

# 21<sup>st</sup> Century Retina Care

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University of the Incarnate Word



# 21<sup>st</sup> Century Retina Care

- Online notes
  - [richardtrevino.net](http://richardtrevino.net)
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  - [rctrevin@uiwtx.edu](mailto:rctrevin@uiwtx.edu)
- Disclosures
  - None



# 21st Century Retina Care

- Instrumentation
- Posterior Seg Disease
  - Clinical Features
  - How to Monitor
  - When to Refer



# Self Assessment Quiz

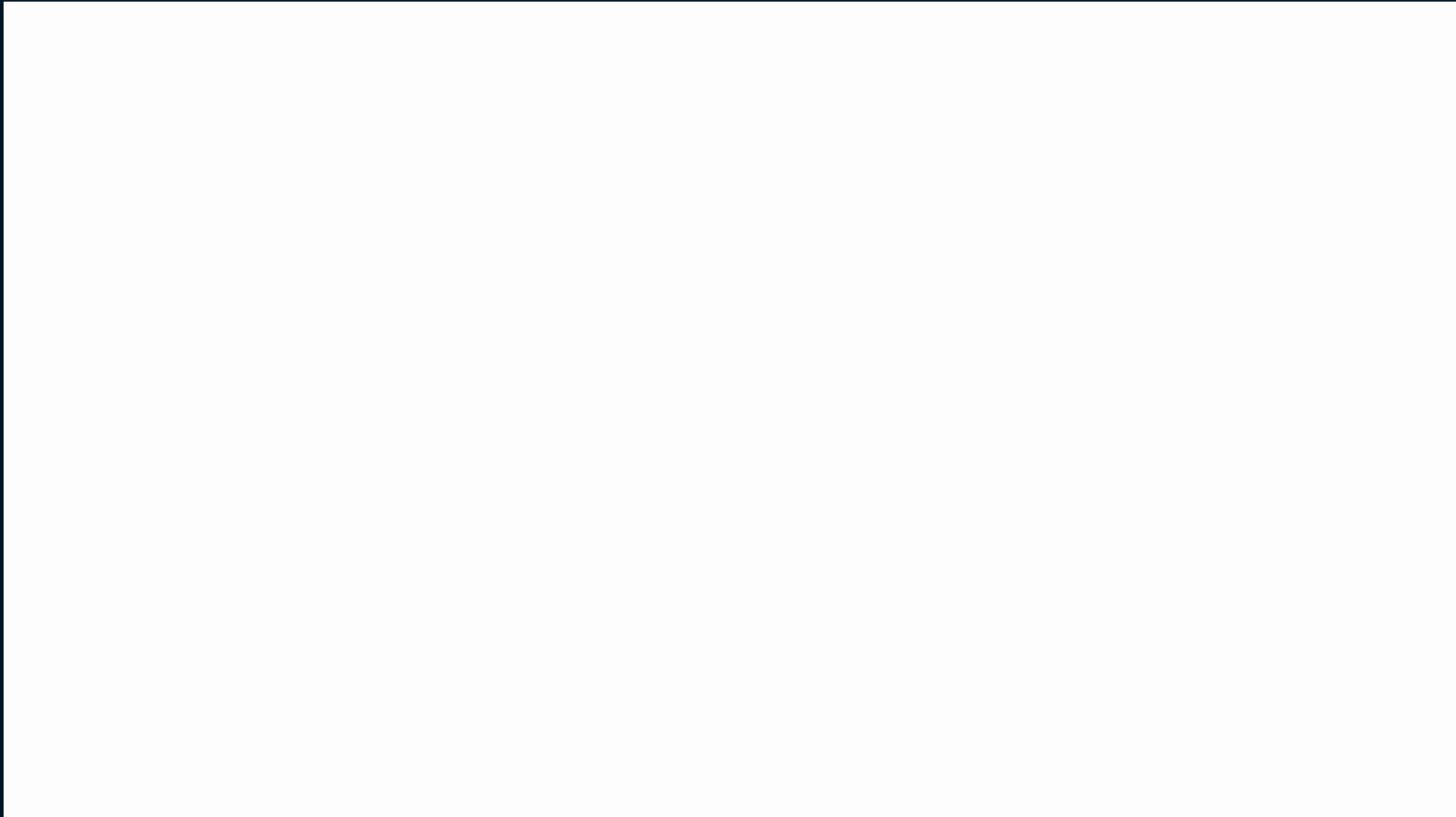
Are you attending this CE course?

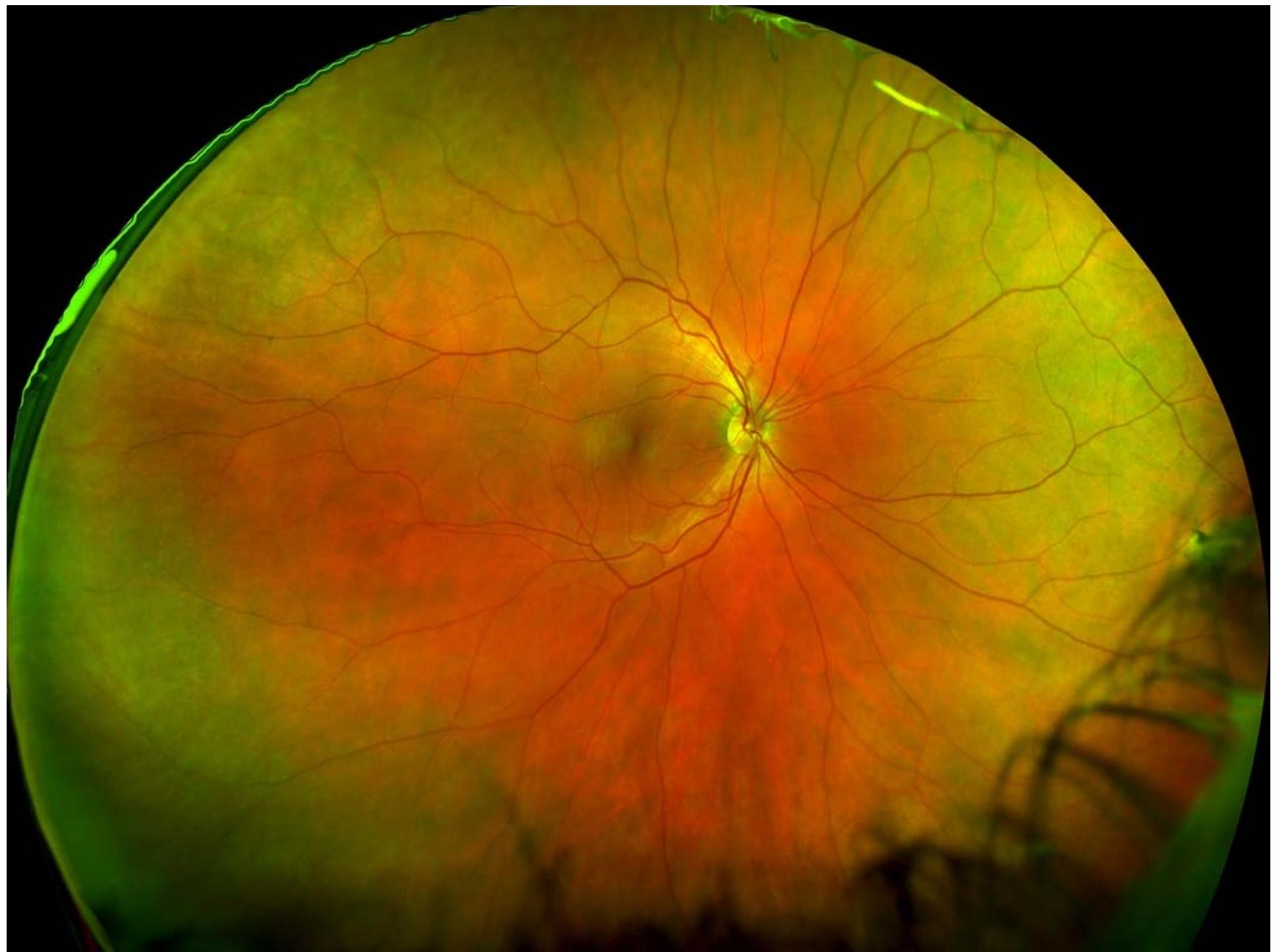
- If so, award yourself 1 point
- If not, award yourself 0 points

# Instrumentation

- Wide-angle Imaging
  - **Scanning laser ophthalmoscopy**
  - Features
    - 200° field of view (80% of the fundus)
    - Multi-modal imaging: Photography, Autofluorescence, Red-free, FA
  - Examples
    - Optos “Optomap”
    - Heidelberg SPECTRALIS & HRA2
    - Zeiss Clarus

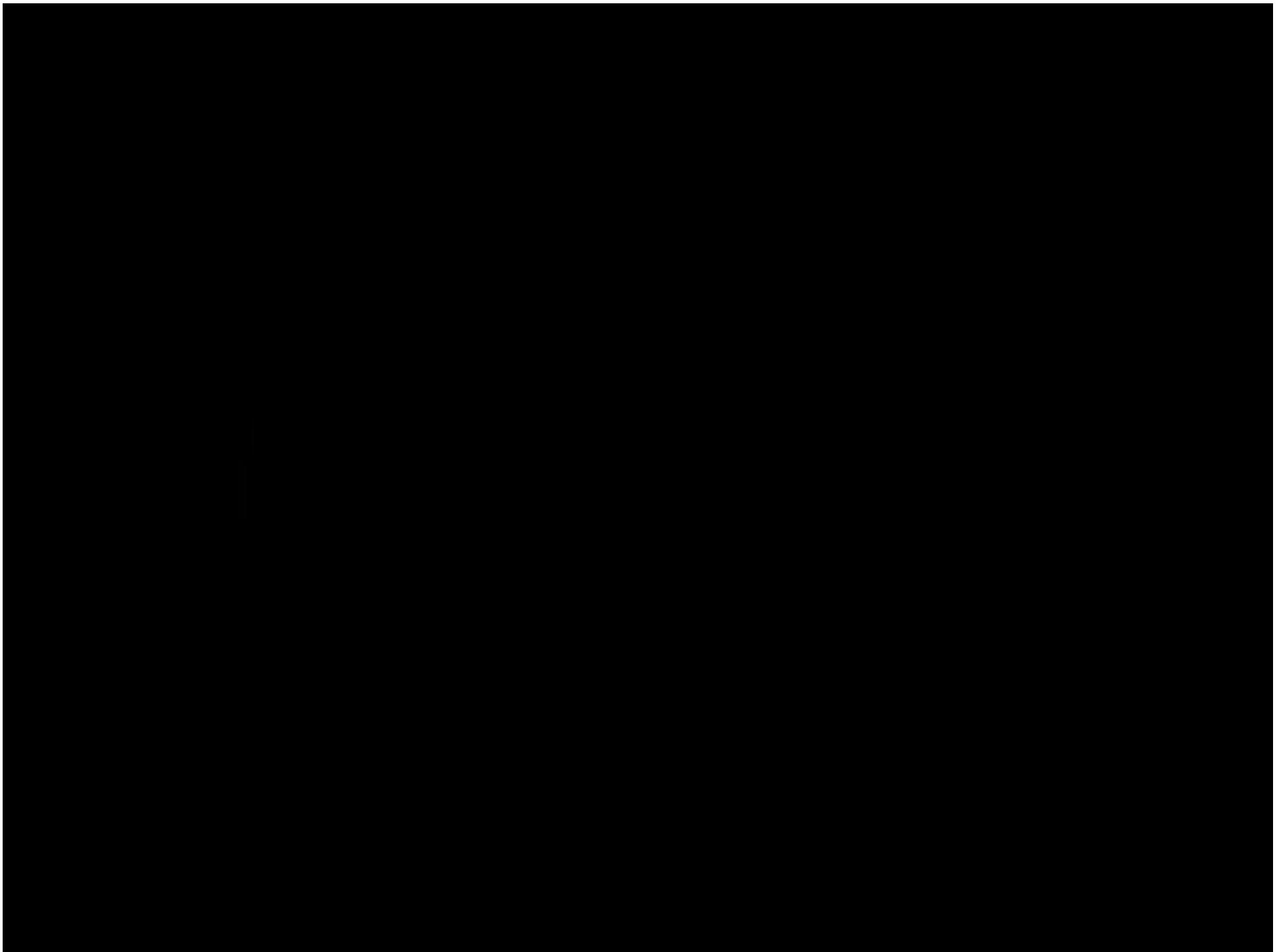
# Ultra-Wide Field Photography











# Is UWF imaging a substitute for DFE?

- No. CMS has declared that fundus photography is not a substitute for DFE
- Most insurance (incl Medicare) will not cover photography as a screening procedure
- Diabetic telemedicine studies comparing photos with DFE indicate good agreement, and superiority to undilated DO



NEW!

# Instrumentation

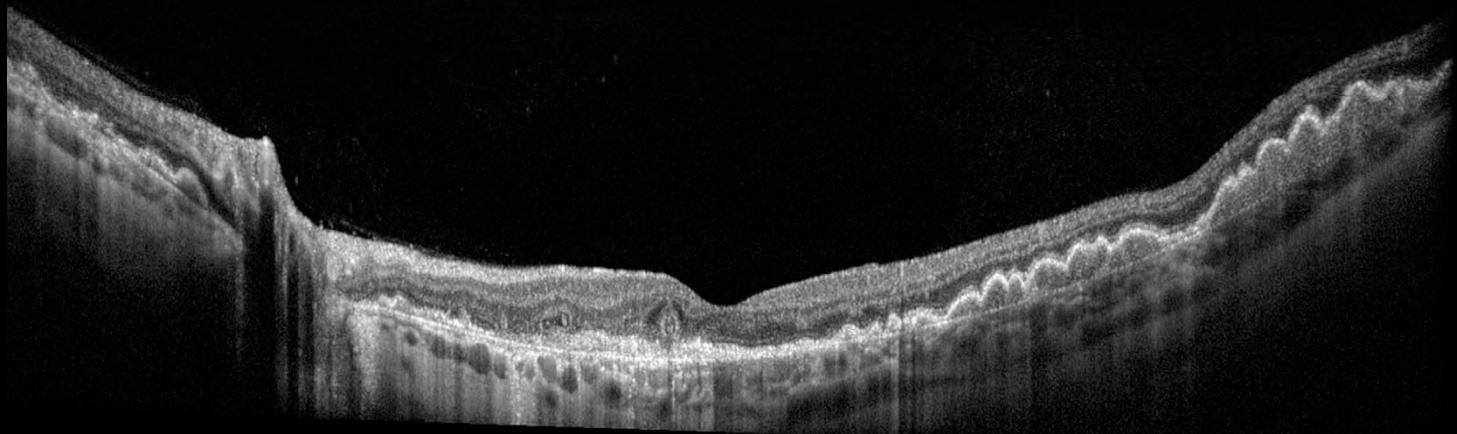
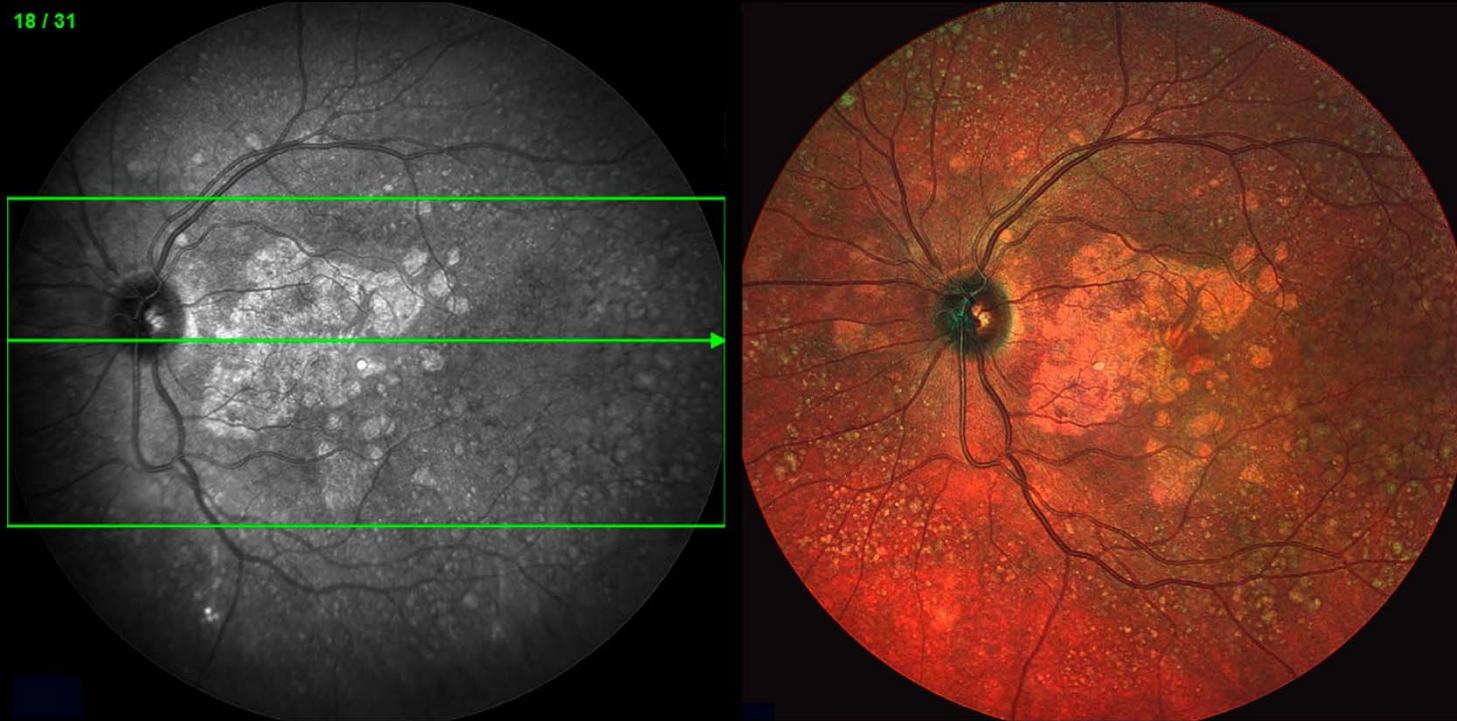
- **Wide-angle OCT**
  - Features
    - Wide-angle and peripheral SD-OCT imaging
    - High-speed scanning. Similar time as standard scan
    - Image stabilization. High resolution images
  - Examples
    - Optovue Avanti ( $40^\circ$ , 12mm)
    - Heidelberg Spectralis ( $55^\circ$ )
    - Zeiss Plex Elite ( $56^\circ$ )

OPTOVUE

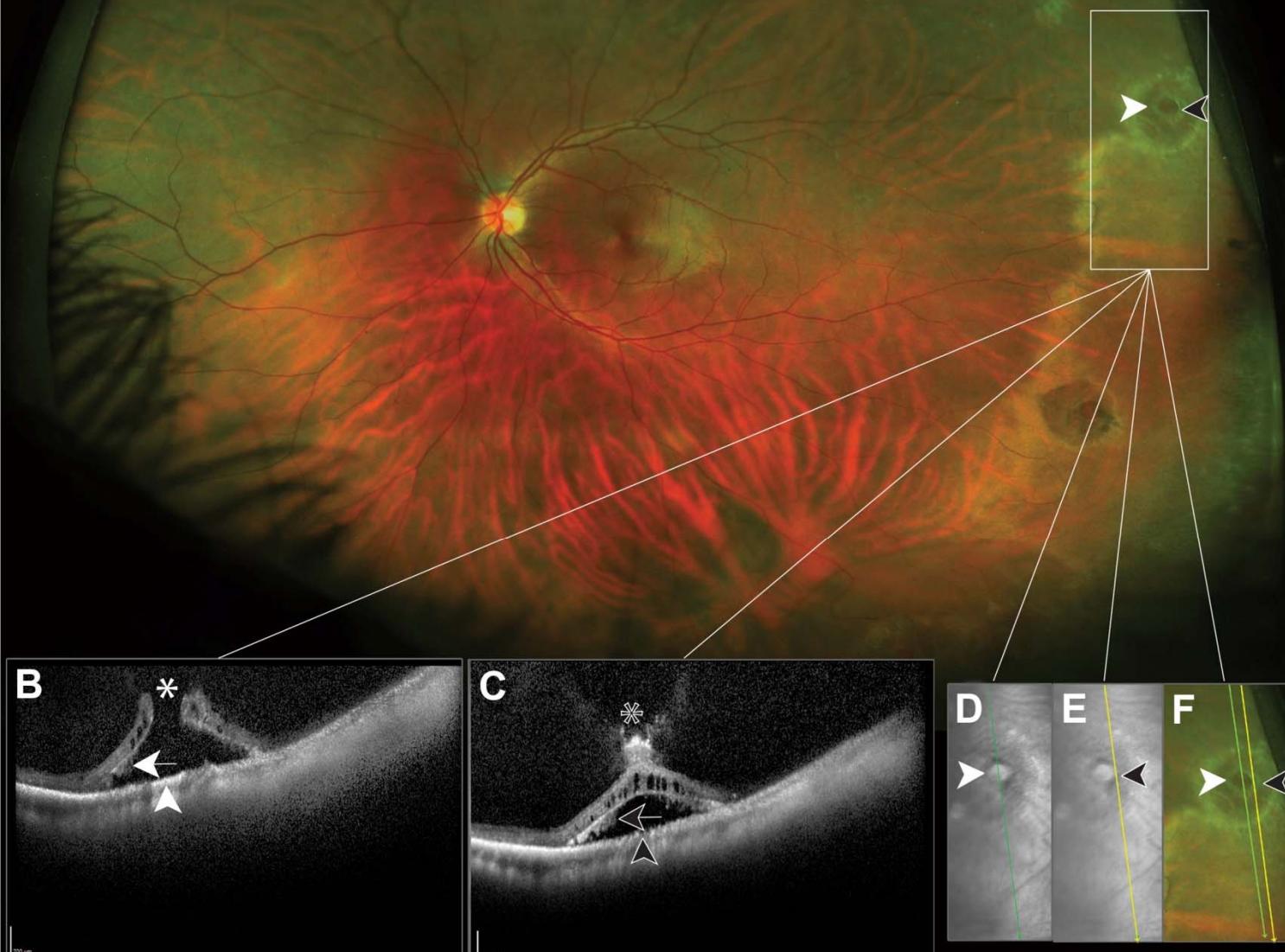
NORMAL

HIGH MYOPIA

18 / 31



SPECTRALIS – Dry AMD

**A****SPECTRALIS – Atrophic hole**

# Instrumentation

- **Fundus Autofluorescence**
  - Fluorescence of fundus pigments, especially lipofuscin
  - Lipofuscin is a toxin found in the RPE
  - Hypofluorescence: Non-functional RPE
  - Hyperfluorescence: Excessive lipofuscin

# Fundus Autofluorescence

- Retinal dystrophies (RP, Stargart's, etc)
- AMD (especially geographic atrophy)
- Choroidal nevus vs melanoma
- Plaquenil screening
- ONH drusen
- Others (central serous chorioretinopathy, diabetes, MacTel-2, etc)

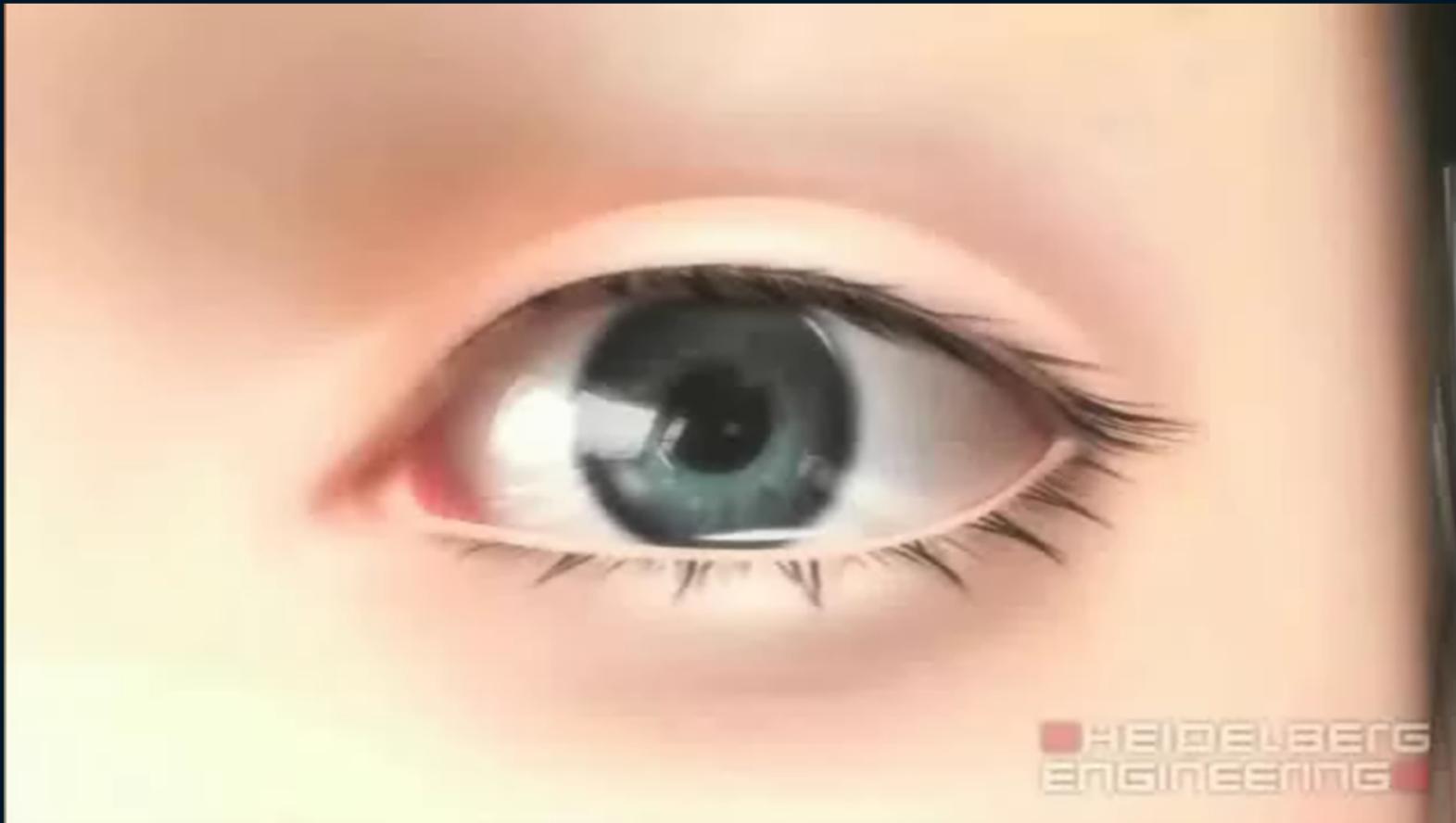
Lipofu  
When  
amour



At so  
lipofu

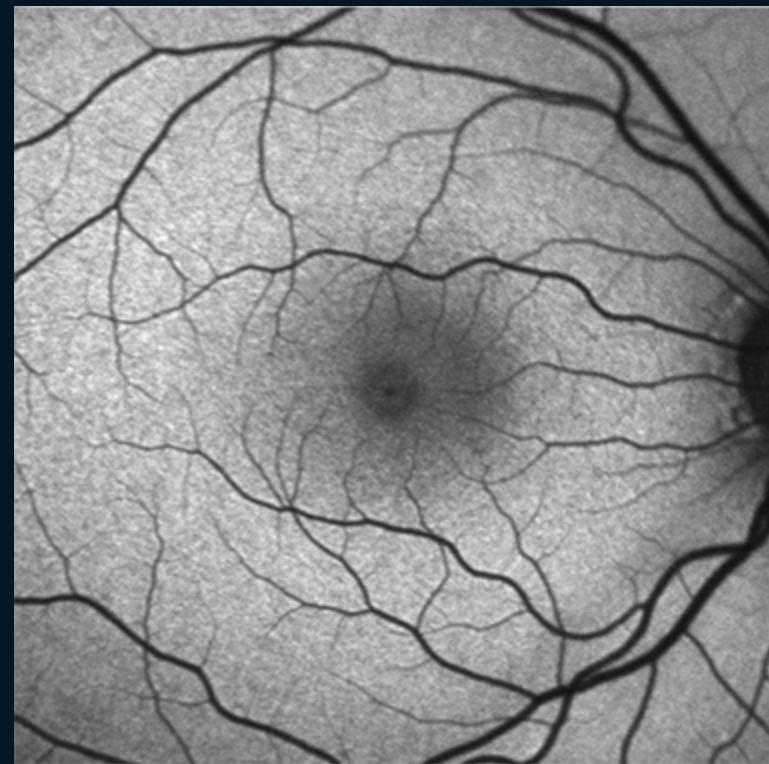
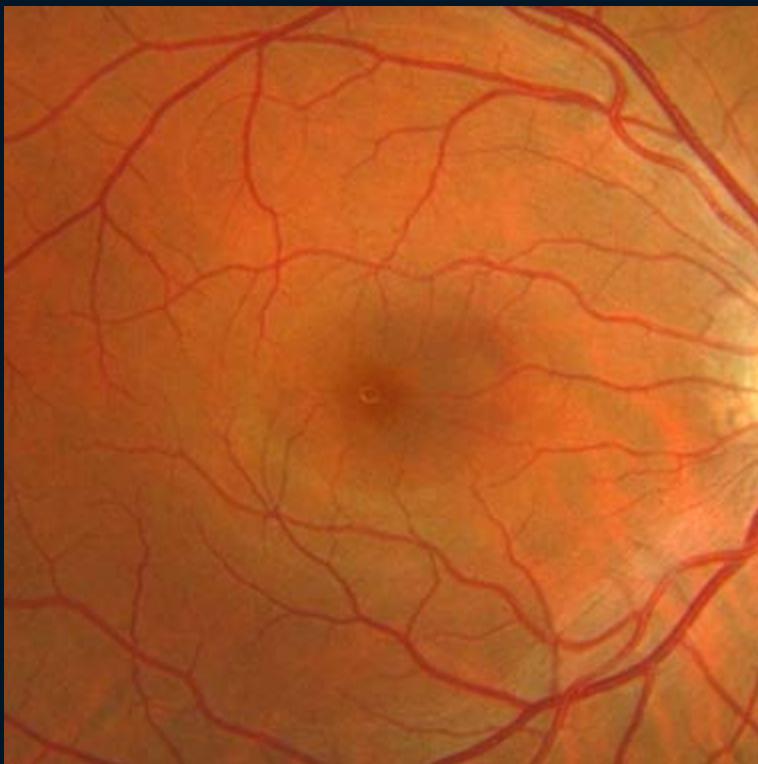
Lipofuscin is toxic, knowing location and over accumulation can be an indicator of cell health.

# Fundus Autofluorescence



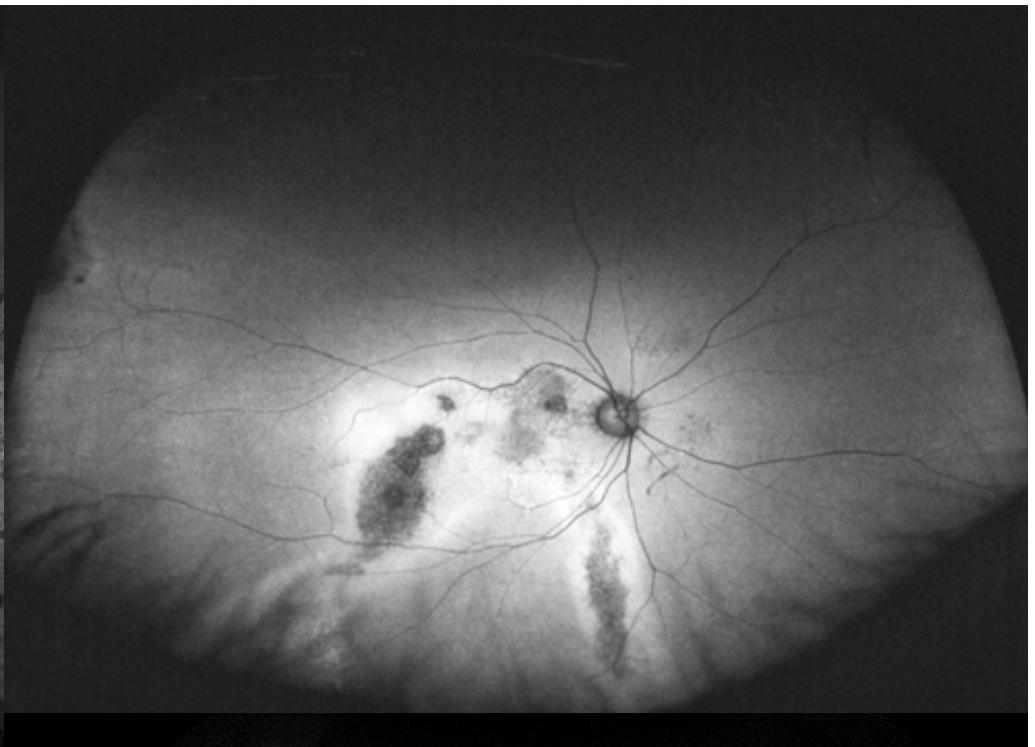
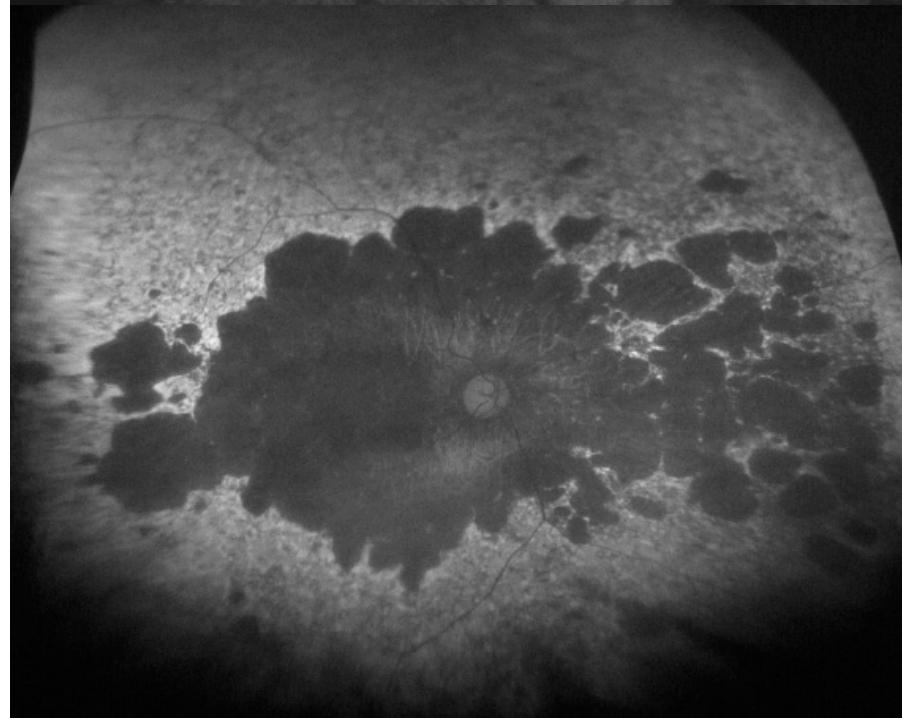
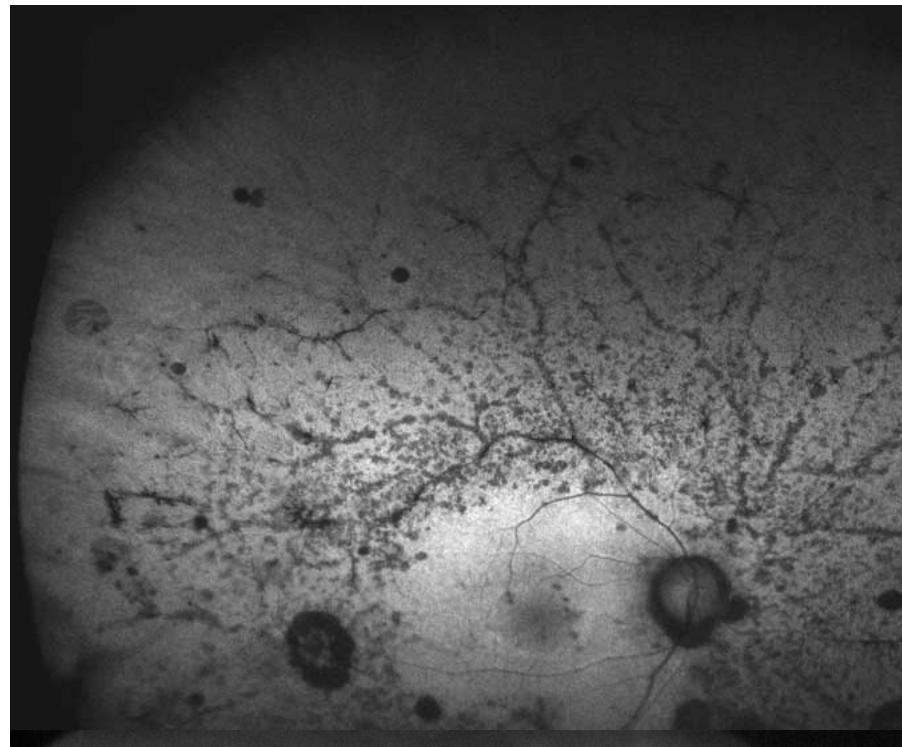
HEIDELBERG  
ENGINEERING

