


The Aging Eye
Impact Lions Gifts

Erik J. van Kuijk, MD, PhD

April 19, 2022




1

Leverage



With Permission: Prof. Edward Dratz Montana State University

2



Leverage

- \$75,000 = R01 Grant for Dr. Gregerson (1.5M)
- \$65,000 kit = Largest ARGUS center in USA (SM)
- 3M MAC center is \$10M gift to Cure AMD
- 4M MLESC = 43M Lion Eye Institute

3

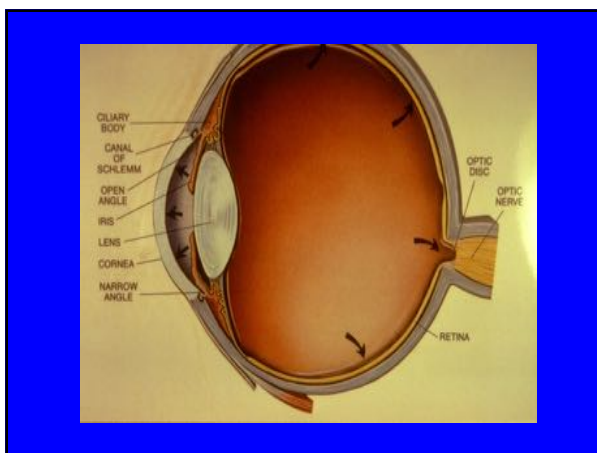
The Aging Eye

Cataract: Retired 6-30-1999; **J. Olson MD**

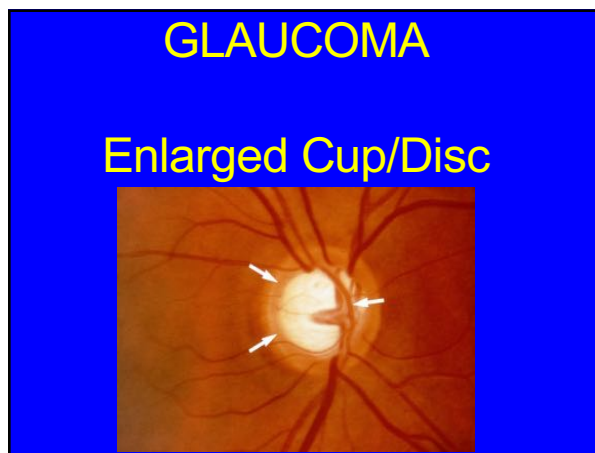
Glaucoma: Brief overview, **MIGS**

Macular Degeneration: Focus topic

4

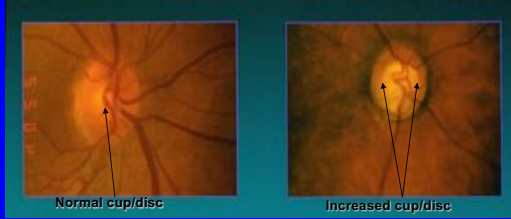


5



6

Normal vs Enlarged Cup/Disc



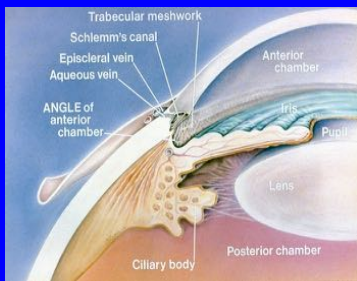
7

Glaucoma

- **Open angle**
 - Much more common
 - Asymptomatic
 - Screening visits, IOP, Visual Fields, RNFL images
- **Closed Angle**
 - Rare
 - Painful
 - Emergency

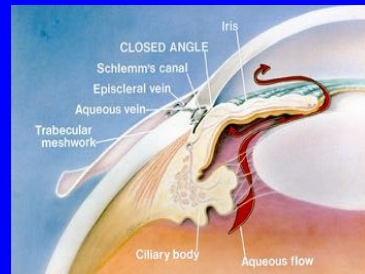
8

Open Angle Glaucoma



9

Closed Angle Glaucoma



10

Angle Closure (Acute) Glaucoma

- More common in small eyes
- Trabecular meshwork occluded
- Pain, photophobia, decreased vision, haloes
- Nausea, vomiting
- My first patient was.....

