

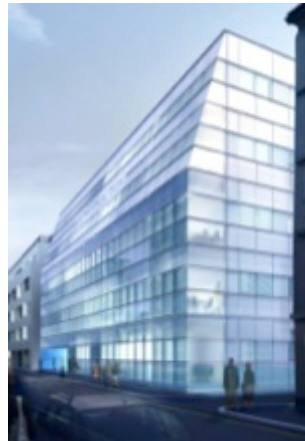
Les outils actuels du diagnostic clinique (autofluorescence, ERG, optique adaptative, OCT)

I Audo, S Mohand-Saïd, JA Sahel

isabelle.audo@inserm.fr

CIC/CMR/Service 4 Quinze-Vingts

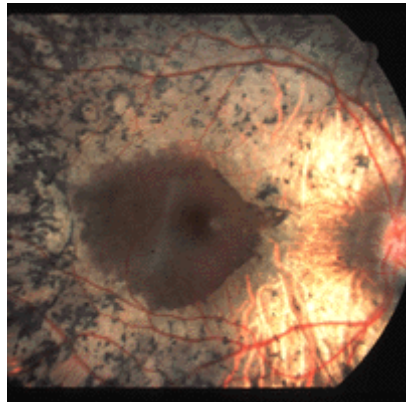
Département de génétique, équipe S6 A-Z, Institut de la vision



Dystrophies rétiniennes génétique: diversité des pathologies et des conséquences visuelles

Rétinopathies pigmentaires

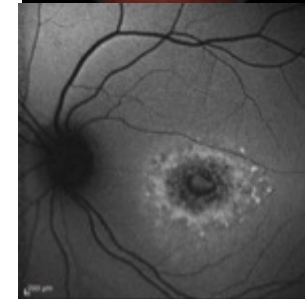
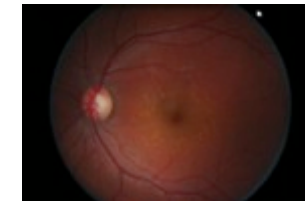
Atteinte de la vision
périphérique plus

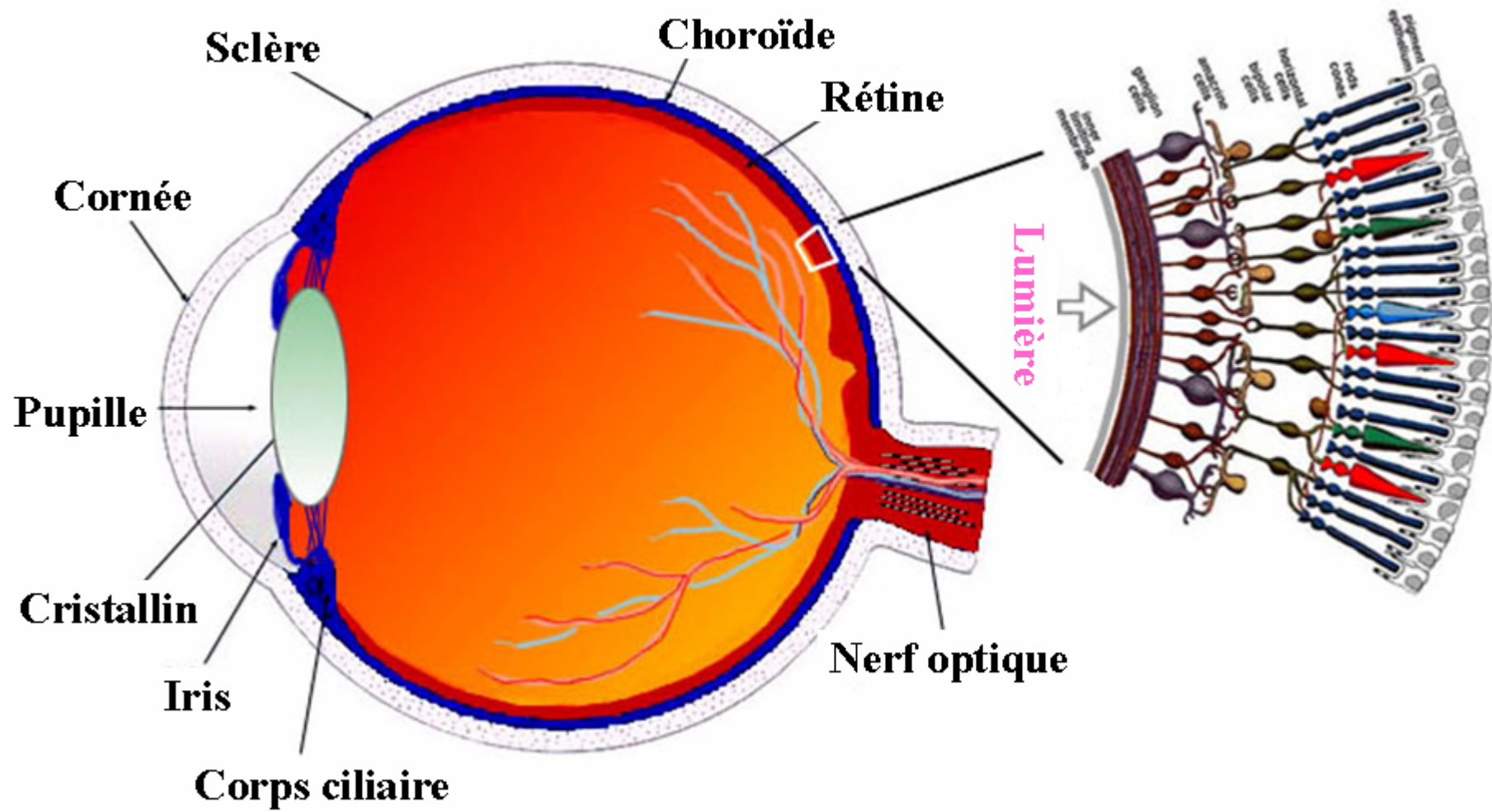


Atteinte de la macula

Dystrophie des cônes

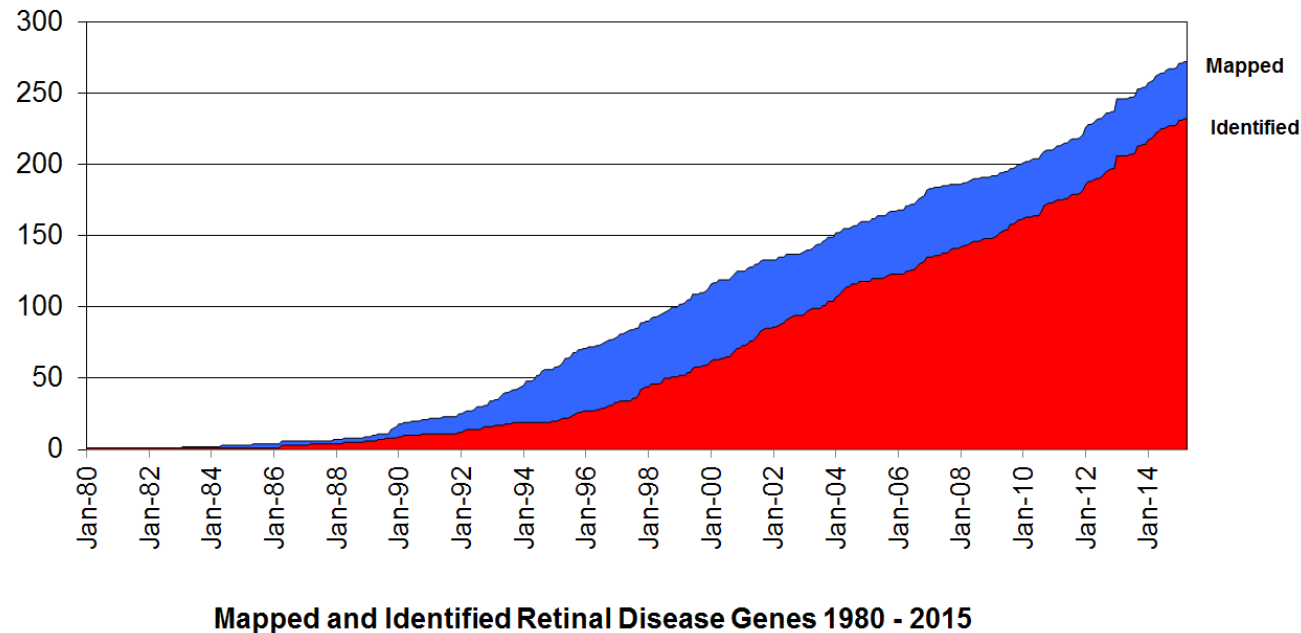
Atteinte de la
vision
centrale voir
plus





Dystrophies rétinienne héréditaires:

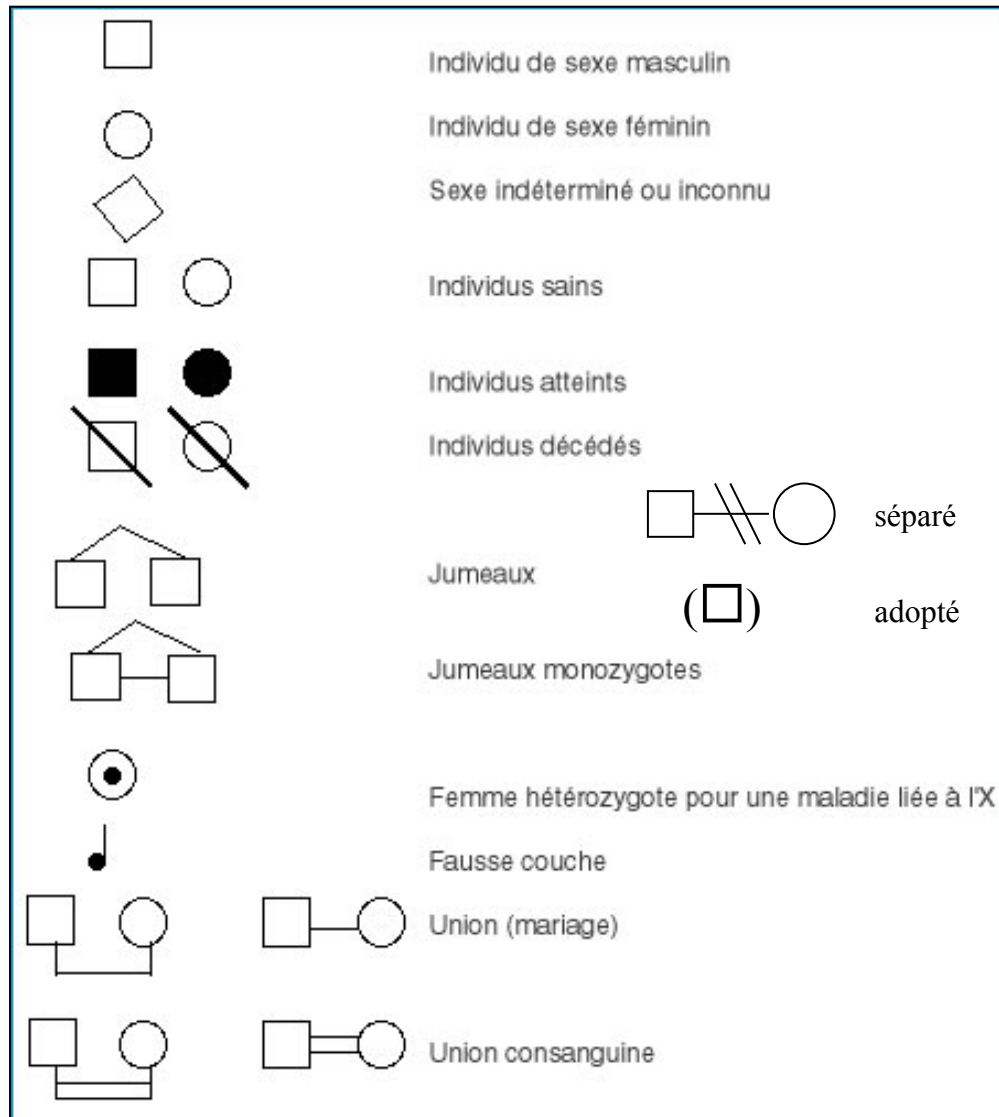
Une grande hétérogénéité génétique



<https://sph.uth.edu/Retnet/>

- Pas de traitement actuel mais des essais très prometteurs
- Nécessaire d'une bonne caractérisation de la maladie:
 - cliniquement et génétiquement

Importance de l'arbre généalogique +++

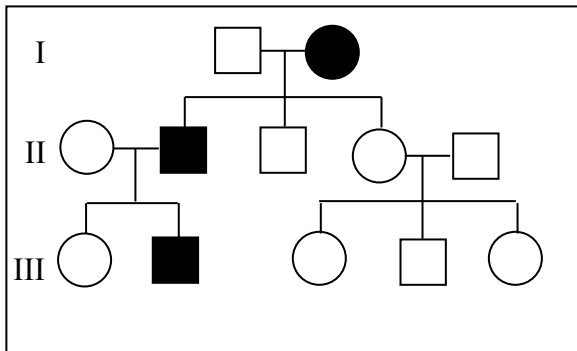


➤ Questions additionnelles:

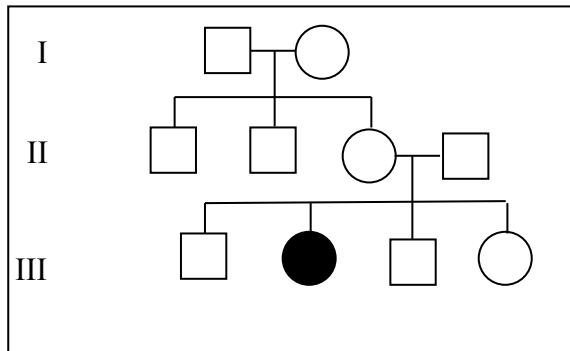
- origine géographique,
- consanguinité
- myopie dans la famille (RPLX),
- nystagmus,
- autres anomalies systémiques (surdit , diab te, ob sitt , hexadactilie),
-  ge de d but des troubles pour le patient et autres membres, hommes et femmes
- sympt mes de d but

Différents modes de transmission

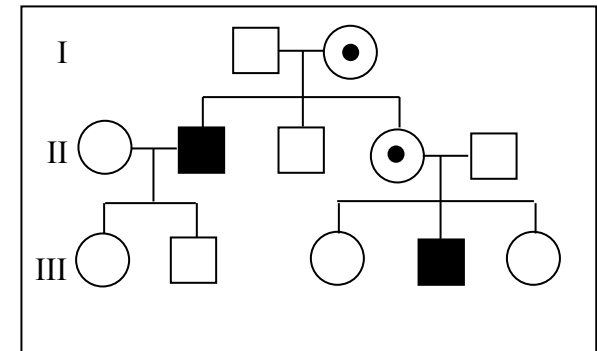
AUTOSOMAL DOMINANT (ex: Best)



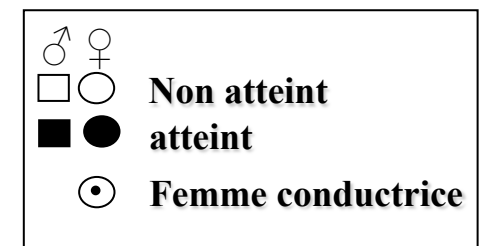
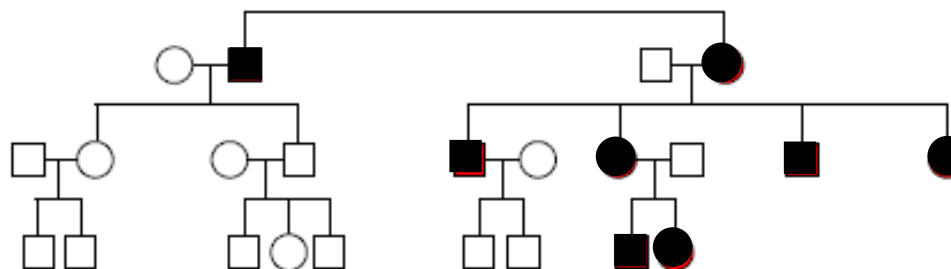
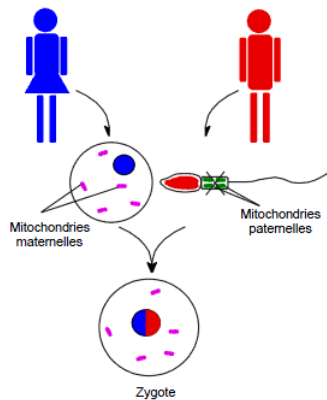
AUTOSOMAL RESSESSIF (ex: stargardt)



LIE AU CHROMOSOME X (ex: choroidémie)



MITOCHODRIAL (ex: neuropathie optique de Leber)



Evaluation de la fonction visuelle

➤ Acuité visuelle

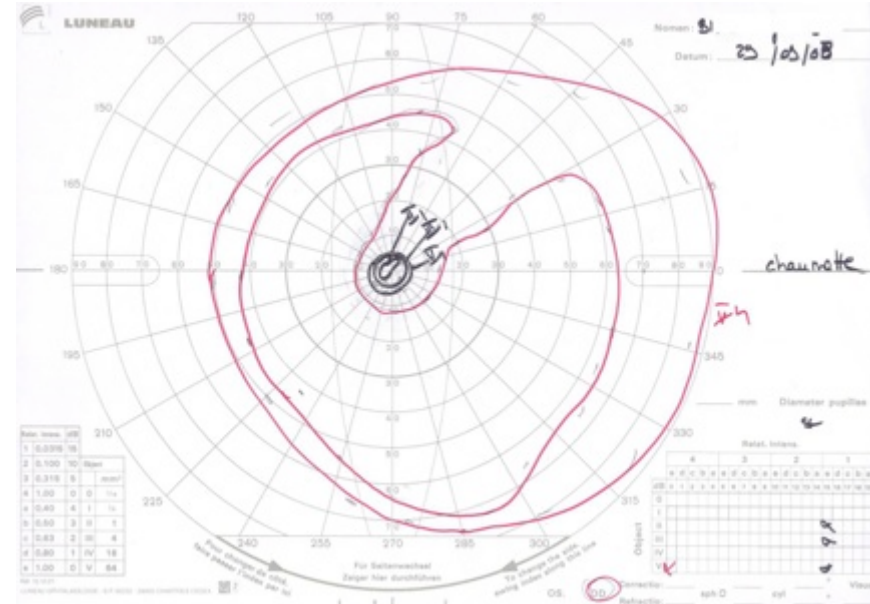
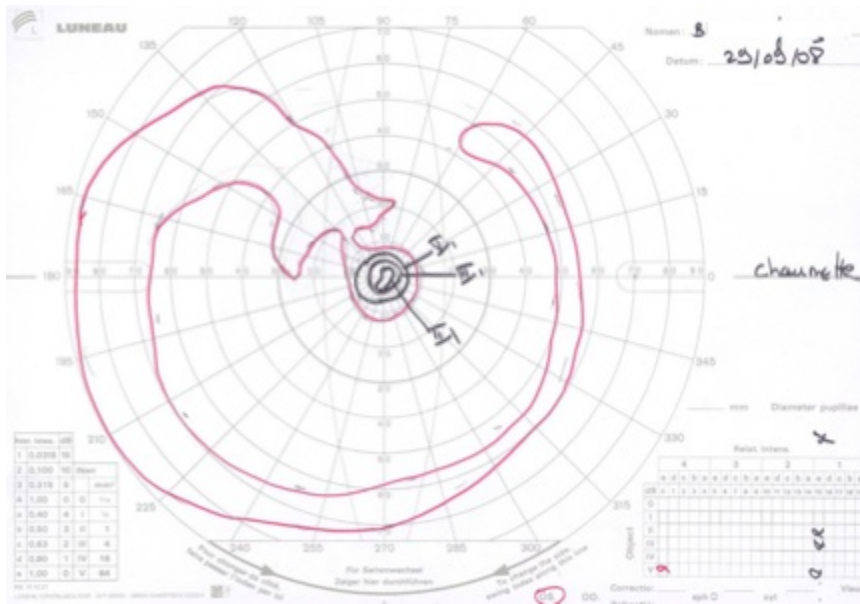
➤ Champ visuel

Périmétrie cinétique (Goldman) et statique

⇒ Meilleure évaluation des conséquences de la maladie

⇒ Important pour établir la légalité par rapport à la conduite automobile+++
(binoculaire III4e)

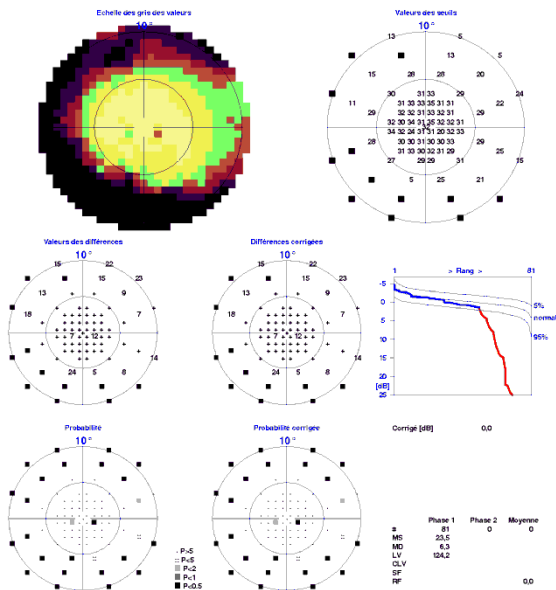
⇒ Important pour la reconnaissance du handicap visuel (binoculaire III4e)



HAAG-STREIT OCTOPUS 101 V 6.07
Seven-in-One

Nom: B
Prénom: F
ID #: 23/04/1943
Date de naissance: 65
Sexe: masculin
Refr. S / C / A: +1.5 / /
Acuité visuelle: 4 asb
Tension oculaire: 252 / 0
Diagnostic: pos 0 / 13, neg 0 / 13
Fichier des données: C:\Program Files\Octopus\ExDat\B.PVD

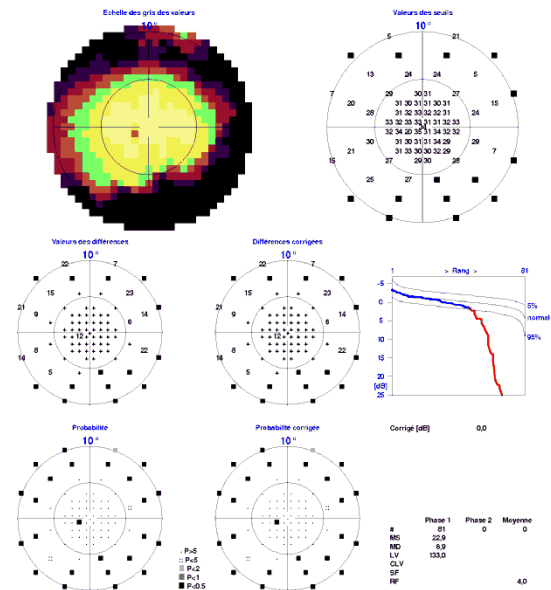
Oeil / Pupil (mm):
Date / Heure: 29/09/2008 11:29
Durée d'examen: 9:10
Programme / Code: dM2 / 0
étapes / Phases: 4 / 1
Stratégie / Méthode: Dynamique / Normale
Taille du stimulus / Durée: III / 100 ms
Luminance de fond: 4 asb
Questions / Répétitions: 252 / 0
Questions pièges: pos 0 / 13, neg 0 / 13
C:\Program Files\Octopus\ExDat\B.PVD