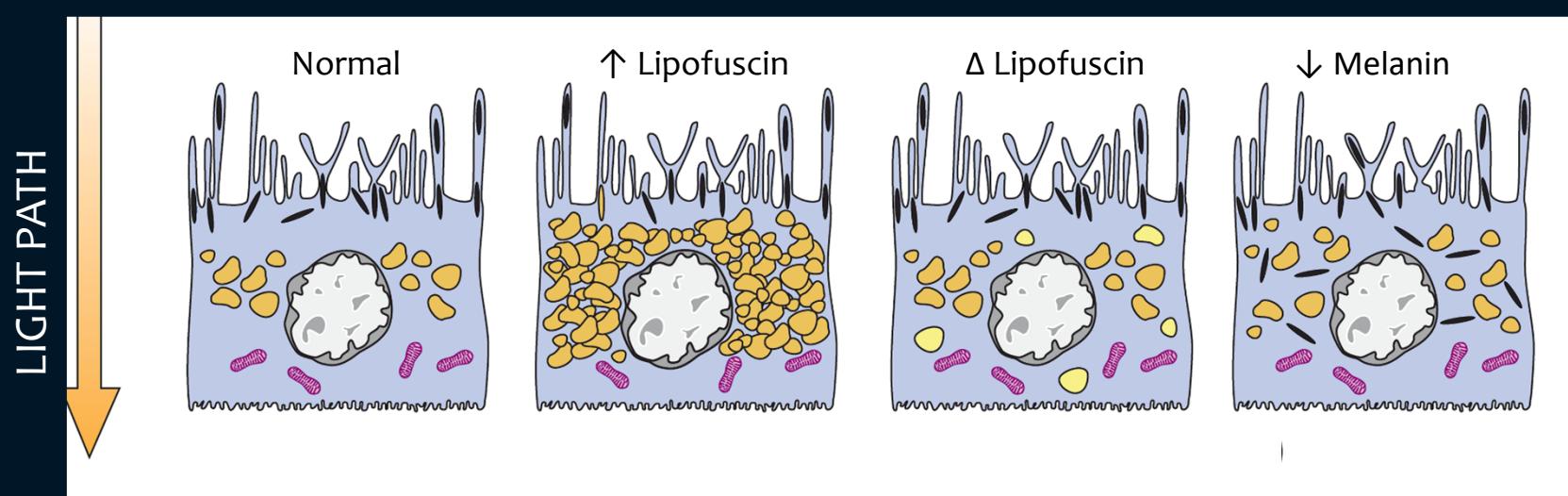
# Normal FAF



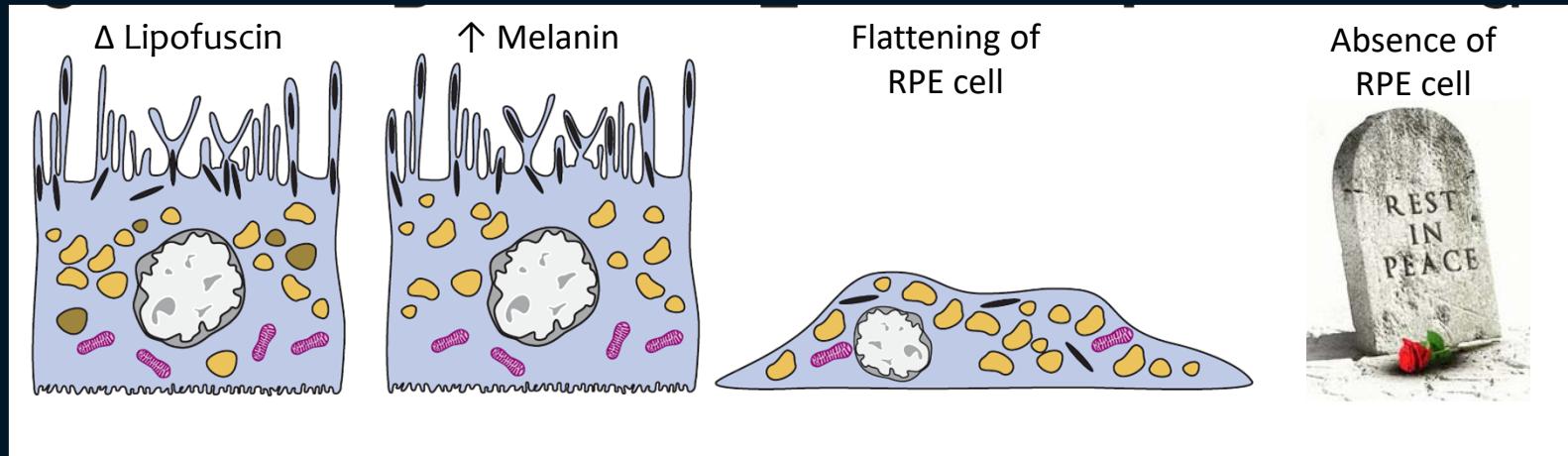


Retinitis pigmentosa





## Potential causes of HYPERAUTOFLOURESCENCE



## Potential causes of HYPOAUTOFLOURESCENCE

IOVS 2019; 60:2481

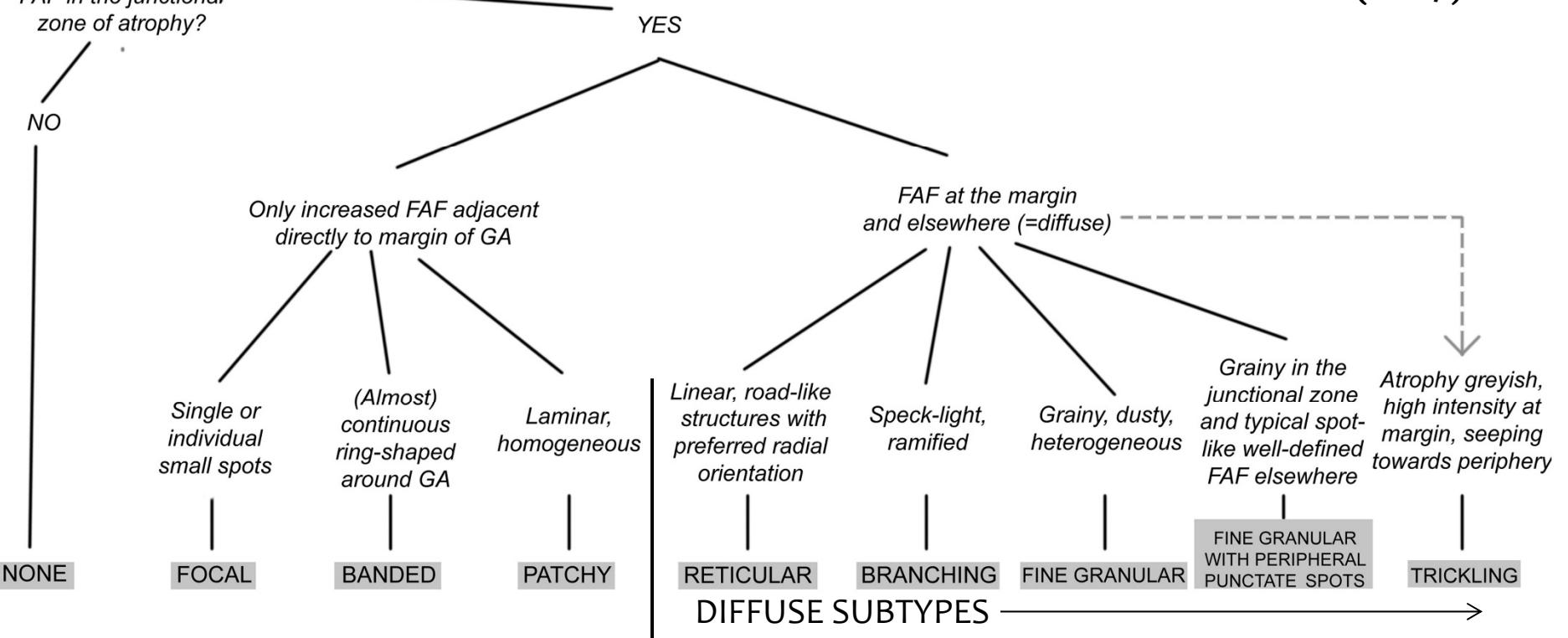
# FAF in Dry AMD

- Holz (2007)
  - FAF patterns impact disease progression and may serve as a **prognostic indicator**
- Gain Study (2015)
  - FAF patterns represent different **stages of GA**.
  - As GA enlarges, the FAF pattern may change

Holz FG, et al. Am J Ophthalmol. 2007;143.  
The GAIN Study. Am J Ophthalmol. 2015;160: 345–353.e5.

Is there any increased FAF in the junctional zone of atrophy?

Holtz (2007)

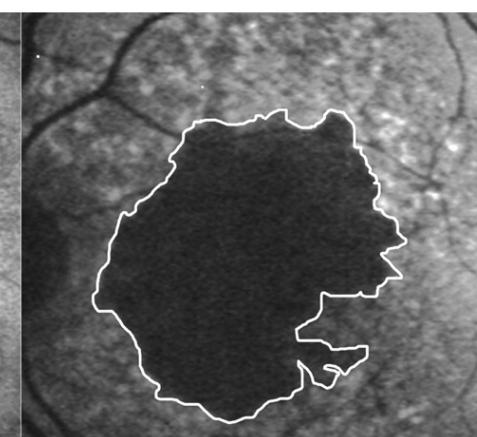
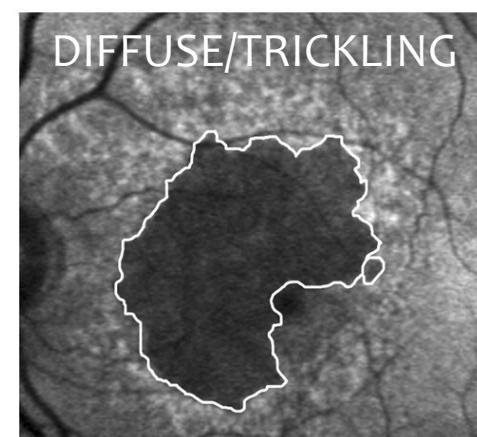
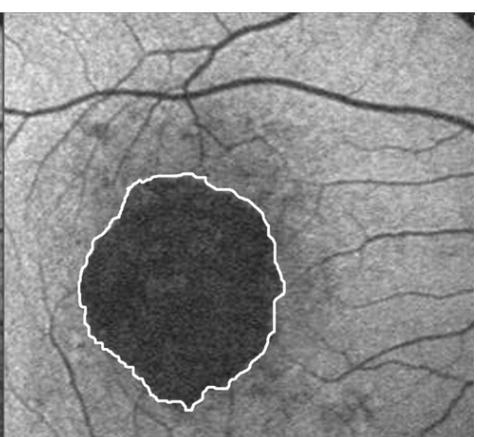
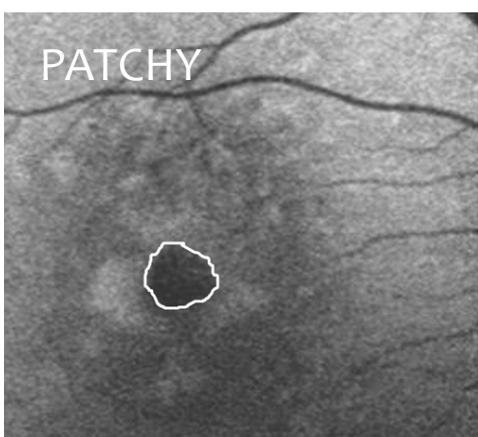
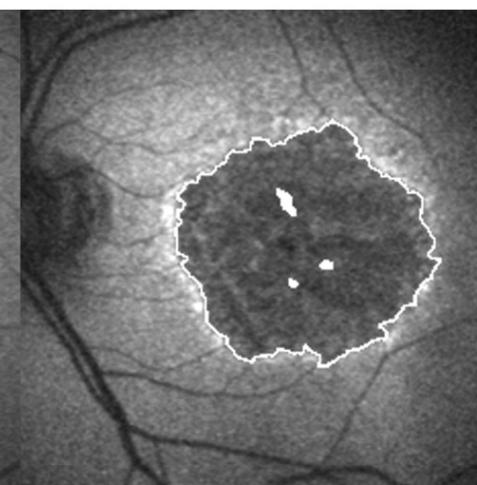
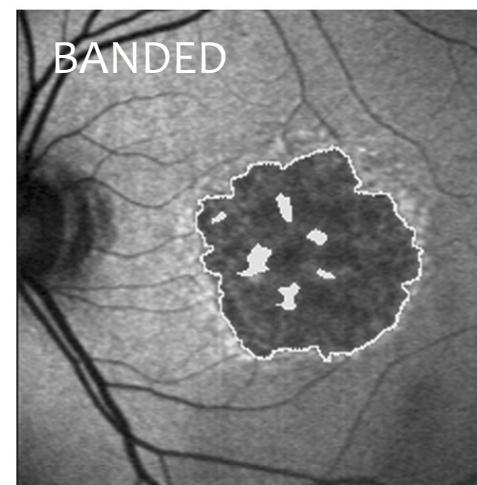
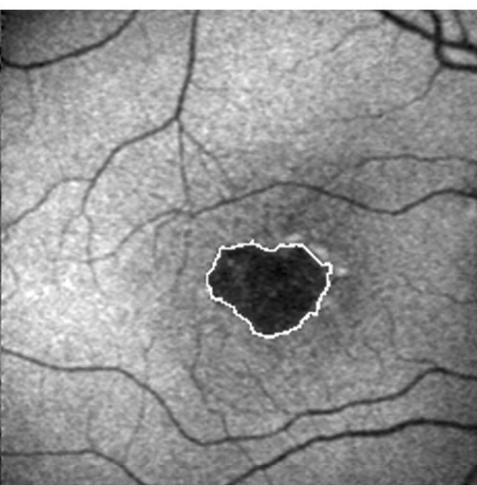
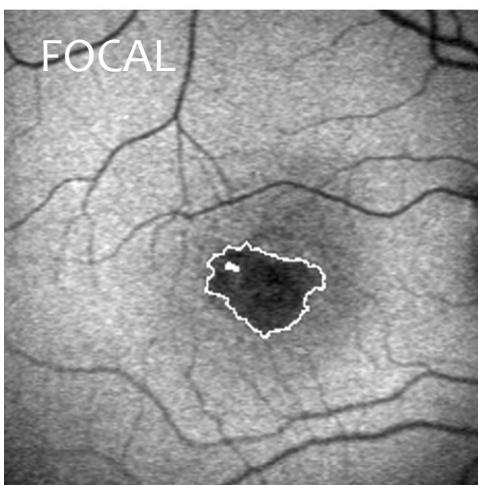
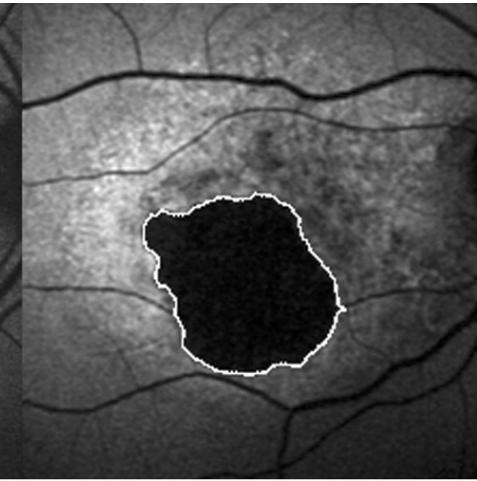
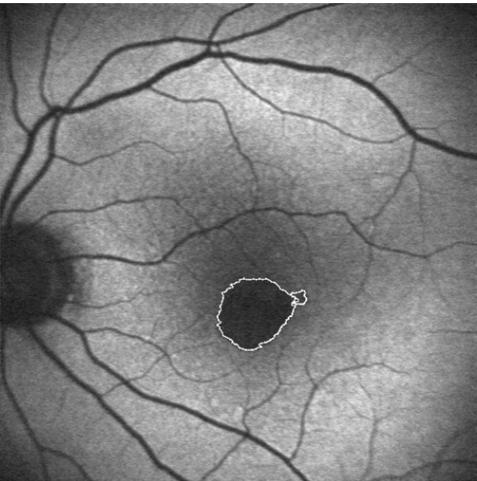
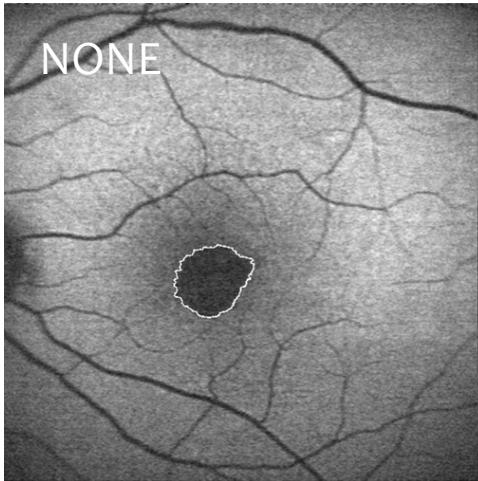


Small GA area

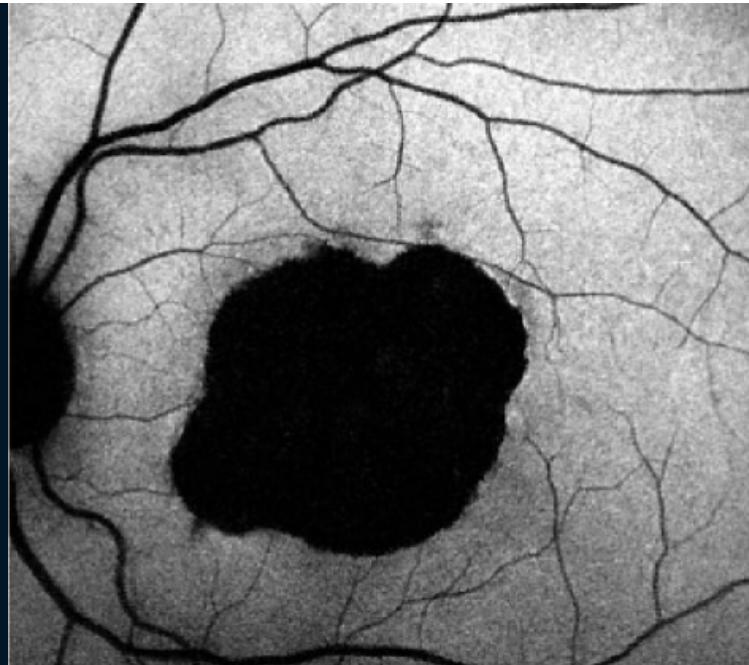
Slow progression

Large GA area

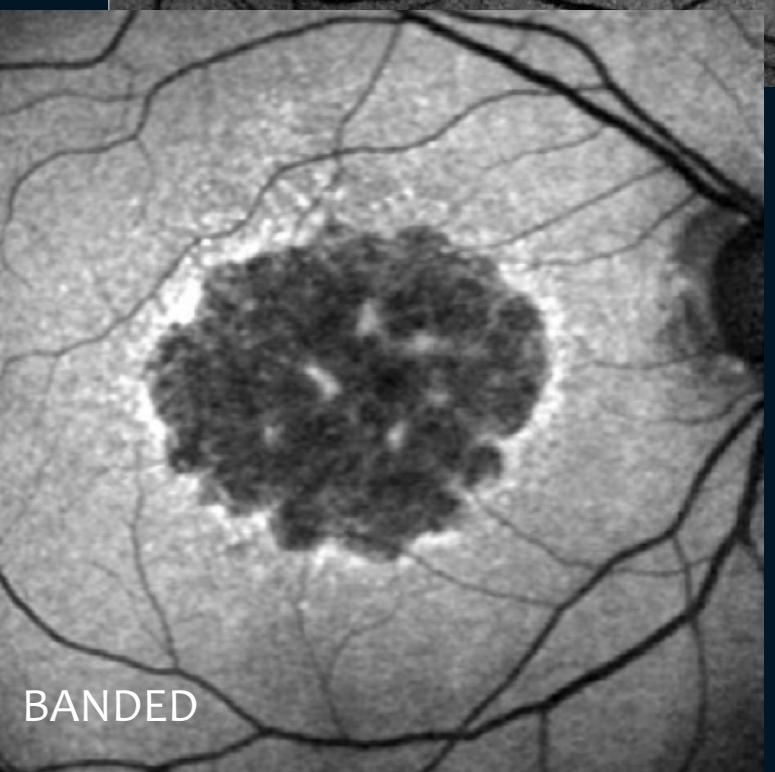
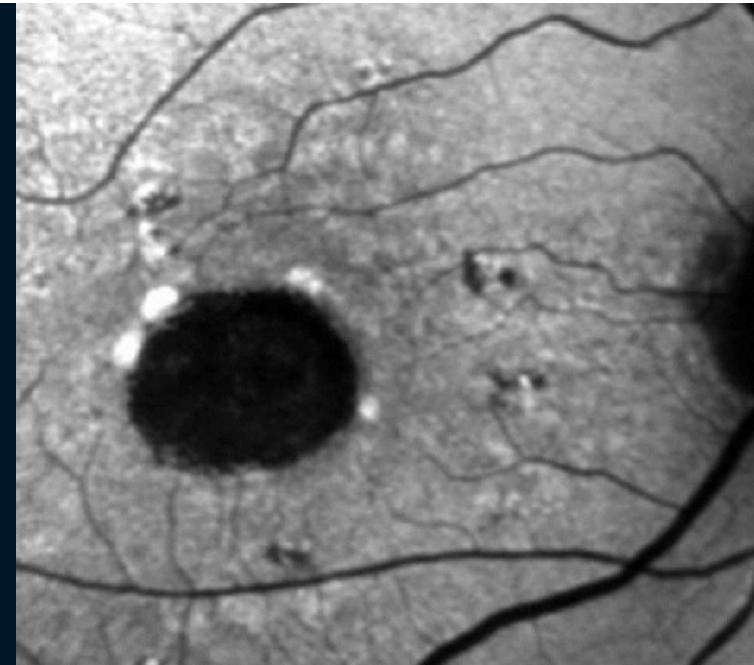
Rapid progression



NONE

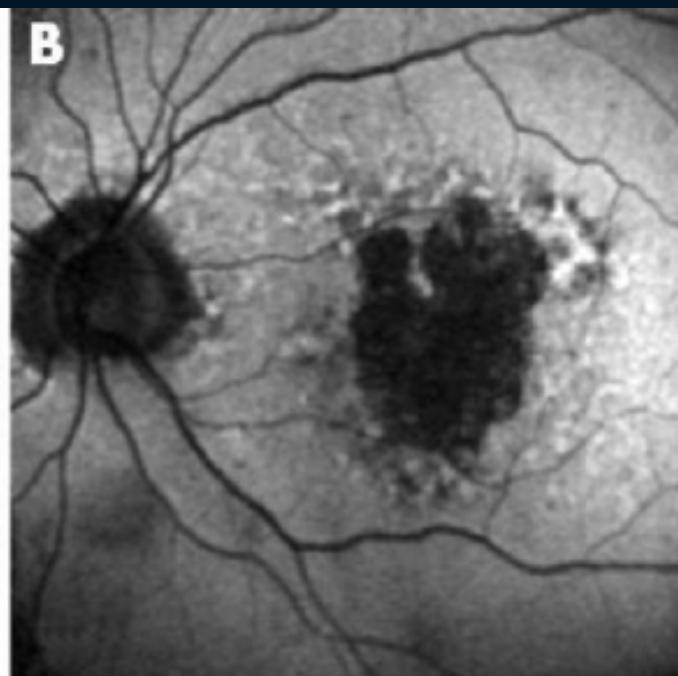
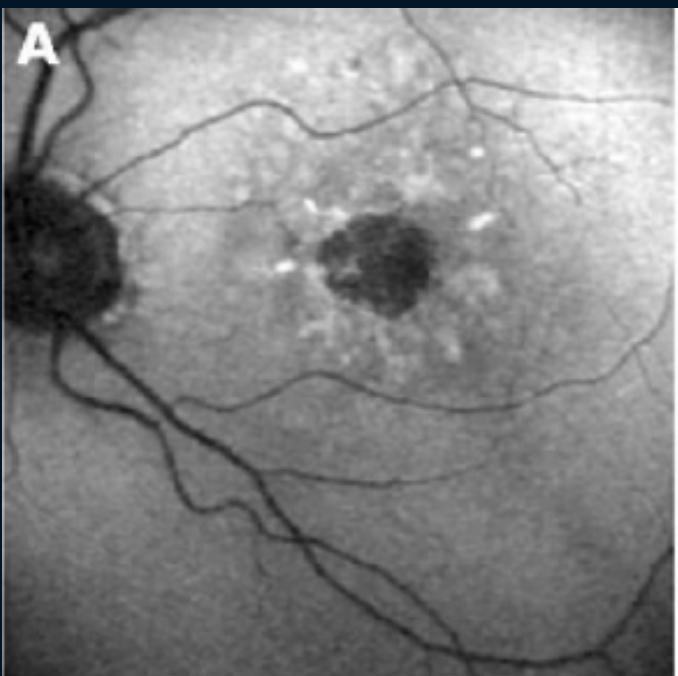


FOCAL

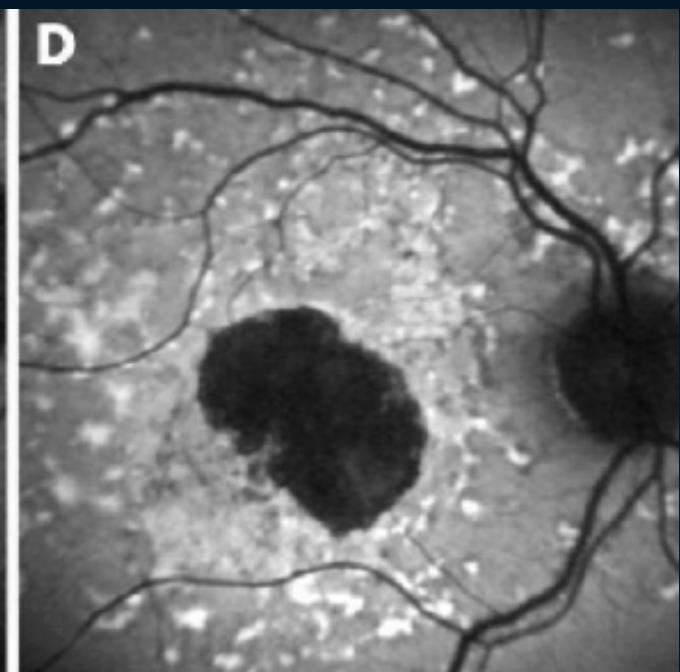
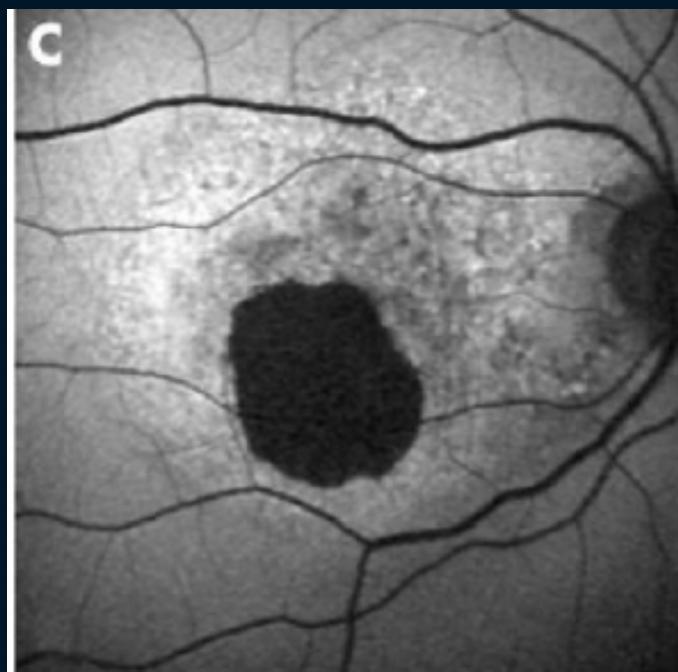


PATCHY





DIFFUSE TYPES



# FAF in Dry AMD

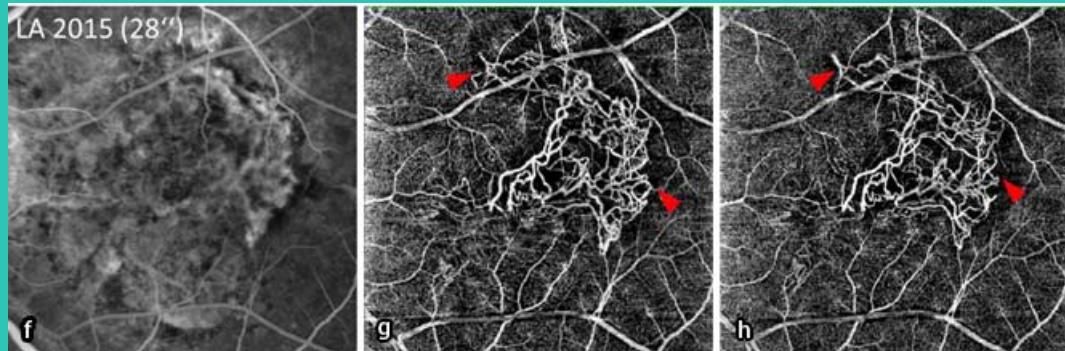
- Factors associated with faster rate of GA enlargement
  - GA arising in region of normal FAF
  - **Abnormal FAF surrounding GA**
  - GA size (faster for larger lesions)
  - Presence of reticular pseudodrusen

NEW!

# Instrumentation

- **OCT Angiography**
  - Non-invasive imaging of blood flow. No dye is used.
  - Software upgrade to some existing OCT devices
  - Does not replace need for fluorescein angiography in some patients (eg. cannot detect leakage or staining)

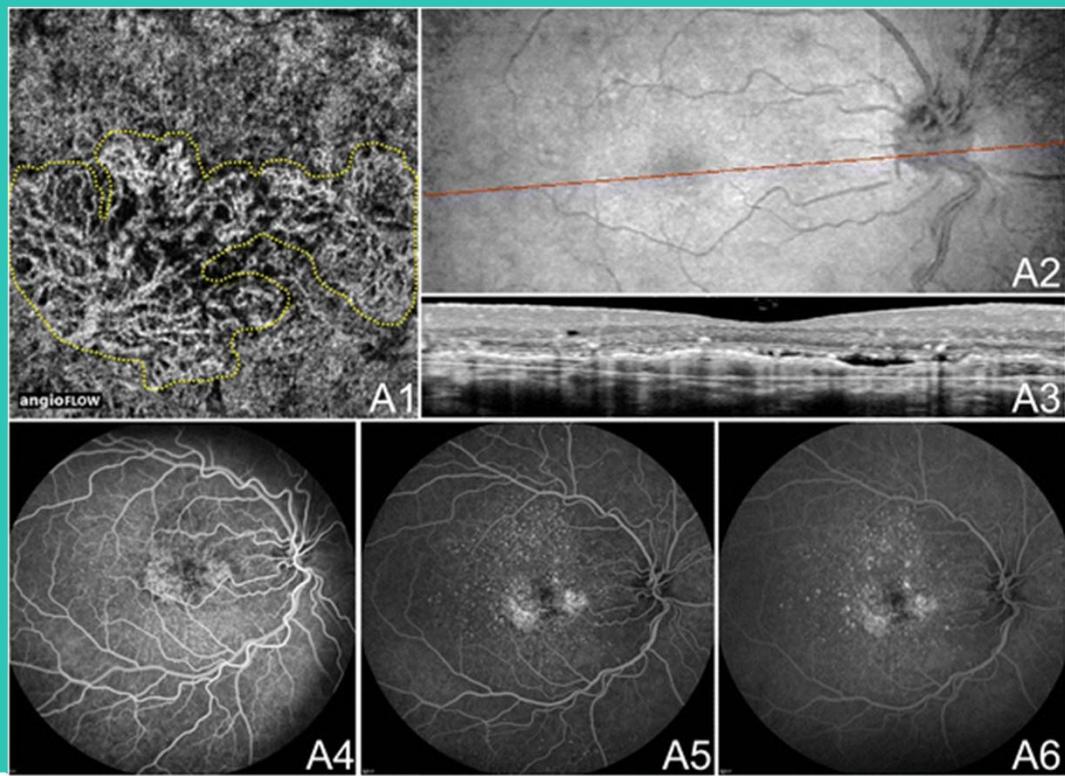
## CLASSIC CNV

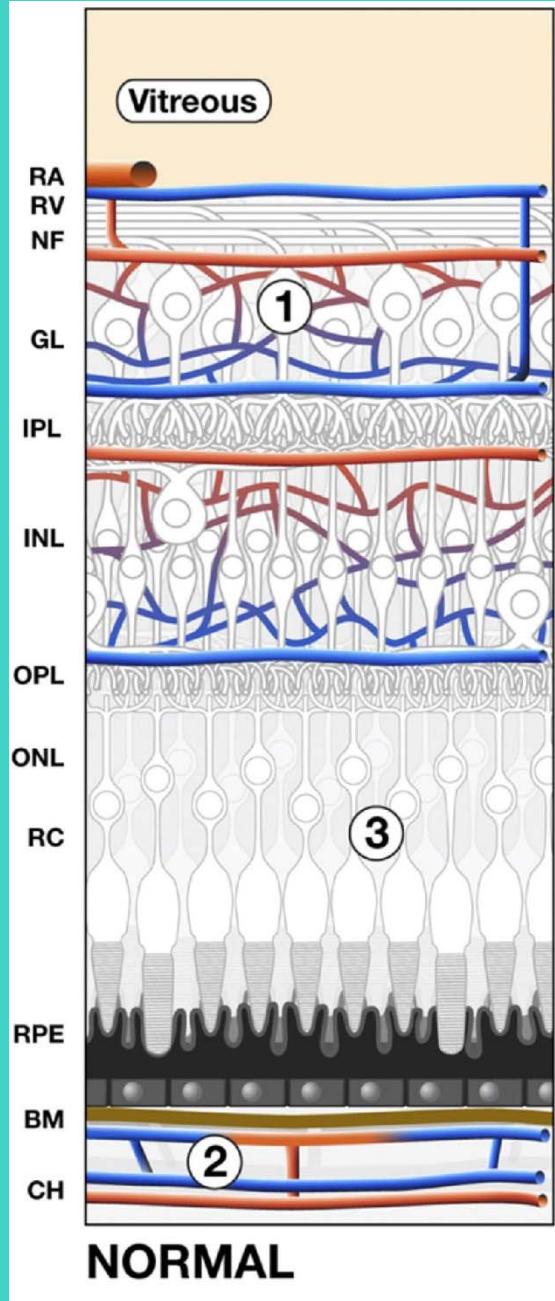


## PDR



## OCCULT CNV





## Retinal Segmentation in OCTA

Superficial retinal vessels

Deep retinal vessels

Outer retina

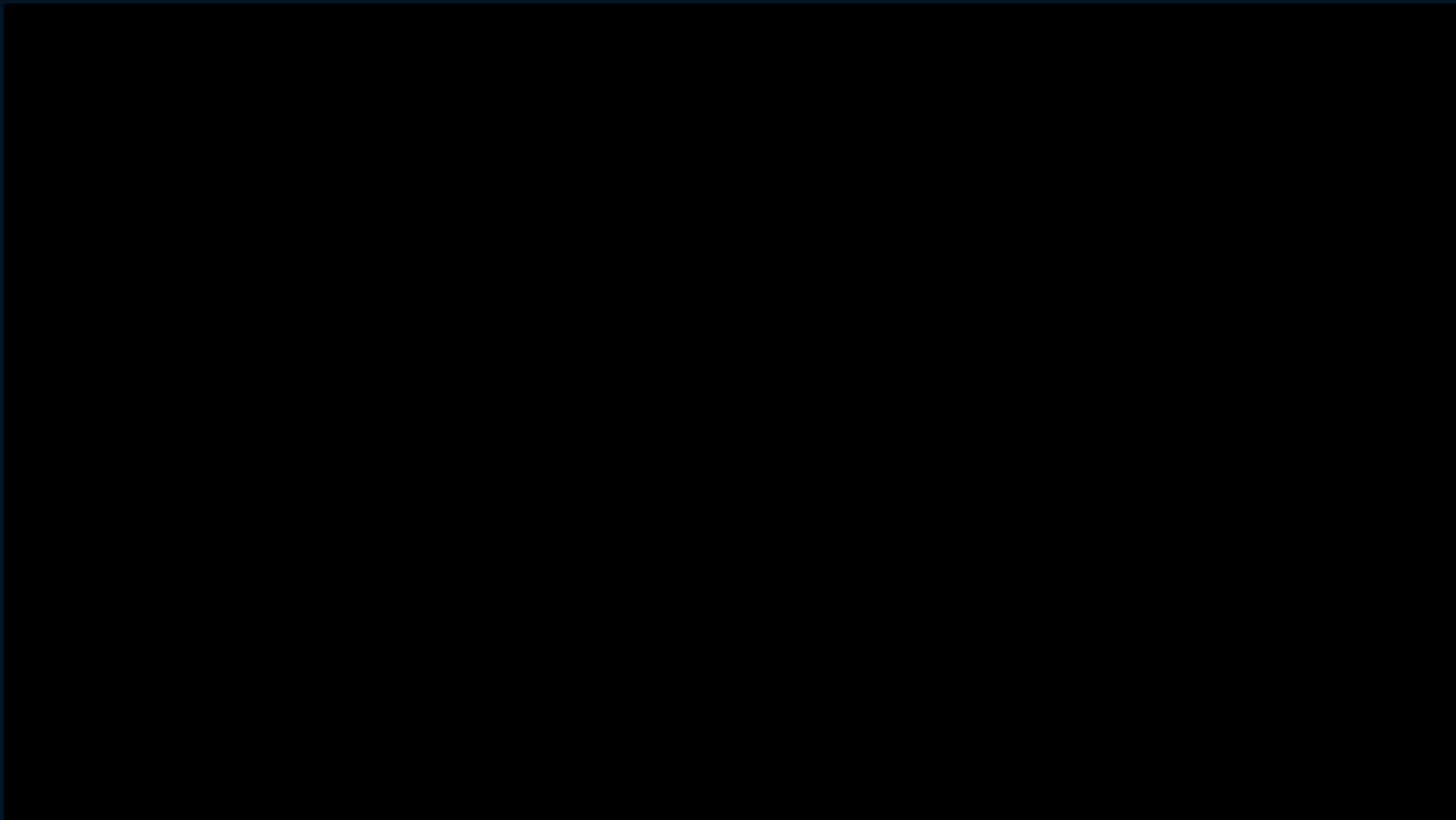
Choroid

The ganglion cell layer and inner nuclear layer are vascularized, but the outer nuclear layer is normally avascular