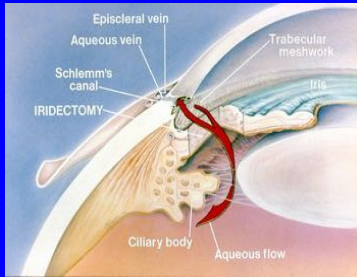
11

Angle Closure Glaucoma

- Decreased vision
- Diffuse conjunctival injection
- Pupil mid-dilated – fixed
- Corneal Edema
- Shallow Anterior Chamber
- Markedly Elevated Intraocular Pressure (40 – 60 + mm Hg)

12

Iridectomy



13

Laser



14

A Cure for AMD: Bridging basic science and clinical ophthalmology

Collaborators:

- Institute of Ophthalmology and Moorfields Eye Hospital, London
 - Fred Fitzke
 - Alan Bird
 - Imre Lengyel
- Neurobiotex Inc, Galveston
 - Christopher Frederickson
- University of Maryland
 - Richard Thompson
- George Mason University
 - Jane Flinn
- UTMB, Galveston
 - Adam Boretsky
 - Massoud Motamedi
 - Faraz Kahn
 - Garrett Burnett MSII
- St. Franziskus Hospital, Muenster
 - Daniel Pauleikhoff

15

AMD

- In developed countries AMD is the leading cause of irreversible visual loss. *Atrophic* ('dry') form accounts for 90% of cases. Most severe visual impairment results from *neovascular* ('wet') form.

- Prevalence in U.S. age groups:
 - 2% (52-64 y)
 - 11% (65-74 y)
 - ~30% (> 75 y)

- In 2050 there will be 80 million people aged over 65 y. 19 million will be > 85 y (5% of total population).

16

AMD RISK FACTORS

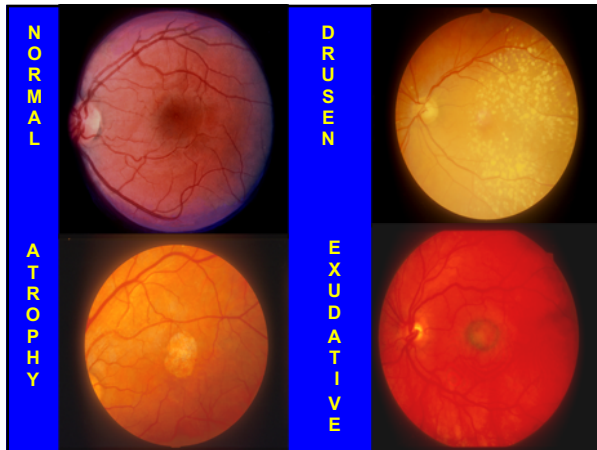
- **AGE**
- **SMOKING** (current or history 3 x 3)
- **LOW DIETARY FRUITS & VEGETABLES**
low serum and tissue anti-oxidant levels associated with low **MACULAR PIGMENT DENSITY (LUTEIN & ZEAXANTHIN)**
- **PARENTS (GENETIC, 70% risk)**
- **SUN EXPOSURE** BLUE and VISIBLE LIGHT

17

AMD PREVENTION

- **DO NOT AGE!**
- No smoking
- Increase dietary intake of fruits & vegetables
- **CHOOSE YOUR ANCESTORS!**
- Wear wrap-around sunglasses with coatings to absorb UV & blue light, and wide-brimmed hat.

18



19

TREATMENT: Wet AMD

- Low Vision Rehabilitation: 1947 (Waele)
- Laser Photo-coagulation 1980
- Photodynamic Therapy Cold Laser 1999
- Anti VGEF: ~~Anecortave Acetate 2001~~
Macugen 2003
Lucentis/Avastin 2005
Eylea 2010

MONTHLY SHOTS!

