitamine A

Fumeurs comme non fumeurs

- Lutéine et Zéaxanthine
- Omega-3 (DHA)

AREDS 2

Addition of lutein + zeaxanthin, DHA + EPA, or both to the AREDS formulation in primary analyses did not further reduce risk of progression to advanced AMD.

However, because of potential increased incidence of lung cancer in former smokers, lutein + zeaxanthin could be an appropriate carotenoid substitute in the AREDS formulation.

Le Figaro, 9 Février 2016

Dans l'étude menée sous la houlette des Prs Demetrios Vavvas et Joan Miller de Harvard, dix patients en Europe et treize aux États-Unis ont donc pris chaque jour une dose de 80 mg d'atorvastatine.

Dix patients ont bien répondu au traitement puisqu'une réduction significative du volume des drusen a été observée chez eux, après un temps de traitement allant de 3 à 22 mois.

Étant donné qu'il s'agissait de patients ayant des drusen de tailles conséquentes au départ, les chercheurs s'attendaient à ce que la maladie progresse pour au moins trois ou quatre d'entre eux pendant la durée de l'étude mais cela ne fut le cas pour aucun des 23 patients demeurés dans l'essai.

Deux ont arrêté à cause des effets indésirables (douleurs musculaires et crampes).

Laser nanosecond

Jobling AI, Guymer RH, Vessey KA, et al. Nanosecond laser therapy reverses pathologic and molecular changes in age-related macular degeneration without retinal damage.

In patients with AMD, nanosecond laser treatment reduced drusen load at 2 yr. Retinal structure was not compromised in human and mouse retina after laser treatment.

Nanosecond laser resolved drusen independent of retinal damage and improved BM structure, suggesting this treatment has the potential to reduce AMD progression

Laser nanosecond

Overall, progression to late AMD was not slowed significantly with SNL treatment compared with sham treatment

.However, a post hoc analysis showed evidence of effect modification based on the coexistence of reticular pseudodrusen:

- progression was slowed for the 222 participants (76.0%) without coexistent RPD at baseline
- increased progression rate was observed for the 70 participants (24.0%) with RPD with SNL treatment.



VALEDA™

Light Delivery System

A DOUBLE-MASKED, RANDOMIZED, SHAM-CONTROLLED, SINGLE-CENTER STUDY WITH PHOTOBIO-MODULATION FOR THE TREATMENT OF DRY AGE-RELATED MACULAR DEGENERATION

SAMUEL N. MARKOWITZ,* ROBERT G. DEVENYI,*† MARION R. MUNK,‡ CINDY L. CROISSANT,§
STEPHANIE E. TEDFORD,§ RENE RÜCKERT,¶ MICHAEL G. WALKER,** BEATRIZ E. PATINO,*
LINA CHEN,* MONICA NIDO,* CLARK E. TEDFORD§

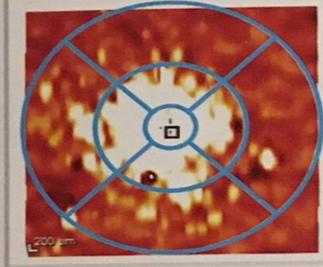
Downloaded from <http://jama.ama-assn.org>

perimetry, central drusen volume and drusen thickness, and quality of life assessments.

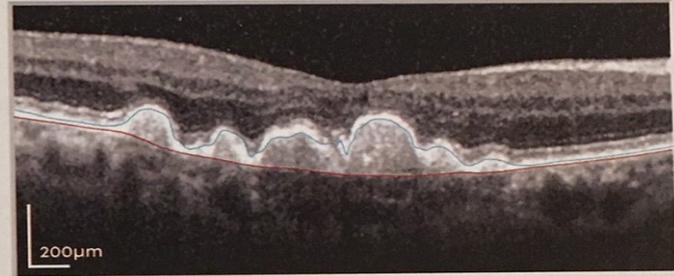
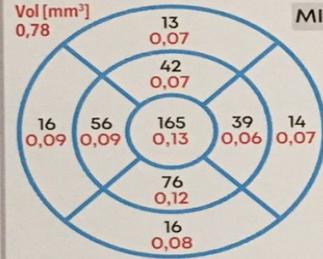
Results: Photobiomodulation-treated subjects showed a best-corrected visual acuity mean letter score gain of 4 letters immediately after each treatment series at Month 1 (M1) and Month 7 (M7). Approximately 50% of PBM-treated subjects showed improvement of ≥ 5 letters versus 13.6% in sham-treated subjects at M1. High responding subjects (≥ 5 -letter improvement) in the PBM-treated group showed a gain of 8 letters after initial treatment ($P < 0.01$) and exhibited earlier stages of age-related macular degeneration disease. Statistically significant improvements in contrast sensitivity, central drusen volume, central drusen thickness, and quality of life were observed ($P < 0.05$). No device-related adverse events were reported.