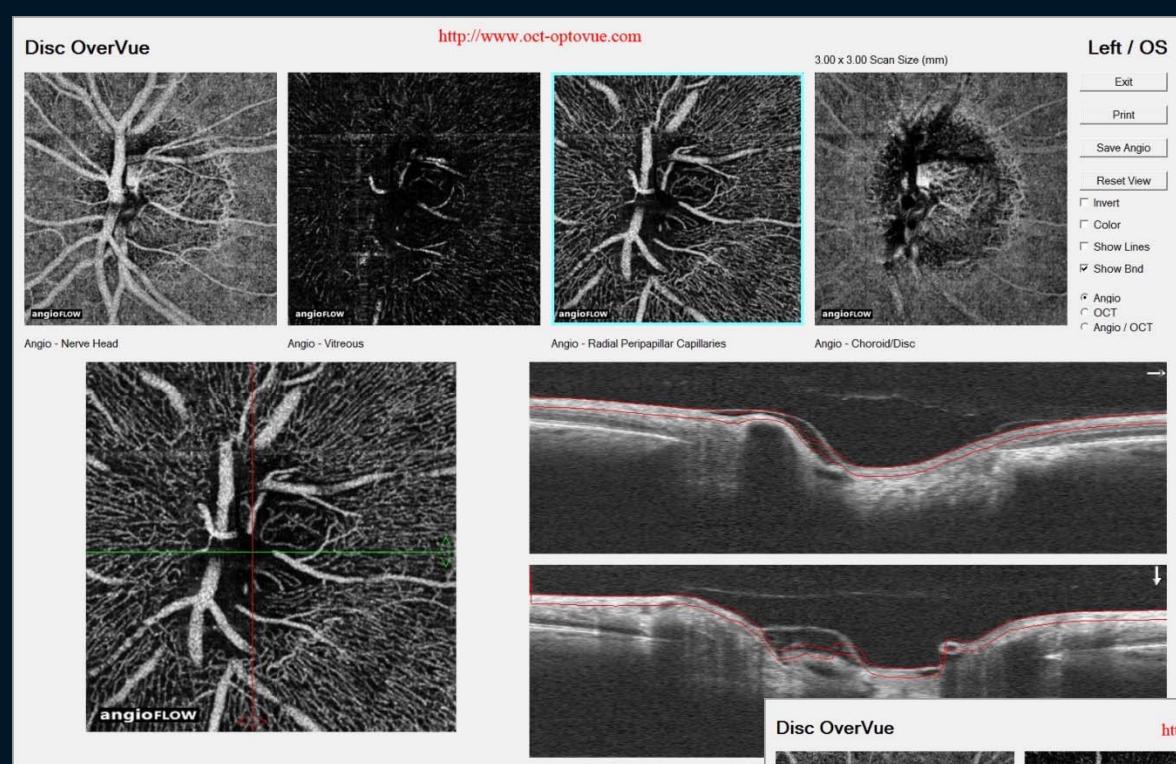
# OCT Angiography



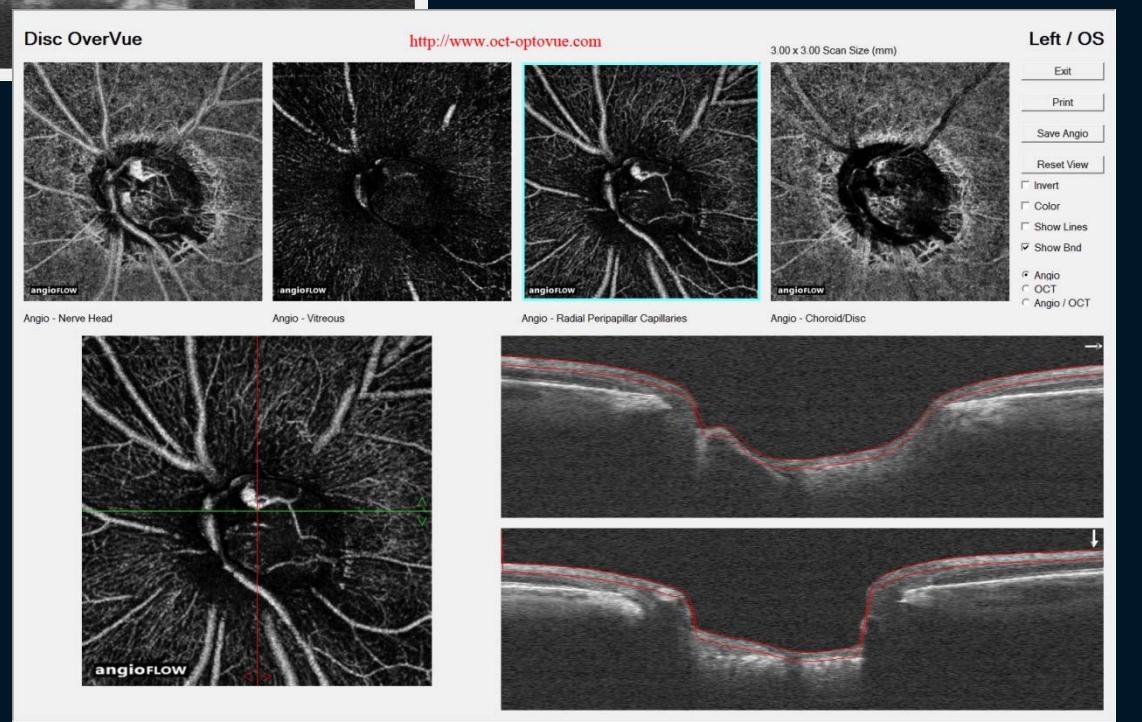
# OCT Angiography



# OCTA Glaucomatous Optic Disc



# OCTA Normal Optic Disc

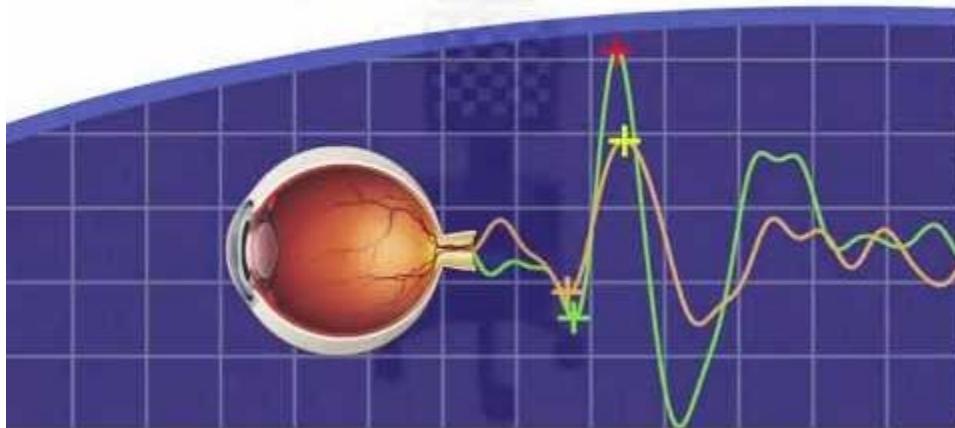


# Instrumentation

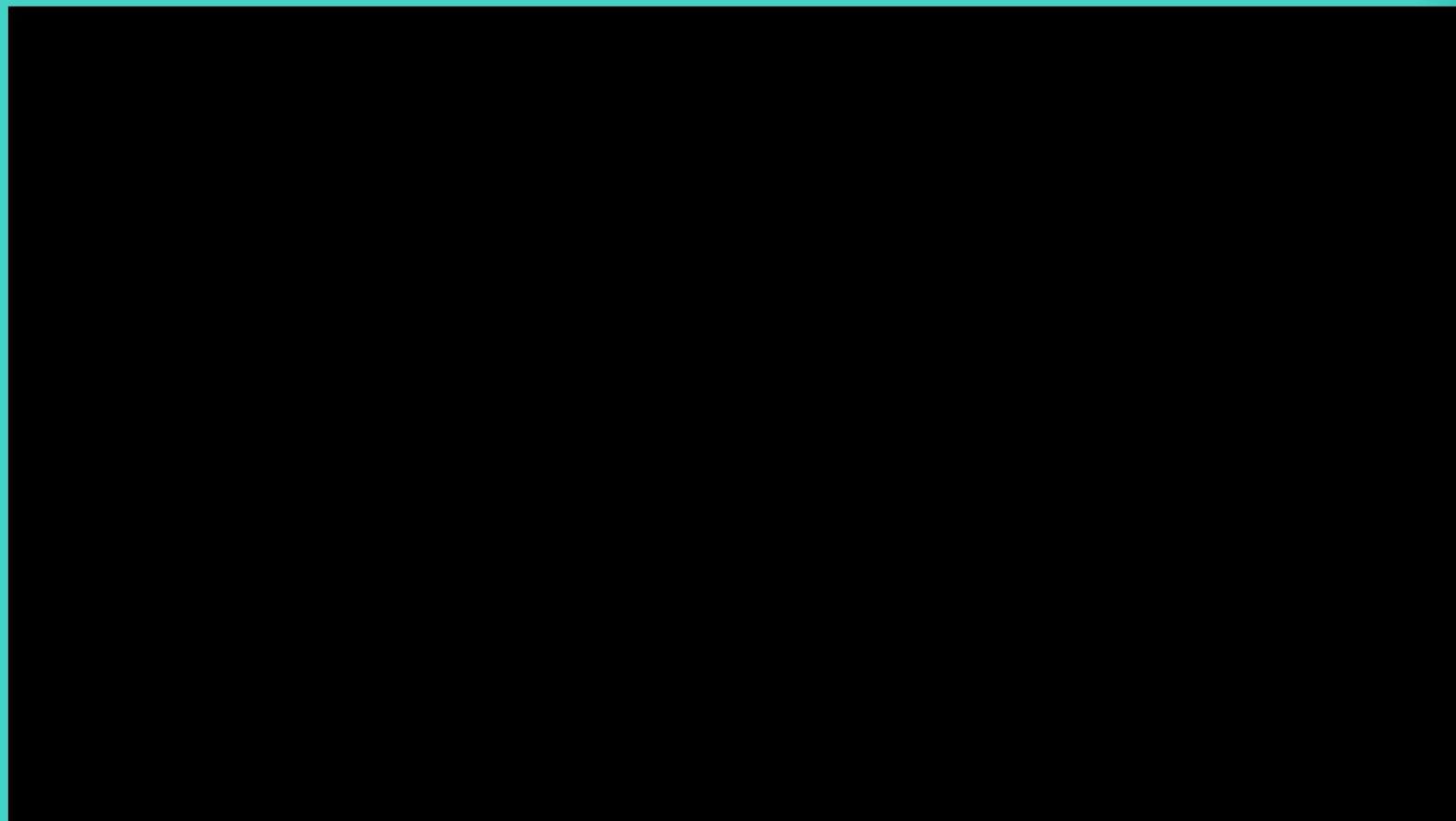
- Electrodiagnostics (EDX)
  - Visual Evoked Potential (VEP): Assess integrity of visual pathway from ganglion cells to visual cortex
  - Electroretinogram (ERG): Assess integrity of various retinal elements (photoreceptors, ganglion cells)



**DIOPSYS® NOVA-VEP**  
OFFICE BASED VISUAL EVOKED POTENTIAL TESTING



# EvokeDX



# Instrumentation

- VEP Applications
  - Amblyopia: Confirm diagnosis, predicting treatment outcome
  - Optic neuropathy: Increased latency in affected eye at all check sizes
  - TBI: Objective measure of functional impairment and track recovery
  - Glaucoma: Diagnosis and prognosis

# Instrumentation

- ERG Applications
  - Maculopathy: Concentric test aids differentiation of local & diffuse abnormality
  - Optic neuropathy: Contrast test aids differentiation of retinal & optic nerve dx
  - Glaucoma: Diagnosis and prognosis

# Self Assessment Quiz

You offer any of these in your practice:

Ultrawide Field Imaging (1 point)

Fundus Autofluorescence (1 point)

Electrodiagnostics (1 point)

OCT Angiography (2 points)

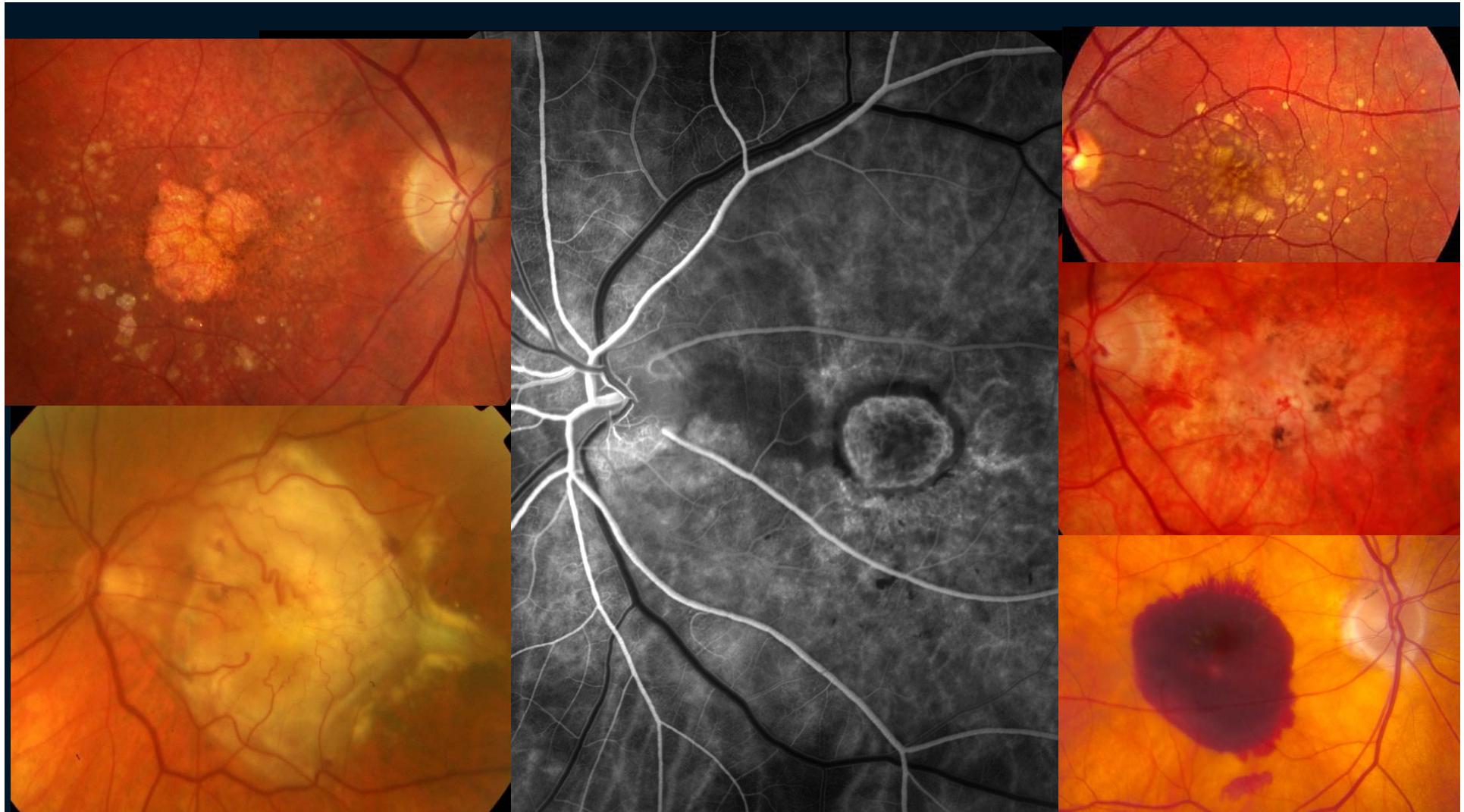
- If so, award yourself points
- If not, award yourself 0 points

# 21st Century Retina Care

- Instrumentation
- Posterior Seg Disease
  - Clinical Features
  - How to Monitor
  - When to Refer

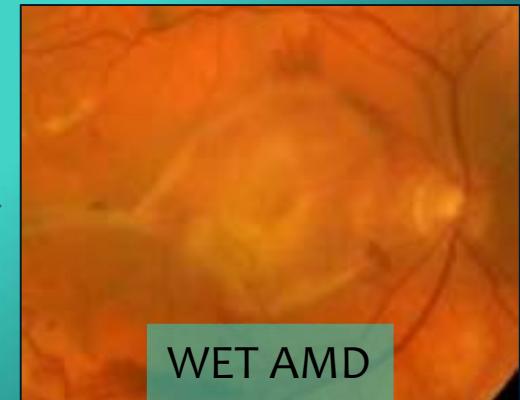
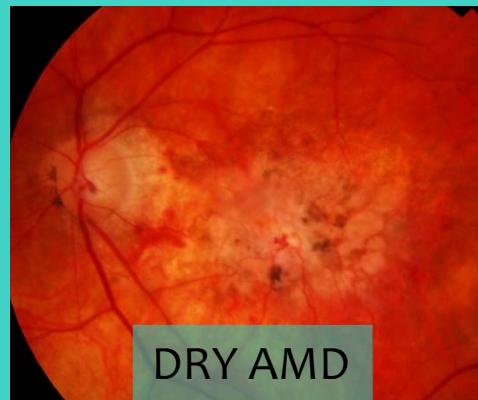
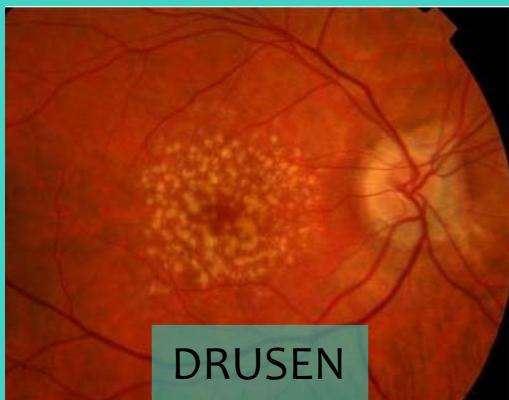


# AMD



# AMD

- Clinical Features
  - Idiopathic. Oxidative damage appears to incite an inflammatory reaction that promotes disease progression
  - **Atrophic phase:** Drusen, pigment atrophy
  - **Exudative phase:** RPE detachments, CNV



# AMD

- **How to Monitor**

- Visual function (VA, CS, Dark adaptation)
- Smoking cessation, low vision care
- Ophthalmoscopy, OCT
- **Amsler grid (or alternatives)**
- **Macular pigment testing**
- **Nutraceuticals & dietary counseling**
- **Genetic testing**

# AMD

- **When to Refer**

- Anti-VEGF therapy:

- Evidence of exudation (OCT, ophthalmoscopy)
    - Unexplained change in vision ( $\downarrow$ VA,  $\uparrow$ metamorphopsia)

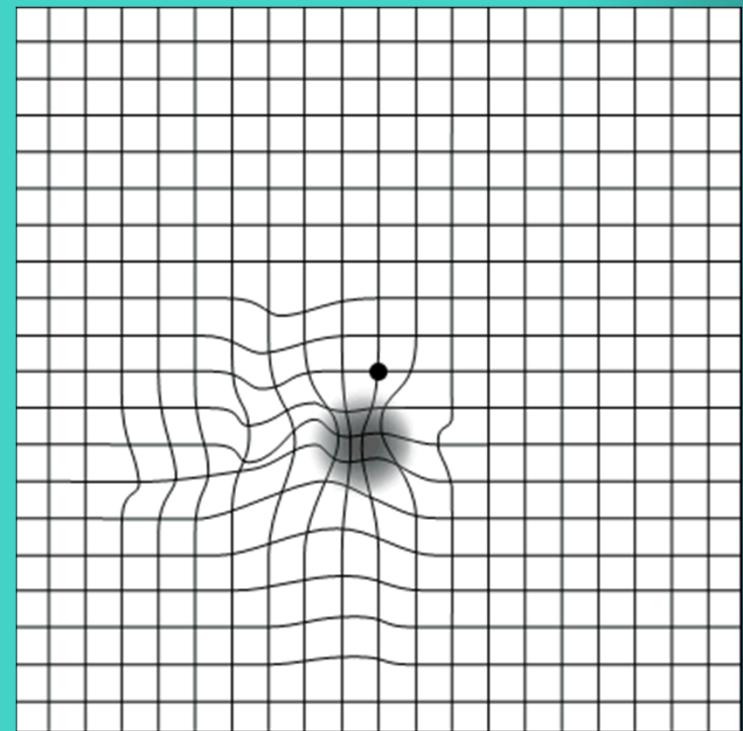
- Low vision

- Functional challenges
    - Social services



# AMD

- **Home Vision Monitoring**
  - Early detection of CNV
- Monitoring Options
  - Amsler grid
  - Environmental Amsler
  - Online vision tests
  - Home devices (PHP)
  - **Mobile apps (mVT)**



## PERSPECTIVE

# The Amsler chart: absence of evidence is not evidence of absence

Michael Crossland, Gary Rubin

*Br J Ophthalmol* 2007;91:391–393. doi: 10.1136/bjo.2006.095315

Early detection of the onset or progression of macular disease is likely to become increasingly important as new treatment modalities are introduced. Current best practice involves issuing patients with an Amsler chart for daily or weekly observation with the instruction to attend for immediate assessment should any new distortion be perceived. However the sensitivity of Amsler charts in detecting macular disease can be less than 50%, implying that presentation may be delayed in over half of patients with advancing disease relying on the Amsler chart to detect progression. A likely explanation for this is the

1874<sup>7,8</sup> and Amsler reports a paper from 1894 which consists of parallel lines to determine “metamorphoma”.<sup>9</sup>

When viewed from the recommended distance of 30 cm, the Amsler chart subtends 20°, with each small square corresponding to one degree of visual angle. Patients are asked a series of structured questions whilst viewing the chart monocularly.

The complete set of Amsler charts consists of seven plates: the conventional white-on-black grid with and without diagonal lines to aid fixation; a red-on-black version; a version with dots in place

**“A simple, cheap, easy to use screening test which patients can use in their own home, which is highly sensitive and specific for development or progression of AMD has yet to be developed.”**

# Google Play Store Search: Macular Degeneration

Apps

Search Android apps All prices

Shop

Games Family Editors' Choice

Account Payment methods My subscriptions Redeem Buy gift card My wishlist My Play activity Parent Guide

Macular degeneration AND EMILY

Central Vision Test healthcare4mobile

Amsler Grid - Eye Test Digital-Meridian

AMD Eye App Srinivas Sastry

MaculaTester Vision Sabina Technology, LLP

MATA (Macular AMD) Khoo Teck Puat Hospital

AMD, A Metamorph app4eyes

Amsler Grid Osibus Software

Eye retina test Jined

Eye Test - Eye Exam healthcare4mobile

Eyecare- Amsler Grid Ira Garoon

My Reading Eyes Free MyWorkingApp.com

MD\_levReader Macular Society

Eye test Designveloper

Macular Degeneration Personal Remedies LLC

Amsler Downloader DroidAppsMaker

Visual Acuity Test healthcare4mobile

etOculus Ludus Codicis

ViaOpta Simulator Novartis Pharmaceuticals

AMD Pro, A Metamorph app4eyes

weZoom - Macular lovlapps

mVT® - Home Vision Vital Art and Science, LLC

Peel Retina Perivision

Eye Vision: Boards Shyri App Studio

Amsler Eye Test DroidAppsMaker

Smart Optometry - Smart Optometry

Eye Test Chart App Park

ForeseeHome Patient Notal Vision

Eye Exam Andrew Brusentsov

12

Lens Navigator

Amsler Grid (Donat)

Color Vision Test G

Complete Eye Doctor

Kuku Kube: color blind

Foods For Eyes

Eye and Vision Test

Glaucoma Vision S

<https://play.google.com/store/apps/details?id=com.maculatester.maculatester>



## mVT® - Home Vision Testing

Vital Art and Science, LLC Medical

Everyone

★ ★ ★ ★ 7

Add to Wishlist

Install

### REVIEWS

2.7

★ ★ ★ ★

7 total



A Google user

★ ★ ★ ★ ★ January 13, 2019

The effect of this app is to REDUCE the income of a doctor. Seriously: mVT asks doctors to pay in order to equip patients with an app that helps avoiding visits. Don't believe it? Google for "multibit" and for the sentence ""The superior quality of the tests enables the app usage to replace many pat...



1



[Full Review](#)



Linda Langos

★ ★ ★ ★ ★ January 1, 2019



3



Instead of helping people they decided to make this test prescription only. For no reason at all, just to make it unavailable for the majority of people living on this planet in many countries, having macular degeneration and other retinal diseases. I wish many people give further negative reviews u...

[Full Review](#)



C Pitts

★ ★ ★ ★ ★ August 24, 2019



1



This App is out for the money requiring a script doctors have to pay for? They should have taken it to a non profit humanitarian company for funding to help people, or given it to the



## Step 1

Download the  
mVT® App



\*\*\*\*\*

## Step 2

Register using a  
10 digit code  
given to you by  
your doctor



## Step 3

Begin testing  
2x per week

# AMD



myVisionTrack®

For Physicians

Media

Our Company ▾

Prescriber Login



**The mVT® is the only FDA cleared App that detects visual function changes in patients with maculopathy, including: AMD & DME**

Our goal is to detect changes in vision early,

[myvisiontrack.com](http://myvisiontrack.com)

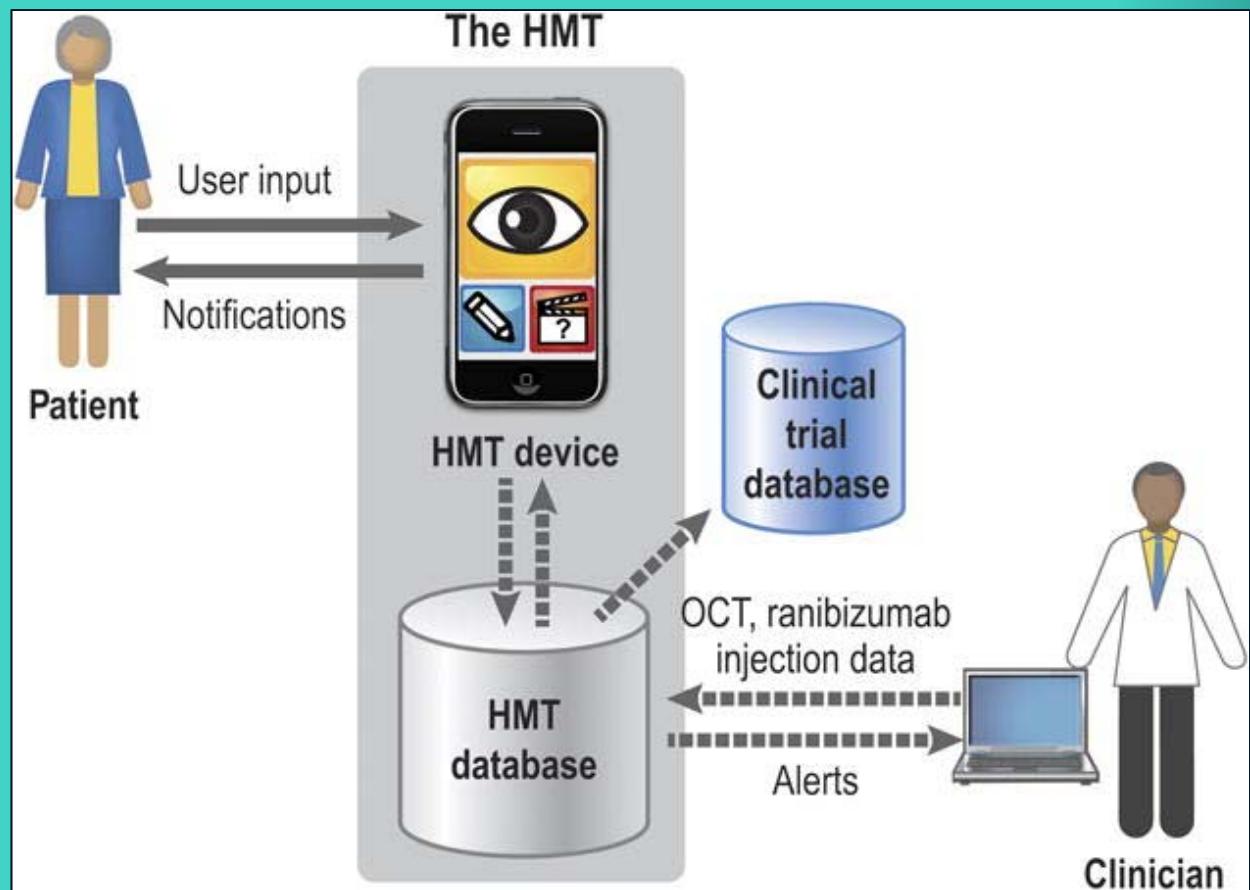
# AMD



# AMD

The prescribing physician receives an alert when a patient's test performance indicates a worsening of metamorphopsia.

**The physician is responsible for following up on abnormal test results.**



# Self Assessment Quiz

Do you educate AMD patients to self-monitor their vision in ways other than Amsler grid?

- If so, award yourself 1 point
- If not, award yourself 0 points



## Vita Risk®

PREDICT AND PROTECT®



Vita Risk® genetic testing identifies patients who have an increased risk of progression to wet AMD after chronic exposure to zinc, allowing patients to avoid supplements that increase their risk of vision loss.

[Learn About Vita Risk®](#)

## Macula Risk®

PREDICT AND PROTECT®



Macula Risk® genetic testing helps doctors identify those at high risk for AMD progression. These patients require increased surveillance and early referral to a specialist to preserve their sight.

[Learn About Macula Risk®](#)

What is the difference between genotyping and sequencing?

Genetic testing services use risk models to calculate your risk of contracting various disorders based on genotype

Special Communication

## Genetic Testing for Age-Related Macular Degeneration Not Indicated Now

Edwin M. Stone, MD, PhD

Age-related macular degeneration is a very common condition that is caused by a complex interplay of genetic and environmental factors. It is likely that, in the future, genetic testing will allow physicians to achieve better clinical outcomes by administering specific treatments to patients based on their genotypes. However, improved outcomes for genotyped patients

**Author Affiliations:** Author affiliations are listed at the end of this article.

*“The costs and risks of routine genetic testing currently outweigh the benefits for patients with AMD.”*

JAMA Ophthalmol. 2015;133:598-600

Only difference between AREDS-1 and AREDS-2 supplements: AREDS-2 substitutes L/Z for  $\beta$ -carotene. Both are equally effective

### AREDS 1

- Zinc
- Copper
- Vitamin C
- Vitamin E
- $\beta$  carotene

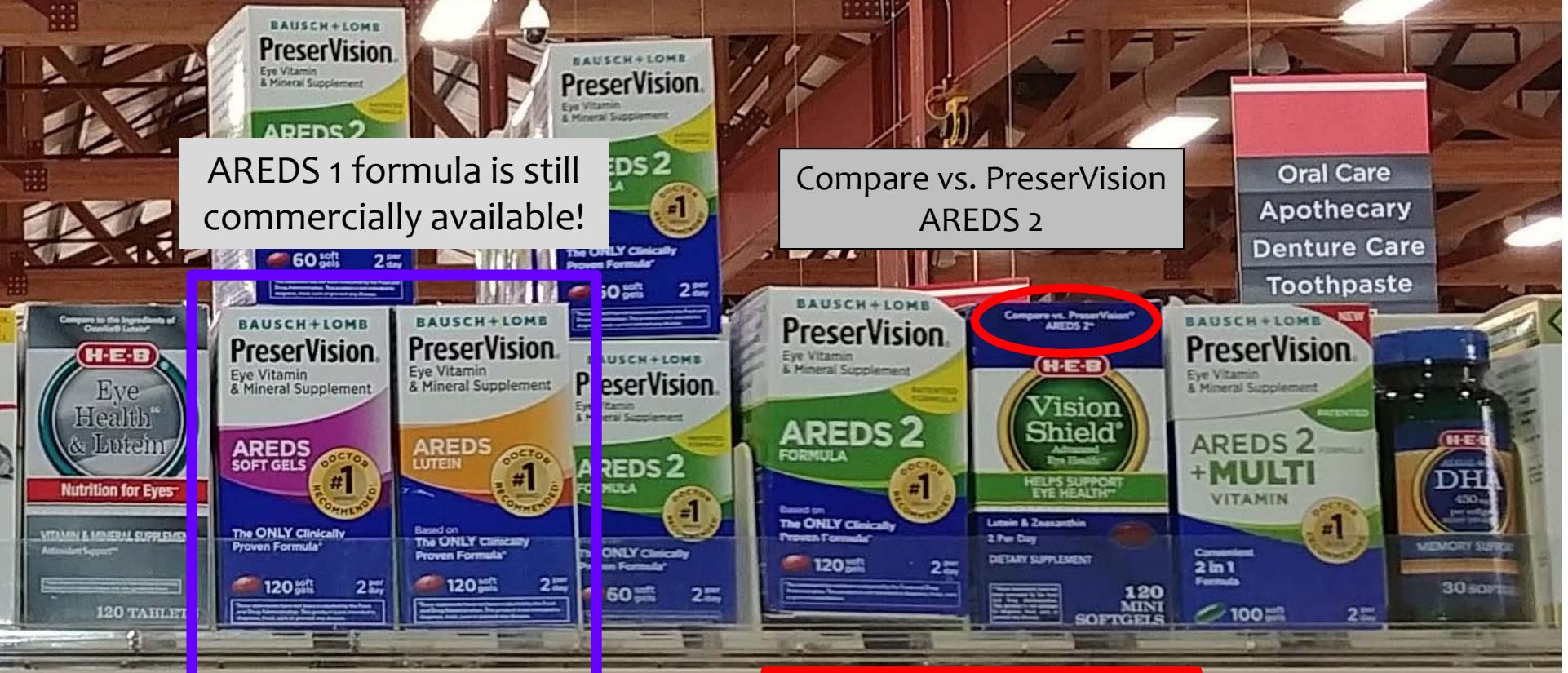
### AREDS 2

- Zinc
- Copper
- Vitamin C
- Vitamin E
- Lutein/Zeaxanthin

AREDS 1 formula is still commercially available!