20

TREATMENT: Wet AMD

LUCENTIS or AVASTIN

- Focus
- Marina
- Anchor
- Horizon
- Pier
- CATT

Miraculous per NEJM

In 1 study, people taking LUCENTIS® monthly saw an average of 22 more letters than those who did not receive therapy

The graph shows the number of letters read over 24 months. The LUCENTIS group (orange line) starts at 0 and rises to +8.5 by month 2, remaining stable. The No therapy group (black line) starts at 0 and falls to -14.5 by month 24. A 22-letter difference is indicated between the two groups at month 2.

21

TREATMENT: Dry AMD

22

TREATMENT: Dry AMD

LIONS EYE INSTITUTE

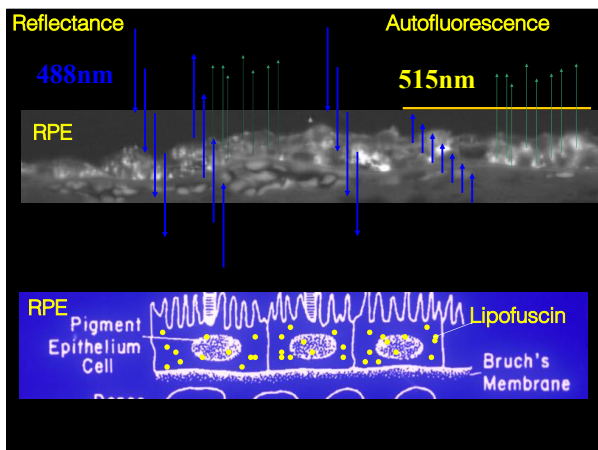
23

AUTOFLUORESCENCE IMAGING

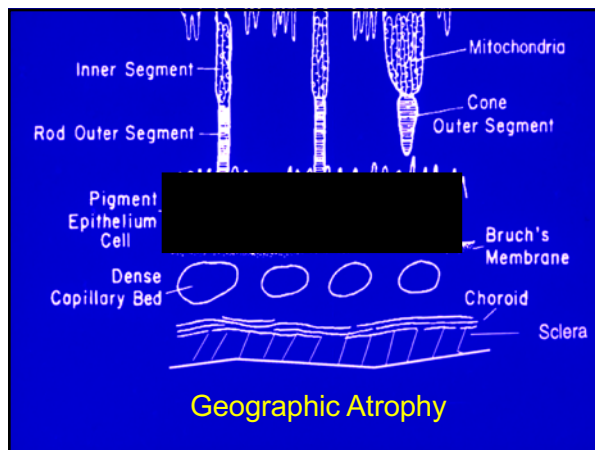
Lions Retinal Imaging Center

- illumination with blue light (488 nm, SLO)
- excitation of natural fluorophores
- lipofuscin in RPE
- use a barrier filter to block blue light
- obtain signal form emitted, green light
- due to weak signal, noisy image
- average 32 images to reduce noise
- von Ruckman, Halfyard, Fitzke, Bird, 1995
- Use barrier filter in camera. Spaide et al, 2001