HAAG-STREIT OCTOPUS 101 V 6.07
Seven-in-One

Nom: B
Prénom: F
ID #: 23/04/1943
Date de naissance: 65
Sexe: masculin
Refr. S / C / A: +1.5 / /
Acuité visuelle: 4 asb
Tension oculaire: 249 / 3
Diagnostic: pos 1 / 12, neg 0 / 13
Fichier des données: C:\Program Files\Octopus\ExDat\B.PVD

Oeil / Pupil (mm):
Date / Heure: 29/09/2008 11:41
Durée d'examen: 9:21
Programme / Code: dM2 / 0
étapes / Phases: 4 / 1
Stratégie / Méthode: Dynamique / Normale
Taille du stimulus / Durée: III / 100 ms
Luminance de fond: 4 asb
Questions / Répétitions: 249 / 3
Questions pièges: pos 1 / 12, neg 0 / 13
C:\Program Files\Octopus\ExDat\B.PVD

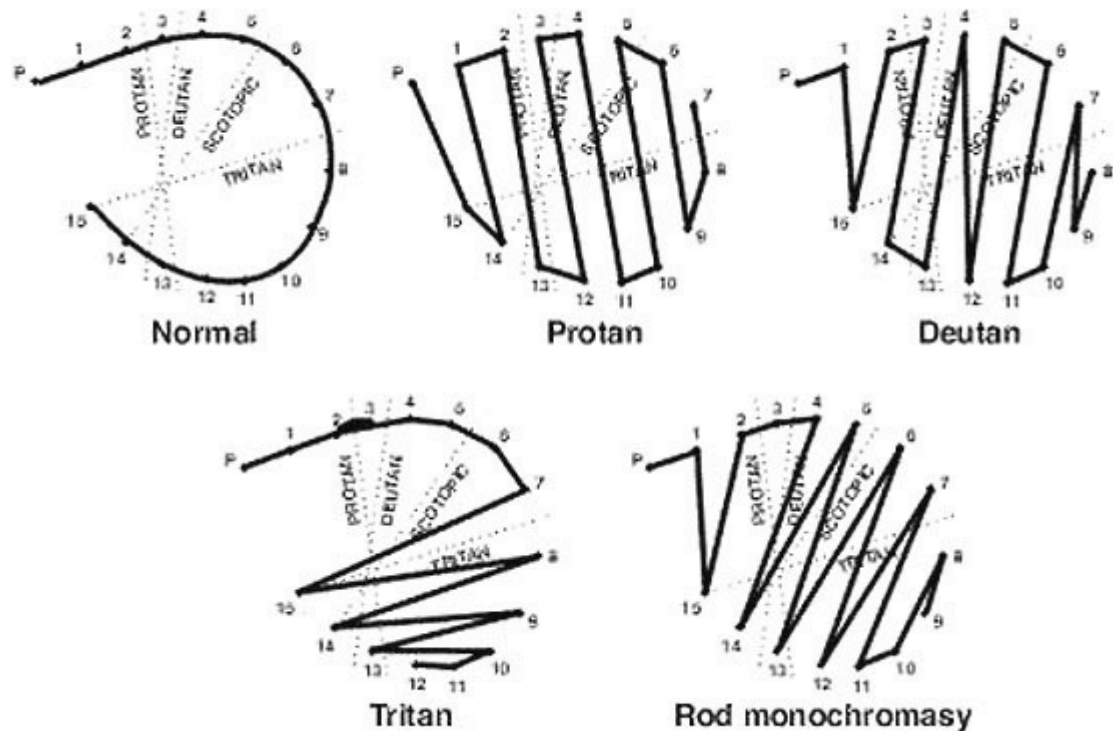


Evaluation de la fonction visuelle

➤ Vision des couleurs

Meilleures évaluation des cônes maculaires

Tests d'appariement



Evaluation de la fonction visuelle

Electrophysiologie: diagnostic and pronostic+++

Electrorétinogramme (ERG) global selon les recommandations de l'ISCEV

Evalue la fonction rétinienne globale

Electrooculogramme (EOG)

Test la fonction de l'épithélium pigmentaire et des photorécepteurs

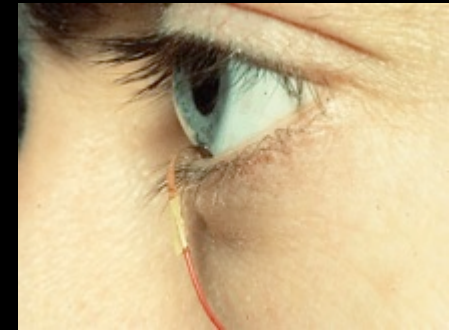
(ERG multifocal ou ERG damier)

Pour évaluer la fonction maculaire



ERG standard ISCEV

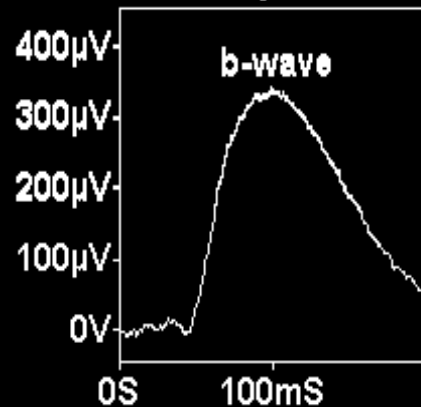
5 enregistrements / flashes achromatiques



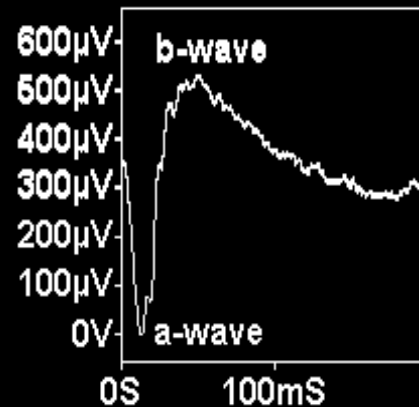
Adaptation à l'obscurité (>20 mn)

Adaptation à la lumière (>10 mn)

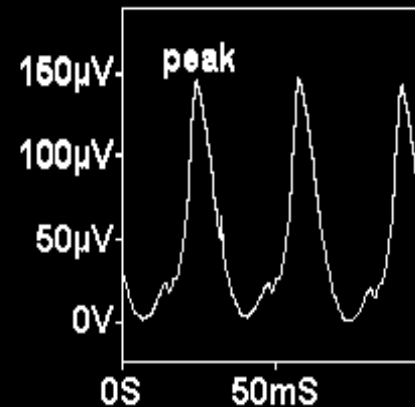
scotopic rod



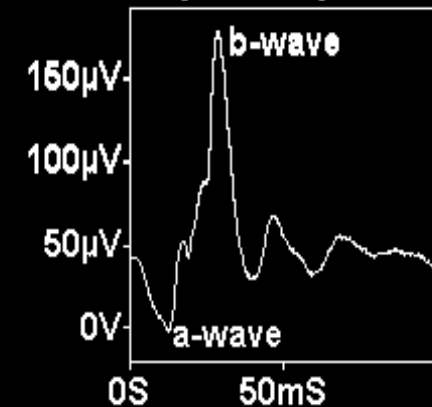
maximal



30Hz flicker



photopic



- ERG scotopique spéc des bts ($\downarrow 2.5 \log U$)
- Réponse «maximum» (mixte, dominée par les bts)
- Potentiels oscillatoires

-ERG Flicker 30Hz (cônes)

- ERG Photopique (cônes)

(flash standard sur 17-34 cd/m^2 d'illumination de fond)

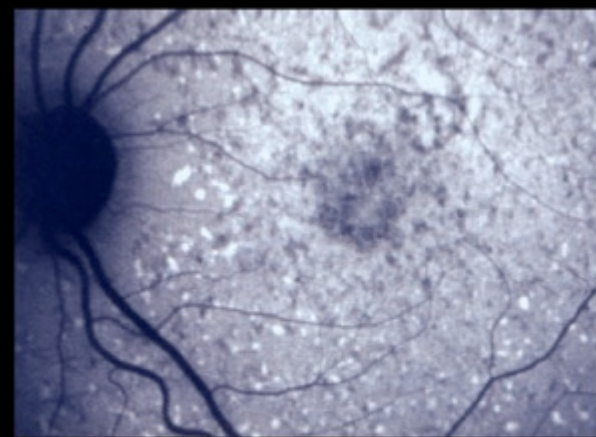
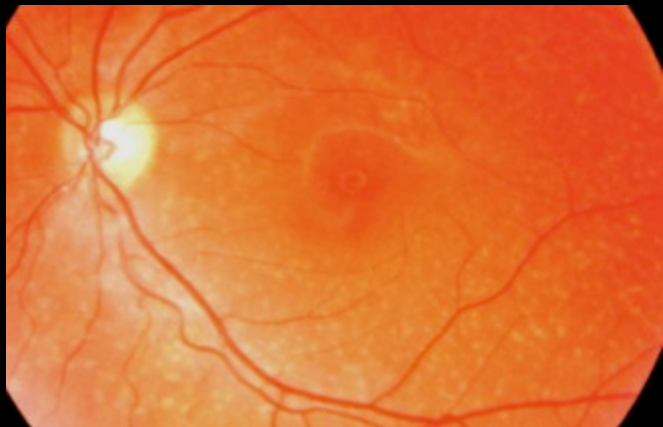
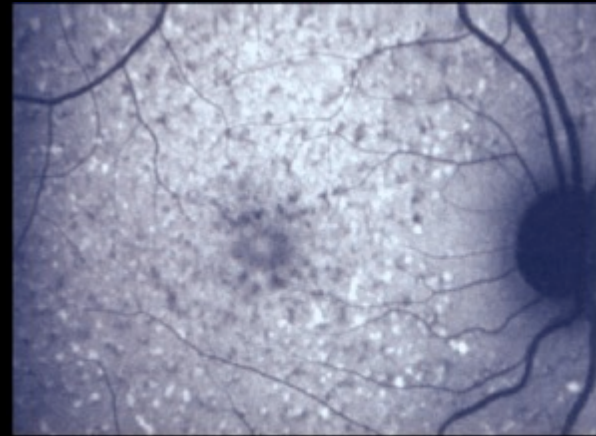
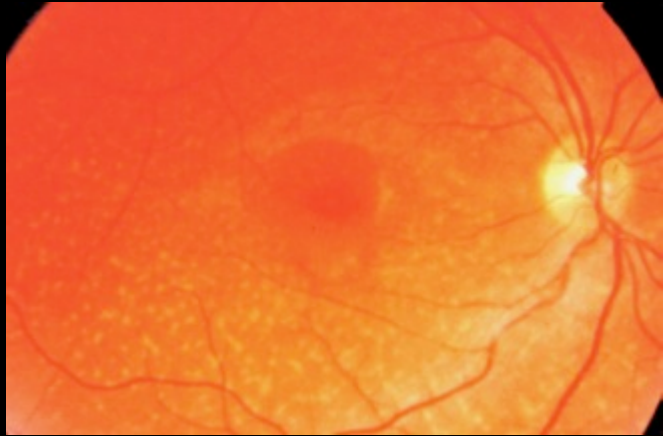
Stargardt/Fundus Flavimaculatus

-ERG prognostic+++

Phenotypic variability+++

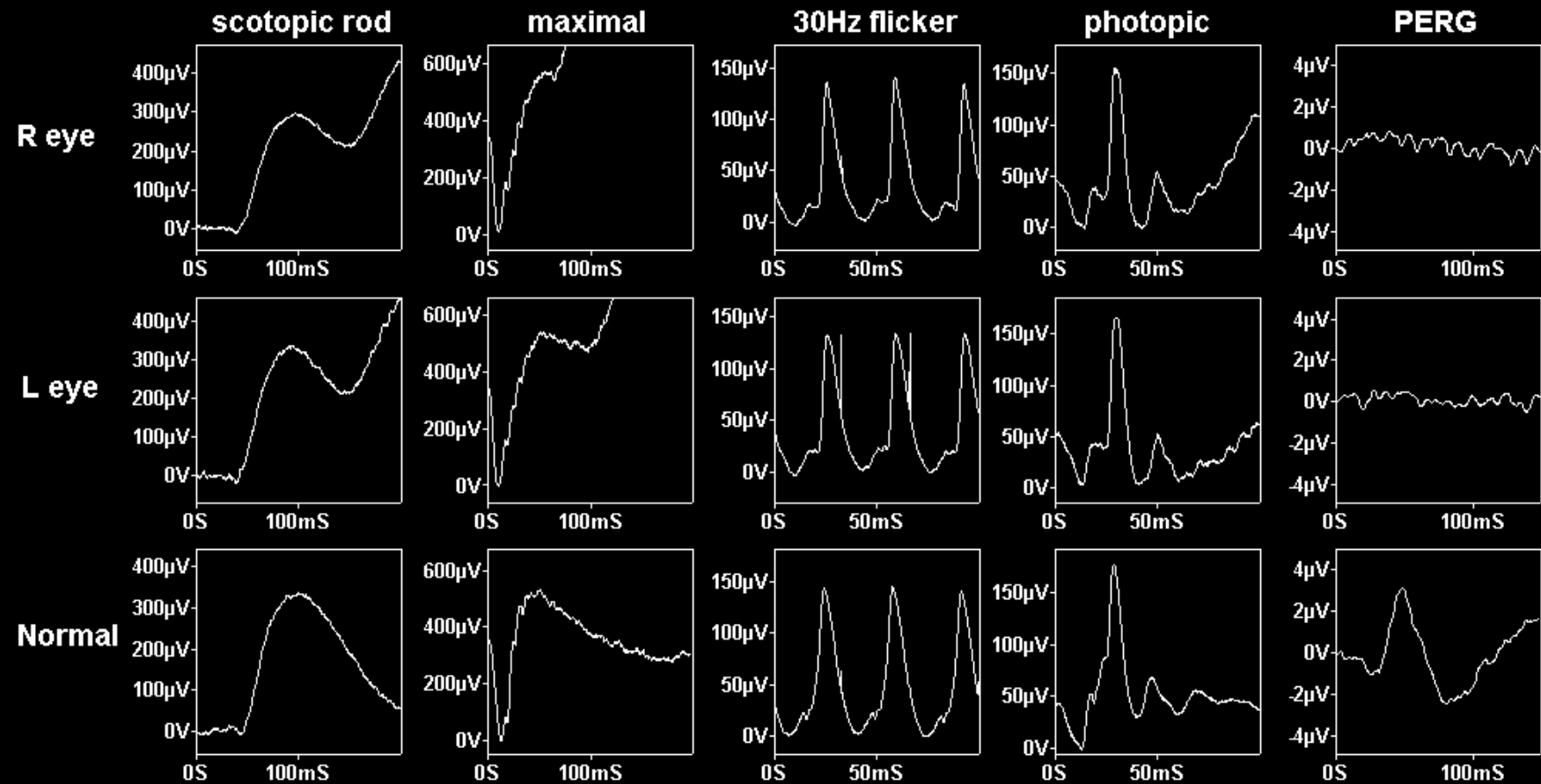
(voir Lois N et al Arch Opht 2001)

**Stargardt fundus flavimaculatus group 1
F, 21a. AV 1/10 OD; 2/10 OG.**

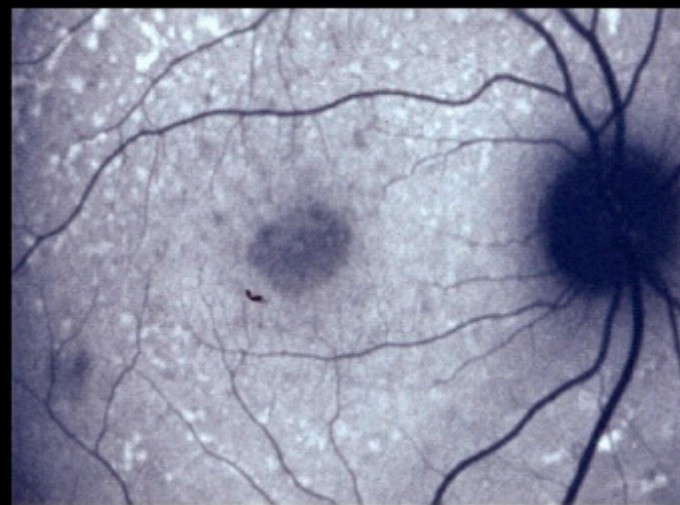
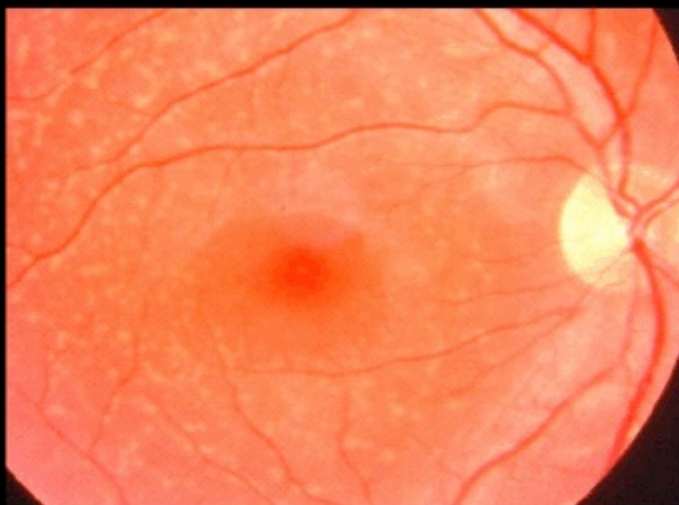


Stargardt fundus flavimaculatus group 1

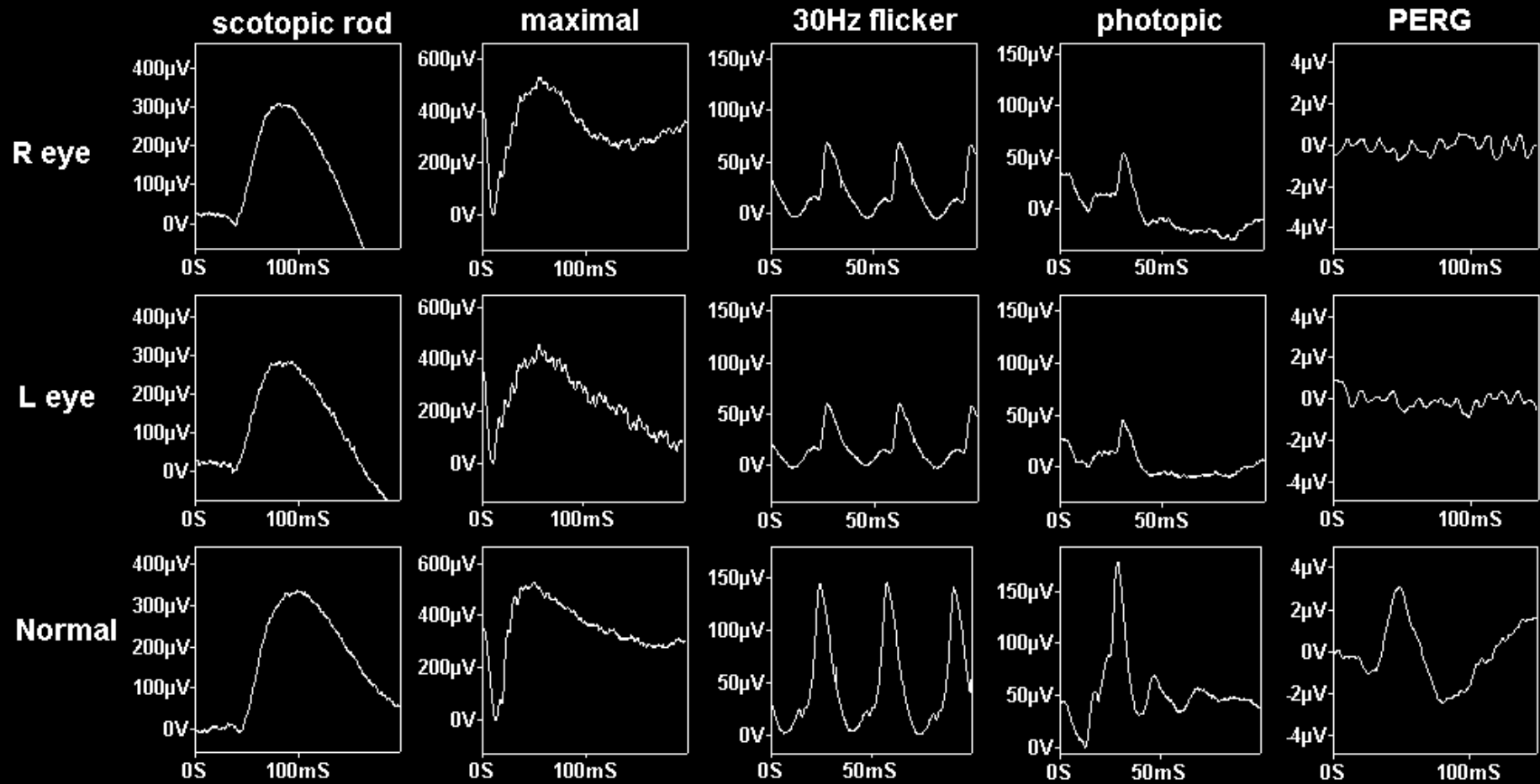
F, 21a. AV 1/10 OD; 2/10 OG.