Compare vs. PreserVision  
AREDS 2

Compare vs. PreserVision®  
AREDS 2®



\$540

\$2484

\$2484

\$1797

\$3097

\$1895

\$3097

\$885



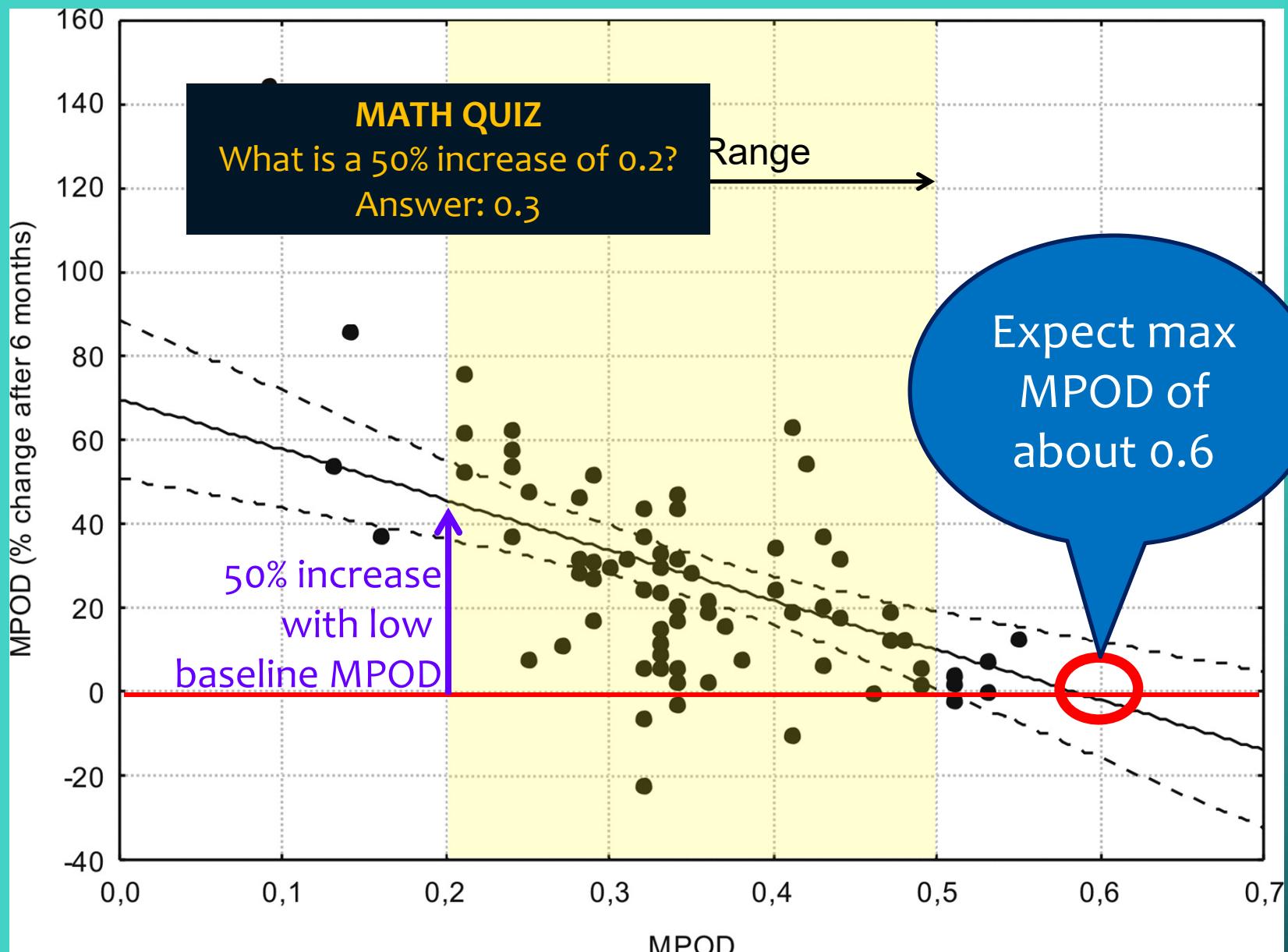
# Macular Pigment

*What is a Carotenoid?*

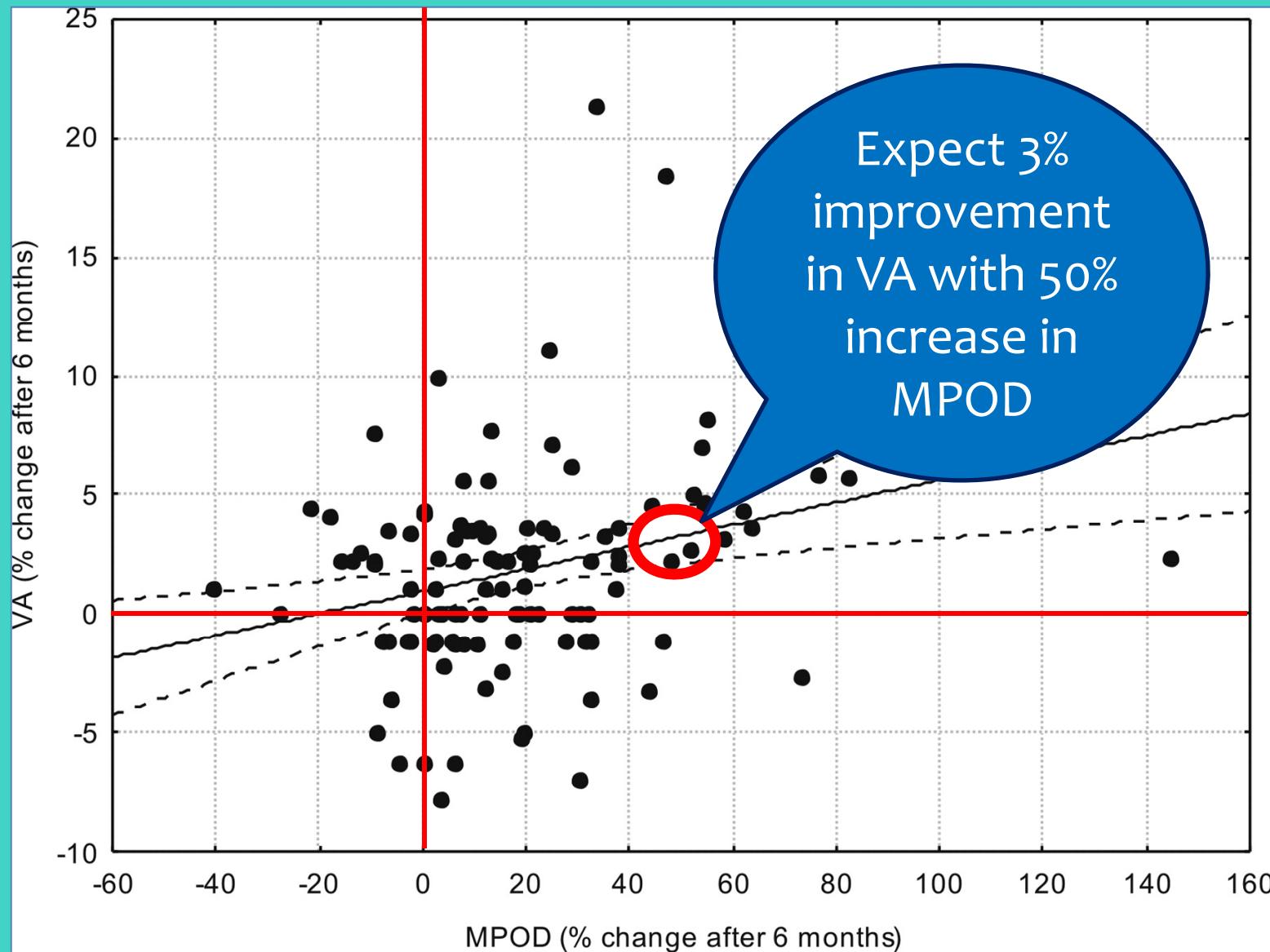
# AMD

- **MPOD and Lutein**
  - Low MPOD is a risk factor for AMD
  - Heterochromatic flicker photometry measures MPOD
  - Lutein supplements:
    - Increase MPOD
    - Improving visual function
    - Decreasing AMD risk





Weigert (2011): Correlation between MPOD at baseline and the change in MPOD after 6 months of lutein supplementation in 84 AMD patients.



Weigert (2011): Correlation between the change in MPOD and the change in VA after 6 months of lutein supplementation.

# MPOD: Protecting the Eyes from Harmful Blue Light with Internal Sunglasses.

Zeaxanthin and Lutein increase Macular Pigment Optical Density

THEORETICAL MAX

## VISION RISK

from harmful blue light

Expect 50% g

100%

300

300 - 400  
UV RANGE

Protect Cornea  
with sun protective  
sunglasses

harmful Blue Light Reaching Photoreceptors

## VISION PROTECTION

from harmful blue light

3%

800

Cell Phones  
Tablets



# A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency

Emily R. Bovier<sup>1</sup>, Lisa M. Renzi<sup>1,2</sup>, Billy

**1** Vision Sciences and Human Biofactors Laboratories, Department of Psychology, The Ohio State University, Columbus, Ohio, United States of America

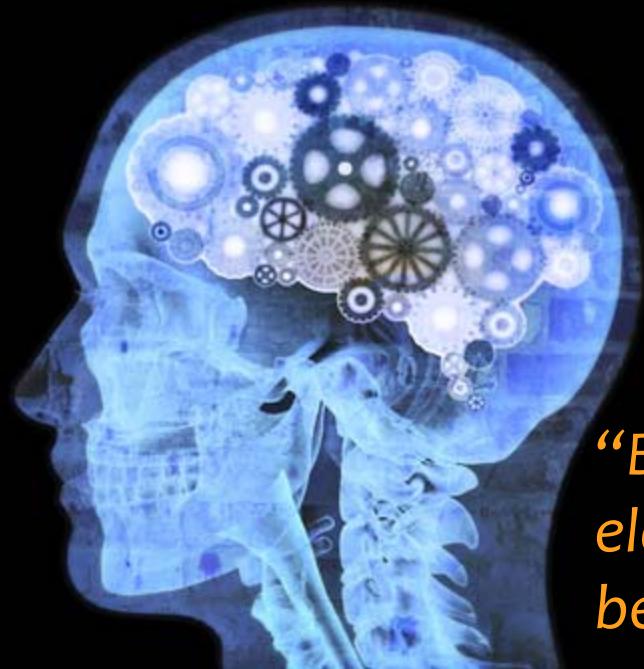
Georgia, United States of America, **2** Abbott Nutrition,

## Abstract

Lutein and zeaxanthin are major carotenoids in the retina. It has been hypothesized that these pigments influence visual performance by increasing macular pigment density within the retina, which may reduce light scatter and improve visual acuity. In this study, we measured macular pigment density (as a biomarker of visual performance), thresholds, and visual motor reaction time in young adults. These variables were assessed after four months of supplementation with a placebo, a pure lutein formulation containing 26 mg/day zeaxanthin, 8 mg/day lutein, and a mixed formulation containing 26 mg/day zeaxanthin, 8 mg/day lutein, and 10 mg/day mixed omega-3 fatty acids. Significant correlations were found between retinal lutein and zeaxanthin (macular pigment) and CFF thresholds ( $p<0.01$ ) and visual motor performance (overall  $p<0.01$ ). Supplementation with zeaxanthin and the mixed formulation (considered together) produced significant ( $p<0.01$ ) increases in CFF thresholds (~12%) and visual motor reaction time (~10%) compared to placebo. In general, increasing macular pigment density through supplementation (average increase of about 10%) was associated with improved visual performance. These findings support the hypothesis that increasing macular pigment density through supplementation may improve visual performance.

*“Increasing macular pigment density through supplementation resulted in significant improvements in visual processing speed, even when testing young, healthy individuals who tend to be at peak efficiency.”*

# Focus is Everything.



*“Both young, healthy adults and the elderly population can gain cognitive benefits from L and Z supplementation.”*

J Ophthalmol. 2015;2015: 865179.

# AMD

## What about meso-zeaxanthin (MZ)?

- MZ is not found in significant quantities in the diet, but is produced by the retina
- Sabour-Pickett (2014)
  - Adding MZ to a lutein supplement resulted in **larger MPOD gains and greater improvement in contrast sensitivity than lutein & zeaxanthin alone**
  - 3 mg L, and 2 mg Z, 17 mg MZ



Contents lists available at [ScienceDirect](#)

# Progress in Retinal and Eye Research

journal homepage: [www.elsevier.com/locate/prer](http://www.elsevier.com/locate/prer)



## Lutein, zeaxanthin, and *meso*-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease



Paul S. Bernstein <sup>a,\*, 1</sup>, Binxing Li <sup>a, 1</sup>, Preejith P. Vachali <sup>a, 1</sup>, Aruna Gorusupudi <sup>a, 1</sup>,  
Rajalekshmy Shyam <sup>a, 1</sup>, Bradley S. Henriksen <sup>a, 1</sup>, John M. Nolan <sup>b, 1</sup>

<sup>a</sup> Department of Ophthalmology and Visual Sciences, Moran Eye Center, University of Utah School of Medicine, 65 Mario Capecchi Drive, Salt Lake City, UT, 84132, USA

<sup>b</sup> Macular Pigment Research Group, Vision Research Centre, School of Health Science, Carriganore House, Waterford Institute of Technology West Campus, Carriganore, Waterford, Ireland

*“Recent studies suggest that supplementation with a formulation containing all three macular carotenoids (i.e. lutein, zeaxanthin, and *meso*-zeaxanthin) offers advantages over formulations not containing all three components of MP.”*

PRER. 2015;50:34–66



## LMZ3 Formula Active Ingredients

Meso-zeaxanthin	10mg
Lutein	10mg
Zeaxanthin	2mg

## Inactive Ingredients

Sunflower Seed Oil	506mg
Vitamin E	3.75 IU
Beeswax & Fatty Acid	39mg
Beef Gelatin	37.5mg

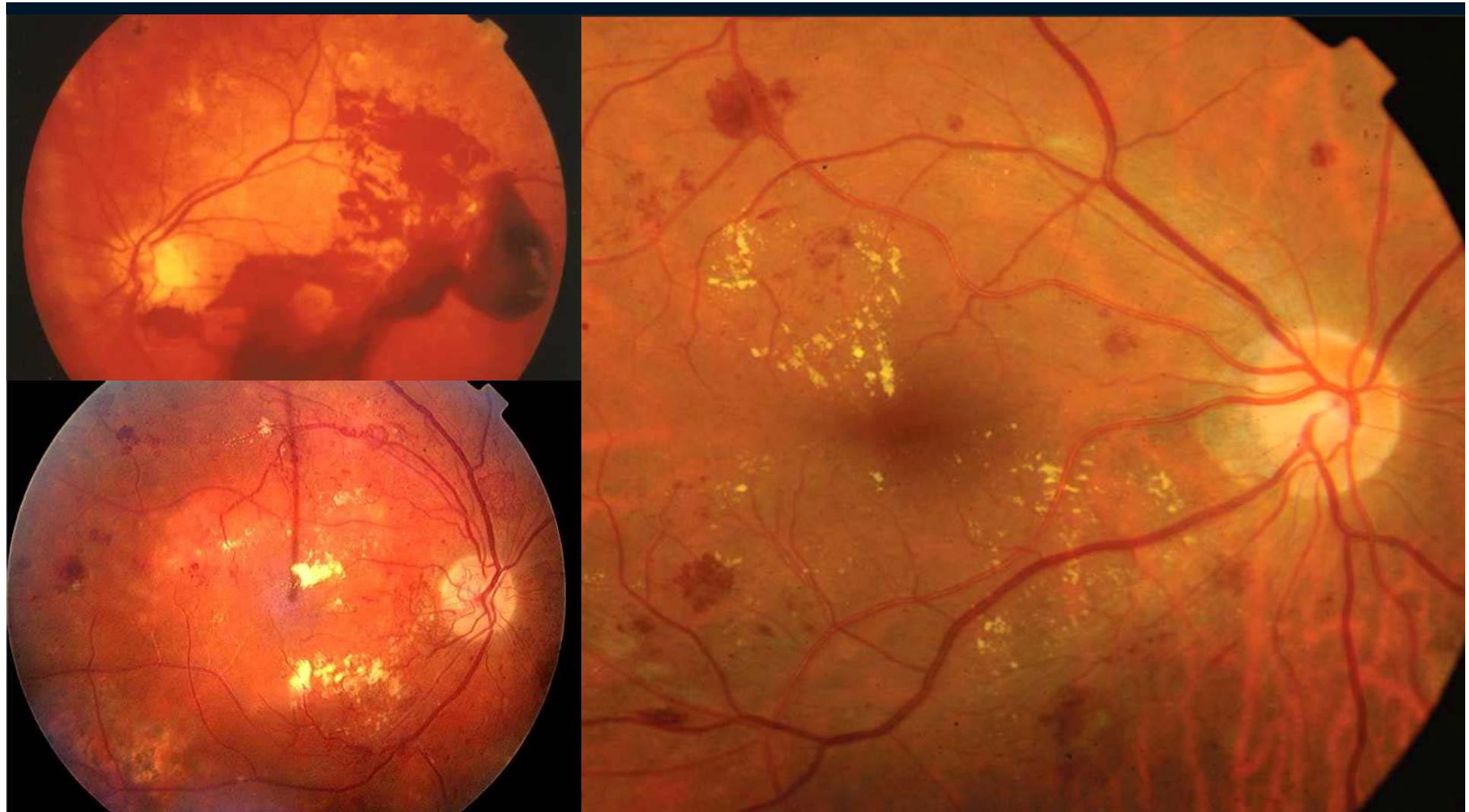


# Self Assessment Quiz

Do you prescribe  
lutein-containing supplements?

- If so, award yourself 1 point
- If not, award yourself 0 points
- BONUS: If you also test MPOD, award yourself 1 bonus point

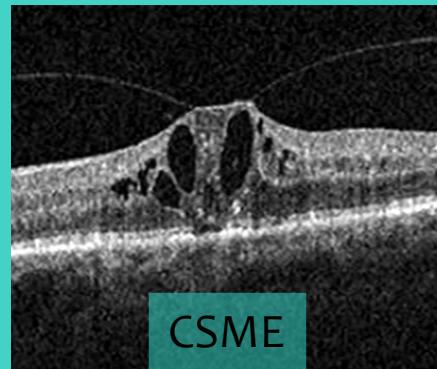
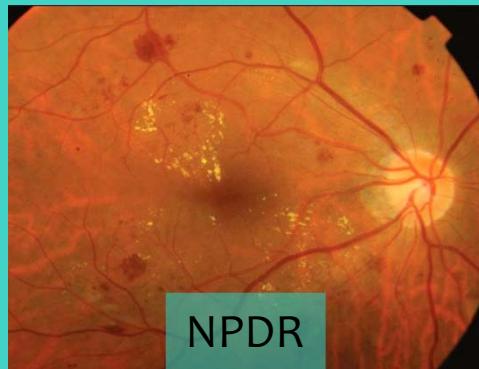
# Diabetic Retinopathy



# Diabetic Retinopathy

- **Clinical Features**

- Loss of pericytes leads to microaneurysms and breakdown of blood-retinal barrier
- Background retinopathy (NPDR)
- Diabetic macular edema (CSME)
- Proliferative retinopathy (PDR)



# Diabetic Retinopathy

- **How to monitor**
  - **Systemic control** (HgA1C, HTN, cholesterol)
  - Routine dilated fundus exams
  - OCT to detect macular edema
  - OCTA: Macular ischemia & early neovascularization
  - **Diet and Nutraceuticals**
  - Other ocular manifestations of diabetes
    - Rubeosis
    - Cranial nerve palsies
    - Ischemic optic neuropathy

# Diabetic Retinopathy

- **When to Refer**
  - Patients needing Avastin
    - Center-involved macular edema
    - High risk patients (monocular, etc)
  - Patients needing PRP
    - PDR
    - Severe NPDR
    - Rubeosis



# Diabetic Retinopathy

- Systemic Control
  - Tight blood glucose control lowers risk of DR and its progression
  - Address co-morbidities & lifestyle
    - Hypertension, Dyslipidemia, **Sleep apnea**
    - Obesity, exercise, smoking



# *Editorial*

---

## **How Was Your Sleep? New Implications for Obstructive Sleep Apnea in Retinal Disease**

It is not uncommon for patients to wonder how well rested their surgeon is; conversely, it is increasingly clear that we should be asking the same of our patients. Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder that has been implicated as a risk factor for an increasing number of systemic and ophthalmic diseases. Consensus estimates place the prevalence of

glaucoma was 2%, similar to the prevalence in the general population.<sup>18</sup> Similarly, a large multicenter study in France reviewed the records of nearly 10,000 patients and after elimination of confounders such as age, no relationship between glaucoma and OSA was found.<sup>19</sup>

The role of OSA in diabetic retinopathy is becoming

*“OSA is an independent risk factor for the development and progression of diabetic retinopathy. More than simply increasing the risk for ophthalmic disease, recent work suggests OSA might hamper the therapeutic benefits of anti-VEGF therapy.”*

Retina. 2016;36: 657–9.

# Diabetic Retinopathy

- **Screening for OSA**
  - Sleepiness, snoring, neck circumference, BMI
  - FES is highly specific for OSA
    - 96% also have OSA
    - FES associated with more severe OSA

Screening tool for OSA: STOP-Bang		
<b>S T O P — B a n g</b>	Does the patient <b>snore</b> loudly (louder than talking or or Do du Ha du Do tre Do Ag Is Ge	<b>Y/N</b>
	<b>THE THREE QUESTIONS</b>	
	1. Do you have a snoring problem?	<b>Y/N</b>
	2. Are you always tired? (While driving, have you ever fallen asleep at a traffic light?)	<b>Y/N</b>
	3. Have you ever been told that you hold your breath in your sleep?	<b>Y/N</b>
	?	<b>Y/N</b>
		<b>Y/N</b>
Scoring:	<b><math>Y \geq 3 = \text{high risk of OSA}</math></b>	
	<b><math>Y &lt; 3 = \text{low risk of OSA}</math></b>	
Developed by Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S, Khajehdehi A, Shapiro C: <i>STOP Questionnaire A Tool to Screen Patients for Obstructive Sleep Apnea</i> , 2008.		

# Self Assessment Quiz

Do you screen for sleep apnea among your diabetic patients?

- If so, award yourself 1 point
- If not, award yourself 0 points

# Diabetic Retinopathy

- How to delay DR and prevent vision loss
  - Earlier diagnosis of diabetes
  - Tighter metabolic control
  - Routine DFE (at least annually)
    - Photography
    - OCT of macula
  - **Nutraceuticals?**
  - Prompt treatment (laser, anti-VEGF, steroids) when indicated



OPEN ACCESS

# The Diabetes Visual Function Supplement Study (DiVFuSS)

A Paul Chous,<sup>1</sup> Stuart P Richer,<sup>2</sup> Jeffry D Gerson,<sup>3</sup> Renu A Kowluru<sup>4</sup>

<sup>1</sup>Private Practice, Tacoma, Washington, USA

<sup>2</sup>Captain James A Lovell Federal Heath Care Center, North Chicago, Illinois, USA

<sup>3</sup>Private Practice, Olathe, Kansas, USA

<sup>4</sup>Kresge Eye Institute, Wayne State University, Detroit, Michigan, USA

**Correspondence to**  
Dr A Paul Chous, FFAO,

## ABSTRACT

**Background** Diabetes is known to affect visual function before onset of retinopathy (diabetic retinopathy (DR)). Protection of visual function may signal disruption of mechanisms underlying DR.

**Methods** This was a 6-month randomised, controlled clinical trial of patients with type 1 and type 2 diabetes with no retinopathy or mild to moderate non-proliferative retinopathy assigned to twice daily consumption of placebo or a novel, multi-component formula containing xanthophyll pigments, antioxidants and selected

the risk of DR and its progression, evidence shows that there is no level of average blood glucose (as reflected by glycosylated haemoglobin) that is totally protective against DR. The current clinical algorithm for delaying DR and preventing STR is earlier diagnosis of diabetes, tighter metabolic control, routine dilated retinal examinations and treatment (laser photocoagulation, intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents and corticosteroids) if/when DR progresses to a level that threatens vision.

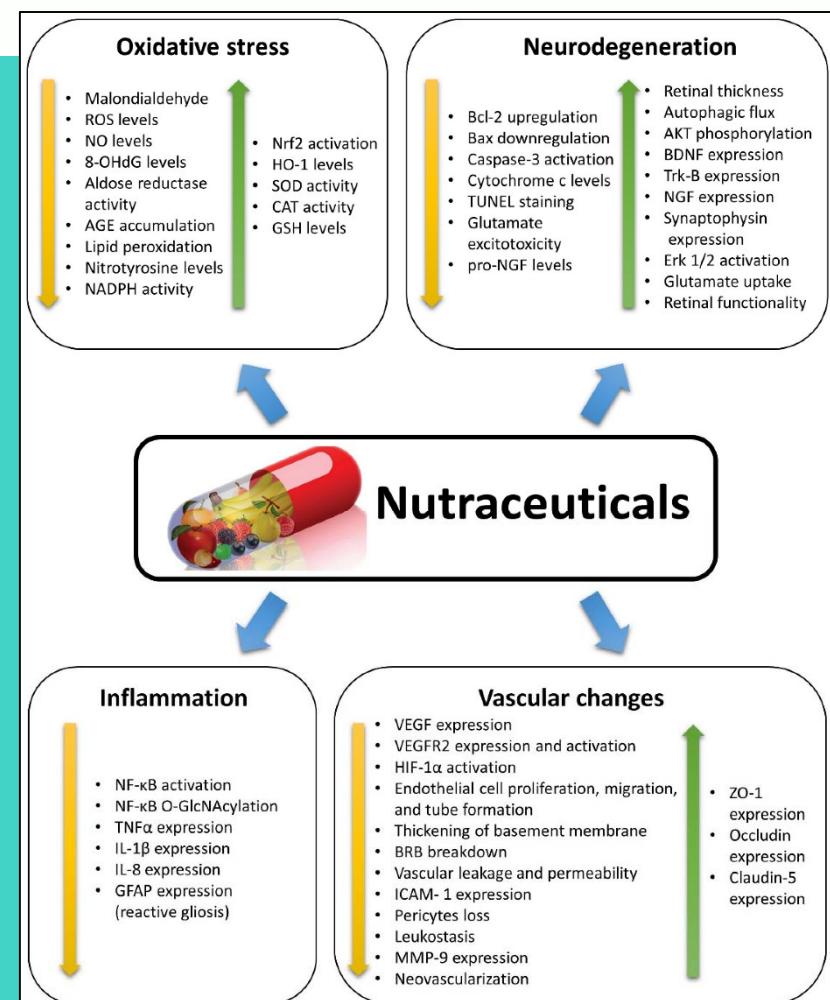
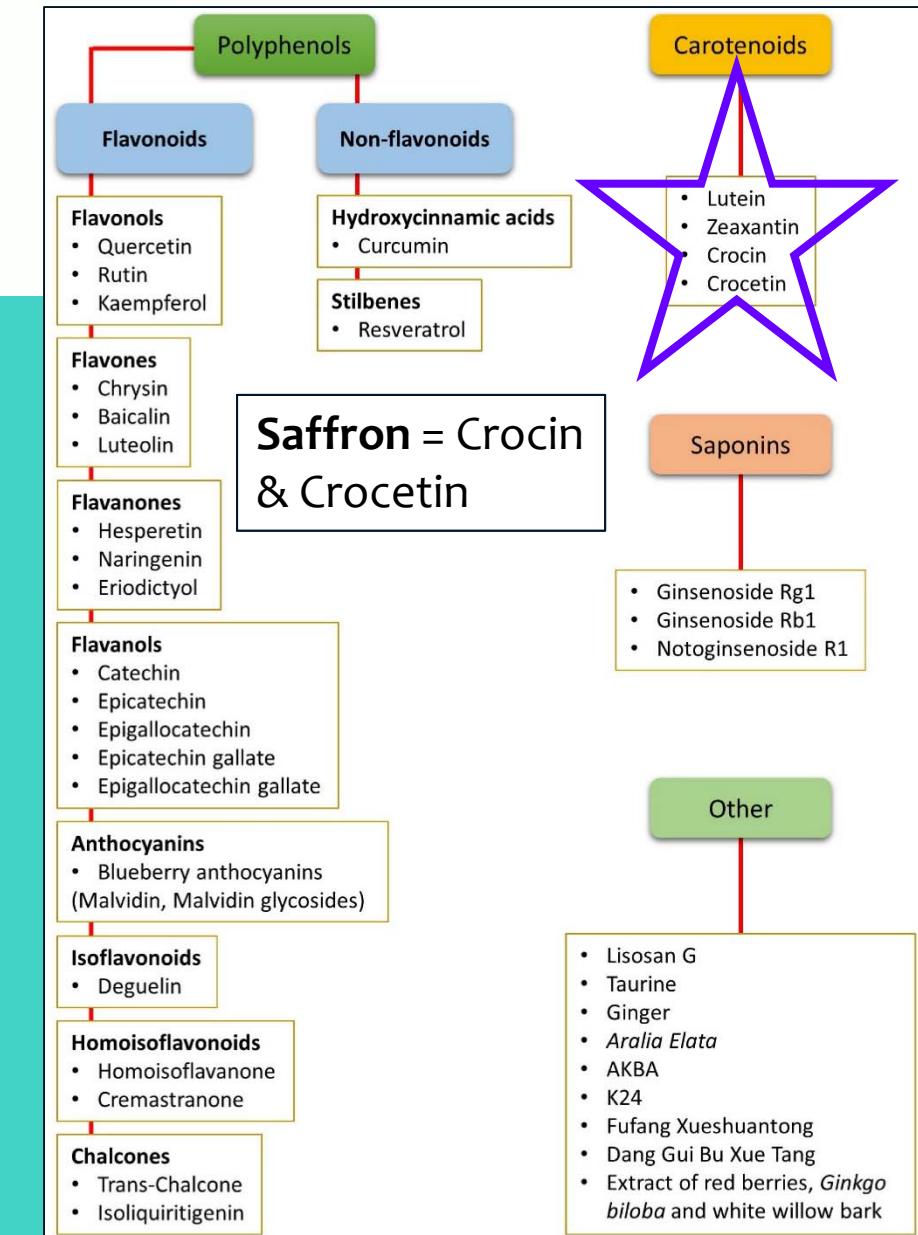
*“This [study] suggests that the DiVFuSS formula positively influences the pathogenesis of diabetes-induced retinal dysfunction... independent of tight or improved blood glucose control.”*

DiVFuSS Constituents	Mitigates DR in animal models	Blocks capillary cell apoptosis	Improves retinal capillary fragility	Reduces VEGF	Reduces oxidative stress	Reduces AGE activity	Reduces Polyol activity	Reduces PKC activity	Reduces NF-K $\beta$
Alpha-Lipoic Acid	•		•	•	•				•
Benfotiamine	•	•				•	•	•	
Vitamins C/E	•				•		•		•
Curcumin	•			•	•	•			•
Vitamin D3	•			•					
DHA/EPA	•	•			•				
Grape Seed Extract		•			•	•			
Resveratrol	•	•			•				
Green Tea Extract				•					
N-Acetyl Cysteine	•			•	•				
CoQ10					•				
Zinc	• (in AREDS)								
Pycnogenol	•		•		•				•
Lutein/Zeaxanthin	•			•	•				•

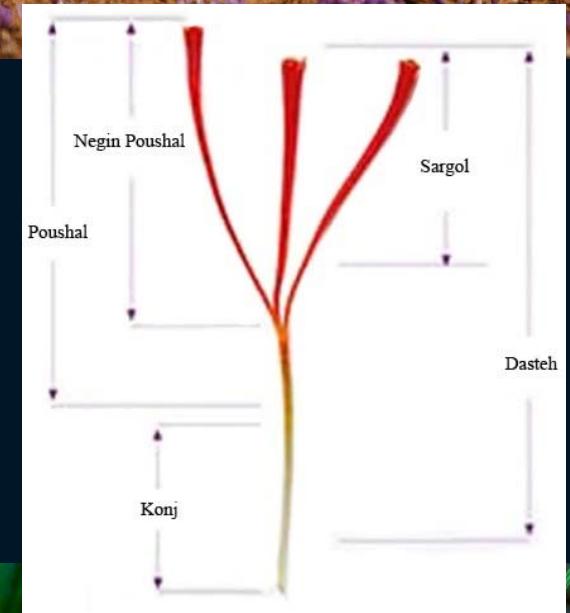
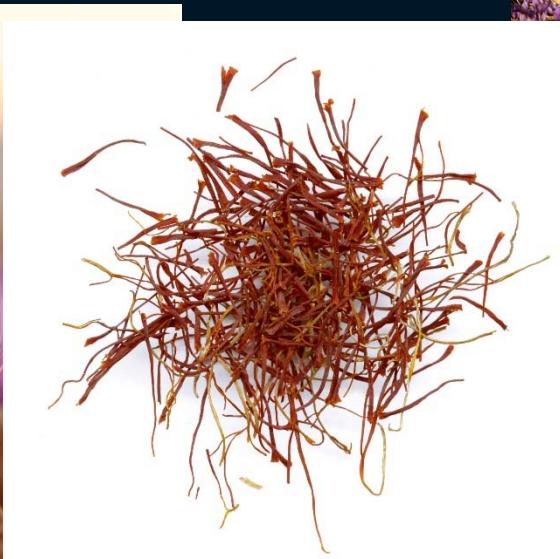
DiVFuSS Constituents	Improves visual function in humans	Reduces retinal edema in humans	Improves endothelial dysfunction in humans	Improves retinal blood flow in humans	Reduces HbA1c in humans	Improves Dyslipidemia in humans	Reduces blood pressure in humans	Reduces DPN symptoms in humans
Alpha-Lipoic Acid			•	•				•
Benfotiamine			•			•		•
Vitamins C/E			•	•		•		
Curcumin	•	•		•				
Vitamin D3					•	•		
DHA/EPA			•			•	•	
Grape Seed Extract								
Resveratrol			•		•			
Green Tea Extract			•			•	•	
N-Acetyl Cysteine								
CoQ10			•					
Zinc						•		
Pycnogenol	•	•		•	•	•	•	
Lutein/Zeaxanthin	•	•						

**Note: Suggested improvements marked by • include published evidence in animal and/or cell models, except as specifically noted, but do not reflect grading of that evidence.**

# Nutraceuticals & DR



# What is saffron?





Saffron is unarguably the most expensive spice you can find on the planet. It's usually sold in a few grams or even ounces, just a few red threads of this delicate and exquisite tasting plant make up a few grams.

On the market, premium quality saffron costs around \$4000 for 1 kilogram (or \$1800 a pound)! That's why it's commonly referred to as "red gold."

[Standards](#)[All about ISO](#)[Taking part](#)[Store](#)

EN ▾

MENU

THIS NEWS BELONGS TO OUR ARCHIVE.

**NEWS**

# HOW TO RECOGNIZE QUALITY SAFFRON ?

20 February 2014

Share on [Twitter](#), [Facebook](#), [Linkedin](#)

Otherwise known as "red gold" and well known in cooking, saffron is the world's most expensive spice

## RELATED INFORMATION

[ISO/TC 34/SC 7](#)**ICS > 67 > 67.220 > 67.220.10**

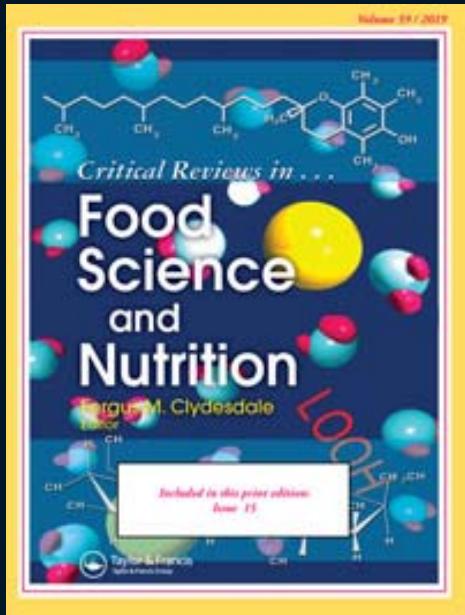
## ISO 3632-1:2011 SPICES -- SAFFRON (CROCUS SATIVUS L.) -- PART 1: SPECIFICATION

that is behind its high value.

