On behalf of Vision Expo, we sincerely thank you for being with us this year.

Reminder to Complete Your Session Evaluations!

Please be sure to complete your digital session evaluations for each course you attended! Your feedback is important to us as our Education Planning Committee considers content and speakers for future meetings to provide you with the best education possible.

vision expo

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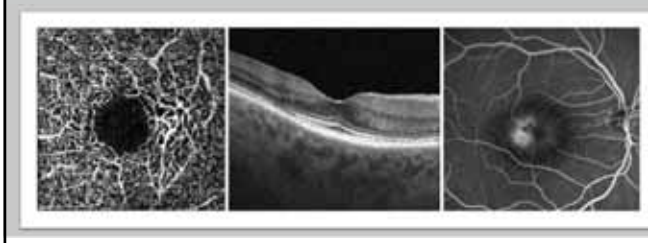
CASE FILES - RETINA



Jay M. Haynie, OD, FAAO, FORS
Sound Retina

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2

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Disclosures:
- Paid consultant/speaker for:
  - Carl Zeiss Meditec
  - Regeneron Pharmaceuticals
  - Iveric Bio (Astellas)
  - Optomed
  - Apellis Pharmaceuticals
- Paid advisory board member for LENZ Therapeutics, Notal Vision, Tarsus, Topcon, Genentech

All relevant relationships have been mitigated

3

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Disclosures:
- Apellis: Advisory Board, Consultant, and Speaker
- Astellas/Iveric Bio: Advisory Board, Consultant, and Speaker
- Glaukos: Advisory Board
- Haag Streit: Advisory Board
- LKC: Advisory Board
- Notal Vision/FSH: Advisory Board and Consultant
- OcuTerra: Advisory Board
- Orasis/Qlosi: Advisory Board
- Reliance Medical Equipment: Advisory Board and Consultant
- Tarsus: Advisory Board
- Topcon: Advisory Board
- Visible Genomics: Advisory Board
- Zeiss: Advisory Board

All relevant relationships have been mitigated

4

Financial Disclosure

Jay M. Haynie is on the advisory board, a consultant and/or considered a Key Opinion Leader (KOL) for the following:

Apellis Pharmaceuticals
Astellas Pharma
Topcon HealthCare
MacuHealth
Orasis Pharma

All relevant relationships have been mitigated

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THE GREAT MASQUERADER

45-year-old female

- CC: Walk-in visit sent from the ER, **Central blur/missing vision OS x 4-5 days**
- Systemic Hx:
  - **DM type 2, HTN, anxiety, hx of stimulant dependence and meth use**
- Ocular Hx: **Sectoral PRP for ischemic BRVO OD 2 years ago**
- VAs @dist cc:
  - OD 20/20
  - **OS 20/40 PH 20/30 (previously 20/20)**
- **SLE: Trace AC cell & flare OS only**
- IOPs: OD 15mmHg, OS 14mmHg

6

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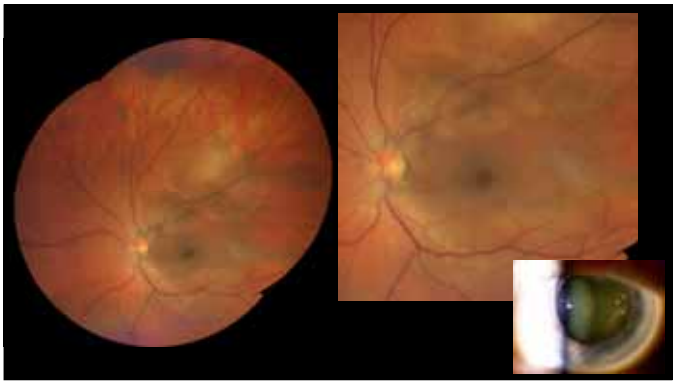

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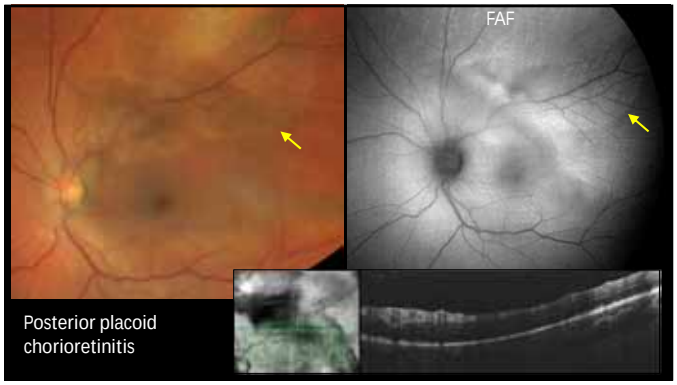
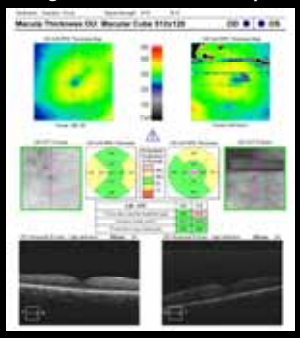


9

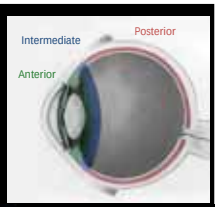
Diagnosis & Work Up?

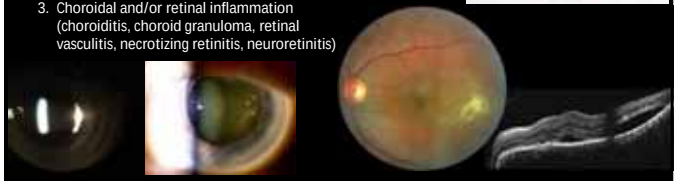


10

PANUVEITIS

- Generalized **inflammation of iris, CB, & choroid (ant + post seg inflammation)**
  - Often affects not only the uvea but **also the retina & vitreous**
- **Often bilateral** and severe
- Diagnosis:
  1. AC cells
  2. Vitreous cells
  3. Choroidal and/or retinal inflammation (choroiditis, choroid granuloma, retinal vasculitis, necrotizing retinitis, neuroretinitis)





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PANUVEITIS

Systemic etiologies & evaluation (always workup!!)

- Sarcoidosis (ACE, serum lysozyme, Chest X-ray or CT)
- Syphilis (FTA-abs, RPR)
- TB (QuantiFERON-TB Gold/PPD, Chest X-ray or CT)
- Tick-borne illness (Lyme/tick panel)
- VKH (HLA-DR1,HLA-DR4)
- Sympathetic ophthalmia
- Lens-induced uveitis
- Behcet disease (HLA-B51)
- Other tests: CBC with diff & platelet count, ESR, ANA, Toxoplasma antibody titers, ANCA panel

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TWO CASES….ONE SYSTEMIC DISEASE

Blood Lab	Results
ESR	**60 (high)**
ANCA	negative
RF	<14.0 (normal)
Lyme IgG/IgM Ab	neg
RMSF IgG, IgM	Negative
FTA-ABS	**Reactive**
RPR	**Reactive**
RPR, Qnt	**1:128**
HIV scr 4th gen	**Non-reactive**
QuantiFERON	Negative
ACE	<5 (normal)
Serum lysozyme	10.2 (normal)
Toxoplasma IgG/IgM	<7.2, <8 (normal)
ANA	Positive 1:320 dense fine speckled pattern
HLA-B51	Negative

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TWO CASES….ONE SYSTEMIC DISEASE

Diagnosis: Panuveitis OS secondary to neurosyphilis

Treatment:
- Contact tracing: patient was Ed on contacting all past sexual partners and advising them to get tested
- Referral to Infectious Disease clinic
- Infectious Disease reported to the local Public Health Agency
- Admitted and started on IV infusion penicillin G 24 million units daily x 10 days

Perform LP in all pts with ocular manifestations
**Ocular syphilis should be managed according to treatment recommendations for neurosyphilis

