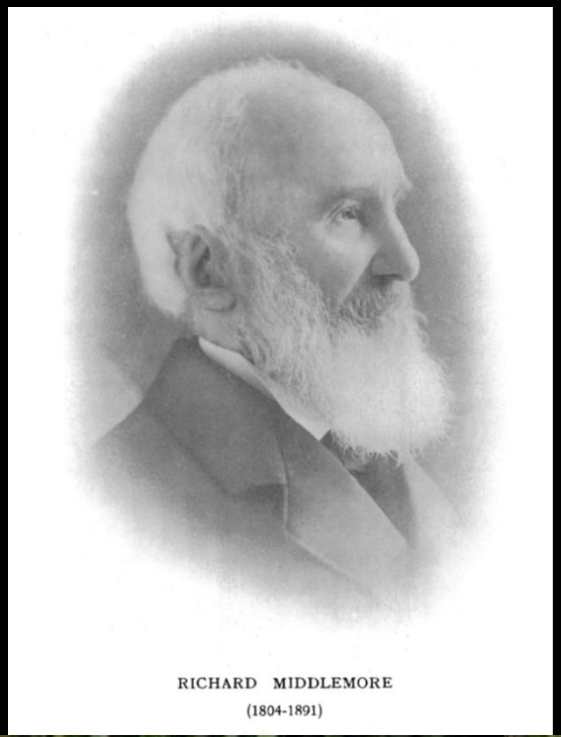
The Middlemore Lecture

Birmingham and Midland Eye Hospital
Midland Ophthalmological Society
Friday 7th October 2016

Yit Yang
Wolverhampton and Birmingham

Richard Middlemore-1804-1891

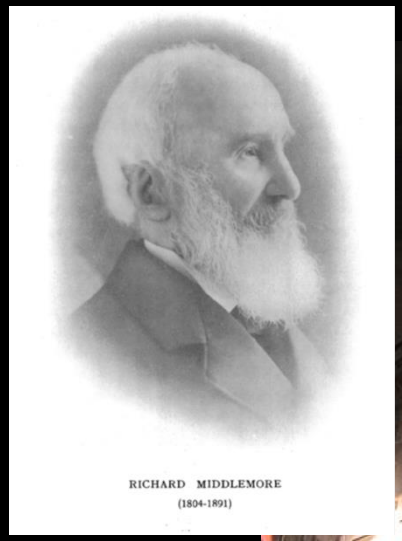


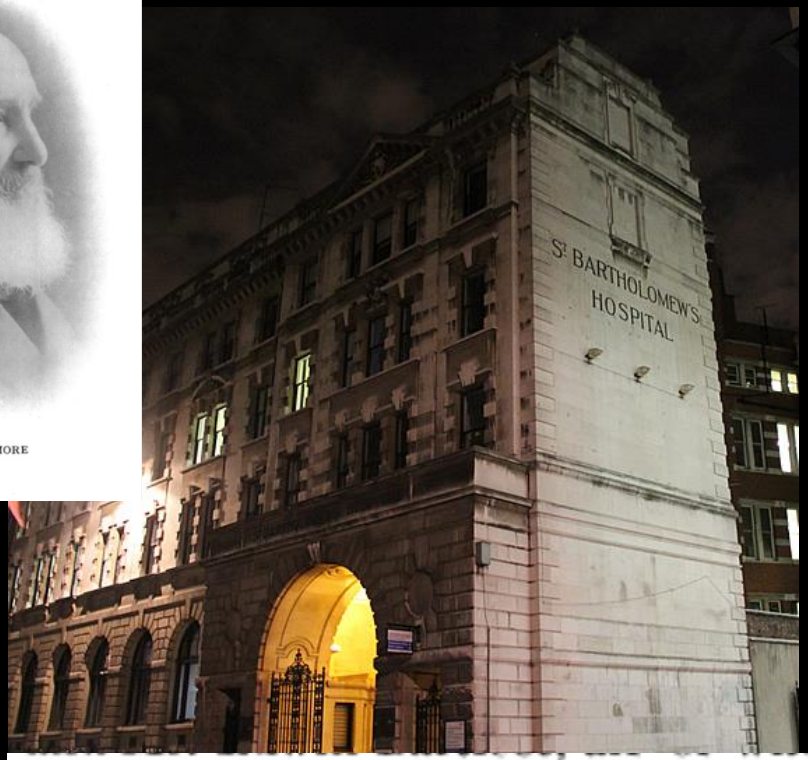
- Born 12 October 1804, Second son
- Middlemores (Hawkesley Branch) of Northfield
- Lords of the Manor of Edgbaston
- Leather Trade

- Solihull School

- 16 yo Apprentice to Mr Chawner (GP) of Lichfield

1823 (19yo) Dresser- Mr Vincent and Mr Abernethy, St Bart's, West Smithfield





14 Bedford Row

him. During his period of dressership for Mr. Vincent he was frequently called upon to dress for Mr. Abernethy, and he prided himself on the fact that he not only never got a

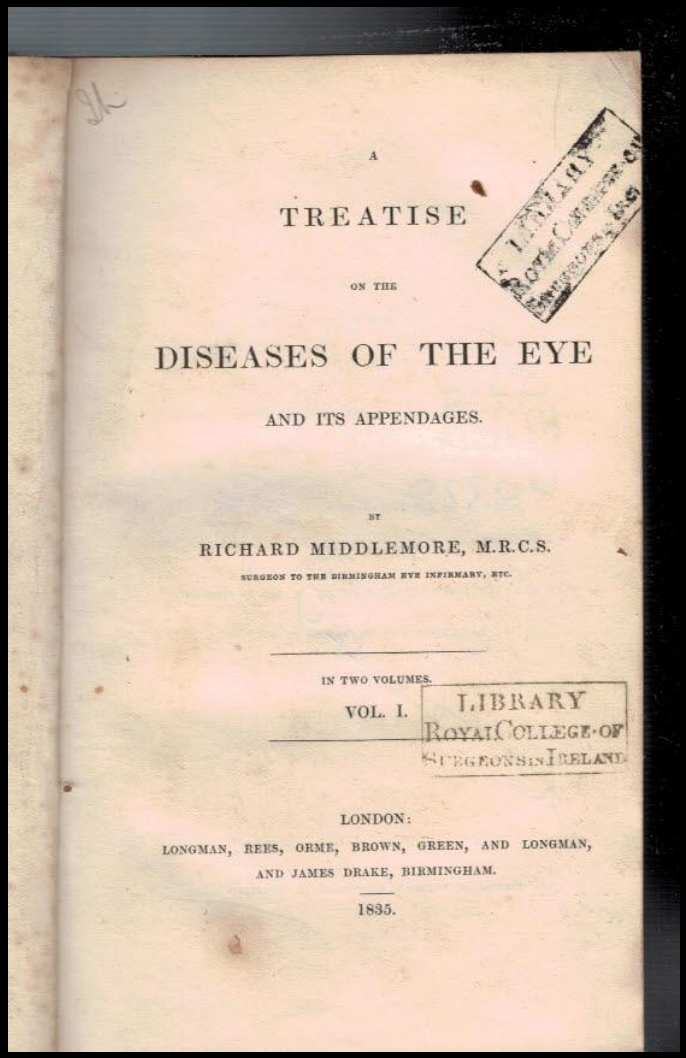
scolding from Mr. Abernethy but received several invitations from him to dine at Bedford Row.

On leaving London he carried a warm recommendation

1828 (24yo) Assistant Surgeon, to Mr Hodgson (founder of Birmingham and Midland Eye Institution in 1823 in Cannon Street)

1831- Jacksonian Prize
1835 -(31yo) ‘DISEASES OF THE EYE’ >1600 pages
1877-Triennial BMA Middlemore Prize
1879 – Retired at age 75,

Birmingham and Midland Eye Hospital,
-Cannon St,
-Steelhouse Lane
-Temple Row


A
TREATISE
ON THE
DISEASES OF THE EYE
AND ITS APPENDAGES.
BY
RICHARD MIDDLEMORE, M.R.C.S.
SURGEON TO THE BIRMINGHAM EYE INFIRMARY, ETC.
IN TWO VOLUMES.
VOL. I.
LIBRARY
ROYAL COLLEGE OF
SURGEONS IN IRELAND
LONDON:
LONGMAN, REES, ORME, BROWN, GREEN, AND LONGMAN,
AND JAMES DRAKE, BIRMINGHAM.
1835.

1879 – Retired at age 75,
1883- Eye Hospital in Church St was opened.

OBITUARY.

RICHARD MIDDLEMORE, F.R.C.S.Eng.

On the 1st of this month, at The Limes, Bristol Road, Birmingham, died Richard Middlemore, F.R.C.S., the accomplished and erudite ophthalmologist. He was a descendant, through the Hawkesley branch, of the ancient and distinguished family of Middlemore, lords of the manor of Edgbaston, and possessors of other manors and great estates in the counties of Worcester and Warwick.

He was born on October 12th, 1804, and so was in his 87th year. At the age of 16 he was apprenticed to a surgeon of wide local reputation, Mr. Chawner, of Lichfield. In 1823 he entered as a student at St. Bartholomew's Hospital, and had for fellow students the following well-known Birmingham men: Dr. Corrie, Dr. James Johnston, Mr. Frederick Ryland, and Mr. Edwin Bartleet, all of whom have long predeceased him. During his period of dressership for Mr. Vincent he was frequently called upon to dress for Mr. Abernethy, and he prided himself on the fact that he not only never got a

did not employ iridectomy.

He did not regard the escape of vitreous with the fear which oppresses most of us. In a hard eye he even thought it a possible advantage. He applied cold, if possible iced, water pads to the closed eye before operation, as he said, to lessen sensitiveness and haemorrhage. I once saw him operate when I was a student in

He delivered a course of lectures on diseases of the eye every year during his connection with the Eye Hospital to students and practitioners; but he was often disheartened, he has told me, by the lack of interest shown. He considered it the duty of all members of our profession connected with public institutions to make the practice subservient to the progress of instruction. His settled convictions on this point found, as he hoped, a permanent expression in the course of post-graduate lectures which he founded and endowed in connection with the Birmingham Eye Hospital in 1889. This course of lectures has been continuous ever since its establishment, the lectures having been delivered by ophthalmologists of eminence. He also endowed a prize in ophthalmology to be

Middlemore Lectures since 1889

Middlemore Lecturers 1889-

Year	Name	Subject
1889	Mr. Lloyd Owen	The Essentials of Ophthalmic Therapeutics
1890	Mr. Henry Eales	Headache and the other results of Ocular Strain and Distress
1891	Mr. E. Wood White	Eye Symptoms in Diseases of the General Nervous System
1892	Dr. Saundby	The Diagnostic and Prognostic Significance of the Retinal Changes in Diabetes and Bright's Disease
1893	Mr. Lloyd Owen	The Nature and Treatment of Purulent Ophthalmia of newly-born infants
1894	Mr. Henry Eales	Ocular Affections caused by Glare
1895	Mr. E. Wood White	Corneal Ulcers and their Treatment
1896	Mr. Lloyd Owen	Pain in Diseases of the Eye; its Character and Treatment.
1897	Mr. Henry Eales	Exophthalmos: its causes and treatment
1898	Mr. E. Wood White	Inflammation of the Conjunctiva
1899	Dr. Jamesson Evans	Eye Affections in Connection with Blood and Vascular Diseases

THE ELEMENTS OF

OPHTHALMIC THERAPEUTICS,

BEING

The Richard Middlemore Post-Graduate Lecture

DELIVERED AT THE

BIRMINGHAM AND MIDLAND EYE HOSPITAL, 1889.

BY

D. C. LLOYD-OWEN, F.R.C.S.I.,

SENIOR SURGEON TO THE HOSPITAL, AND CONSULTING OPHTHALMIC SURGEON TO THE CHILDREN'S HOSPITAL, BIRMINGHAM.

BOSTON MEDICAL LIBRARY. JUN 5 1903

BIRMINGHAM:

CORNISH BROTHERS, 37, NEW STREET.

INTRODUCTION.

IN delivering the first of the annual series of lectures established by Mr. RICHARD MIDDLEMORE, I am privileged in being able to act as the mouthpiece of the medical profession in this district, in expressing their cordial appreciation of his generosity, and of the service done to his professional brethren in founding and endowing these lectures.

Although Mr. MIDDLEMORE has reached a very advanced age, he is well known to take a warm interest still in the progress and advancement of medical science, and especially of ophthalmology, to which his life has been devoted.

From his earliest connection with this branch of medicine, which now dates back some sixty-odd years, Mr. MIDDLEMORE has always laboured, by his lectures and his writings, to place the results of special research before his brethren in general practice,—a high-minded line of conduct which has now culminated in the establishment and endowment of the "RICHARD MIDDLEMORE Post-

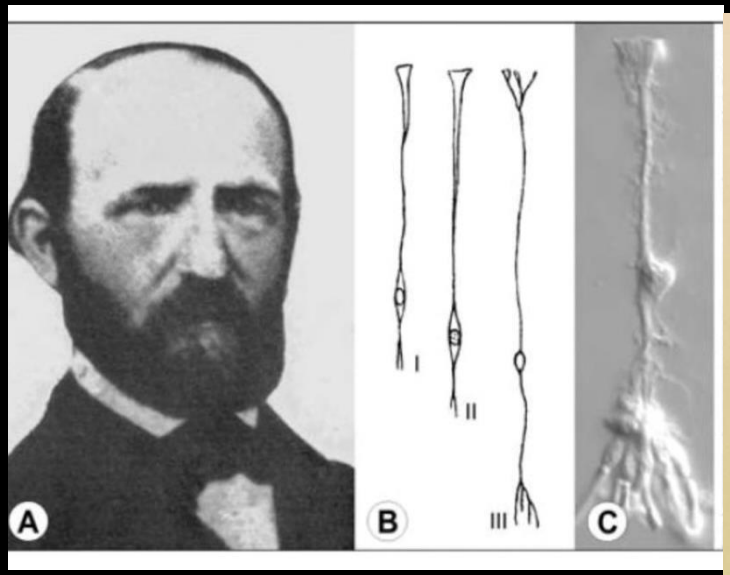
Richard Middlemore Lectures
The Remit

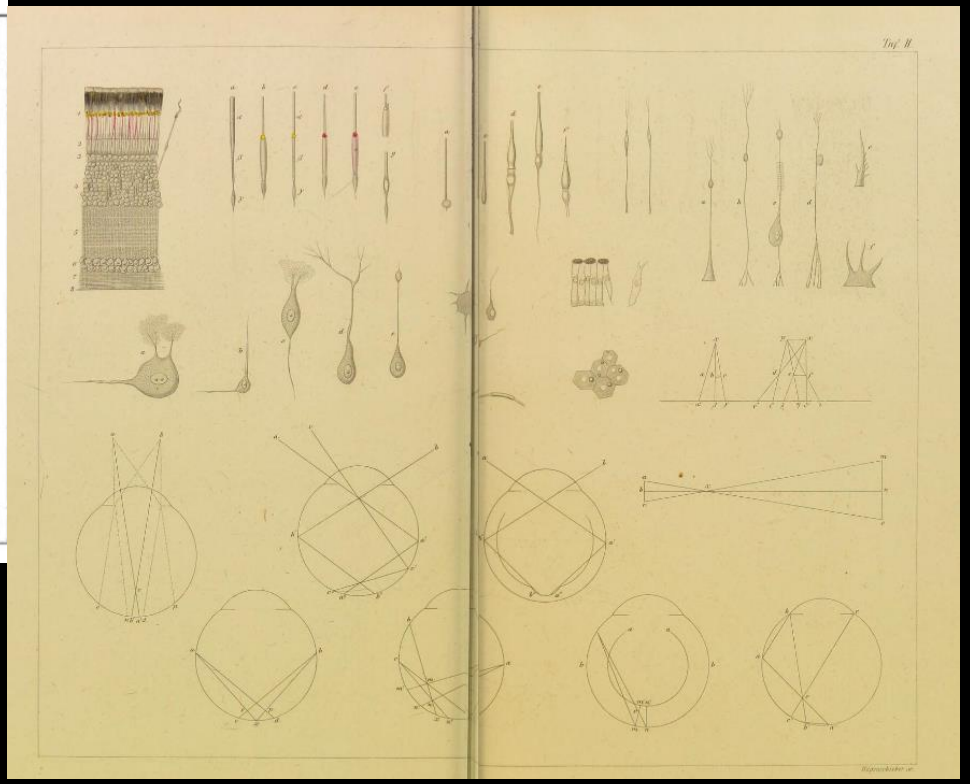
- To digest and arrange, …
- …the research and experience of those who devote themselves to the advancement of ophthalmology ….
- …for the service of those who are engaged in the absorbing duties of ophthalmic practice…

Middlemore Lecture 2016

Role of the Muller Cell
in
Retinal Pathology and Physiology

Illustrating:
-Some research…
-Some skills for clinical practice….





Heinrich Muller (1820-1864)

DISEASES OF THE EYE

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MAN, REES, ORME, BROWN, GREEN, AND LONGMAN,

AND JAMES DRAKE, BIRMINGHAM.

1835.

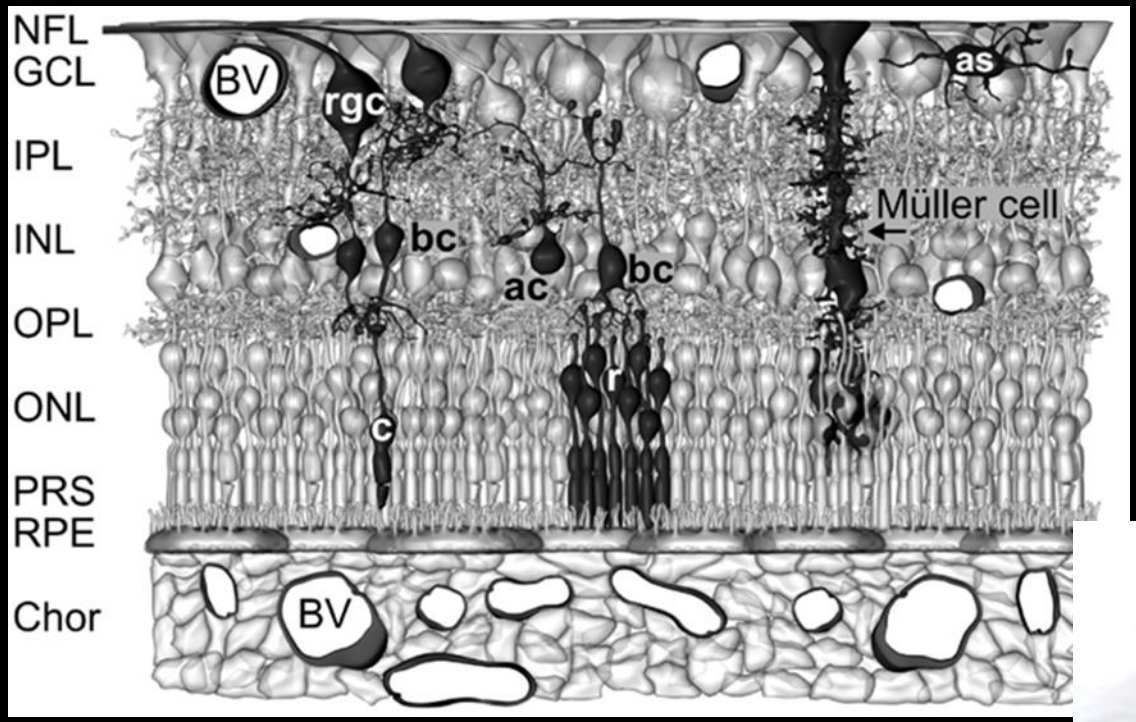
BIBLIOTHECA LAUDIANA

eye there exists a small aperture in the bony cup which indicates the place where the optic nerve passed through it to be expanded into the retina. Many well authenticated cases of ossification of the choroid are upon record: MR. WARDROP has witnessed several, and he has collected others from the writings of BICHÀT, HALLER, MORGAGNI, PELLIER, MORAND, SCARPA, and GÜNZ. MACKENZIE and TRAVERS allude to this pathological change but do not appear to have seen any example of it in the course of their own practice. Ossification of the choroid has also been witnessed by LENHOSSECK, MÜLLER, and JACOBSON.

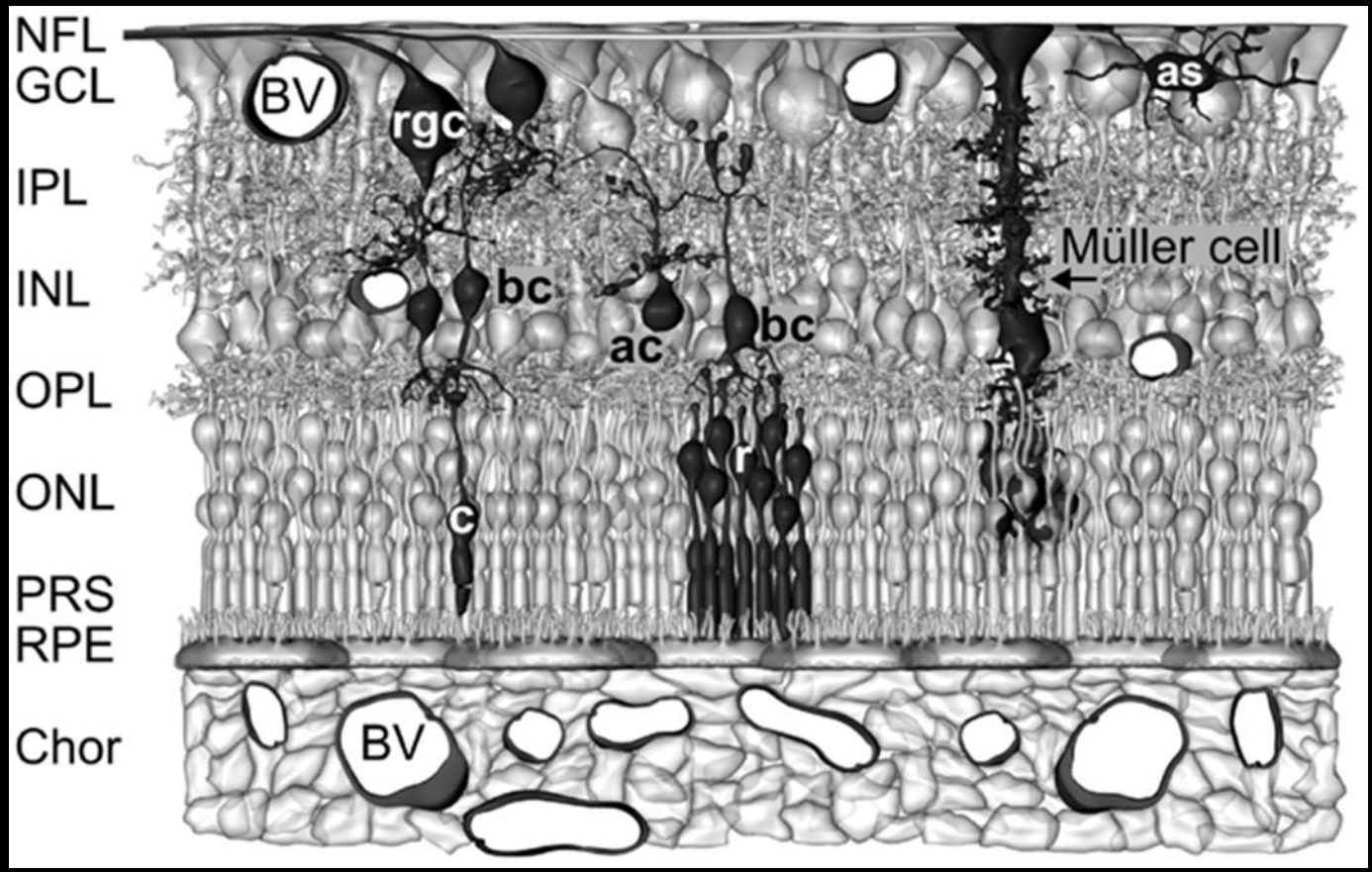
The vessels of the choroid are liable to become ossified and to undergo the same morbid changes as occur in blood-vessels in other situations.

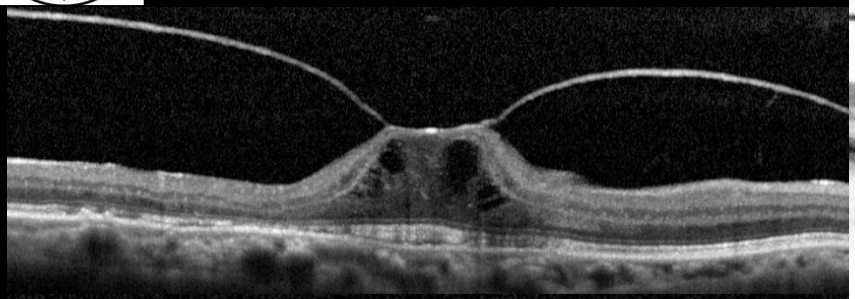
ü

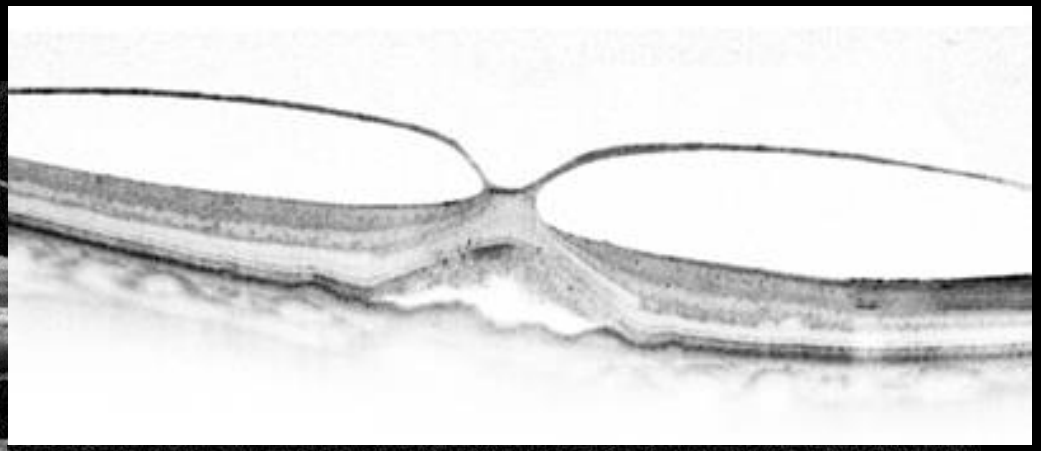
The Muller cell

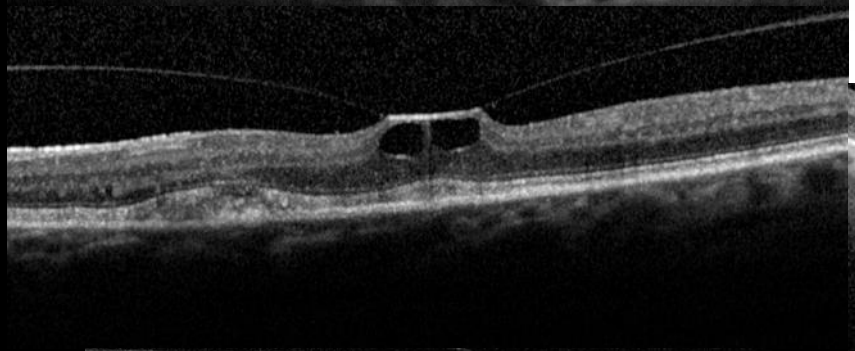


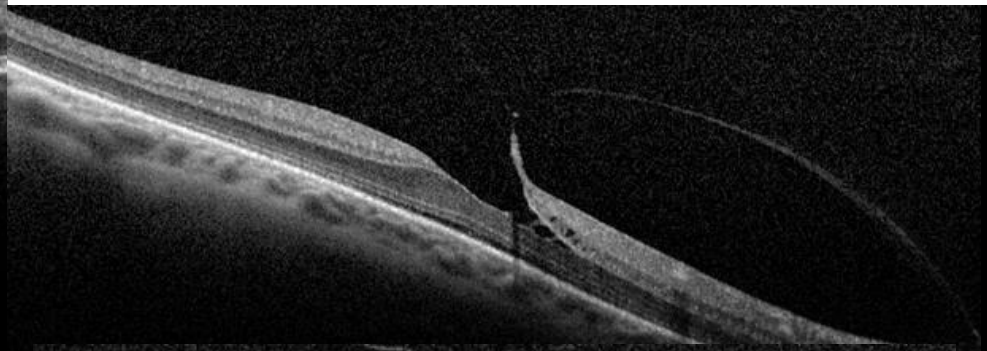
1) Role of Muller Cells in VMT

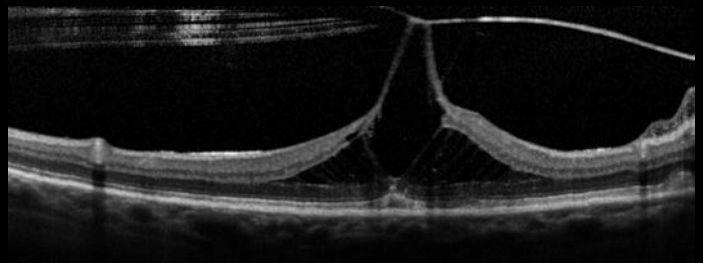


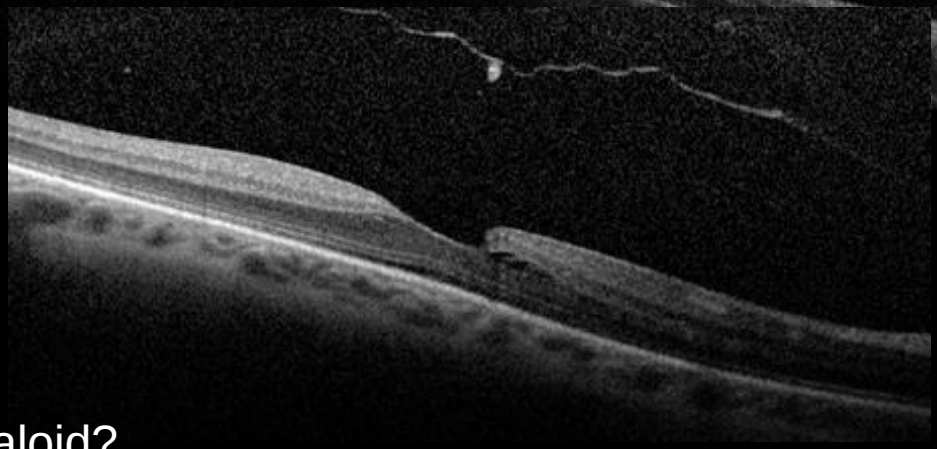






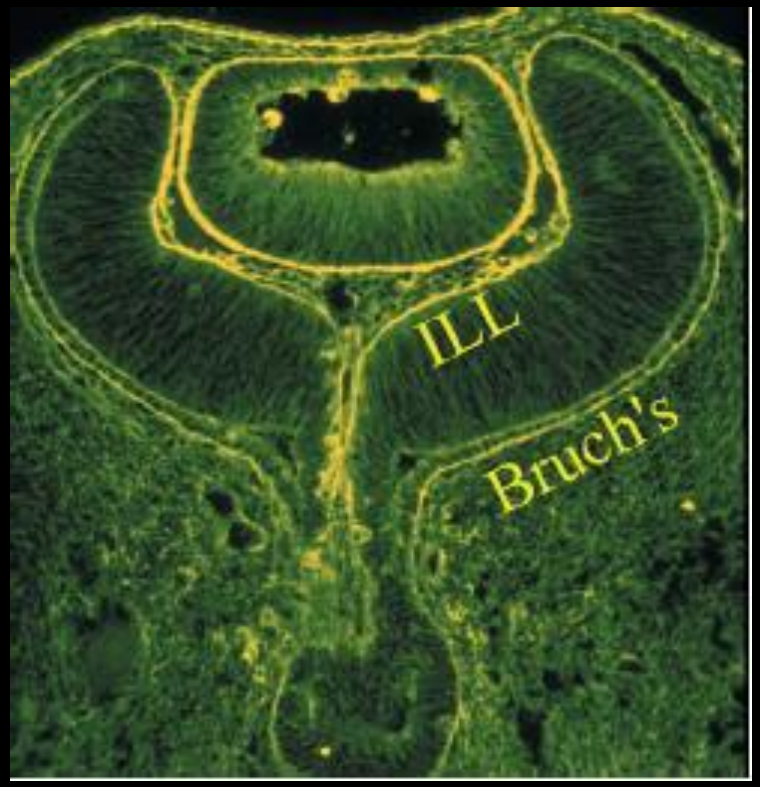






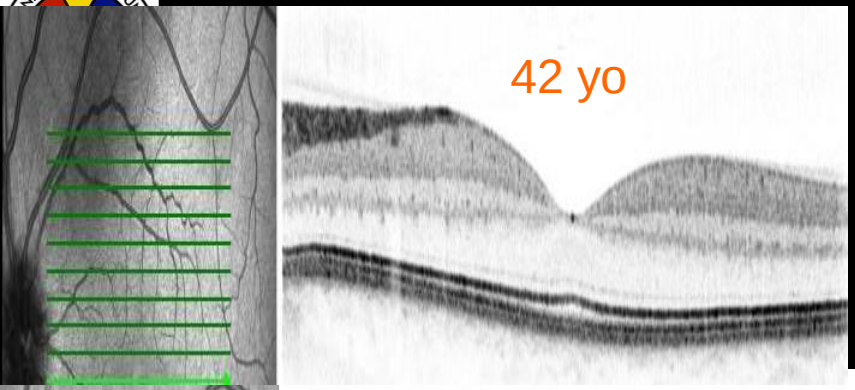
Why is fovea so sticky to ILM/Post Hyaloid?

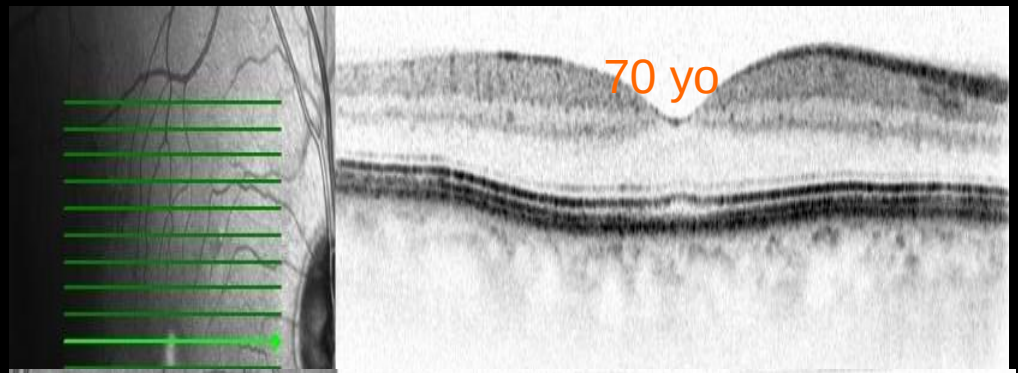
Vitreous Embryology

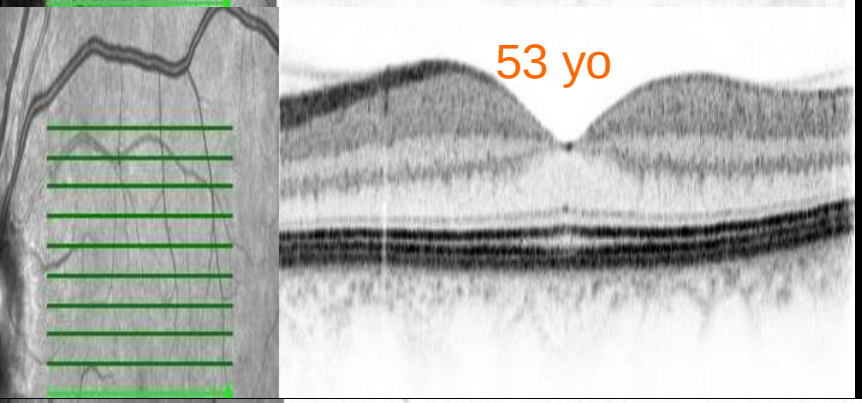


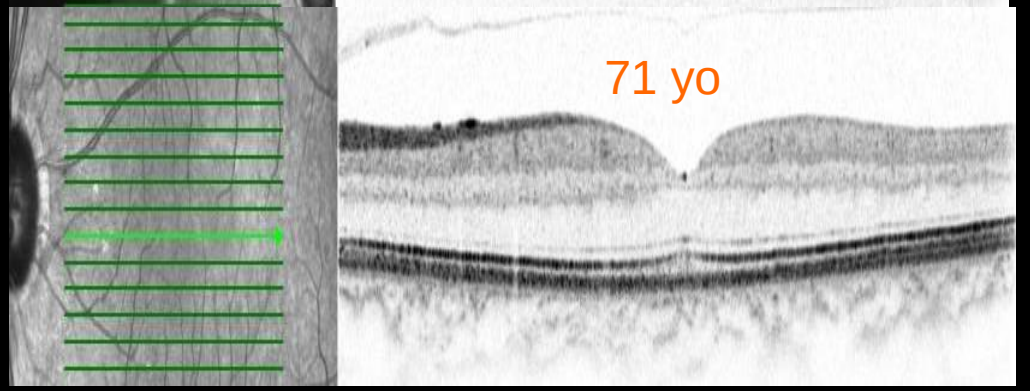
ILM and Bruch's are continuous in early embryogenesis
(coded by same genes)

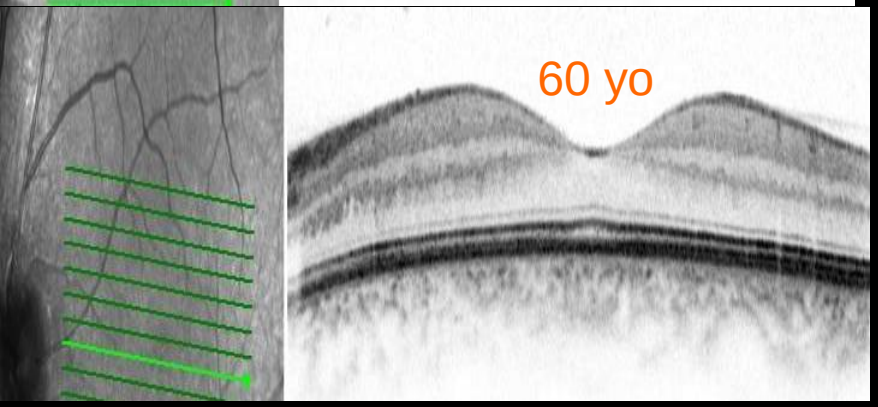
Gregory Hageman PhD

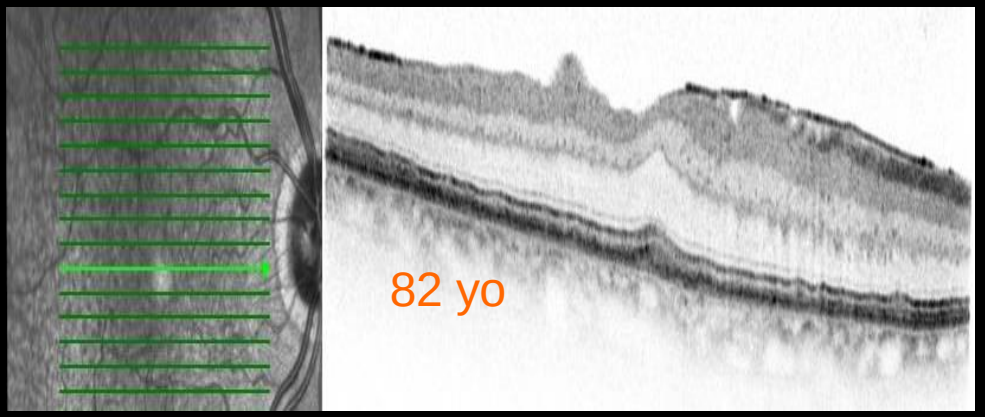












RPE/Bruch’s complex in different age groups.