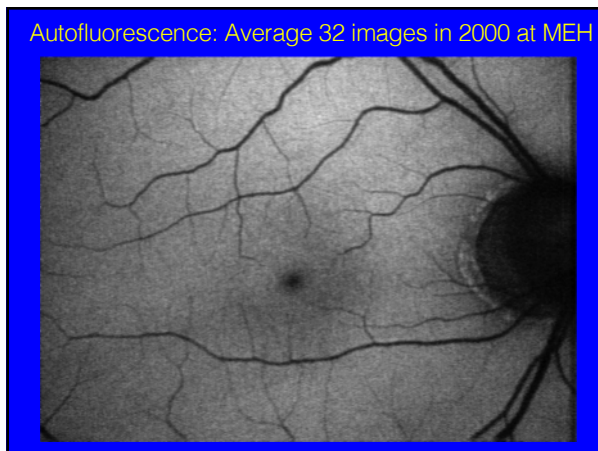
24



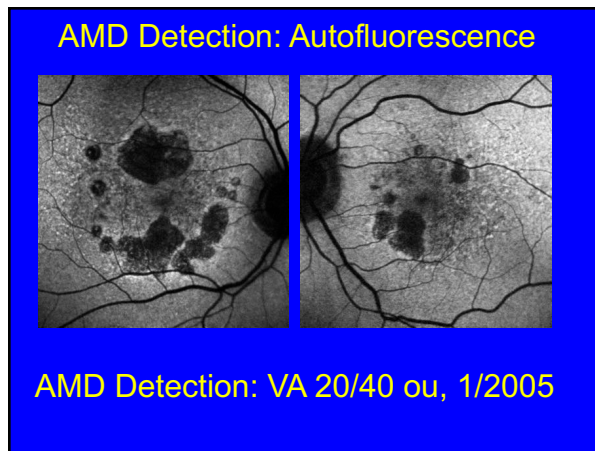
25



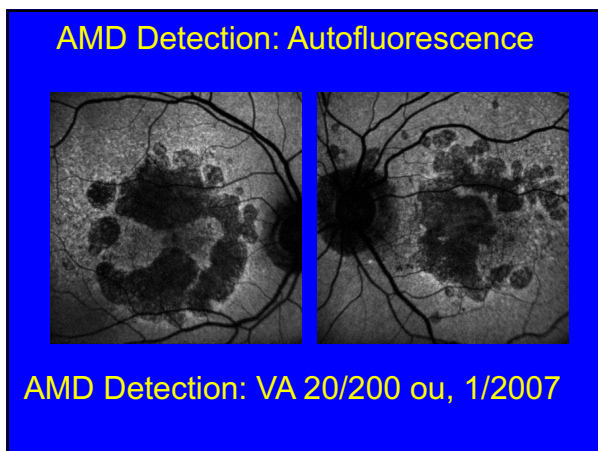
26



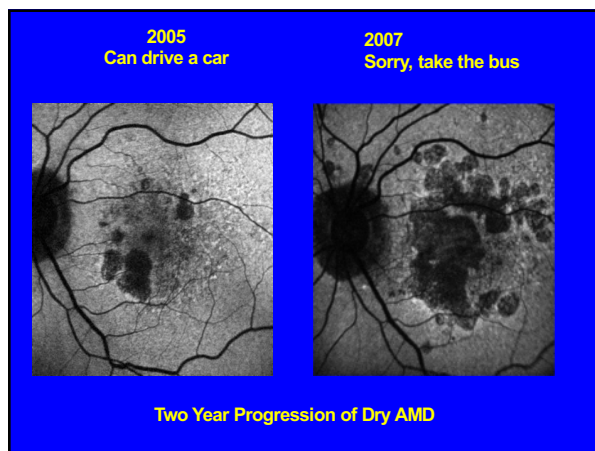
27



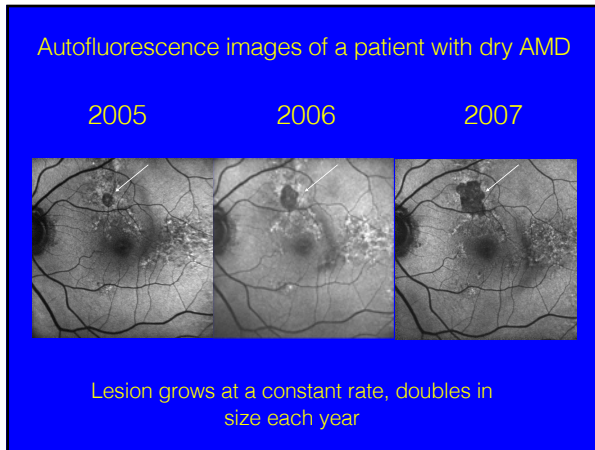
28



29



30



31



32

Philanthropy

Mr. Sidney Wolfenson, 1941 UofM graduate and Men's Gymnastics

Dr. Robert Wilkins, Galveston

Mr. Duer and Mrs. Genevieve Wagner, Fort Worth