Début de l'étude

Épaisseur de l'épithélium pigmentaire rétinien [μm]

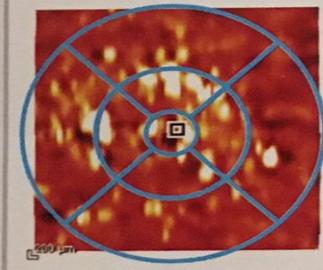


Épaisseur moyenne [μm]

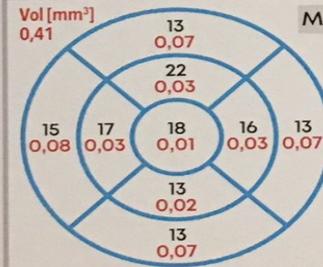


Mois 12

Épaisseur de l'épithélium pigmentaire rétinien [μm]



Épaisseur moyenne [μm]



Réduction significative du volume occupé par les drusen séreux

LUMITHERA LIGHTSITE III STUDY

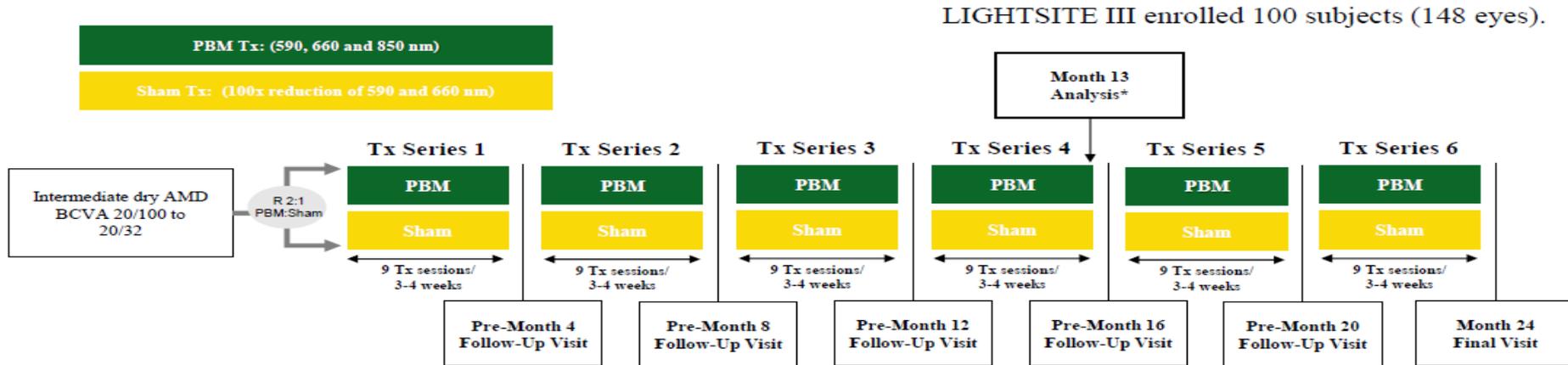
LIGHTSITE III enrolled 100 subjects (148 eyes) across 10 centers in the US

LIGHTSITE III Clinical Sites

Principal Investigator	Clinic	Location
Diana Do	Byers Eye Institute, Stanford University	Palo Alto, CA
Richard Rosen	New York Ear and Eye Infirmary of Mount Sinai	New York, NY, USA
David Boyer	Retina Vitreous Associates Medical Group	Beverly Hills, CA, USA
Victor Gonzalez	Valley Retina Institute	McAllen, TX
Samantha Xavier	Florida Eye Clinic	Altamonte Springs, FL
Allen Hu	Cumberland Valley Retina Consultants	Hagerstown, MD
David Warrow	Cumberland Valley Retina Consultants	Chambersburg, PA
Eleanora Lad	Duke Eye Center	Durham, NC
Todd Schneiderman	Retina Center NorthWest	Silverdale, WA
Allen Ho	Mid Atlantic Retina	Cherry Hill, NJ

LUMITHERA LIGHTSITE III STUDY

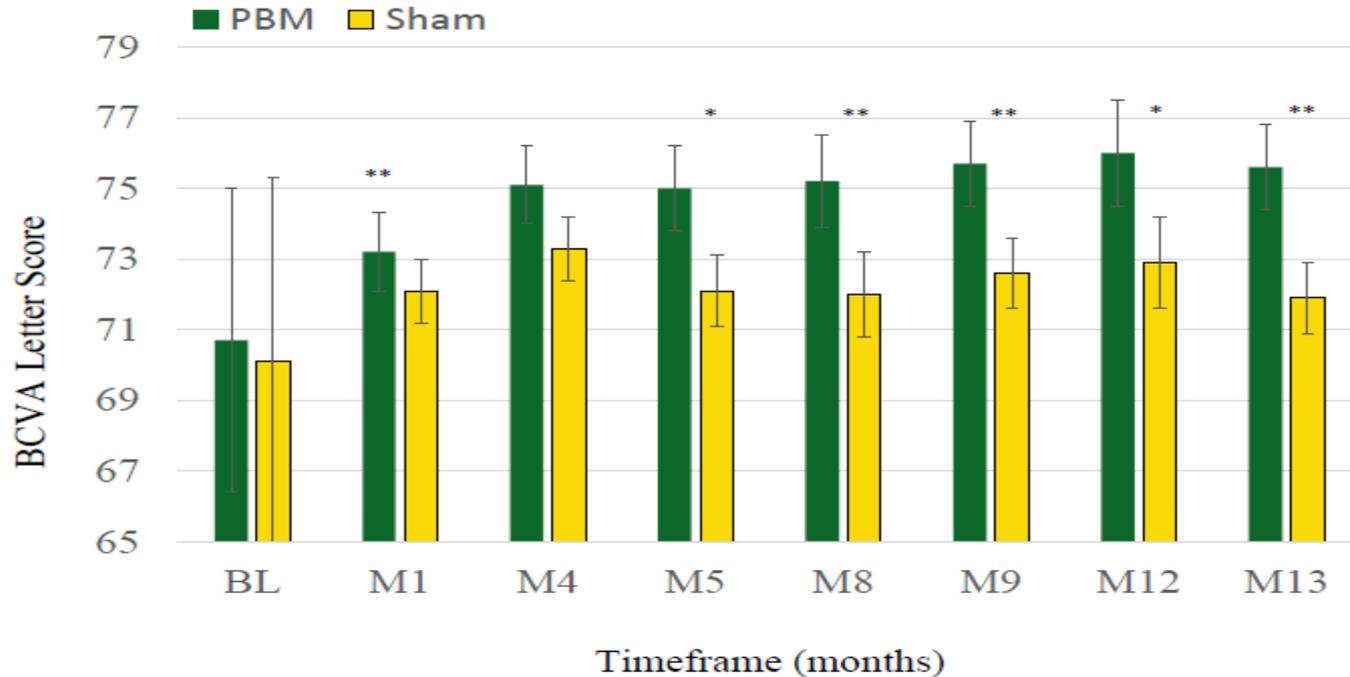
The **LIGHTSITE III** study is a double-masked, randomized, sham-controlled, parallel group, multi-center study to assess the safety and efficacy of photobiomodulation (PBM) in subjects with dry age-related macular degeneration.