Aging vitreous

Slit microscopy

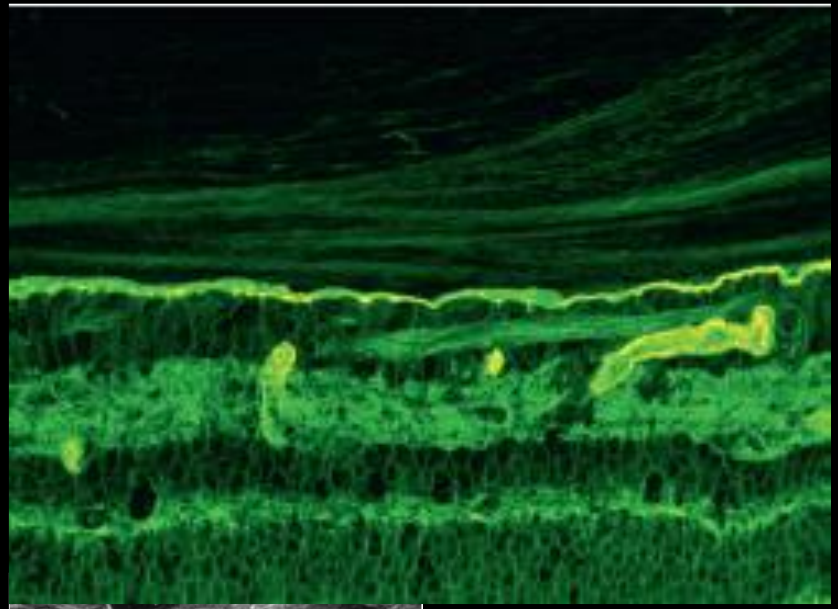
Embryo
– dense cortex

Young adult
- collagen fibrils

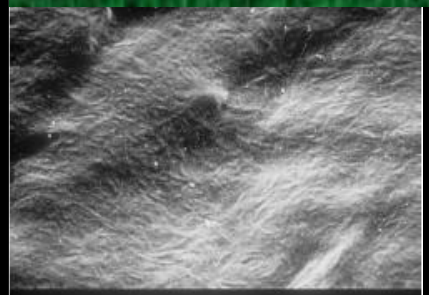
Elderly
-lacunae

Jerry Sebag MD

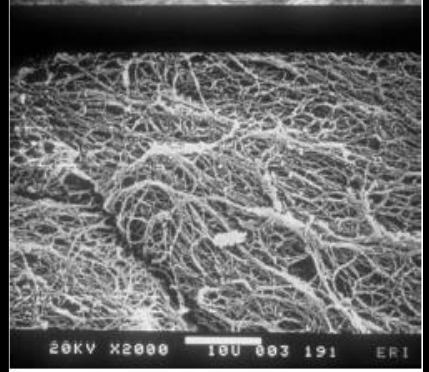
Vitreo-retinal Interface



- Dense sheets of collagen fibrils
- Not attached to ILM but ‘glued’ to it



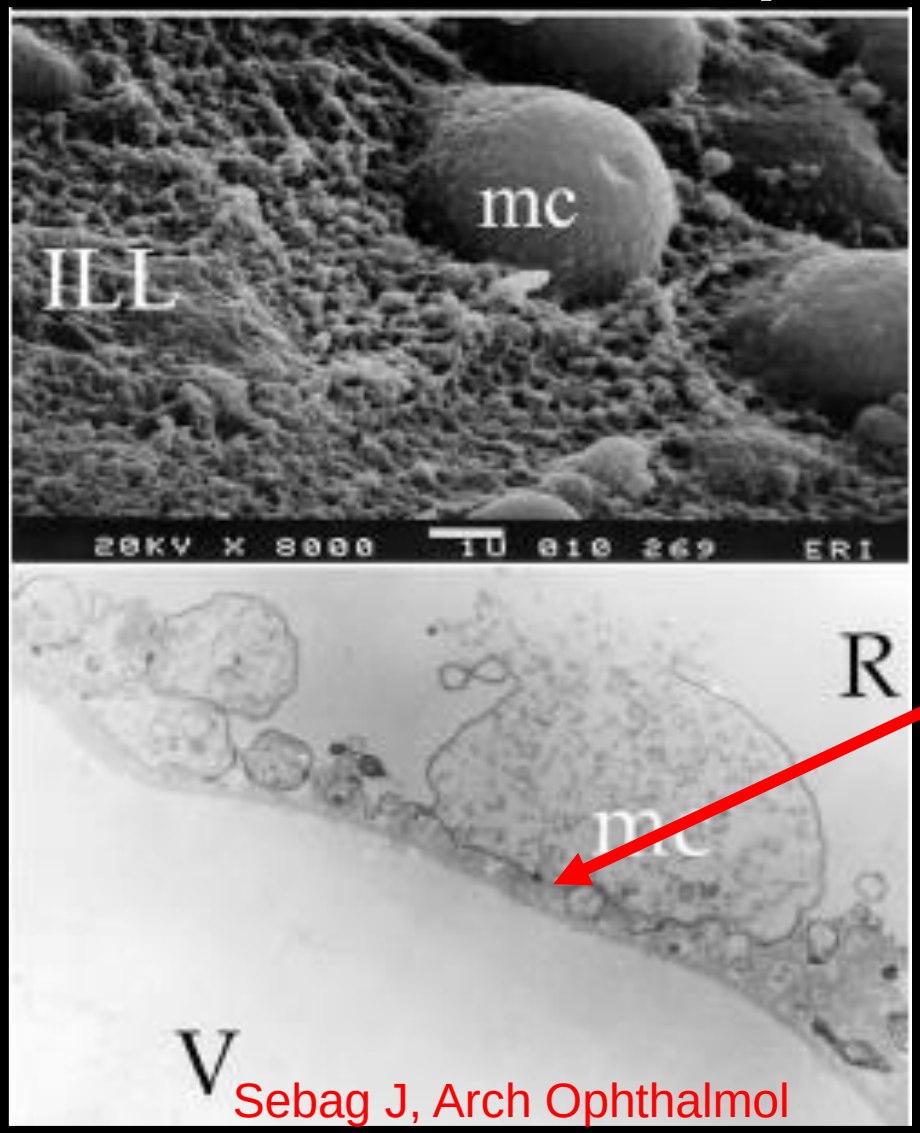
Posterior Surface of vitreous cortex (posterior Hyaloid)



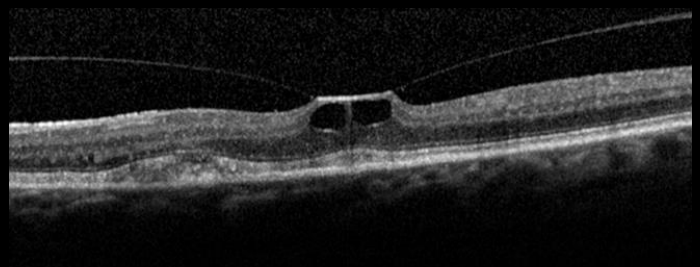
Anterior surface of ILM

Encyclopedia of the Eye, Darlene A Dartt, J Sebag, Elsevier, 2010

Muller cells ‘poke through’ ILM

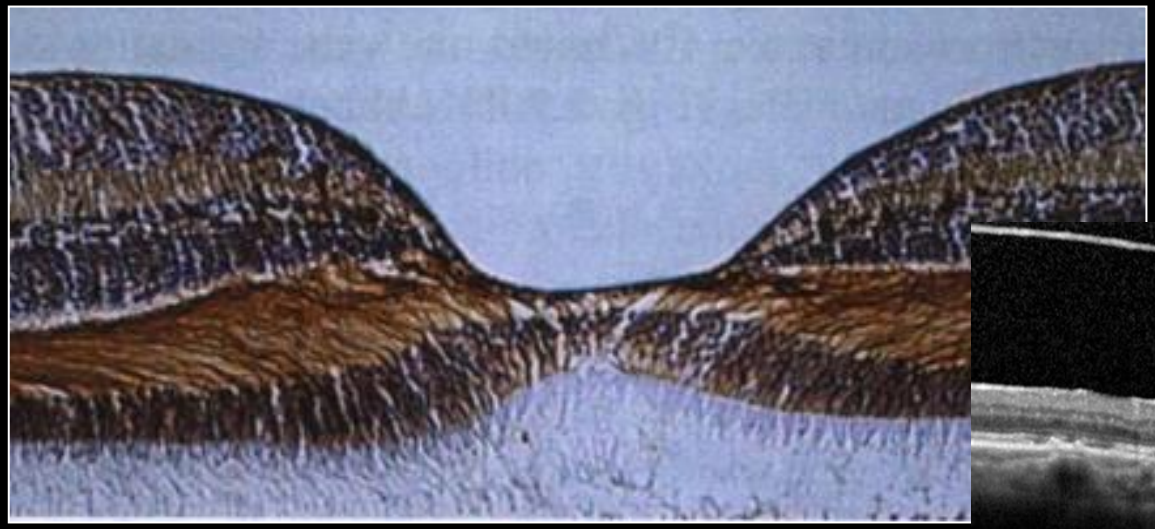


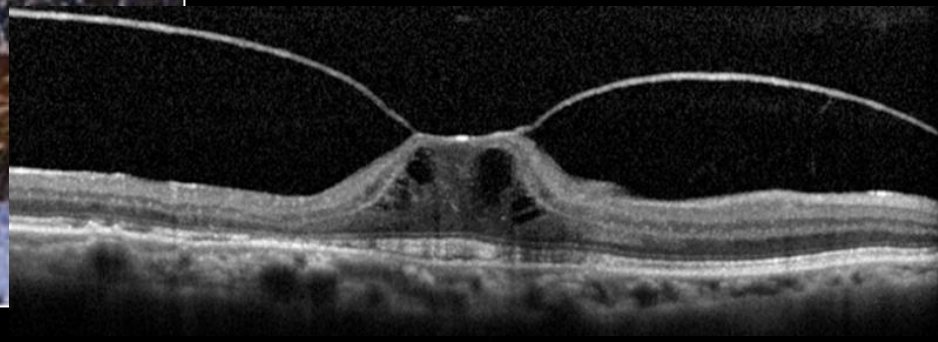
- Scanning EM of anterior surface of ILM- muller cell imprints
- Transmission EM showing ILM between Muller cell plate and Posterior surface of Vitreous Cortex
- ? Strong ‘glue’ at this interface which weakens with age.

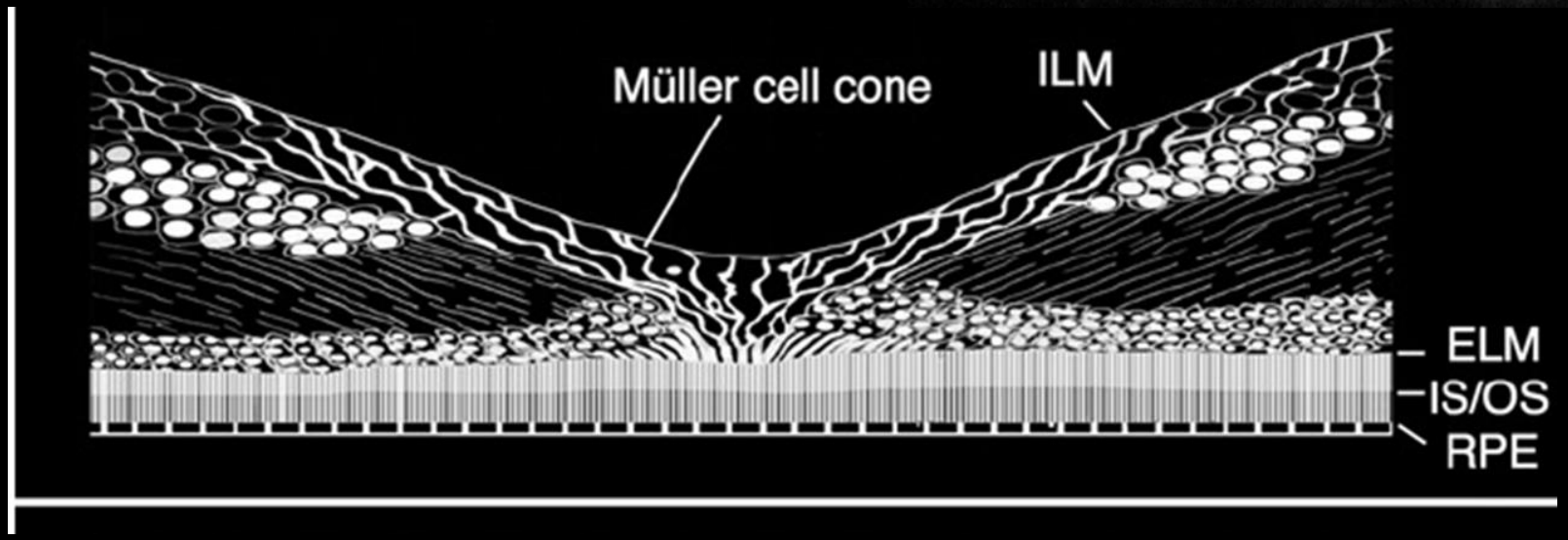


Sebag J, Arch Ophthalmol 109:966-971, 1991

Center of foveola and Muller cell cone



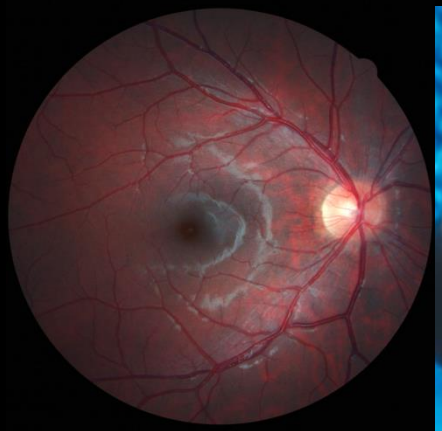


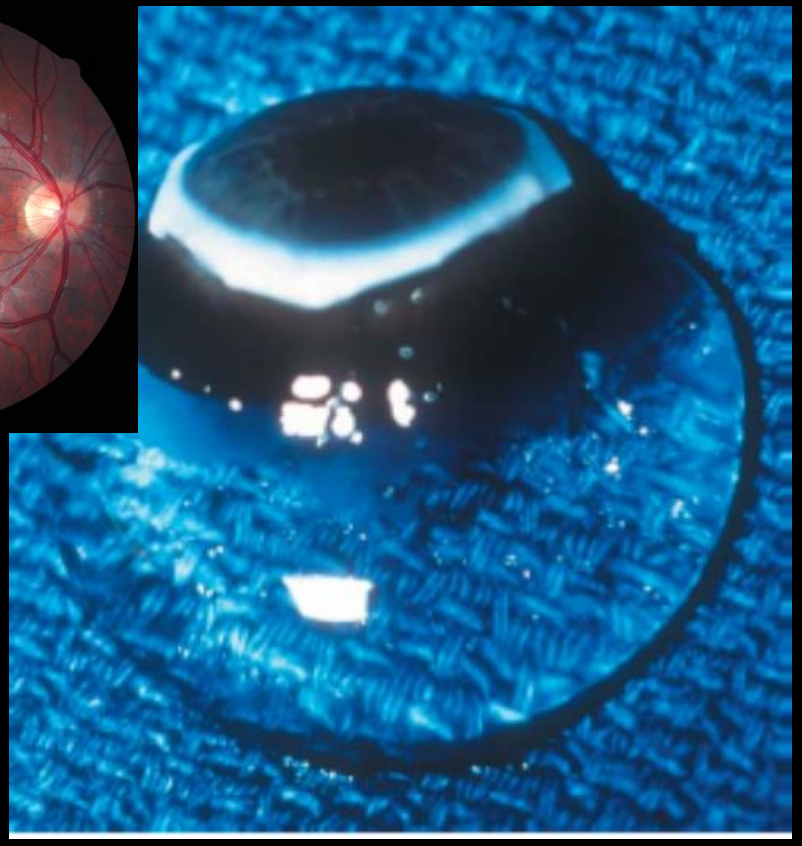


1. Bringmann A, *et al. Prog Retin Eye Res* 2006;25:397–424.

Muller cells play a role in vitreo-retinal adhesion

- Strongest at
  - Vitreous Base, Equator,
  - Optic disc margin
  - fovea
  - but not posterior pole.

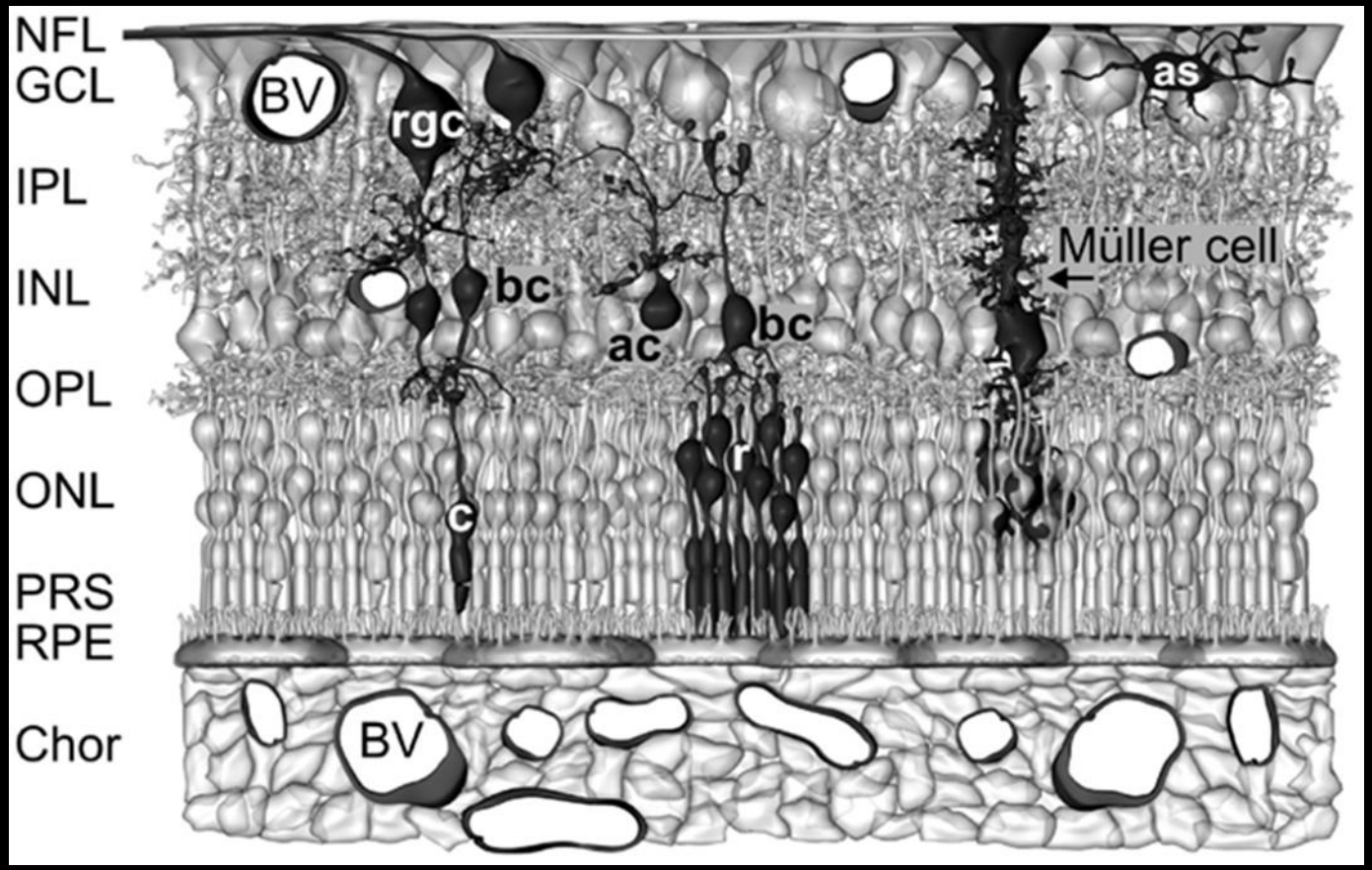




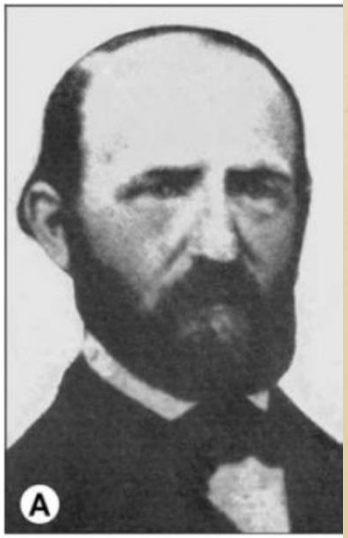
- ?Implications for NVE and NVD and VMT
- ? Implications for ILM peel technique

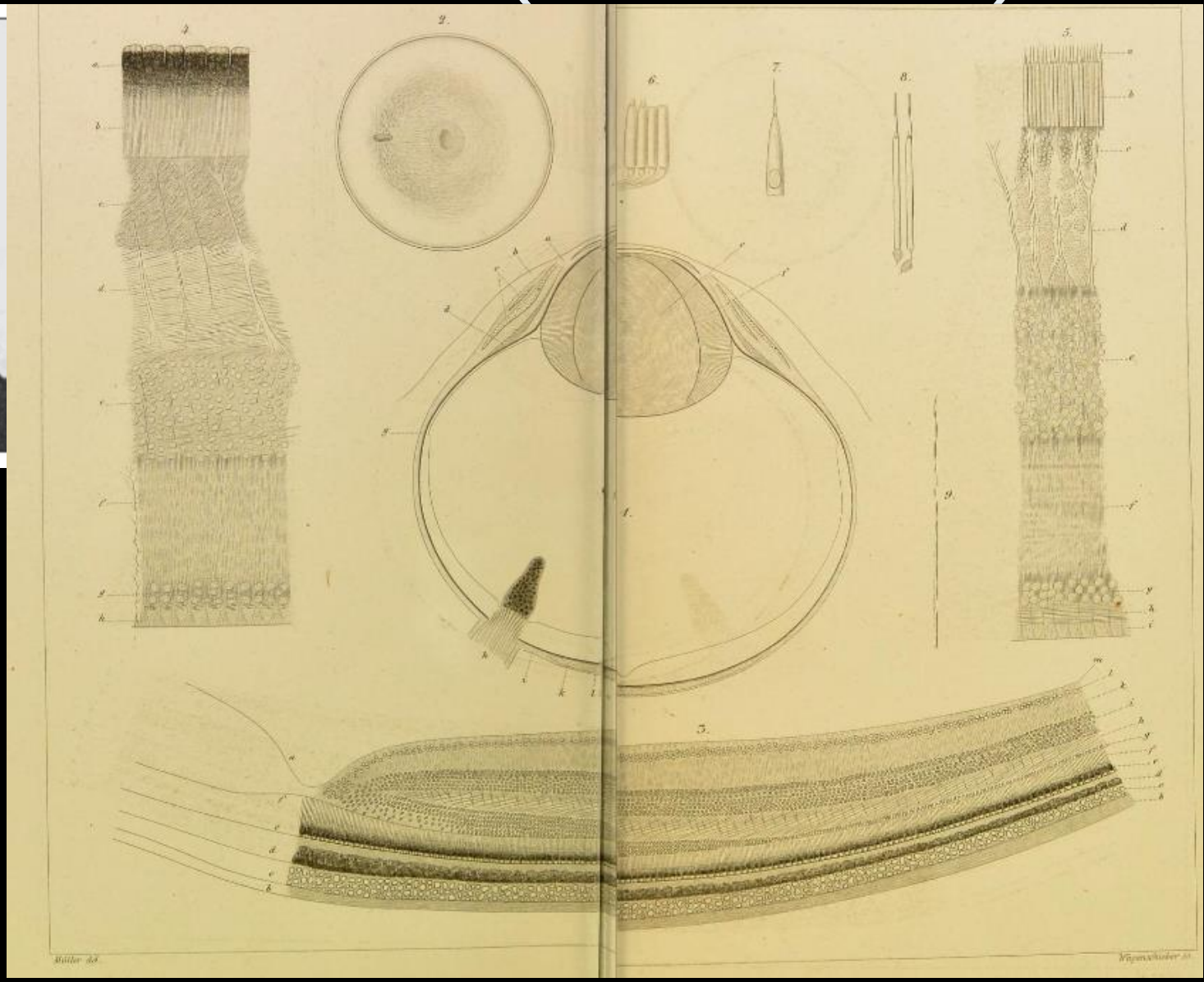
Russell SR, Shepherd JD, Hageman GS, Distribution of glycoconjugates in human ILM. IOVS, 32, 1991

2) Role of Muller cells in directing light on the fovea

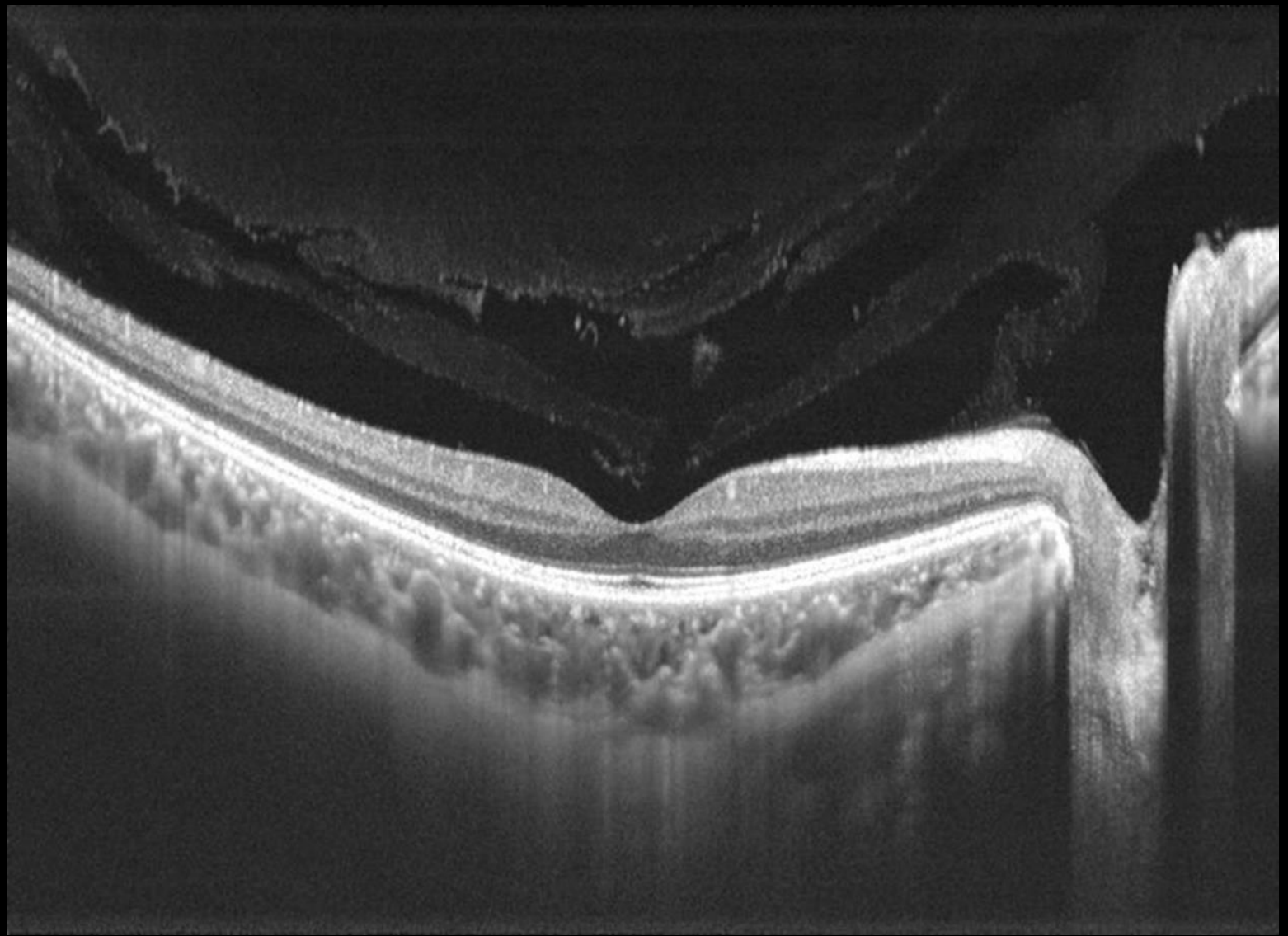


Heinrich Muller (1820-1864)

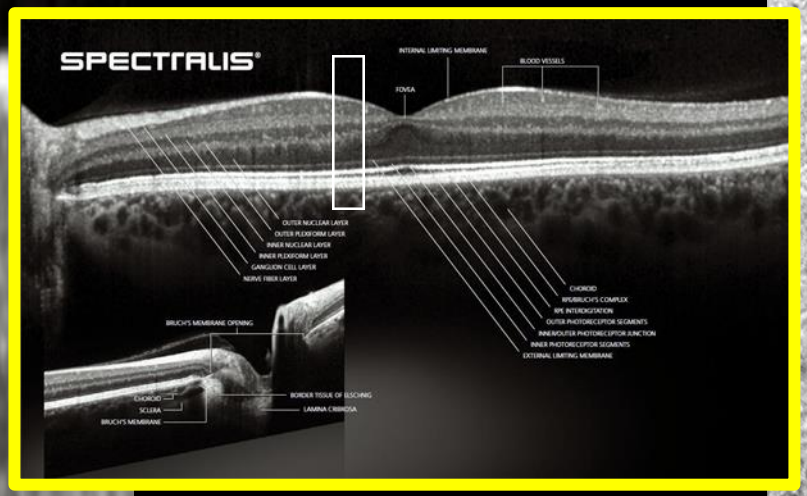




Bursa Premacularis and Posterior vitreous lacunae

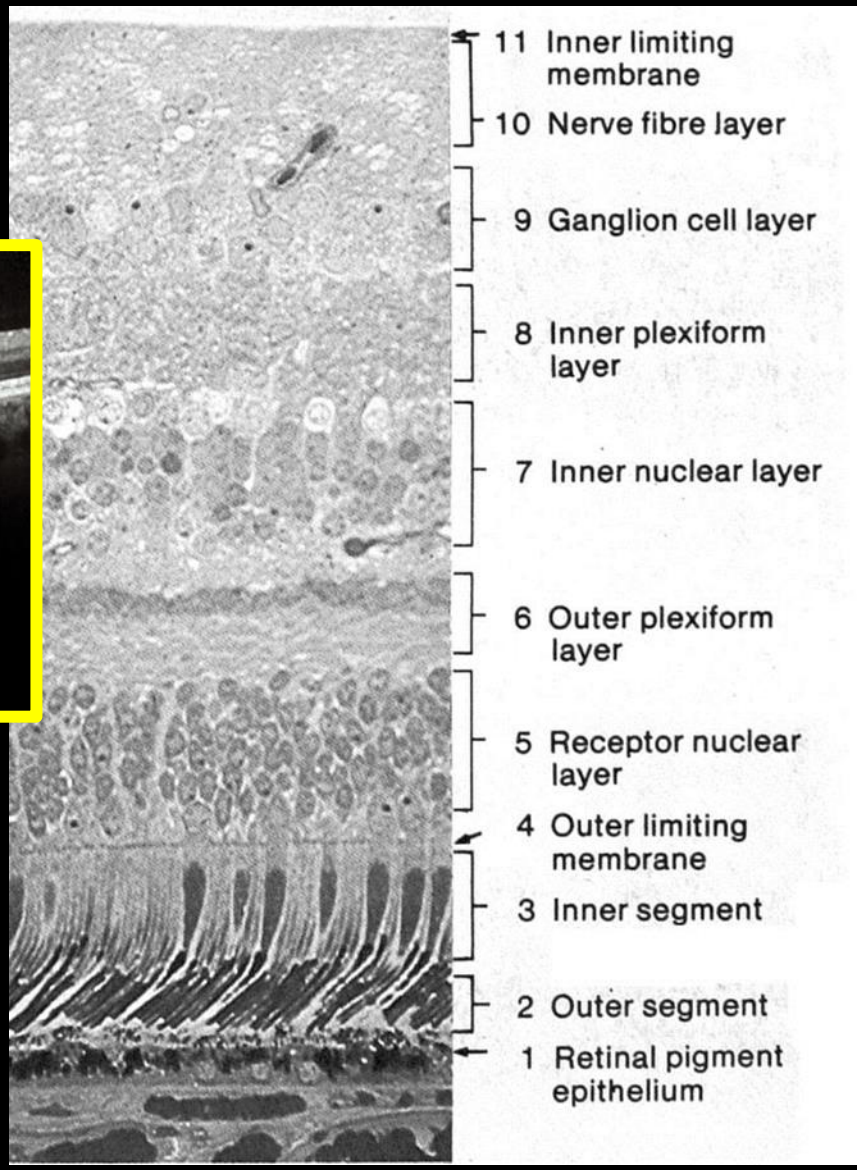


OCT layers- assignment



ELM

RPE



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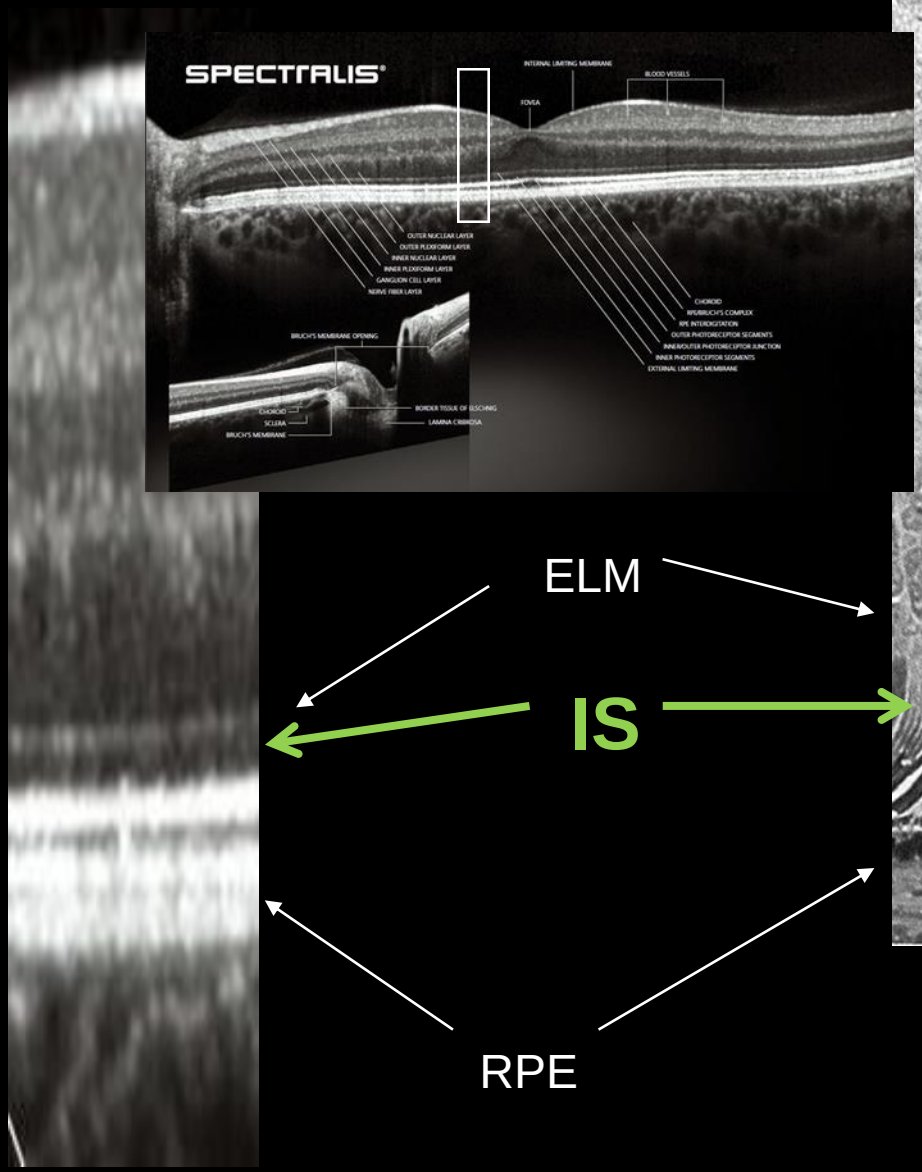