Dr. A. Jayathilak, Chairman of the ISO subcommittee ISO/TC 34/SC 7, *spices*,

**STANDARDS**

***"It's high value has made saffron the object of frequent adulteration." International Standards Organization***



# Critical Reviews in Food Science and Nutrition

Publication details, including instructions for authors and subscription information:  
<http://www.tandfonline.com/loi/bfsn20>

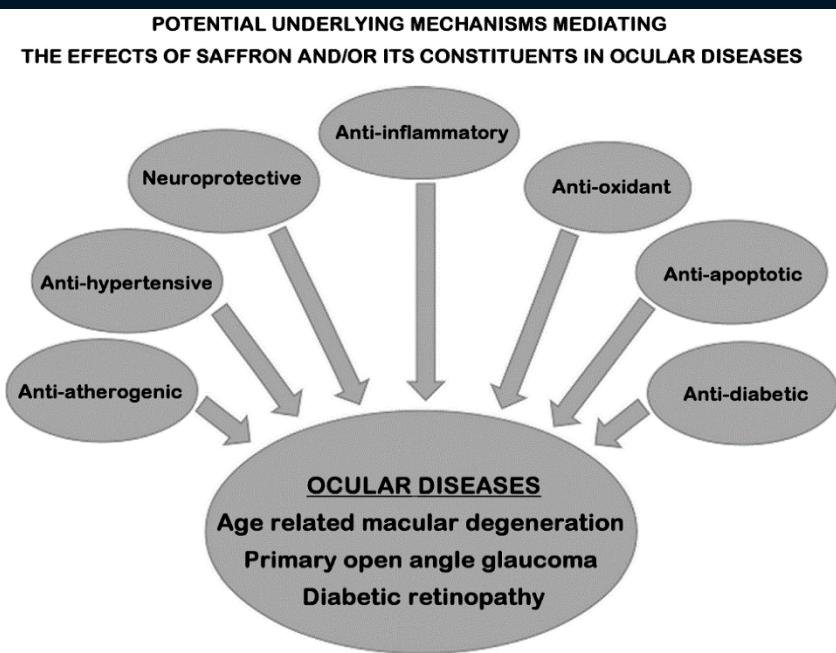
## Efficacy and Safety of Saffron Supplementation: Current Clinical Findings

G. K. Broadhead<sup>a</sup>, A Chang<sup>a</sup>, J Grigg<sup>a</sup> & P McCluskey<sup>a</sup>

<sup>a</sup> Save Sight Institute, The University of Sydney, Sydney, Australia

Accepted author version posted online: 15 Apr 2015.

Saffron [30 mg/day], and its constituents such as crocetin and crocin, are effective in reducing damage mediated by reactive-oxygen species. **There is evidence from clinical trials that this research translates into measurable clinical benefits.**



NEW!



*nutrients*

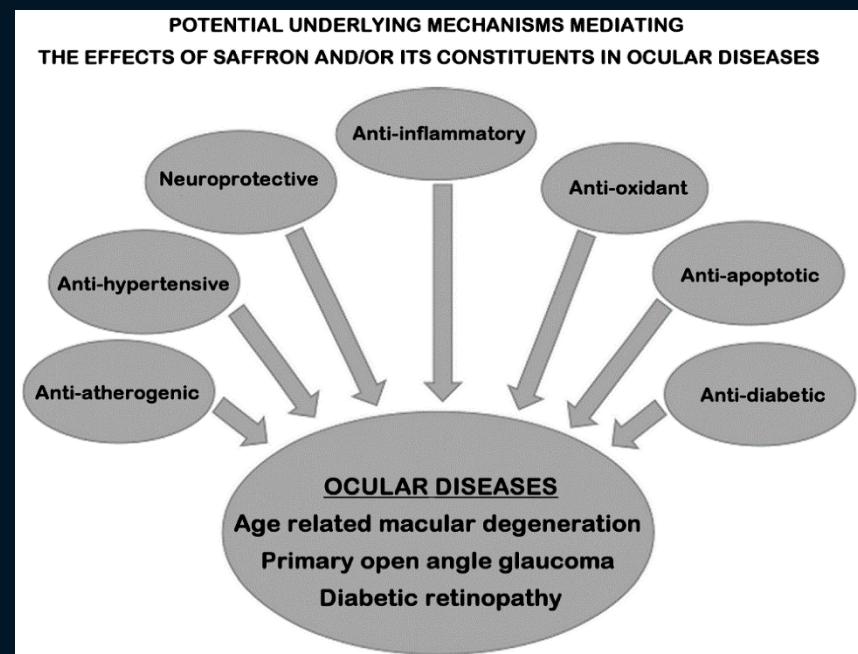


Review

## Saffron (*Crocus sativus* L.) in Ocular Diseases: A Narrative Review of the Existing Evidence from Clinical Studies

Rebekka Heitmar <sup>1,\*</sup>, James Brown <sup>1</sup> and Ioannis Kyrou <sup>2,3,4</sup>

*Saffron supplementation appears to have promising potential as an effective and safe adjunct therapy in certain ocular diseases. [There is a need for] RCTs in order to form evidence-based recommendations for the potential therapeutic role of oral saffron supplementation in ocular diseases.*





# Saffron 2020-PRO Eye Supplement

**\$84.97**

Saffron eye health supplement  
and helps maintain good health.

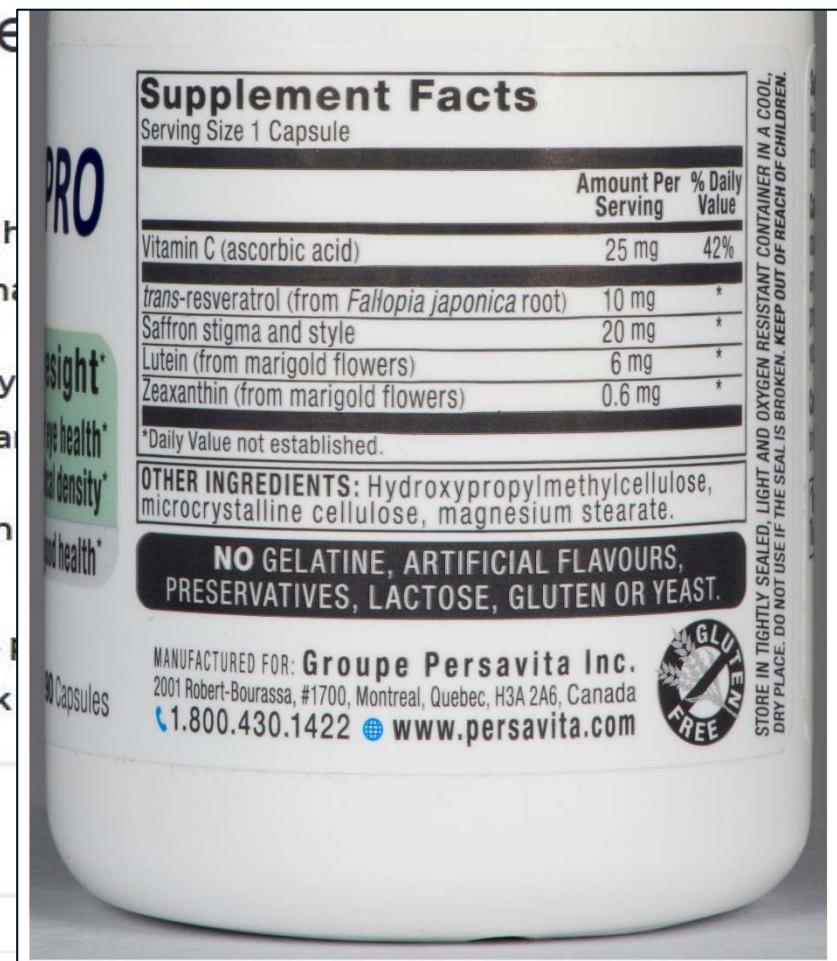
Approved by

Without vitamins

With saffron  
eye health.

90 capsules

Money-Back



NEW!

*nutrients*

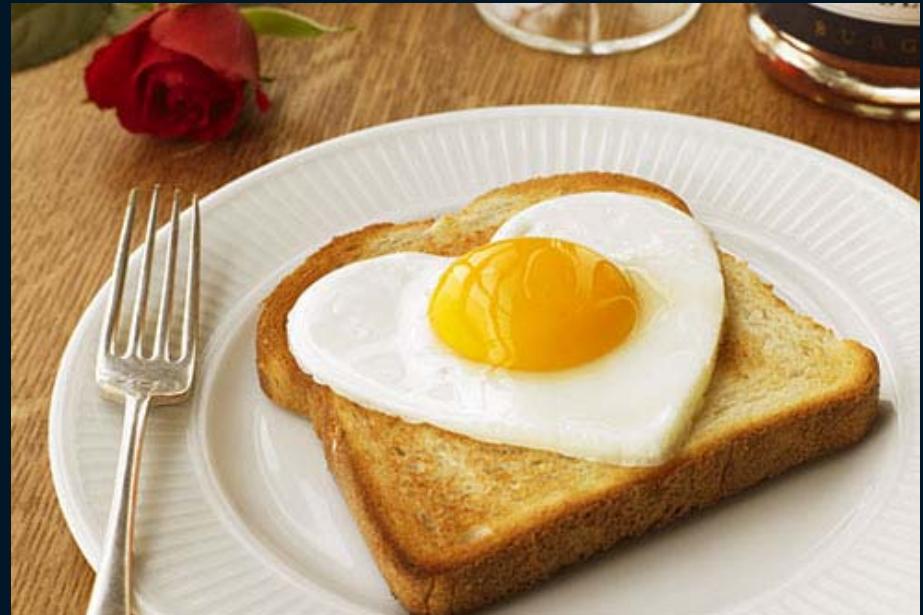


Review

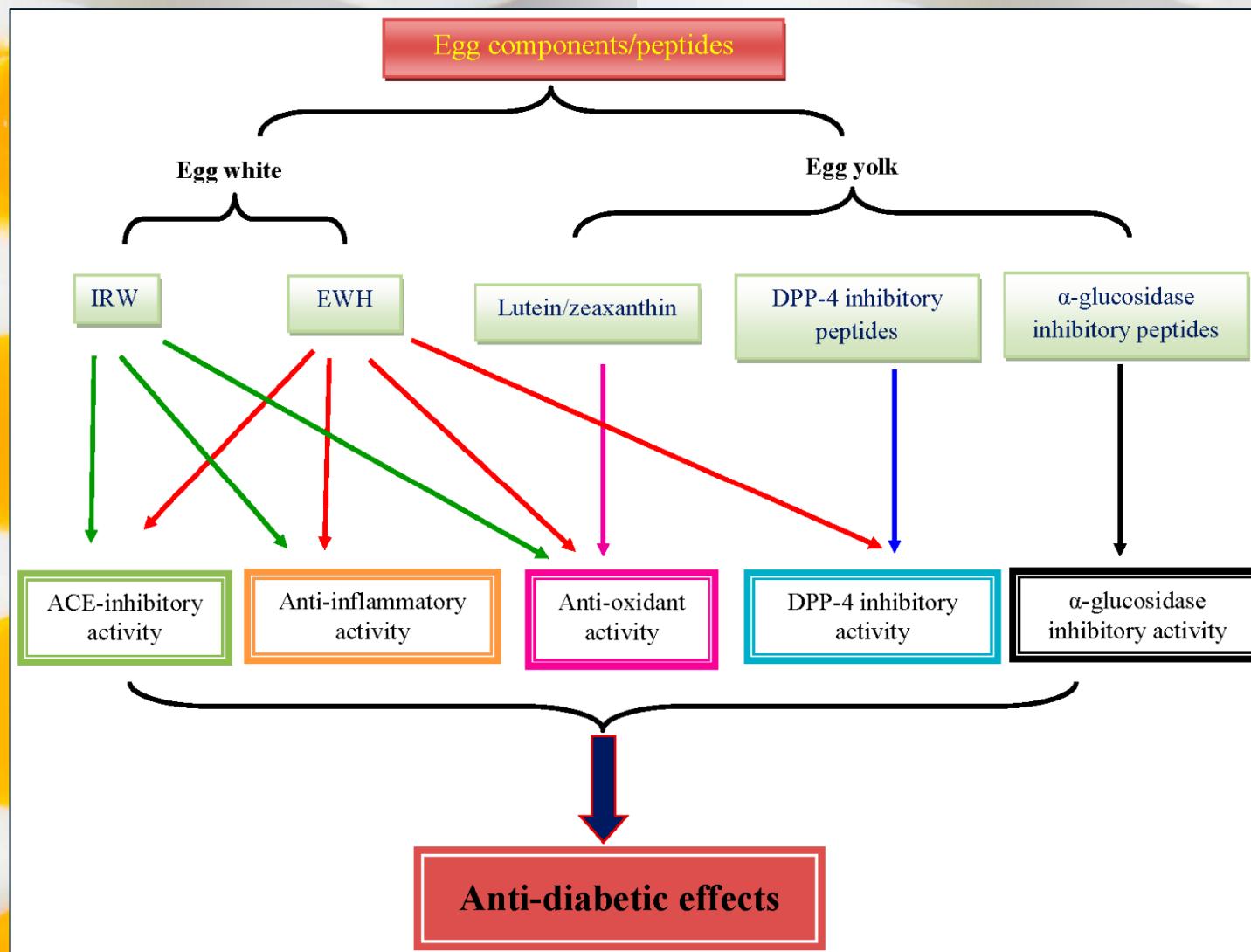
# Mechanism and Potential of Egg Consumption and Egg Bioactive Components on Type-2 Diabetes

Xiaofeng Wang <sup>1</sup>, Myoungjin Son <sup>1</sup>, Chalamaiah Meram <sup>1</sup> and Jianping Wu <sup>1,2,\*</sup>

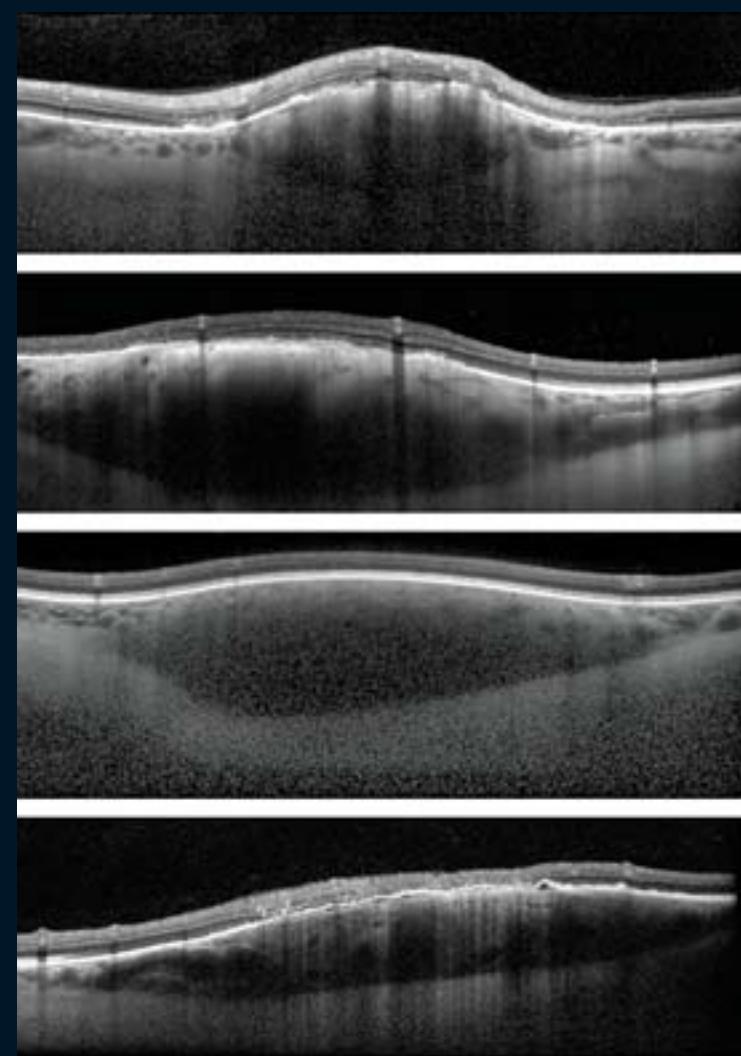
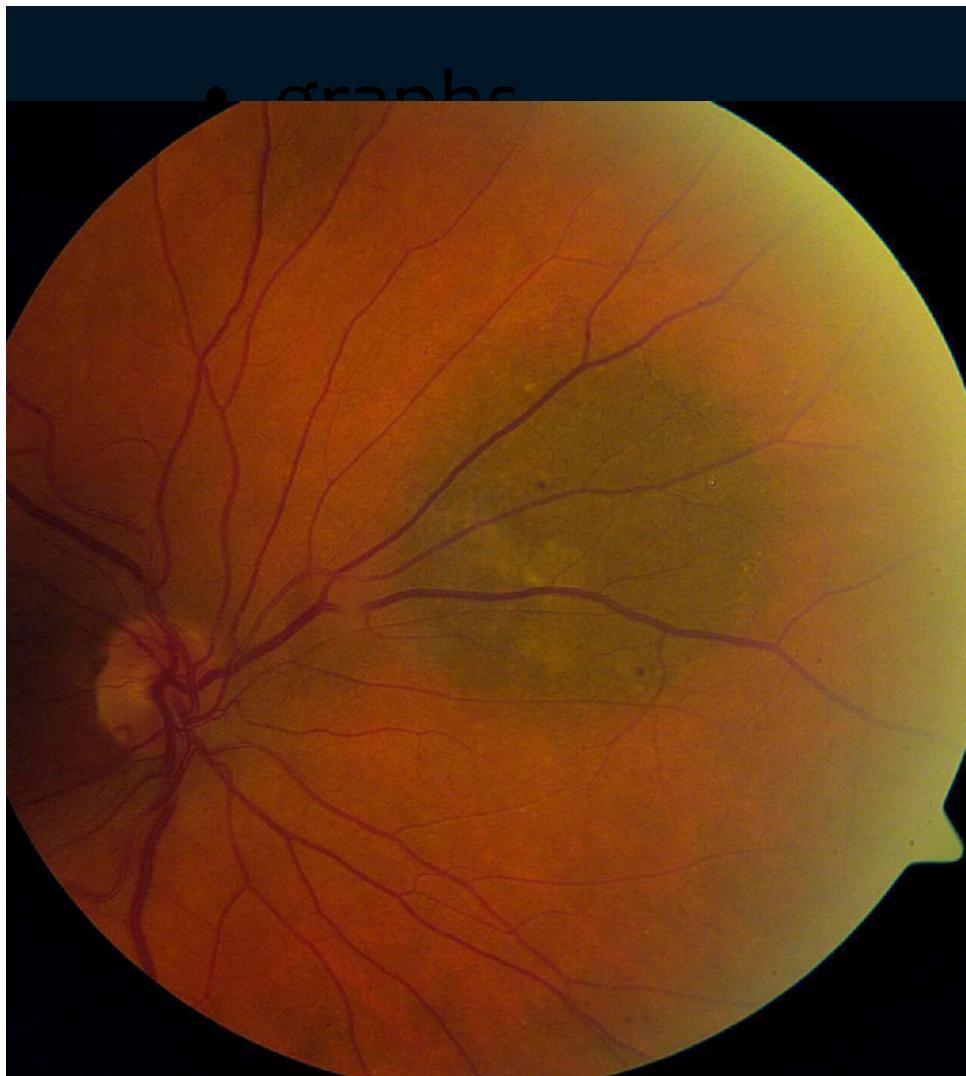
*There is association between higher egg consumption and improved blood lipid profile, insulin sensitivity, and glucose response in interventional clinical trials.*



Nutrients. 2019;11:357



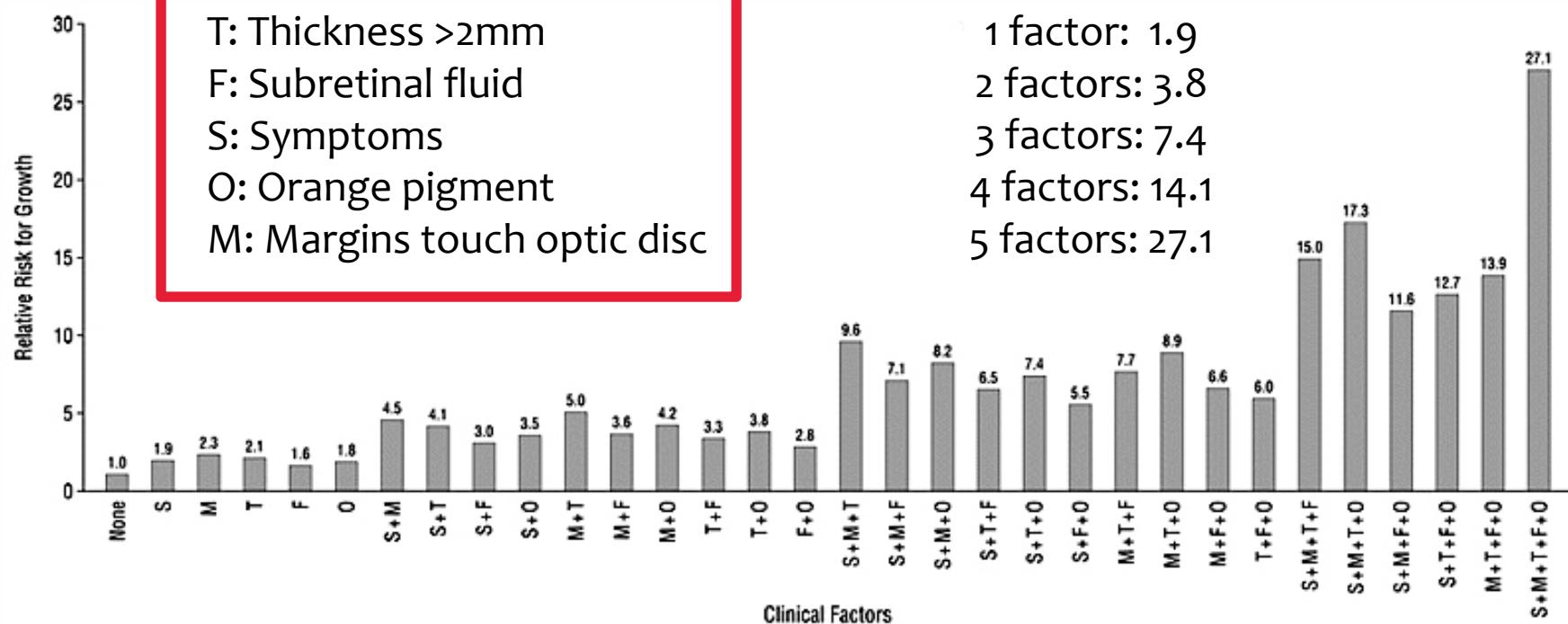
# Choroidal Nevus



# Choroidal Nevus

- **Clinical Features**

- Clinically indistinguishable from melanoma
- Documented growth is best evidence of malignancy
- Other features suggestive of malignancy:  
**T**o **F**ind **S**mall **O**cular **M**elanomas
- **T**hickness, **F**luid, **S**ymptoms, **O**range, **M**argin
- Risk of transformation: **1 in 8,845**



Relationship between number of risk factors and documented growth of 1287 small melanocytic tumors ( $\leq 3$  mm thickness) over an average 51mo follow-up period.



This 37yoWF had photopsia and a 1.7-mm-thick choroidal pigmented mass touching the optic disc. Note the prominent orange pigment and subtle subretinal fluid. This patient had 4 of 5 risk factors for tumor growth, including symptoms, orange pigment, SRF, and margin touching the optic disc. In keeping with traditional management in 1985, serial observation was advised. Left: Baseline photograph (1985). Right: Follow-up photograph (1986). Growth was documented in base and in thickness 1 year later. Enucleation was performed. Eight years later, she died from metastatic melanoma.

NEW!

# CHOROIDAL NEVUS IMAGING FEATURES IN 3,806 CASES AND RISK FACTORS FOR TRANSFORMATION INTO MELANOMA IN 2,355 CASES

**The 2020 Taylor R. Smith and Victor T. Curtin  
Lecture**

CAROL L. SHIELDS, MD, LAUREN A. DALVIN, MD, DAVID ANCONA-LEZAMA, MD,  
MICHAEL D. YU, BS, MAURA DI NICOLA, MD, BASIL K. WILLIAMS, JR., MD,  
J. ANTONIO LUCIO-ALVAREZ, MD, SU MAE ANG, BS, SEAN MALONEY, BS, R. JOEL WELCH, MD,  
JERRY A. SHIELDS, MD

To Find Small Ocular Melanoma Doing IMaging

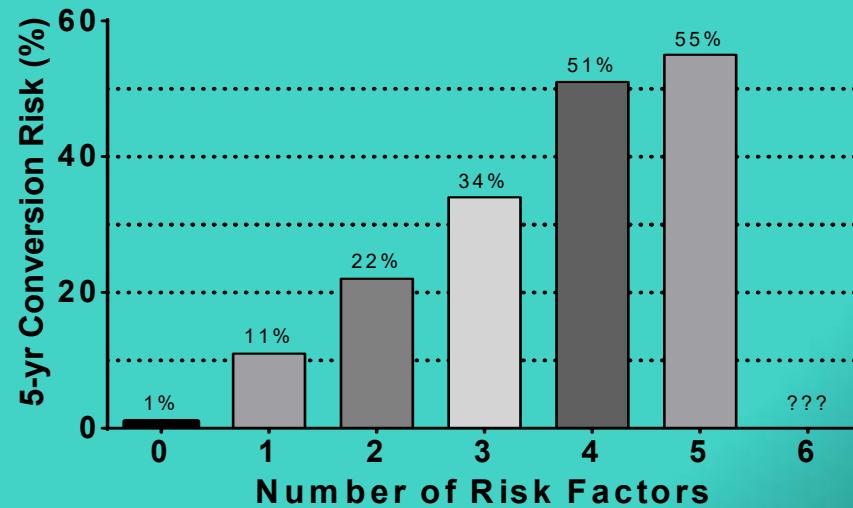
**TFSOM-DIM**

Retina. 2018 Dec 31.

NEW!

# Choroidal Nevus

- **Imaging features associated with malignant transformation**
  - Thickness >2 mm (US) ← Ultrasound – not OCT
  - Fluid subretinal (OCT)
  - Symptoms & vision loss (VA 20/50 or worse)
  - Orange pigment (FAF)
  - Melanoma hollow (US) ← No longer “Margin touching ONH”
  - DiaMeter >5mm (photography) ← NEW!

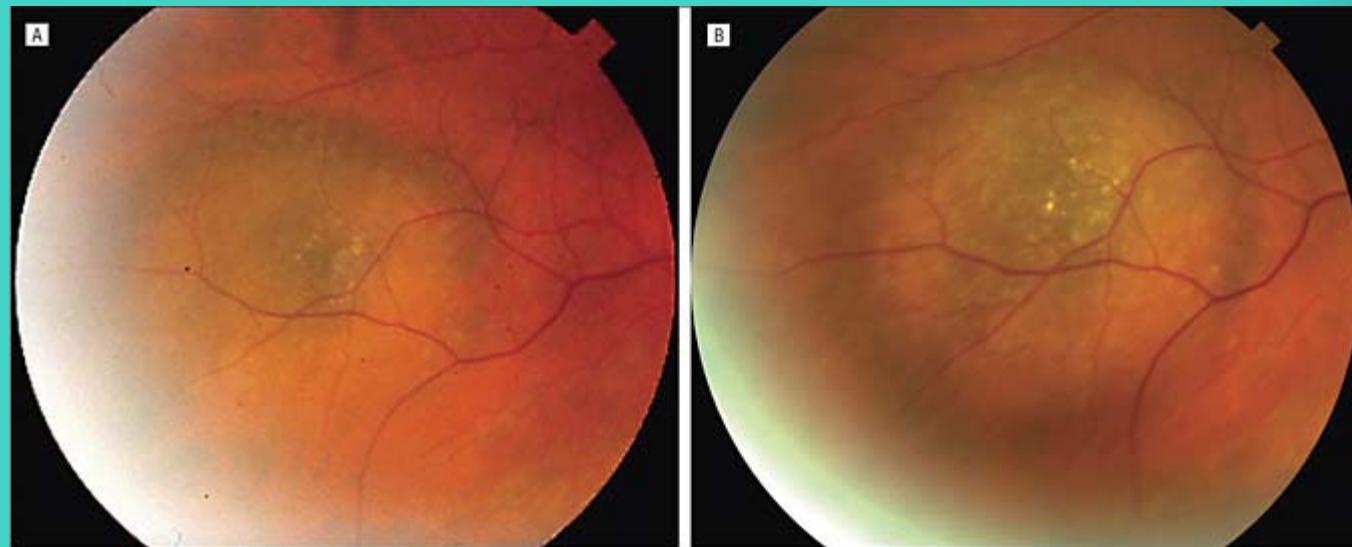


# Choroidal Nevus

- How to Monitor
  - **NEVER monitor a nevus with even a single high-risk feature**
  - Annual exams with DFE
  - **Photographs:** 2 disc diam  $\approx$  5mm, growth
  - **FAF:** Orange pigment
  - **OCT:** Subretinal fluid, thickness, growth
  - Document TFSOM-DIM evaluation in chart

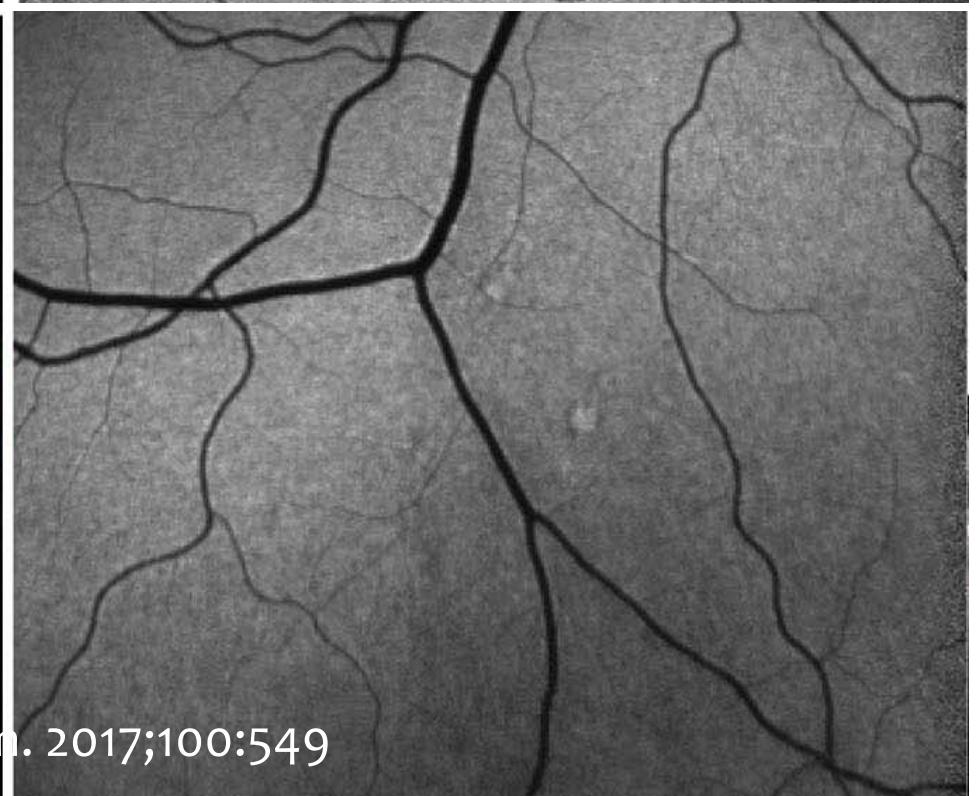
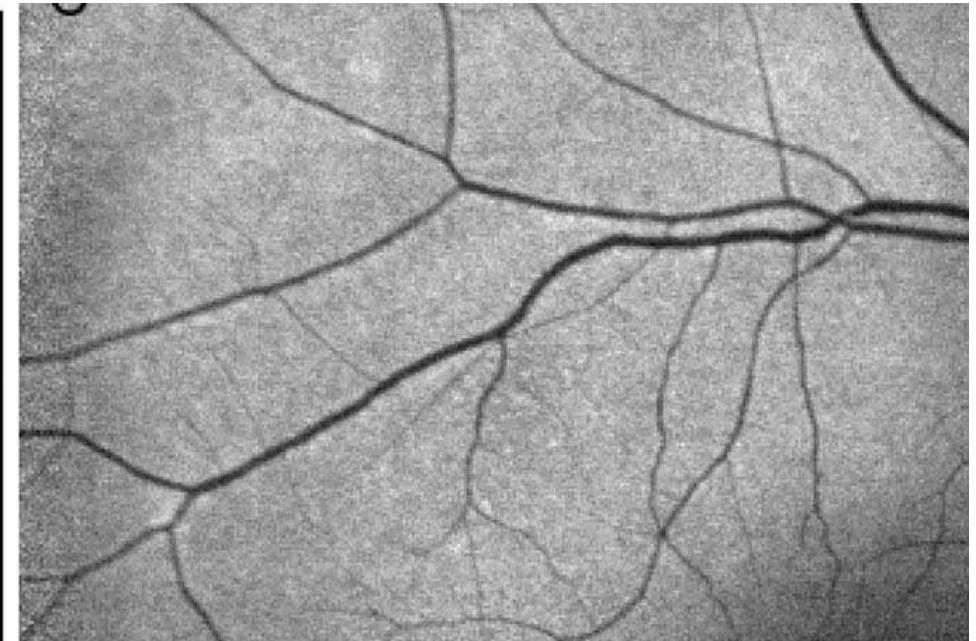
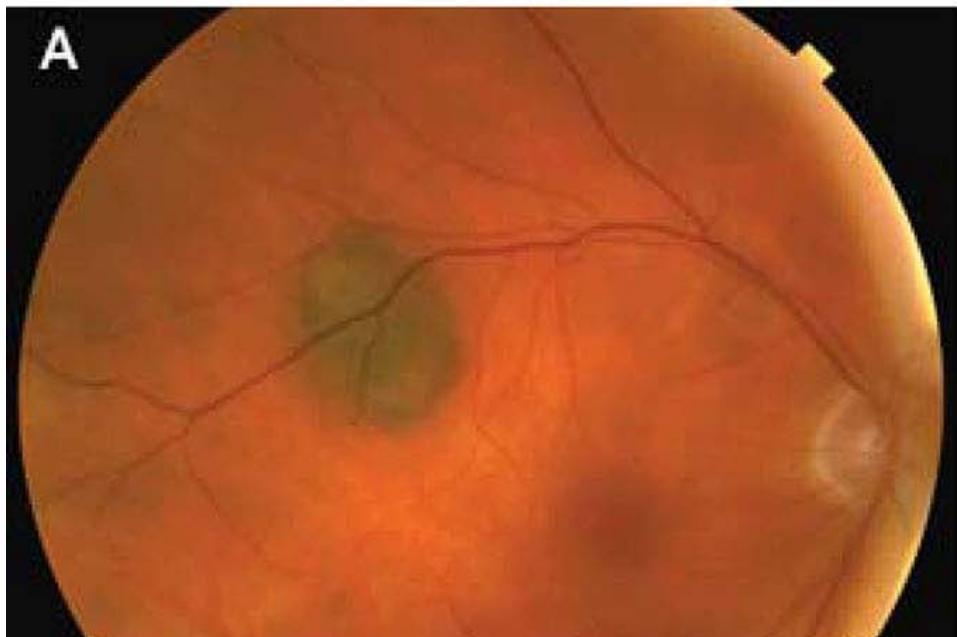
# Choroidal Nevus

- When to Refer
  - Any high-risk features (TFSOM-DIM)
  - Documentation of *growth*