LUMITHERA LIGHTSITE III STUDY

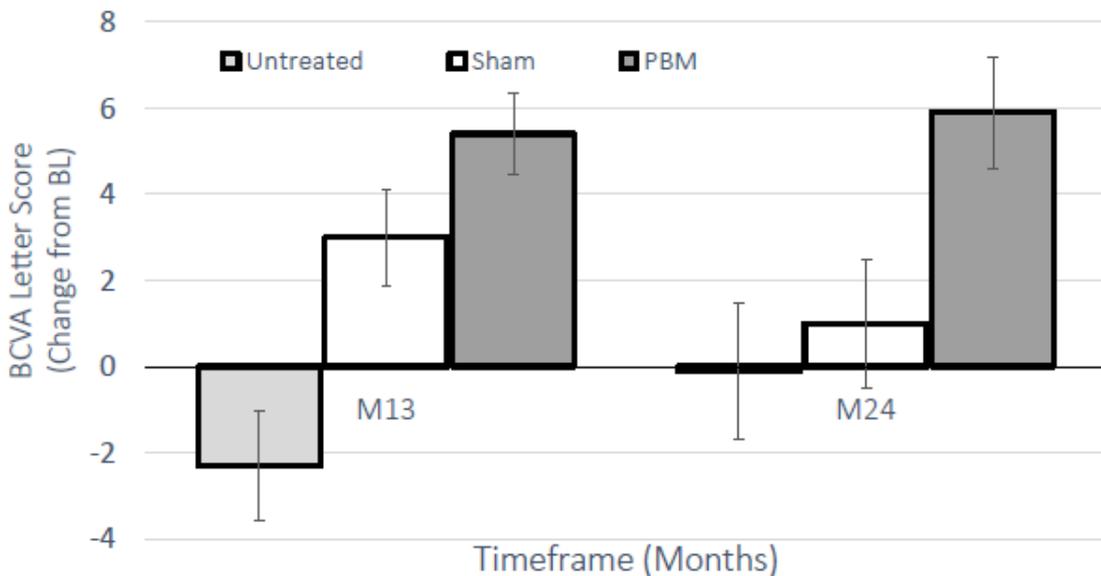
	LIGHTSITE III
Subjects	100
Eyes	148 (2:1 PBM to Sham)
Race	99% Caucasian, 1% Black/African American
Gender	32 M (32%), 68 F (68%)
Age	75
Time from Diagnosis	4.9
AREDS supplements	86 (86%) yes 14 (14%) no
BCVA BL Letter Gain	+5.5 (M13)
BCVA BL Letter Score	Masked 70.6 ± 5.3