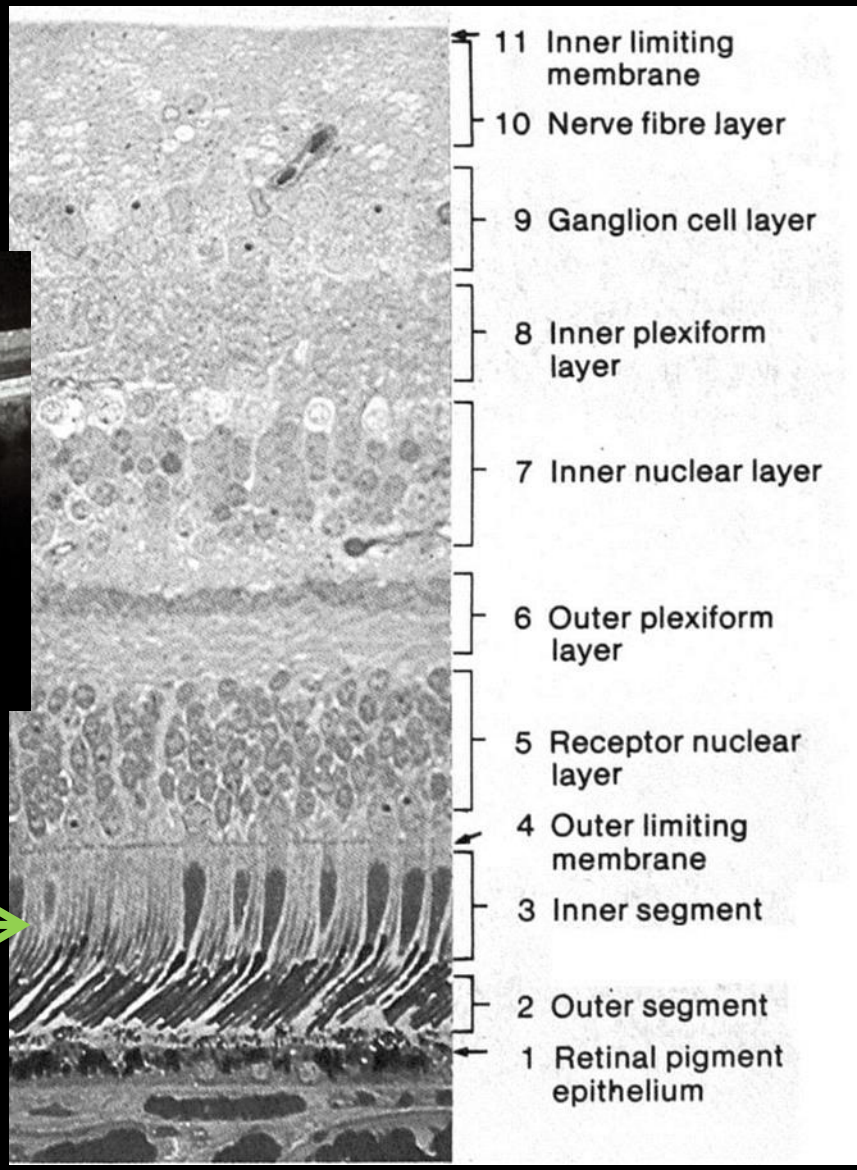

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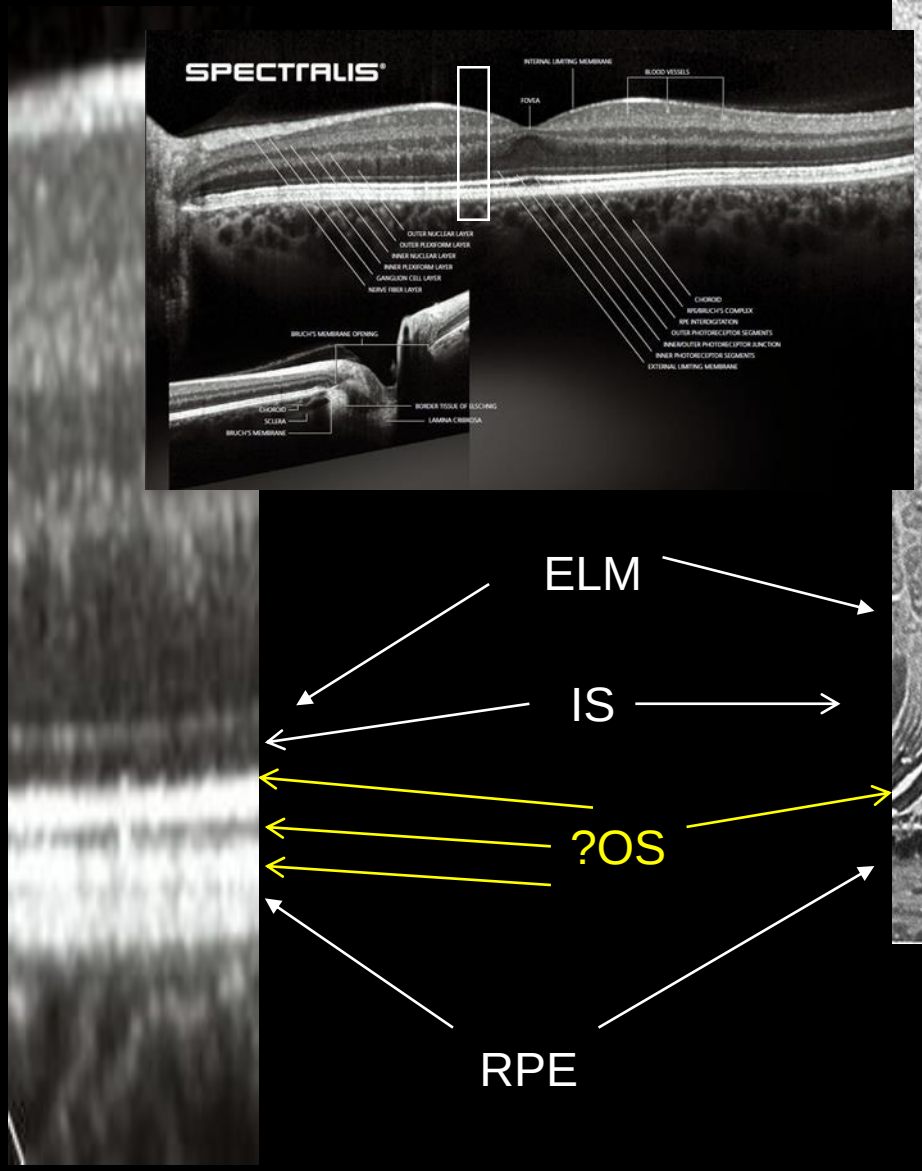
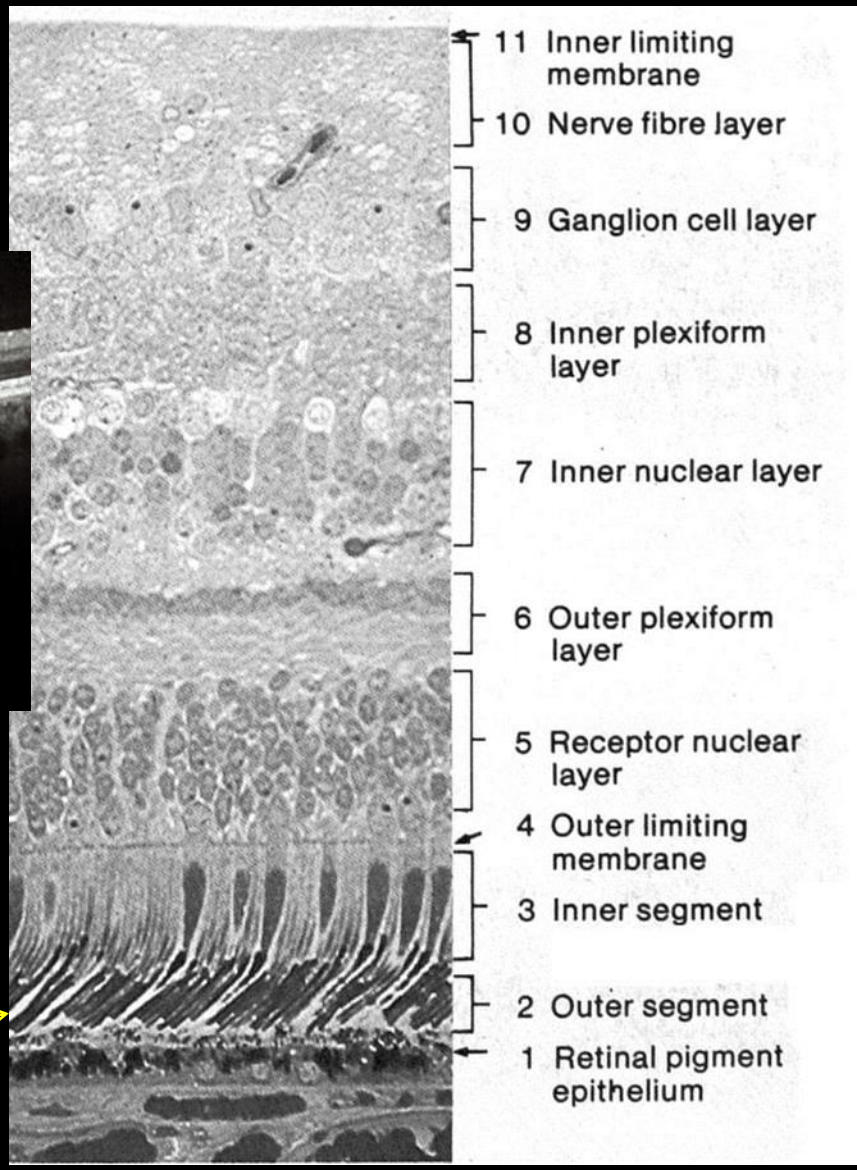




Nomenclature of lines- are the assignments correct?

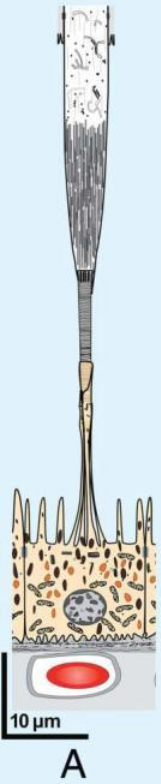
ANATOMICAL CORRELATES TO THE BANDS SEEN IN THE OUTER RETINA BY OPTICAL COHERENCE TOMOGRAPHY

Literature Review and Model

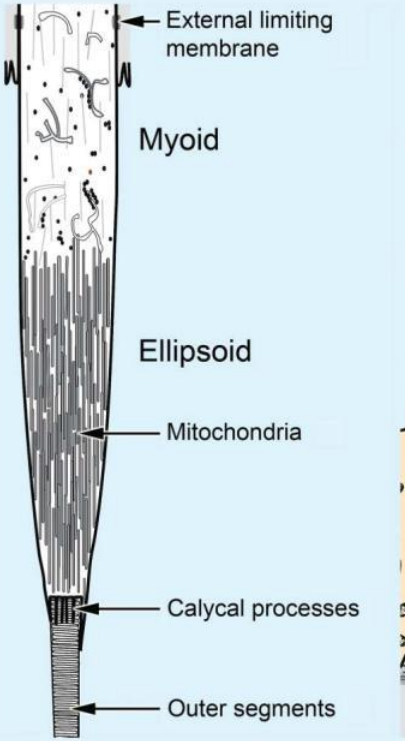
RICHARD F. SPAIDE, MD,*† CHRISTINE A. CURCIO, PHD‡

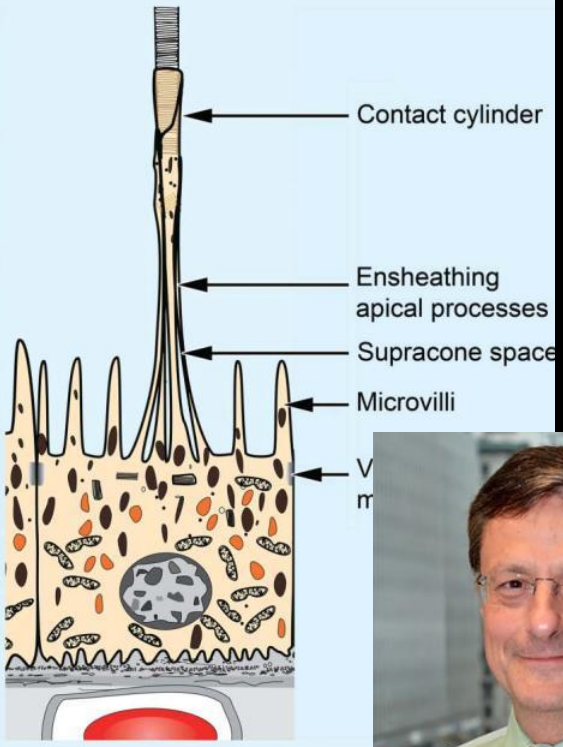
Retina Vol 31, pg1609-1619, 2011

Perifovea
Cones



A

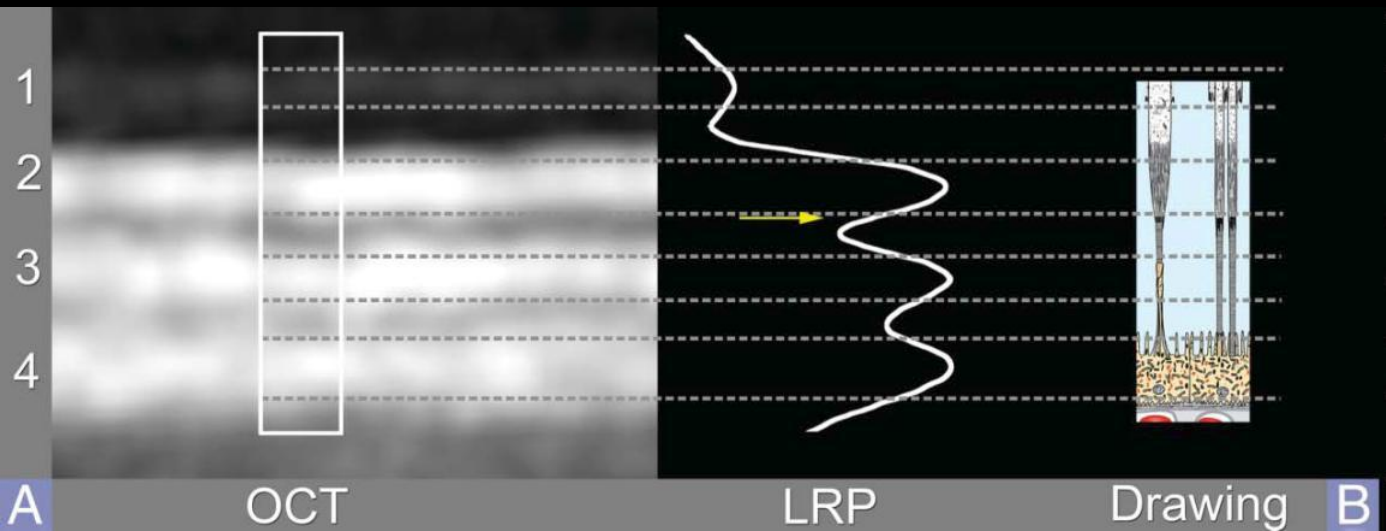


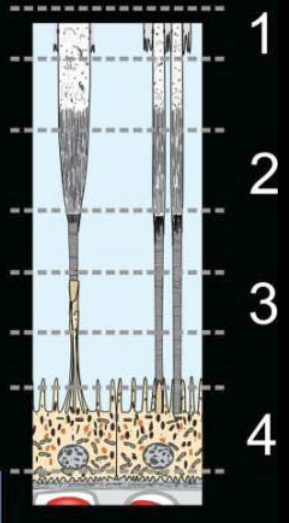


B

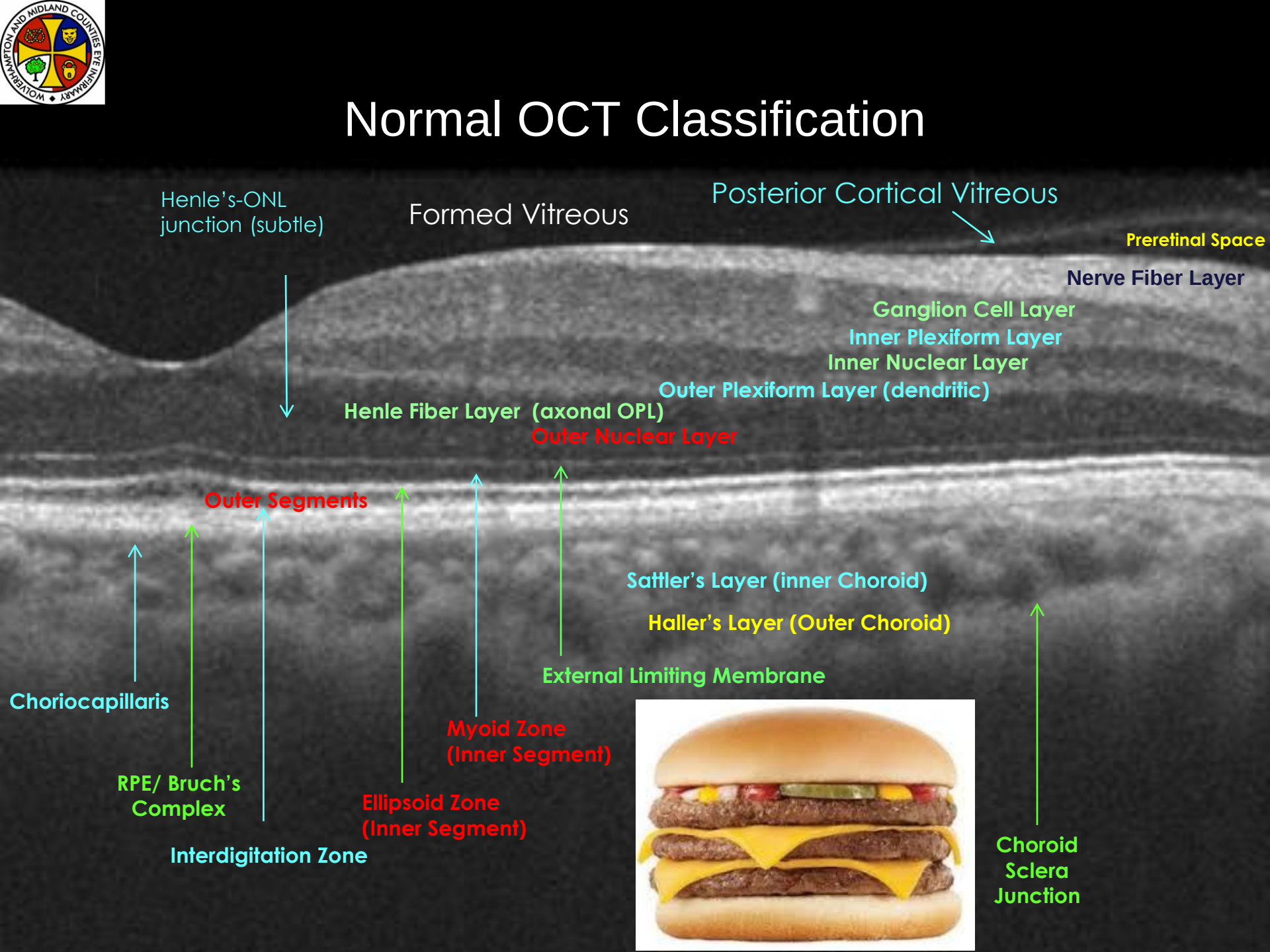
Scale drawing of inner segment and outer segment

Cones



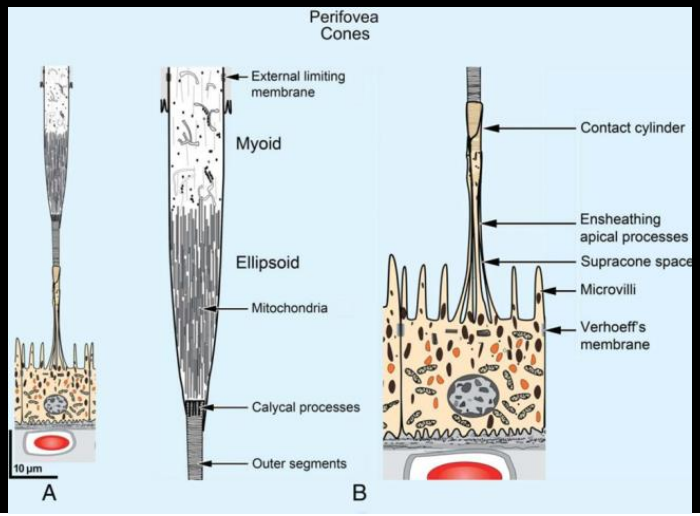


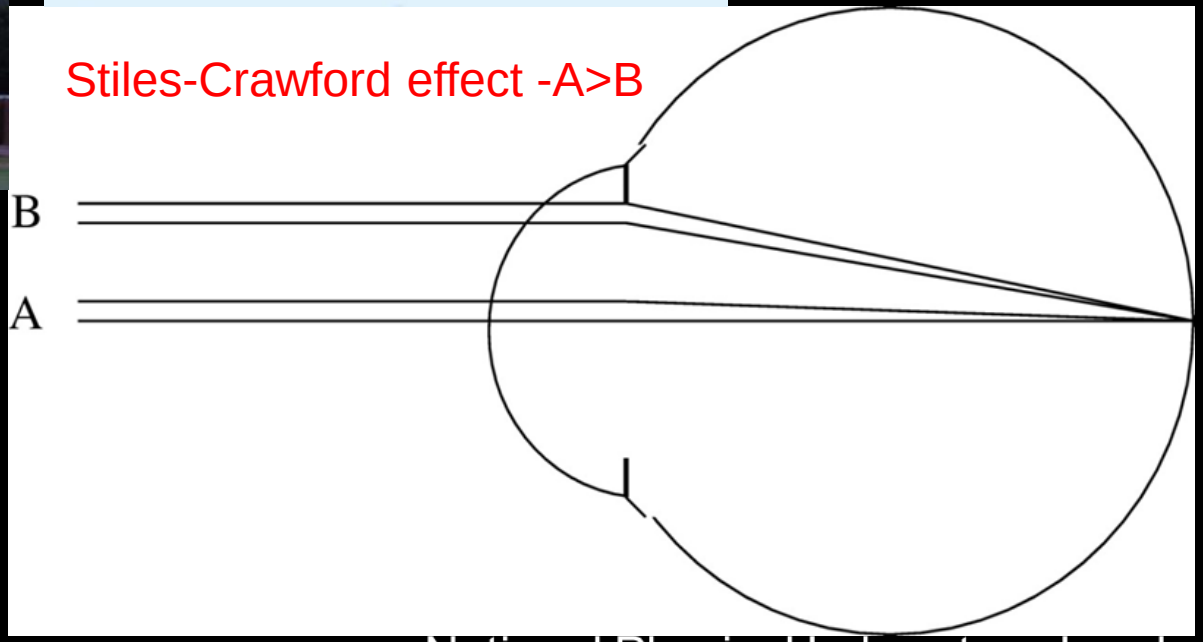
Normal OCT Classification



OCT Nomenclature group- Venice 2012.

Foveal centre, Mitochondria and light path





National Physical Laboratory, London.

1. Bringmann A, *et al. Prog Retin Eye Res* 2006;25:397–424.

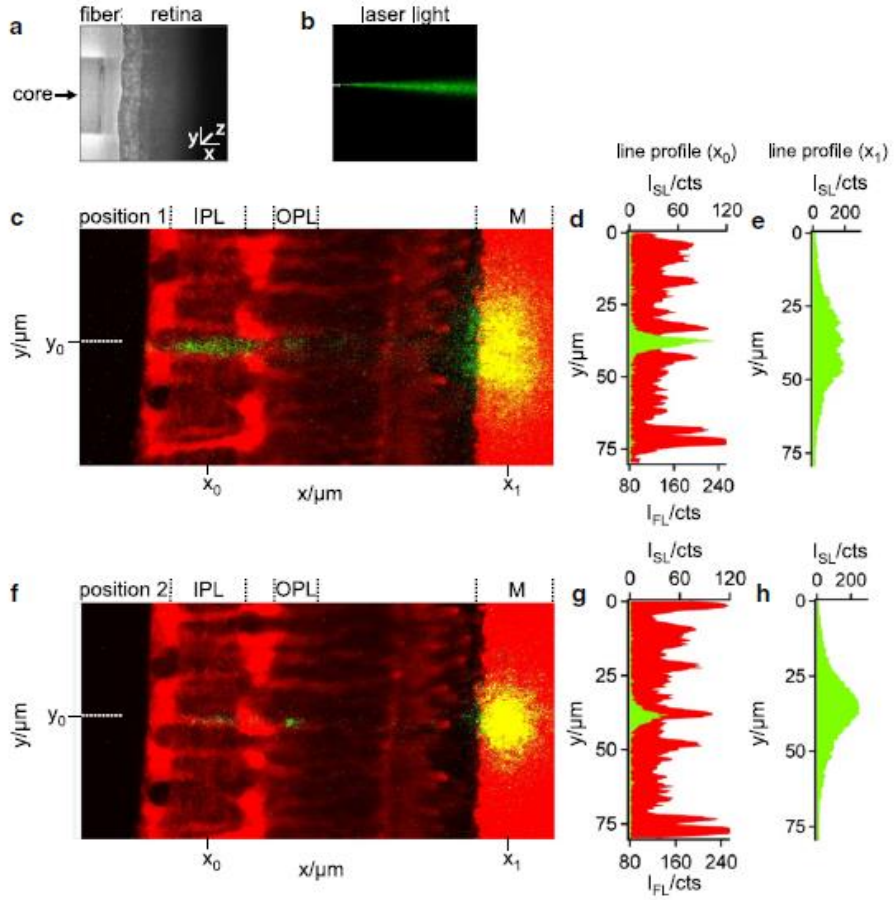
Biophysical Journal Volume 101 December 2011 2611–2619

Müller Glial Cell-Provided Cellular Light Guidance through the Vital Guinea-Pig Retina

Silke Agte,[†‡*] Stephan Junek,[§¶‖] Sabrina Matthias,[†] Elke Ulbricht,[†] Ines Erdmann,[†] Antje Wurm,[†] Detlev Schild,[§] Josef A. Käs,[‡] and Andreas Reichenbach[†]

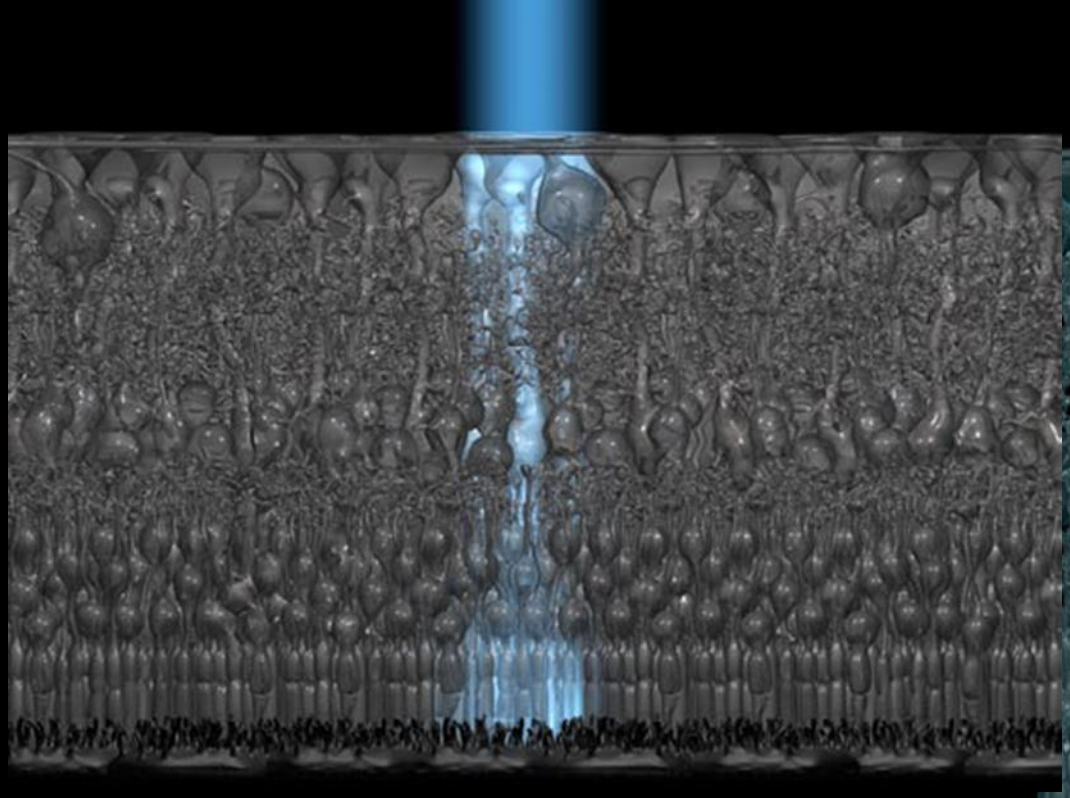
[†]Paul Flechsig Institute for Brain Research and [‡]Institute for Experimental Physics I, Department of Physics and Geosciences, Universität Leipzig, Leipzig, Germany; [§]Physiology Department, University of Göttingen and Deutsche Forschungsgemeinschaft Cluster of Excellence, Göttingen, Germany; [¶]Deutsche Forschungsgemeinschaft Research Center Molecular Physiology of the Brain, Universität Göttingen, Göttingen, Germany; and [‖]Max Planck Institute for Brain Research, Frankfurt, Germany

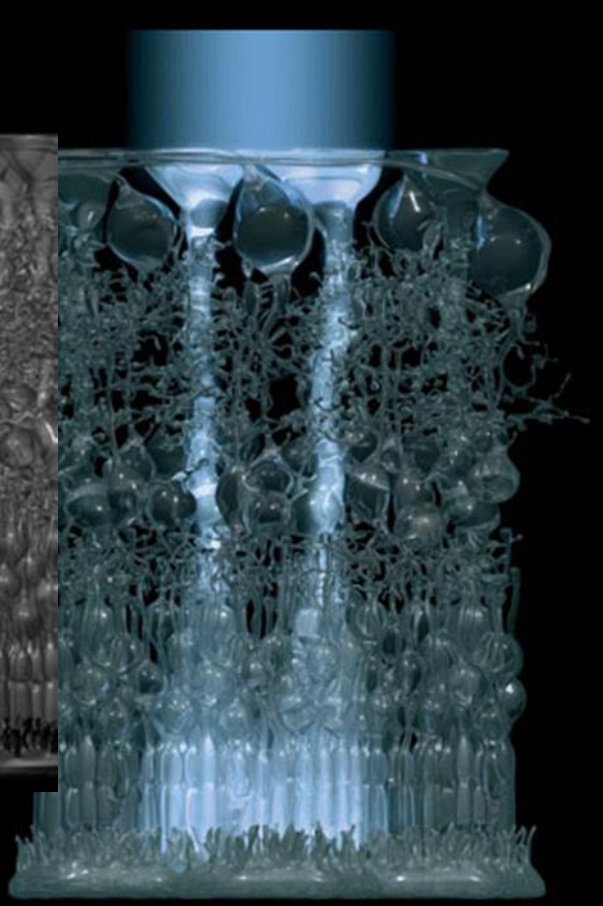
Optical Pathway through the Retina

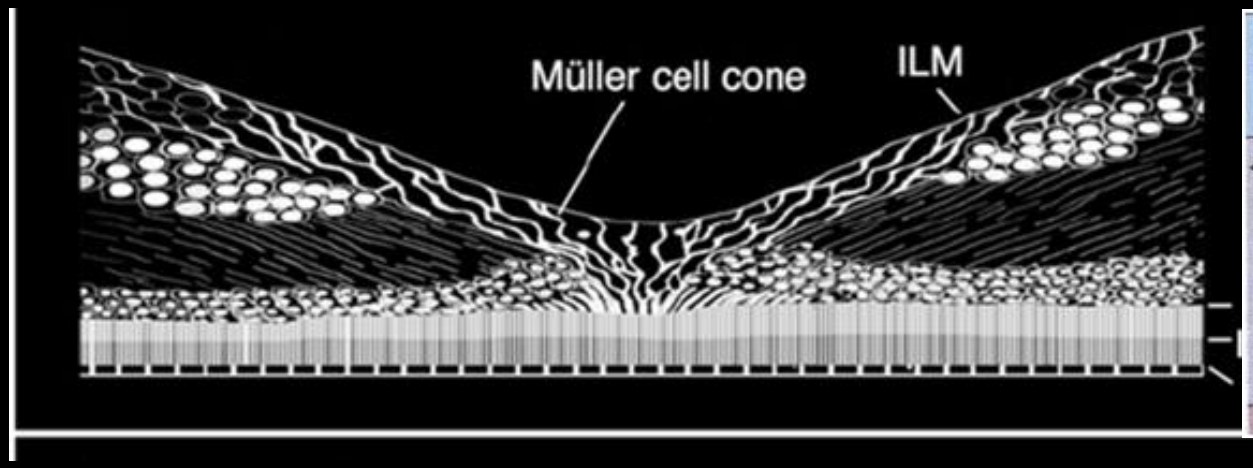


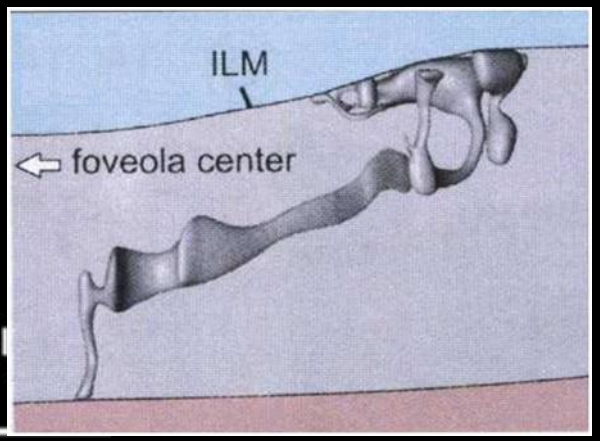
projected onto an inverted retina where light passes all retinal layers on its way to this tissue should impair vision. We show that radial glial (Müller) cells in the living onserve the diameter of a beam that hits a single Müller cell endfoot. Thus, light intensity. This leads to an optimized signal/noise ratio, which increases visual that the ratio between Müller cells and cones—responsible for acute vision—is poral resolution may be achieved by each cone receiving its part of the image