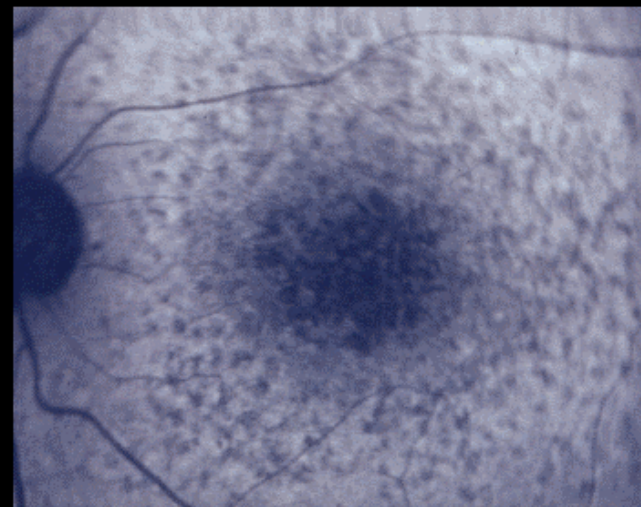
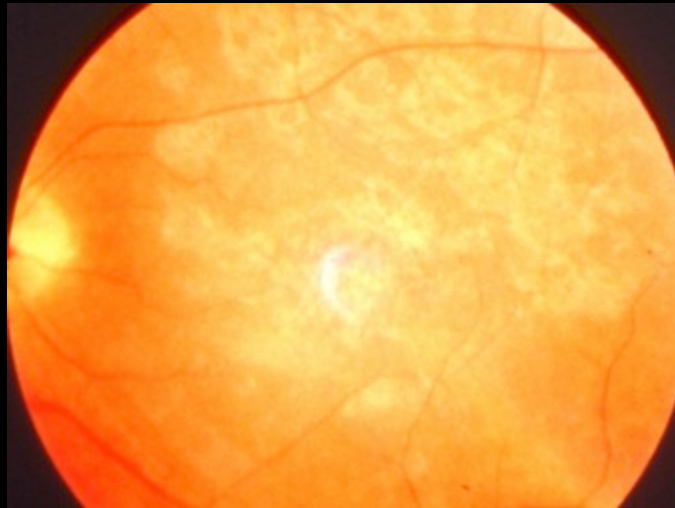
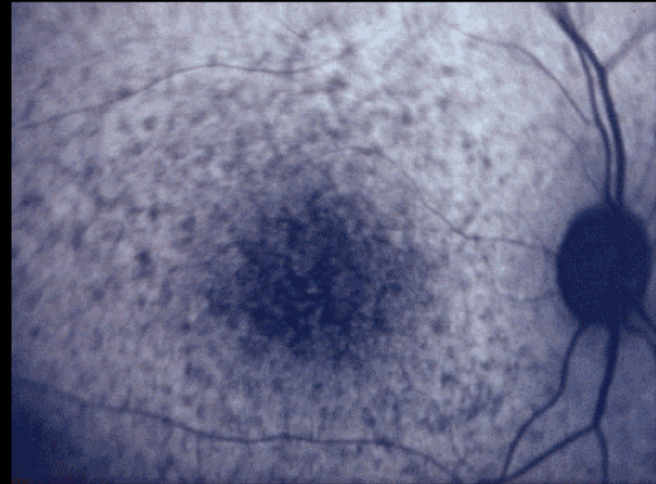
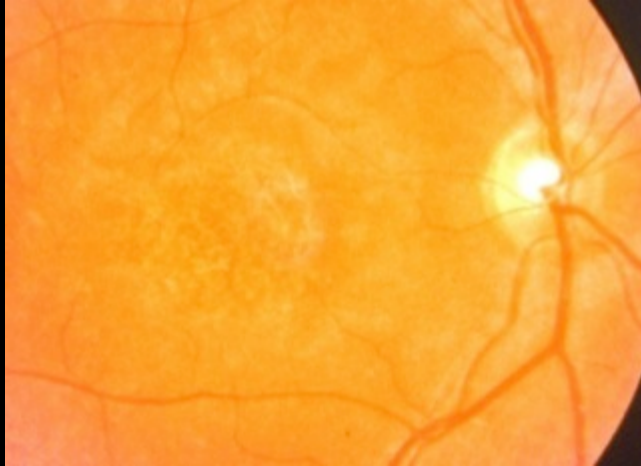
Stargardt fundus flavimaculatus group 2
H, 15a. AV 1/10 ODG.



Stargardt fundus flavimaculatus group 2 H, 15a. AV 1/10 ODG.

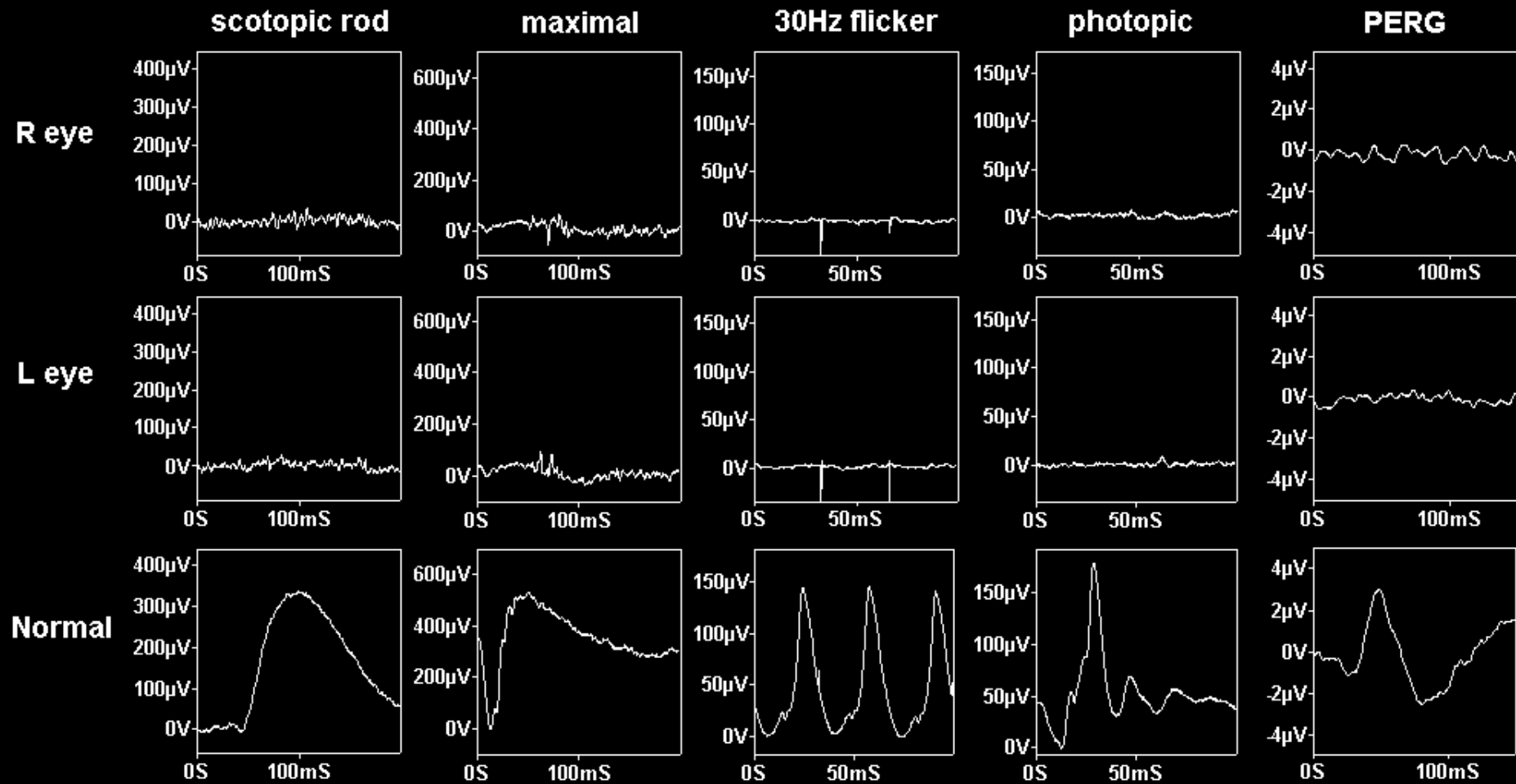


**Stargardt fundus flavimaculatus groupe 3
H, 16a. AV 1/20 ODG.**



Stargardt fundus flavimaculatus group 3

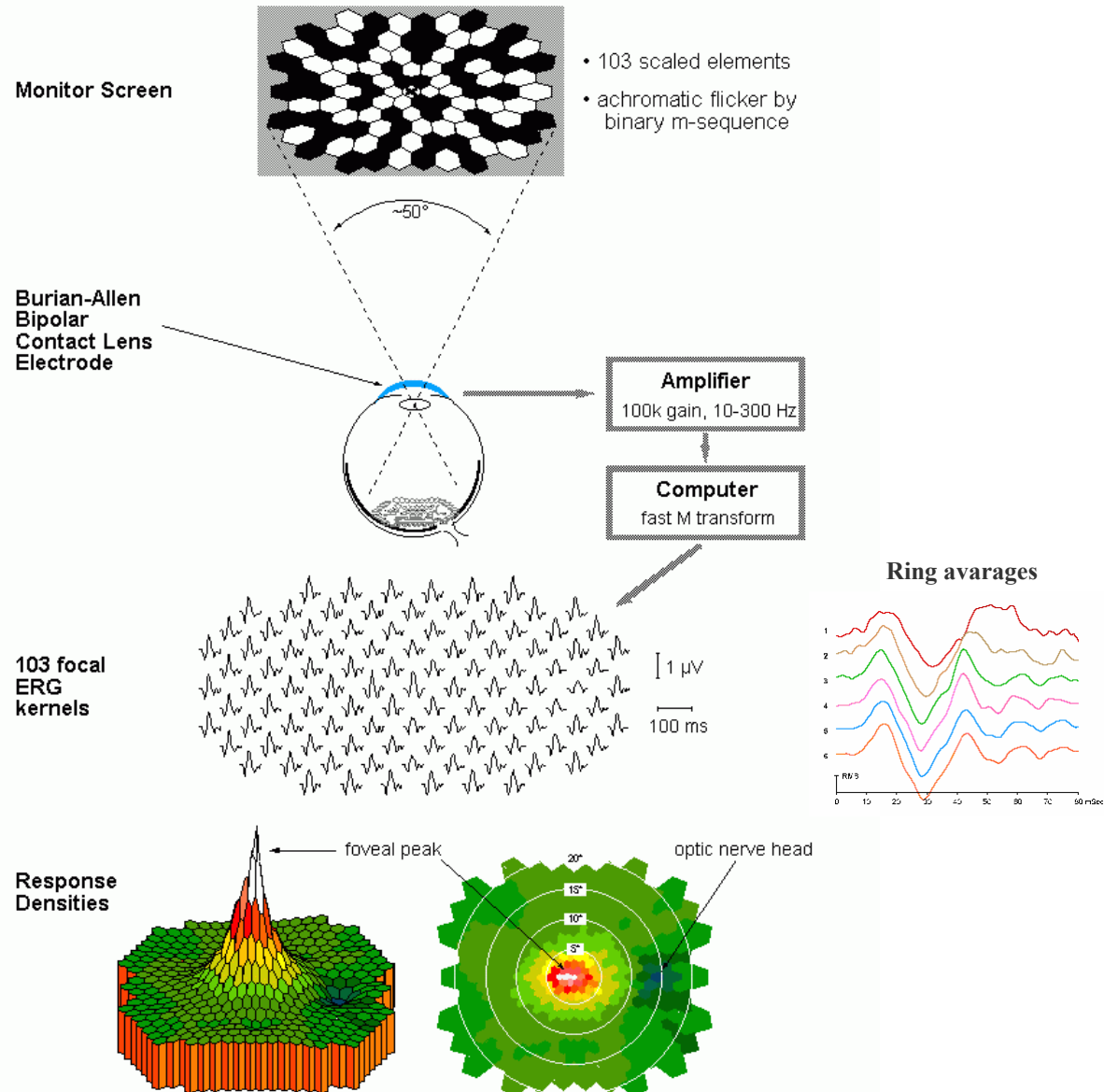
H, 16a. AV 1/20 ODG.



Stargardt-fundus flavimaculatus

- **Group 1: maculopathy => normal peripheral visual field**
- **Group 2: maculopathy + cone dysfunction**
- **Group 3: maculopathy + cone and rod dysfunction**
 - => Groupe 2/3: will evolved toward more generalized disease... cone-rod...**

ERG multifocal (mfERG)

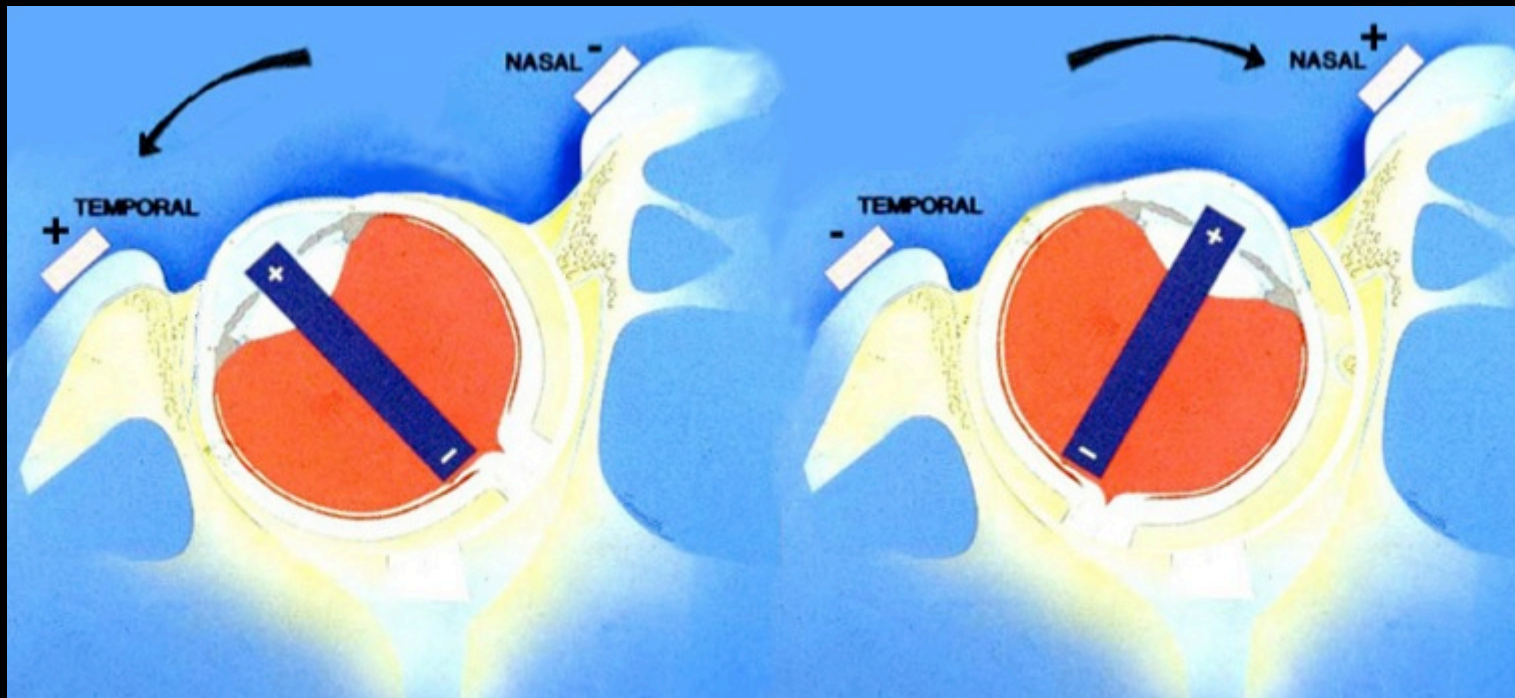


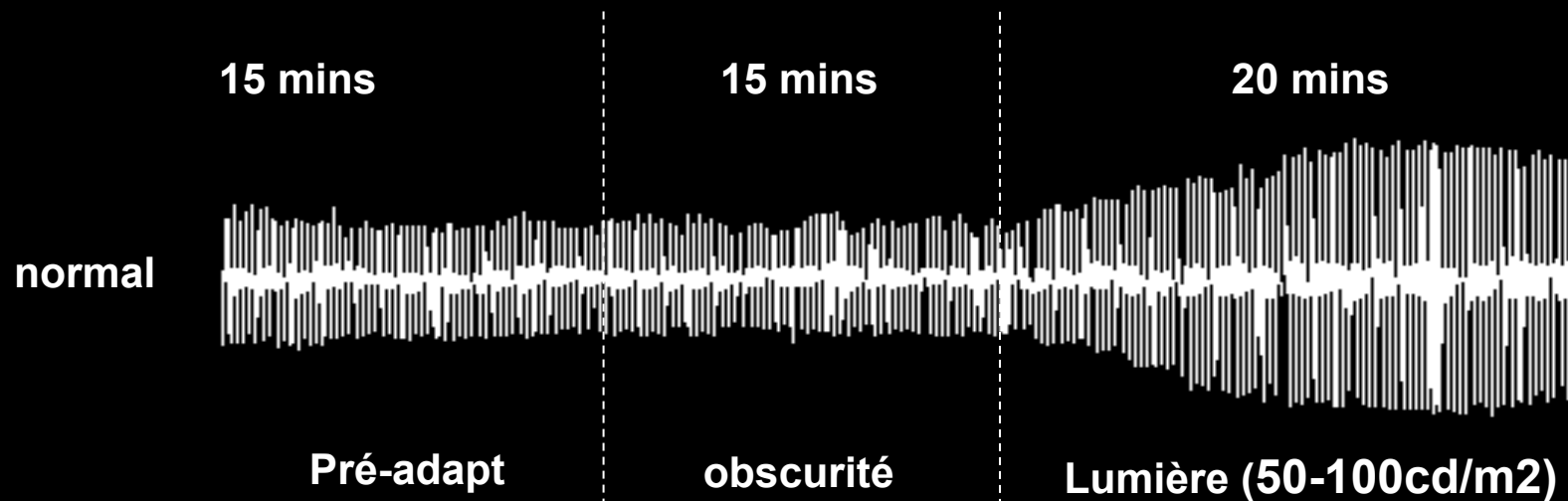
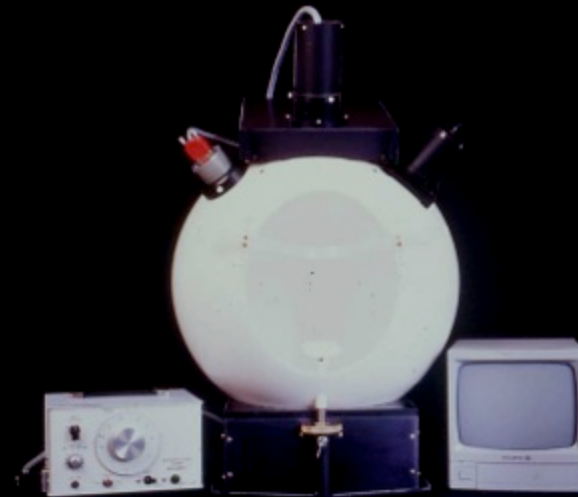
Electrooculogramme (EOG)

Dipôle cornéo rétinien:

reflet du bon fonctionnement du couple PR/EPR

Pas d'EOG sans ERG+++++

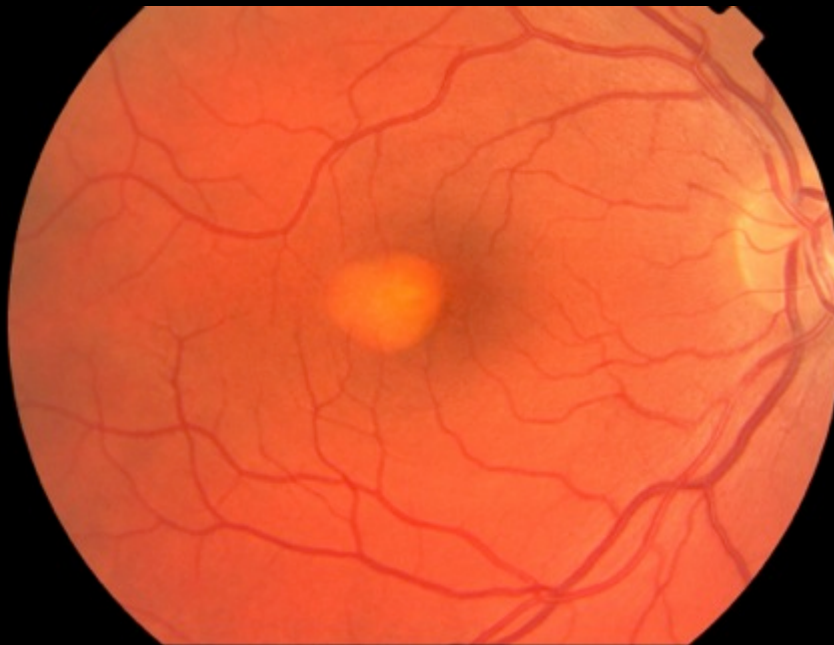




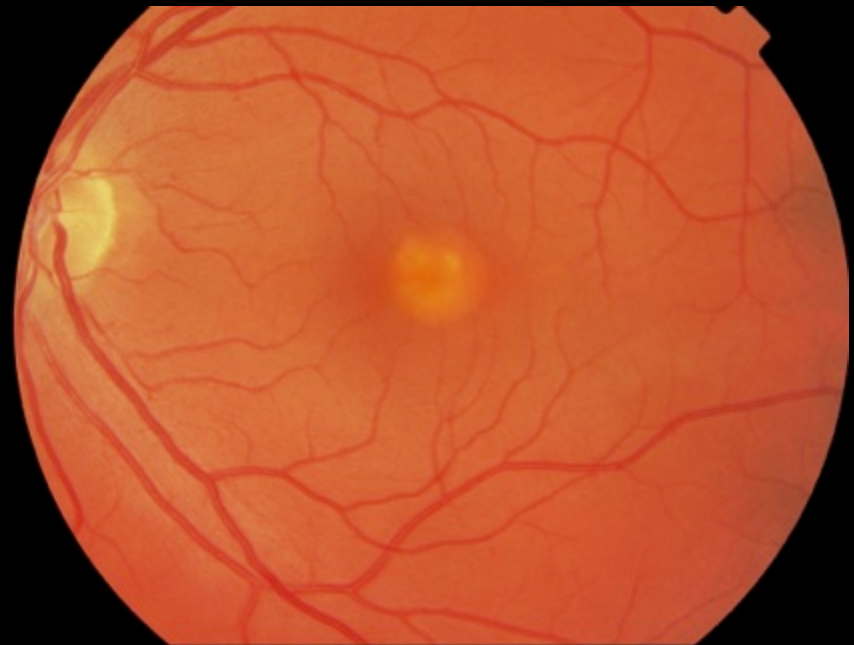
Mouvements oculaires toutes les 1 - 2.5 secs; 10 saccades/min
EOG rapport d'Arden = light rise/dark trough

h A. 36a.