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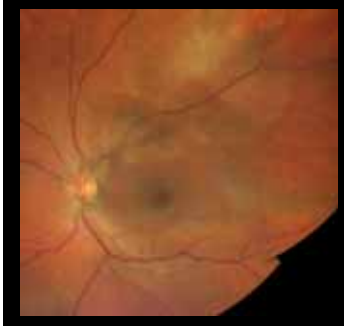
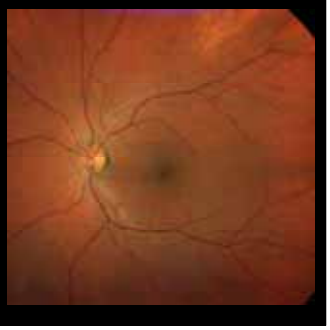
Baseline
20/40 PH 20/30



4 months post PCN tx
20/25+



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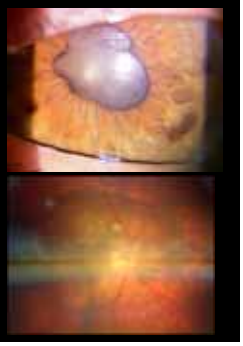
Syphilis- Ocular Manifestations

- **One of the great masqueraders!**
- Uveitis
  - Posterior uveitis, panuveitis most common
  - May or may not be granulomatous
  - Retinitis, vitritis possible
- Chorioretinitis
  - Typically multifocal and associated with heavy vitritis
- Vasculitis
- Papillitis/optic neuropathy
- Interstitial keratitis
- Conjunctivitis
- Episcleritis or scleritis
- CN palsies
- Argyll Robertson pupils



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Photobiomodulation for AMD

A New (non invasive) Treatment Option

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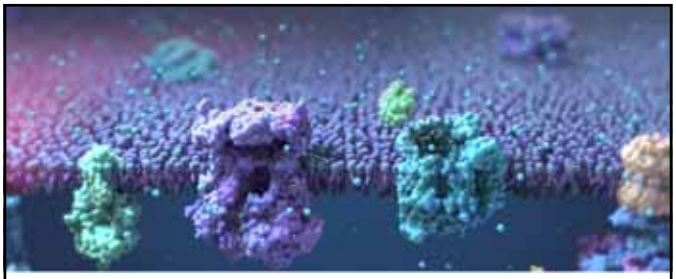

Photobiomodulation is the medical application of low-level light wavelengths to stimulate cellular function leading to beneficial clinical effects.

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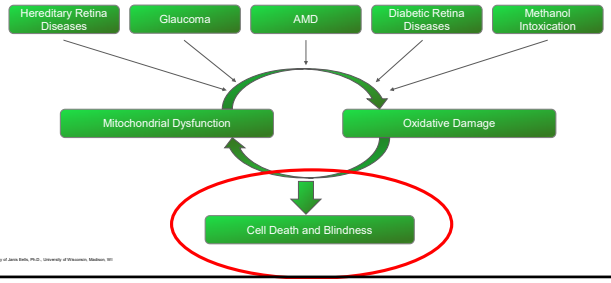
Mitochondrial Function – Create Cellular Energy
Mitochondrial Dysfunction: An Important Role in Retinal Disease & Injury



Courtesy of Janis Eells, Ph.D., University of Wisconsin, Madison, WI

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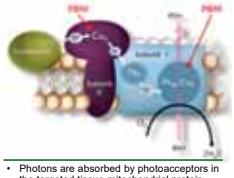
Valeda Photobiomodulation Approach

Valeda uses low-level light to stimulate cells, restore energy production, and improve cellular health



- Photons are absorbed by photoacceptors in the targeted tissue mitochondrial protein, cytochrome C oxidase (CcO) to restore energy production
- Sustained cellular changes also occur through activation of transcription factors

Valeda Wavelengths (nm)	Cellular Targets and Effect
590	Increases nitric oxide synthesis and vasodilation which can improve local oxygenation and nutrient delivery
660	Promotes O^2 binding (CU_B), stimulates metabolic activity (ATP) and inhibits inflammation and cell death
850	Drives electron transfer (CU_A) stimulates metabolic activity (ATP) and inhibits inflammation and cell death

Valeda wavelengths were selected based on their cellular targets and importance in AMD

Wong-Riley MTT, et al. J Biol Chem. 2005; 280: 4761-71.
Ball KA, et al. J Photochem Photobiol B Biol. 2012; 102: 182-91.

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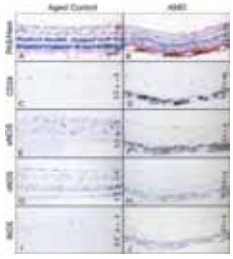
Role of Nitric Oxide in AMD

Nitric oxide is reduced in patients with AMD



- Nitric oxide (NO) is a potent vasodilator with diverse physiological functions such as regulation of ocular blood flow and retinal neurotransmission
- Expression pattern of the NO synthase (NOS) isoforms (eNOS, nNOS, iNOS) in aged control human eyes show significant reductions in immunoreactivity levels of eNOS and nNOS in eyes with AMD
- Immunohistochemical findings suggest that there is less NO produced in AMD eyes
- Reduced NO may play critical role in reducing blood volume to submacular choroid which is critical for central visual function
- The decrease in eNOS and nNOS expressions could be associated with neuronal degeneration in retina and vasoconstriction and hemodynamic changes in AMD choroid

Bhutto IA, et al. Exp Eye Res. 2010; 90: 698-707.

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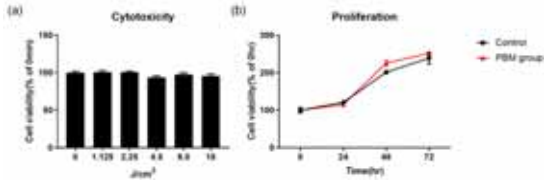
No Toxicity of Multiwavelength PBM in Cultured RPE Cells



Multiwavelength PBM has no effect on cell viability and cell proliferation of ARPE-19 cells. (a) Cell viability was measured after the irradiation of multi-wavelength PBM at an intensity of 0, 1.125, 2.25, 4.5, 9.0, and 18 J/cm^2. (b) After the irradiation of multi-wavelength PBM at 4.5 J/cm^2, cell proliferation was measured in control and PBM-treated groups for 24, 48 and 72 h.

Guo H, et al. Int J Mol Sci. 2023; 24.

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FDA Authorizes Valeda Treatment to Improve Vision in Dry AMD (November 04, 2024)

Valeda Light Delivery System

- First and only FDA-authorized treatment for dry AMD to improve vision
- U.S. LIGHTSITE III 24-month pivotal trial met BCVA primary endpoint and was used to support Valeda FDA submission
- CE Marked in Europe and available in select countries in Latin America
- Non–invasive treatment with a favorable safety profile with no signs of phototoxicity

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U.S. Indications for Use

Indications for Use
The Valeda Light Delivery System is intended to provide improved visual acuity in patients with best corrected visual acuity (BCVA) of 20/32 through 20/70 and who have dry age-related macular degeneration (AMD) characterized by:

- The presence of at least 3 medium drusen (> 63 µm and ≤125 µm in diameter), or large drusen (> 125 µm in diameter), or non-central geographic atrophy, AND
- The absence of neovascular maculopathy or center-involving geographic atrophy

After about two years, the Valeda Light Delivery System treatment provides improved mean visual acuity of approximately one line of visual acuity (ETDRS) compared to those not receiving the treatment.

Contraindications
As a precaution, patients have not been tested and should not be treated with Valeda if they have any known photosensitivity to yellow light, red light, or near-infrared radiation (NIR), or if they have a history of light-activated central nervous system disorders (e.g., epilepsy, migraine). In addition, patients should not receive treatment within 30 days of using photosensitizing agents (e.g., topicals, injectables) that are affected by 590, 660, and/or 850 nm light before consulting with their physician.

Refer to the Valeda User Manual for full Important Safety Information.