Dr Andreas Reichenbach, Leipzig, 2011

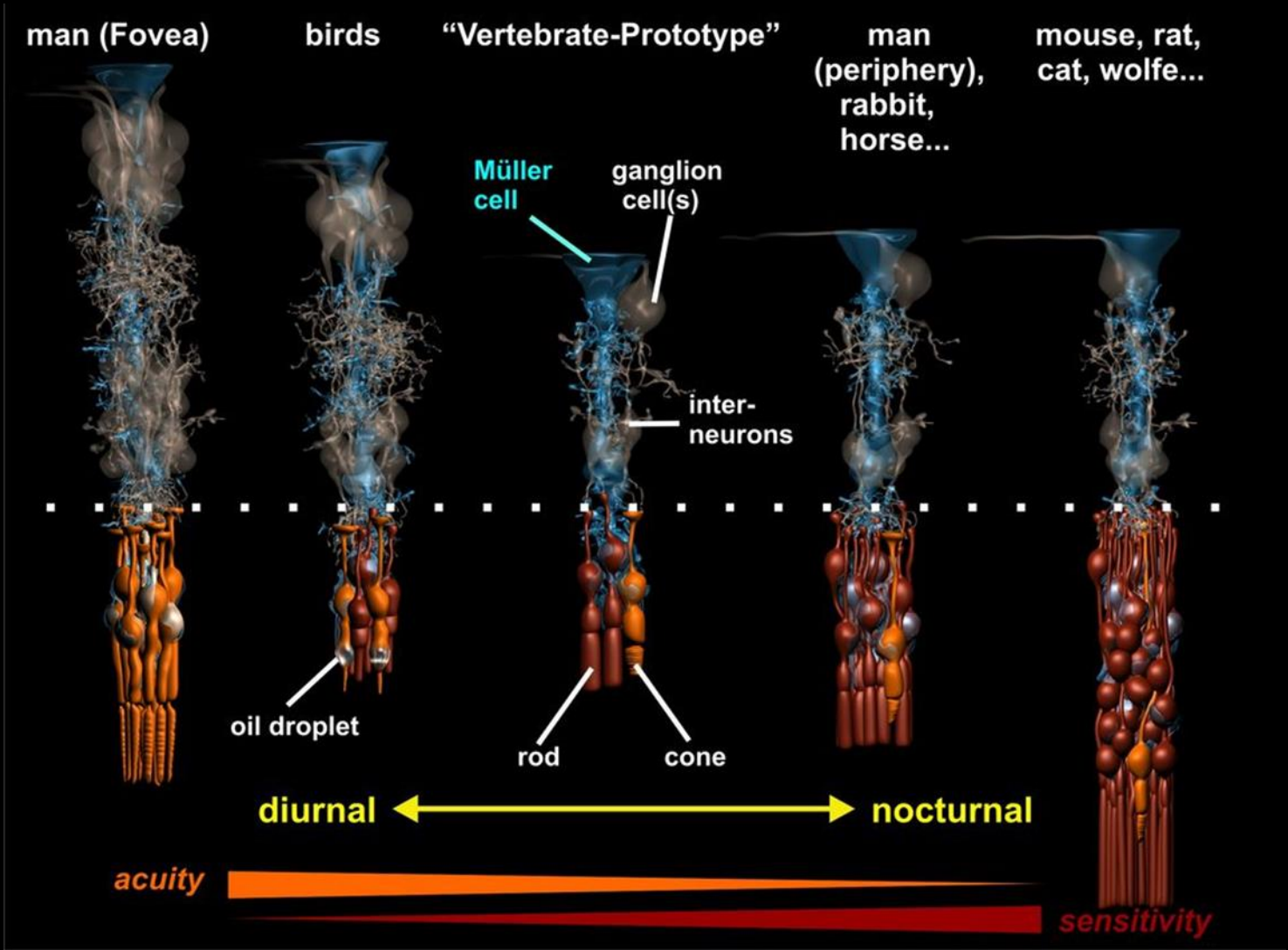




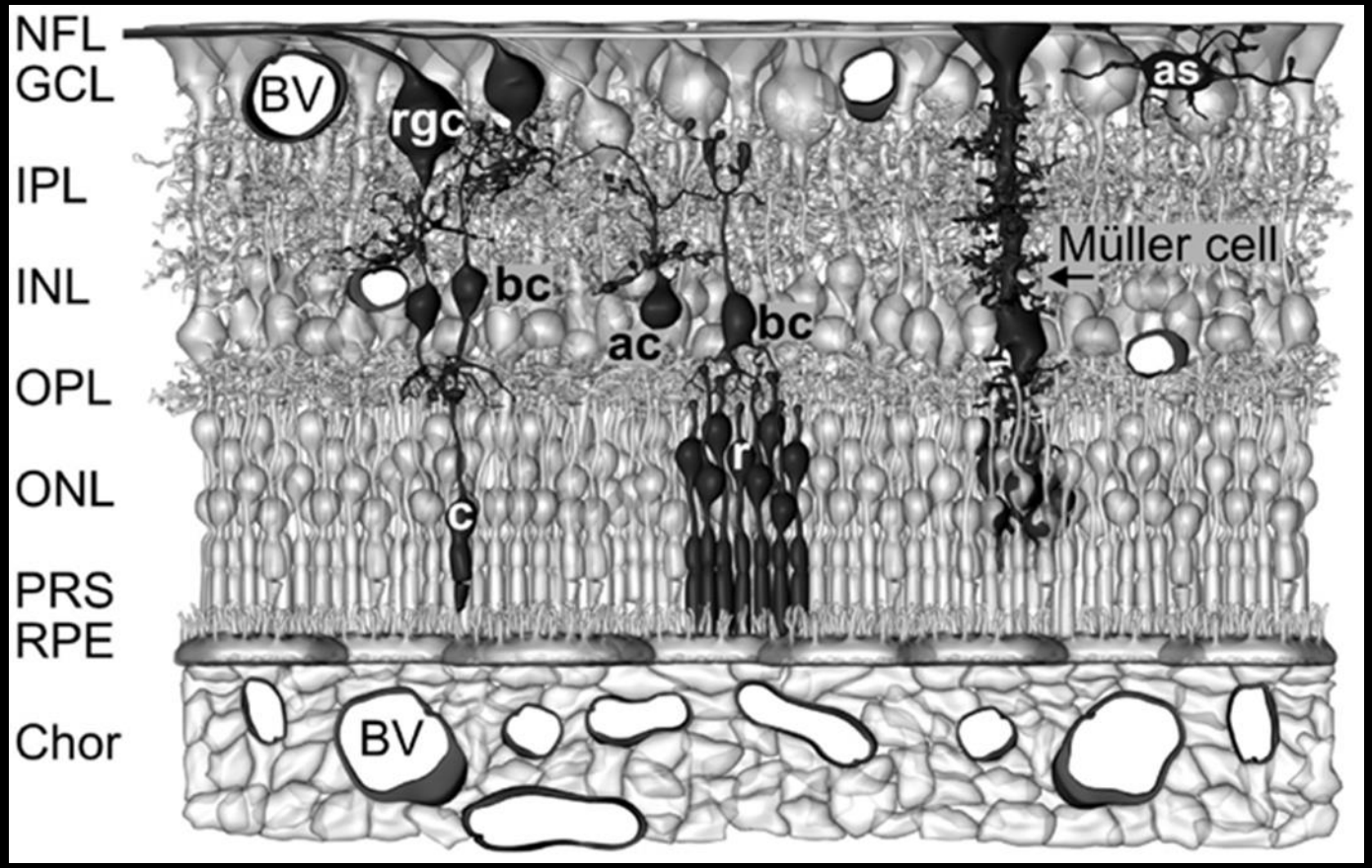

Müller cell cone
ILM


ILM
foveola center

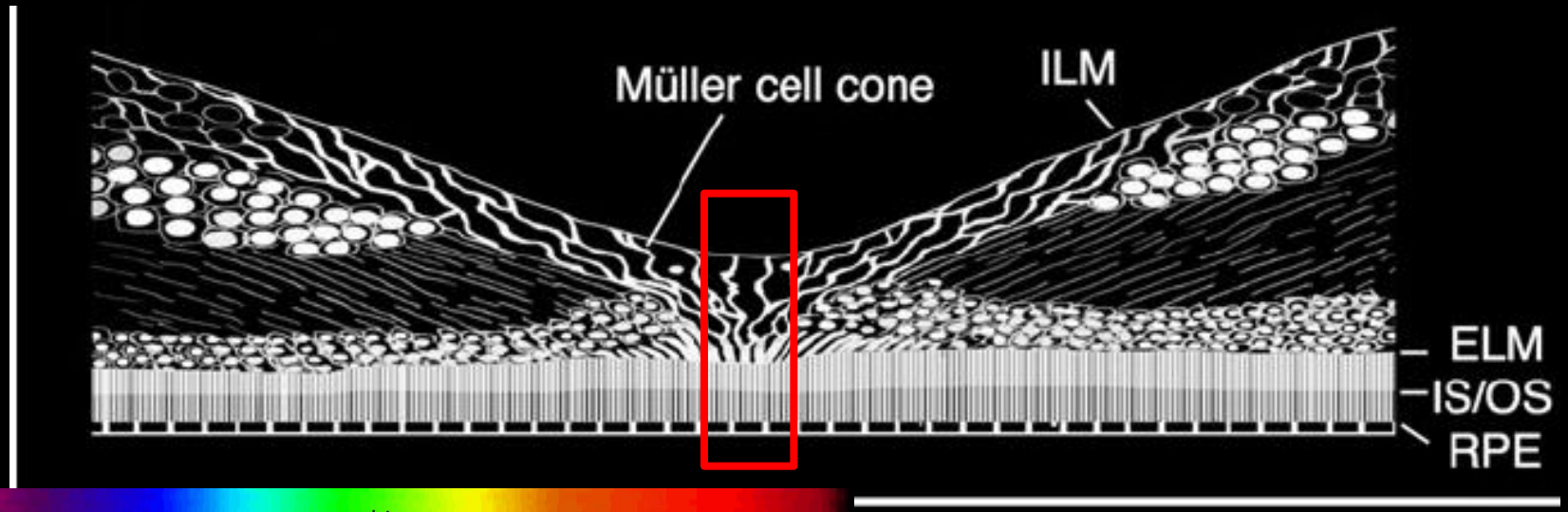
Muller cells better developed in high acuity system

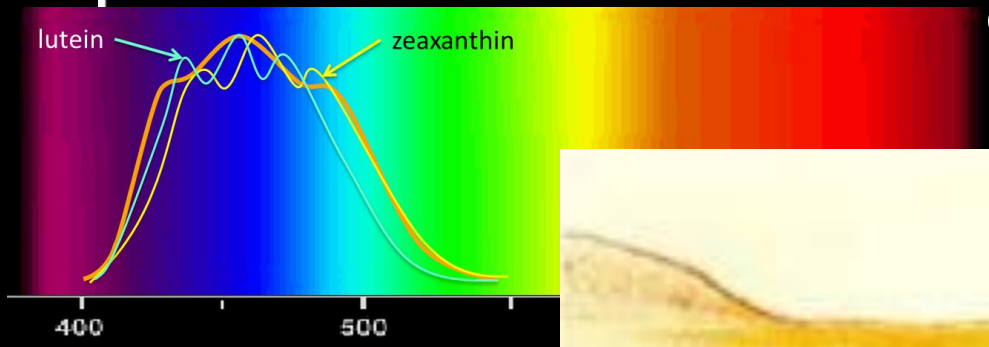


3)Role of Muller cells in macular protection



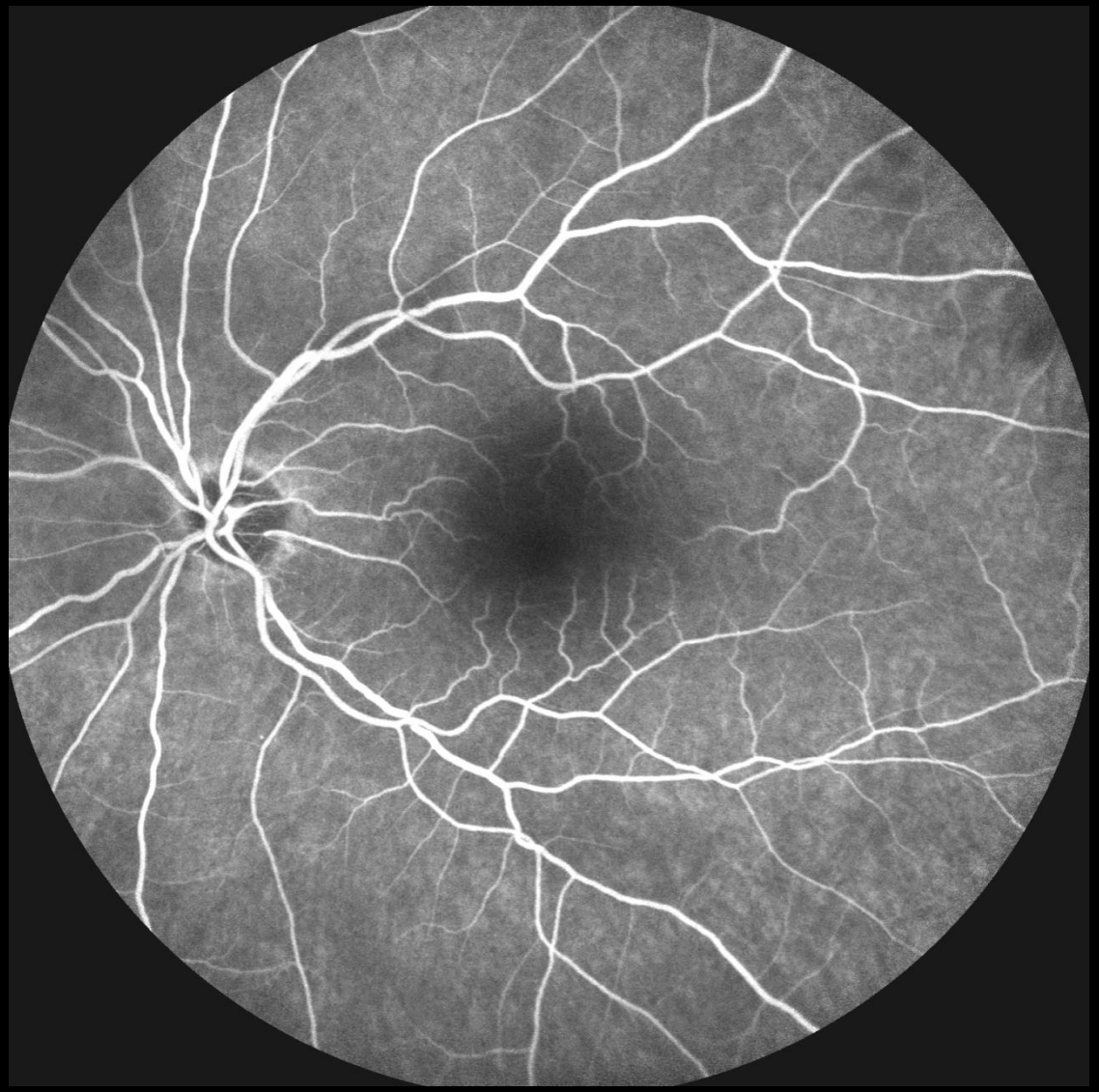
Muller cells contain Lutein and Zeaxanthin

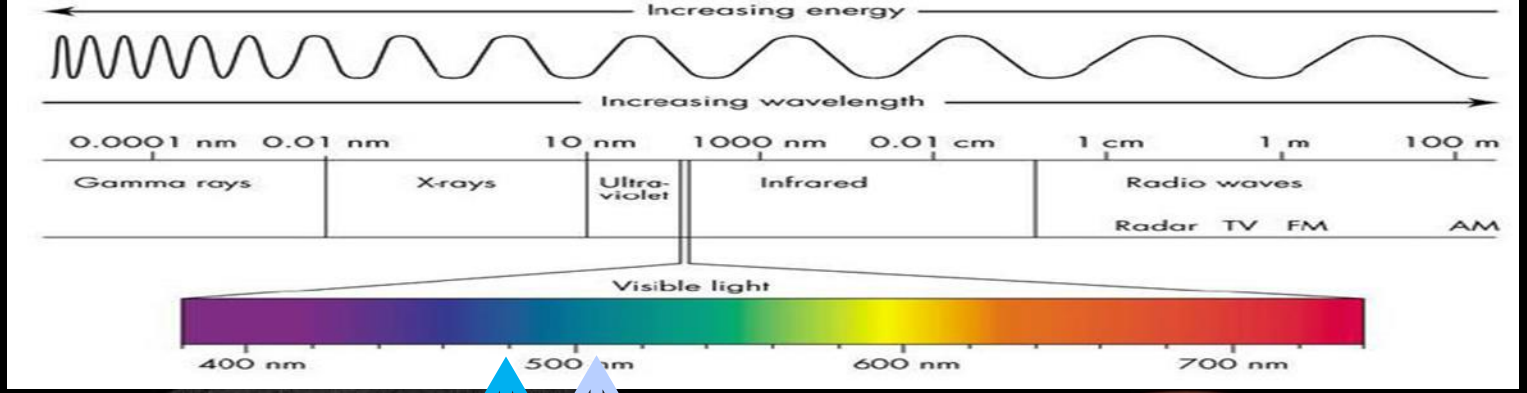




1. Tsujikawa A, *et al. Am J Ophthalmol* 2009;148:83–9; 2. Gass JD. *Arch Ophthalmol* 1968;80:550–68.

Blocked flourescence in centre of macula in normal eyes





Filter 521nm

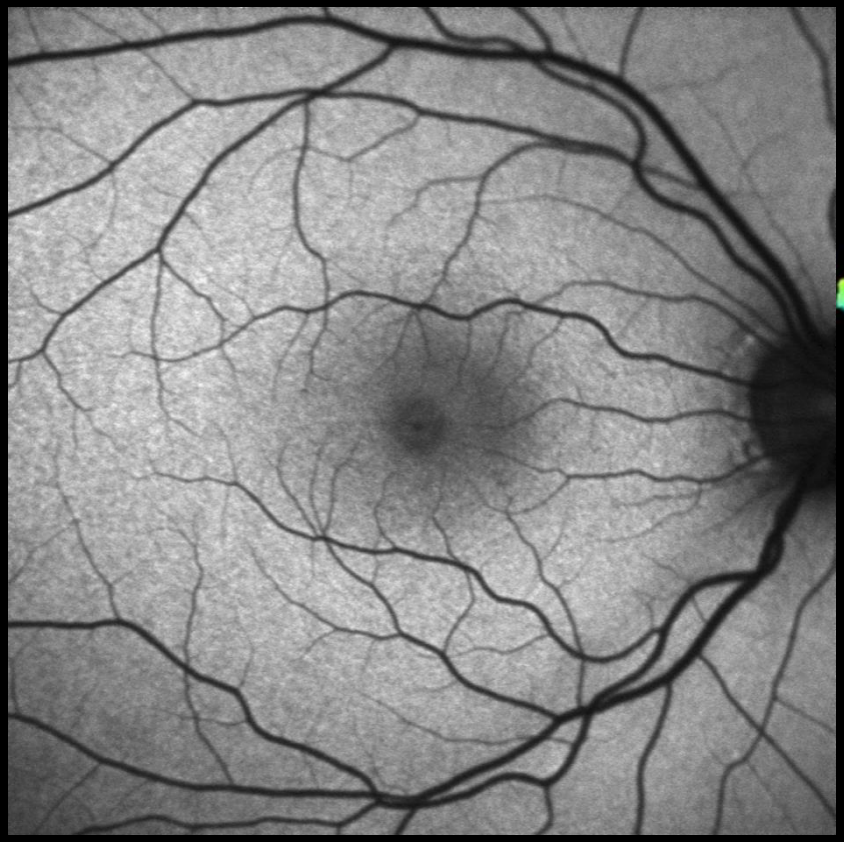
Excite 488nm

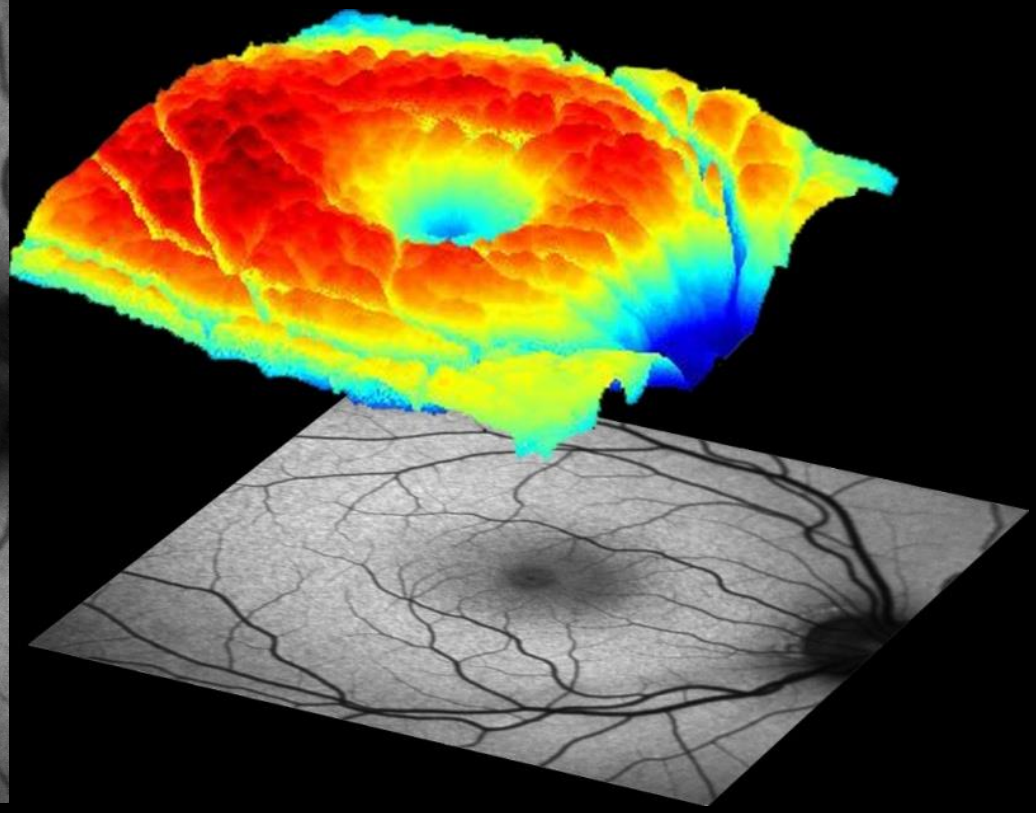
Normal Blue Peak Auto fluorescence imaging

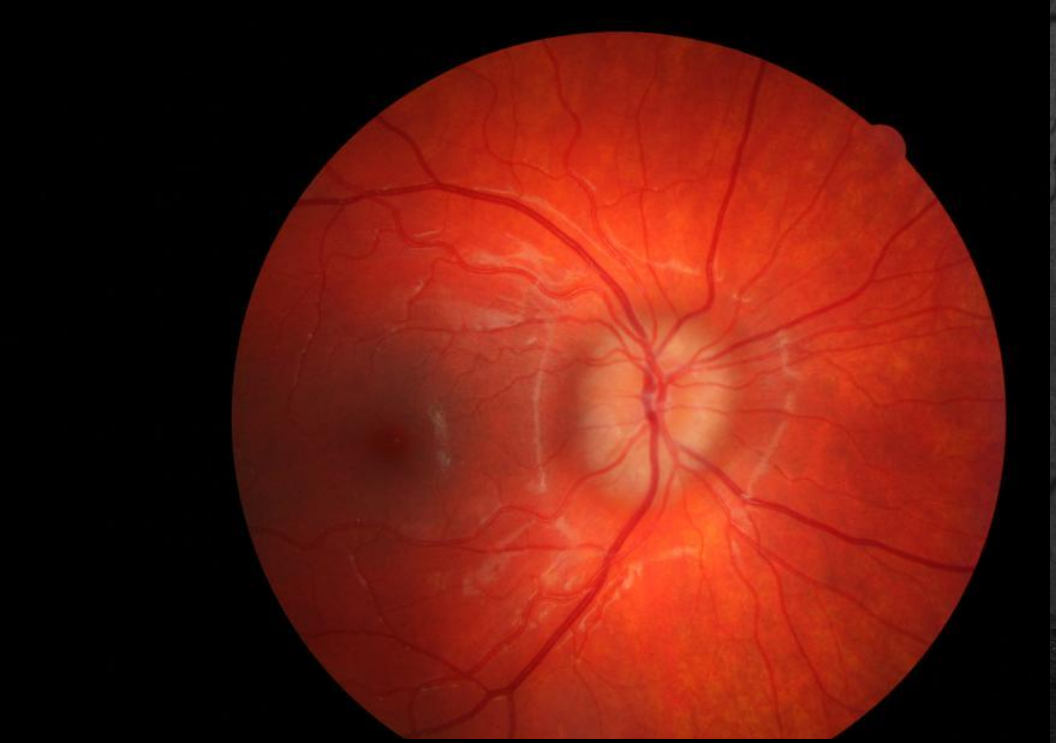
200 µm

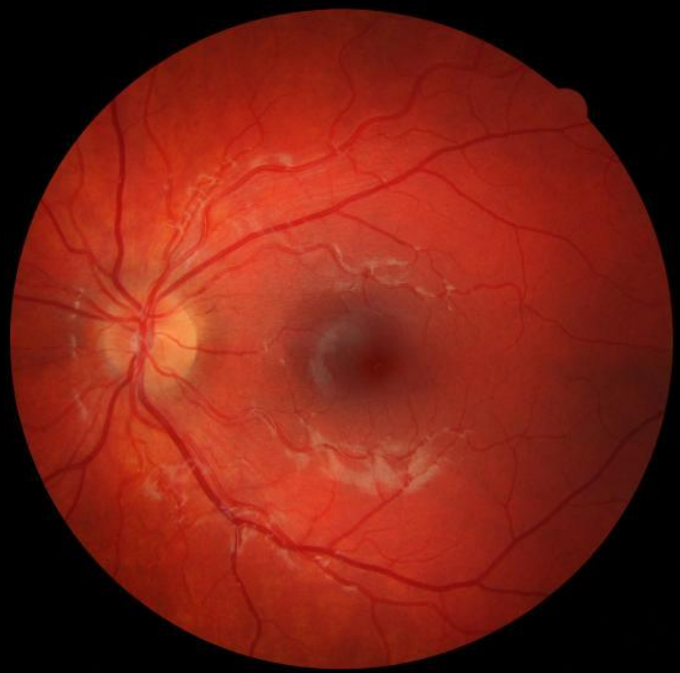
FAF Imaging in Normals

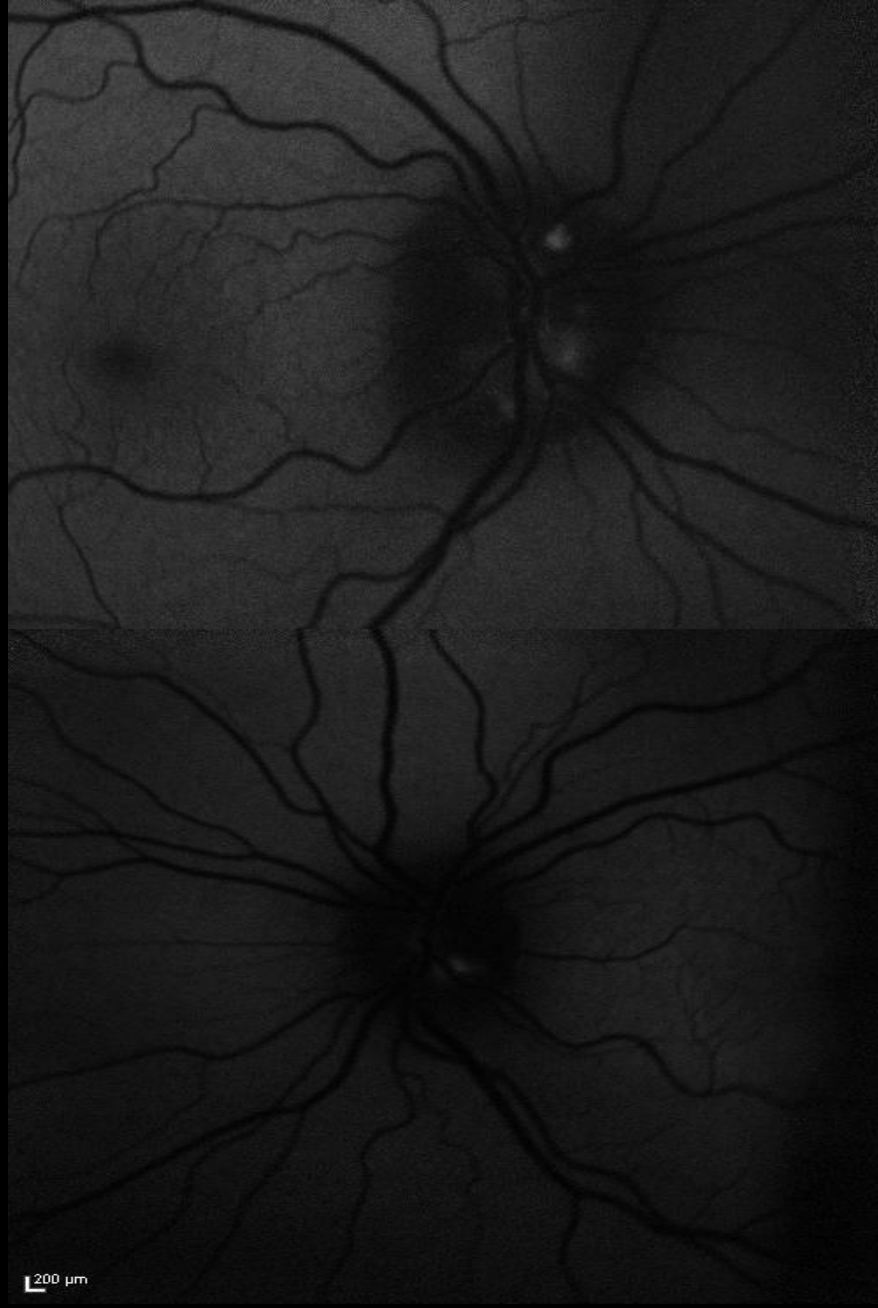
- Distribution of lipofuscin over the posterior pole
- Relative decreased signal in the central macula
    - Absorption by luteal pigment
    - Increased RPE melanin deposition
    - Lower density of lipofuscin granules











15/06/2011, OS

AF 30° ART(28) [HR]

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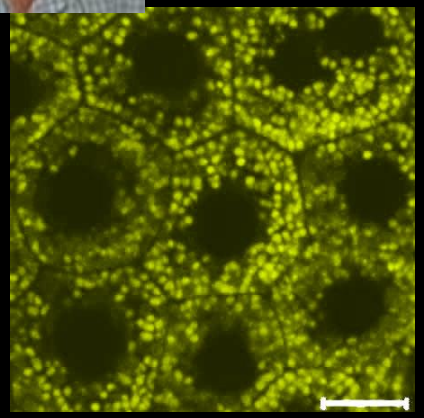
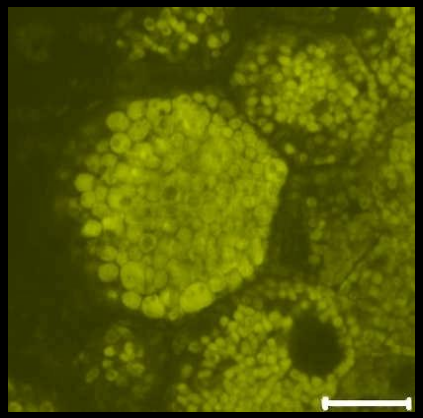
RPE Lipofuscin (Francois Delori and Alan Bird)

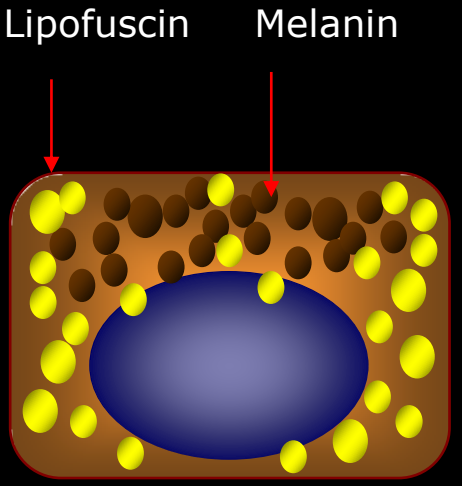
- Lipofuscin in the lysosomal compartment
- Mainly derived from incompletely digested photoreceptor discs
- Accumulation with age and in various retinal disease