LUMITHERA LIGHTSITE III STUDY



**P<0.005, * 0<0.05

BCVA Through Month 24 - Change from Baseline: Sustained Benefits



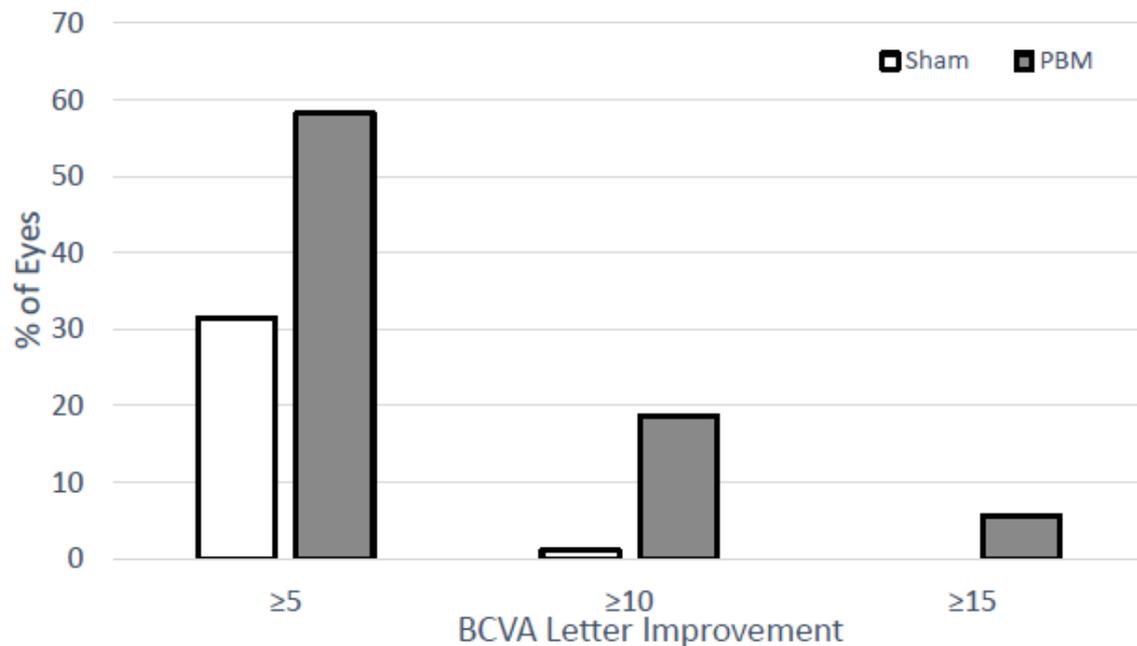
- Non-study untreated control eyes (no PBM treatment or Sham) that showed >75 letters in BCVA at baseline (n = 12) show a mean BCVA loss of 2.3 letters at Month 13 and 0.1 letters at Month 24
- Sham eyes show a mean BCVA gain of 3.0 letters at Month 13 and 1.0 letters at Month 24
- PBM-treated eyes show a mean BCVA gain of 5.4 letters at Month 13 and 5.9 letters at Month 24

LIGHTSITE III BCVA >5 Letter Vision Gain at Month 24

58.2% of PBM eyes responded with a ≥ 5 letter gain with a mean of 8.5 ± 0.5 letters

18.7% of PBM eyes responded with a ≥ 10 letter gain with a mean of 13.4 ± 0.6 letters

5.5% of PBM eyes responded with a ≥ 15 letter gain with a mean of 16.6 ± 0.8 letters

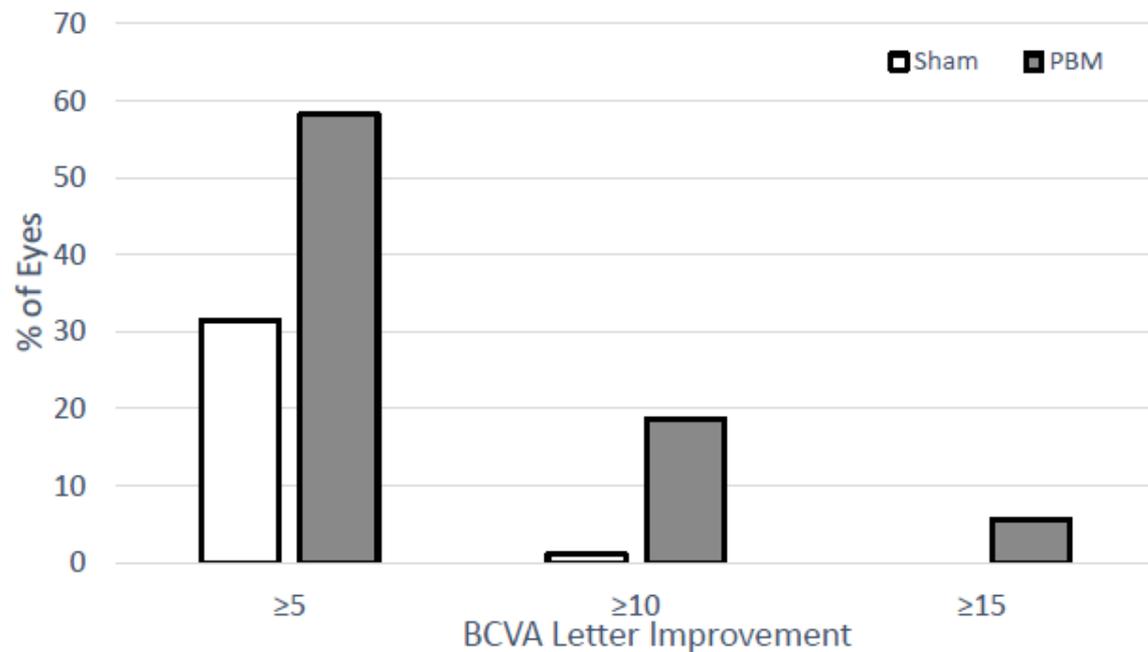


LIGHTSITE III BCVA ≥ 5 Letter Vision Gain at Month 24

58.2% of PBM eyes responded with a ≥ 5 letter gain with a mean of 8.5 ± 0.5 letters