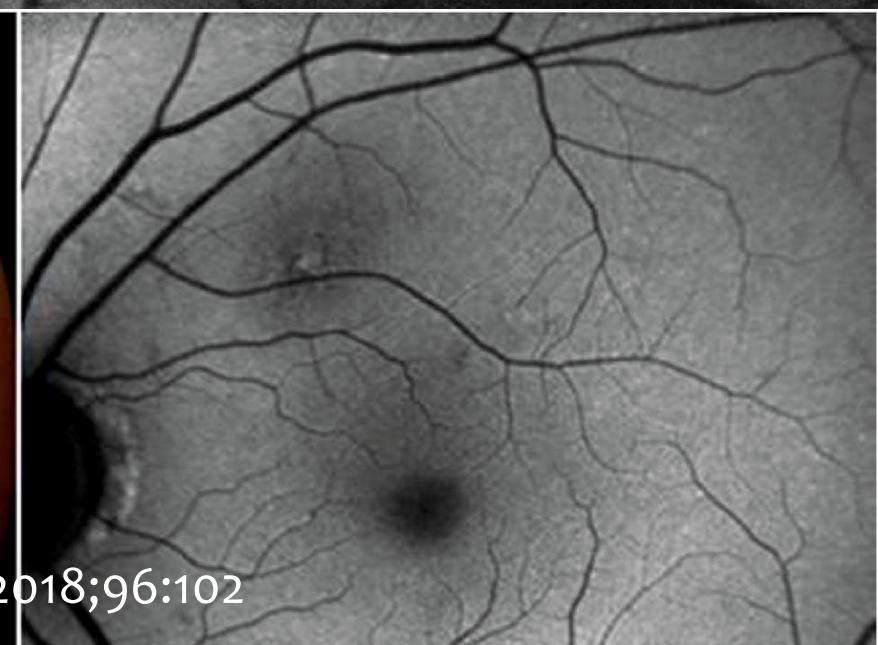
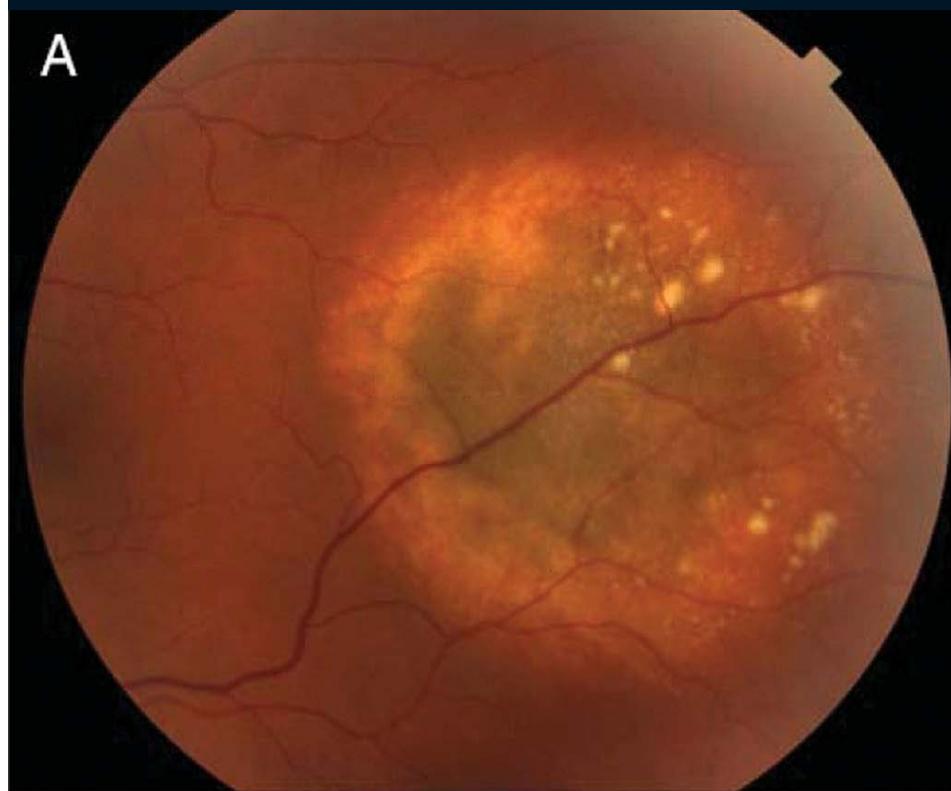


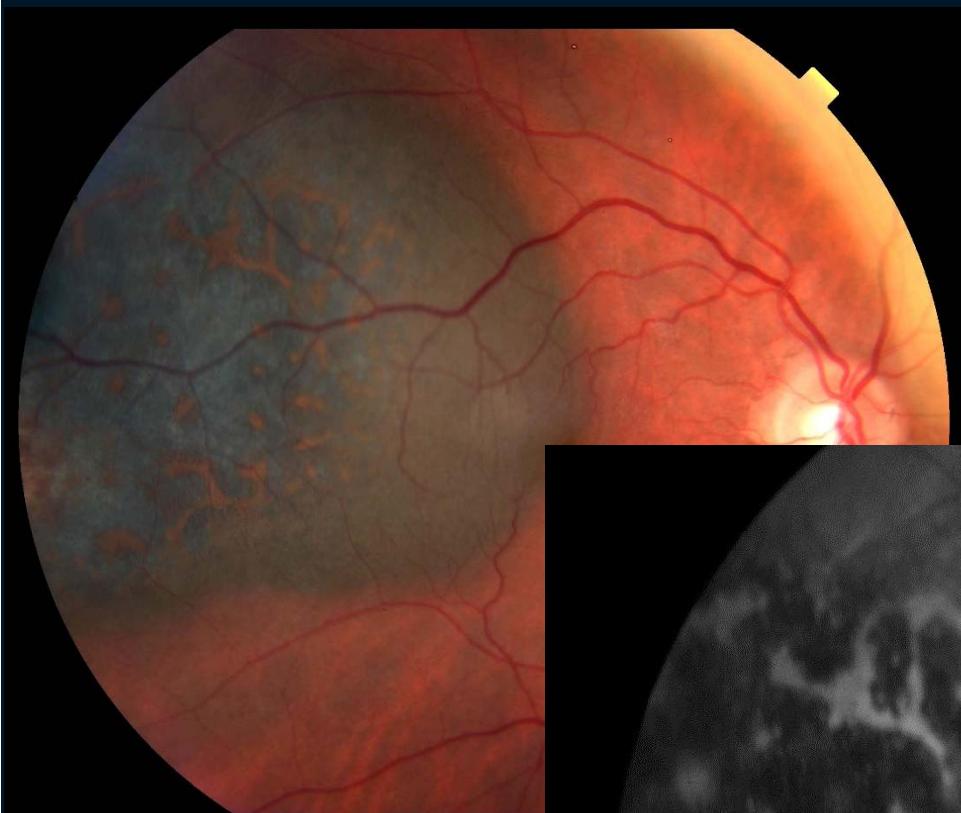
# Choroidal Nevus

- **FAF features of choroidal nevus**
  - Hypo-autofluorescence (56%) – RPE degeneration
  - Hyper-autofluorescence (25%) – Drusen
  - Normal autofluorescence (19%) – No change
- **FAF features of choroidal melanoma**
  - Tumor itself is not autofluorescent
  - Autofluorescence of lipofuscin and SRF



A

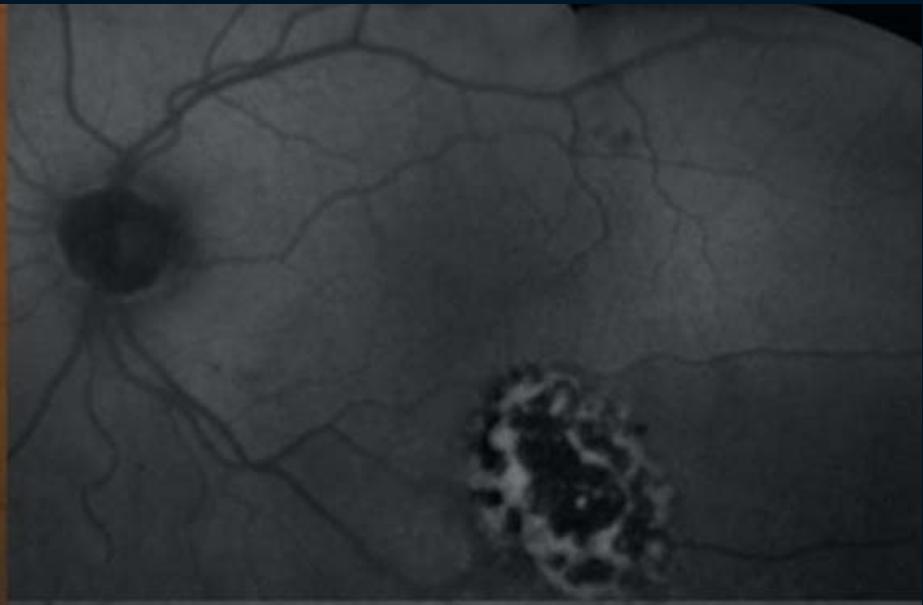
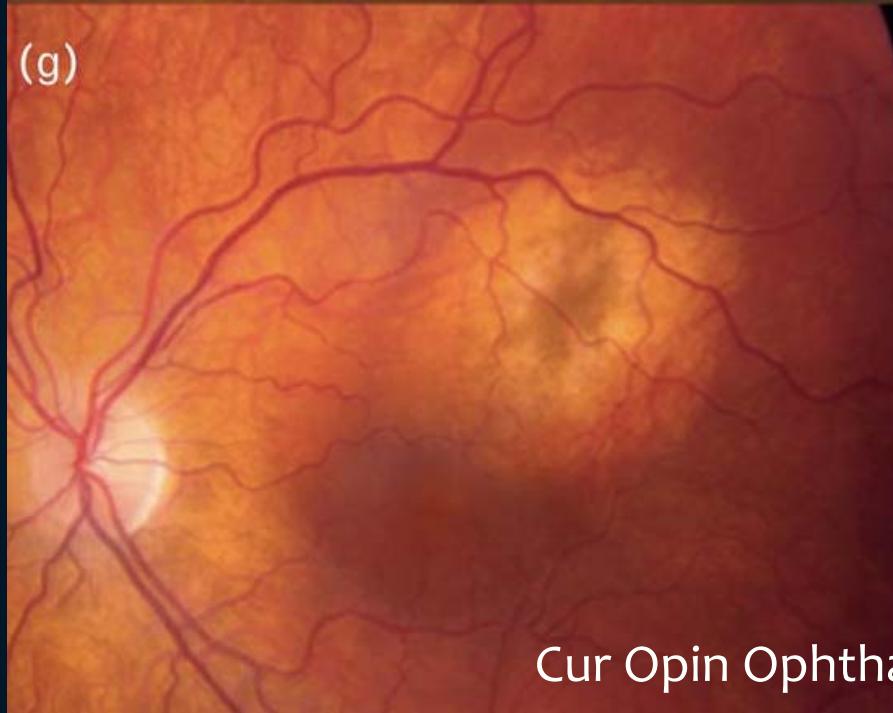
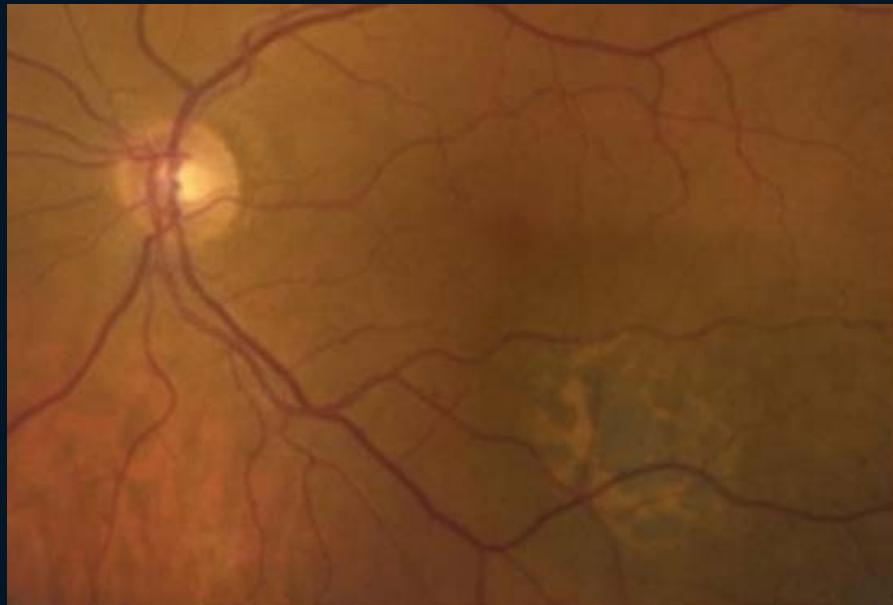




Orange lipofuscin plaques may occur in melanomas and will intensely autofluoresce

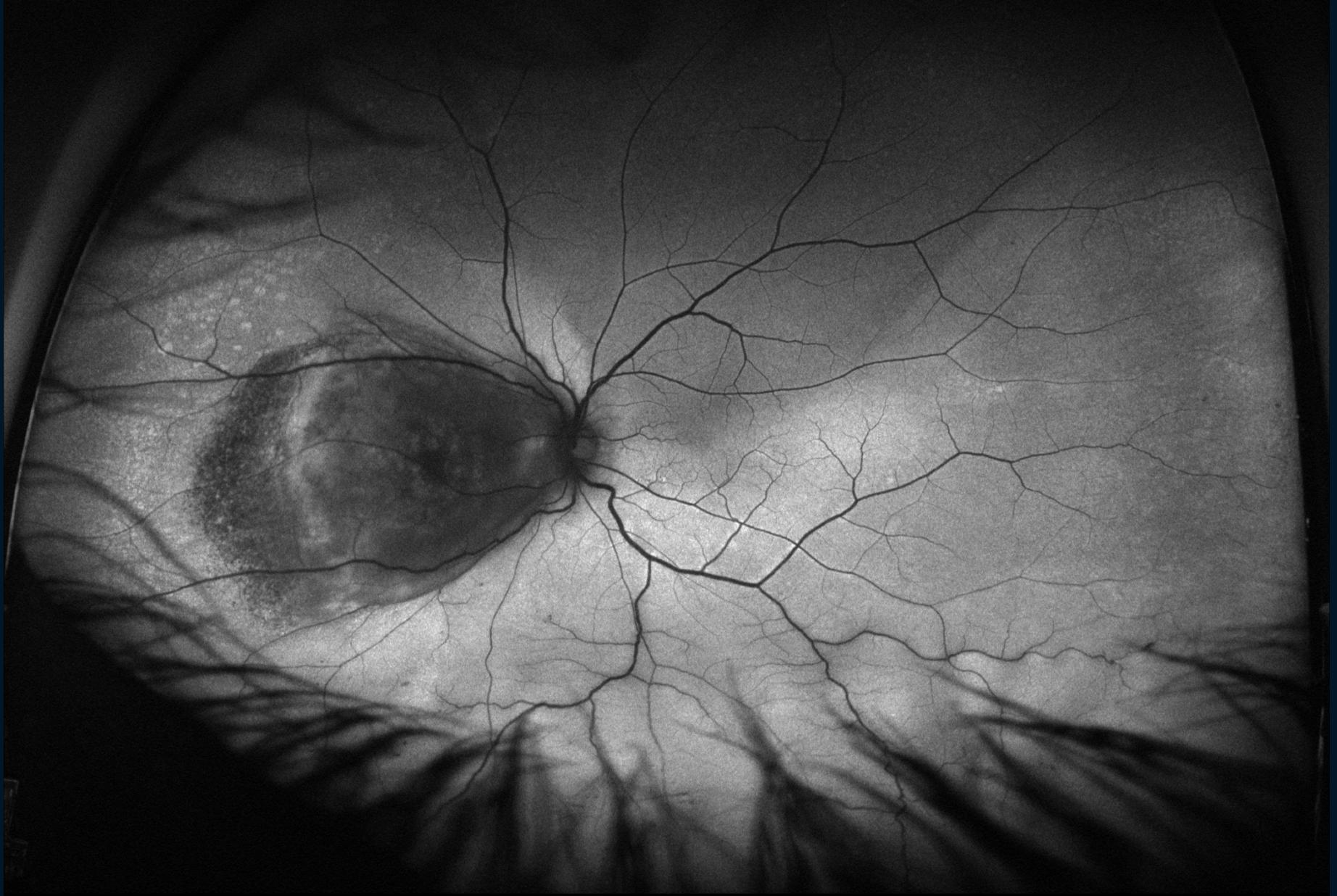


Examples of small melanomas associated with hyperautofluorescent lipofuscin pigment



(h)

Example of an inferior melanoma-associated exudative RD demonstrating hyper-autofluorescence of subretinal fluid

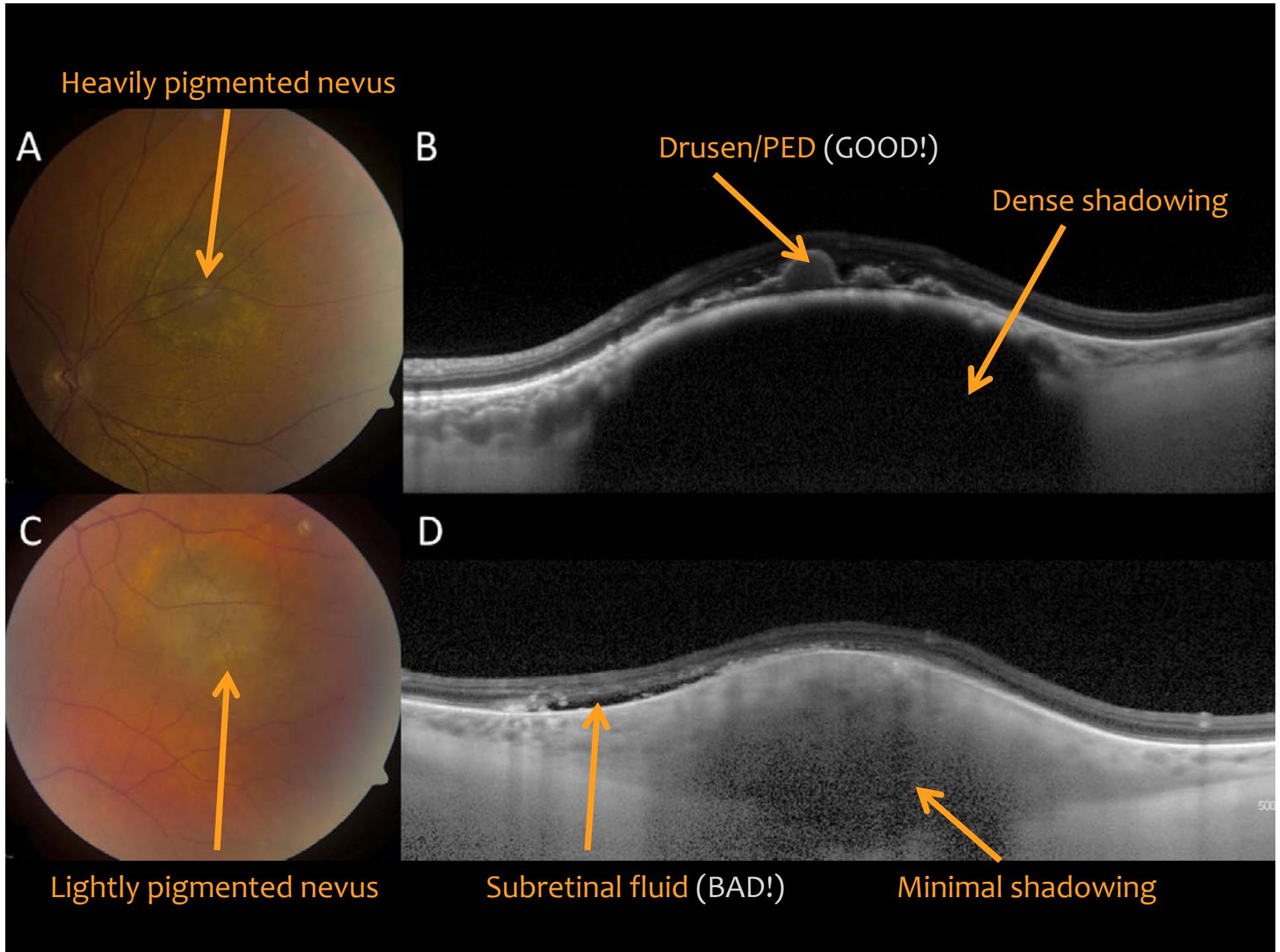


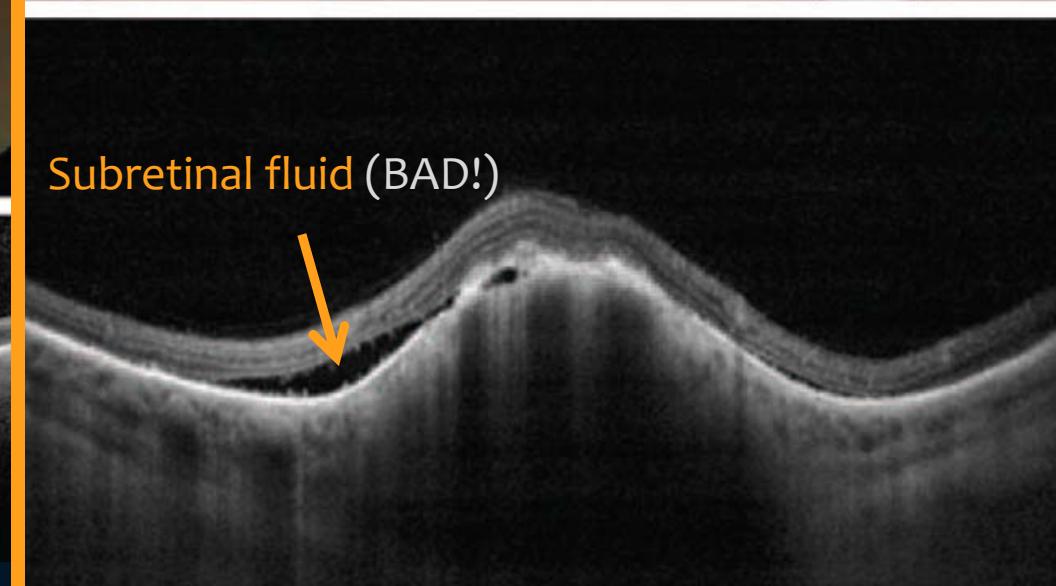
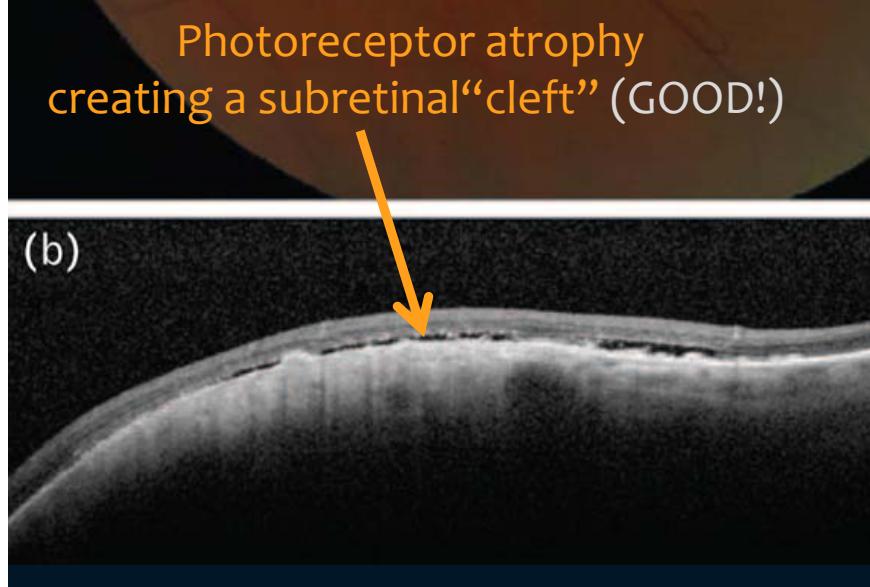
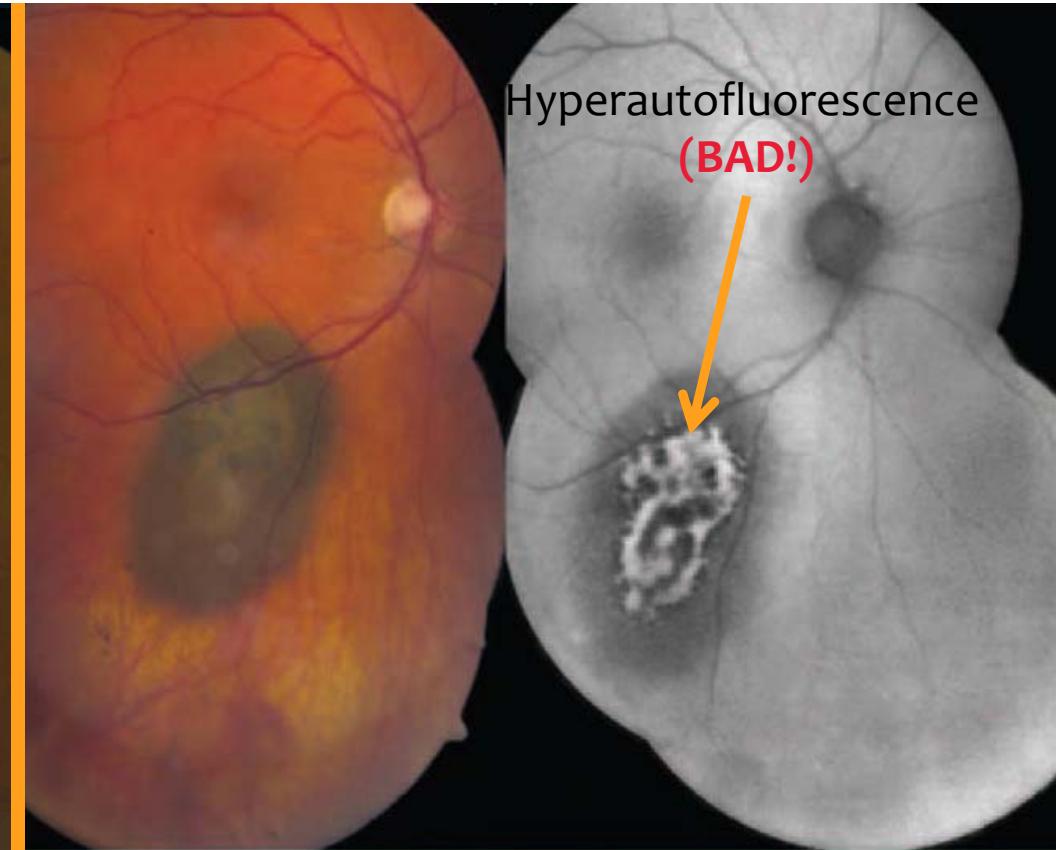
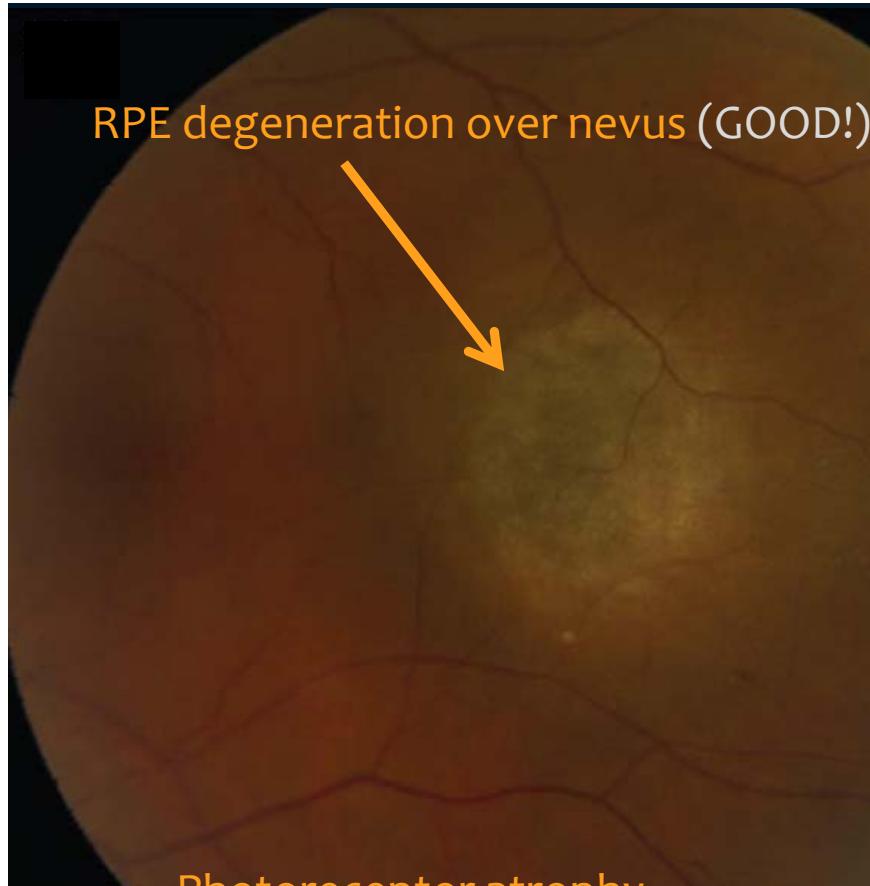
Example of hyper-autofluorescence of subretinal fluid surrounding a melanoma

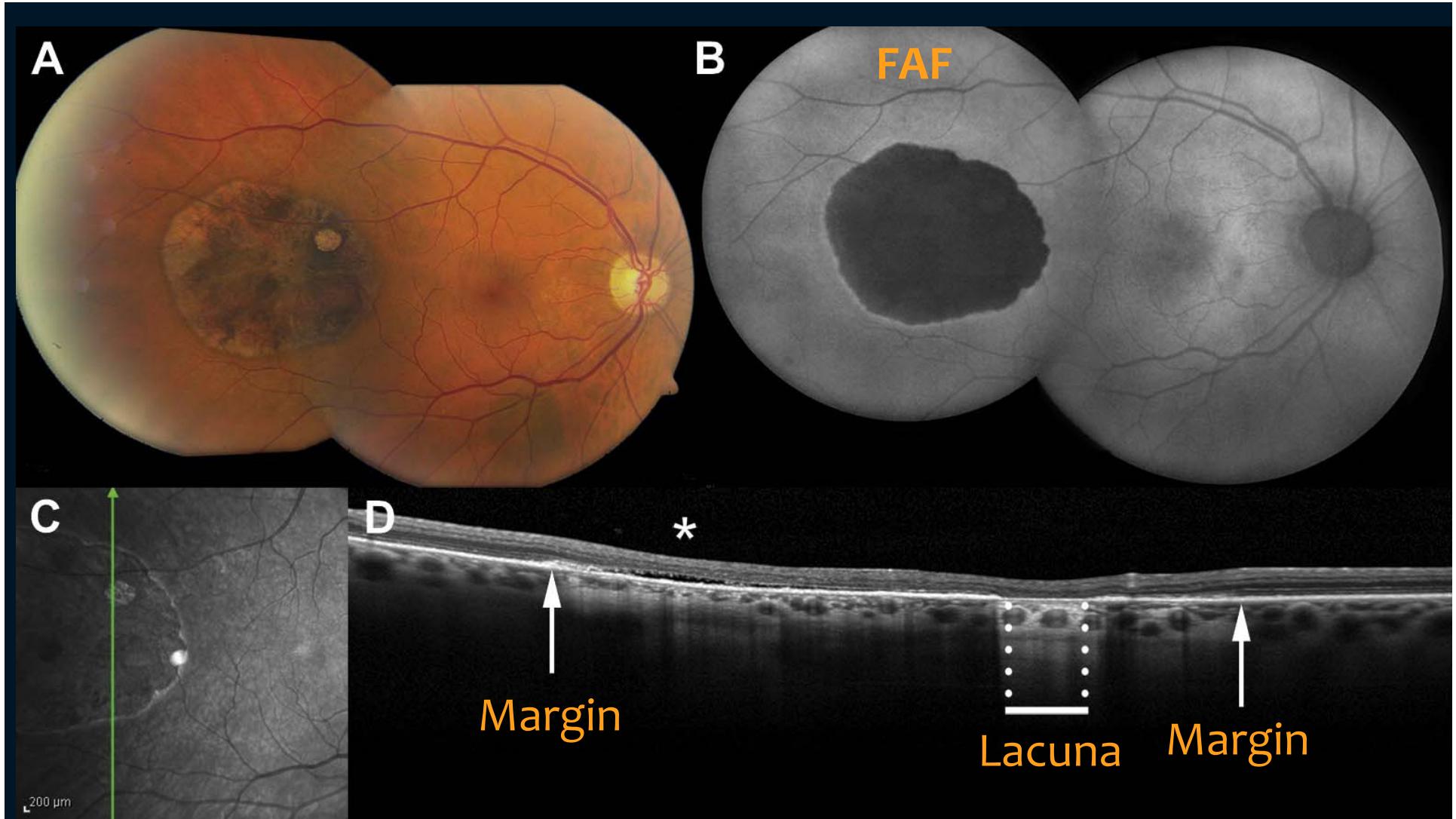


# Choroidal Nevus

- **OCT features of choroidal nevus**
  - Gently sloping smooth surface
  - Overlying RPE and retinal degeneration
  - Choroidal shadowing varies with pigment
  - Absence of exudation
  - **Lesion thickness**
    - <2mm = nevus
    - 2-3mm = suspicious for melanoma
    - $\geq 3$ mm = melanoma



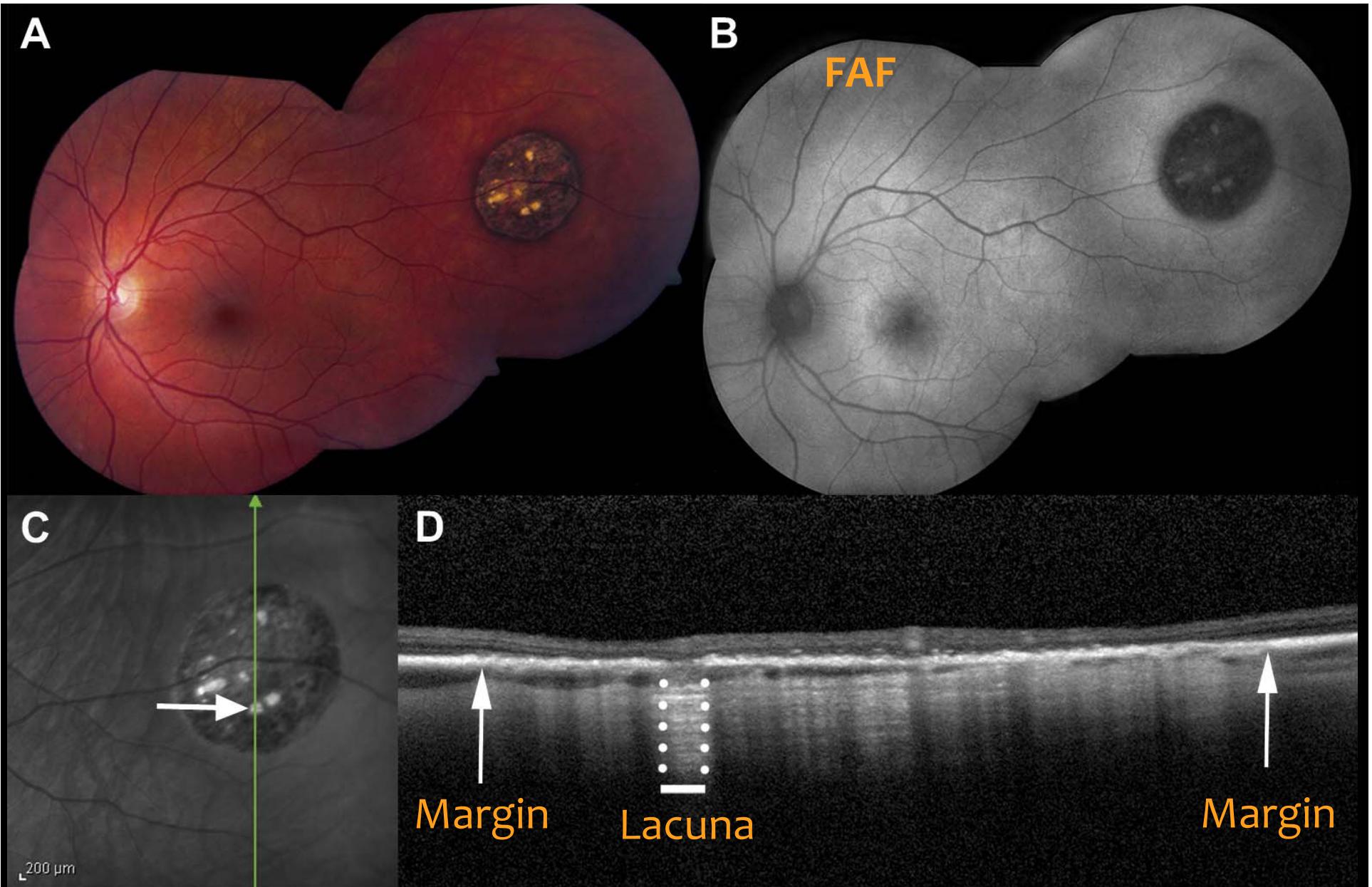




## Congenital hypertrophy of RPE (CHRPE)

Both choroid and retina is thinned within the margins of the lesion.

Lacunae are window defects that permit light transmission through the lesion. \* marks intraretinal cleft caused by photoreceptor atrophy.