10/10

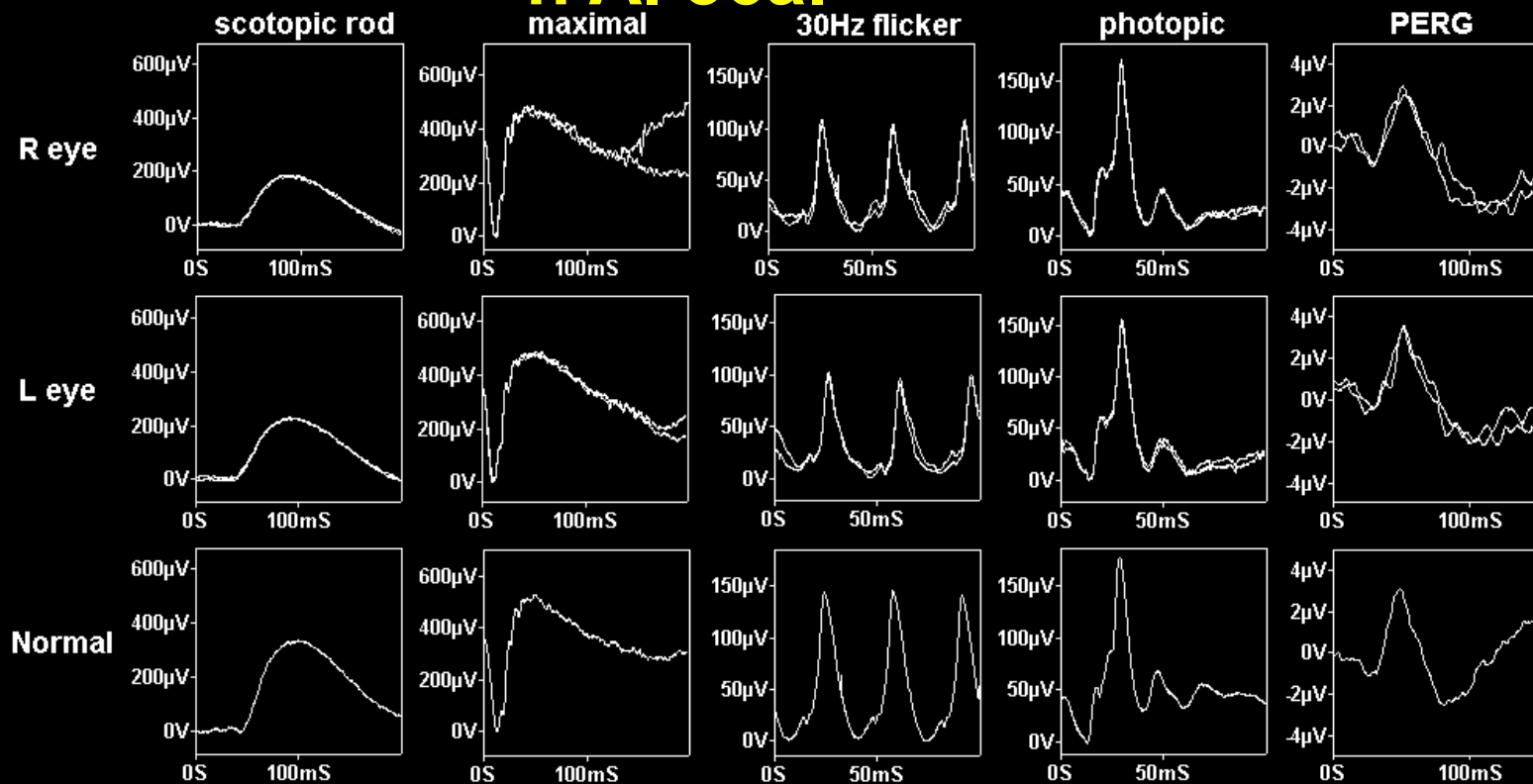


10/10

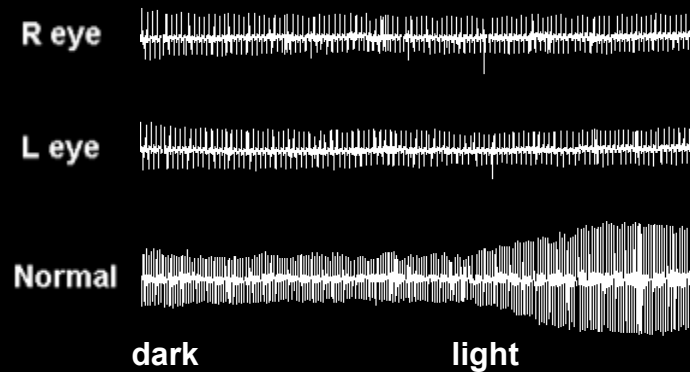


h A. 36a.

ERG



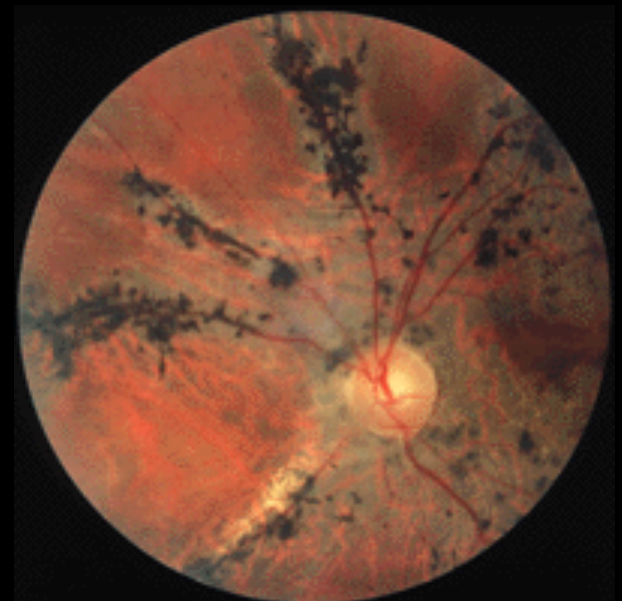
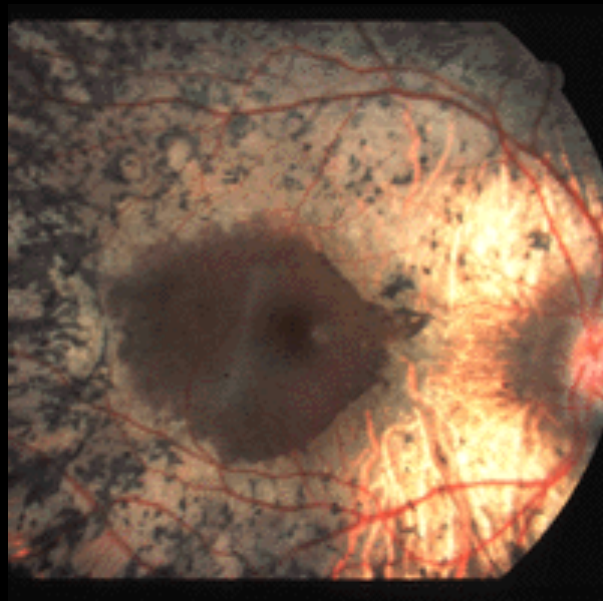
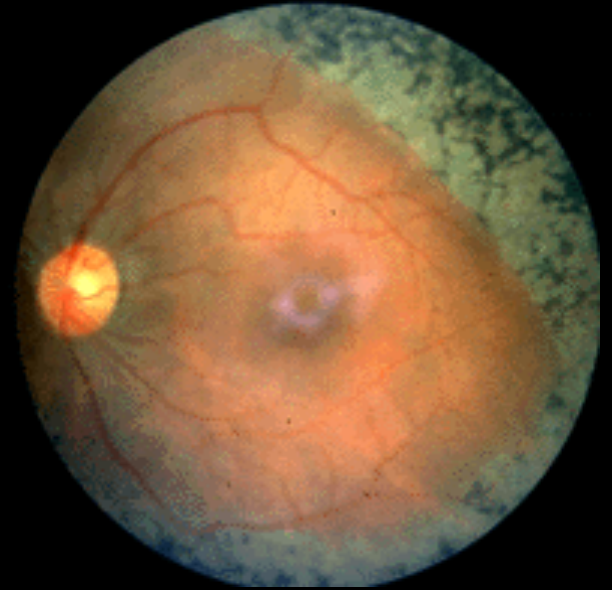
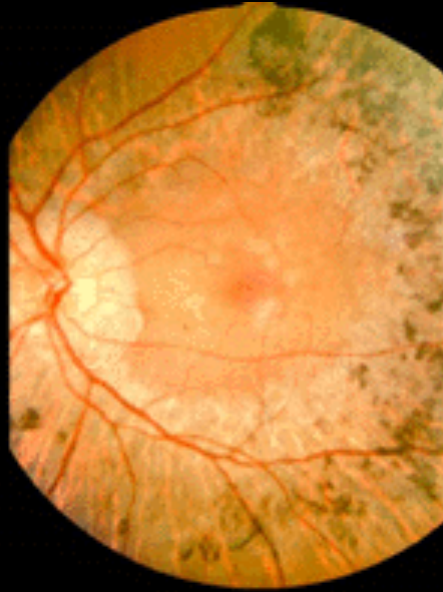
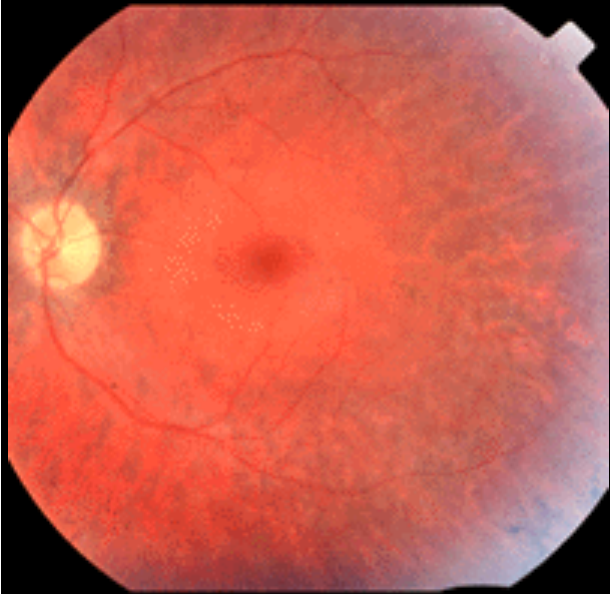
EOG



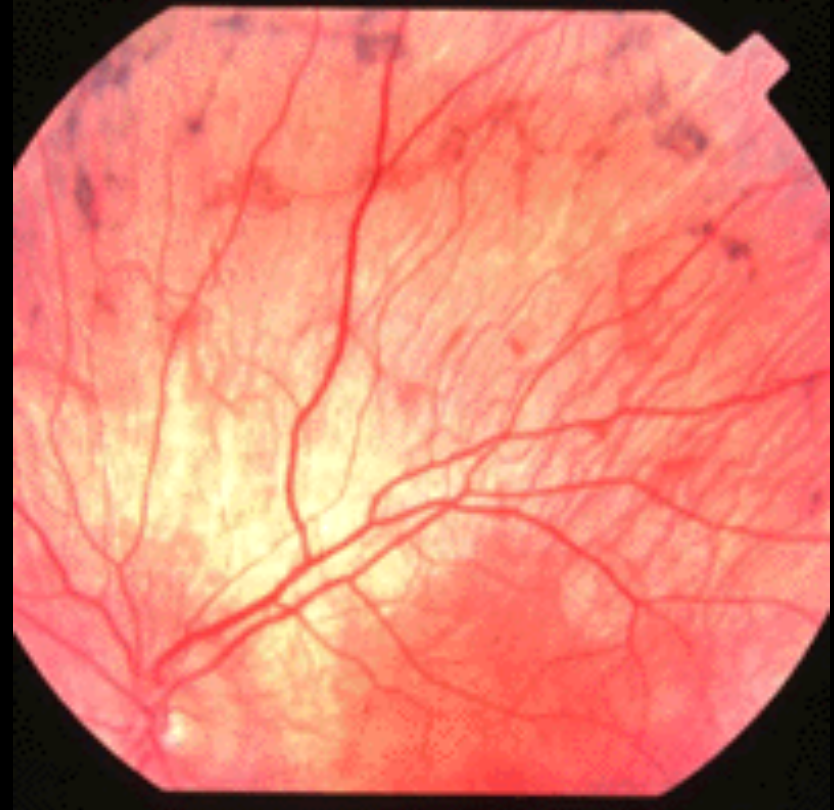
Best disease

Evaluation de la structure de la rétine

➤ examen du fond d'œil



Choroidérémie



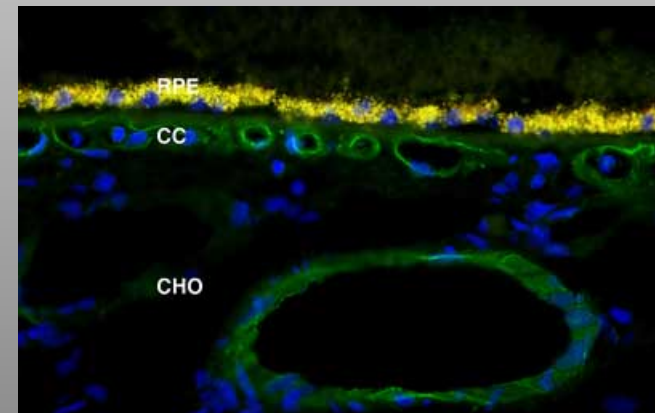
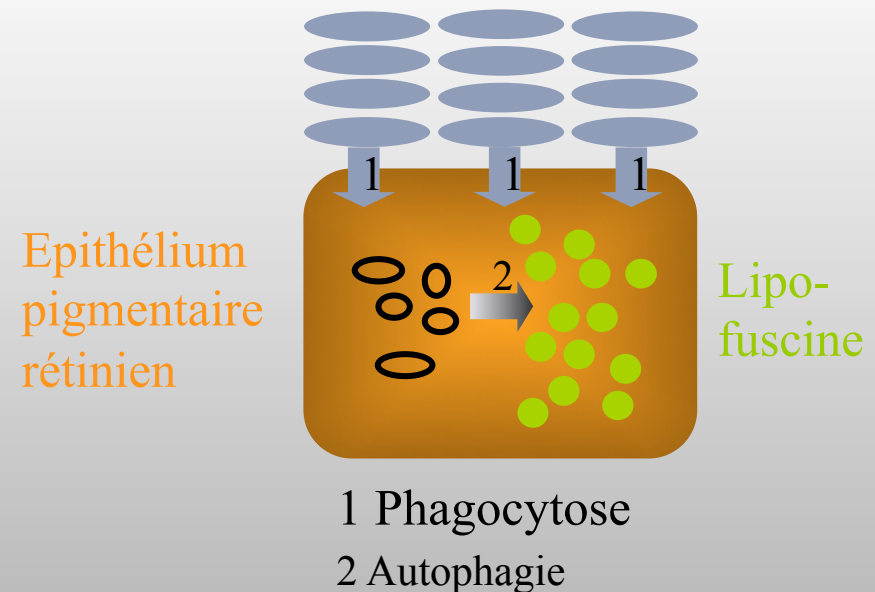
Qu'est-ce que l'autofluorescence (AF) du fond d'œil?

= visualisation de la LIPOFUSCINE (LF), marqueur fonctionnel du renouvellement des segments externes des photorécepteurs (=PR/EPR)

- AF: reflète l'accumulation de LF, principalement A2E, dans les cellules de l'EPR
- Associée au renouvellement cyclique des segments externes des photorécepteurs
- = « déchets » de la phagocytose incomplète, soumis à l'auto-oxydation
- Accumulation dans les cellules post-mitotiques
- Augmente avec l'âge
- Modifiée dans les pathologies rétinienne (DMLA, SGDT, Best...)

Delori FC, et al. 2001

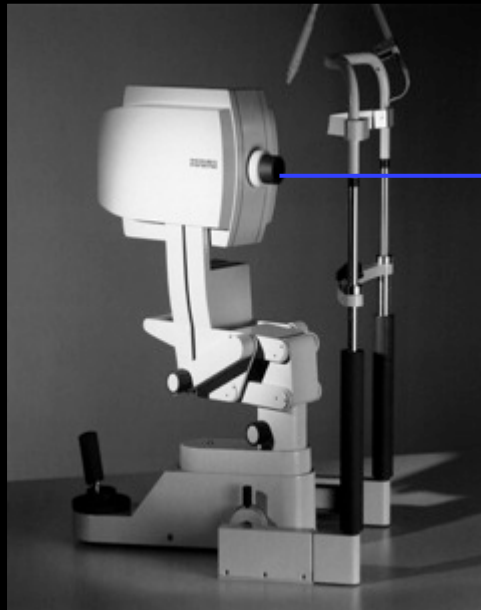
Segments externe des photorécepteurs



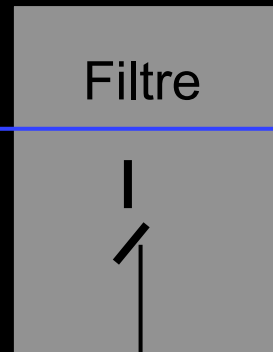
Technique(s) d'imagerie

Non invasive+++

- SLO confocal, type HRA2



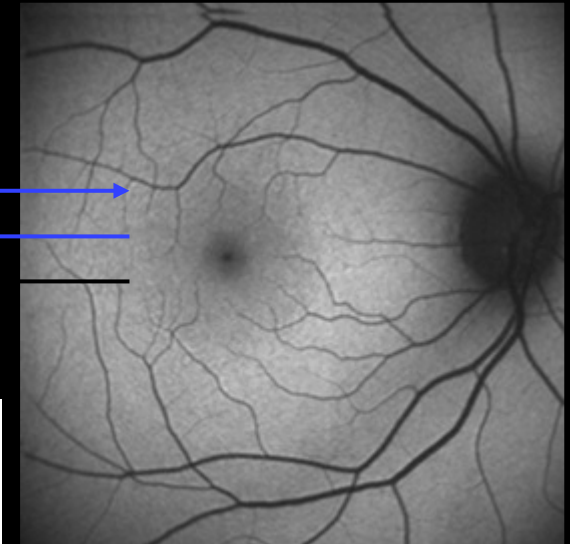
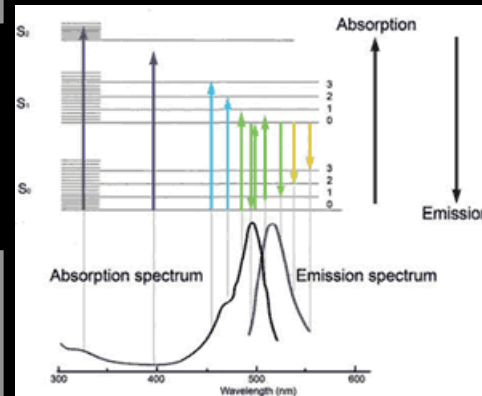
Laser/488 nm



Filtre

488 nm

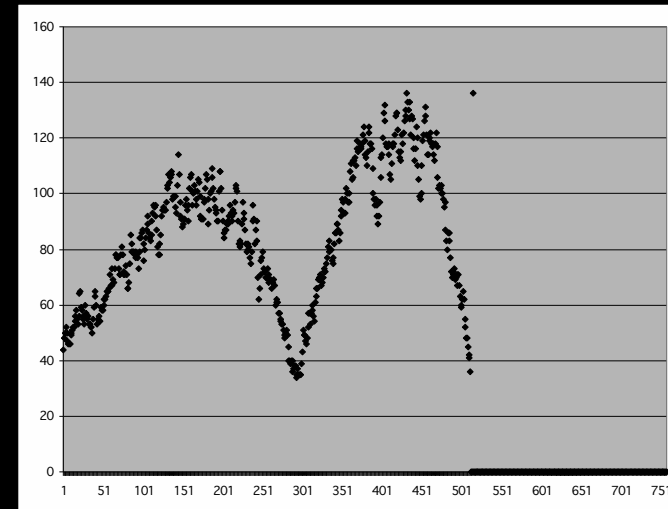
> 521 nm



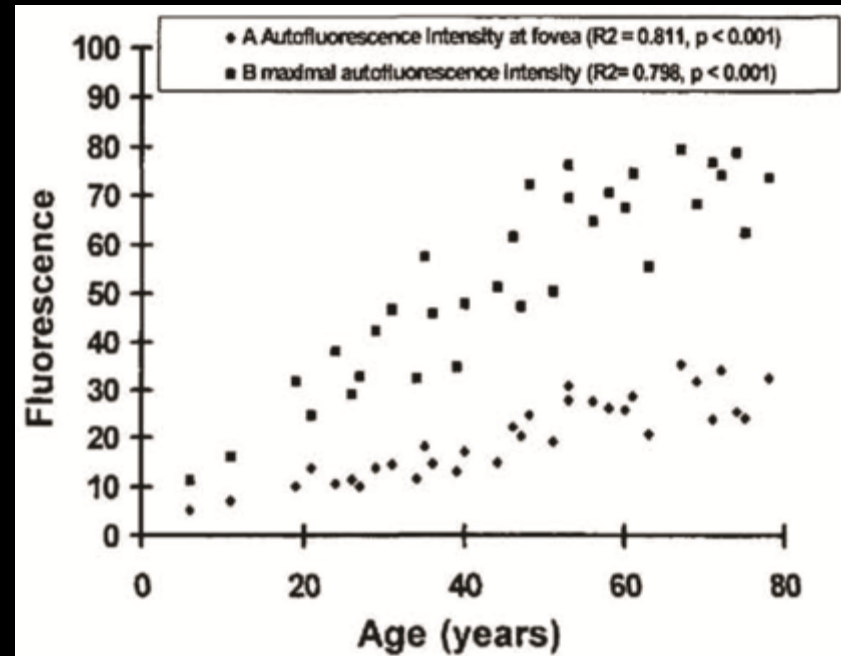
Autofluorescence (AF)
in vivo
Après sommation

- Rétinographe, type Topcon, avec filtres spéciaux

Autofluorescence normale



Von Rückman et al., 1999



Anomalies de l'autofluorescence du fond d'œil

Visualise la LF au niveau de l'EPR

– **augmentée**

- Turn-over augmenté des segments externes des PR
- Incapacité à recycler les métabolites

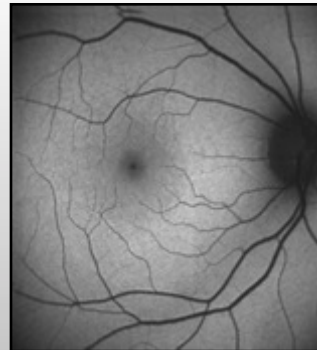
– **diminuée**

- Masquage
- Absorption (pigment lutéal)
- Réduction de la densité de l'EPR
- Diminution du renouvellement des SE