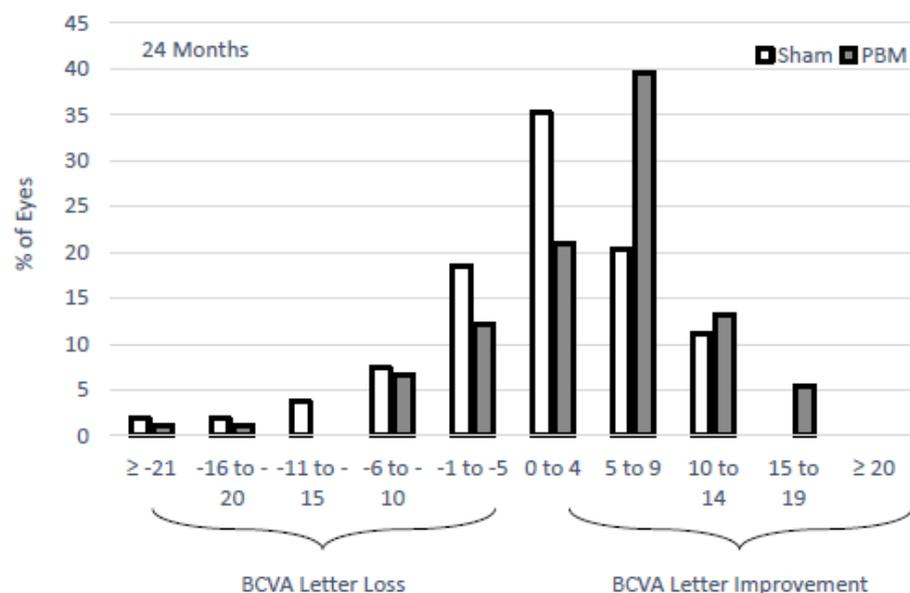
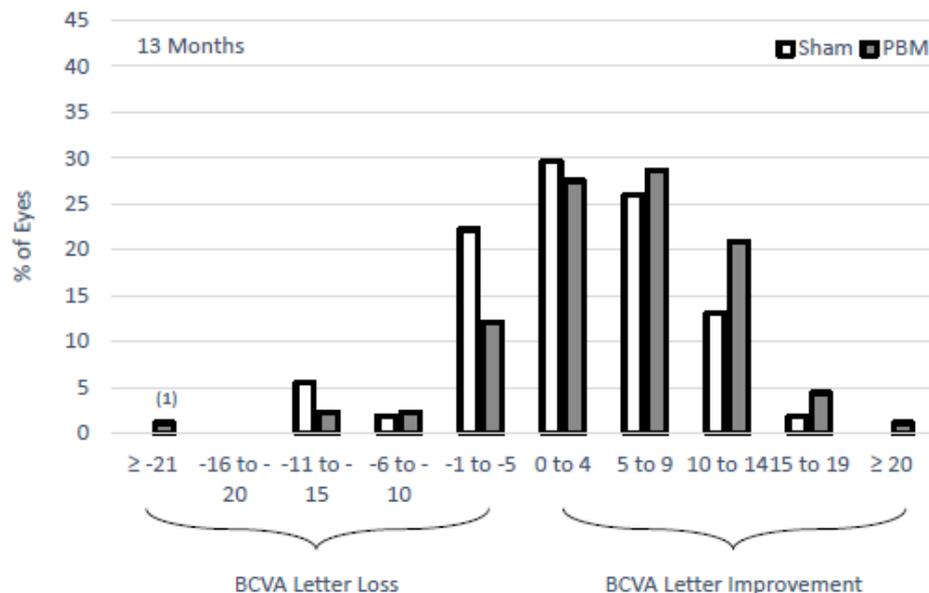
18.7% of PBM eyes responded with a ≥ 10 letter gain with a mean of 13.4 ± 0.6 letters

5.5% of PBM eyes responded with a ≥ 15 letter gain with a mean of 16.6 ± 0.8 letters



LIGHTSITE III BCVA Vision Loss Accelerates from M13 to M24 in Sham

At 24 Months BCVA Letter Loss Increases in the Sham Groups but PBM groups show BCVA Increases to >60% with >5 letter benefits