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Valeda® Light Delivery System Treatment

- Treatment is straightforward with minimal training required
- No pupil dilation required
- A treatment series is nine (9) treatments delivered 3x/week over the course of 3-5 weeks
- A treatment series should be delivered every 4 months
- Implementation support available from LumiThera Customer Success

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Valeda® Light Delivery System Specifications

Parameter	Specification
Size	530 mm height x 300 mm width x 330 mm depth (20.8" x 11.8" x 13")
Weight	10.8 Kg (23.8 lbs.)
Light Sources	Light Emitting Diodes (LEDs)
Light Emission	590 nm output: 5 mW/cm² 660 nm output: 65 mW/cm² 850 nm output: 8 mW/cm²
Beam Diameter	30 mm (nominal) at treatment plane
Treatment Exposure Time	A total of 250 seconds (4 minutes 10 seconds) There are 4 phases: • Phase 1: 590 and 850 nm pulsed: 35 seconds • Phase 2: 660 nm continuous waveform: 90 seconds • Phase 3: 590 and 850 nm pulsed: 35 seconds • Phase 4: 660 nm continuous waveform: 90 seconds

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Photobiomodulation Delivery Specifications

- Valeda delivers eye-safe photobiomodulation treatment using LEDs
- The eye is uniquely accessible to PBM treatment. No other tissue or bone interferes with treatment directed to the eye
- Valeda is NOT a LASER. Valeda delivers a non-coherent, homogenized, light beam produced by LEDs
- Valeda meets all requirements set forth by ANSI Z80.36 and IEC 62471 for light exposure safety
- Valeda does not deliver thermal treatment or produce local cellular damage
- No phototoxicity or serious adverse events considered related to PBM treatment have been reported in Valeda clinical trials

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LIGHTSITE III: US Pivotal 24-Month Trial

The LIGHTSITE III was an FDA, IDE-approved, prospective, double-masked, randomized, sham-controlled, parallel group, multi-center trial to assess the safety and efficacy of photobiomodulation (PBM) in subjects with dry age-related macular degeneration (AMD)

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LIGHTSITE III: Principal Investigators

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

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LIGHTSITE III: Clinical Trial Design

Key Trial Criteria:

Inclusion
- Diagnosis of Dry AMD
- BCVA between 20/32 to 20/100

Exclusion
- Current or history of neovascular maculopathy
- Presence of center involving geographic atrophy (GA) within central ETDRS 1 mm diameter
- Visually significant disease in any ocular structure apart from dry AMD

Study Duration: 24-Months; Focus on Month 13, Month 21 (Final Tx series), and Month 24 (3 months after final Tx series) timepoints
Randomization: 2:1 randomized PBM to Sham
Sham Control (Active low dose control): 10x reduction of 590, 100x reduction of and 660 nm, and no 850 nm wavelengths
Masking: Triple masked (subjects, sites, sponsor)
Outcome Measures: Best Corrected Visual Acuity (BCVA); Low Luminance BCVA (LLBCVA); MARS Contrast Sensitivity (CS); Radner Reading; Visual Function Questionnaire 25 (VFQ-25, Quality of Life); D-15 Color Vision; Perimetry; OCT/FAF/Fundus photo imaging (Heidelberg Spectralis, Duke Reading Center)

Boyer D. et al., Retina, 2020

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Duke Reading Center (DRC): Image Analyses

- Secondary, exploratory, and safety endpoints
- Image Acquisition: FAF/NIR: Heidelberg blue light, OCT: Spectralis (97 line, HR) and FP
- GA Analysis
  - Identify GA with OCT (cRORA)
    - cRORA criteria
    - Hypertransmission (≥250u), RPE loss (≥250u), outer retinal layer loss
  - Quantification of GA by FAF (supplemented by OCT/NIR)
  - GA quantification with region finder
- Drusen Volume Analysis
  - Quantified with custom in-house software (DRCV)
- Assessment of EZ by Macular Location

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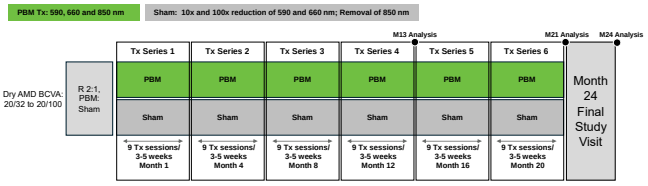
LIGHTSITE III: Clinical Trial Design

A double-masked, randomized, sham-controlled, parallel group, multi-center study to assess the safety and efficacy of PBM in subjects with dry AMD



Primary Endpoint: *BCVA change from baseline at Month 13 or Month 21. Comparison between the PBM and Control arms to demonstrate statistical superiority of the PBM treatment. (α of 0.025 to control for multiple testing), at both Month 13 and 21 with Month 13 tested first.*

Secondary and Exploratory Endpoints: *BCVA, MARS CS, Radner Reading, LLBCVA, Quality of Life (VFQ-25), and anatomical outcomes via OCT/FAF/Fundus photo imaging were conducted at selected timepoints over 24-months with a focus on Month 13, 21 (Final Tx series), and 24 (3 months after final Tx series).*

Boyer D. et al., Retina, 2024

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LIGHTSITE III: Subject Baseline Characteristics

LIGHTSITE III Baseline Characteristics	
Subjects	100
Eyes	148 (2:1 randomized into PBM and Sham Treatment groups)
Race	99% Caucasian, 1% Black/African American
Gender	32 M (32%), 68 F (68%)
Age	Mean 75.0 years
BCVA BL Letter Score	PBM: 70.7 (SD 5.2) Sham: 70.1 letters (SD 4.3)
Clinical Classification (Beckman*)	Early: 32 (21.6%); Intermediate: 105 (71.0%); Late: 11 (7.4%)
AREDS Categories	AREDS II: 19 eyes (13%); AREDS III: 129 eyes (87%)
Risk Factors for AMD Progression^	
Low Risk (1-2 risk factors)	48 eyes (32.4%)
Moderate to High Risk (3-4 risk factors)	100 eyes (67.6%)
Time from Diagnosis	Mean 4.9 years
AREDS Supplements	86 (86%) Yes; 14 (14%) No

*Ferris FL 3rd, Wilkinson CP, Bird A, et al. Clinical classification of age-related macular degeneration. Ophthalmology. 2013;120(4):844-851. doi:10.1016/j.ophtha.2012.10.036. ^A modified Ferris risk factor scoring system was used to identify the total risk factors for each eye indicating potential risk for further progression of disease (max of 4 points for high risk).

Boyer D. et al., Retina, 2024

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LIGHTSITE III: Risk Scoring for Disease Progression

Modified Ferris Simplified Scoring System

Criterion	Point Designation
Per eye for drusen size (1 large or ≥3 medium drusen)	1
Per eye for pigmentary changes (study eyes only, pigmentary changes were not collected at screening for the 52 ineligible non-study eyes)	1
Per eye for nAMD or central/non-central GA	2
Overall Risk Estimate Score	**= Sum of points from each eye (Total of 4 points)**

- Majority of eyes (67.6%): moderate-to high-risk for dry AMD disease progression
- Average # of risk factors for disease progression:
  - PBM group: 3.0 risk factors
  - Sham group: 3.4 risk factors

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Dry AMD Trial Discontinuation Comparison

LIGHTSITE III showed a lower rate of discontinuation than other dry AMD studies that have recently completed

Valeda® Light Delivery System

LIGHTSITE I (12 Months)[1]
- PBM (2 series): 0/15 (0.0%)
- Sham: 2/15 (13.3%)

Overall rate: 2/30 (6.7%)

LIGHTSITE II (10 Months)[2]
- *PBM (3 series): 6/29 (20.7%)*
- *Sham: 2/15 (13.3%)*

*Overall rate: 8/44 (18.2%)**

LIGHTSITE III (24 Months)[3]
- PBM (6 series): 12/65 (18.5%)
- Sham: 8/35 (22.9%)

*Overall rate: 20/100 (20.0%)**

Pegcetacoplan (Syfovre)

OAKS (24 Months)[4]
- Tx (15 mg; monthly): 69/213 (32.4%)
- Tx (15 mg; EOM): 43/212 (20.3%)
- Sham: 54/212 (25.5%)

Overall rate: 166/637 (26.1%)

DERBY (24 Months)[4]
- Tx (15 mg; monthly): 59/206 (28.6%)
- Tx (15 mg; EOM): 47/208 (22.6%)
- Sham: 46/207 (22.2%)

Overall rate: 166/637 (26.1%)

Avacincaptad pegol (Izervay)

GATHER 1 (18 Months)[5]
- Tx (2 mg): 28.4%
- Tx (4 mg): 44.6%
- Sham: 26.7%

Overall rate: 33.2%

GATHER 2 (12 Months; 24 Month data unavailable)[6]
- Tx (2 mg): 25/225 (11.1%)
- Sham: 17/222 (7.7%)