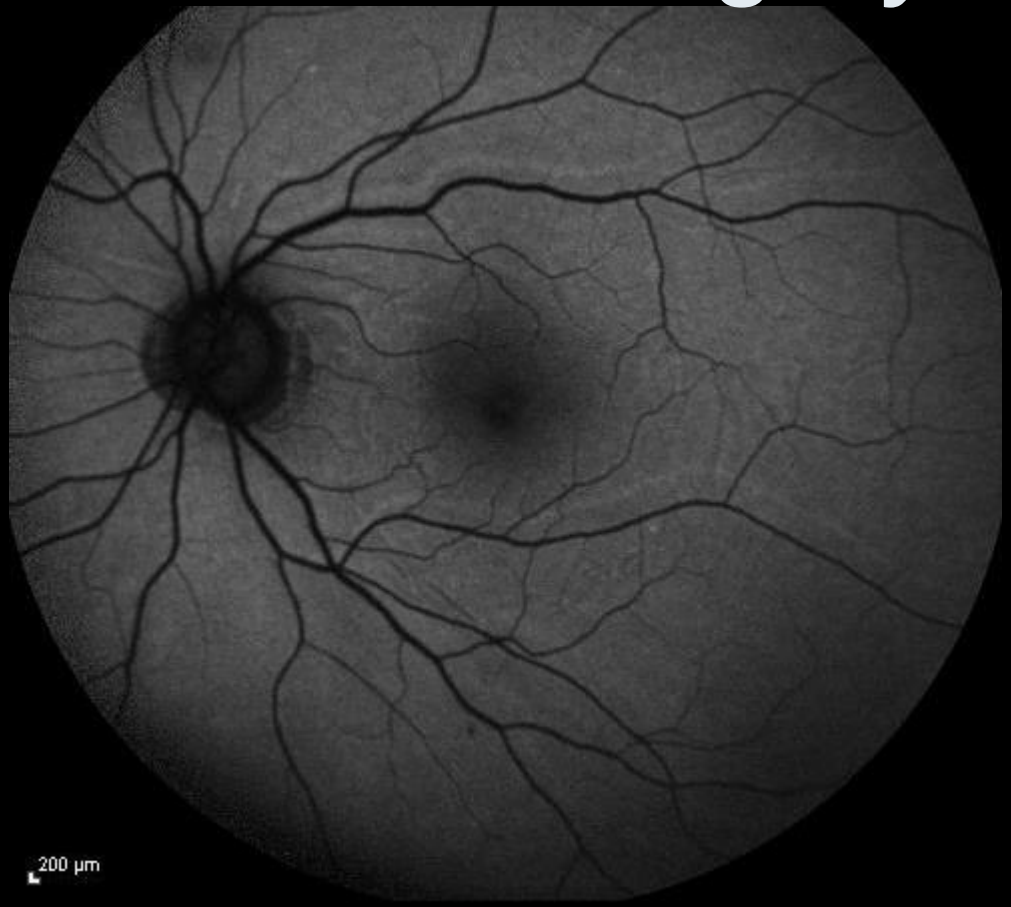
19 years



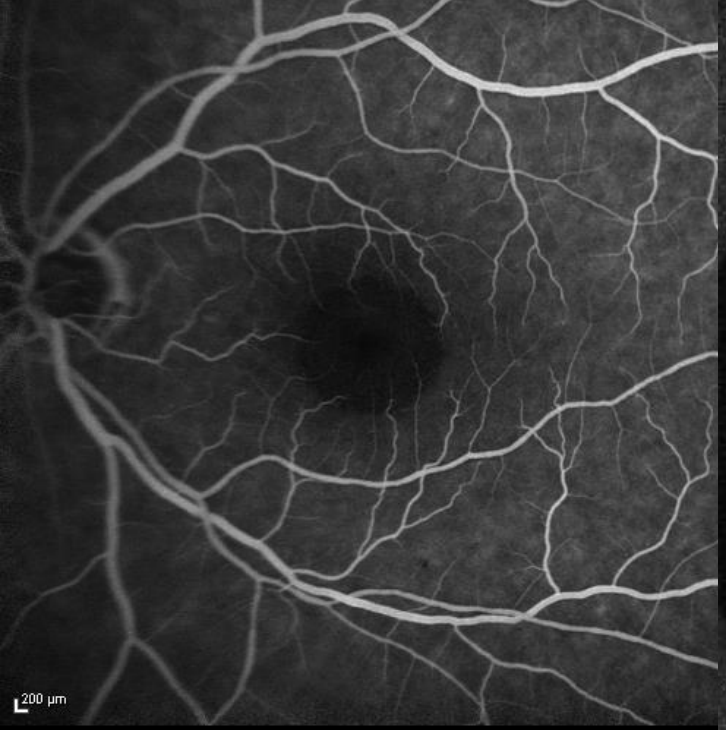
64 years

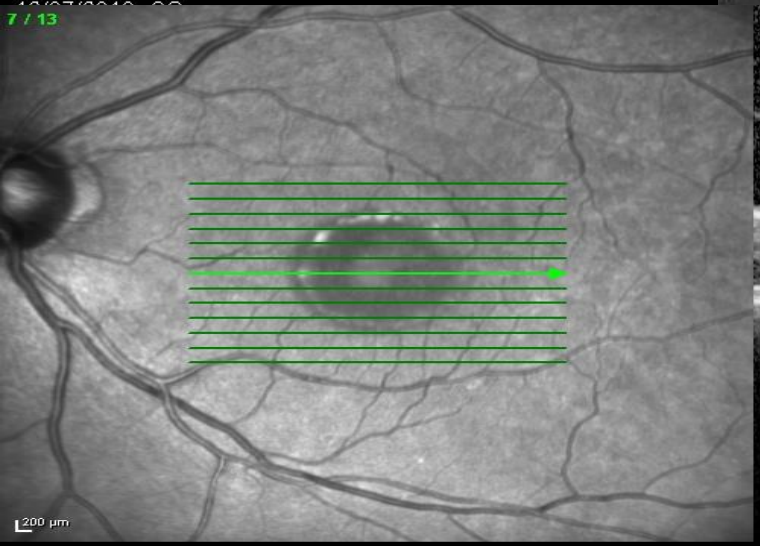


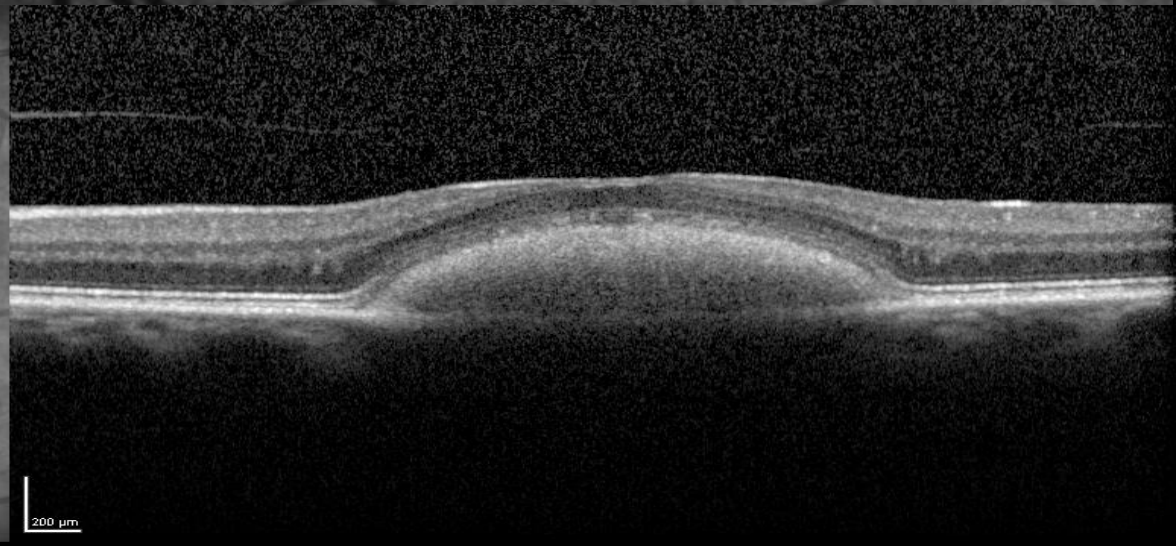
Post RD surgery



Vitelliform lesion diagnosis







12/07/2010, OS
IR&OCT 30° ART [HR] ART(14) Q: 22

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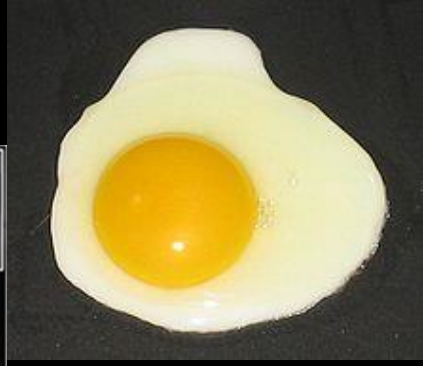
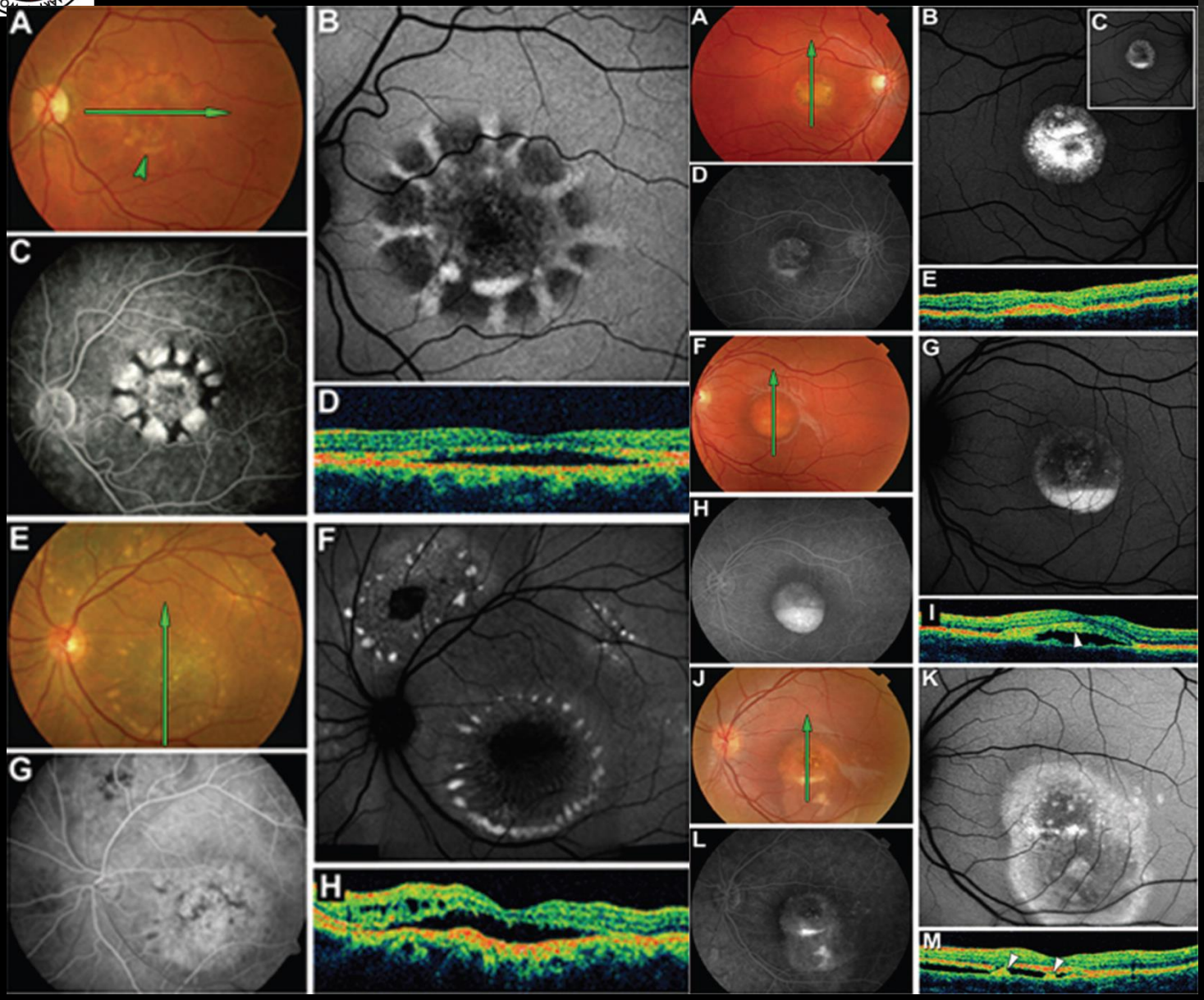
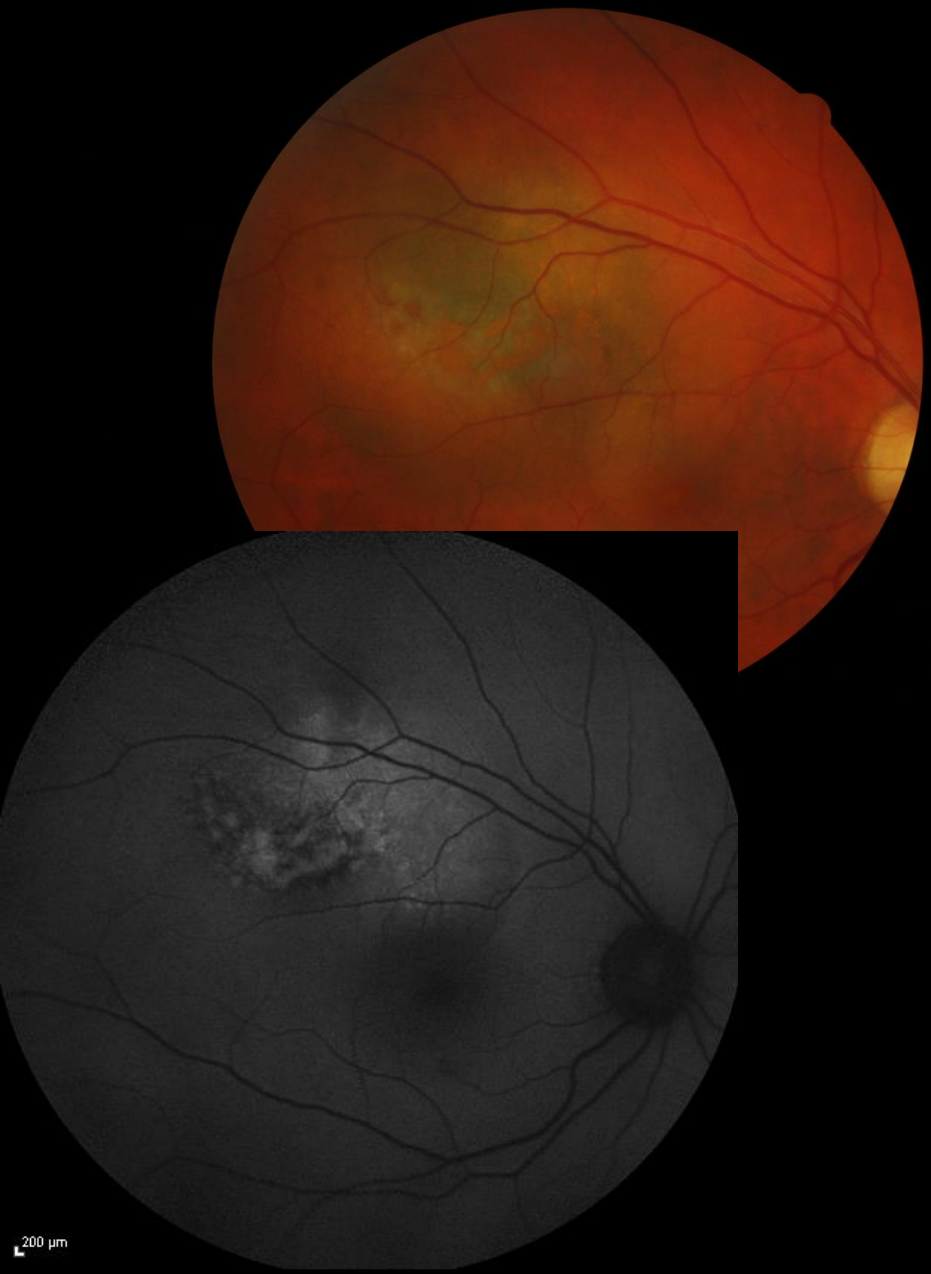
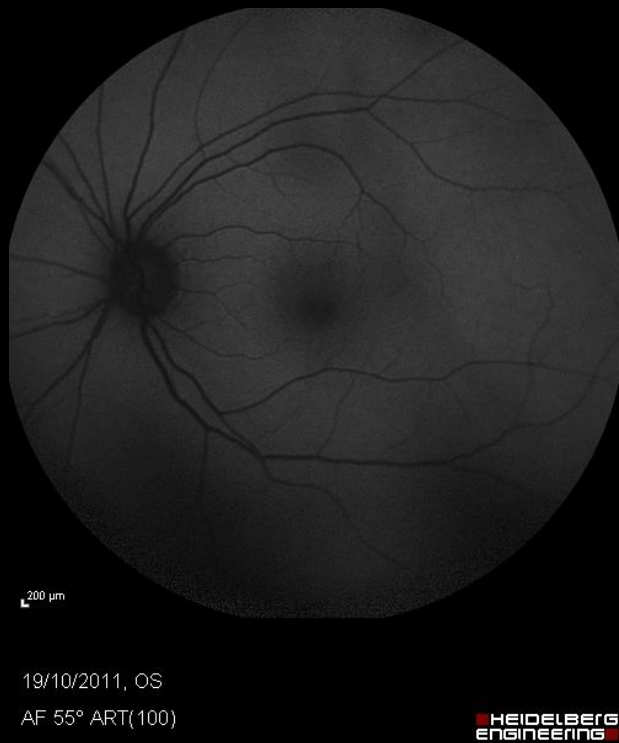
Vitelliform lesions





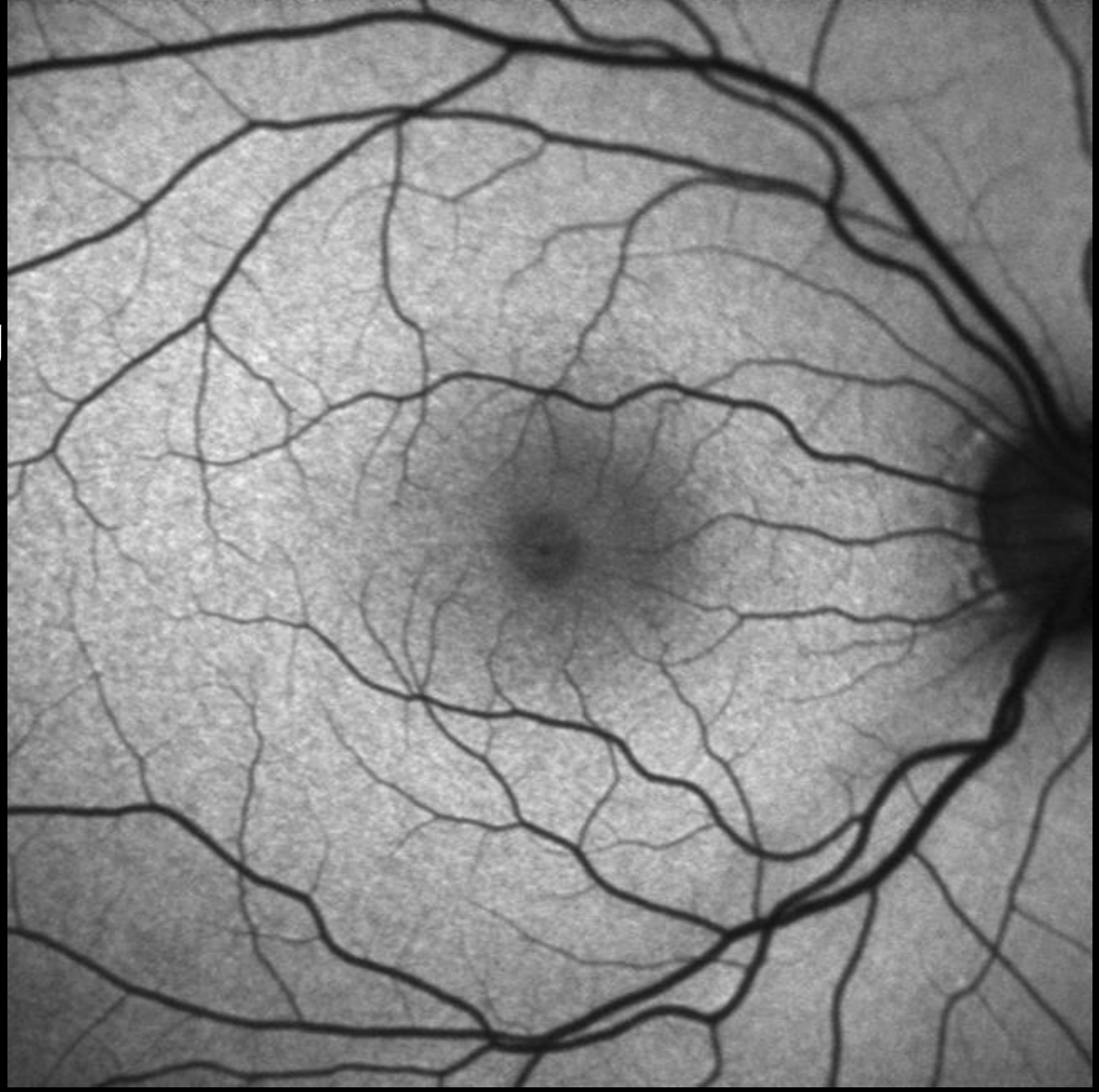
From
Boon et al





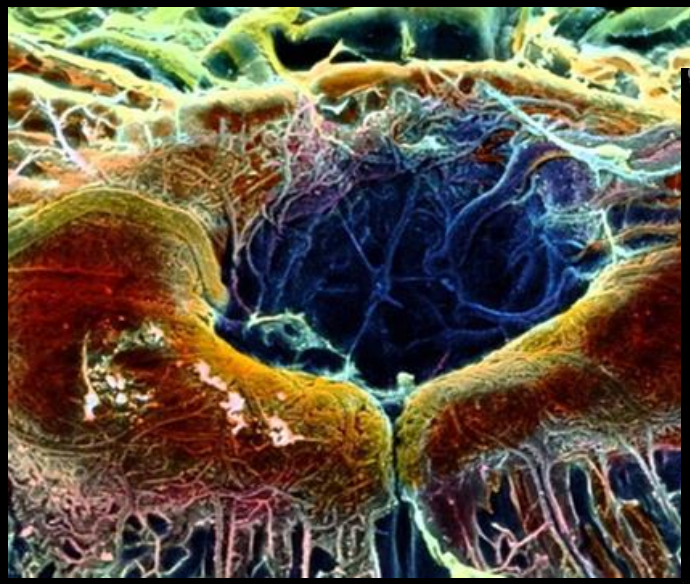
Orange pigment on Melanoma

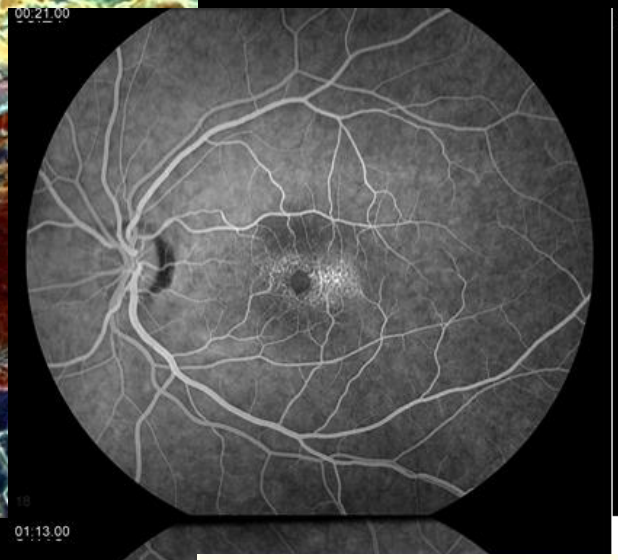
AF imaging

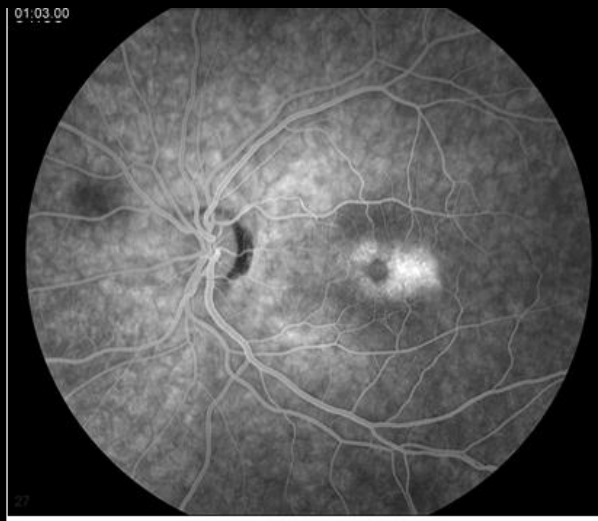


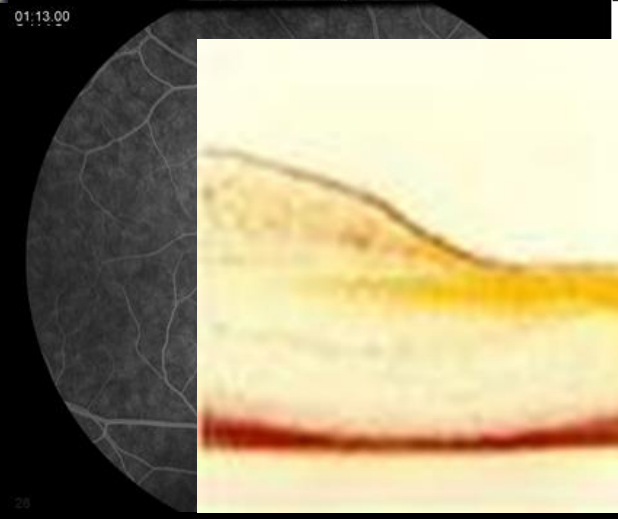
Healthy Foveal Muller cell pigment blocks RPE Lipofuscin autofluorescence

4)Role of Muller cells in Macular Telangiectasia





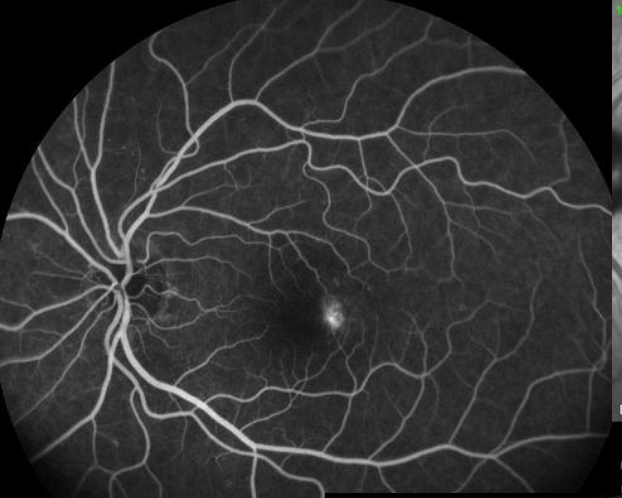


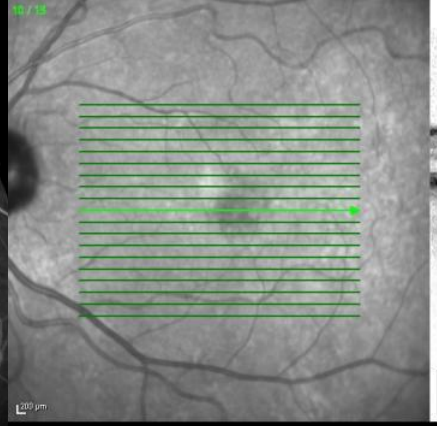


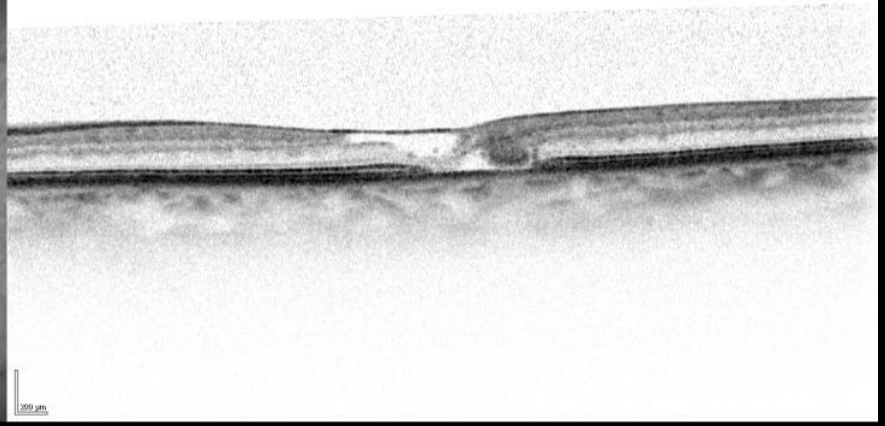
Clinical features in Macular Telangiectasia Type II (MacTel)

- Slightly reduced central vision, Bilateral
- FFA- Juxta foveal, hyperfluorescent lesion
- Cysts on OCT, no lipid
- Macular thinning, sometimes thickening

- Increased Auto Fluorescence - macula centre brighter than normal..







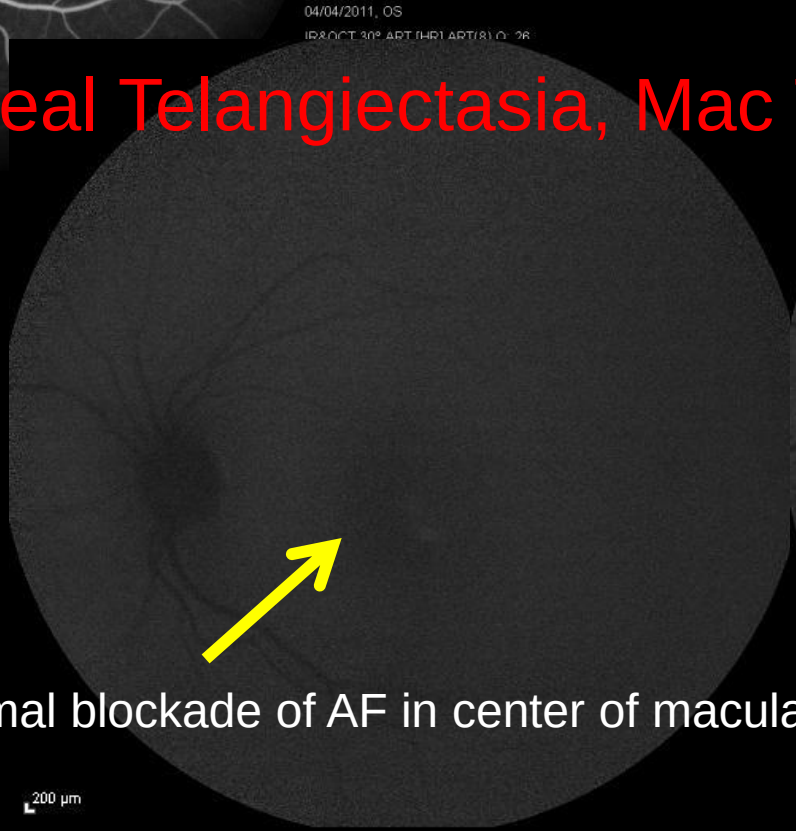
04/04/2011, OS

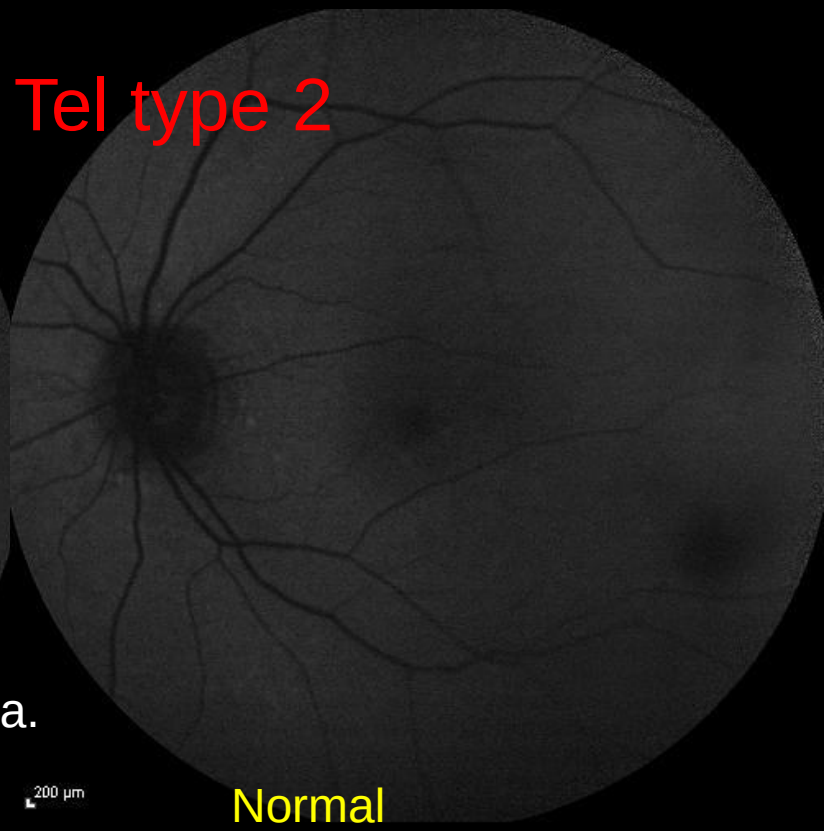
Parafoveal Telangiectasia, Mac Tel type 2

200 µm

04/04/2011, OS

FA Stereo 0:38.71 55° ART(17)





Loss of normal blockade of AF in center of macula.

200 µm

04/04/2011, OS

AF 55° ART(19)

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200 µm

Normal

10/10/2011, OS

AF 55° ART(31)

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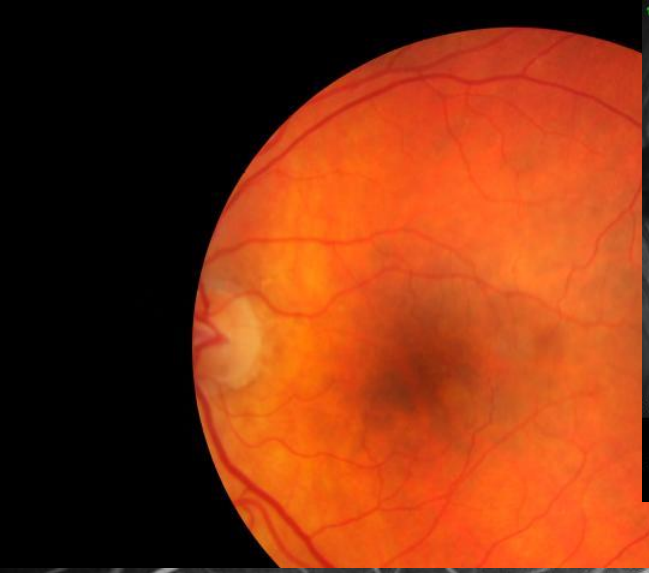
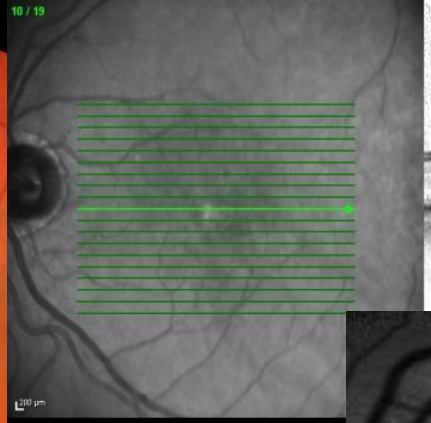
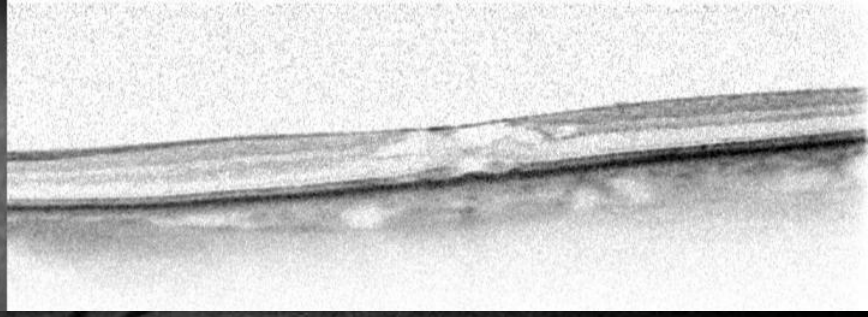
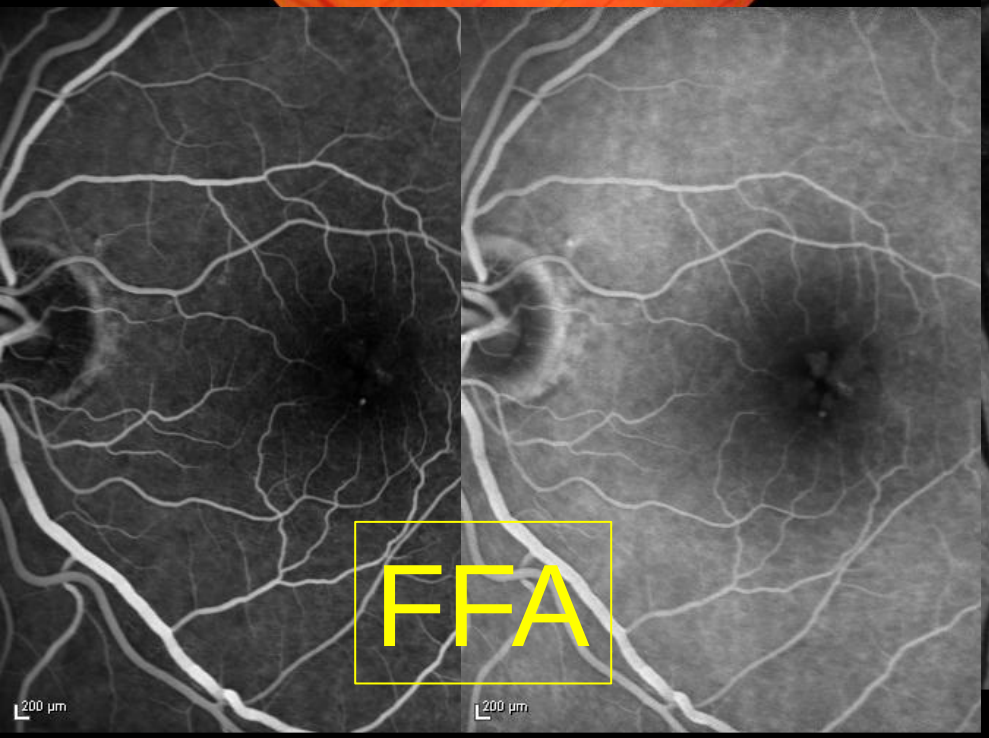




31/10/2011, OS
IR&OCT 30° ART [HR] ART(9) Q: 21

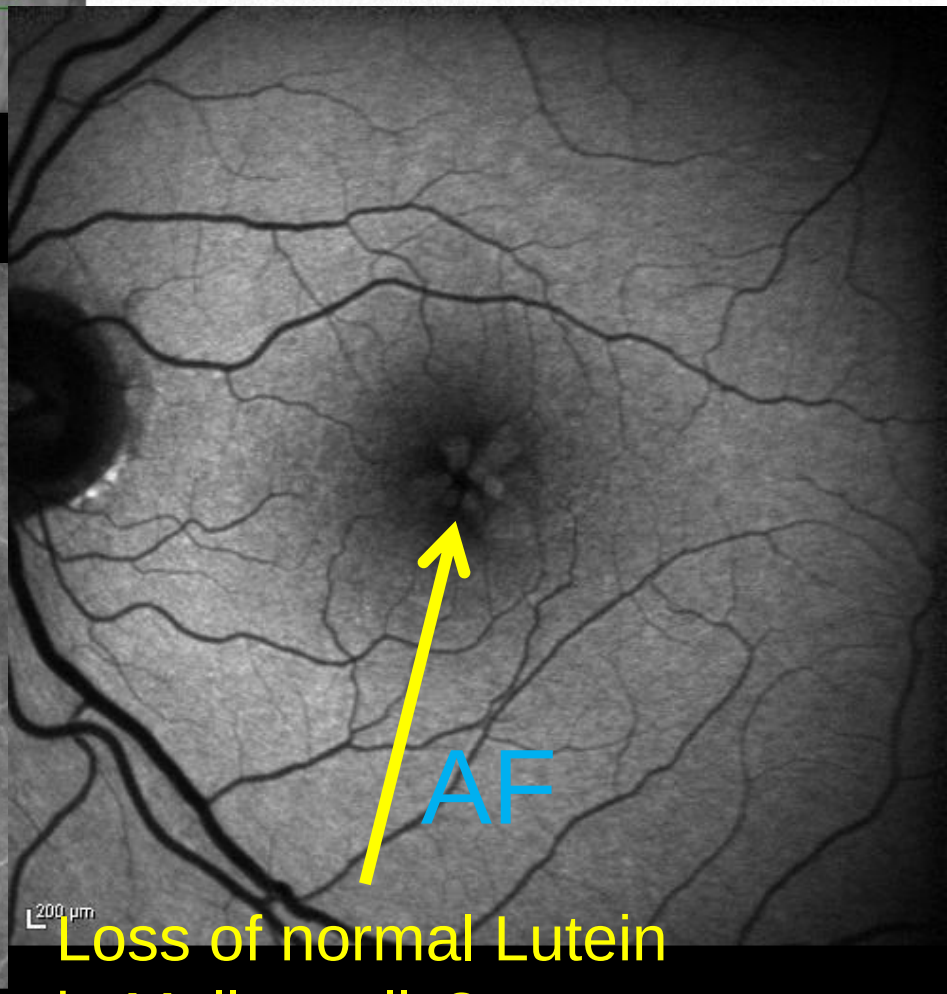




FFA

31/10/2011, OS
FA 0:38.93 30° ART(7) [HR]

31/10/2011, OS
FA 10:33.31 30° ART(9) [HR]



Loss of normal Lutein in Muller cells?

31/10/2011, OS
AF 30° ART(15)

HEIDELBERG ENGINEERING

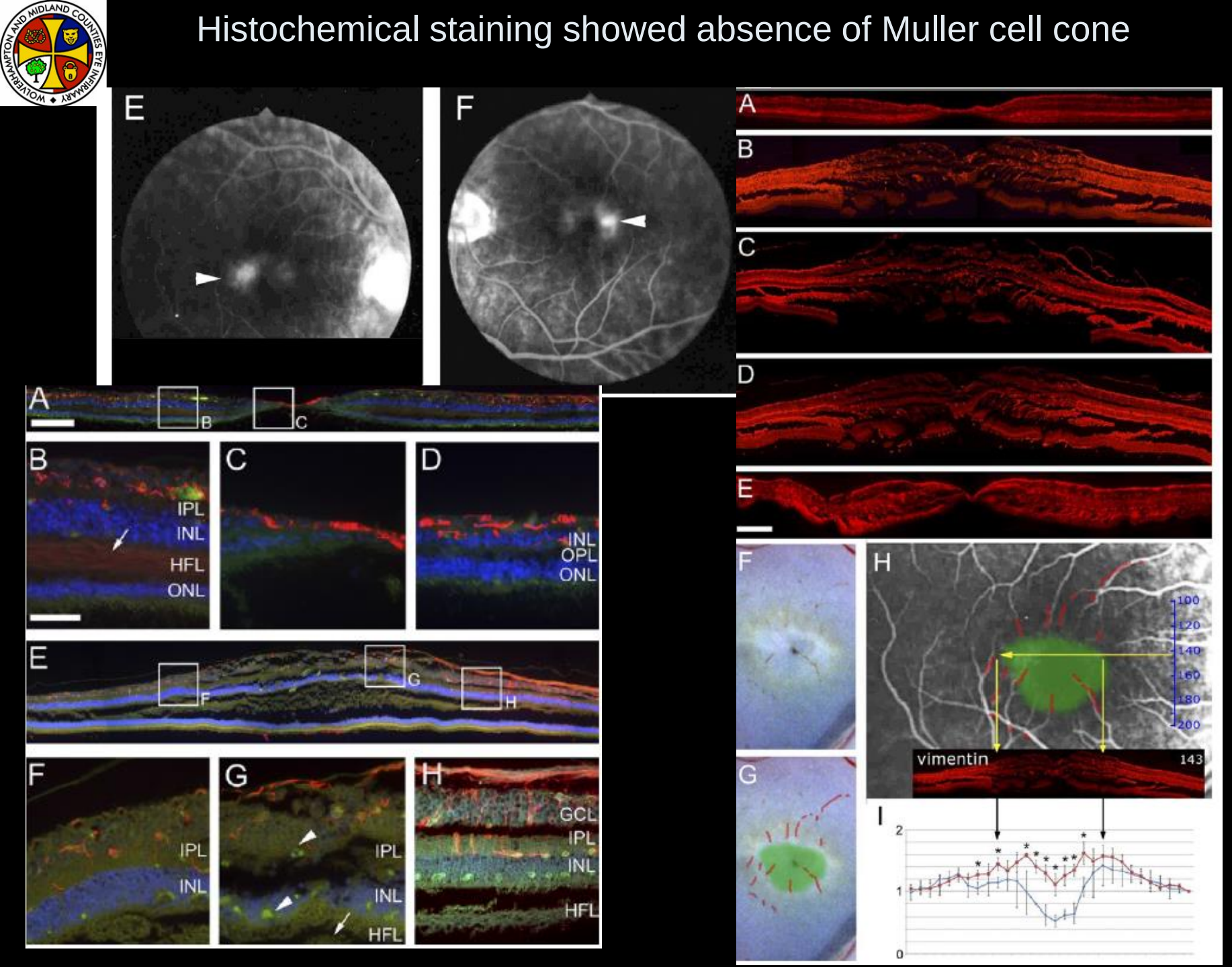
Perifoveal Müller Cell Depletion in a Case of Macular Telangiectasia Type 2

Michael B. Powner, BSc(Hons),[1] Mark C. Gillies, MBBS, PhD,[2] Marina Tretiach, PhD,[2]
Andrew Scott, MD, MRCOphth,[1] Robyn H. Guymer, MBBS, PhD,[3] Gregory S. Hageman, PhD,[4]
Marcus Fruttiger, PhD[1]

Third published clinico-pathologic study of Mactel 2 in literature

Ophthalmology 2010:117

Histochemical staining showed absence of Muller cell cone



MacTel 2

Dear Editor:

I read with interest and admiration the recent article, "Perifoveal Müller cell depletion in a case of macular telangiectasia type 2."[1]

This study is not the third pathologic study of this entity but is the first, and indeed, the only one.