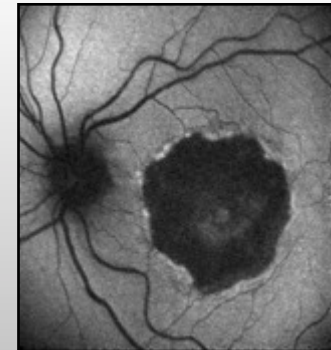
– **Absent**

- Atrophie ou mort cellulaire

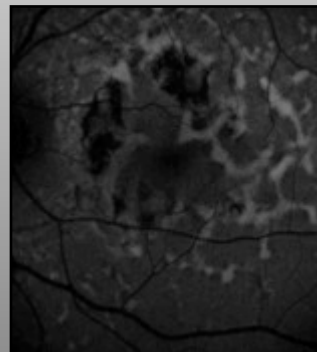
Normal



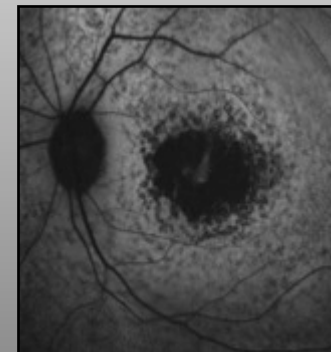
DMLA



Pattern dystrophy



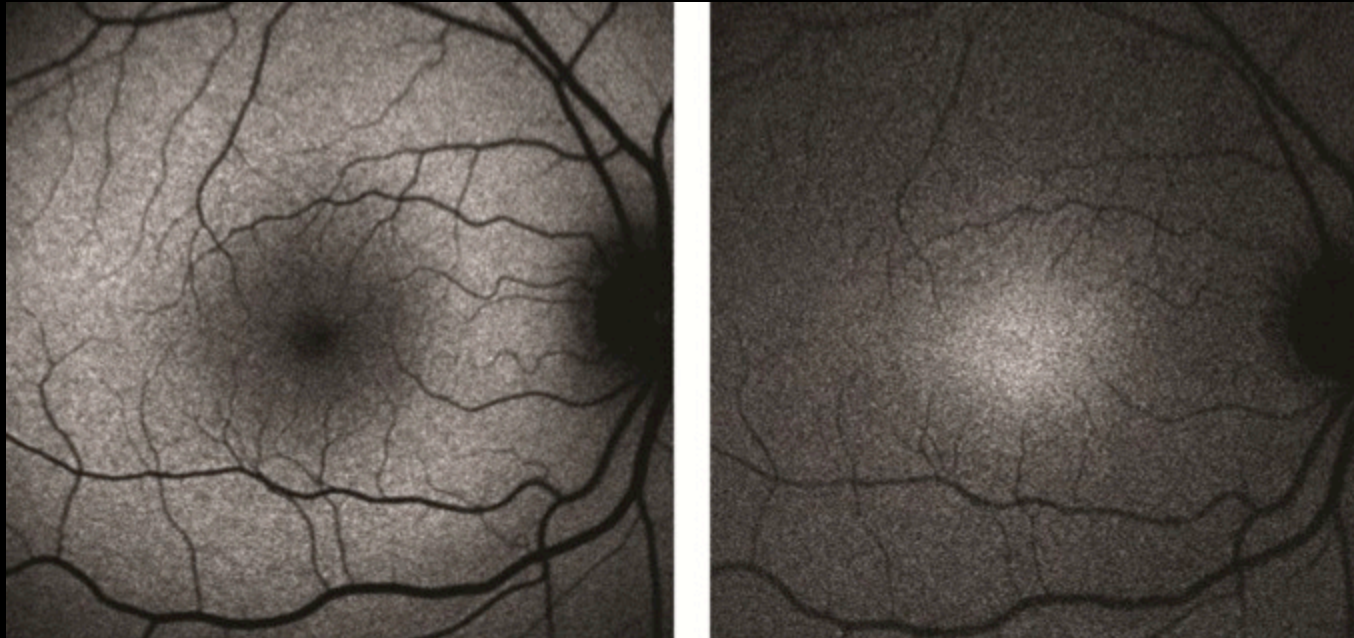
Stargardt



Correlation FAF

Argon bleu vs proche IR

Kellner et al., 2009



(Ex 488nm/Em >500nm)
(OS PR/RPE)

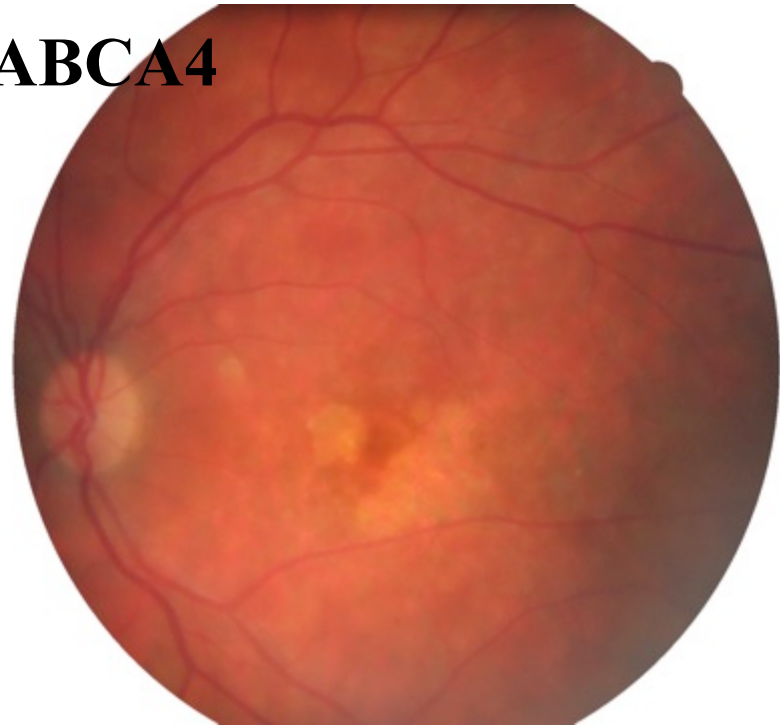
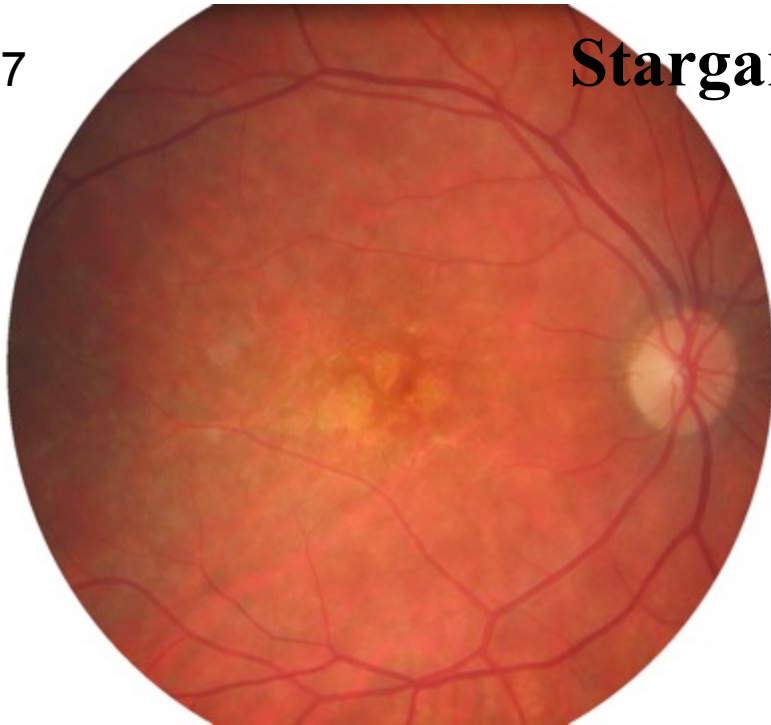
(Ex 787nm/Em >800nm) (évite la lumière bleue)

Mélanine des mélanosomes, essentiellement dans la partie apicale du RPE

- **Diminution:** blocage ou déplacement des mélanosomes ou perte de l'EP
- **Augmentation:** redistribution ou diminution de mélanine, mélanolysosomes,, mélanolipofuschine

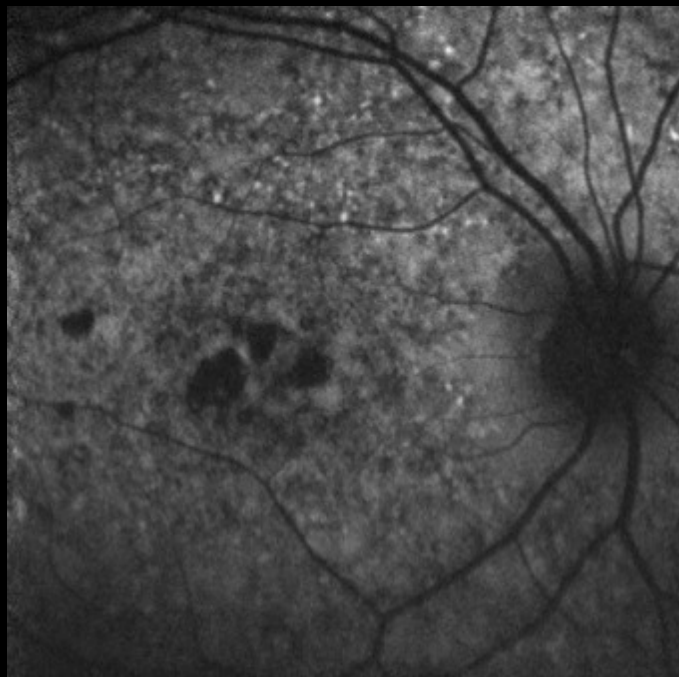
2007

Stargardt/ABCA4

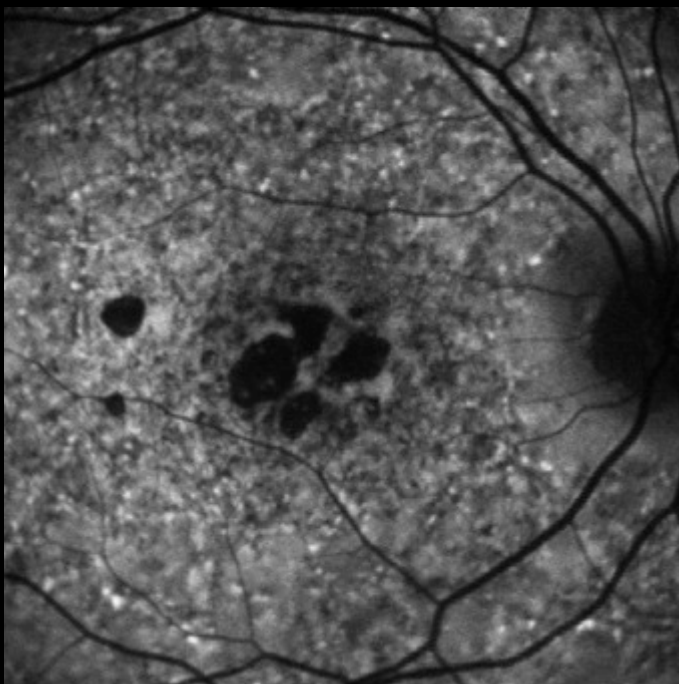
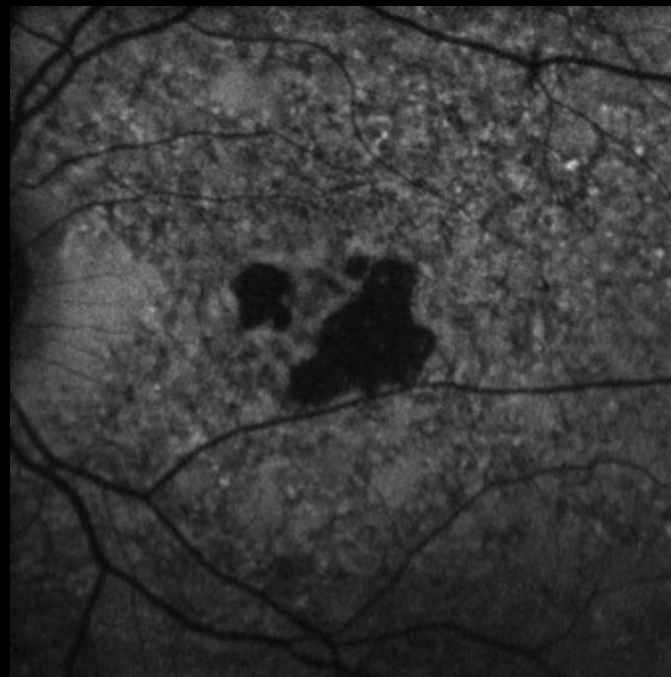


2008

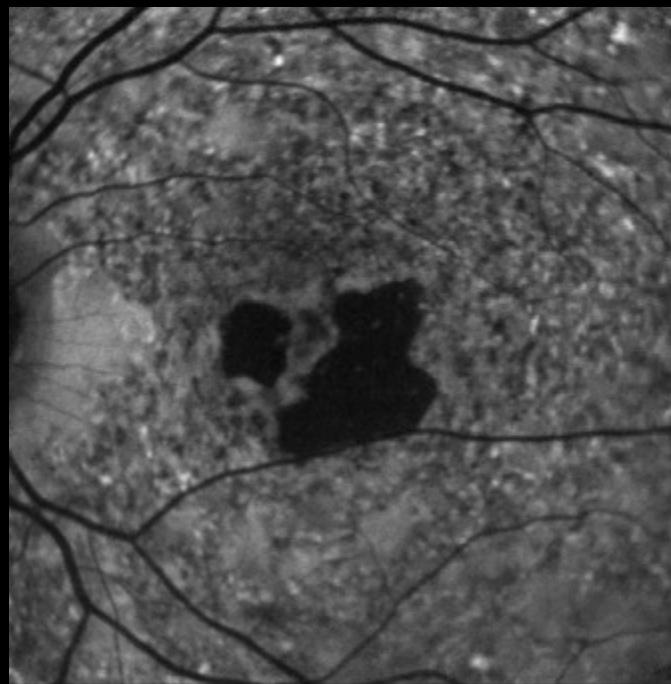


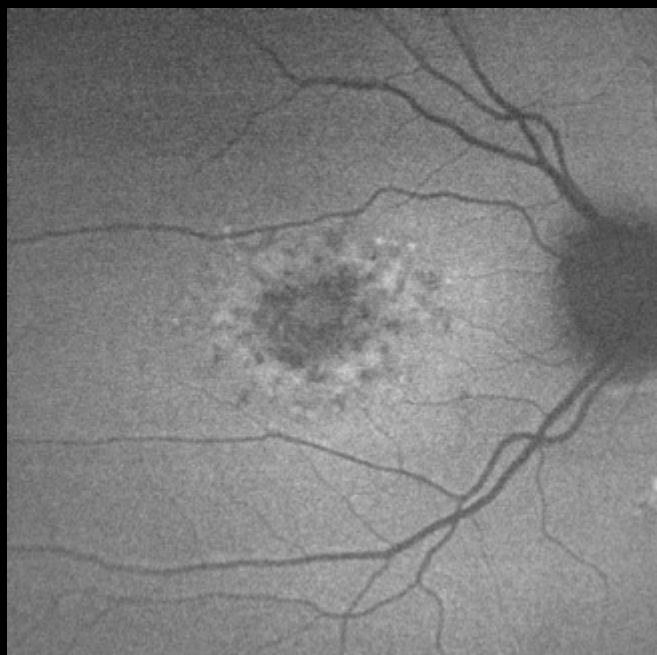
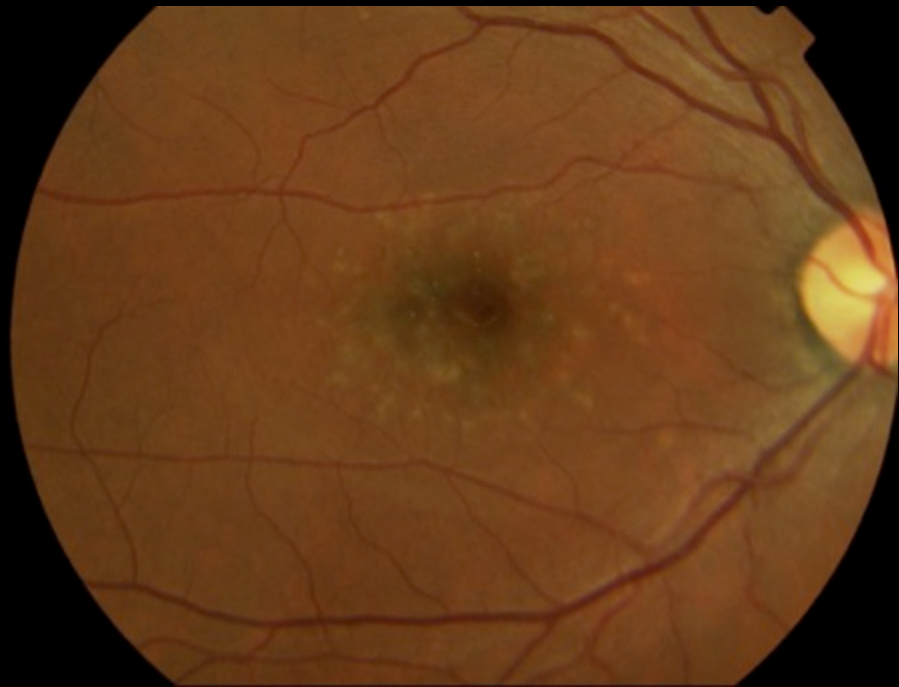


2007

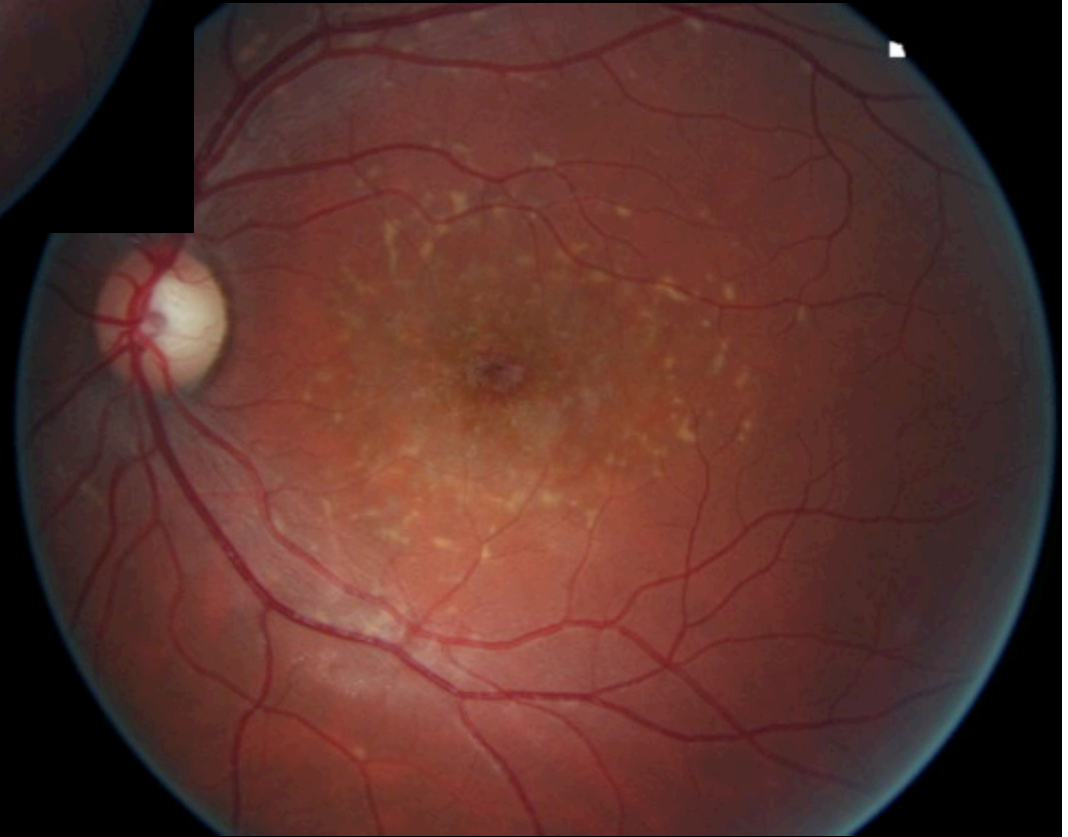
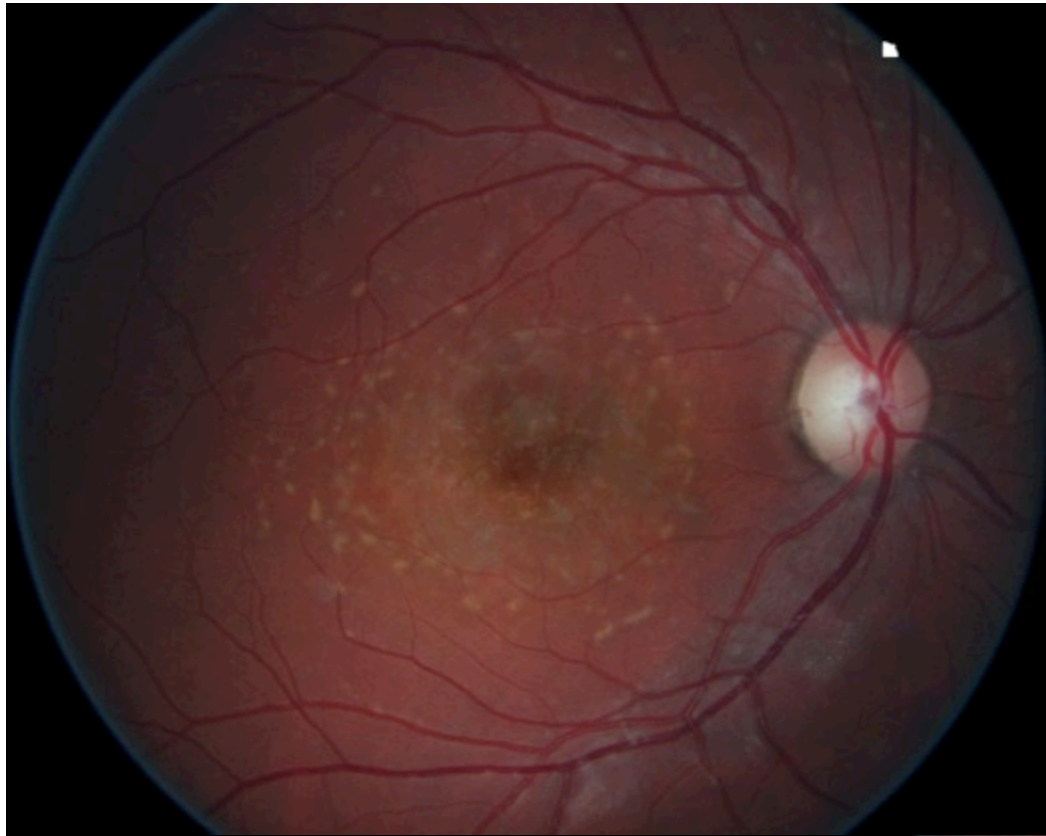