Dr. Arnold Beckman: BIMR

Anonymous donor 2013, 10 million to cure AMD

Minnesota Lions Vision Foundation

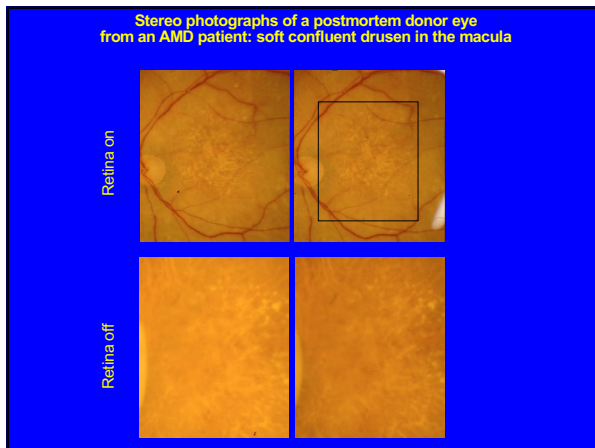
33

Beckman Initiative for Macular Research 2008-present

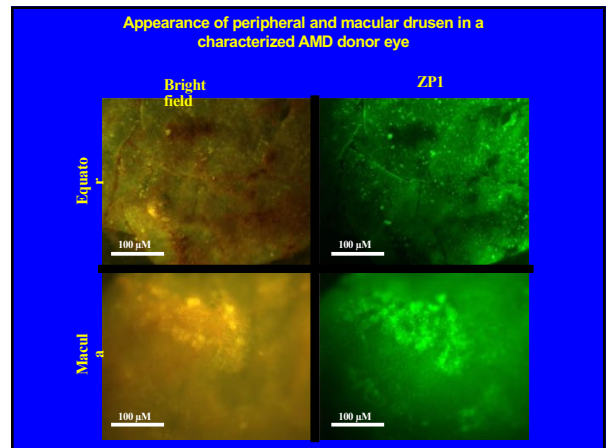
Multidisciplinary Approach to Dry AMD:

- Imaging
- Stem cell therapy
- Cell transplants
- Clinical Ophthalmology
- Nanotechnology
- Genetics
- Immunology
- Molecular Biology