The first study by Green et al[2] we now know was not of an eye with Type 2 MacTel but of an eye that had previously received radiation. For in the text of the second study is the statement, "Neither that patient nor her family had a history of diabetes but the patient had received radiation to the orbit. This previously reported case likely fits into Group 3 because of the history of radiation."[3]

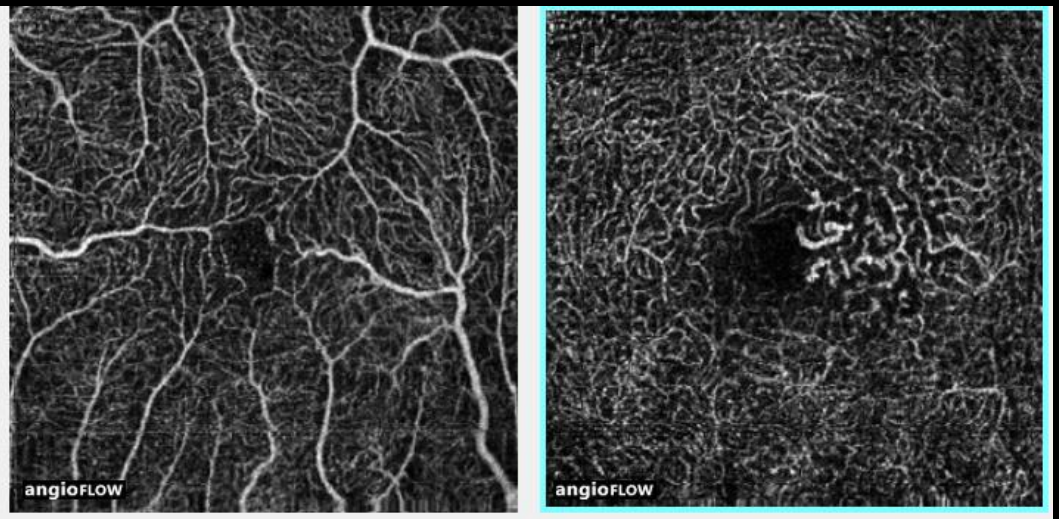
This second study is also suspect because a diagnosis of MacTel 2 was not made before death and the clinical diagnosis was not supported by the usual criteria of ophthalmoscopy and fluoroscein angiography.

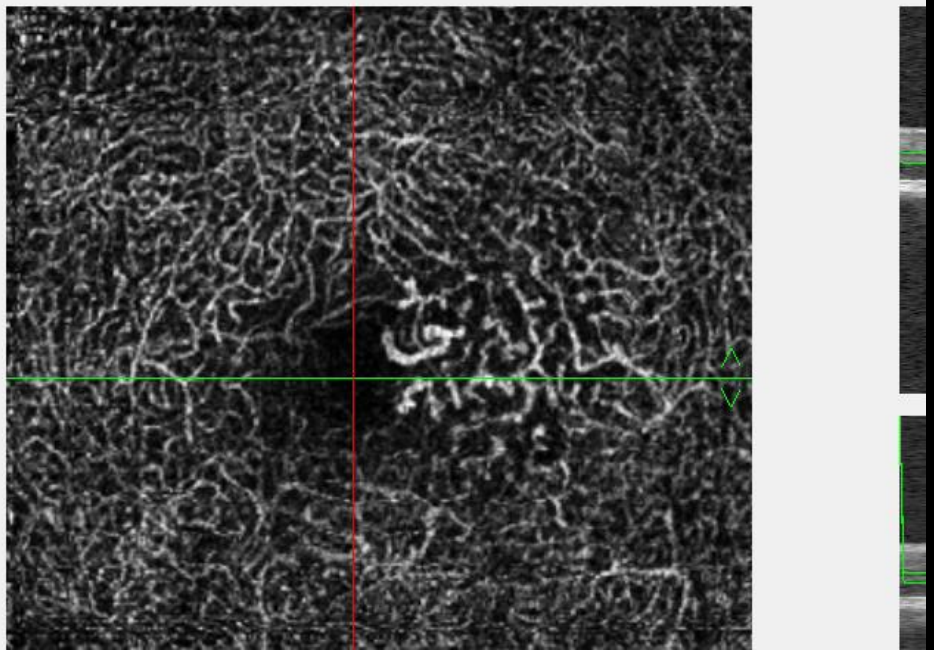
I suggest that the report by Powner et al[1] is really the first clinicopathologic study of this entity and should be recognized as such.

ROBERT C. WATZKE, MD
Portland, Oregon

OCT Angiography of Mactel II

Superficial Plexus





Deep Plexus

Powner et al- discussion about vascular changes

well be detectable in vivo. Because Müller cells are intimately related to the retinal vasculature, it is quite possible that their dysfunction is associated with clinically visible telangiectasis. Müller cell processes are closely apposed to retinal blood vessels in the deeper plexus of retinal vasculature and are believed to contribute to induction of blood retina barrier integrity.[32,33] Blood vessels in the RGC layer

Does the Muller Cell have a role in the pathogenesis of other types of macular telangiectasia?

(Types I and III and Retinal Telangiectasia, Coats disease and Coats syndrome)

Retinal telangiectasis

1. retinal vascular disorder
2. developmental or acquired
3. central or peripheral retina
4. ectasia of capillaries
5. irregular capillary dilation and incompetence

Al Khars et al

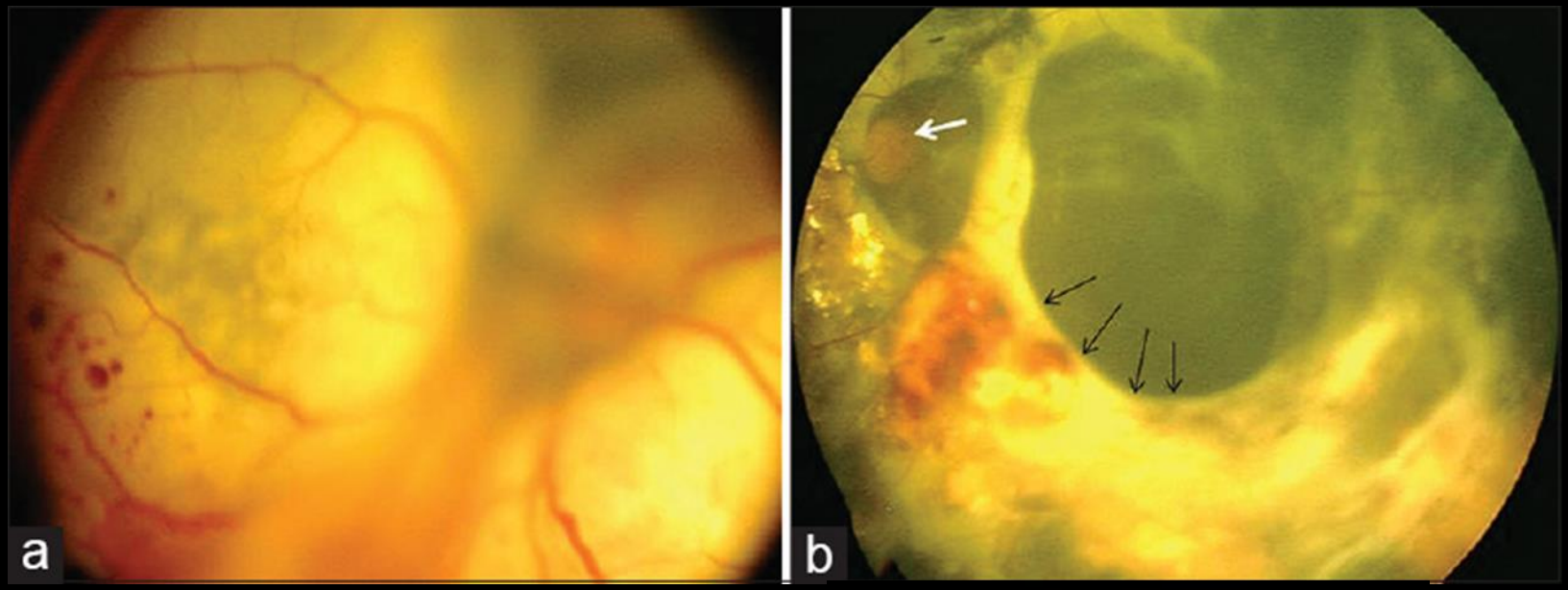
Middle East Afr J Ophthalmol. 2010 Jul-Sep; 17(3): 224–241

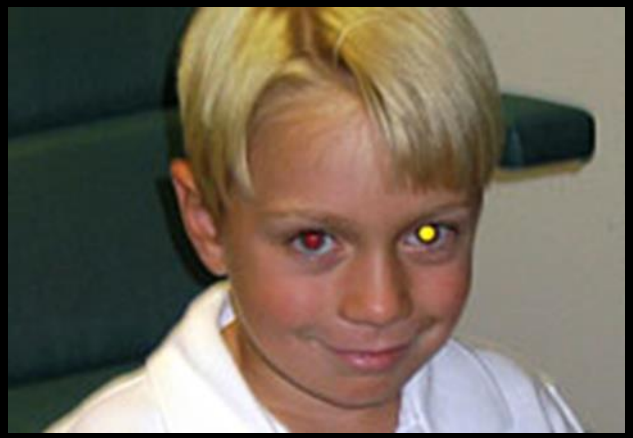
According to Gass and Blodi[2]→	I-A: Visible & Exudative	I-B: Visible, Exudative & Focal	II-A: Occult & Nonexudative	II-B: Juvenile, occult and familial	III-A: Occlusive	III-B: Occlusive Associated with Central Nervous System Vasculopathy
Frequency	Second most common	Rare	Most common	Extremely rare	Very rare	Very rare
Gender	Male (90%)	Male	Male=Female		Female	Male=Female
Age (Mean yrs)	15–54 (40)	middle age	35–65 (56)	2 siblings< 12 yrs	40–60	middle age
Congenital/Acquired	Congenital	Congenital	Acquired	Acquired	Acquired	Dominant inheritance
Biomicroscopic Features						
Laterality	Unilateral	Unilateral	Bilateral (asymmetric)	Bilateral	Bilateral	Bilateral
Juxtafoveolar telangiectasis location	Temporal half of macula	Temporal half of macula	Temporal to fovea++++ up to entire perifovea	Temporal to fovea	Perifoveal	Perifoveal
Juxtafoveolar telangiectasis size	≥ 2DD	< 2 clock hours	≈ 1DD around foveola	Small	Variable	Variable
Visual acuity at presentation	≈20/40	≥ 20/25	20/20-20/300	NM	20/25-20/50	variable
Visible macular edema	+++	±	− (unless SRNV)	−	NM	NM
Loss of retinal transparency	+	±	+	+	+	NM
Easily visible microaneurysms/telangiectasis	+++	+	−	−	+	+
Yellow exudates	+	±	−(unless SRNV)	−	Minimal	Minimal
Blunted right-angled venules	−	−	+	−	−	−
Superficial crystalline deposits	−	−	+	−	−	−
ntraretinal pigment plaques/hyperplasia	−	−	+	−	−	−
Fibrous metaplasia	−	−	+	NM	−	−
Subretinal neovascularization/RCA	−	−	+ (in stage 5)	+ (OU)	−	−
Fluorescein Angiographic Features						
Visible telangiectasia	+++	±	±	±	± *	+
Late intraretinal staining	+	+	+	+	+	M
Capillary occlusion	Minimal	−	−	NM	+++ *	+
Cause of Vision Loss	Macular edema, exudation	No visual loss	Foveal atrophy SRNV	SRNV	Capillary occlusion & obstruction	C
Systemic Associations	None	None	Possible diabetes mellitus	None	Polycythemia Hypoglycemia Gouty arthritis Ulcerative colitis Multiple myeloma Chronic lymphocytic Leukemia	C te

Working Classification of Retinal Telangiectasia

1. Mac Tel II (Loss of Muller cells)
   - Neurodegeneration
   - No Lipid (crystals and pigment)
   - Hyperfluorescence on FFA but No swelling
2. Other types of Retinal Telangiectasia
   - Predominantly vascular leakage
   - Lipid exudate
   - Spectrum from Coats disease, to Type 1 , Type 3, adult Coats syndrome