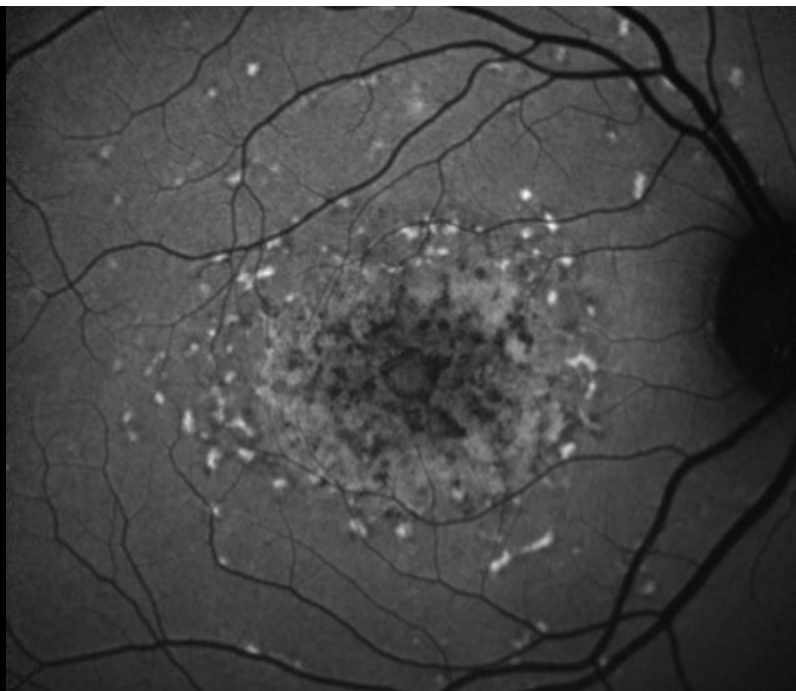
2008



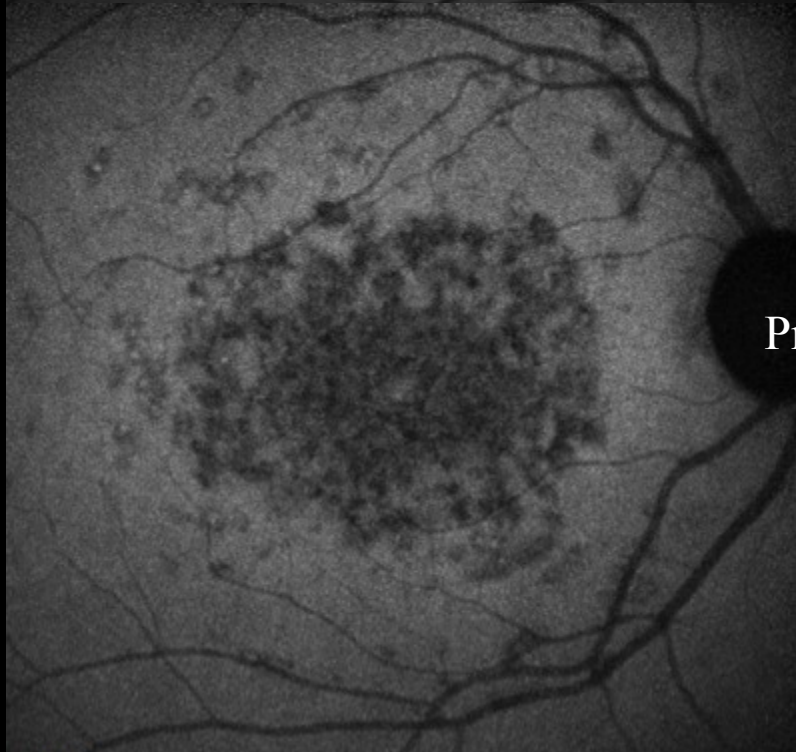
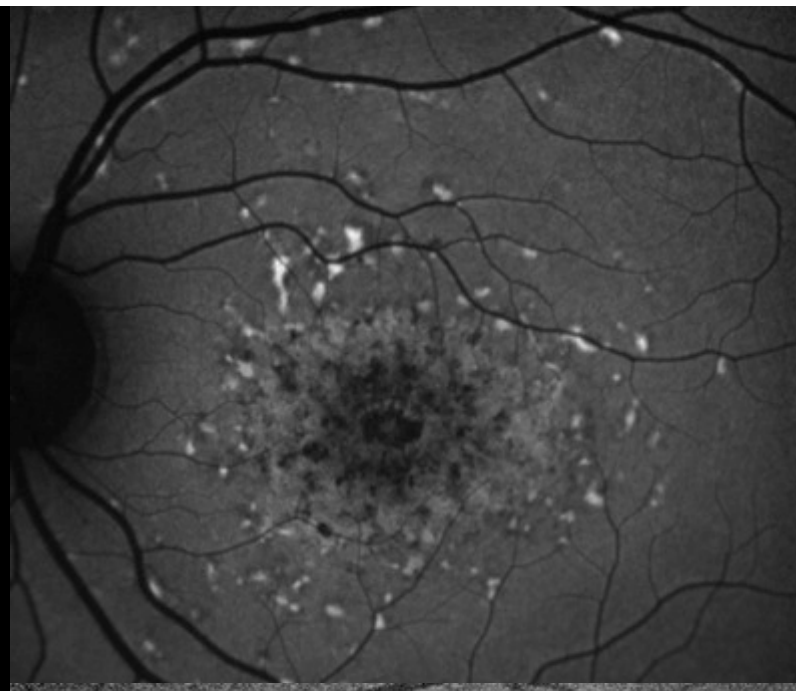


**Maladie de Stargardt/
silence choroidien**

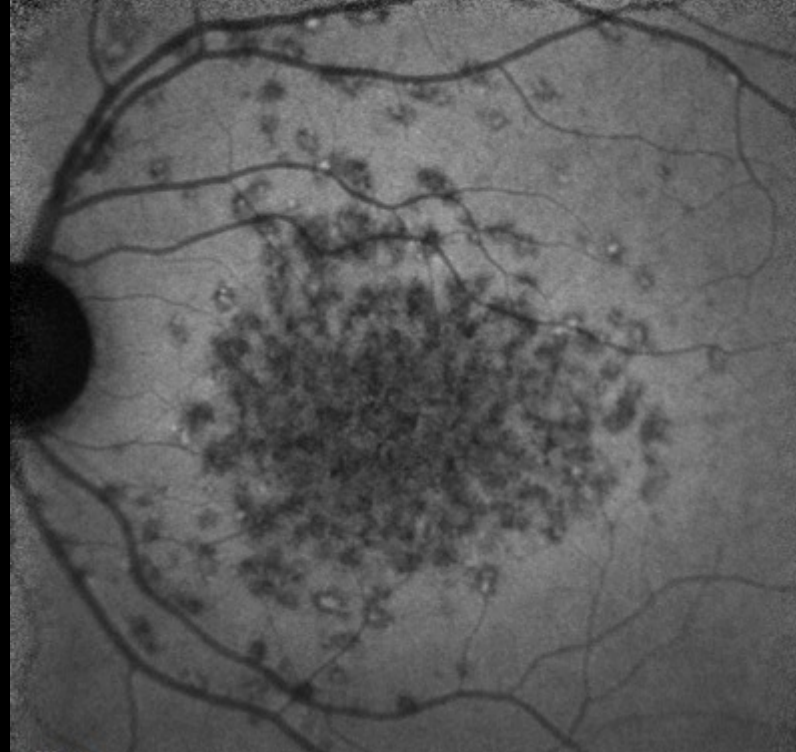


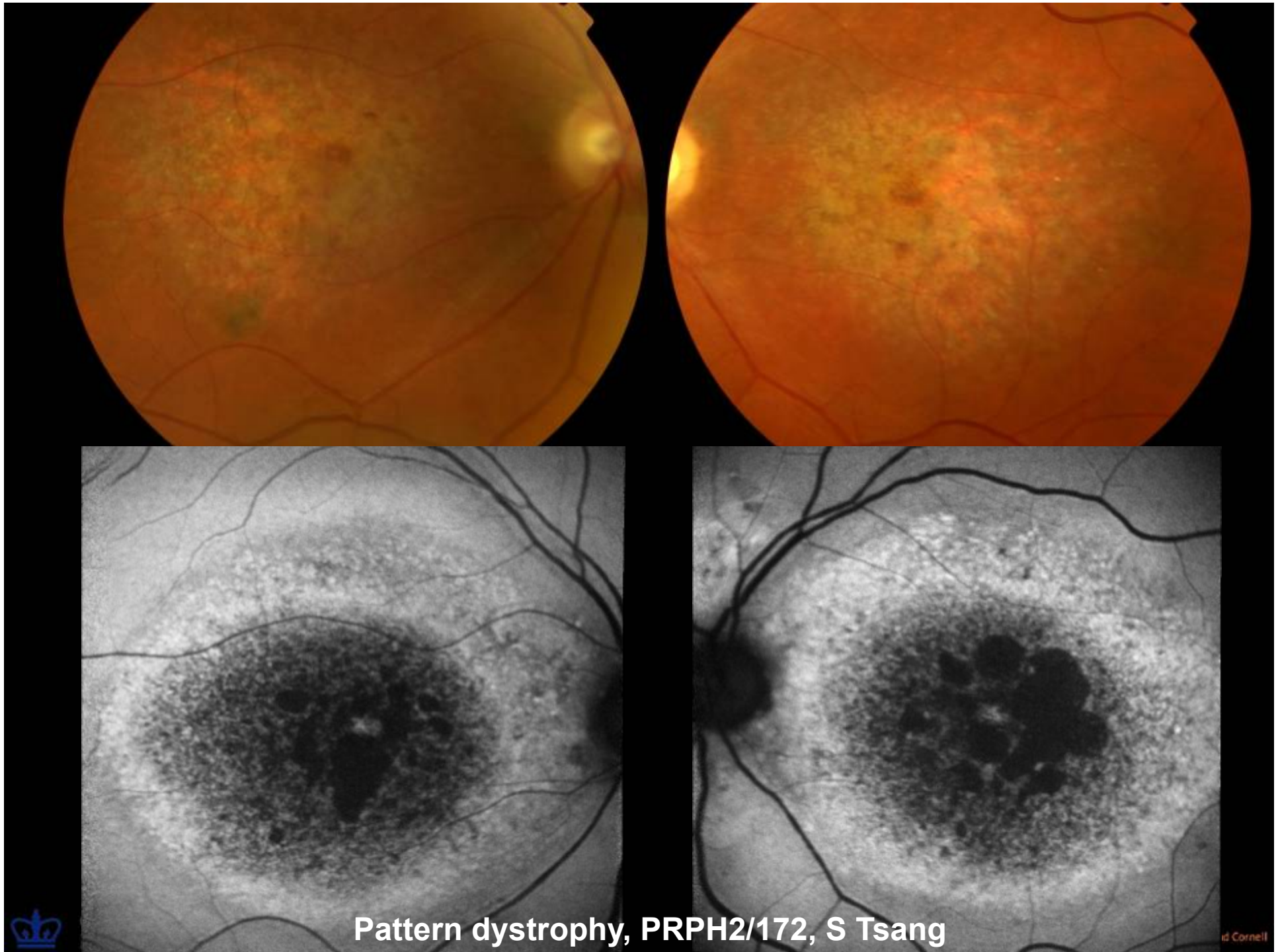


Bleu



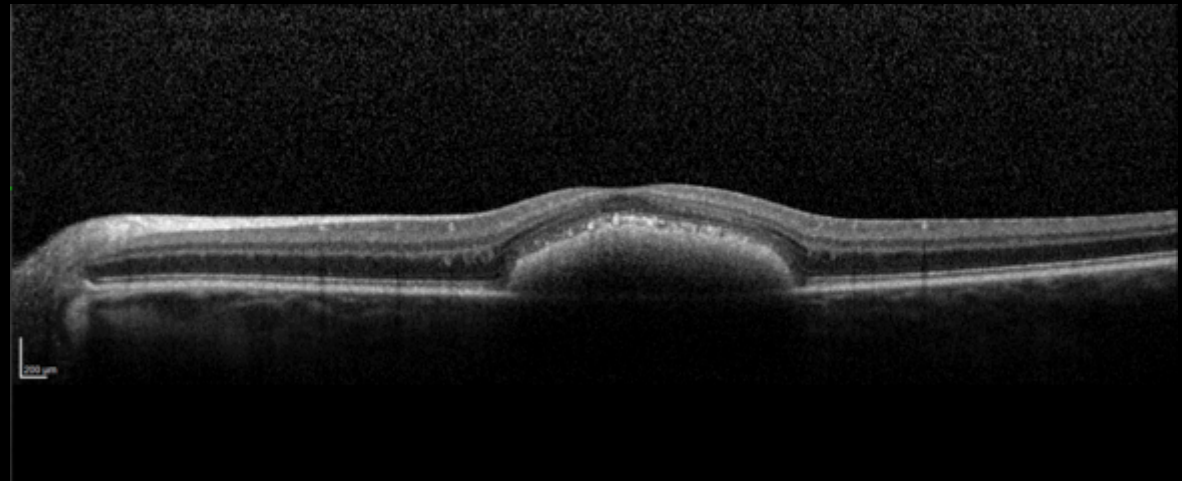
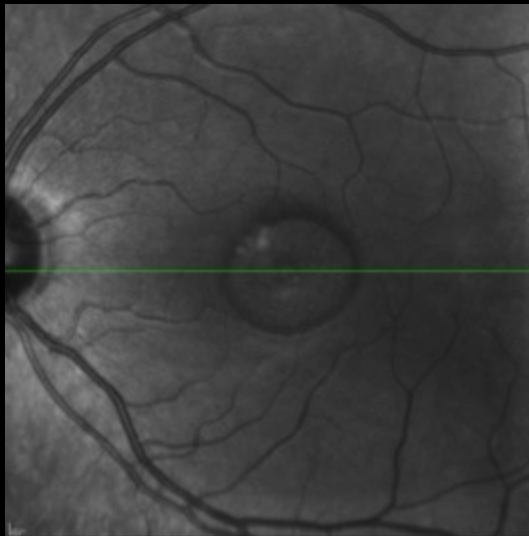
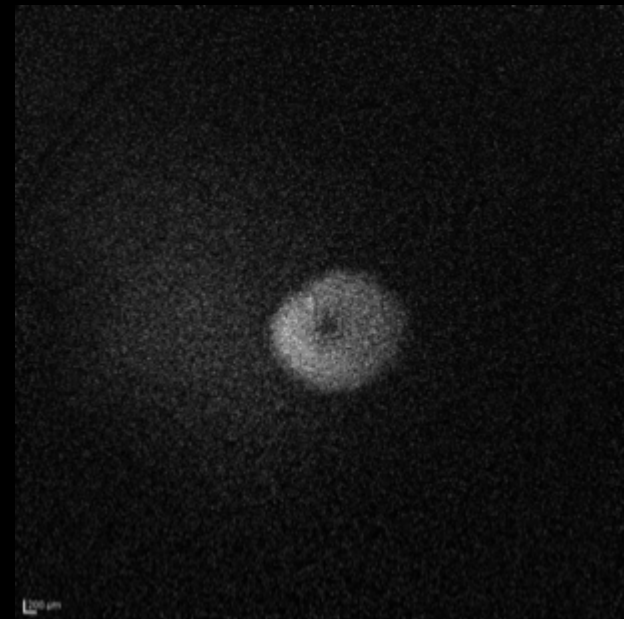
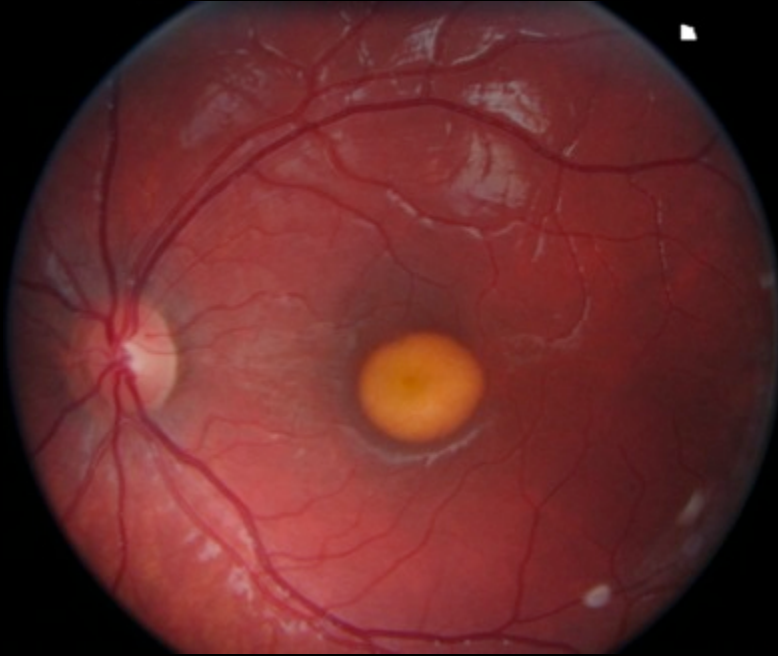
Proche IR