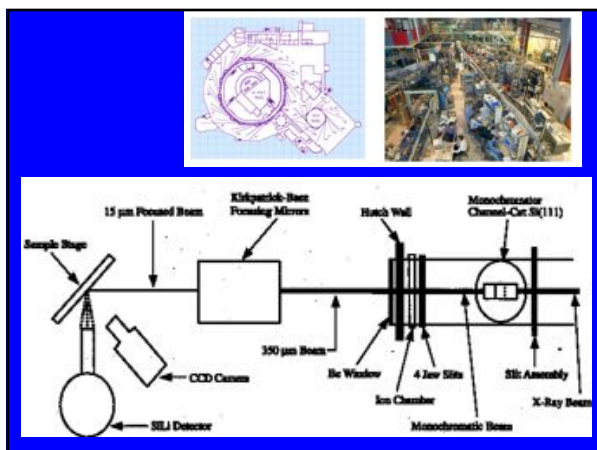
34



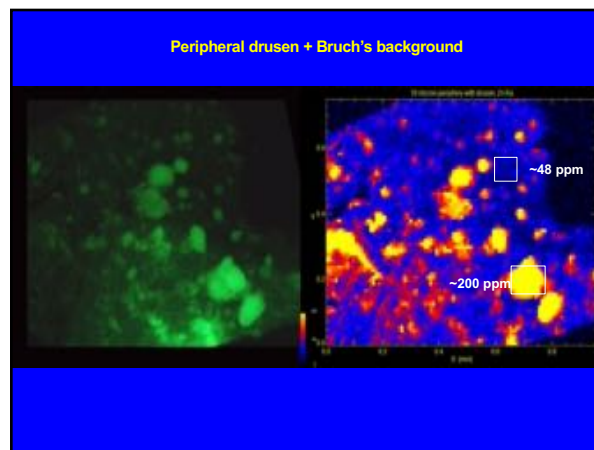
35



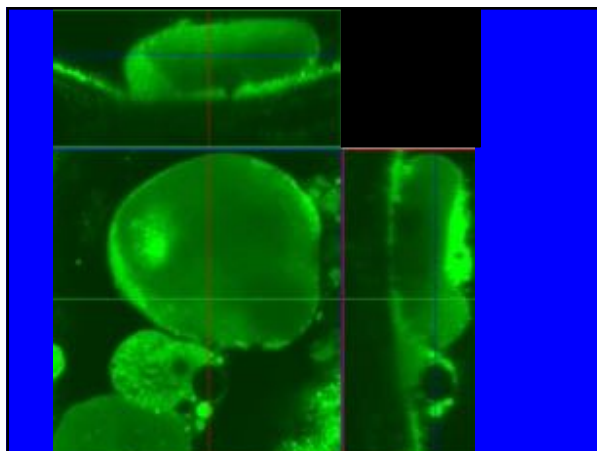
36



37



38



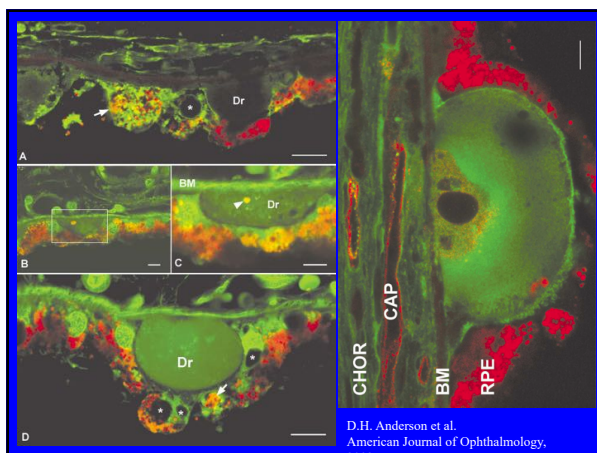
39

Table 1. Most common proteins in drusen

Most common protein	Accession no.*	Normal donors		AMD donors	
		Match	No.	Match	No.
Normal donor drusen					
Clusterin	P13003	10	36	5	4
TIMP1	P29215	14	36	6	3
Serum albumin	P62768	10	11	27	3
Vitellogenin	P64004	8	11	7	3
Complement component 9	P62728	8	10	5	3
Apolo. beta	A44983B3	5	6	5	3
Amyloid A	AF134733	3	8	12	2
Retinol B E C	C9980	5	7	1	2
Lectinoglobulin, beta A chain	P62714	5	7	3	3
Apolipoprotein E	A48557B	4	6	2	2
Complement component 3	P61014	6	6	2	2
Complement component 8	P62758	2	6	1	1
Retinol B A a	P29070	3	6	4	1
Serum amyloid P	156125	3	6	4	1
AMBP protein	P62760	4	5	1	1
Retinol B A b 2	P29021	2	5	3	3
Novel leucine-rich protein	U481372	2	5	3	3
Vitelminin	P69070	4	5	4	2
AMD donor drusen					
Crystalin, beta B1	P53078	7	2	15	5
Lectinoglobulin, beta A chain	P62714	5	7	3	5
Clusterin	P13003	10	36	5	4
Complement component 9	P62728	8	10	5	3
Crystalin, alpha B1	P53111	5	1	7	3
Crystalin, beta A3	P53073	4	1	8	3
Crystalin, beta A4	P53073	2	1	4	3
Crystalin, beta B2	P53220	2	1	9	3
Crystalin, beta 5	P29114	2	2	8	3
Retinol B beta 2	P62223	4	2	5	3
Retinol B A b 2	P29021	2	1	3	3
Serum albumin	P62768	10	11	27	3
TIMP1	P29215	14	36	6	3
Vitellogenin	P64004	8	11	7	3

1408 | www.pnas.org/cgi/doi/10.1073/pnas.2205388115
AMD donor drusen maximum number of peptides/peptide identified per analysis by LC/MS/MS sequence analysis. No. indicates the number of donors exhibiting the indicated protein.
 *Accession database accession nos. are shown in regular text and National Center for Biotechnology Information database accession nos. are in italics.