Spectrum of Retinal Telangiectasia: Coats disease

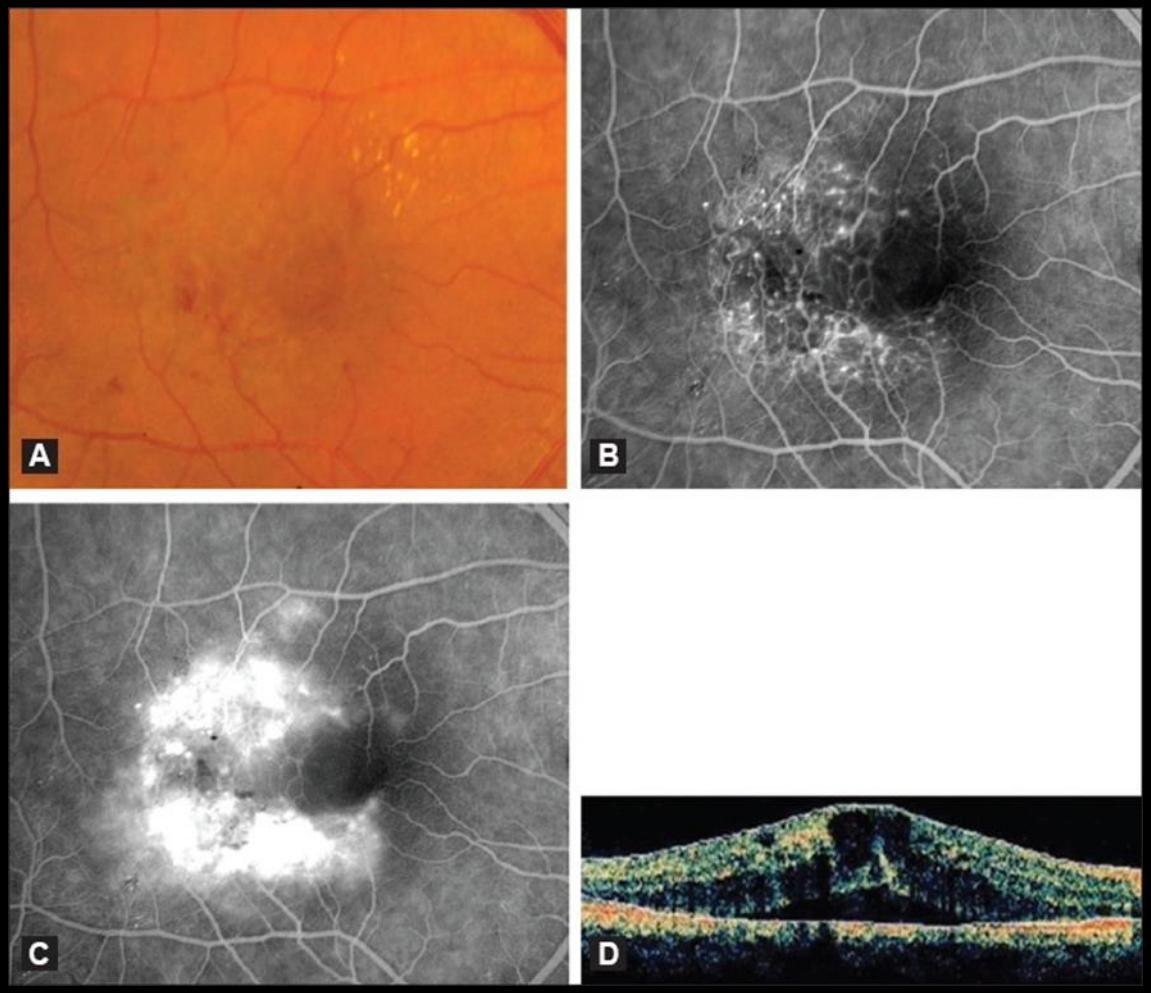




George Coats 1876 - 1915

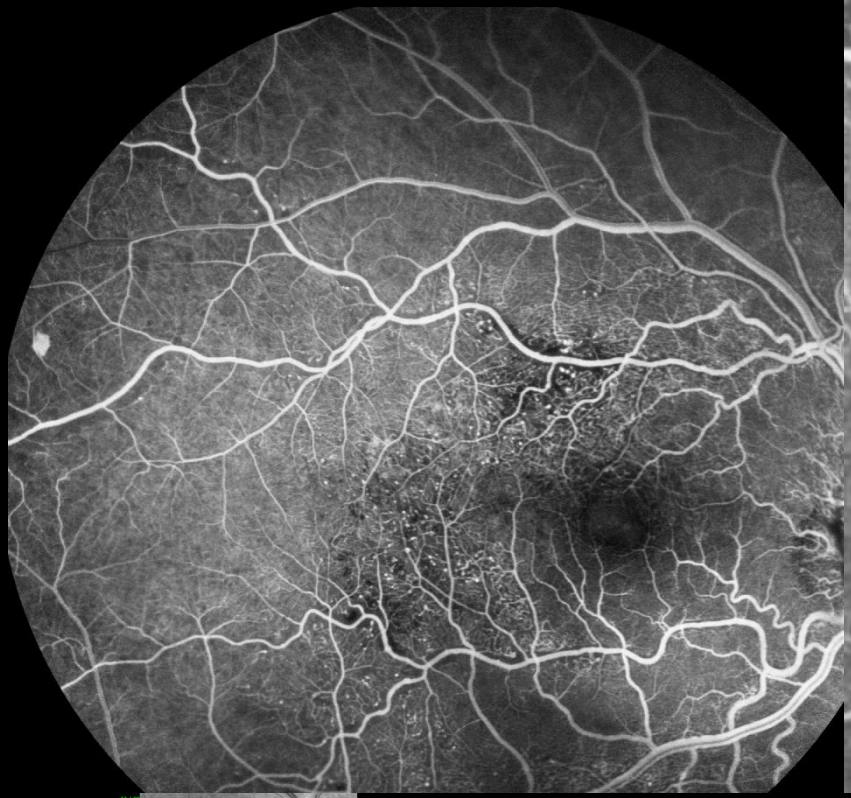
Spectrum of Retinal Telangiectasia

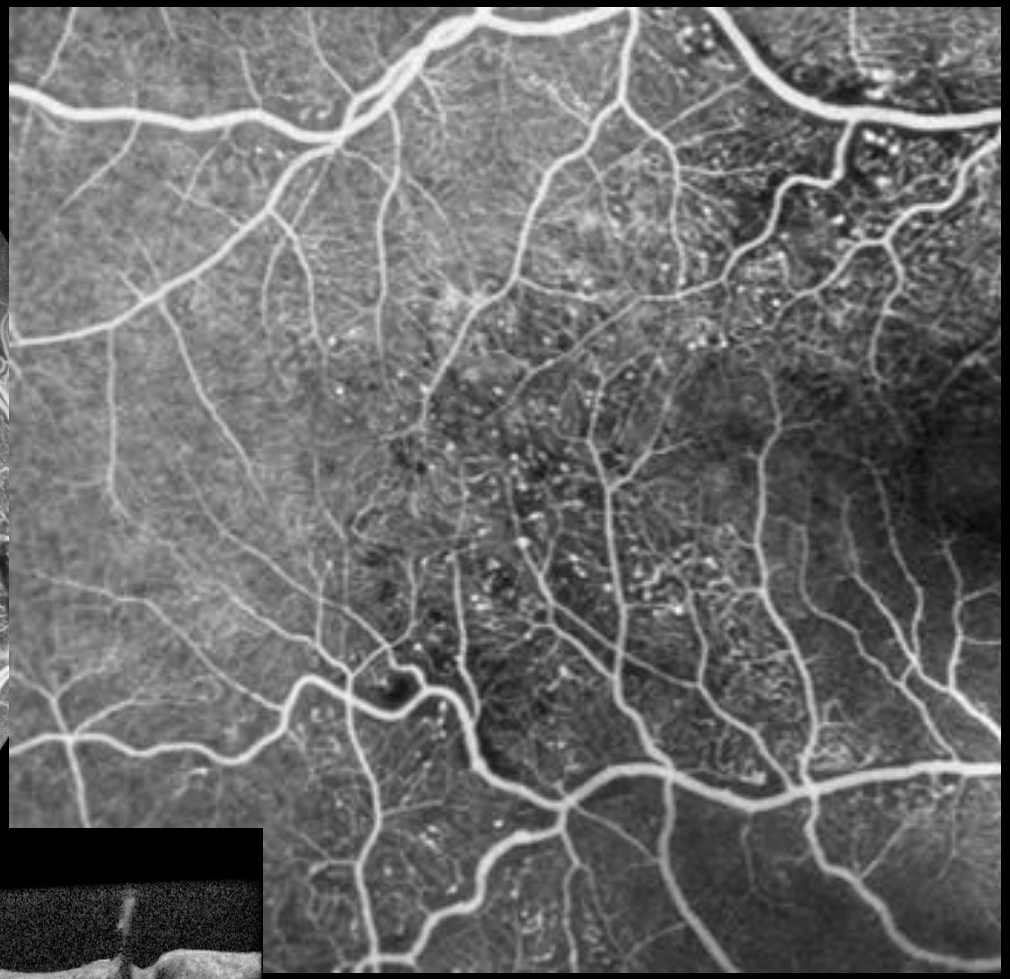
Type 1, Macular Telangiectasia

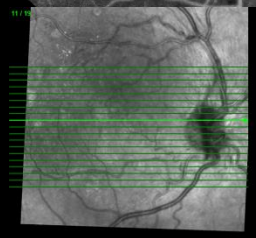


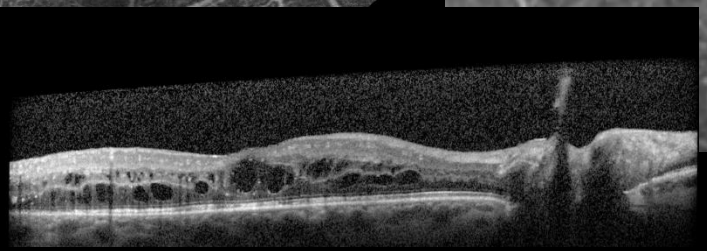
Spectrum of Retinal Telangiectasia

Type 1, N301997



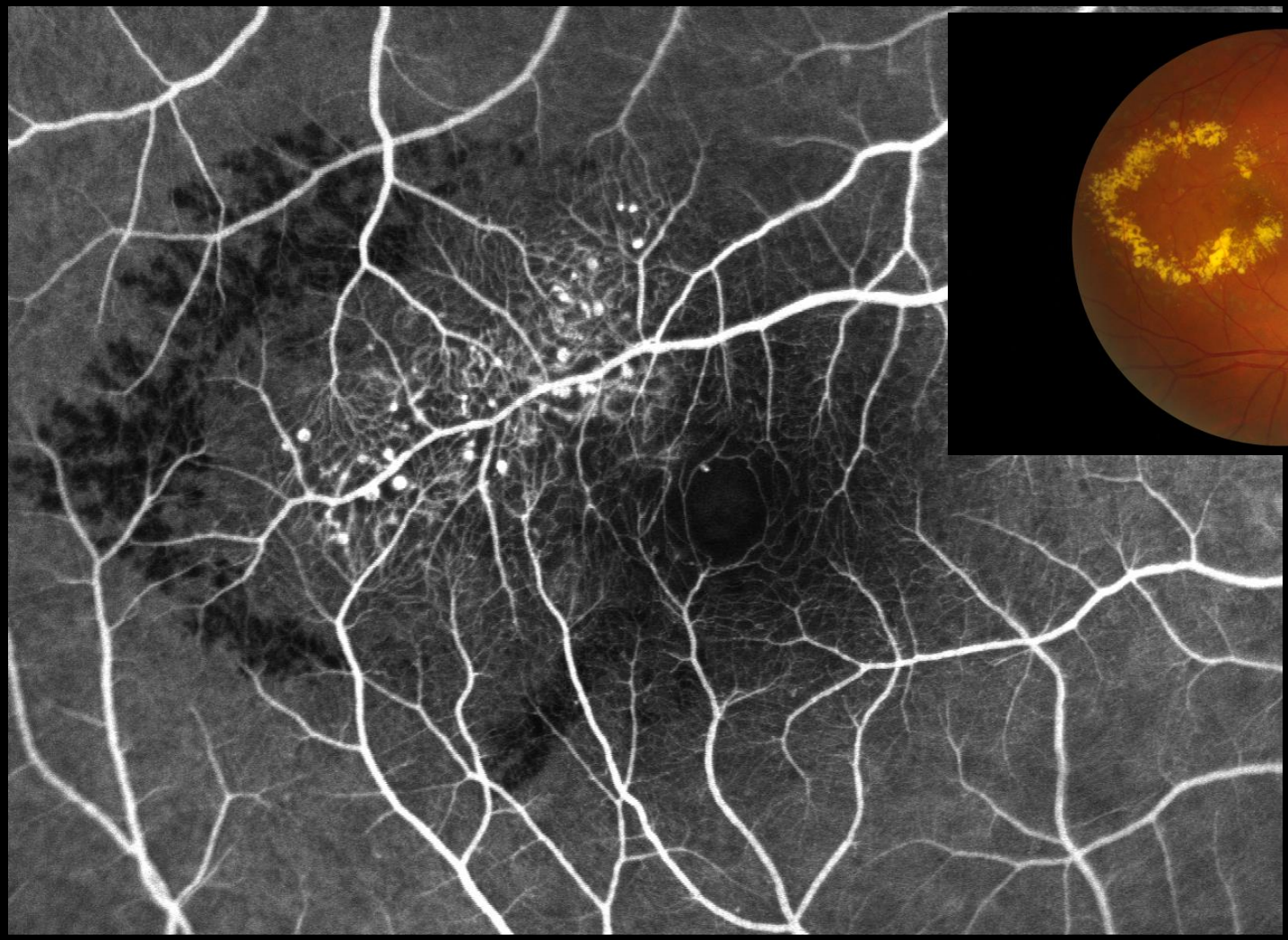






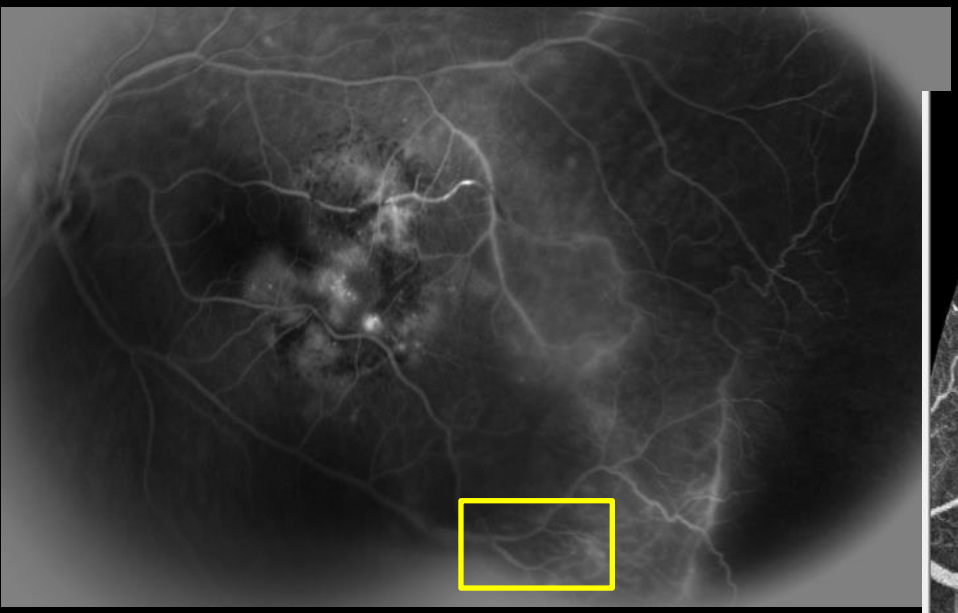
Spectrum of Retinal Telangiectasia

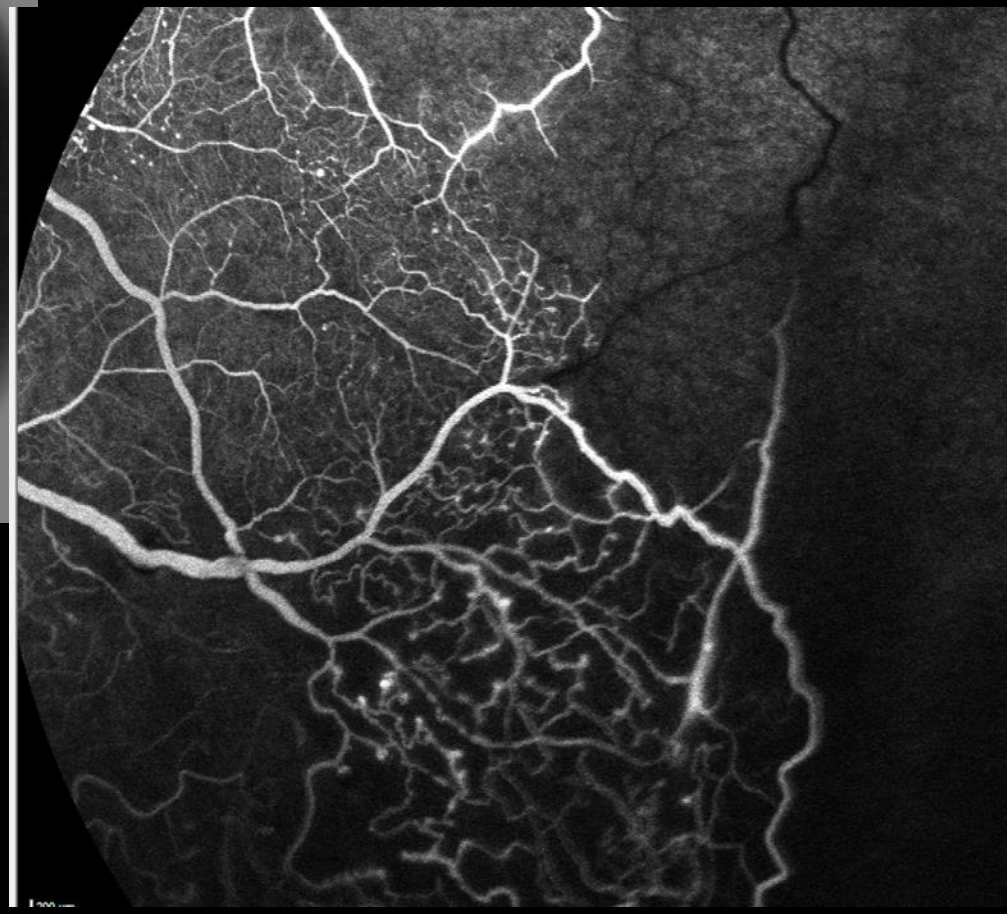
Type 1 Macular Telangiectasia



E60792

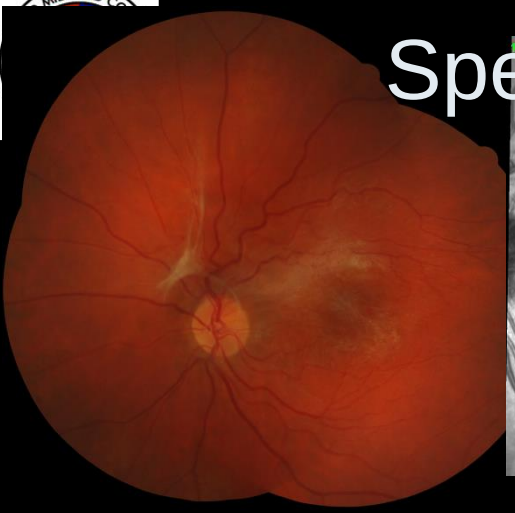
Spectrum of Retinal Telangiectasia

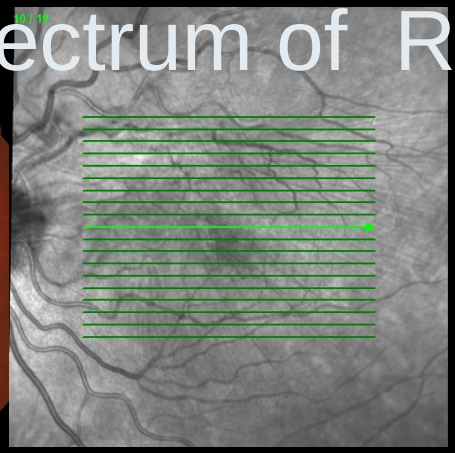


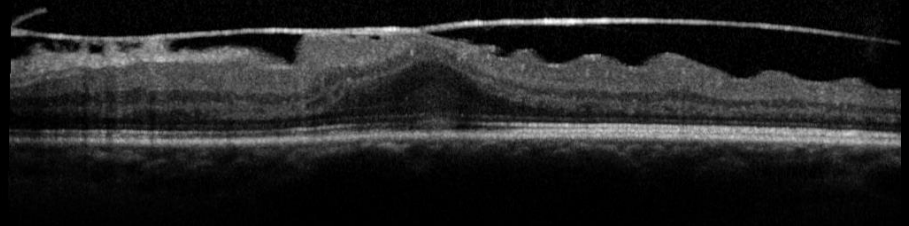


N251310

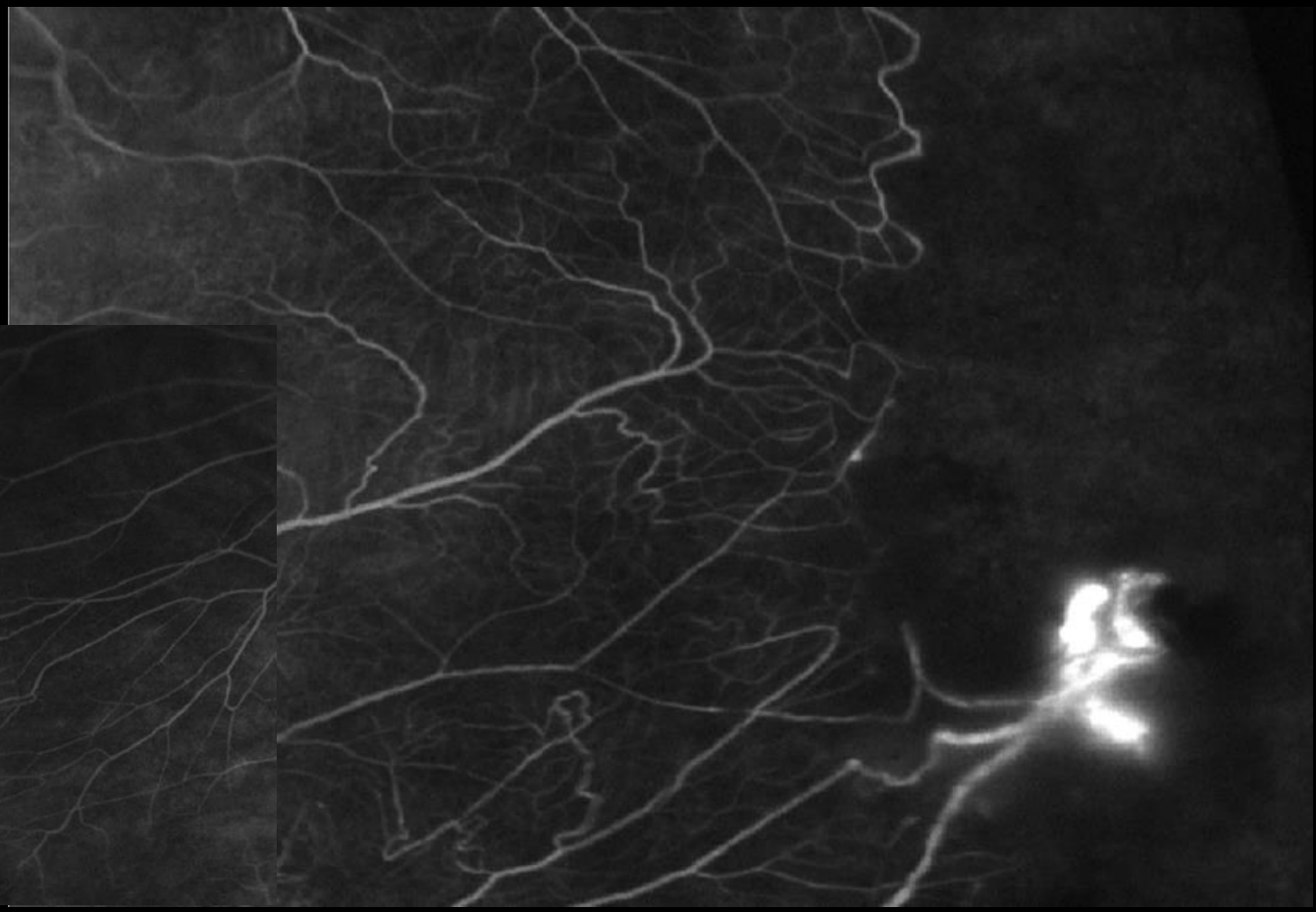
Spectrum of Retinal Telangiectasia

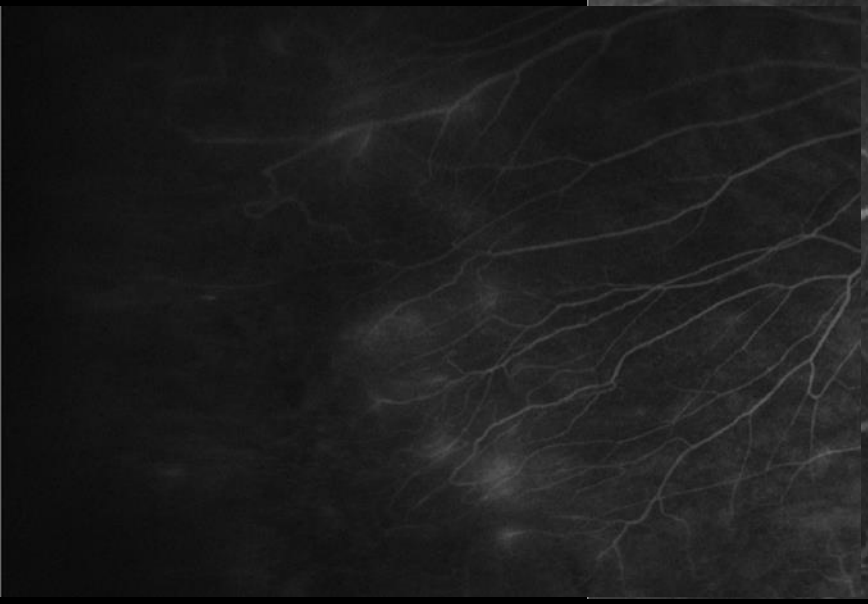




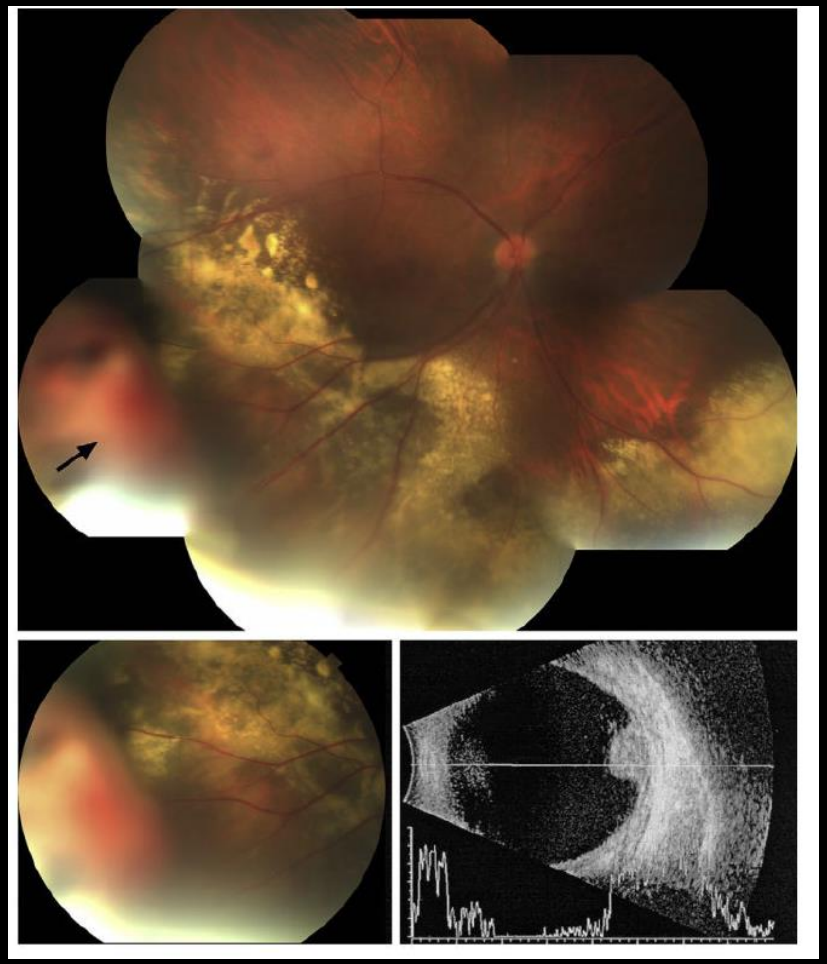


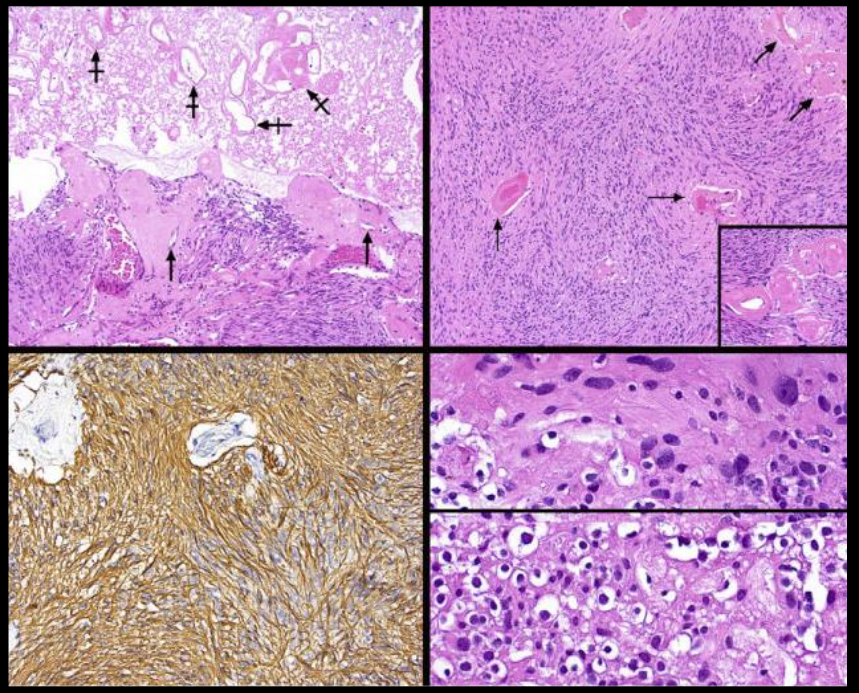
N732804, 39 YO lady



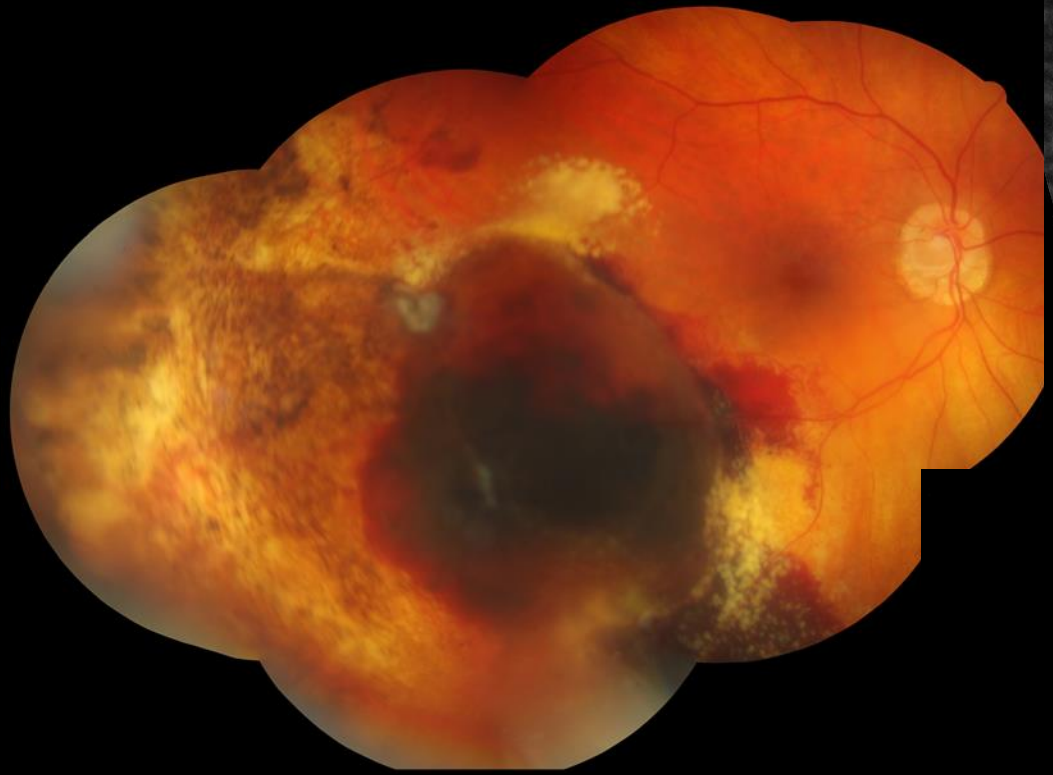


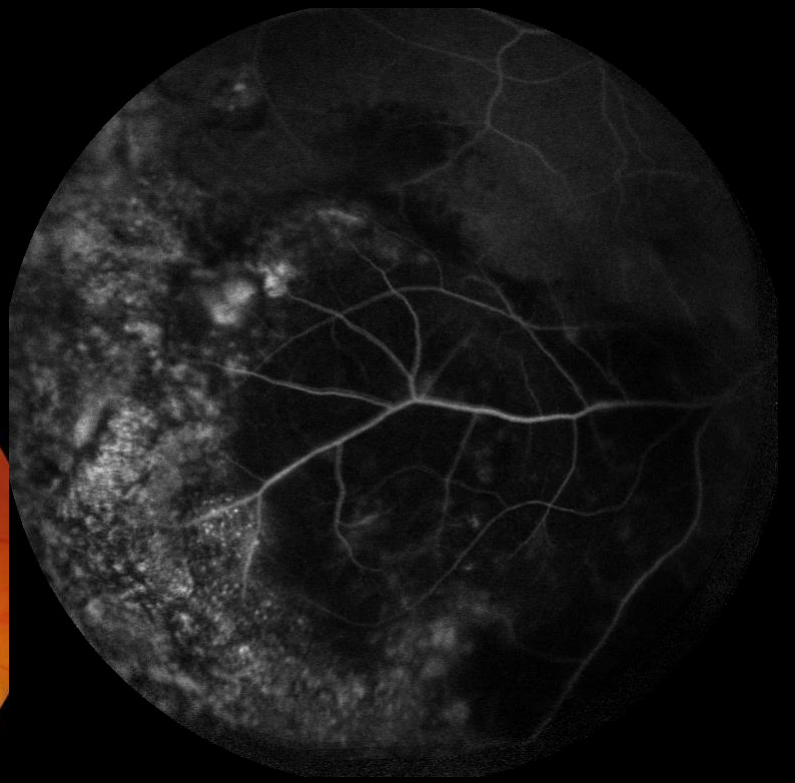
Not Coat's: Peripheral vasoproliferative tumours
(Reactive Retinal Astrocytic Tumors)

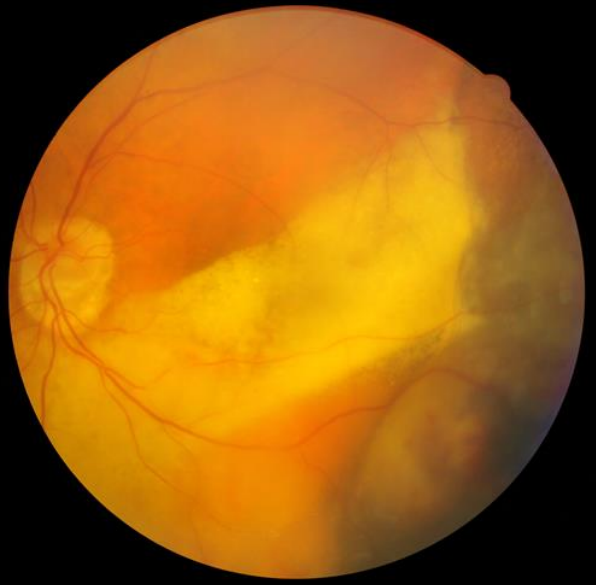




Not Coats- PCV





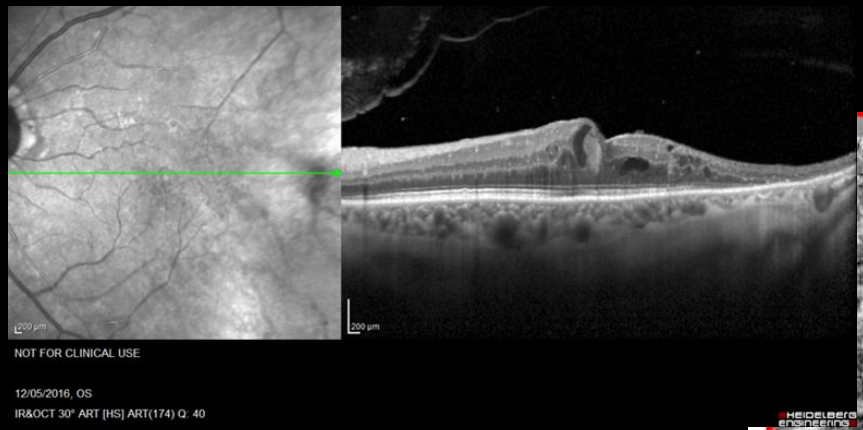


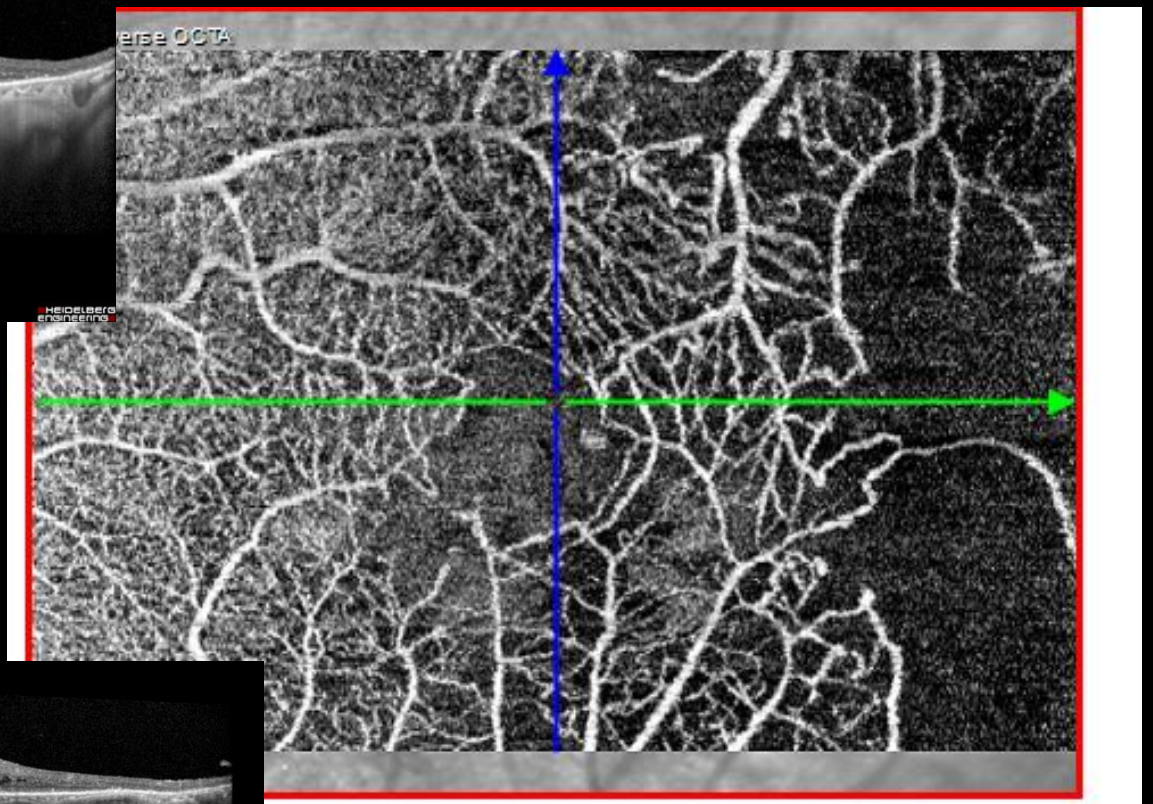
n361137

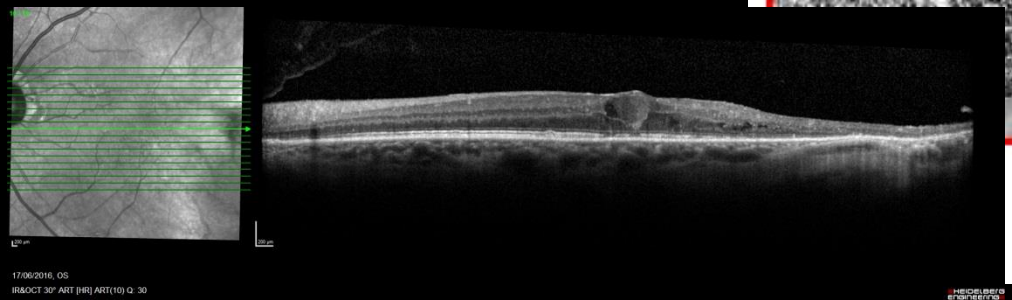
Spectrum of Retinal Telangiectasia

Type III Retinal Telangiectasia

Radiation Retinopathy- Ruthenium N308704





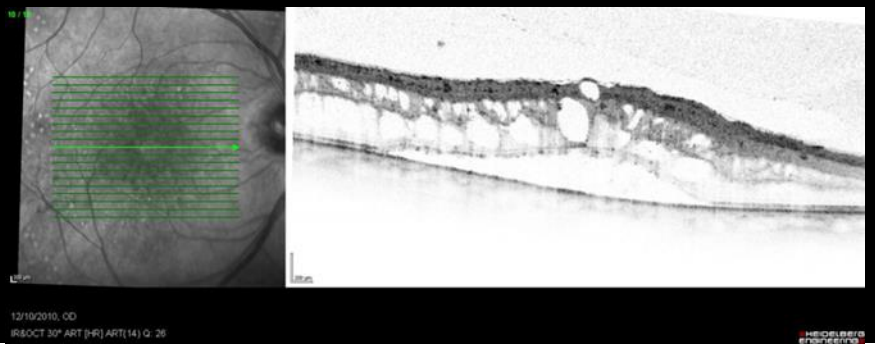


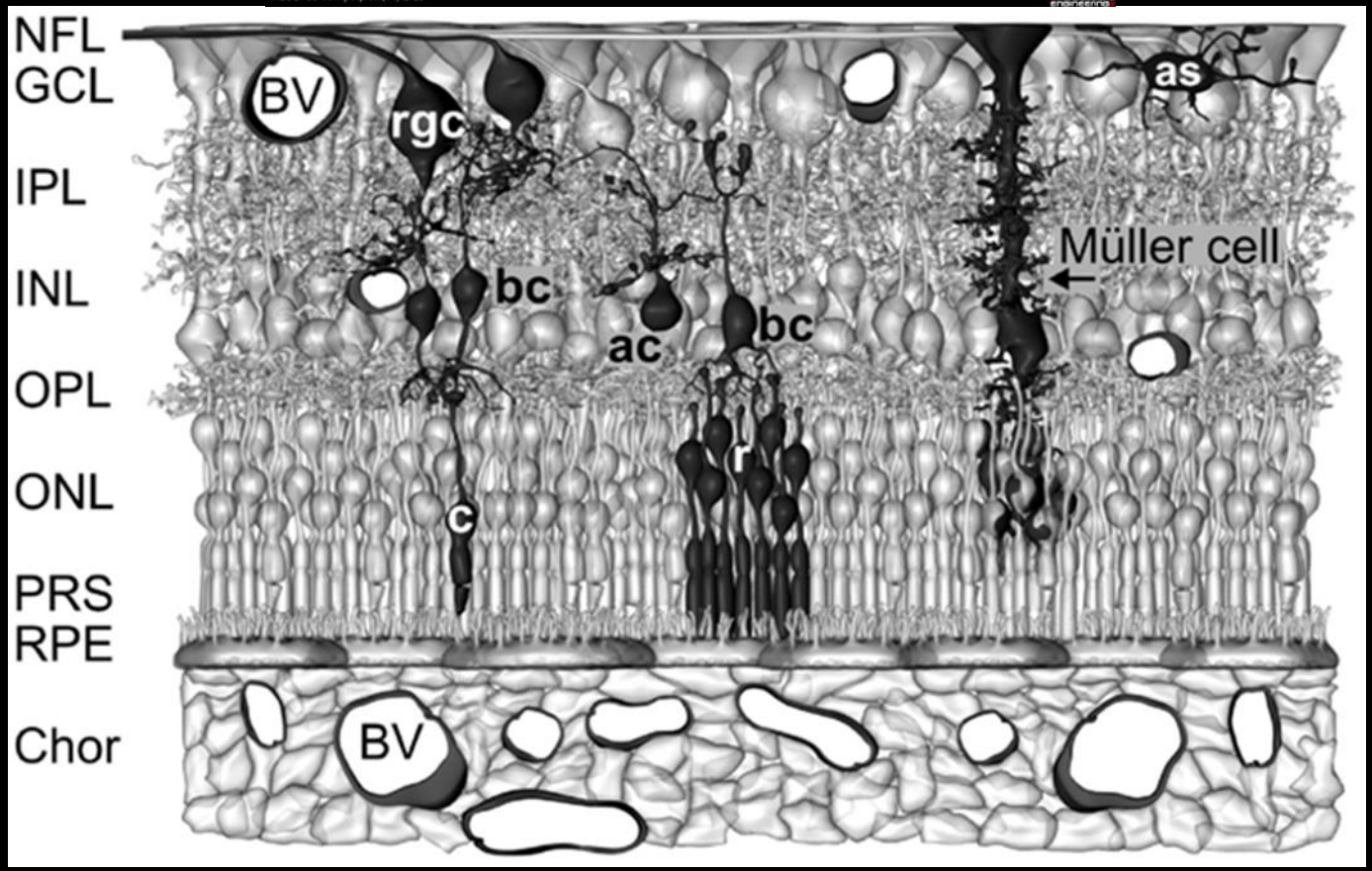
Does the Muller Cell have a role in the pathogenesis of other types of macular telangiectasia?

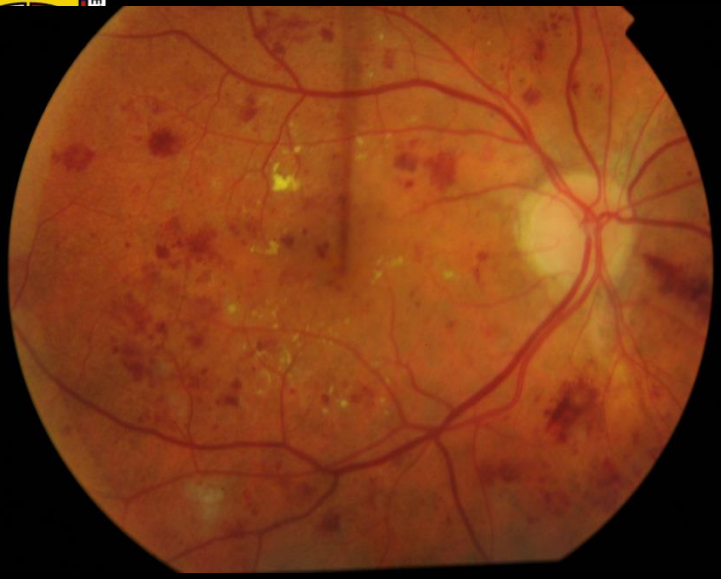
(Types I and III and Retinal Telangiectasia, Coats disease and Coats syndrome)

Probably NOT as direct a role as in MacTel 2

5)Muller cells also have a role in Macular Oedema

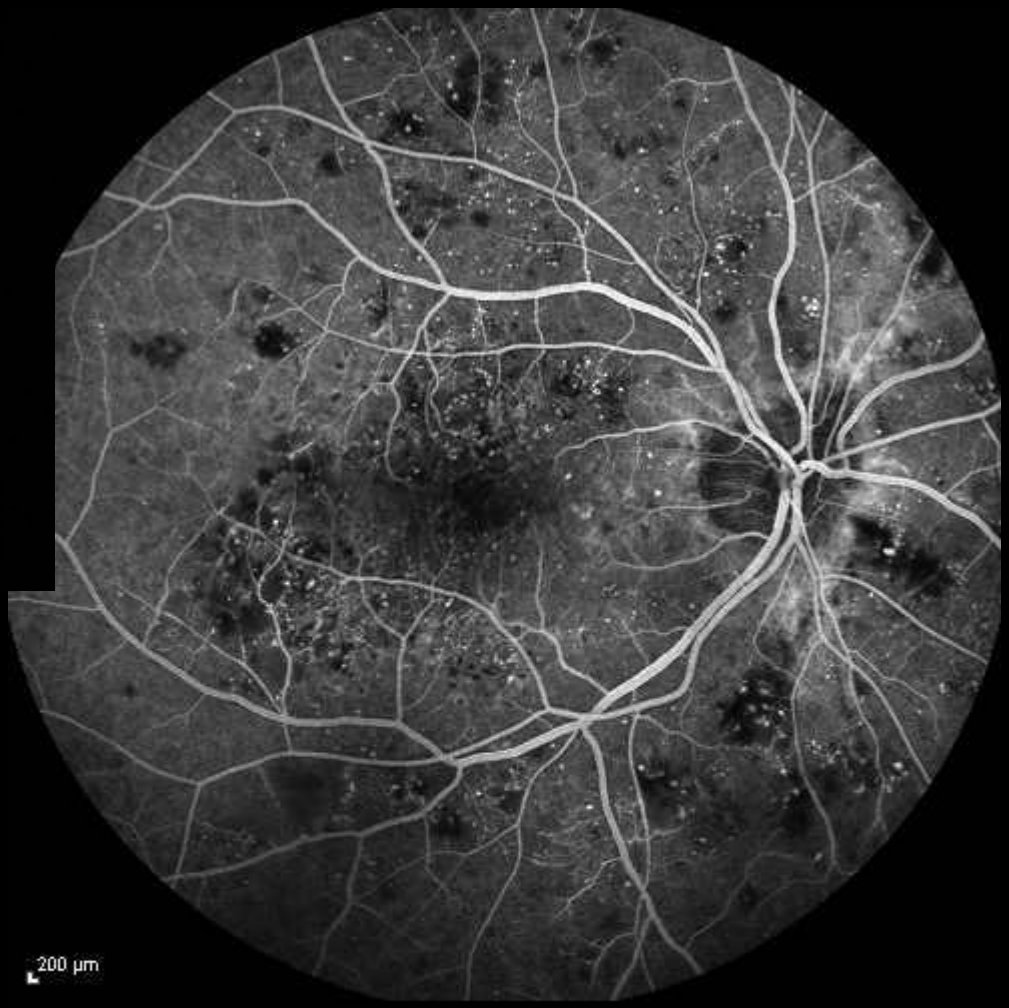






Diabetes

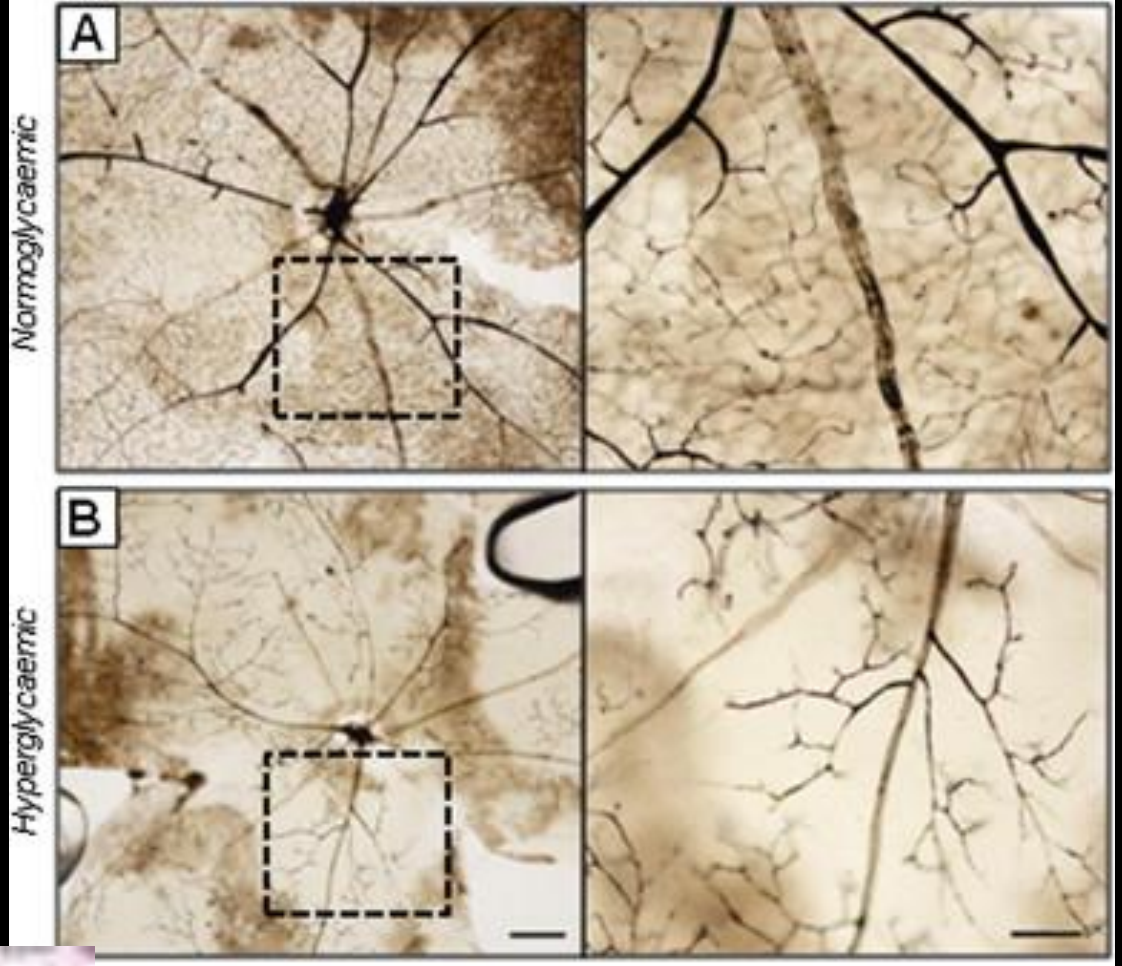
Micro angiopathy

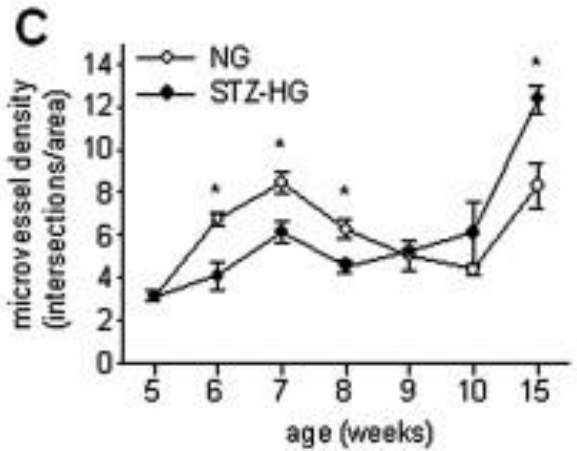


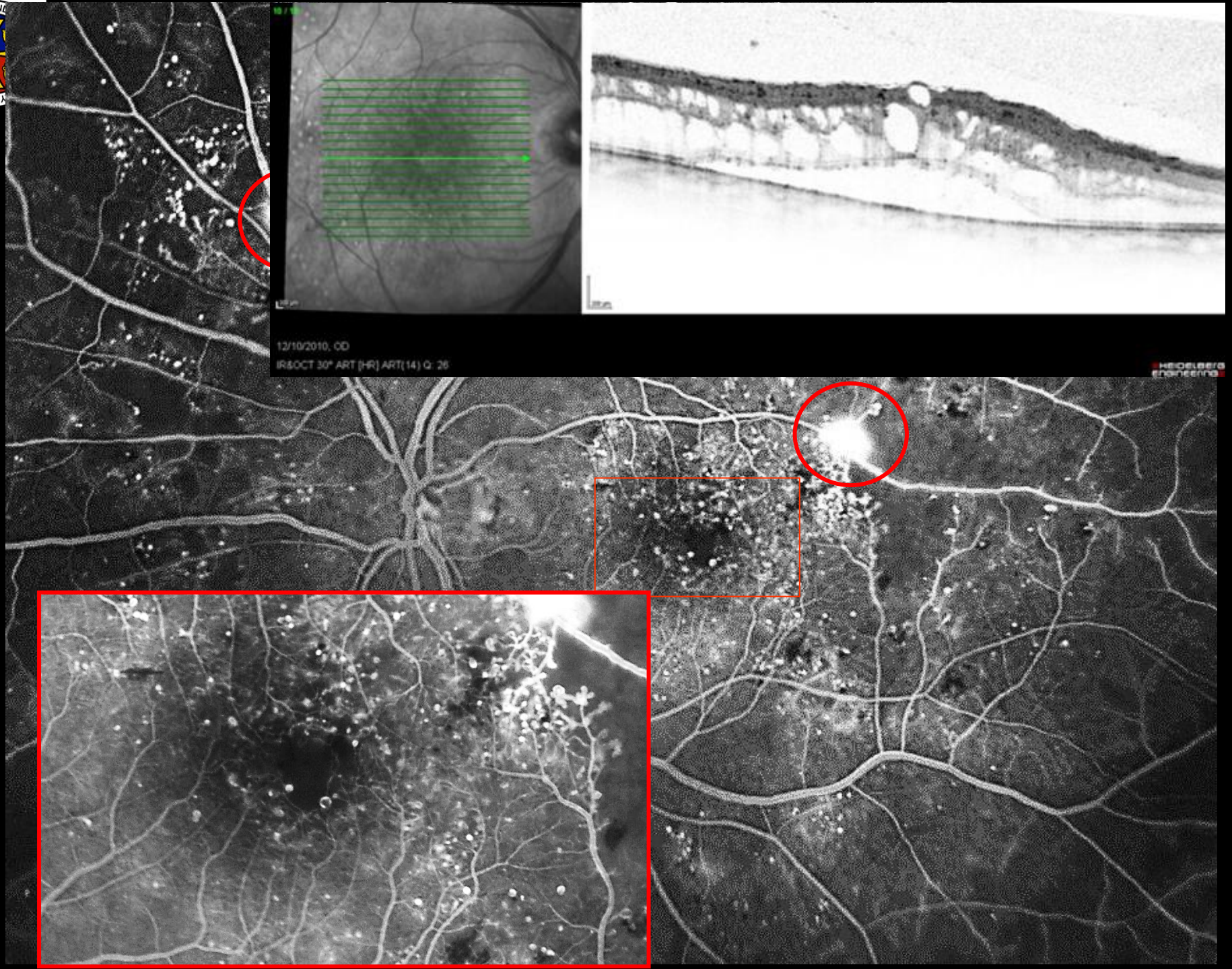
India Ink retinal mounts of diabetic rat retina

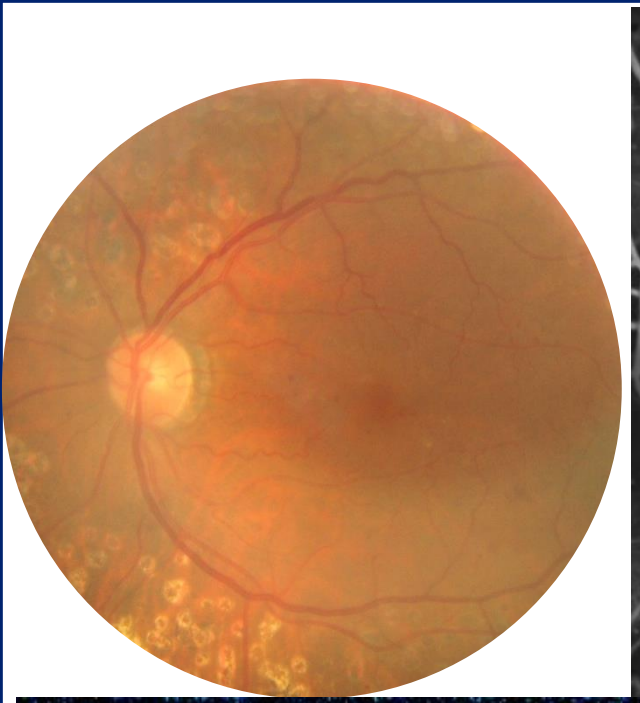
Animal Model of DR

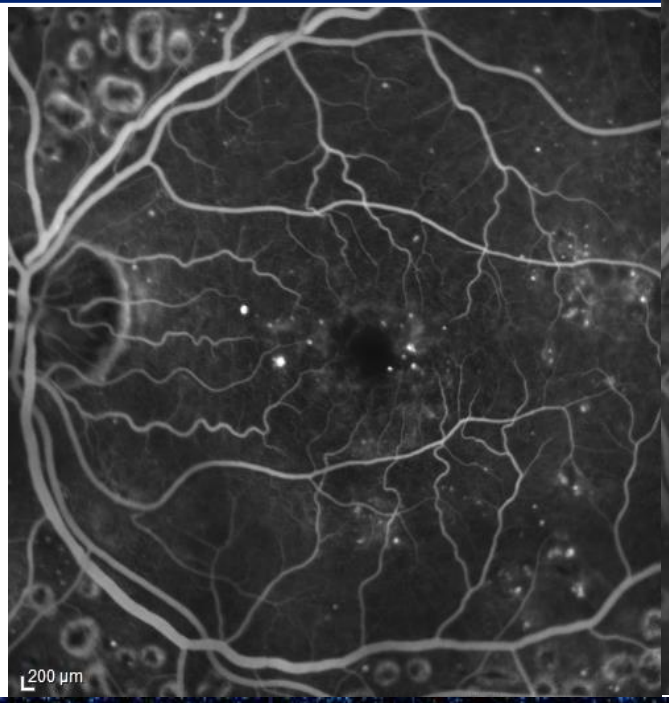
Stretozotocin

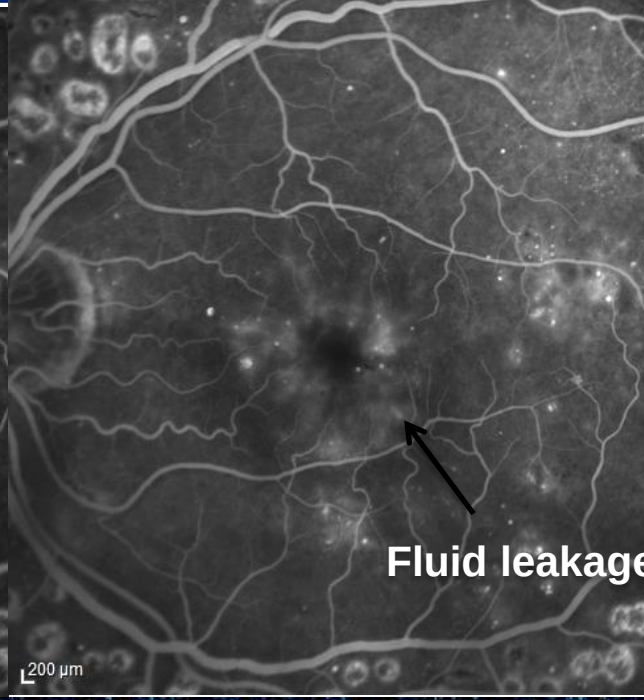




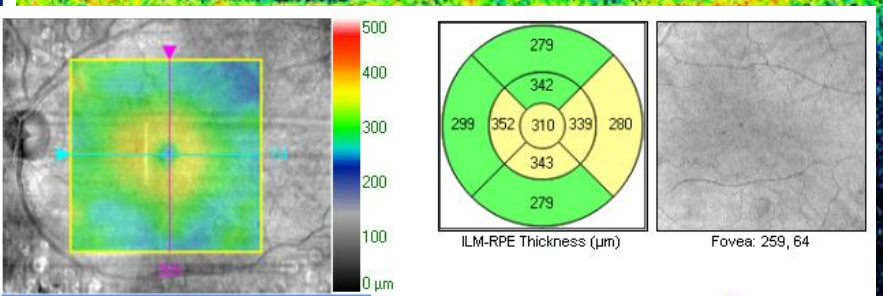

12/10/2010, OD
IR&OCT 30° ART [HR] ART(14) Q: 26
HEIDELBERG ENGINEERING







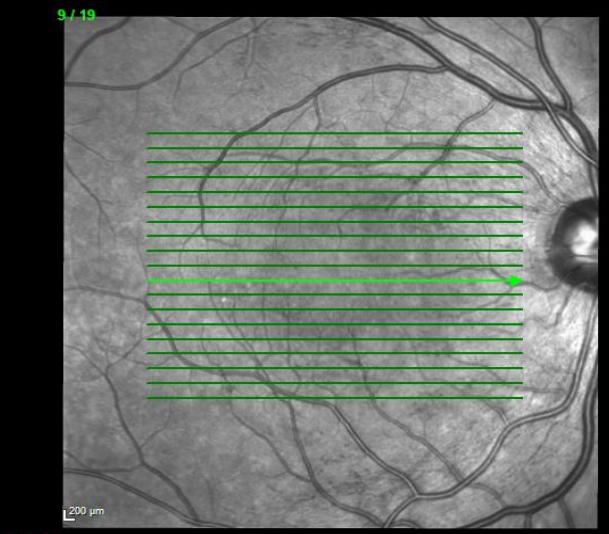
Diabetic retinopathy with good vision (VA 20/25)