Overall rate: 9.4%

** Of note, trial was ongoing during COVID-19, several subjects discontinued due to COVID-19 impact (LT2, 25%; LT3, 5%). EOM, every other month. [1]Markowitz et al., Retina, 2019; [2]Burton et al., Ophthalmol Ther, 2023; [3]Do et al., AAO, 2024; [4]Heier et al., Lancet, 2022; [5]Patel et al., Eye, 2023; [6]Khanani et al., Lancet, 2023.*

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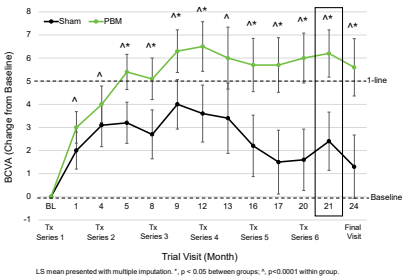
LIGHTSITE III: Primary BCVA Efficacy Endpoint Met

Valeda Improves Vision

- The trial met the predetermined primary efficacy BCVA endpoint at Month 21 (p = 0.0036) with a gain of 6.2 letters in the PBM group (mean letter difference of 3.8 letters between Tx groups)
- A mean letter gain of 5.6 letters in the PBM group was maintained at Month 24 (mean letter difference of 4.3 letters between Tx groups, p = 0.0024)



LS mean presented with multiple imputation. *, p < 0.05 between groups; ^, p<0.0001 within group.

Do, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA. October 20, 2024.

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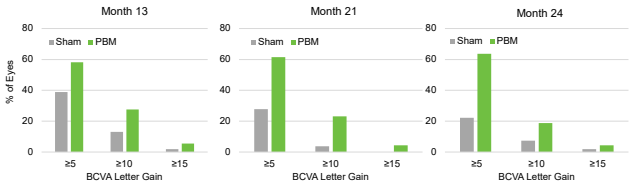
LIGHTSITE III: BCVA Letter Gain Distribution

The PBM group showed a higher frequency of ≥ 5 letter, ≥ 10 letter, and ≥ 15 letter gains compared to the Sham group at Months 13, 21, and 24



Data presented with multiple imputation. Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA, October 20, 2024.

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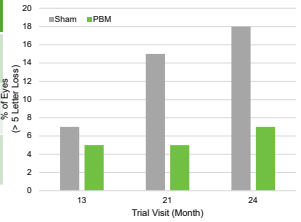
LIGHTSITE III: Percentage of BCVA Loss (> 5 Letters)

PBM reduced the % of eyes with vision loss of >5 letters compared to the Sham group over 24 Months

Timepoint	Sham	PBM
Month 13	7%	5%
Month 21	15%	5%
Month 24	18%	7%



- Sham-treated eyes lost vision due to progression of disease: All eyes with >5 letter loss at Month 24 converted to GA

Data presented with actual values. Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA, October 20, 2024.

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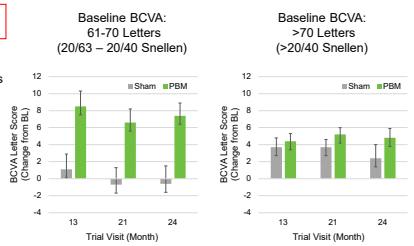
LIGHTSITE III: BCVA Change Stratified by Baseline Acuity

- Eyes with worse baseline BCVA show larger visual gains
- At baseline, 30.0% of eyes (n=45) had BCVA <70 letters; 70.0% of eyes (n=103) had BCVA ≥ 70 letters (mean of 72.4 letters - near normal/ mild visual impairment)
- Eyes with baseline BCVA between 61-70 letters showed more robust increases in acuity following PBM compared to eyes with baseline letter scores ≥ 70 letters



Data presented with last observation carried forward (LOCF). Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA, October 20, 2024.

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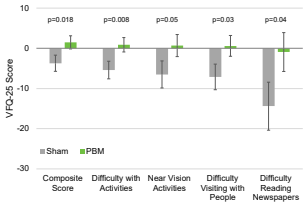
LIGHTSITE III: Quality of Life Improvement

- Additional clinical outcome measures for Quality of Life (QoL, VFQ-25)
- Significant improvement in overall VFQ-25 QoL Composite Score (p = 0.018)
- At Month 21, PBM-treated subjects showed improvement in overall VFQ-25 composite score and sub-score assessments of difficulty with activities, near vision activities, difficulty visiting with people, and difficulty reading newspapers compared to deterioration observed in the Sham group



Data presented with actual values. Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA, October 20, 2024.

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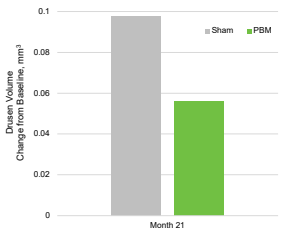
LIGHTSITE III: Macular Drusen Volume

Baseline drusen volume levels:

- Sham: 0.947 mm^3
- PBM: 0.973 mm^3

- A greater numerical increase (~2x) in change from baseline macular drusen volume was observed in Sham vs. PBM at Month 21



Data presented with multiple imputation. Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA, October 20, 2024.

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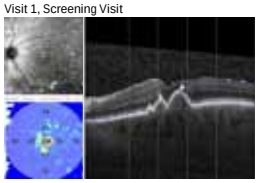
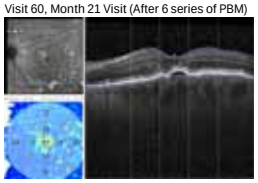
LIGHTSITE III: Macular Drusen Volume Reduction

Visit 1, Screening Visit



Visit 60, Month 21 Visit (After 6 series of PBM)



Representative OCT imaging from a 77-year-old female subject showing a significant reduction in macular drusen volume after the final series of PBM treatment at Month 21 without visible loss of photoreceptor or retinal pigment epithelium.

Starting BCVA: 75 letters

Month 13 BCVA (4 series of PBM): 79 letters; 4 letter gain

Month 21 BCVA (6 series of PBM): 84 letters; 9 letter gain

Month 24 BCVA (3 months after final PBM Tx): 82 letters; 7 letter gain

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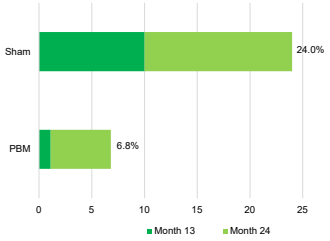
LIGHTSITE III: Incident Geographic Atrophy

Disease progression to incident GA significantly higher in the Sham group vs PBM group at Month 24:

- Month 13, p = 0.024 (Fisher exact test, odds ratio 9.4)
  - Sham group: 5/50 (10.0%)
  - PBM group: 1/87 (1.1%)
- Month 24, p = 0.007 (Fisher exact test, odds ratio 4.2)
  - Sham group: 12/50 (24.0%)
  - PBM group: 6/87 (6.8 %)



Data presented with actual values. Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA. October 20, 2024.