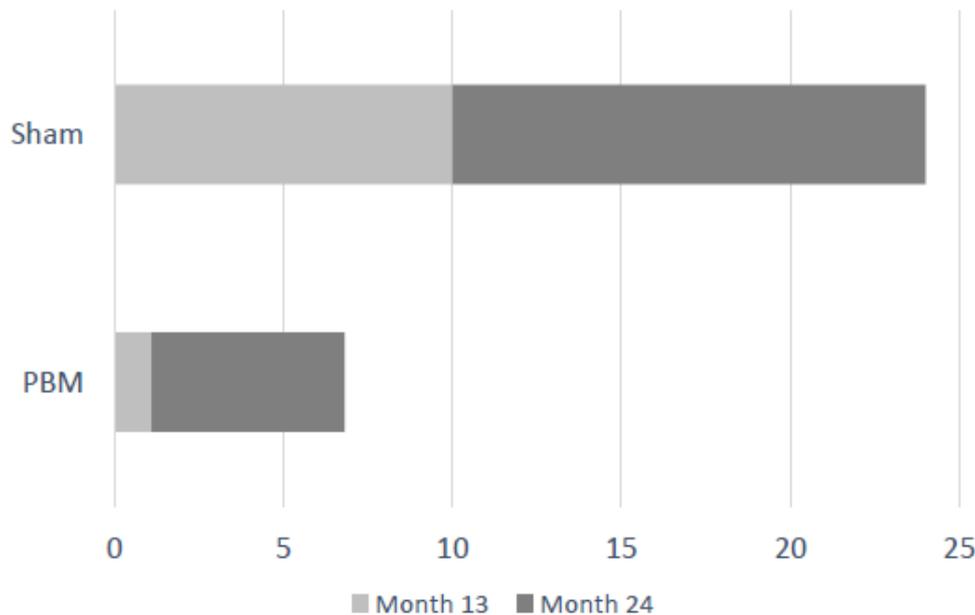


Note: (1) Patient had vision loss due to worsening of cataract

Valeda Treatment Benefit on New Onset GA Occurrence: Slows Progression

Occurrence of new GA in LIGHTSITE III:

- Month 13
 - 5 of 50 (10.0%) of Sham eyes
 - 1 of 87 (1.1%) of PBM eyes
- The occurrence of new GA was significantly higher in the Sham group than in the PBM group ($p = 0.024$, Fisher exact test, odds ratio 9.4)
- Month 24
 - 12 of 50 (24.0%) of Sham eyes
 - 6 of 87 (6.8 %) of PBM eyes
- The occurrence of new GA was significantly higher in the Sham group than in the PBM group ($p = 0.007$, Fisher exact test, odds ratio 4.2)



LIGHTSITE III Summary

LIGHTSITE III met the predetermined primary efficacy BCVA endpoint with a statistically significant difference between the PBM group versus the Sham group at M13 ($p = 0.02$) and M24 ($p = 0.0015$)

An improved BCVA with a mean > 5 letter gain in PBM eyes from BL values at M13 and M24 was seen ($p < 0.0001$). At Month 24:

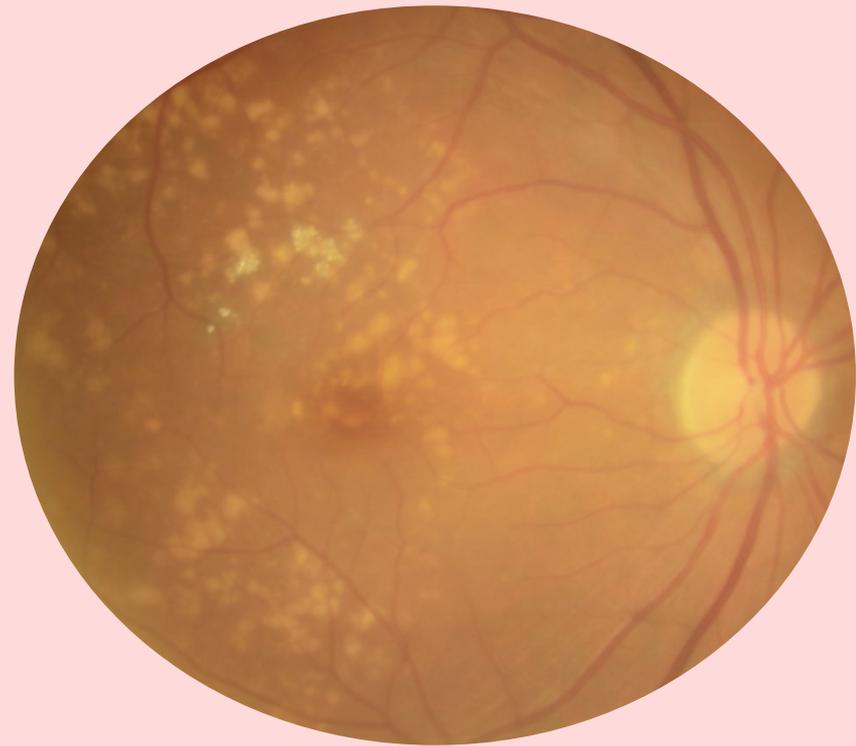
- 58.2% of PBM eyes responded with a >5 letter gain with a mean of 8.5 ± 0.5 letters
- 18.7% of PBM eyes responded with a >10 letter gain with a mean of 13.4 ± 0.6 letters
- 5.5% of PBM eyes responded with a >15 letter gain with a mean of 16.6 ± 0.8 letters

Approximate 2x decrease in patients with lost BCVA letter scores in the PBM-treated eyes versus the Sham eyes at 13 months and significant loss in vision at 24 months in the Sham group

A non-significant numerical increase in central drusen volume was observed in the Sham group, vs no increase in central drusen volume in the PBM group at M13 and M24 (~ 4 -fold over PBM) consistent with LT I and II, suggesting a disease modifying benefit