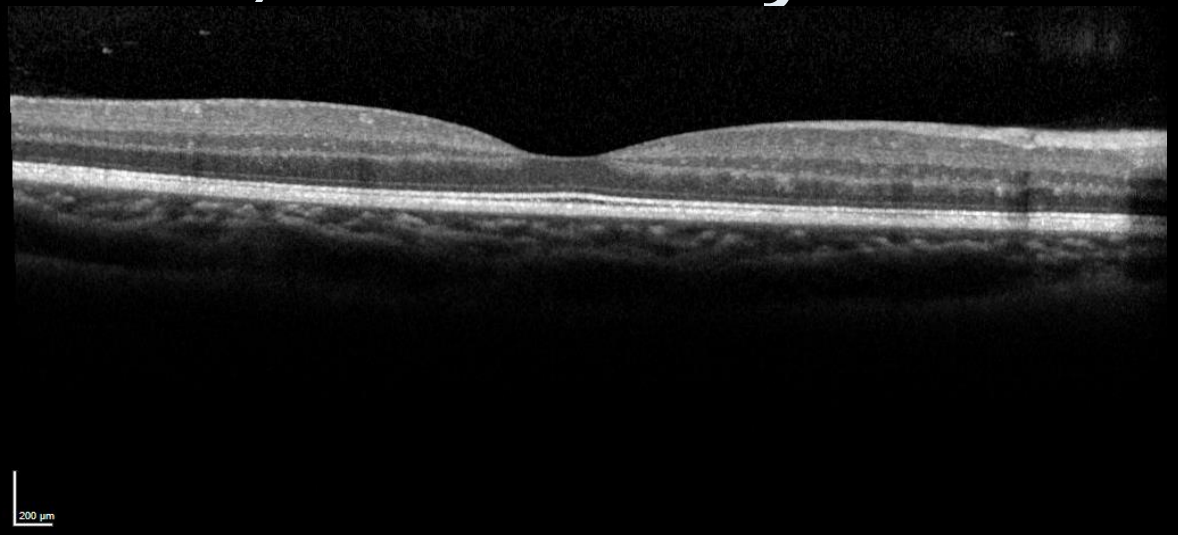


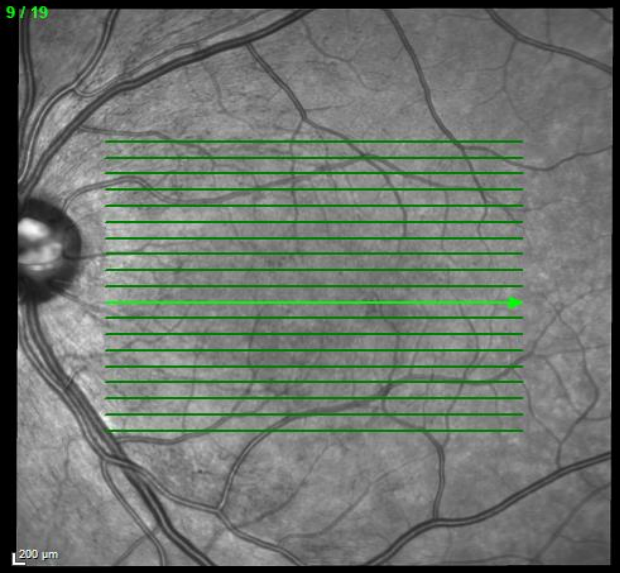
Only microcysts associated with mild retinal thickening

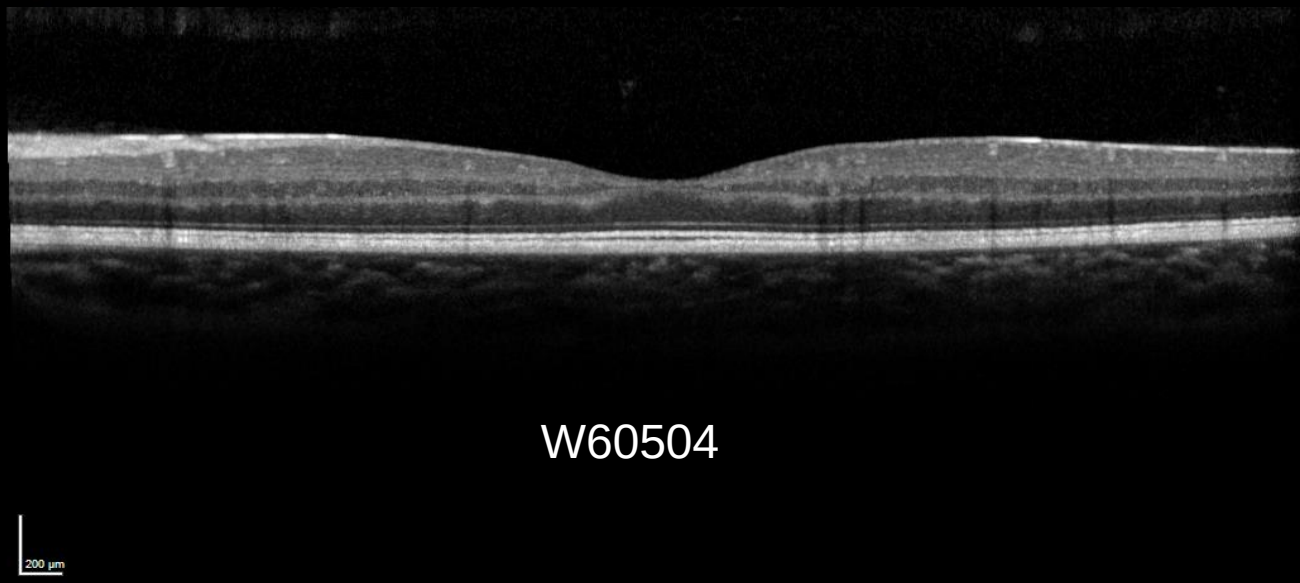
Images provided by authors

Young type 1 diabetic, reduced vision 6/9, in both eyes



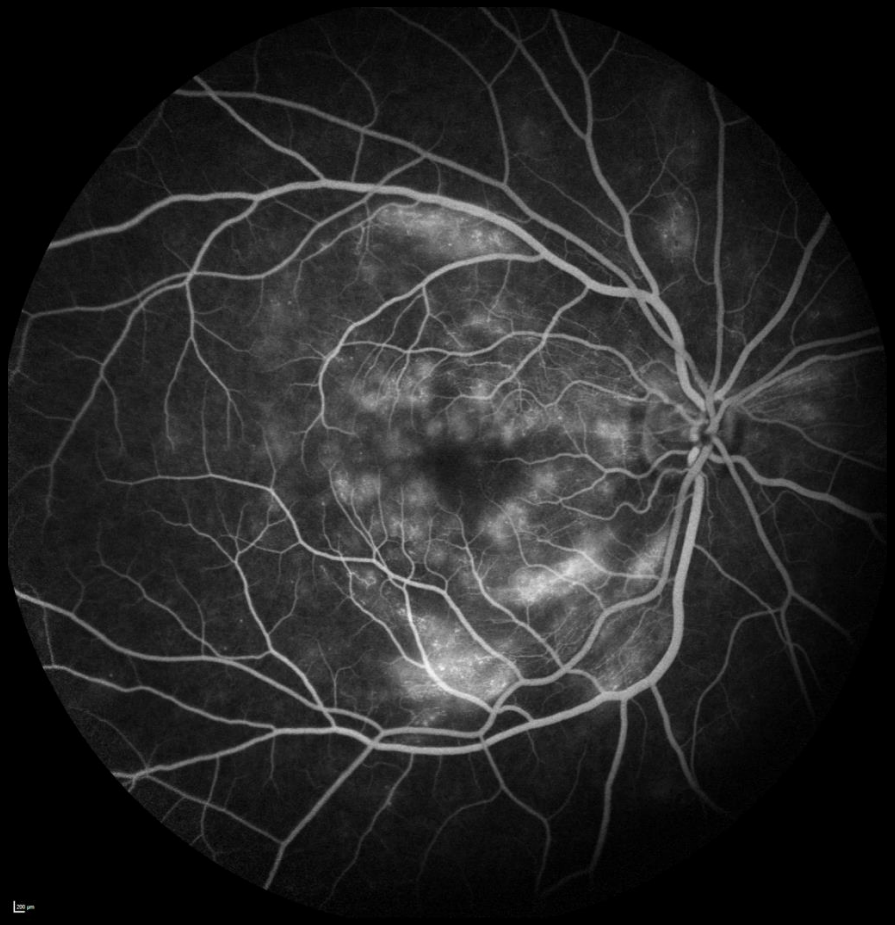


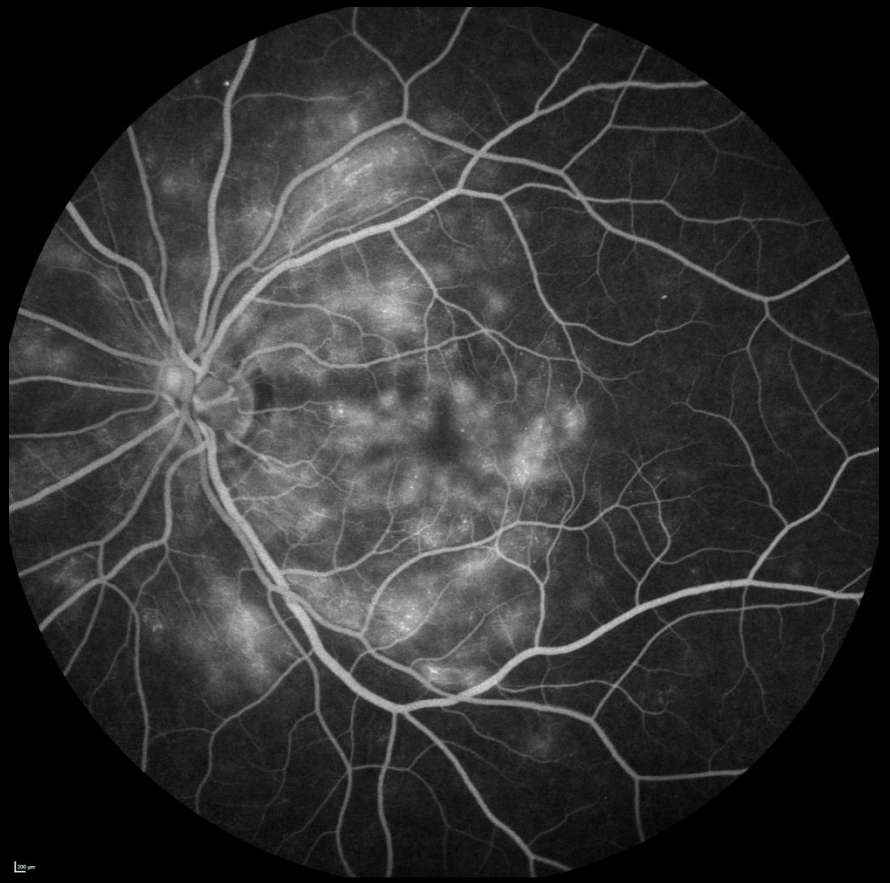




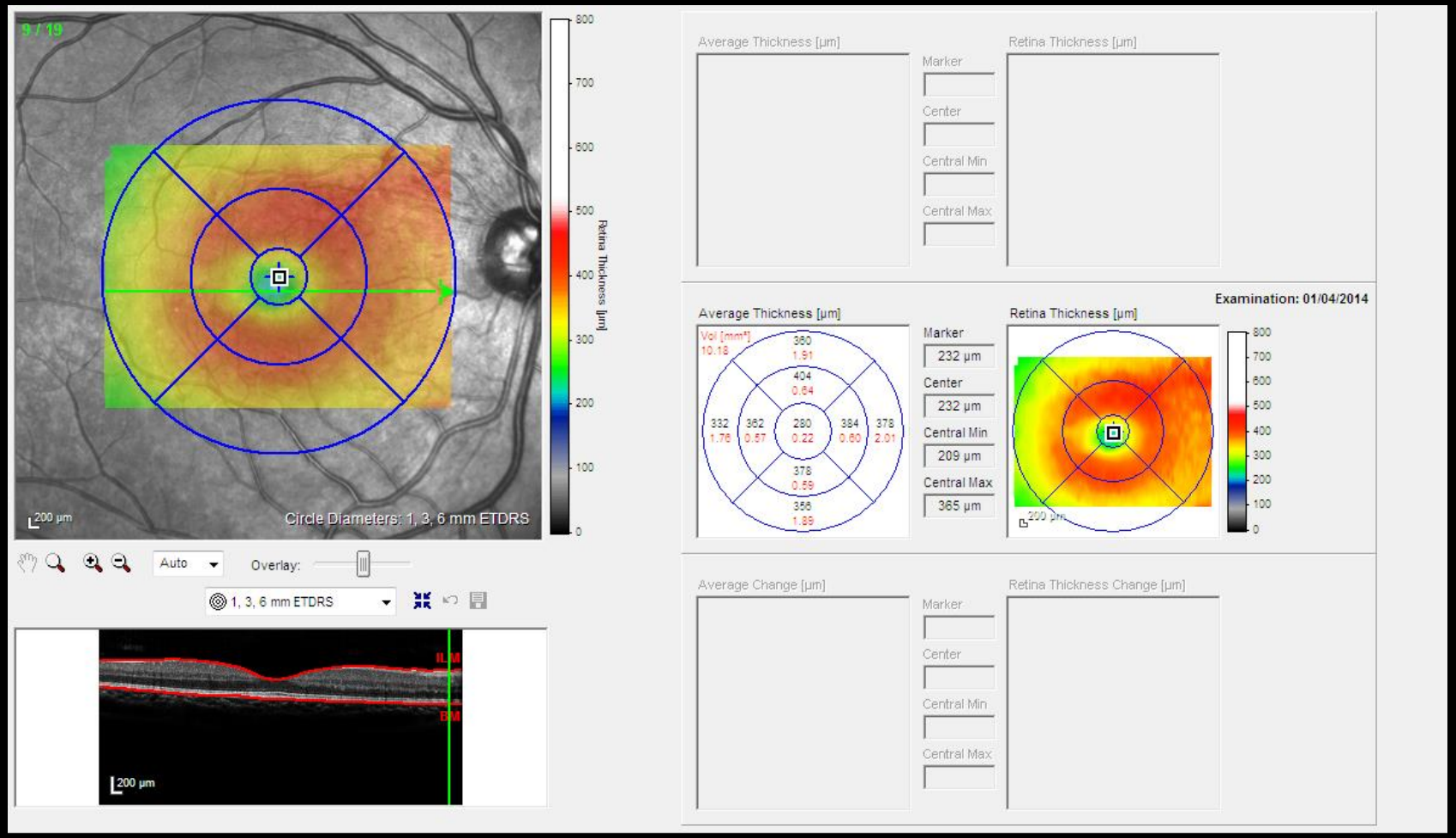
W60504

FFA showed bilateral diffuse leakage from capillaries with no microangiopathy signs



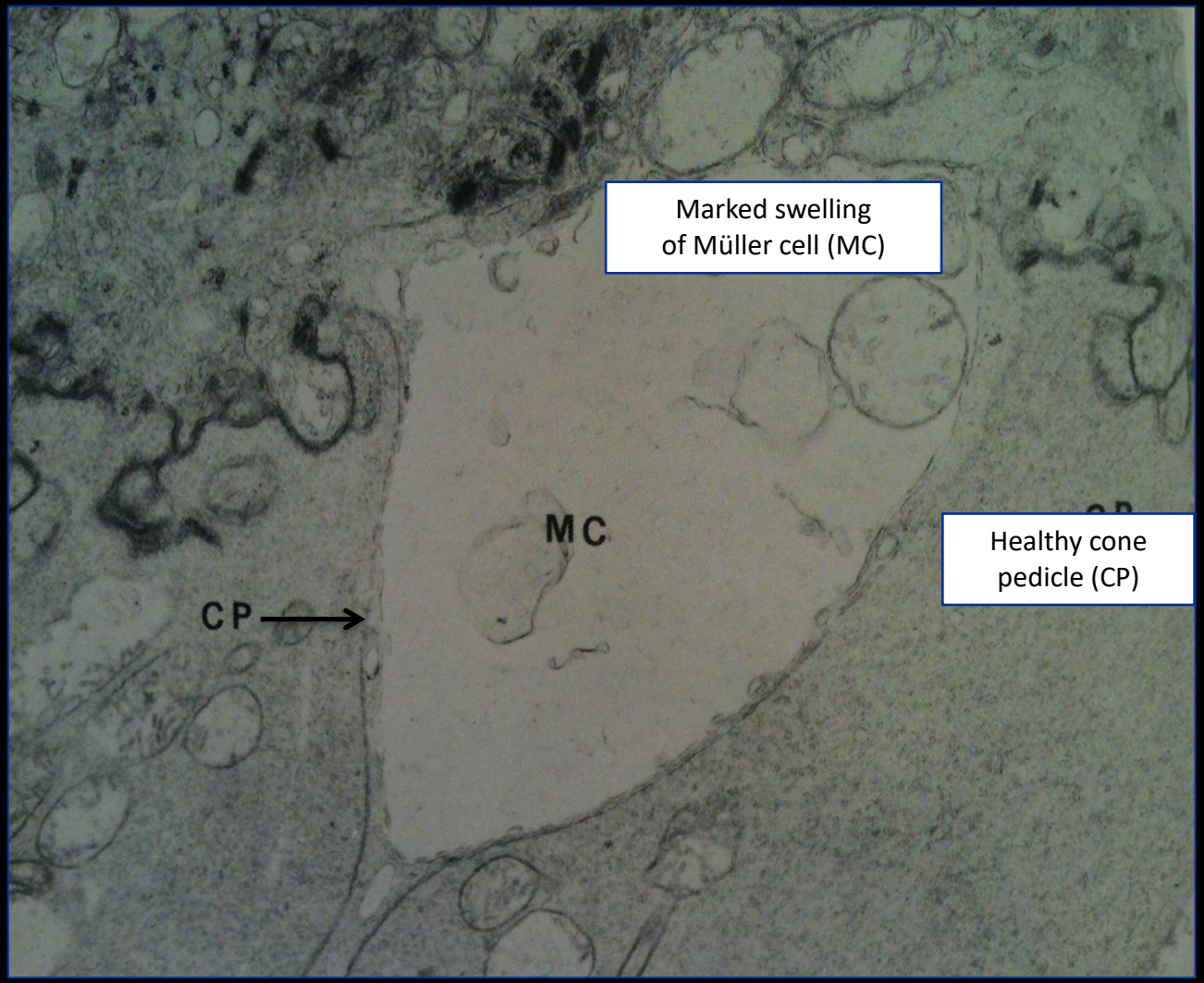


Thickness map showed thickening> 400 microns



01/04/2014, OD

Retinal swelling starts *inside* Müller cells (Ballooning)

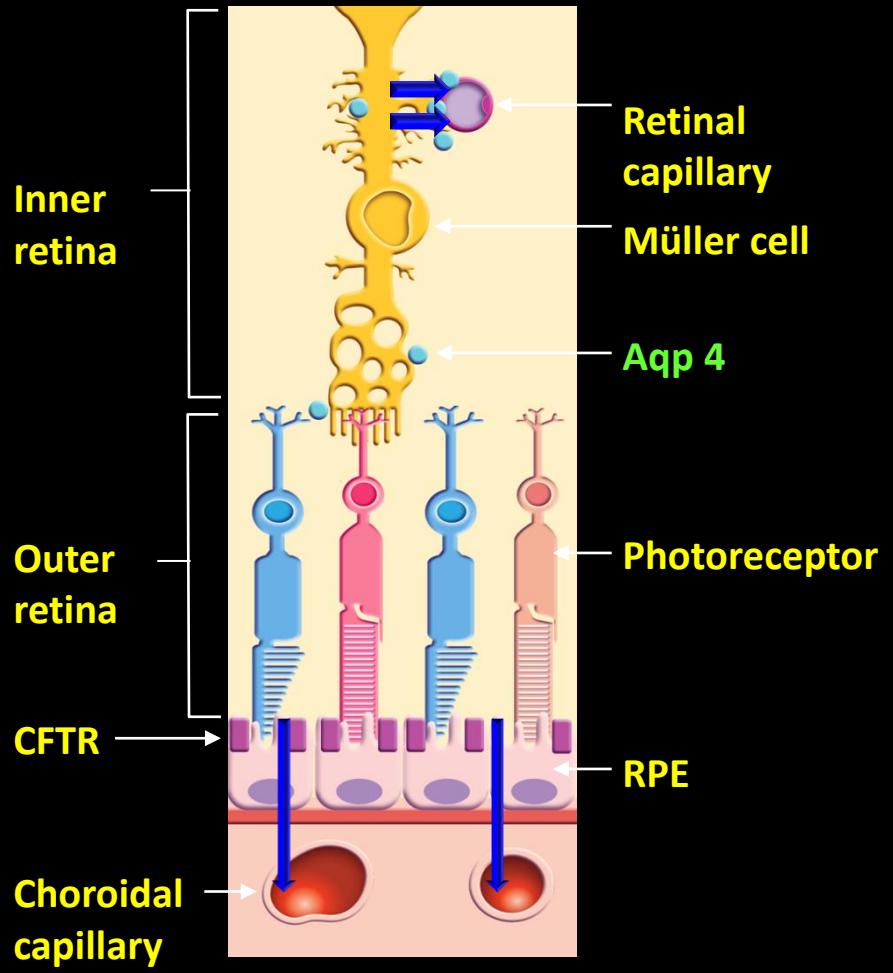


- **Ballooning of the Müller cells is the first step, not clinically detectable**[1]
- **Foveomacular region of an eye with cystoid macular edema (electronic microscopy) from diabetic retinopathy: the intercellular spaces (arrow) are usually normal or slightly enlarged**[1]

1. Fine BS and Brucker AJ. *Am J Ophthalmol* 1981;92:466–81.

‘Intracellular Oedema’

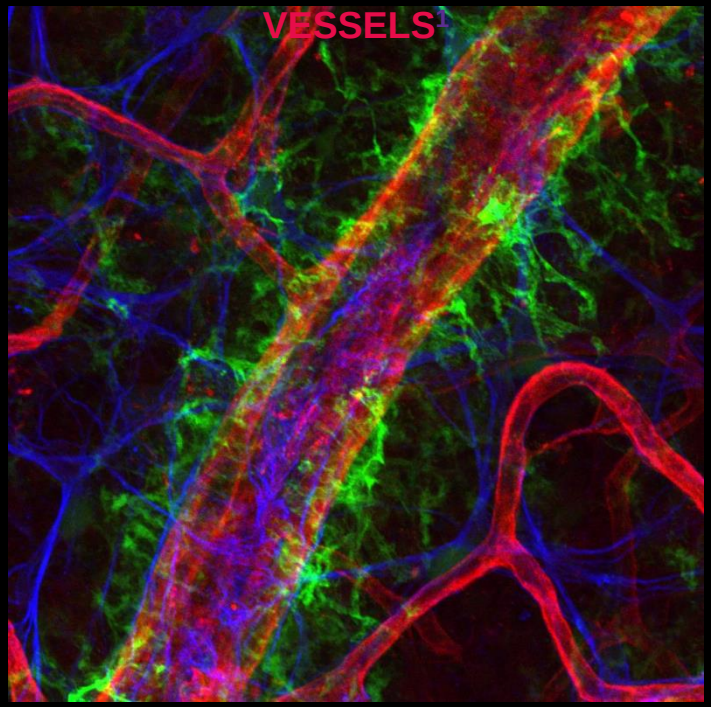
- **Intracellular**
  - Müller cell swelling
  - Neuronal swelling
- **Intercellular**
  - Retinal vessel leakage
  - RPE cell leakage



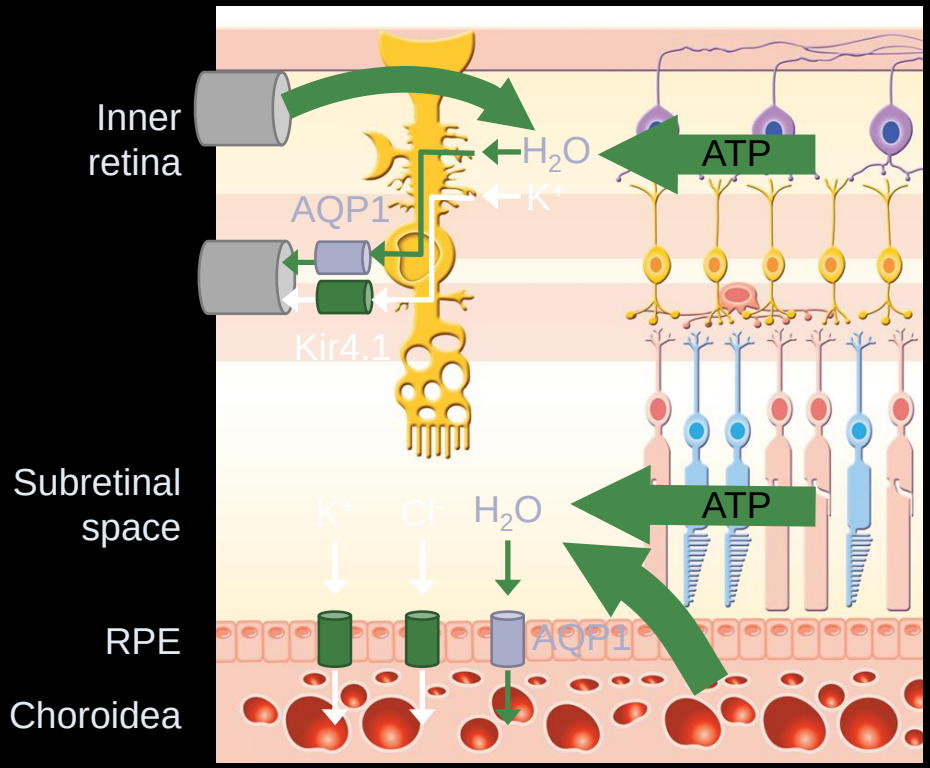
1. Yanoff M, *et al. Surv Ophthalmol* 1984;28:505–11. 2. Fine BS and Brucker AJ. *Am J Ophthalmol* 1981;92:466–81.
3. Adapted from Levin MH and Verkman AS. *J Membr Biol* 2006;210:105–15.

Müller cells are important for regulation of fluid transfer in the retina (through ionic channels)

ASTROCYTES, MÜLLER GLIAL CELLS & VESSELS[1]



Müller cells are wrapped around vessels[1,2]

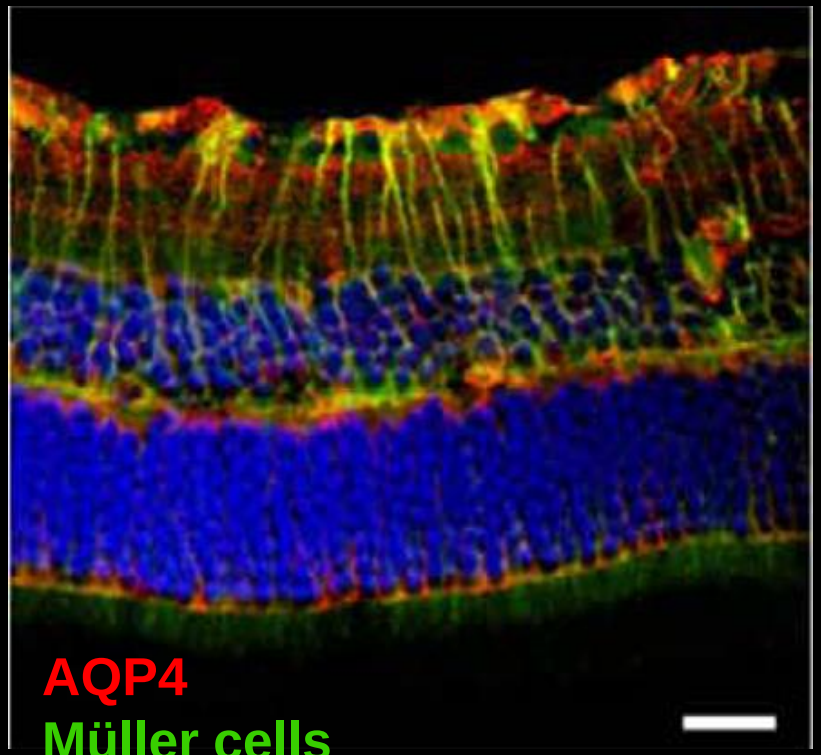


Müller cells active fluid reabsorption (retinal dehydration control) and ionic

As long as Müller cells keep functioning, visual function can be maintained or repaired[2]

1. Rendon A. Personal data. 2. Reichenbach A, *et al. Graefes Arch Clin Exp Ophthalmol* 2007;245:627–36.

Aquaporin-4 is the principal water channel in Müller cells

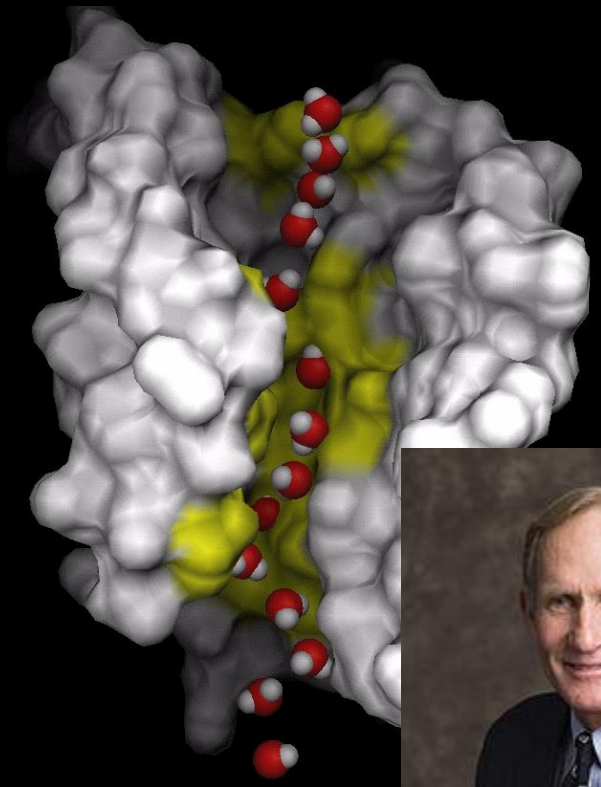


GCL

INL

OPL

ONL



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Group.

Peter Agre MD, Johns Hopkins, Nobel Prize 2003

1. Iandiev I, *et al. Neurosci* Lett 2005;388:96–9; 2. Figure ©2006 Computational Biomolecular Dynamics Group. www3.mpibpc.mpg.de/groups/de_groot/concept_design/gallery.html Accessed May 2013.

Summary

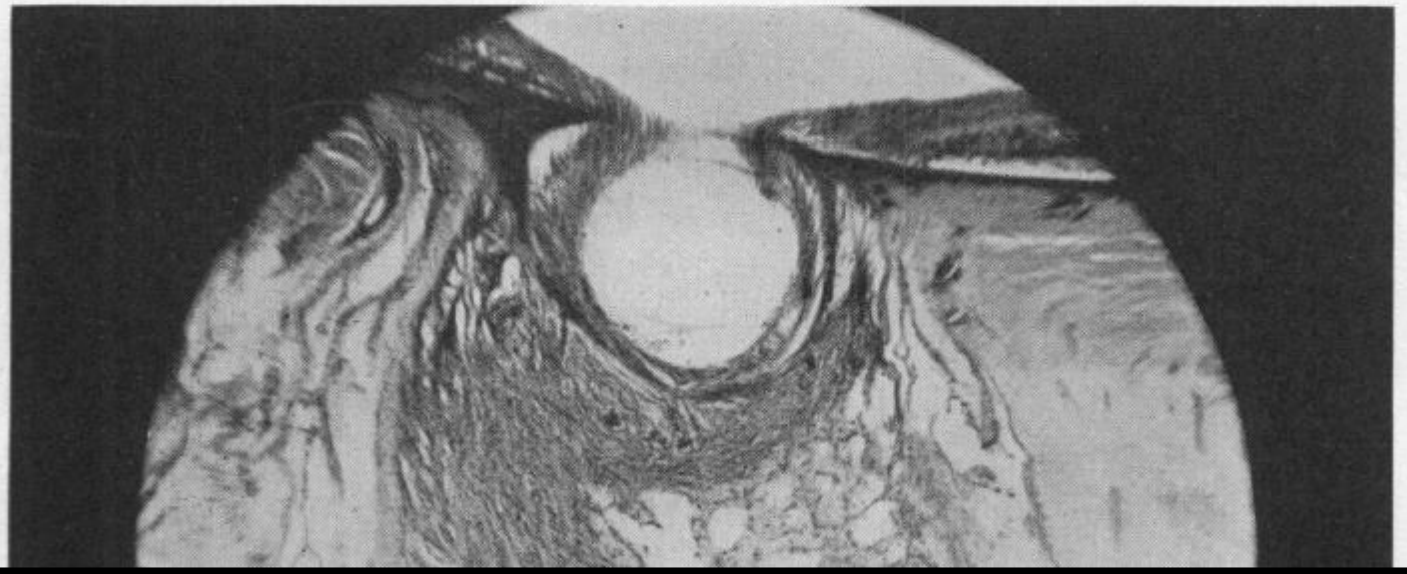
- Muller Cells have multiple roles:

1. Glue for VR adhesion
2. Directing light (Muller cell cone)
3. Storing Lutein to block Blue and UV light
4. Changes in Mactel II
5. Early ‘Intra-cellular’ Macular Oedema (aquaporin failure)
6. Etc Etc

The Richard Middlemore Lectures Remit

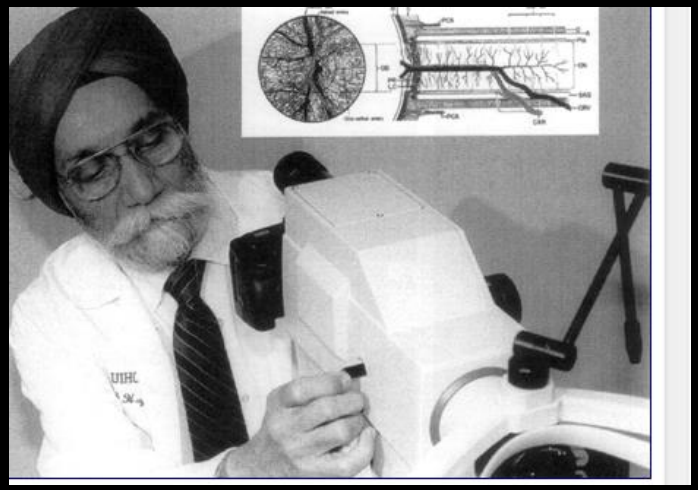
- To digest and arrange, …
- …the research and experience of those who devote themselves to the advancement of ophthalmology ….
- …for the service of those who are engaged in the absorbing duties of ophthalmic practice…

raised or when the blood pressure is lowered. The diastolic pressure is of greatest importance in this respect. Troncoso (1902) believed that the optic atrophy of glaucoma was due to degeneration following on chronic vascular disease. Earlier still Schnabel (1892) held that the optic atrophy was due to an essential shrinking



and not to the effects of intra-ocular pressure, though his contention did not then meet with much support. In this thesis it is held that the optic atrophy of chronic and of acute glaucoma is due to defective circulation involving either an actual ischaemia through sclerosis of the arterioles supplying the retina and optic

P Jameson Evans, Middlemore Lecture, December 1939



Sohan Singh Hayreh, MD, MS, PhD, FRCS, FRCOphth, DSc
Born Amritsar 1927,
1964 (37yo) SHO BMEC,
1987 DSc

In 2008, he wrote this about the laminar part of the optic nerve in glaucoma.

…this concept was received with marked skepticism. Since then, however, evidence that vascular insufficiency in the optic nerve head (ONH) plays an important role in pathogenesis of glaucomatous optic neuropathy has progressively accumulated; so that now its vasogenic origin is widely accepted.2

Middlemore Lecture 2016

Role of the Muller Cell
in
Retinal Pathology and Physiology

Illustrating:

-Some research…

-Some skills for clinical practice….

-Medical Retina Practice in 2016.

Acknowledgments

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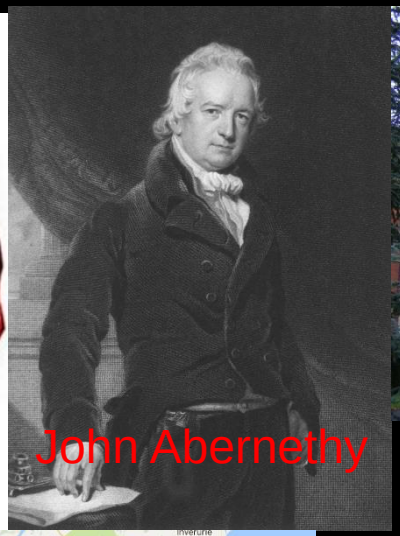
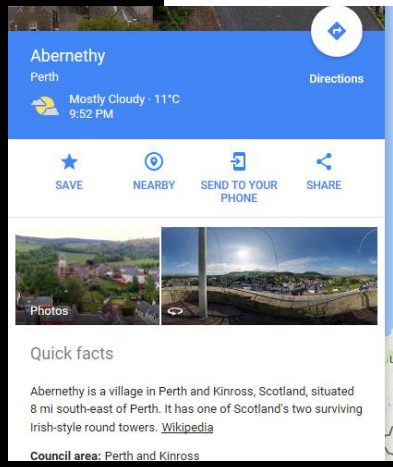
- Prof Simon Harding

Colleagues

- Miss Sharon Hughes
- Consultant colleagues


John Abernethy


Wolverhampton Grammar



Thank you for Listening

RICHARD MIDDLEMORE
(1804-1891)