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LIGHTSITE III: Incident Geographic Atrophy Baseline Characteristics

	PBM	Sham
Incident GA	6/87 (6.8%)	12/50 (24.0%)
Central-involving	0/0 (0.0%)	7/12 (58.3%)
Non-central	5/6 (83.3%)*	5/12 (41.7%)
High Risk for progression (Category 4)	6/6 (100%)	9/12 (75%)
Companion Non-study eye with Central GA	3/6 (50%)	1/12 (8.3%)

* 1 eye converted to nAMD prior to month 24

- The majority of eyes that converted to GA in the PBM group showed development of non-central GA (n=5/6, 83.3%)
- The majority of eyes that converted to GA in the Sham group showed development of central-involving GA (n=7/12, 58.3%)
- PBM eyes that developed GA were at higher risk for GA conversion compared to the Sham group

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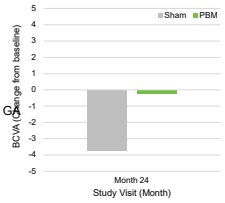
LIGHTSITE III: Geographic Atrophy BCVA Summary

In eyes that developed GA, PBM-treated eyes showed better BCVA outcomes

Month 24 incident GA, p = 0.007
- Sham group: 12/50 (24.0%)
  - 7/12 (58.3%) eyes developed central-involving GA
  - 5/12 (41.7%) eyes developed non-central involving GA
- PBM group: 6/87 (6.8 %)
  - 5 (83.3%) eyes developed non-central-involving GA*
  - No eyes developed central-involving GA

Month 24 BCVA (Mean change from baseline) in eyes with new GA
- Sham group (All, n=12): -3.75
  - Eyes with Central GA (n=7): -6.14 letters
  - Eyes with non-central GA (n=5):-0.4 letters
- PBM group (All, n=5): -0.2 letters
  - Eyes with non-central GA (n=5): -0.2 letters



* 1 eye converted to nAMD and BCVA data not available

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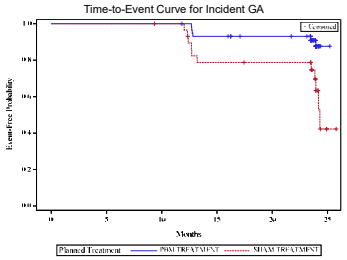
LIGHTSITE III: Reduction of Incident GA

- A post-hoc Cox proportional hazards model time to event hazard ratio of GA incidence
- The hazard ratio (HR) for GA incidence was 0.27, (p < 0.006) indicating a statistically **significant risk reduction of 73% to new incident GA over 24-months with PBM vs. Sham treatment**



Du, D. et al., Photobiomodulation for Dry AMD. Presented at the American Academy of Ophthalmology, Chicago, IL, USA. October 20, 2024.

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LIGHTSITE III: Ocular Adverse Event Reporting

System Organ Class Preferred Term	Sham (N = 55) n (%)	PBM (N = 93) n (%)	Total (N = 148) n (%)
Serious Adverse Events	**3 (5.5)**	**7 (7.5)**	**10 (6.8)**
nAMD (neovascular AMD)	2 (3.6) [7.3%]*	7 (7.5)	9 (6.1)
Cystoid Macular Edema	1 (1.8)	0 (0.0)	1 (0.7)
Adverse Events	**14 (25.5)**	**24 (25.8)**	**38 (25.7)**
Vitreous Floaters	4 (7.3)	1 (1.1)	5 (3.4)
Dry Eye	2 (3.6)	1 (1.1)	3 (2.0)
Punctate Keratitis	2 (3.6)	1 (1.1)	3 (2.0)
Vitreous Detachment	1 (1.8)	2 (2.2)	3 (2.0)
Blepharitis	0 (00.0)	2 (2.2)	2 (1.4)
Conjunctival Haemorrhage	0 (00.0)	2 (2.2)	2 (1.4)
Conjunctivitis Allergic	0 (00.0)	2 (2.2)	2 (1.4)
Cystoid Macular Oedema	2 (3.6)	0 (0.0)	2 (1.4)
Eye Pain	0 (00.0)	2 (2.2)	2 (1.4)
Foreign Body Sensation In Eyes	0 (00.0)	2 (2.2)	2 (1.4)
Lacrimation Increased	0 (00.0)	2 (2.2)	2 (1.4)
Lamellar Macular Hole	0 (00.0)	2 (2.2)	2 (1.4)
Photopsia	0 (00.0)	2 (2.2)	2 (1.4)
Posterior Capsule Opacification	1 (1.8)	1 (1.1)	2 (1.4)
Abnormal Sensation In Eye	1 (1.8)	0 (0.0)	1 (0.7)

*Prevalence of High-Risk Eyes (comparison eye with nAMD at Baseline) was 3x higher (12:4) in the PBM group vs. Sham group - when Sham is normalized to the higher rate, development frequency would be estimated at 7.3%.

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LIGHTSITE III: Ocular Adverse Event Reporting

System Organ Class Preferred Term	Sham (N = 55) n (%)	PBM (N = 93) n (%)	Total (N = 148) n (%)
Adverse Events (Continued)			
Amaurosis Fugax	0 (0.0)	1 (1.1)	1 (0.7)
Angle Closure Glaucoma	1 (1.8)	0 (0.0)	1 (0.7)
Cataract	1 (1.8)	0 (0.0)	1 (0.7)
Diplopia	0 (0.0)	1 (1.1)	1 (0.7)
Eye Discharge	1 (1.8)	0 (0.0)	1 (0.7)
Eye Irritation	0 (0.0)	1 (1.1)	1 (0.7)
Eye Pruritus	0 (0.0)	1 (1.1)	1 (0.7)
Open Angle Glaucoma	1 (1.8)	0 (0.0)	1 (0.7)
Photophobia	0 (0.0)	1 (1.1)	1 (0.7)
Retinal Vein Occlusion	0 (0.0)	1 (1.1)	1 (0.7)
Visual Perseveration	1 (1.8)	0 (0.0)	1 (0.7)
Vitreous Degeneration	0 (0.0)	1 (1.1)	1 (0.7)
General Disorders And Administration Site Conditions	0 (0.0)	1 (1.1)	1 (0.7)
Application Site Warmth	0 (0.0)	1 (1.1)	1 (0.7)
Infections and Infestations	0 (0.0)	1 (1.1)	1 (0.7)
Hordeolum	0 (0.0)	1 (1.1)	1 (0.7)
Vascular Disorders	1 (1.8)	0 (0.0)	1 (0.7)

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Dry AMD Trial nAMD Conversion Comparison

LIGHTSITE III showed a lower or comparable rate of nAMD conversion than other recently completed dry AMD trials

Valeda® Light Delivery System	Pegcetacoplan (Syfovre)	Avacincaptad pegol (Izervay)
LIGHTSITE I (12 Months)[1] PBM (2 series): 1/24 (4.2%) Sham: 0/22 (0.0%)	**OAKS (24 Months)[4]** • Tx (15 mg; monthly): 24 (11.0%, 25 events) • Tx (15 mg; EOM): 16 (8.0%, 17 events) • Sham: 4 (2.0%, 4 events)	**GATHER 1 (18 Months)[5]** • Tx (2 mg; monthly): 11.9% • Sham (2 mg): 2.7% • Tx (4 mg; monthly): 15.7% • Sham (4 mg): 2.4%
LIGHTSITE II (10 Months)[2] PBM (3 series): 1/34 (2.9%) Sham: 1/19 (5.3%)	**DERBY (24 Months)[4]** • Tx (15 mg; monthly): 27 (13.0%, 30 events) • Tx (15 mg; EOM): 12 (6.0%, 12 events) • Sham: 9 (4.0%, 11 events)	**GATHER 2 (12 Months; 24 Month data unavailable)[6]** • Tx (2 mg; monthly): 15 (7.0%) • Sham: 9 (4.0%)
LIGHTSITE III (24 Months)[3] PBM (6 series): 7/93 (7.5%) Sham: 2/55 (3.6%)[7.3]*		

*Prevalence of High-Risk Eyes (companion eye with nAMD at Baseline) was 3x higher (12:4) in the PBM group vs. Sham group - when Sham is normalized to the higher rate, development frequency is estimated at 7.3%. EOM (every other month). [1]Markowitz et al., Retina, 2019; [2]Burton et al., Ophthalmol Ther, 2023; [3]Do et al., AAO, 2024; [4]Heier et al., Lancet, 2023; [5]Patel et al., Eye, 2023; [6]Khanani et al., Lancet, 2023

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LIGHTSITE III: Trial Summary

LIGHTSITE III results show significant effect on clinical and anatomical outcomes that support vision improvement and disease modifying effects

- LIGHTSITE III met the primary efficacy endpoint with a statistically significant improvement in BCVA in the PBM versus the Sham group
- Eyes with worse BCVA at baseline showed larger magnitude gains in BCVA following PBM
- Increased rate of > 5, 10, and 15 letter BCVA gains following PBM compared to BCVA loss in the Sham group
- Cox proportional analyses showed a significant reduction in the hazard ratios for BCVA vision loss and incident GA in PBM vs Sham groups
- Reduced occurrence of incident GA and other exploratory markers of disease progression (reduced conversion incident iRORA, conversion to GA/cRORA) following PBM
- Reduced macular drusen volume following PBM
- Improved QoL in VFQ-25 Composite score and select subscales following PBM
- A favorable safety profile was observed following PBM with no signs of phototoxicity and no deterioration in other visual outcomes including contrast sensitivity, low luminance BCVA, Radner reading, perimetry, or color vision observed