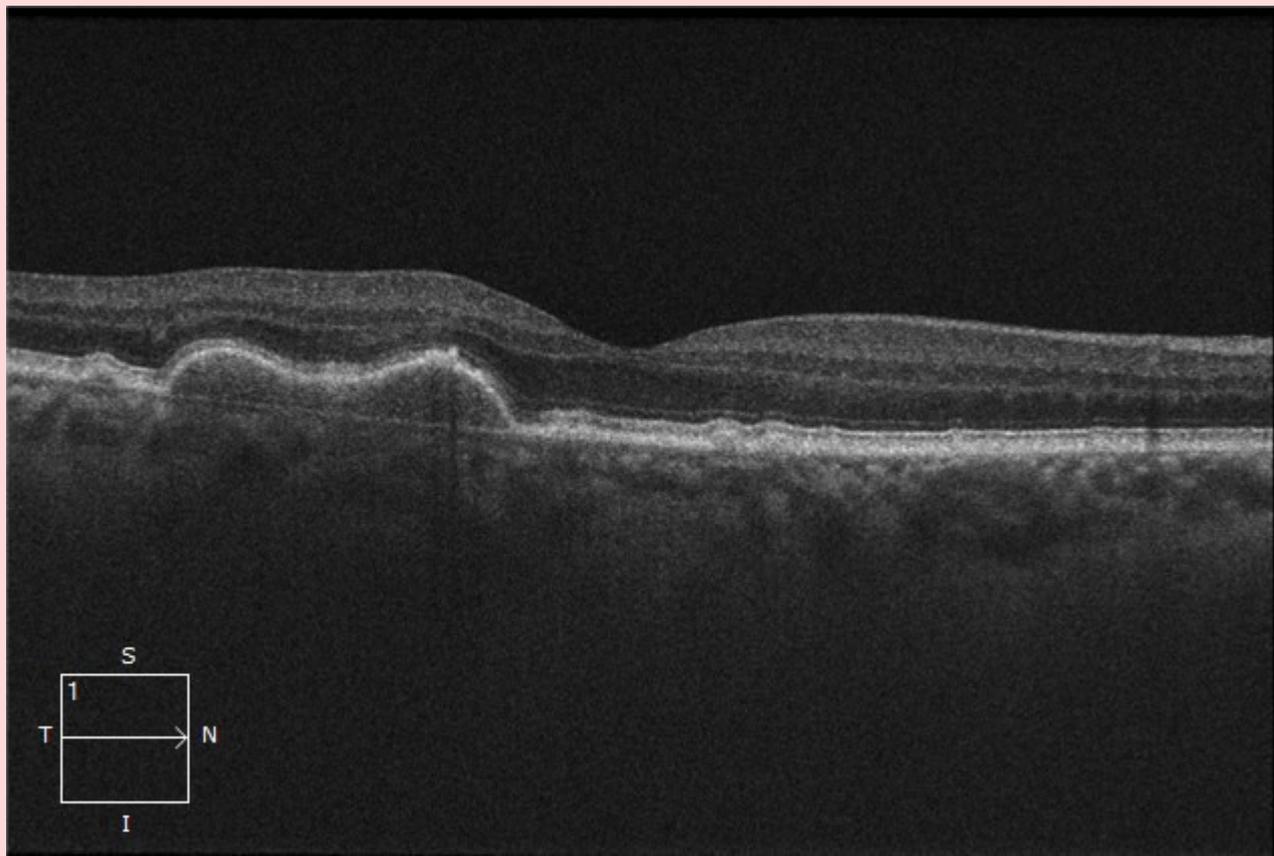
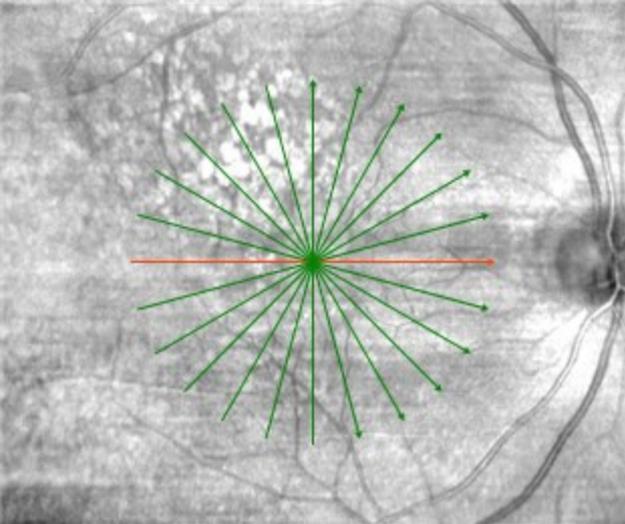
PBM treatment with Valeda shows an excellent safety profile