40



41

Zinc as an early biomarker for Dry AMD

- Have two animal models at the UofM that mimic the human eye with early AMD
- **Detection of Zinc in drusen *in vivo***: Do drusen form and trap zinc or does zinc contribute to the drusen formation?
- Funding: BMR grant s #1113 and #1408

42

Towards imaging the single cell: Hubble

- Current capabilities that are translatable to AMD studies
- Future possibilities

Available Imaging
Techniques

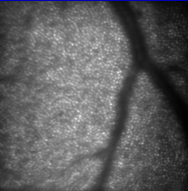
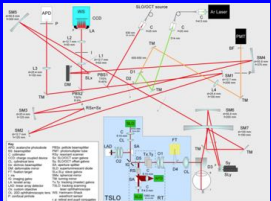
What You
Want

BIMR 2011

43

Adaptive Optics

- Imaging of retina uses lens as objective and result in aberrations that limit resolution
- Adaptive optics (AO) corrects for this using a wavefront sensor and deformable mirror
- The application of AO to current imaging technology enables *in vivo* cellular resolution


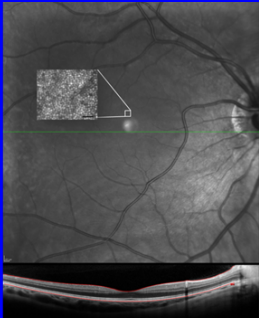



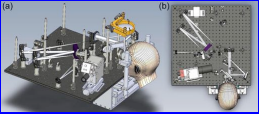
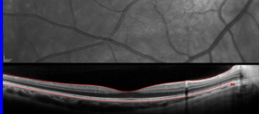
BIMR 2011

44

Adaptive Optics Scanning Laser Ophthalmoscopy

WAGNER RETINAL IMAGER

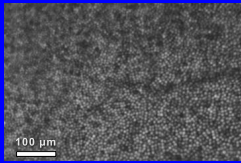
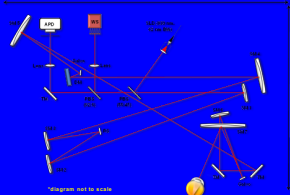



BIMR 2011

45

Adaptive Optics Confocal Scanning Laser Ophthalmoscope (AO-cSLO)

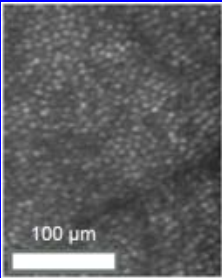
Macular cone photoreceptors in a healthy volunteer

Optical and Sensing Components	
APD – Avalanche Photodiode	(%T : %R)
SLD – Superluminescent Diode	TM - Turning Mirror
DM – Deformable Mirror	RS – Resonance Scanner
SM – Spherical Mirror	WS – Wavefront Sensor
PBS – Pellicle Beam Splitter	

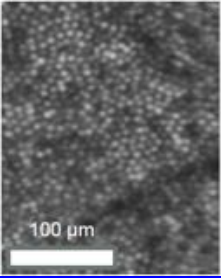
Wagner Retinal Imager

46

AO-SLO Image Enhancement



Single Frame Image

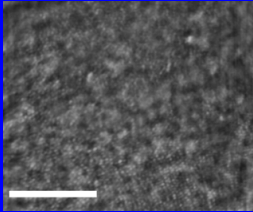


Registered Average of
20 Frames

BIMR 2011

47

Initial Experience Wagner Retinal Imager: HEALTHY

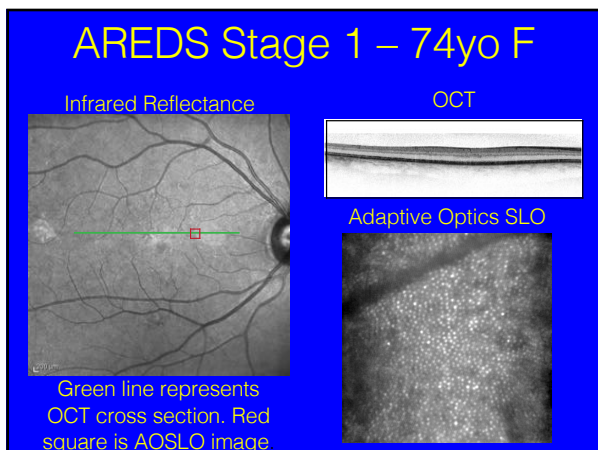



AREDS Category I.