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LIGHTSITE IIIB: Trial Summary

LIGHTSITE IIIB results show sustained visual gains

- LIGHTSITE IIIB was delayed 20 months after the conclusion of LIGHTSITE III
  - PBM treated eyes lost on average 2.2 letters during the treatment gap
  - SHAM treated eyes lost on average 5.7 letters during the treatment gap
  - PBM treated eyes in LIGHTSITE IIIB regained more than 5 letters
  - SHAM treated eyes in LIGHTSITE IIIB did not improve although did not continue to decline
  - ANALYSIS:
    - Suggests that PBM treated eyes sustained benefit over approximately 54 months with a cumulative gain of 5 letters
    - By month 13 of LIGHTSITE IIIB there was a 10 letter gap between eyes originally treated with PBM and those originally assigned to the SHAM group.
    - LIGHTSITE IIIB also concluded continued reduction in development of GA

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Snap shot of patients treated and completed 2 sessions

Number of Eyes: 131
Visual Acuity at enrollment 20/20 - 20/100
Staging of AMD at enrollment
Early / Intermediate AMD (110 eyes)
Advanced AMD with non central GA (21 eyes)

Eyes with > 5 letter gain = 92 (70%)
Eyes with >10 letter gain = 23 (18%)
Eyes with >15 letter gain = 6 (5%)

Development of non central GA lesion – 2 eyes
(collapsed drusenoid fibrovascular PED)
Conversion to nAMD – 2 eyes (also receiving Syfovre)

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Snap shot of patients treated and completed 9/9 sessions Subjective Assessment of Visual Function

Improved clarity of road signs while driving and watching TV

Increased reading comprehension

Less distortion on home amsler grid

Less trouble in lower light settings

Improved dark adaptation

Reduced glare sensitivity

Reduced size of dark spot noted in lower light settings (AM)

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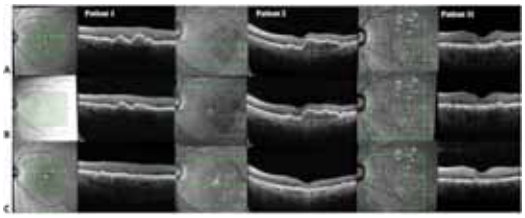
Investigator-Initiated Clinical Support

Valeda Improves Anatomical Outcomes in AMD



B-scan OCT demonstrating drusen reduction in dry AMD treated by Valeda. Baseline (A) imaging showing large macular drusenoid pigment epithelial detachment (PED) in patients 1 and 2 and soft drusen in patient 11. Week 5 (B) B-scan SD-OCT showing drusen volume evolution with a main reduction at the time points between week 5 and month 6. Month 6 (C) imaging illustrates the complete reduction of the drusenoid PED and soft drusen after a series of 10 Valeda treatments.

Benlahbib et al., Retina, 2023

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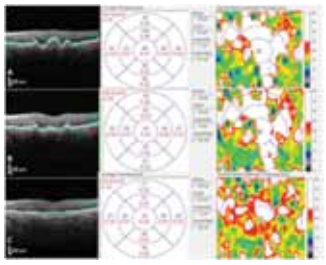
Investigator-Initiated Clinical Support

Valeda Improves Anatomical Outcomes in AMD

Evaluation of a low reflective homogenous drusen larger than 125 mm using SPECTRALIS HRA system after segmentation of the RPE and Bruch membrane (BM) within the central 6-mm diameter of the macula. Drusen volume (DV) and mean central drusen thickness reduction in an eye categorized as AREDS 3 treated by Valeda. Baseline (A) SD-OCT illustrates DV of 0.31 mm3 with CDT of 89 mm. On the left side, the color-coded drusen thickness map illustrated the anatomical improvement. Week 5 (B) SD-OCT showed DV reduction to 0.24 mm3 with CDT of 43 mm. On the left side, the color-coded drusen thickness map illustrated the anatomical improvement. At month 6 after Valda therapy (C) SDOCT demonstrated a global decrease in DV (0.15 mm3) and CDT (32 mm). SD-OCT confirmed no newly development of GA, or irregularity of the photoreceptor.



Benlahbib et al., Retina, 2023

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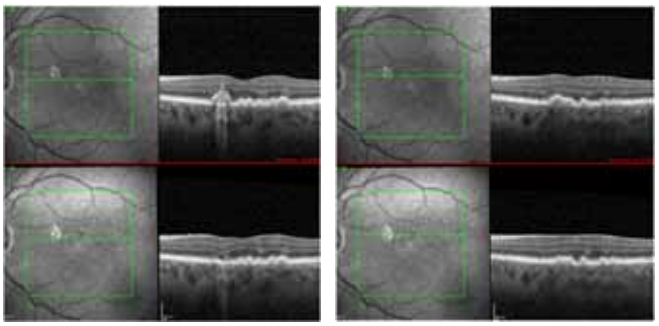
Anatomic changes noted post 9/9 sessions



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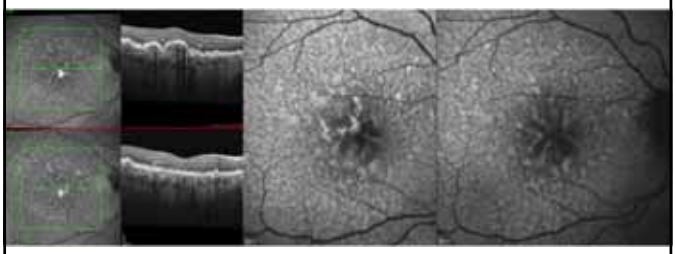
Anatomic changes noted post 9/9 sessions



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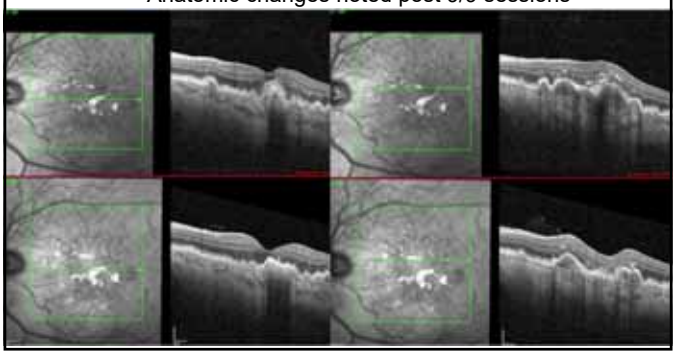
Anatomic changes noted post 9/9 sessions



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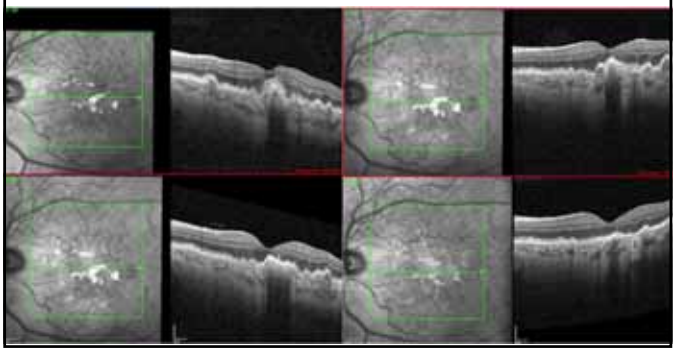
Initial and post 9/9 | Beginning and end of second session



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Growing and Robust Dossier of Clinical Data

Increasing number of publications using PBM in Ophthalmology

- >10,000 published articles in PBM
- >200 articles of PBM in Ophthalmology
  - At least 12 published clinical studies conducted in AMD

Consistent demonstrations of PBM effects improving visual outcomes in AMD with low to no reports of any adverse effects
- Global publications across multiple centers
- Variety of outcome measures
- Differing treatment populations
- Translation to other ocular indications

	No. of Subjects/Eyes
Valeda Studies (peer reviewed and presented study data)	493 subjects; 739 eyes
Other PBM devices*	>900 subjects; >1500 eyes
Total Estimate of PBM use in ocular studies*	>1300 subjects; >2,200 eyes

** Estimates reflect publications in retinal disease.*

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Case Presentation: The patient's husband

- This patient was not actually referred to me…he was attending his wife's retina appointment when he told me the following story:

Patient (78 yo white male) states that he was watching a volleyball game on 11/1/24 when he had sudden, complete loss of vision in the left eye. He had called CEI and was told to go to the ER. 85% carotid blockage on the left side. He immediately underwent a carotid endarterectomy. Patient realizes his vision may not come back in the left eye.