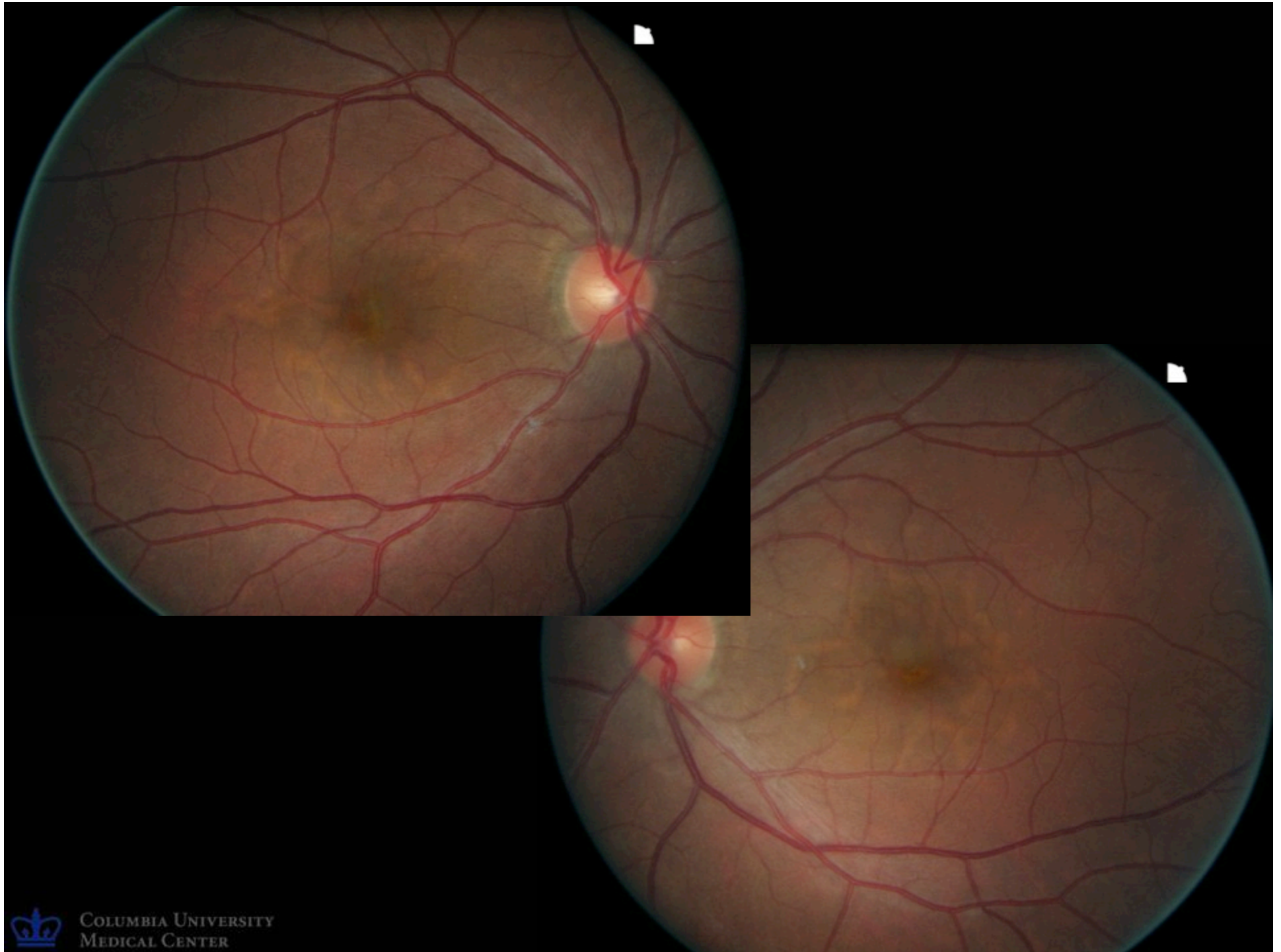


Pattern dystrophy, PRPH2/172, S Tsang

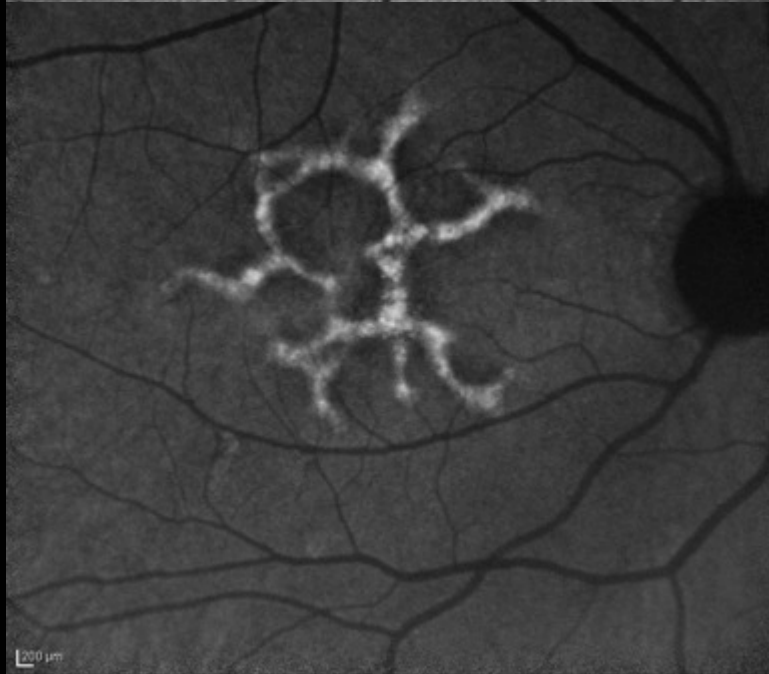
vitelliform

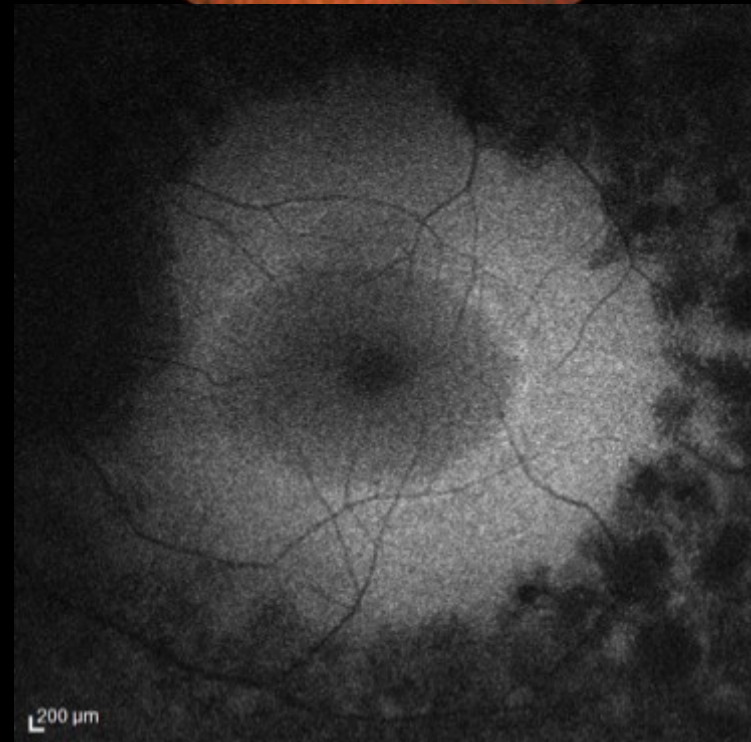
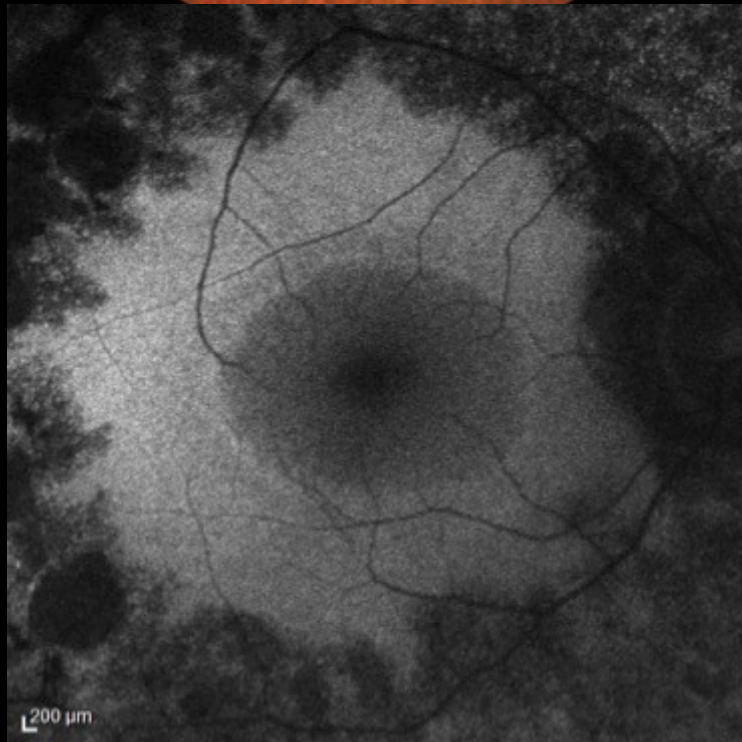
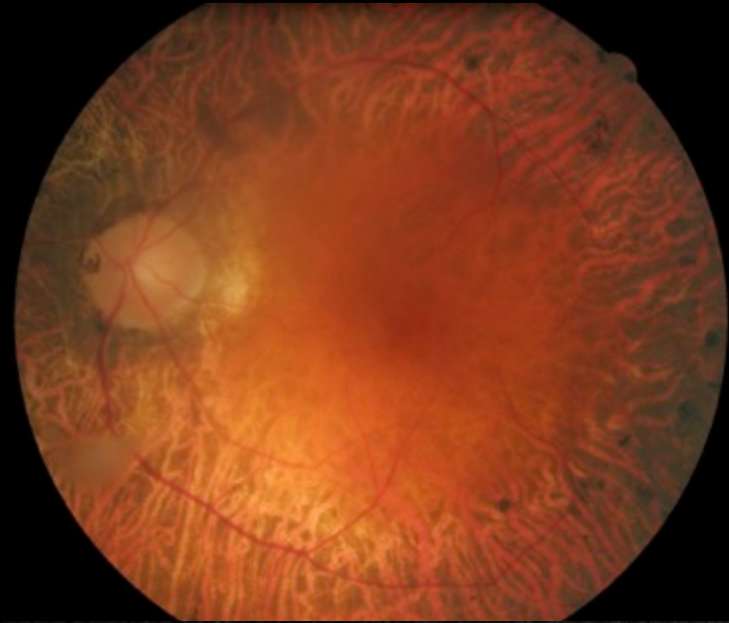
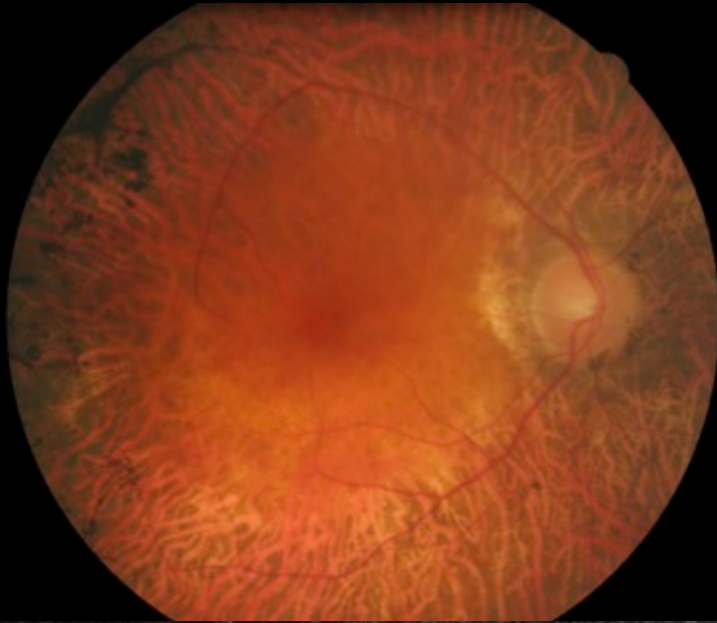


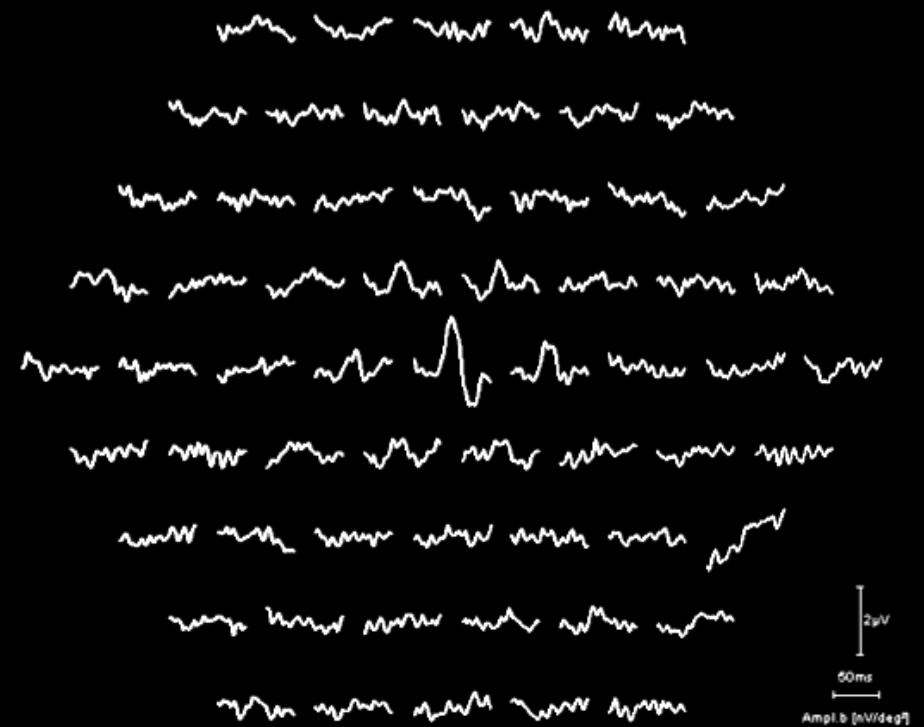
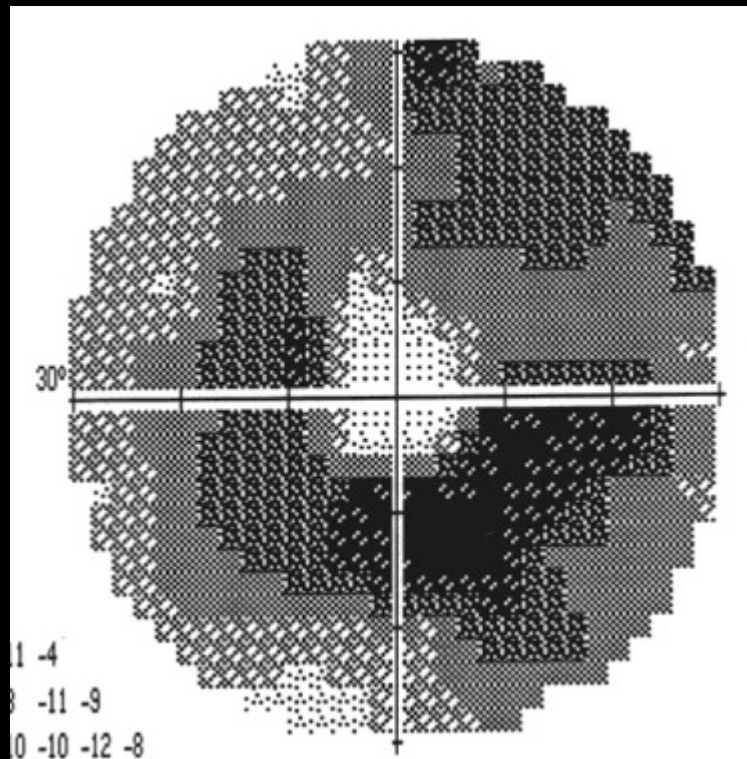
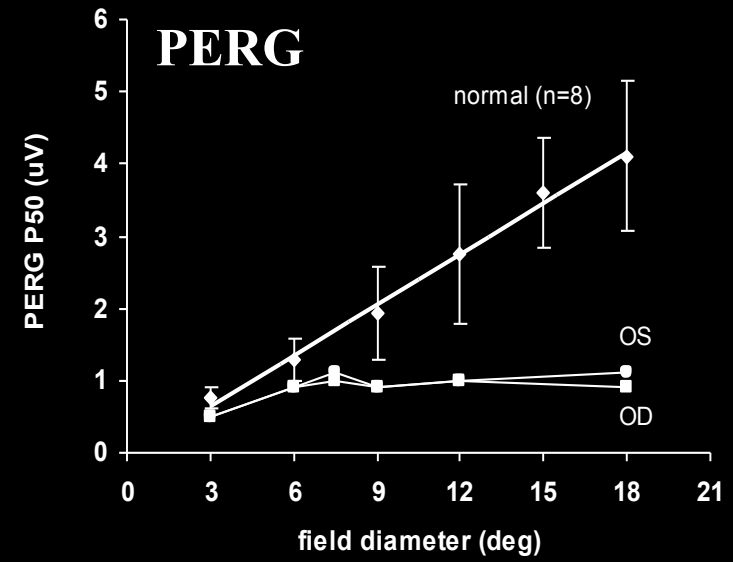
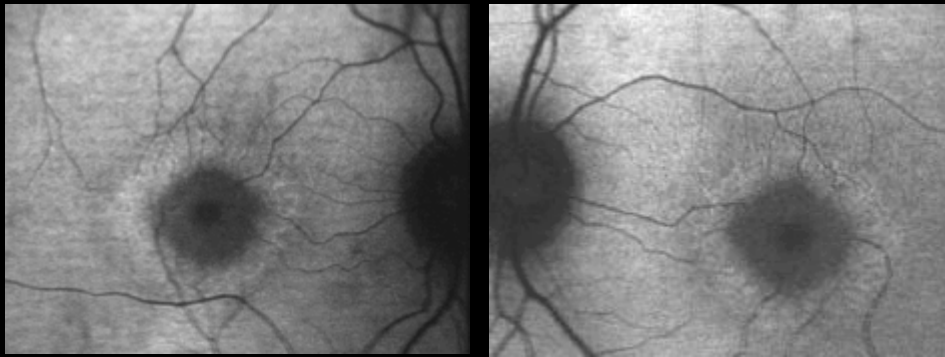
F 4 ans, CIC02569

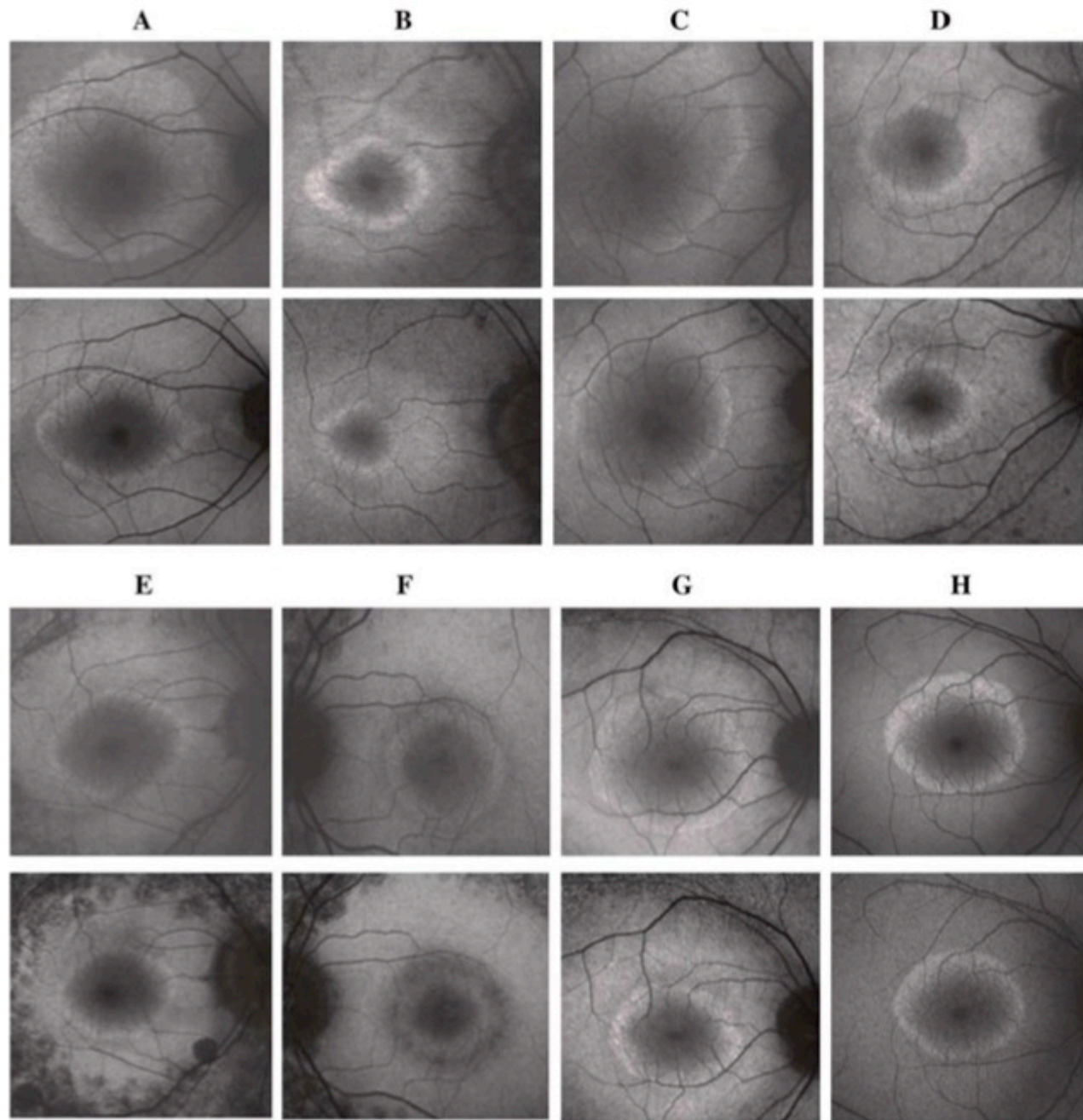


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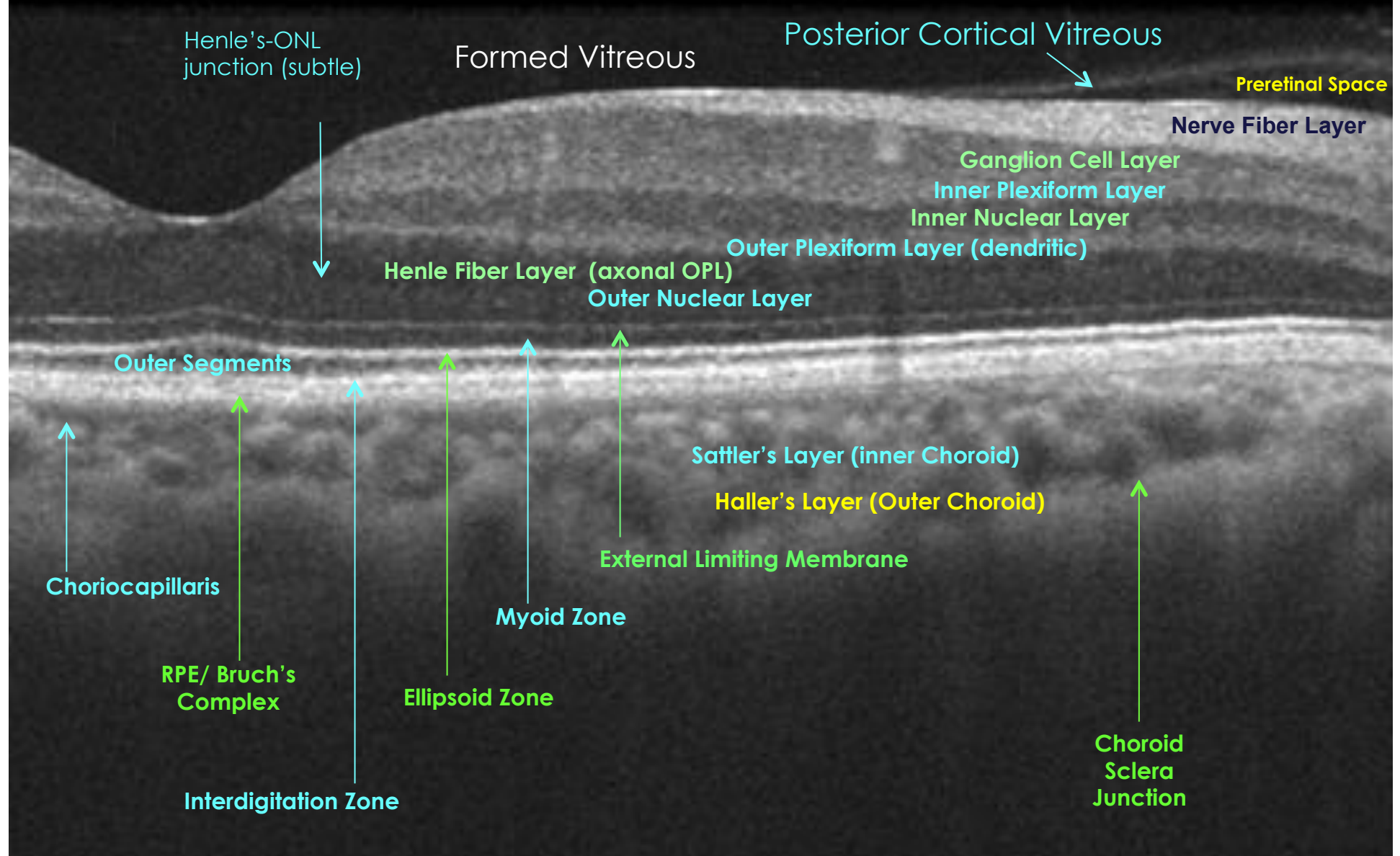