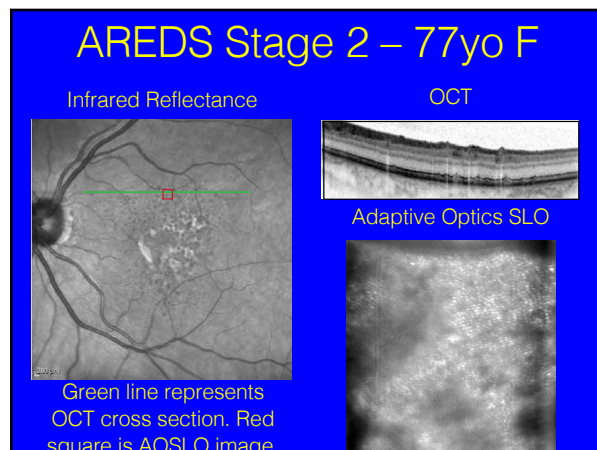
- Future Investigations
- Age matched controls
- Is AREDS I normal?
- Implications AMD classification?

BIMR 2012

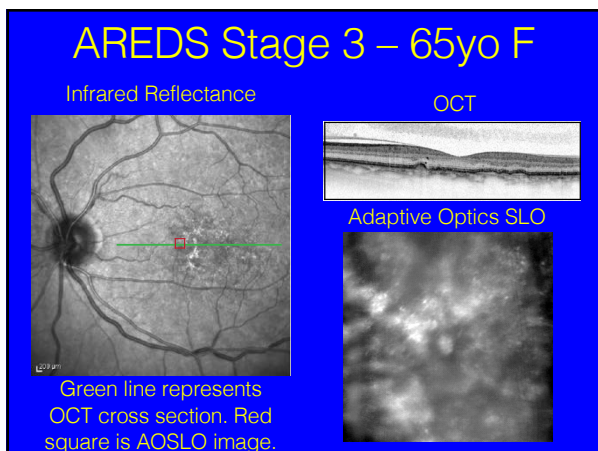
48



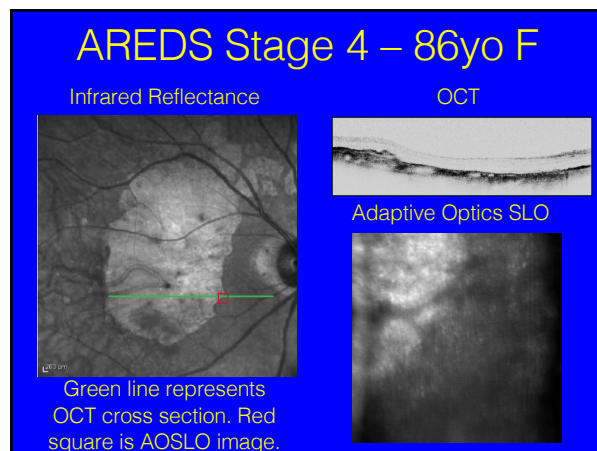
49



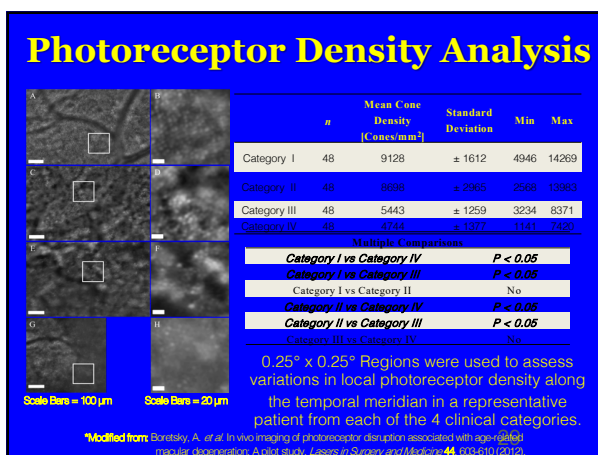
50



51



52



53



54