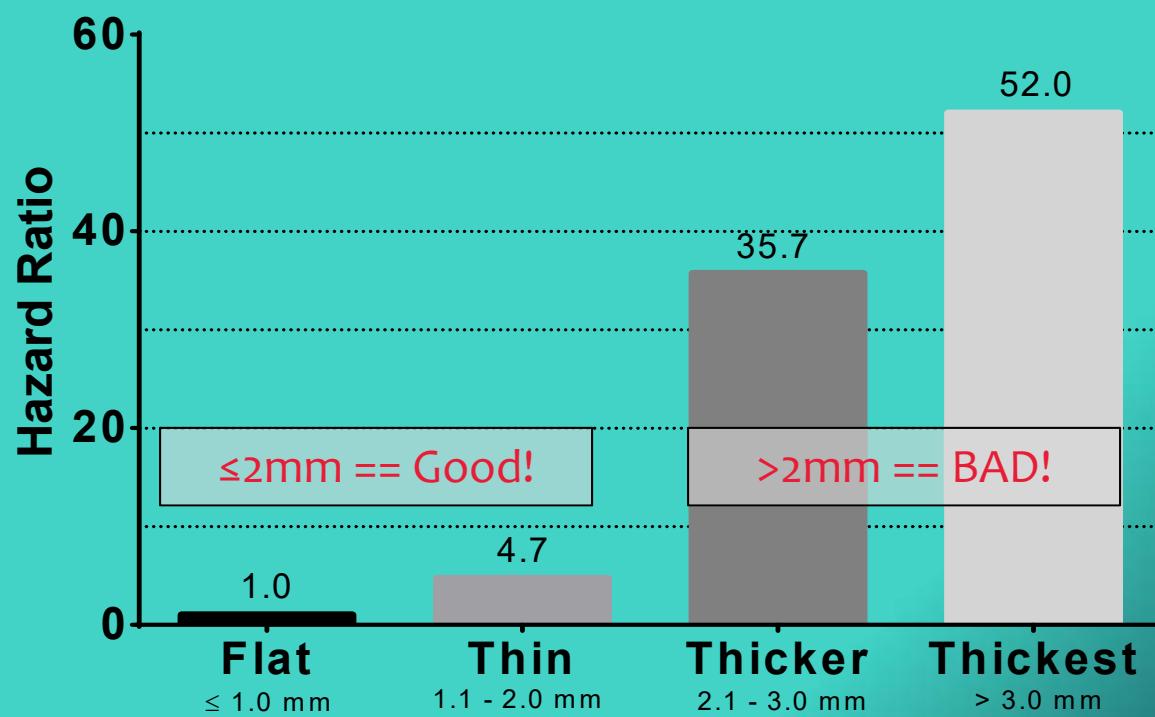
Congenital hypertrophy of RPE (CHRPE)

NEW!

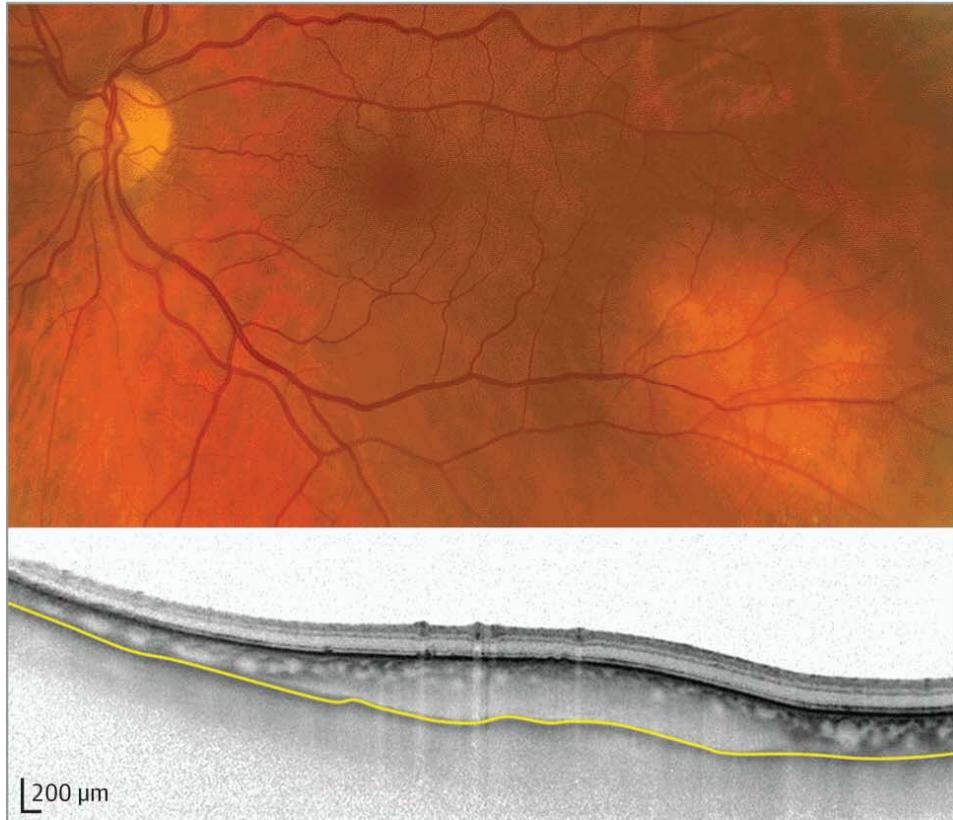
# Choroidal Nevus

## • IMPORTANCE OF LESION THICKNESS

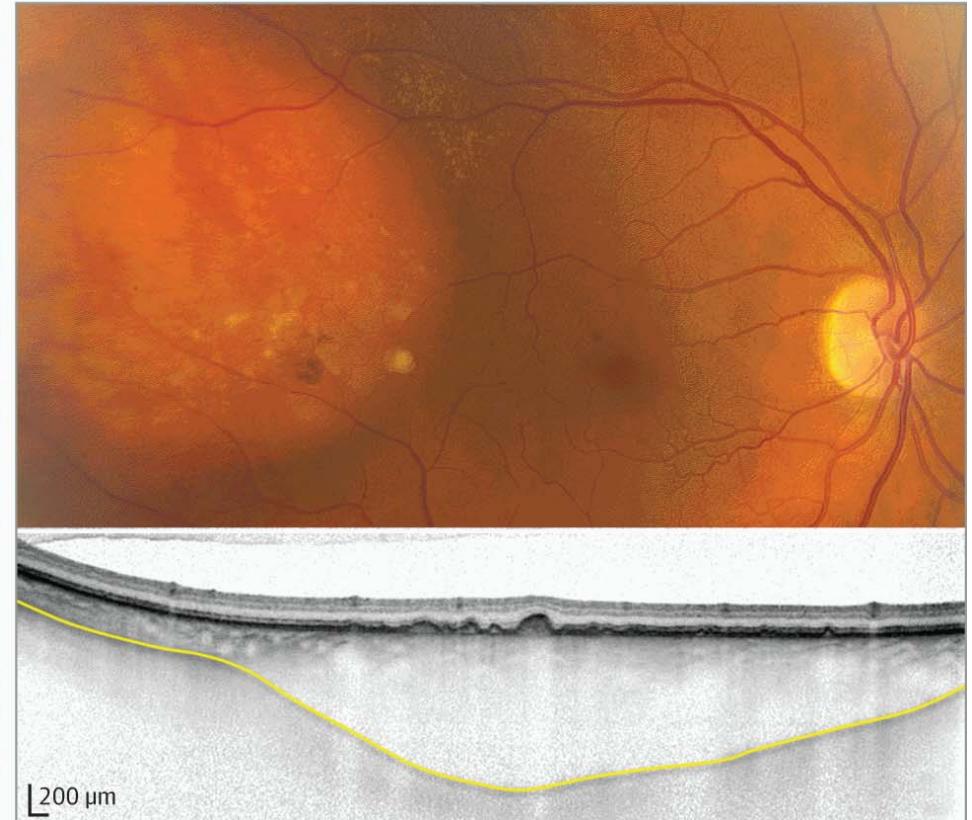
- Higher risk of malignant transformation for nevi  $>2.0$  mm compared with those  $\leq 2.0$  mm



**A** Without posterior scleral bowing



**B** With posterior scleral bowing



Nevi typically extend inwardly, elevating the retina (LEFT). Sometimes they extend outwardly, causing bowing of the sclera and little or no elevation of the retina (RIGHT).

# Choroidal Nevus

- **Importance of subretinal fluid**
  - Choroidal nevus
    - Retinal degeneration & photoreceptor death
    - Photoreceptor loss → subretinal “**cleft**”
  - Choroidal melanoma
    - Fluid leakage creates a “puddle” at lesion margin
    - Photoreceptors shed outer segment discs, which appear “**shaggy**” on OCT

## SMALL MELANOMA

A

Orange pigment

SRF & shaggy PR

E

SRF & shaggy PR



I

SRF & shaggy PR



## NEVUS

D



Irregular RPE

L

P

PR retraction & cleft

Drusen & PED

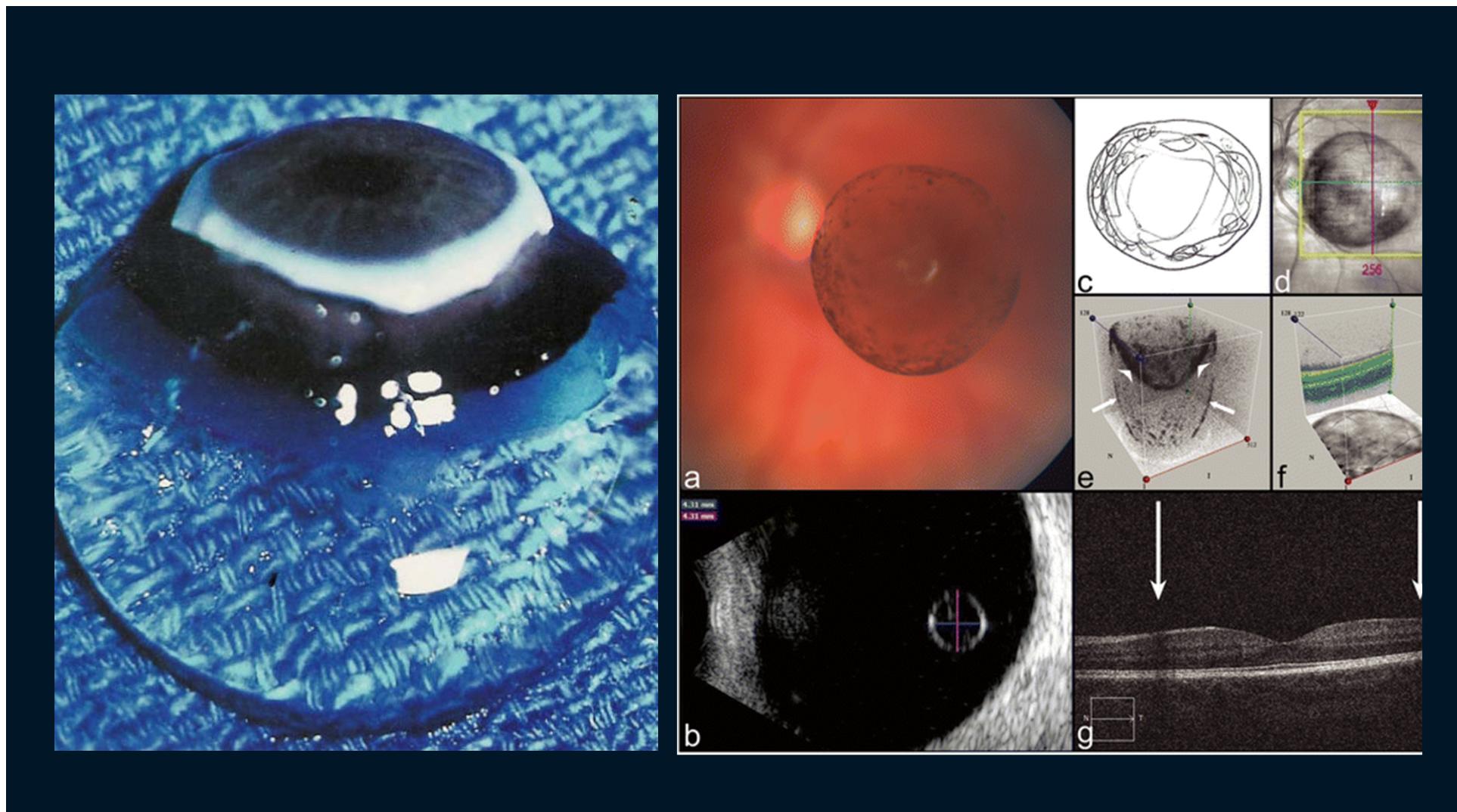


# Self Assessment Quiz

You obtain OCT and photographs of all choroidal nevi.

- If so, award yourself 1 point
- If not, award yourself 0 points

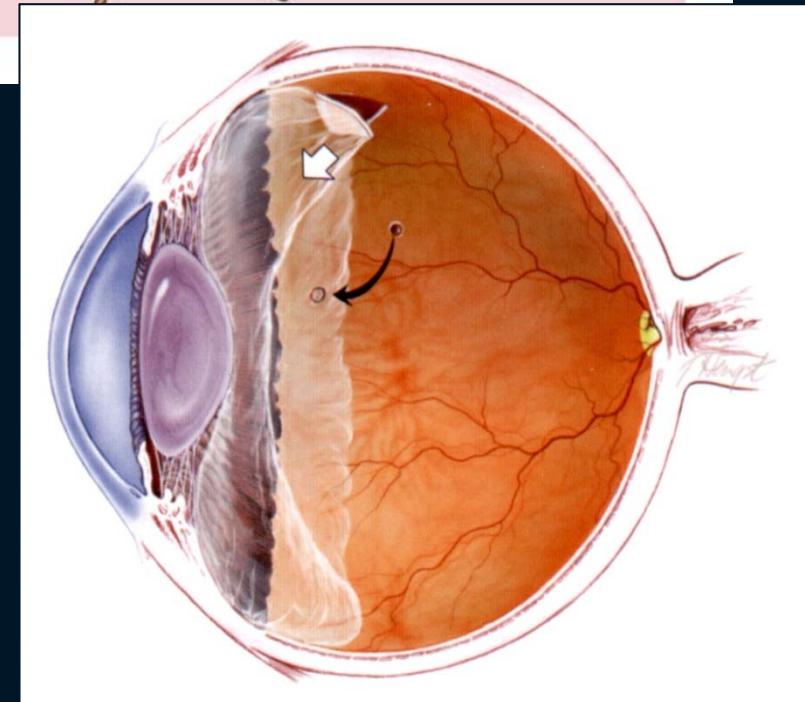
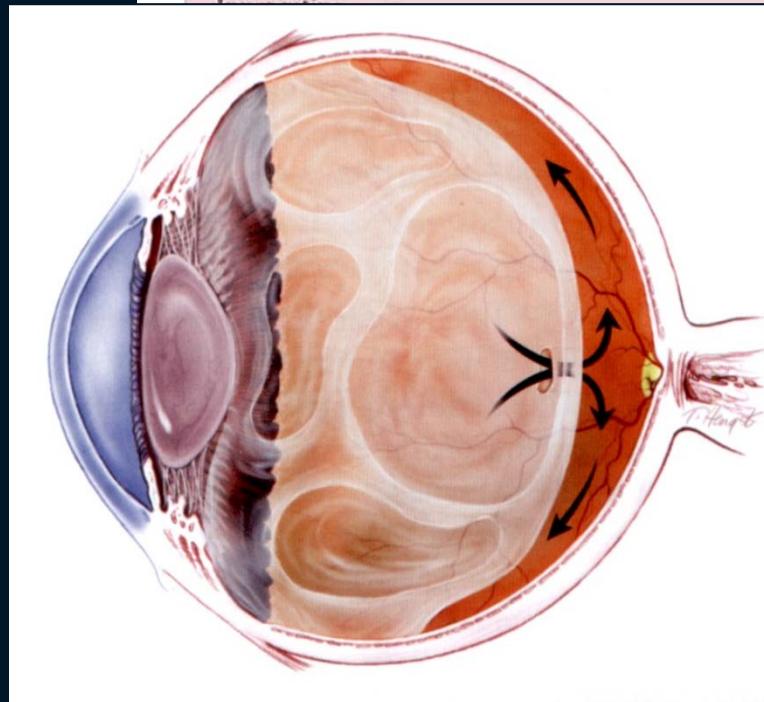
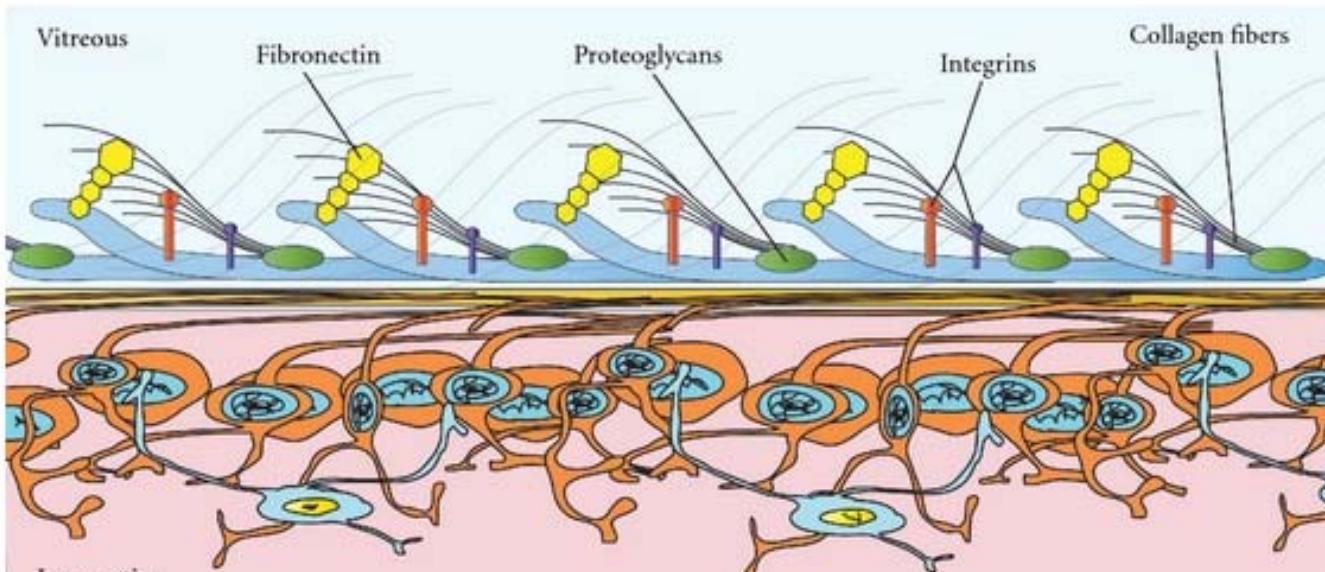
# Posterior Vitreous Detachment



# Posterior Vitreous Detachment

- **Clinical Features**

- Vitreous shrinkage & separation from the retina
- Requires **weakening of vitreoretinal adhesions**
- Inadequate weakening of vitreoretinal adhesions may lead to complications (eg. retinal tears, maculopathy, vitreous hemorrhage)
- **Floaters & photopsia** are a normal consequence of vitreous detachment

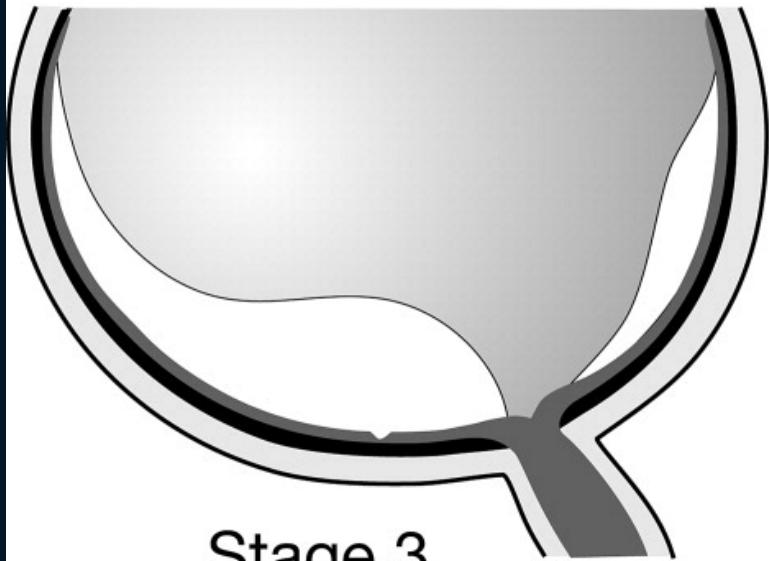




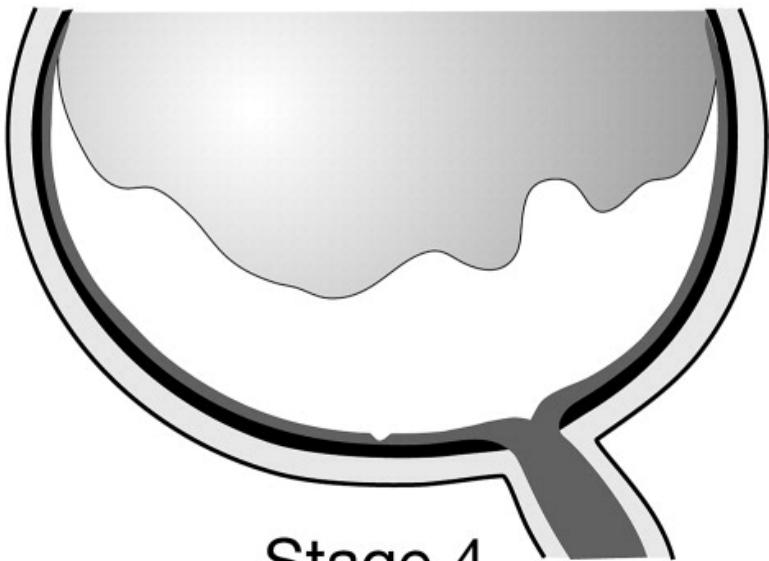
Stage 1



Stage 2



Stage 3



Stage 4

Stage 1: Perifoveal vitreous detachment with vitreofoveal adhesion

Stage 2: Perifoveal vitreous detachment with no vitreofoveal adhesion

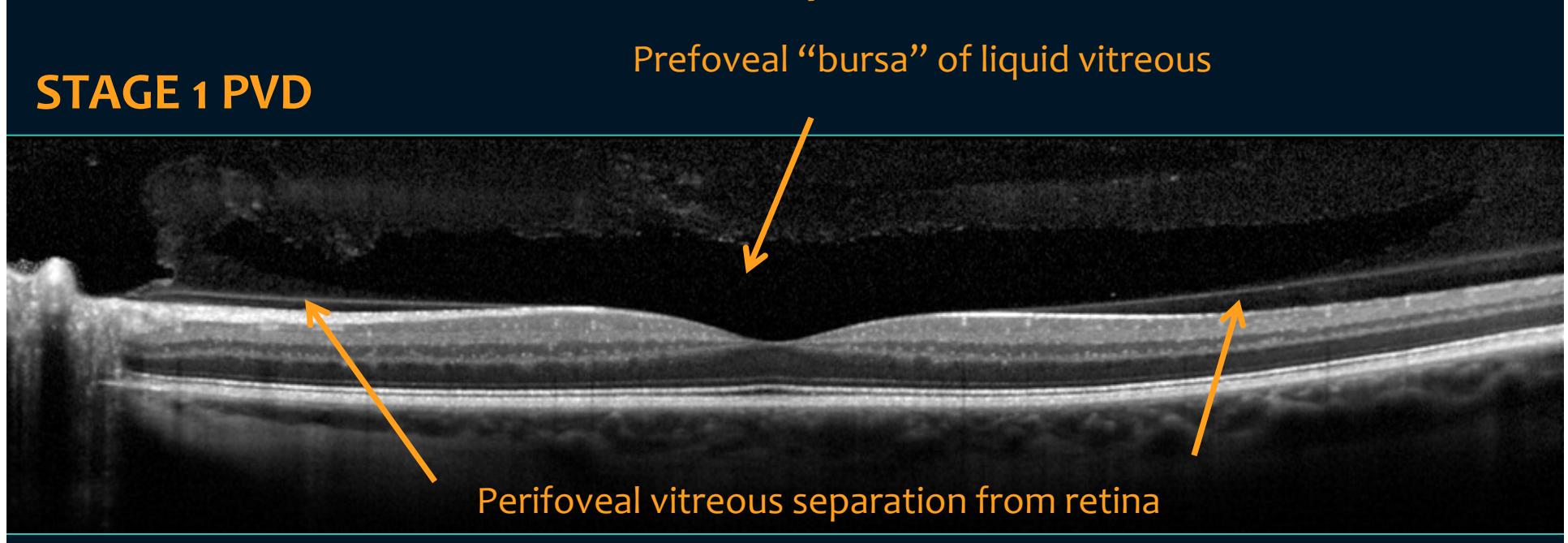
Stage 3: Complete PVD except for vitreopapillary adhesion

Stage 4: Complete PVD

**STAGE 0 PVD**



**STAGE 1 PVD**

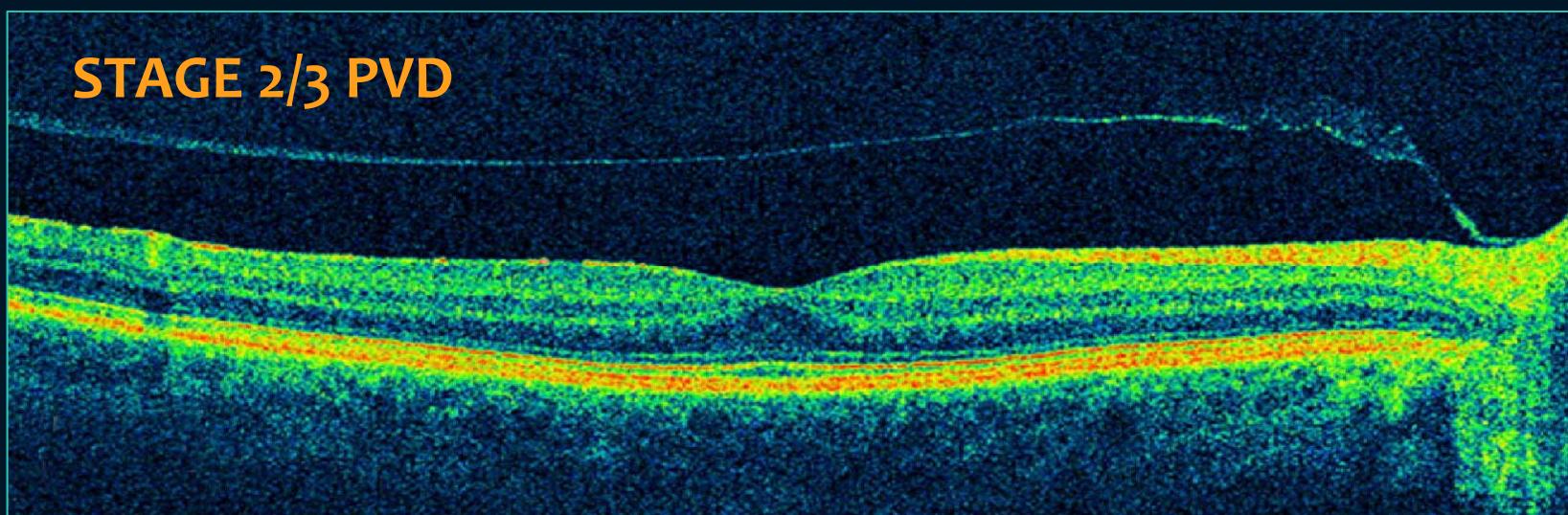


**STAGE 1 PVD**

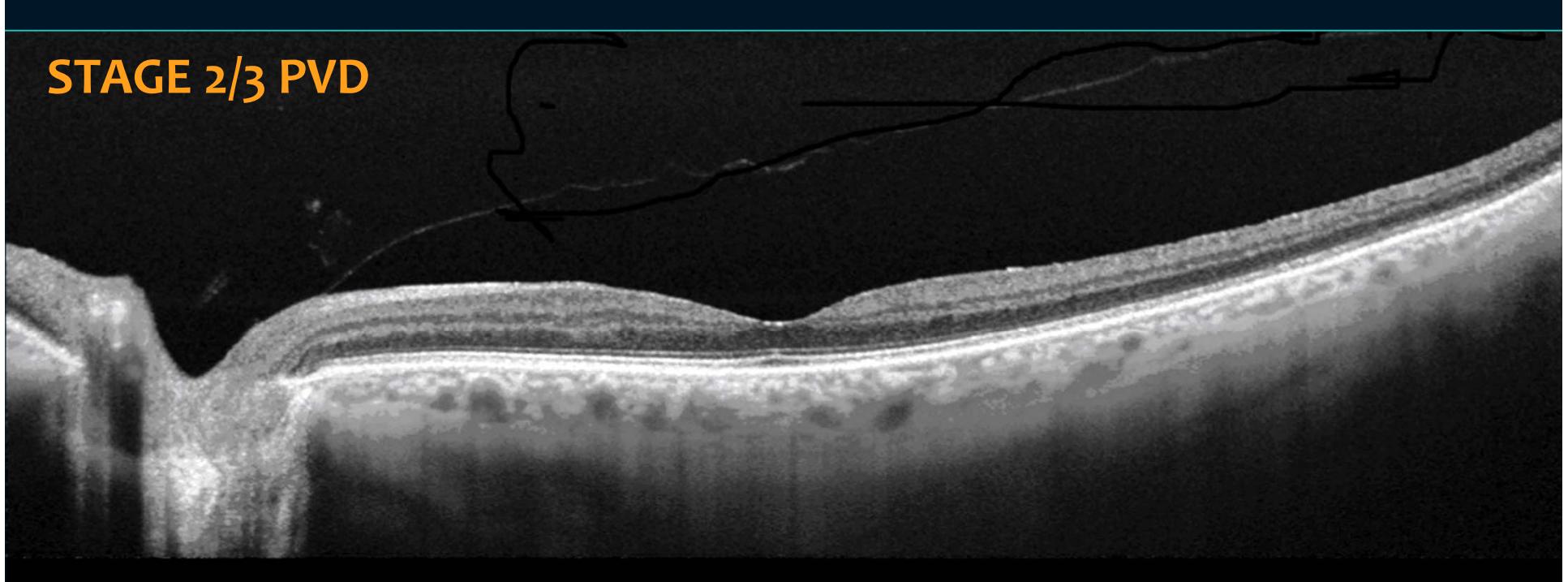
Perifoveal vitreous separation from retina



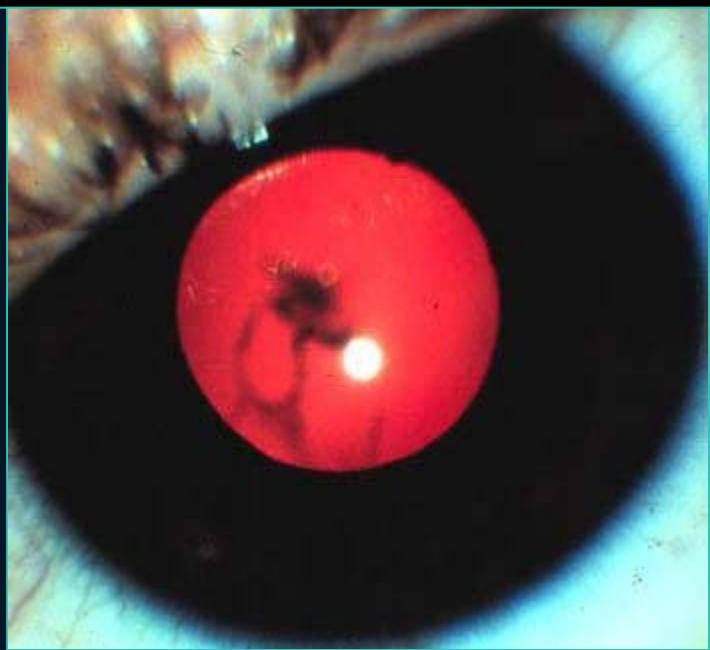
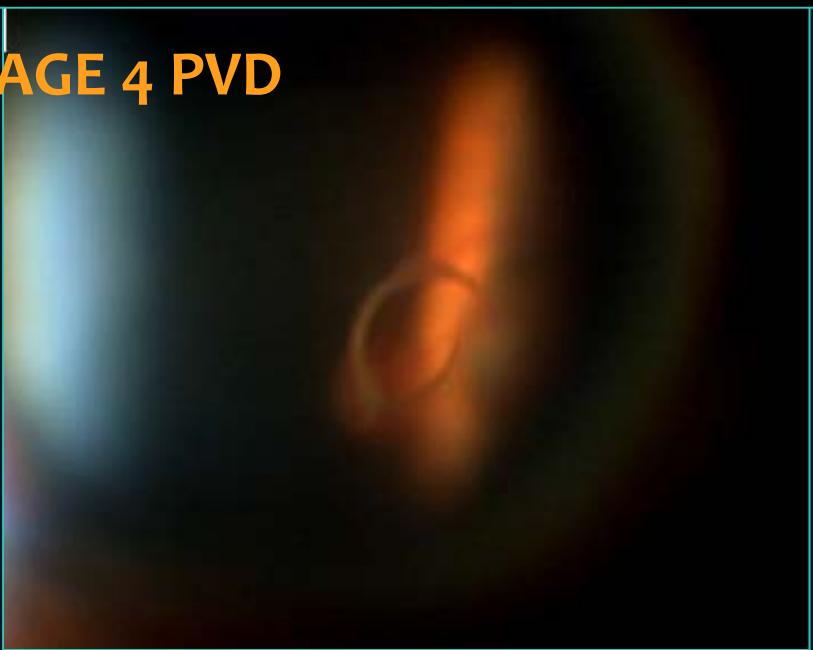
**STAGE 2/3 PVD**



**STAGE 2/3 PVD**



**STAGE 4 PVD**



# Posterior Vitreous Detachment

- Symptoms of acute PVD: **Photopsia**
  - Due to vitreoretinal traction
  - Last < 1 second in duration (95% eyes)
  - **Lightning streak** or flash (94% eyes)
  - Located in the **temporal periphery** (86% eyes)

# Posterior Vitreous Detachment

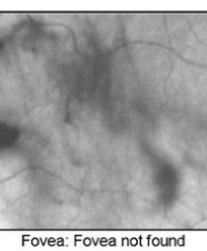
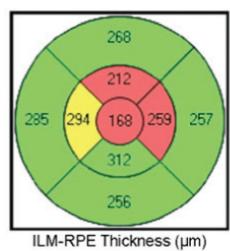
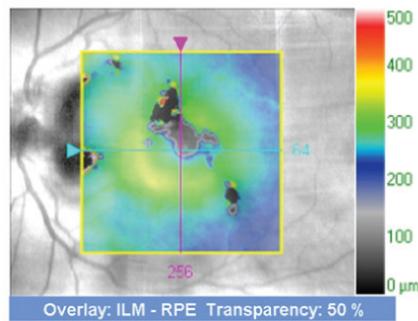
- Other Causes of Photopsia
  - **Migraine**
    - Central blind spot surrounded by photopsias
    - Constant, lasting average of 15 min
    - Commonly travels across the visual field
  - **Neovascular maculopathy**
    - Central (80% eyes)
    - Several seconds or longer (76% eyes)
    - Twinkling, pinwheels, strobes, or circles (96% eyes)

# Posterior Vitreous Detachment

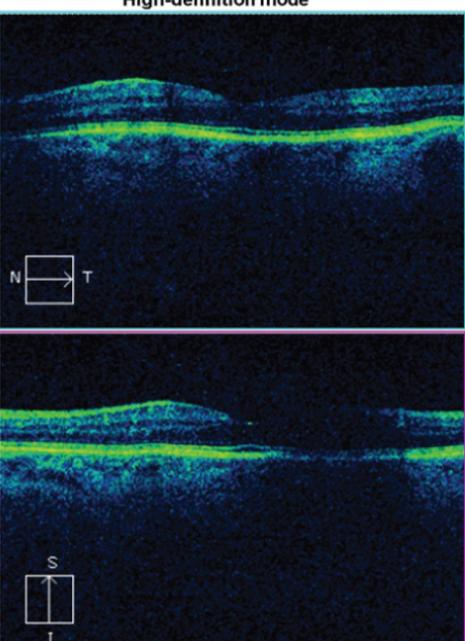
- Symptoms of acute PVD: **Floaters**
  - Onset of 1-2 large floaters is typical
  - May appear without concurrent photopsia
  - Onset of many small floaters (“pepper shaker”) is suggestive of **vitreous hemorrhage**

### Macula Thickness : Macular Cube 512x128

OD OS

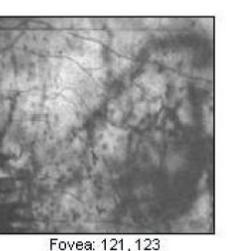
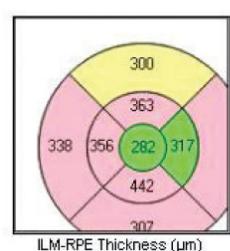
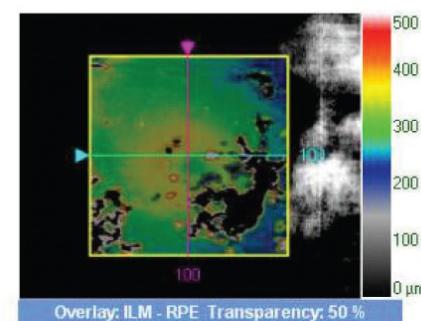