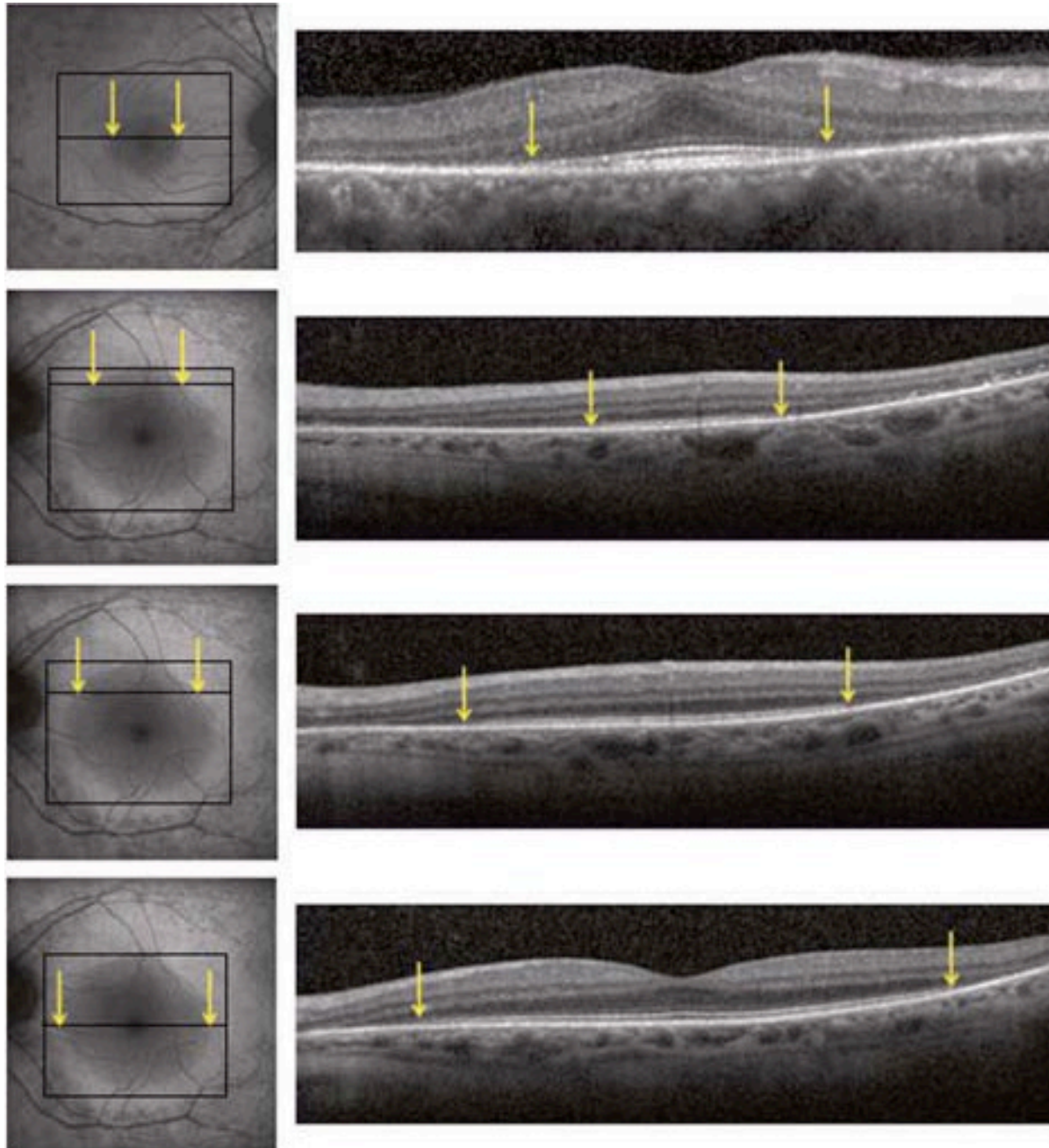




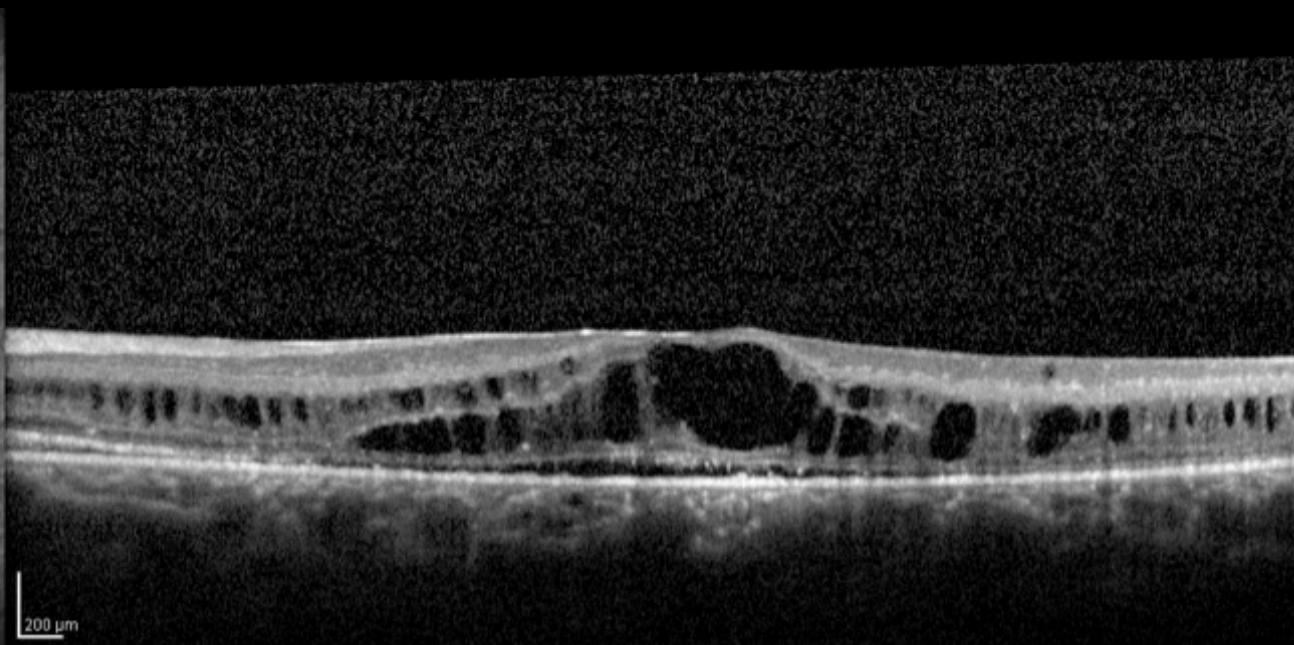
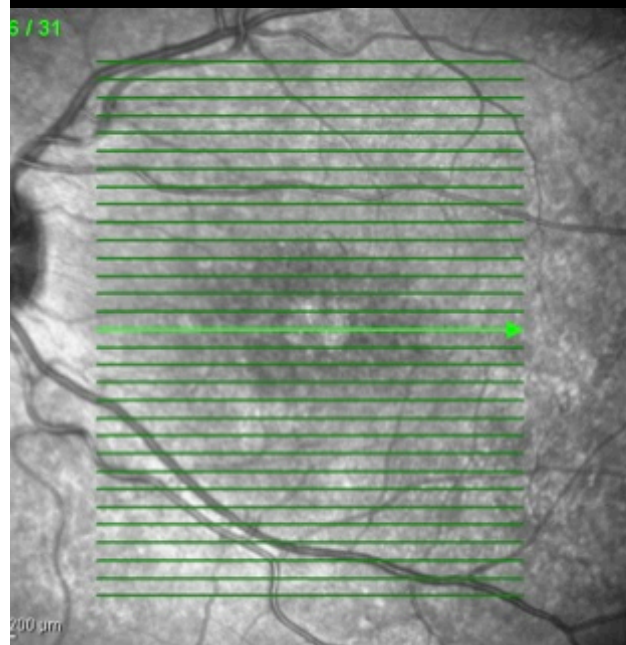
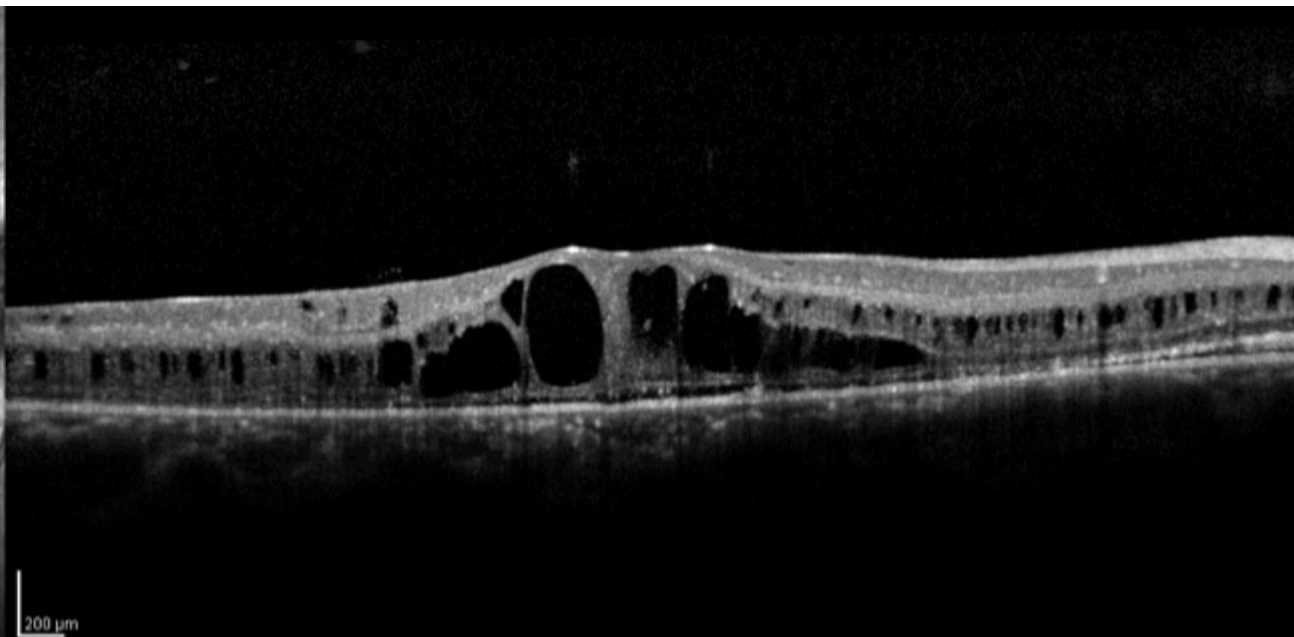
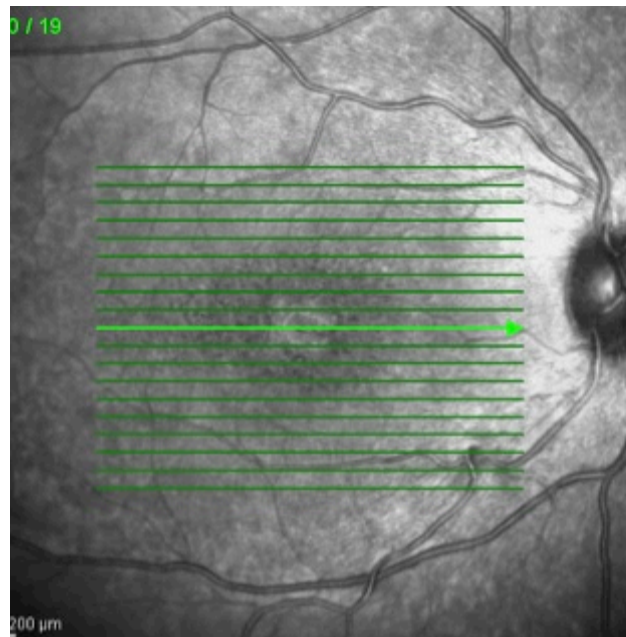
*Robson et al 2011, Retina,
Serial imaging and structure-
function correlates of high
density ring of fundus
autofluorescence in RP*

Pre-Euretina Normal OCT Classification



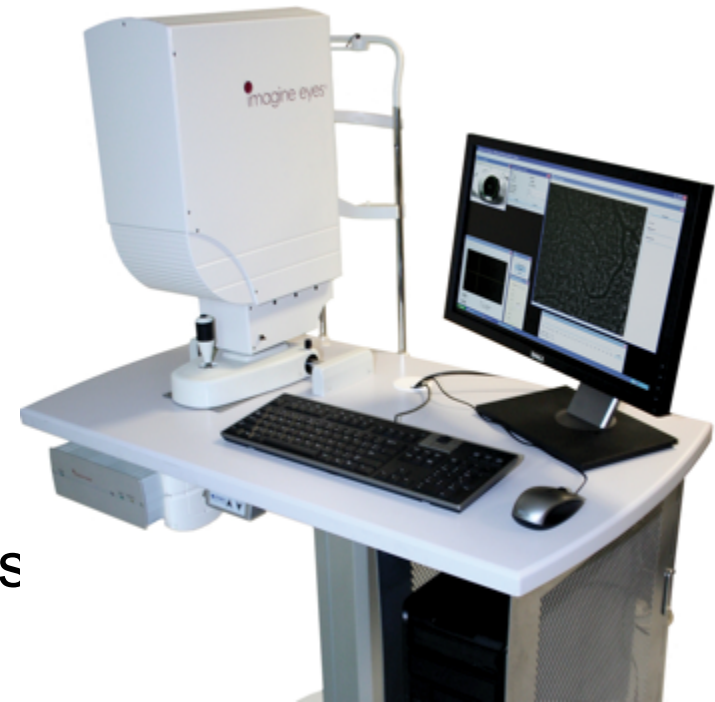


Robson et al 2011, Retina, Serial imaging and structure-function correlates of high density ring of fundus autofluorescence in RP



Adaptive Optics Retinal Camera

- 52-actuator electromagnetic deformable mirror
- 1024-lenslet Shack-Hartmann sensor
(both Imagine Eyes, France).
- SLD 750nm for optical aberrations
- LED 830nm for retinal imaging
- Image size : 4x4 deg at retina
- Simple & Compact for clinical use



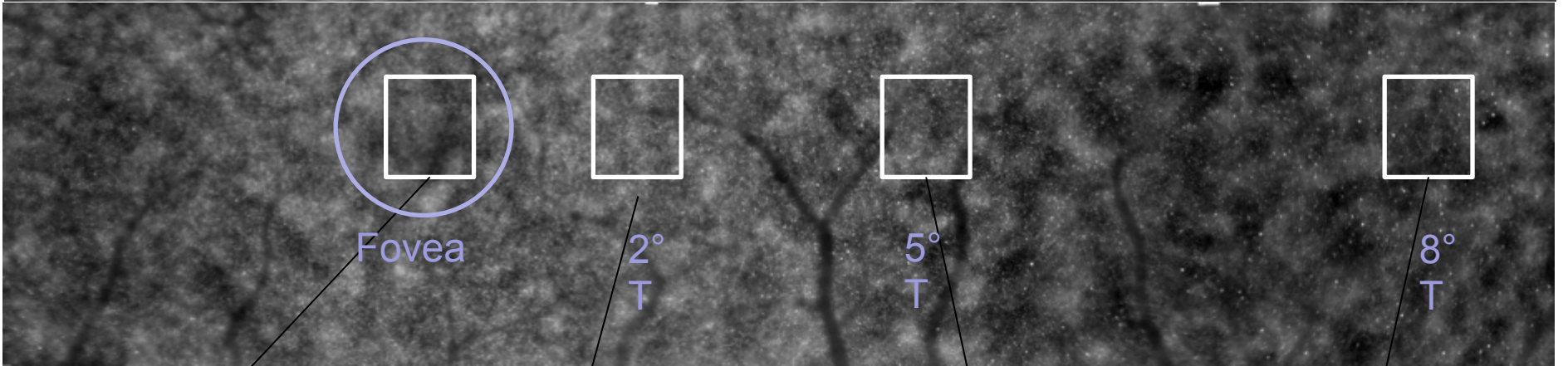
Adaptive Optics Retinal Camera
“rtx1”

By Imagine Eyes, Orsay, France





Normal subject , male, 41 year



nasal

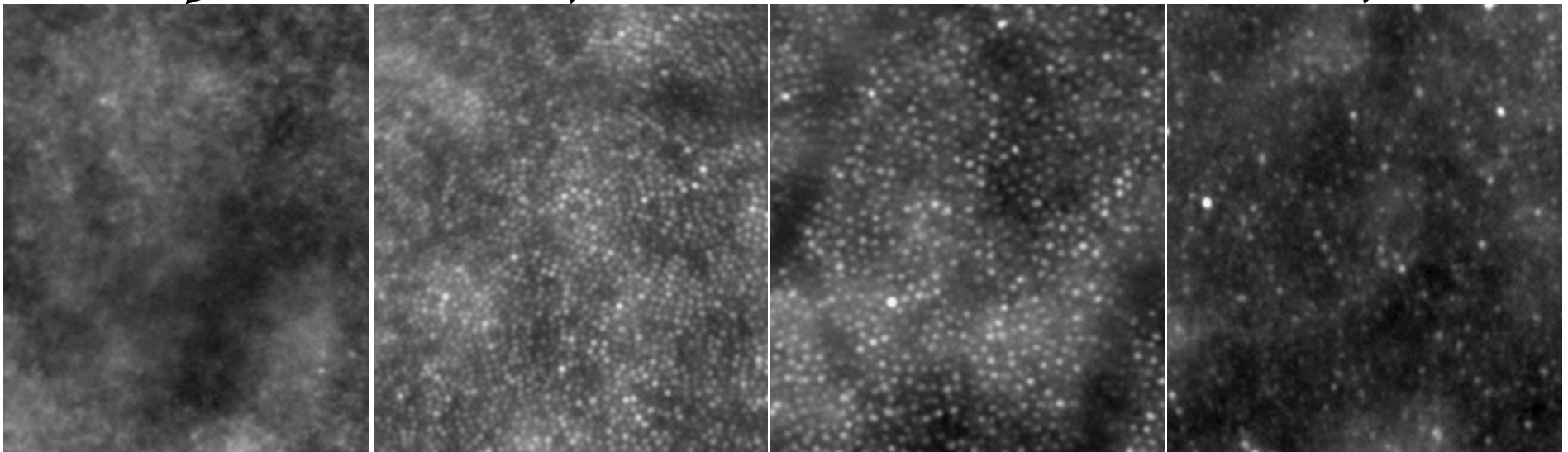
Fovea

$$\frac{2^\circ}{T}$$

5°
T

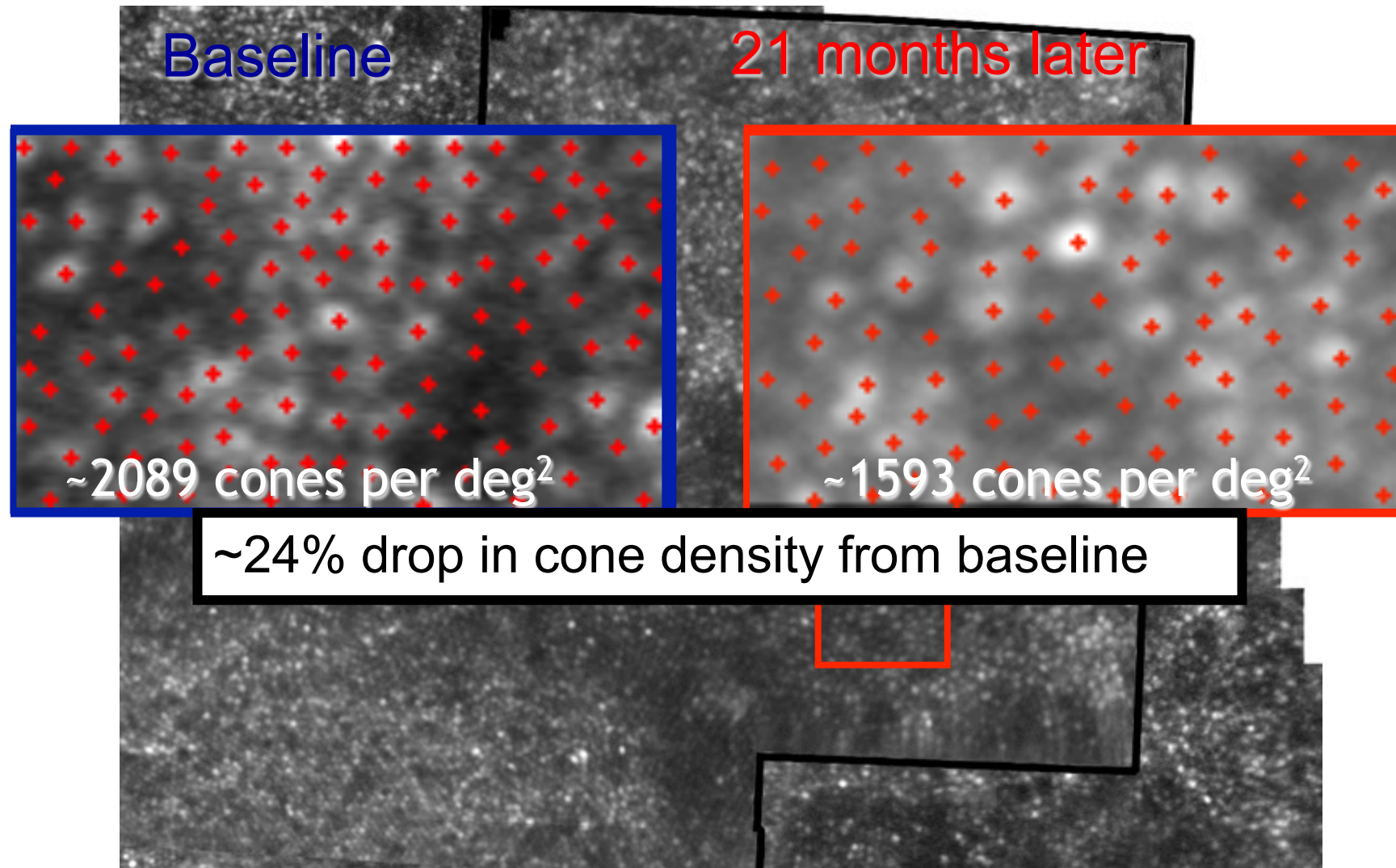
$$\frac{8^\circ}{T}$$

Temporal

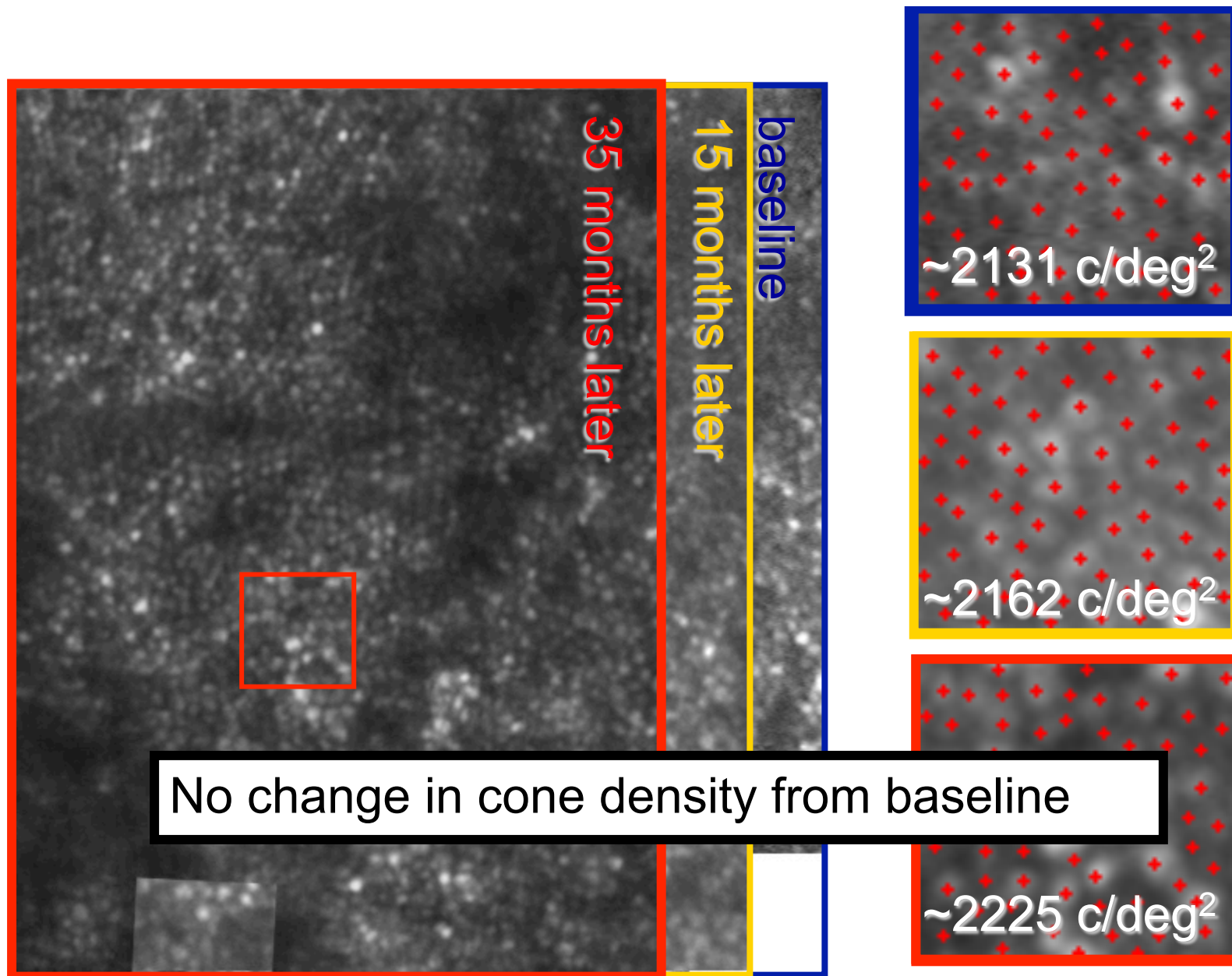


K. Gocho-Nakashima

CNTF and adaptive optic follow-up (J. Duncan, A. Roorda, UCSF)



CNTF treated eye, inferotemporal



Merci de votre attention...