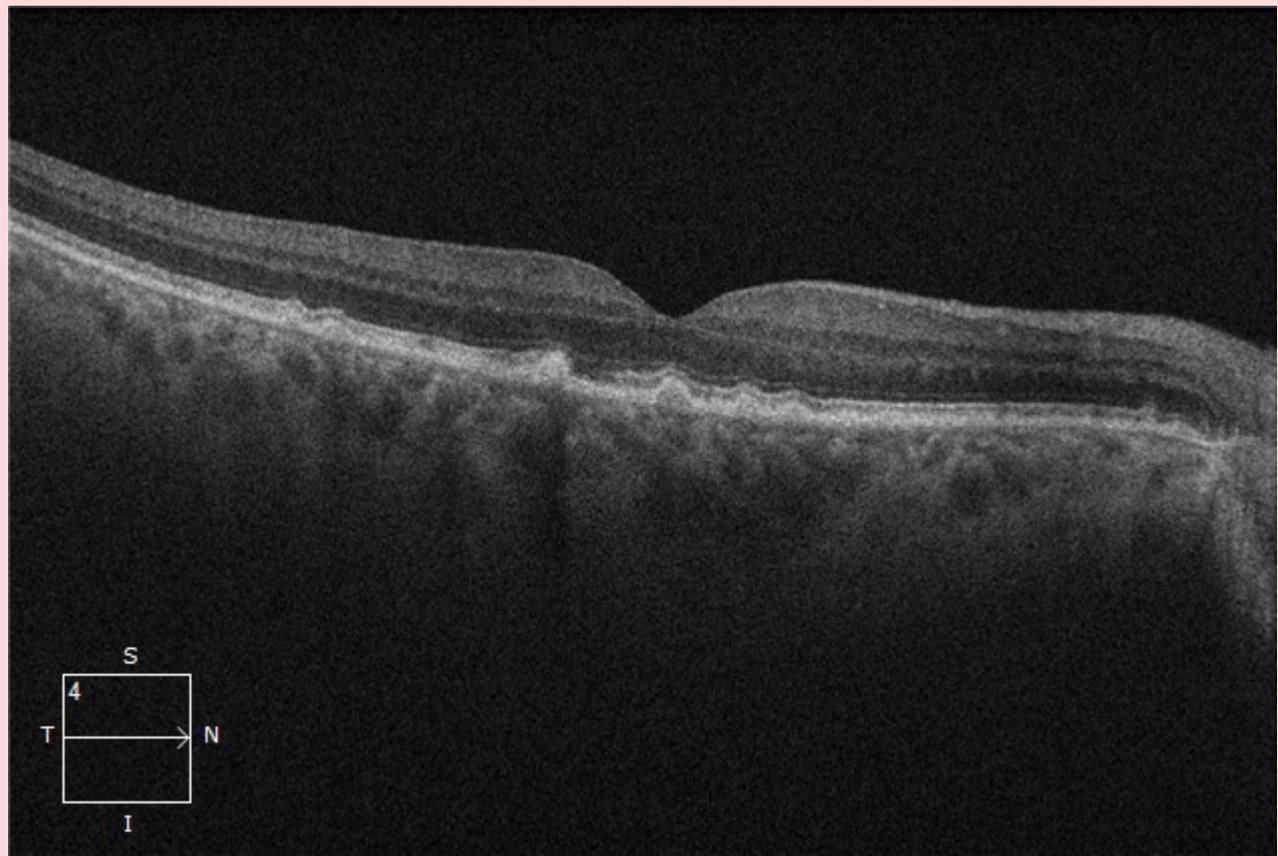
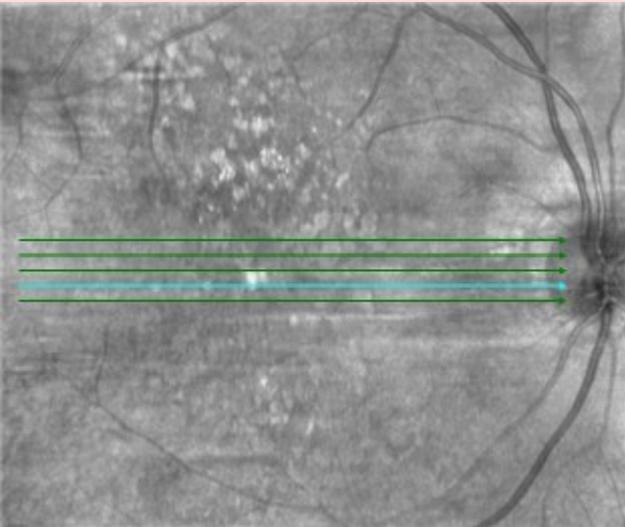
Occurrence of later stage, new GA observed in 24.0% of Sham vs 6.8% of PBM eyes. Occurrence of new GA was significantly higher in the Sham group than in the PBM group ($p = 0.007$, Fisher exact test, odds ratio 4.2) demonstrating slowing of disease progression.



Avant et 18 mois après photobiomodulation pour drusen séreux







Ça bouge peut-être en traitement des drusen

Une trentaine de patients traités aux CIL

Pas d'amélioration de l'AV moyenne

Des patients améliorés subjectivement, dont améliorés en AV luminance normale et/ou basse luminance et quelques patients améliorés anatomiquement, mais pas de retraitement le plus souvent.

Ça bouge peut-être en traitement des drusen

Photobiomodulation

Ce qu'on sait:

- bien toléré par les patients
- pas de complication rapportée à ce jour
- effet variable selon les patients
- Etude randomisée (100 patients) positive

Ça bouge peut-être en traitement des drusen

Photobiomodulation

Ce qu'on ne sait pas:

- protocole idéal ? 9 séances / 3 semaines
- protocole idéal ? 3 fois par an ?
- meilleurs répondeurs ?
- effet à long terme ? Rassurant sur atrophie
- effet durable ?

Ça bouge peut-être en traitement des drusen

Photobiomodulation

On en parle aux patients avec drusen séreux

On leur envoie la documentation existante et les conditions (pas de prise en charge SS)

On fait le traitement si le patient accepte la part d'inconnu dans tout nouveau traitement

Points importants

1. Différents types de drusen, avec pronostic différent
2. Reconnaissance des pseudo-drusen +++
3. Surveillance avec un rythme différent selon le risque
4. Règles hygiéno-diététiques + Vitamines anti-oxydantes + lutéine/zéaxanthine +/- omega 3
5. Photobiomodulation ?