Fovea: Fovea not found

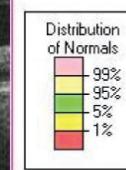
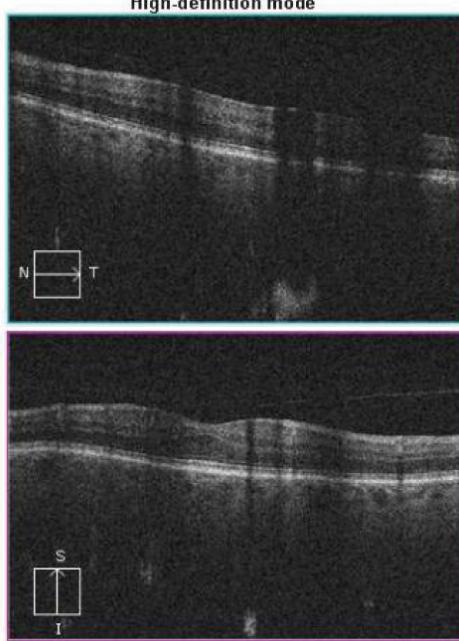


### Macula Thickness : Macular Cube 200x200

OD OS



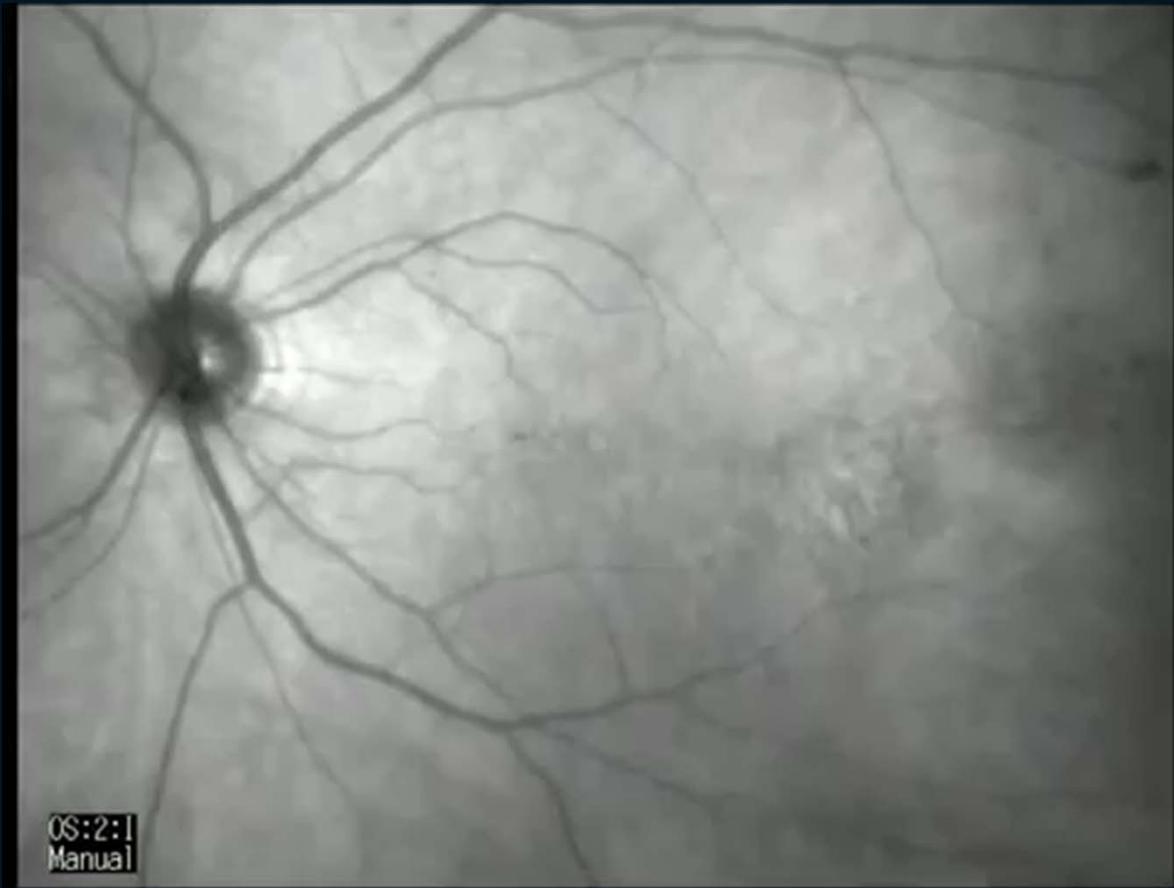
Fovea: 121, 123



	Central Subfield Thickness (μm)	Cube Volume (mm³)	Cube Average Thickness (μm)
ILM - RPE	282	10.4	288

OCT can be used to document symptomatic vitreous floaters

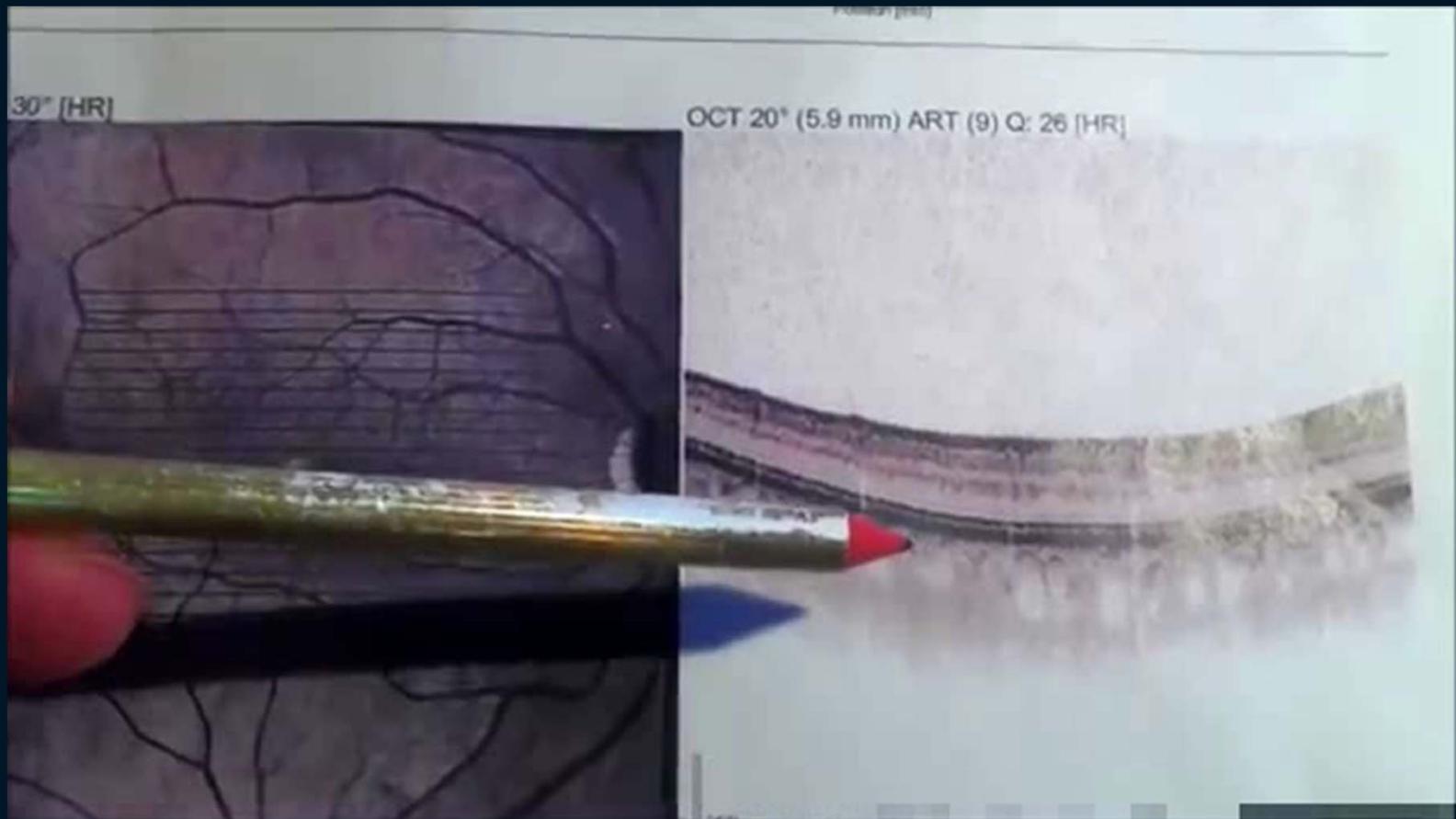
Ophthalmic Surg Lasers Imaging Retina. 2013;44:415-418



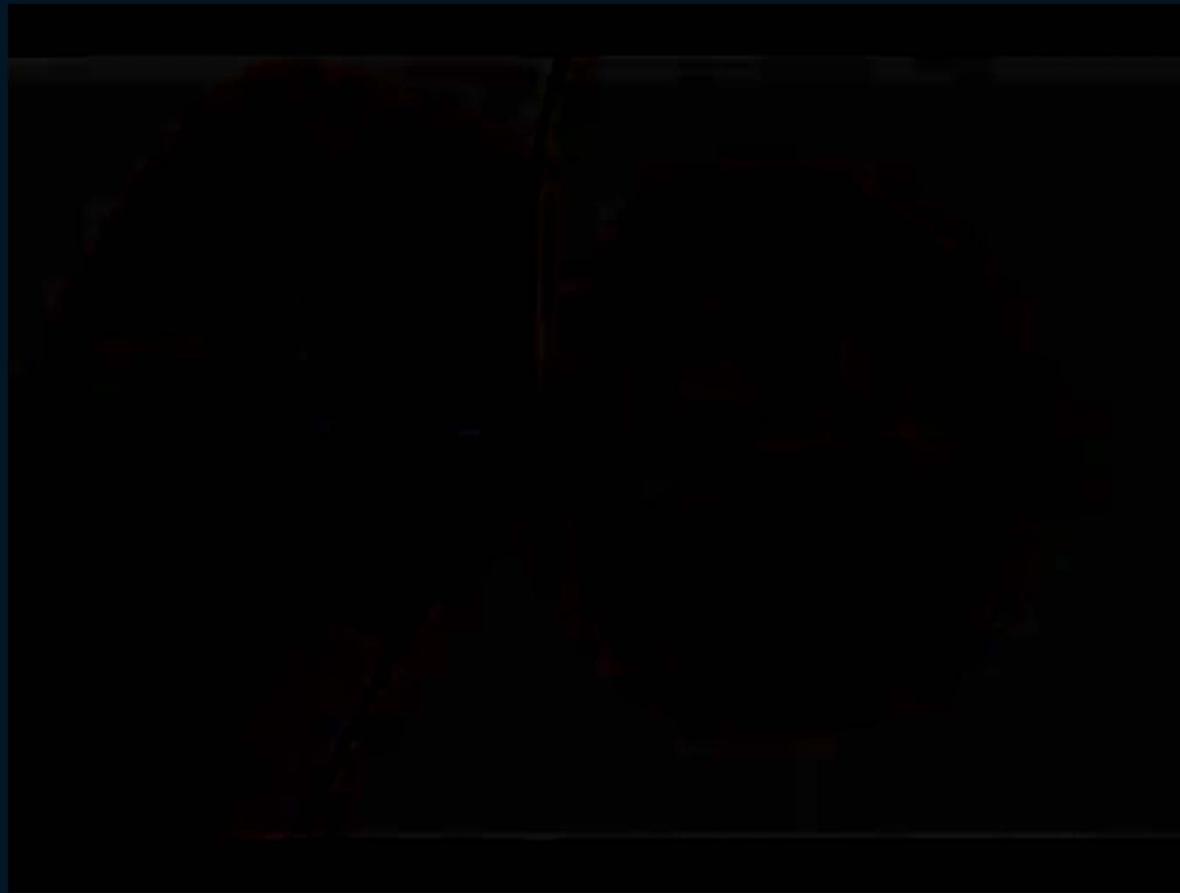
OCT can be used to document symptomatic vitreous floaters

# Posterior Vitreous Detachment

- Floater Treatment Options
  - **Observation**
    - May become less bothersome over time
  - **Floater-Only Vitrectomy**
    - “Gold standard” therapy, 95% success rate
    - Potential for severe complications
  - **YAG Vitreolysis**
    - Few studies, Variable efficacy, Potential risk?



<https://www.youtube.com/watch?v=XMJ8P3FCoBI>



[https://www.youtube.com/watch?v=uTNLt\\_pmUB0](https://www.youtube.com/watch?v=uTNLt_pmUB0)

# Posterior Vitreous Detachment

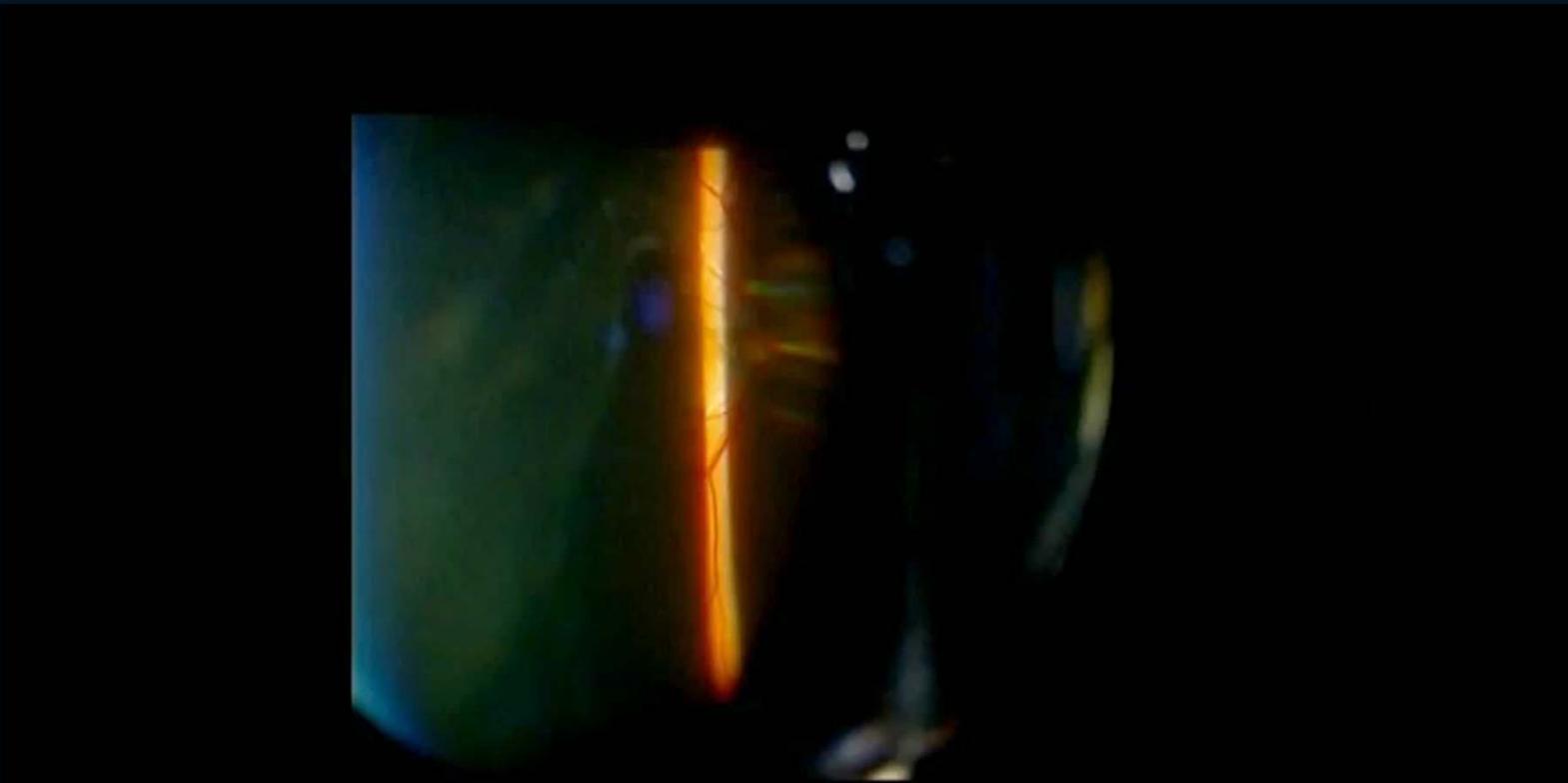
- **How To Monitor**
  - Initial assessment
    - History of photopsia and floaters
    - **Detailed DFE including scleral depression**
    - Slitlamp exam of vitreous including 78/90D lens
    - **OCT posterior vitreous and macula**
  - 4-6 week follow-up, sooner PRN
    - Search for delayed onset retinal tears



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Volk 90D exam of complete (stage 4) PVD (inverted image)

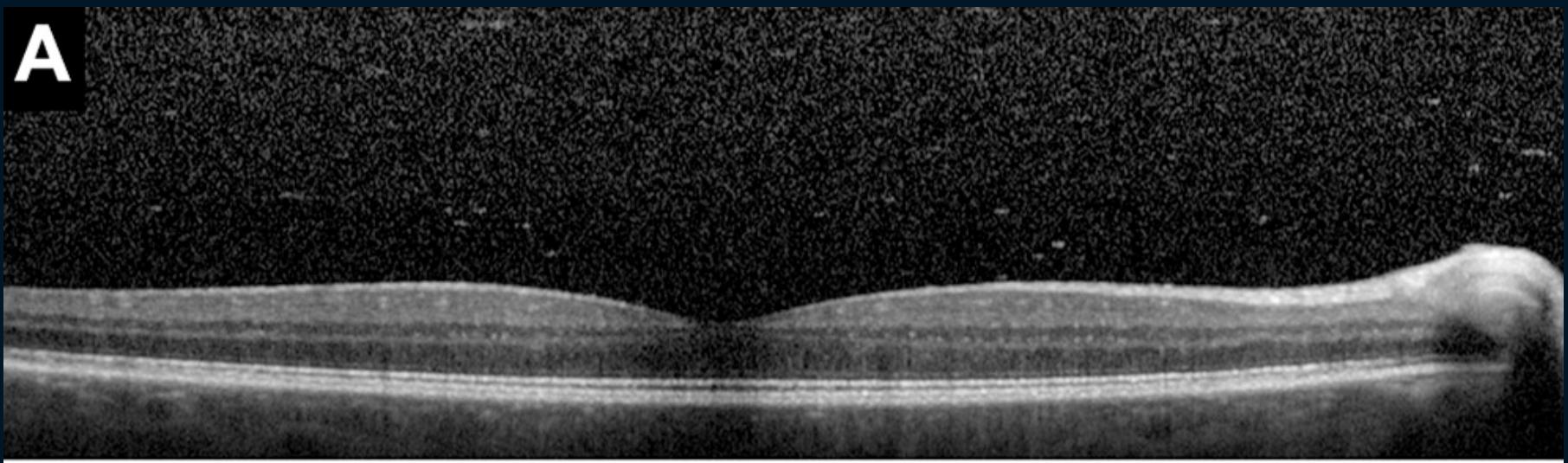
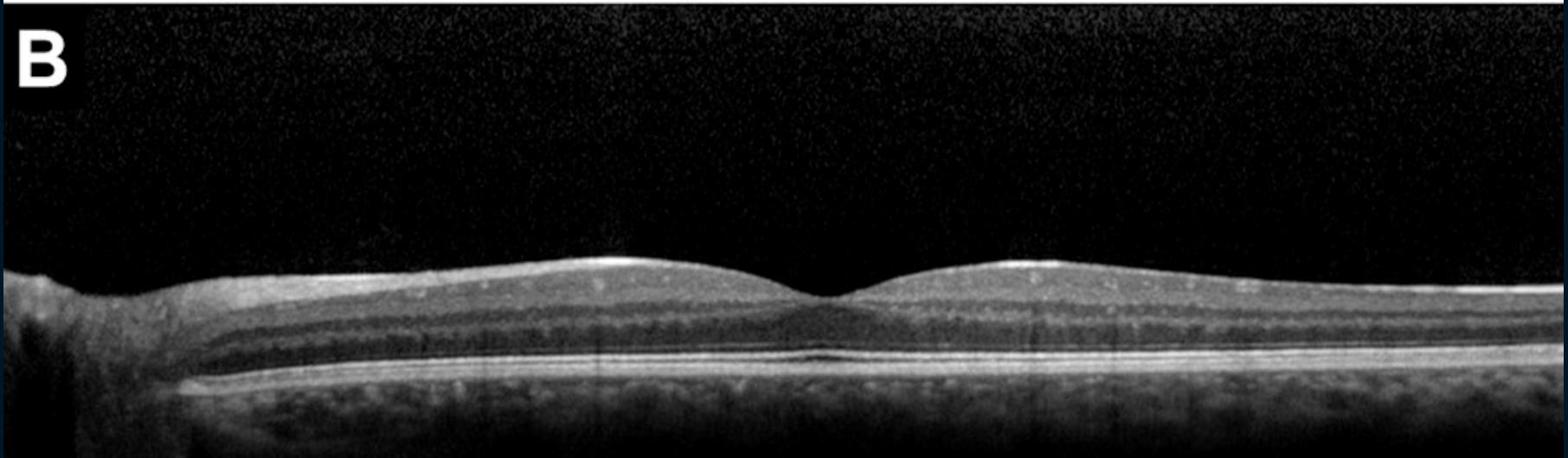
Clin Ophthalmol 2014;8:1-10



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Volk 90D exam of partial (stage 3) PVD (inverted image)

Clin Ophthalmol 2014;8:1-10

**A****B**

Enhanced vitreous imaging in spontaneous acute posterior vitreous detachment for a patient (A) with a retinal tear and associated hyper-reflective dots (“falling ash” sign) in the vitreous and subhyaloid region and for a patient (B) without a retinal tear with absence of hyper-reflective dots in the vitreous/subhyaloid region

Ophthalmology. 2015;122: 1946–1947.

# Posterior Vitreous Detachment

- **When to Refer**

- Acute PVD

- Vitreous hemorrhage or pigment
    - Retinal tears and detachments
    - Predisposing degenerations (eg. lattice)

- Floaters

- Chronic impairment of quality of life

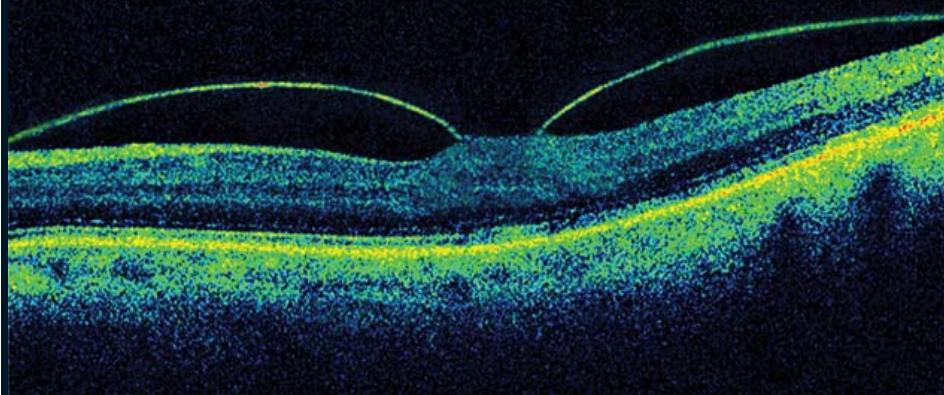
- **Vitreomacular Traction**

- Visual acuity loss
    - Evidence of macular hole development

GRADE 1

Retinal anatomy intact

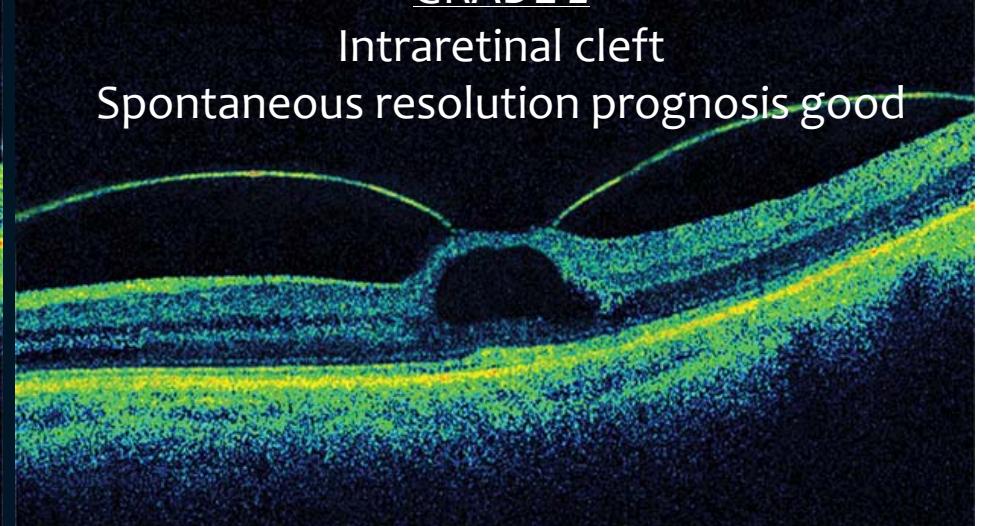
Spontaneous resolution prognosis good



GRADE 2

Intraretinal cleft

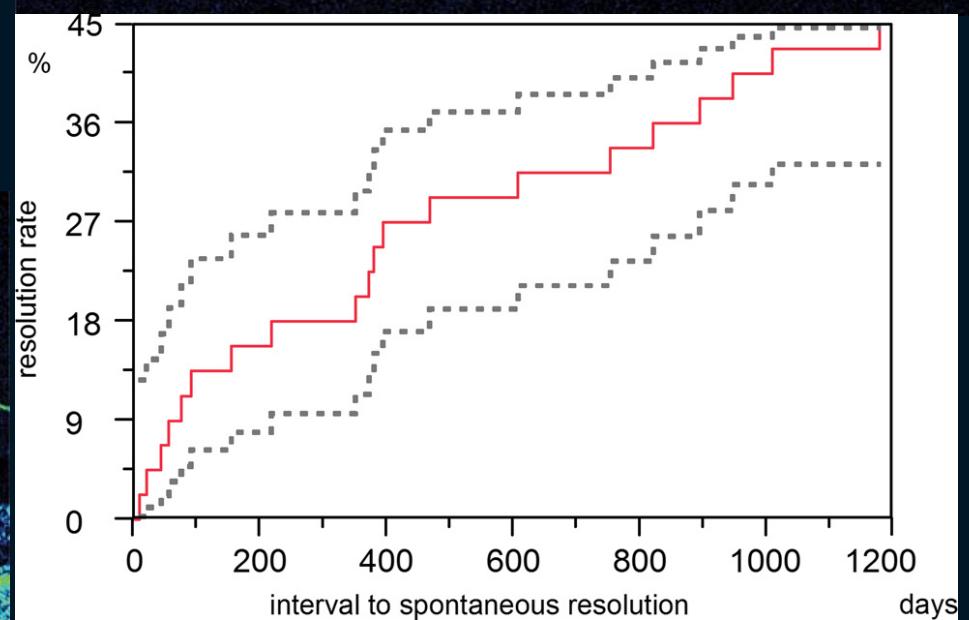
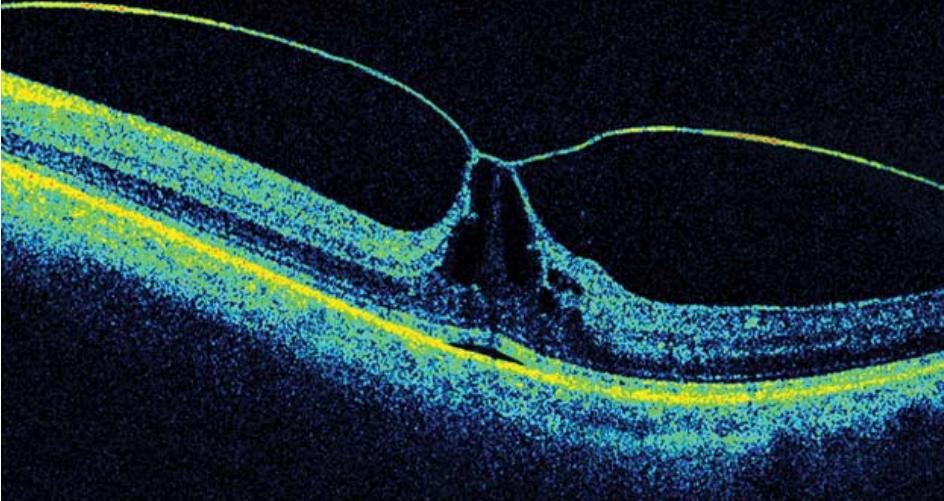
Spontaneous resolution prognosis good



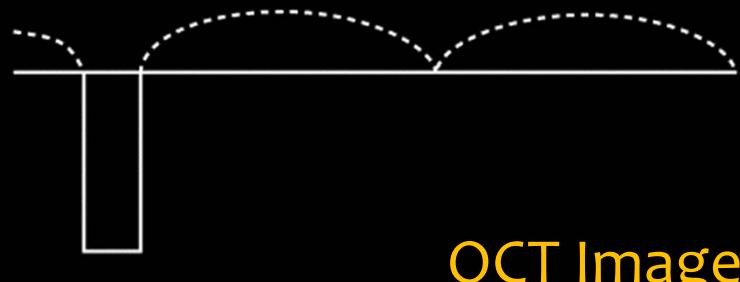
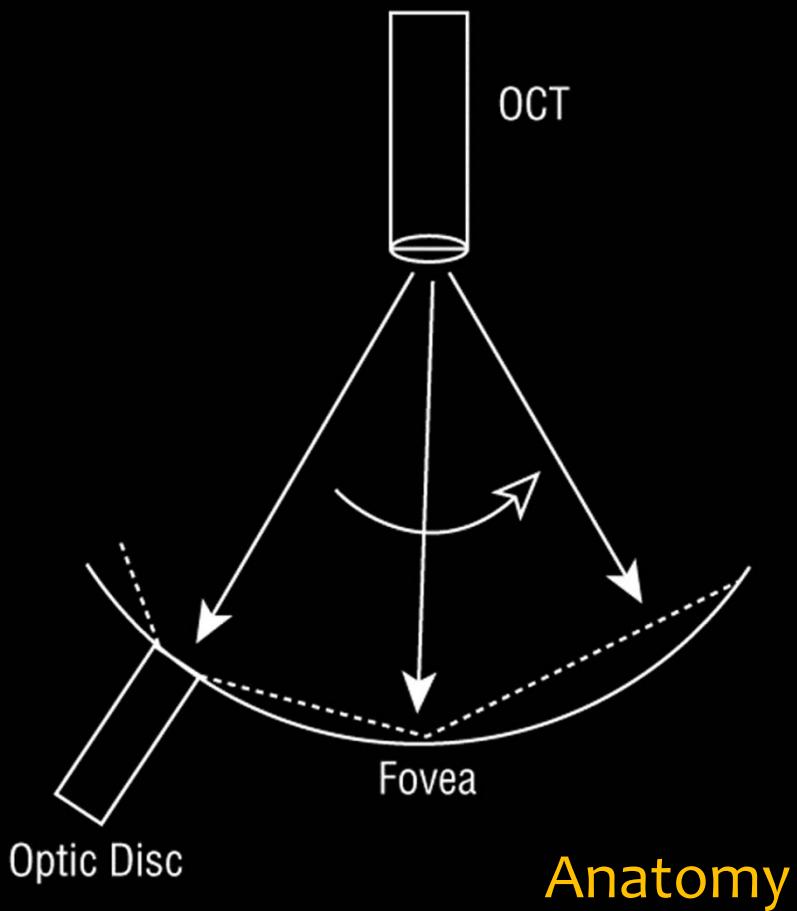
GRADE 3

Subretinal fluid

Spontaneous resolution prognosis guarded



Worse: Progression to higher grade be first to undergo surgery



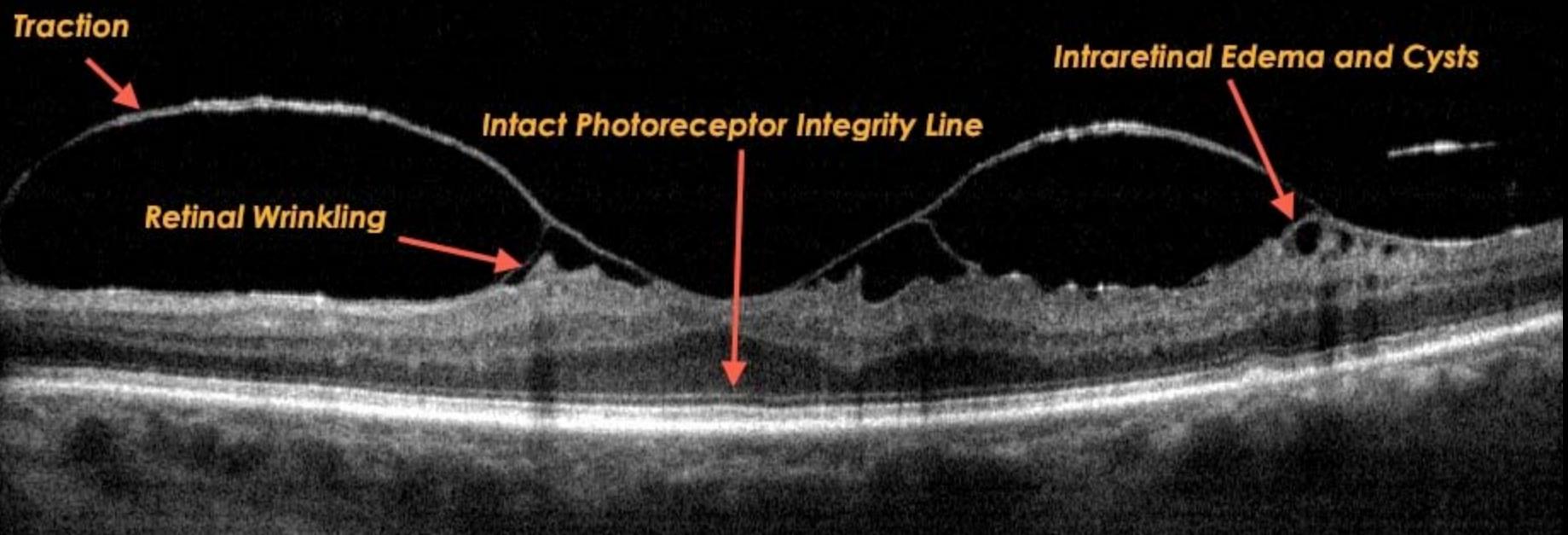
## Explanation of the double-convex OCT signal

TOP: The OCT beam (straight arrows) is scanned across the posterior pole.

BOTTOM: Most points on the concave retinal surface are equidistant from the OCT, thus appearing flat on the image obtained. Those on a partially detached posterior vitreous face (dotted line) are not, resulting in an artifactual convexity.

1

**Very Significant Vitreo-Retinal Traction Creating  
Wrinkling of the Retinal Surface , Intraretinal  
Edema and Cysts, and Retinal Lift**



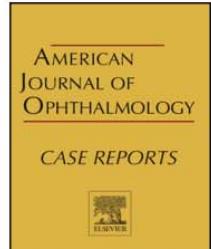
NEW!

Contents lists available at ScienceDirect



## American Journal of Ophthalmology Case Reports

journal homepage: [www.elsevier.com/locate/ajoc](http://www.elsevier.com/locate/ajoc)



Case report

### Focal vitreomacular traction: Resolution after ocular massage

José Javier García-Medina<sup>a,b,c,\*</sup>, Mónica del-Río-Vellosillo<sup>d</sup>, Elena Rubio-Velázquez<sup>a</sup>, María Dolores López-Bernal<sup>a</sup>, Juan José Zafra-Pérez<sup>a</sup>



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#### ARTICLE INFO

Keywords:

Vitreomacular traction

Adhesion

OCT

#### ABSTRACT

**Purpose:** Vitreomacular traction (VMT) is a relatively common ocular disorder that may distort the foveal structure causing visual symptoms. The influence of ocular massage (OM) on this condition has not been considered yet. We aim to report clinical and OCT features of VMT release associated with OM.

**“OM was performed placing the two index fingertips on the nasal and temporal side of the eyeball, with the eyelid of the patient shut, and pressing alternatively with both fingers. The patient was instructed to perform the same OM (1 minute, moderate intensity massage) every 8 hours at home”**

AJO Case Reports. 2019;14:61

# Posterior Vitreous Detachment

- Management of VMA
  - **Observation**
    - Spontaneous release in  $\approx 30\%$  of cases over 18mos
  - **Pneumatic vitreolysis**
    - High success ( $\approx 80\%$ ) with few complications
  - **Enzymatic vitreolysis**
    - Risk of adverse effects & 20% still require surgery
  - **Vitrectomy**
    - Gold standard, risks of intraocular surgery

# Self Assessment Quiz

**Have you paid attention to what I was saying for the past 10 min?**

- +1 point if you know what I was talking about
- -10 points if you were sleeping for the past 10 minutes

# Self Assessment Quiz

## SCORE

0-2      1980's

3-5      1990's

6-8      Early 2000's

>8      I need a new OD, are you  
accepting new patients?

# THANK YOU!