- On 11/8/24: He was diagnosed with a Central Retinal Artery Occlusion that was by one of CEI's Comprehensive Ophthalmologists
- He sees me the next day, 12/5/24
  - Med History: HTN, High Cholersterol, Type 2 Diabetes A1C 7 (11/1/24), Heart disease
  - BCVA OD 20/20-1, OS HM
  - +APD OS
  - IOP: 10 mmgHg OD and 17 mmHg OS

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Anatomy refresher

- The retina receives a dual blood supply,
  - inner retina supplied by the central retinal artery
  - outer retina supplied by the choroidal circulation via branches of the posterior ciliary arteries
- Both sets of arteries arise from the ophthalmic artery, the first branch of the internal carotid artery.
- The ophthalmic artery passes through the optic canal inferolaterally to the optic nerve.
- On entering the orbit, the central retinal artery leaves the ophthalmic artery and travels within the optic nerve.
- Approximately 15%-30% of the population has a cilioretinal artery, a branch of the short posterior ciliary artery. It supplies blood to part or all of the fovea. If a CRAO occurs in such eyes, the cilioretinal artery is spared, typically preserving visual acuity at 20/50 or better, although peripheral visual field is still severely impaired.

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CRAO is an ocular emergency!!

- Profound, acute, painless monocular visual loss
  - 80% of affected individual have a final visual acuity of counting fingers or worse.
- CRAO is the ocular analogue of a cerebral stroke—and, as such, the clinical approach and management are relatively similar to the management of stroke:
  - Treat the acute event, identify the site of vascular occlusion, and try to prevent further occurrences.
- The incidence of CRAO is approximately 1 to 2 in 100,000, with a *male* predominance and mean age of *60-65 years*.

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Risk Factors: Nonarteritic vs Arteritic

- **Nonarteritic.** More than 90% of CRAOs are nonarteritic in origin.
  - Ipsilateral carotid artery atherosclerosis is the most common cause of retinal artery occlusion with a prevalence as high as 70% reported among patients with CRAO or branch retinal artery occlusion.
  - Other causes of nonarteritic retinal artery occlusion:
    - cardiogenic embolism, hematological conditions (sickle cell disease, hypercoagulable states, leukemia, lymphoma, etc.), and other vascular diseases, such as carotid artery dissection, moyamoya disease, and Fabry disease
- **Arteritic.** CRAO of arteritic etiology is mostly caused by giant cell arteritis (GCA)
  - Other vasculitic disorders such as Susac syndrome, systemic lupus erythematosus, polyarteritis nodosa, and granulomatosis with polyangiitis have also been associated with retinal artery occlusion.

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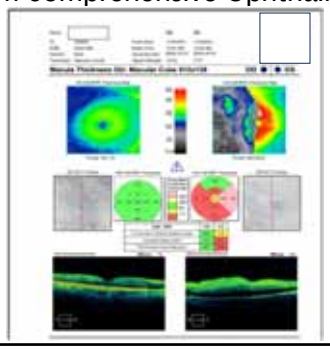
OCT from Comprehensive Ophthalmologist



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Visual Field of Left Eye

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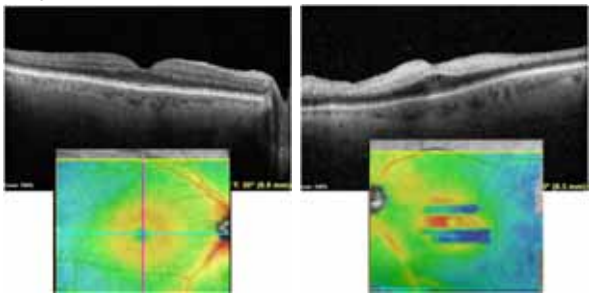
My exam 12/5/24: OCT



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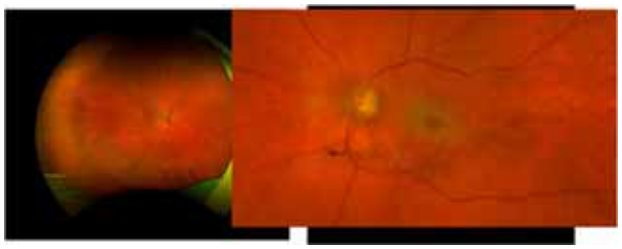
Cherry red spot remains even 1 month later OS

12/5/24



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And then there was this…

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Fluorescein Angiography

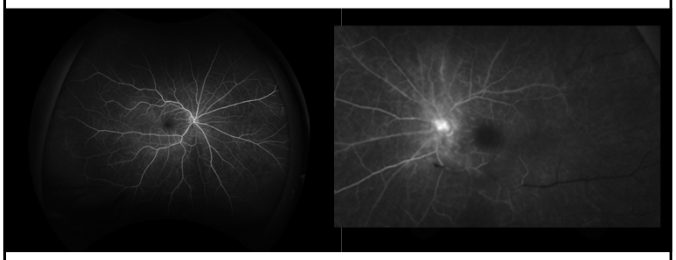

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Table 1 Treatment Options for CRAO

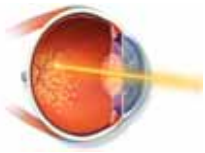
TREATMENT	MECHANISM OF ACTION
Pharmacological	
IV acetazolamide	Reduce intraocular pressure
IV mannitol	Reduce intraocular pressure
Topical antiglaucoma medications	Reduce intraocular pressure
Pentoxifylline	Vasodilation to increase blood oxygen content
Inhalation of carbogen	Vasodilation to increase blood oxygen content
Sublingual isosorbide dinitrate	Vasodilation to increase blood oxygen content
IV methylprednisolone	Reduce retinal edema, only given in arteritic CRAO
IV or intra-arterial recombinant tissue plasminogen activator (rt-PA)	Thrombolytic therapy to dissolve clot
Hyperbaric oxygen therapy	Increase blood oxygen tension
Surgery/Procedures	
Anterior chamber paracentesis	Reduce intraocular pressure
Ocular massage	Fluctuations in intraocular pressure to mechanically dislodge clot
Nd:YAG laser embolectomy	Lyse or dislodge the clot
Pars plana vitrectomy	Surgical removal of the clot
Lifestyle Modification	
Optimization of atherosclerotic diseases	Secondary prevention

www.aao.org/eyenet/article/diagnosis-and-management-of-crao

72

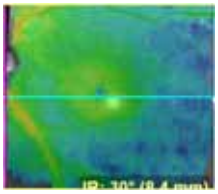
Treatment:
Stat to the RS for CRAO with NVD and NVI/A OS

- Stat IVA OS q 1 month
- Schedule PRP OS x 3 aggressive treatment plan
- Patient is on Eliquis and ASA as per Cardiovascular surgeon



73

After one month of treatment:
12/05/24 to 1/9/2025



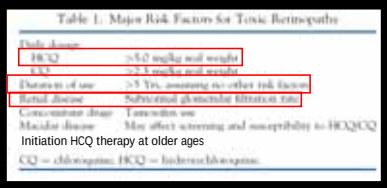
74

75

IT'S THE LITTLE THINGS THAT MATTER MOST

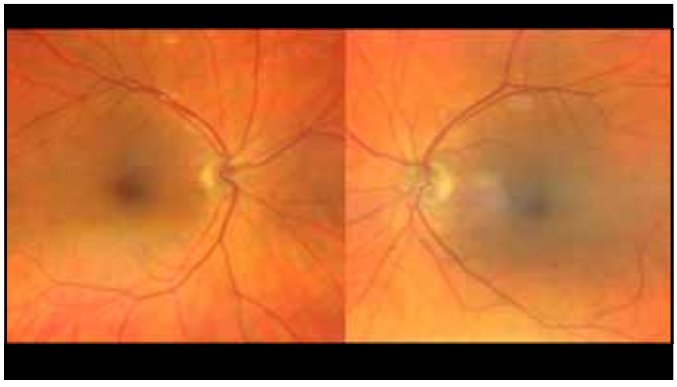
70yo Native American female

- Taking Plaquenil 200mg BID x **15-20 years for RA**
- Weight: 157lbs (**max daily dose = 356mg**)
- **Stage 3 CKD**, former smoker
- BCVAs OD 20/20, OS 20/20



Initiation HCQ therapy at older ages

76



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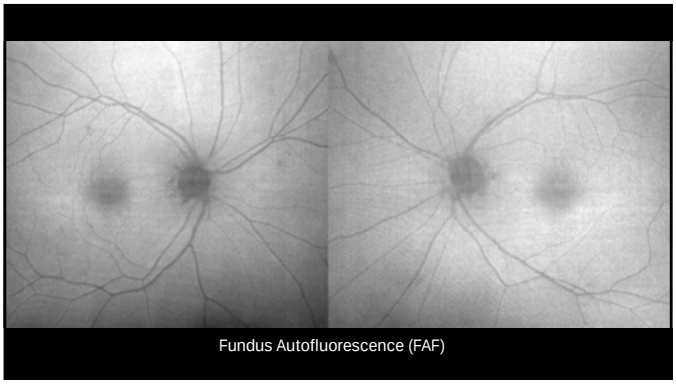
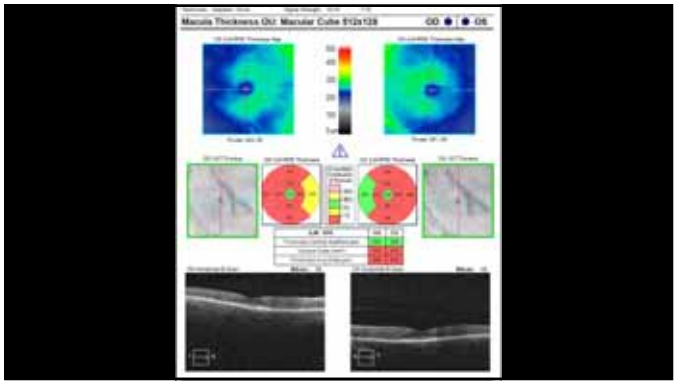


Fundus Autofluorescence (FAF)

78



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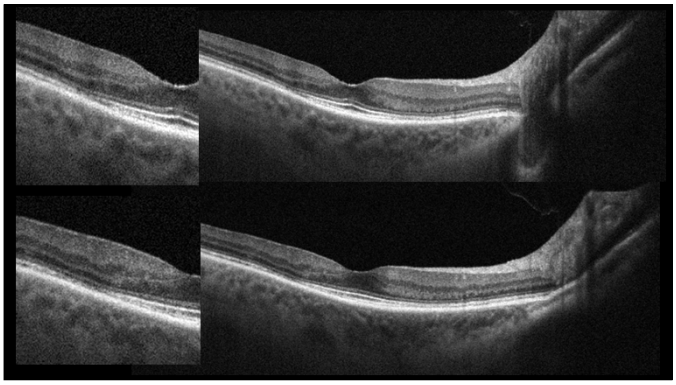

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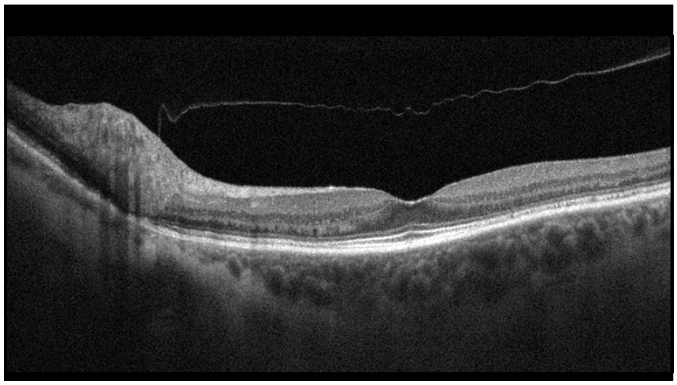

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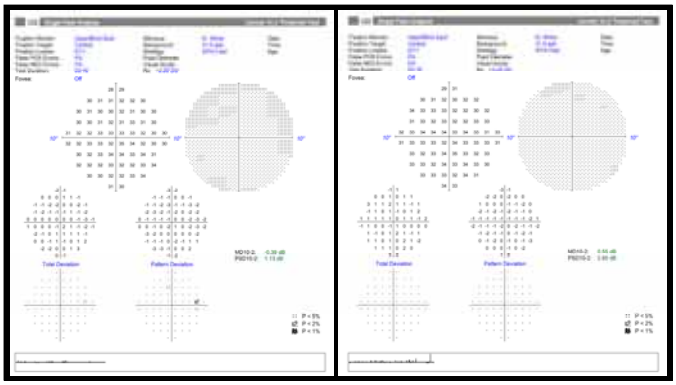

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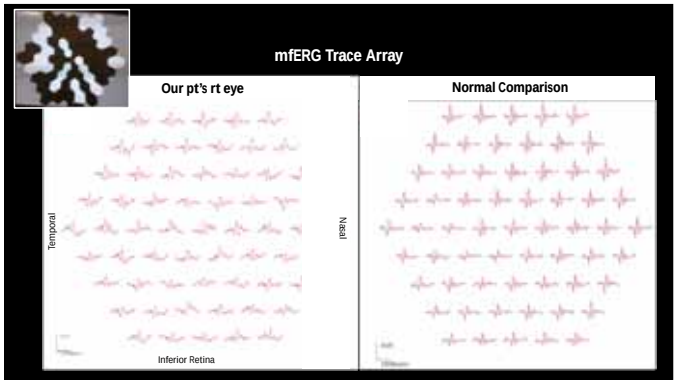

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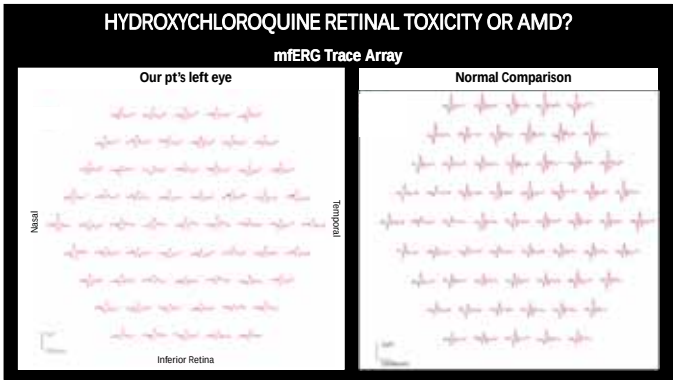

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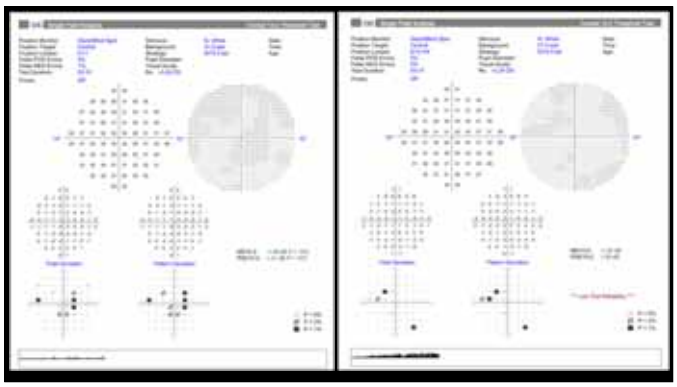


85

Hydroxychloroquine Retinal Toxicity

AAO 2026 Recommendations on Screening: Primary Screening Methods

Spectral Domain (SD) -OCT

- Diffuse outer retinal thinning/change may be detected by comparison of sequential en face images of retinal thickness (progressive thinning may be evident several years before EZ alteration becomes evident in the OCT B-scan images)
- Focal thinning of the interdigitation zone (IZ line) and EZ; May lead to the appearance of a "bright line" sign under the fovea caused by central EZ & IZ preservation

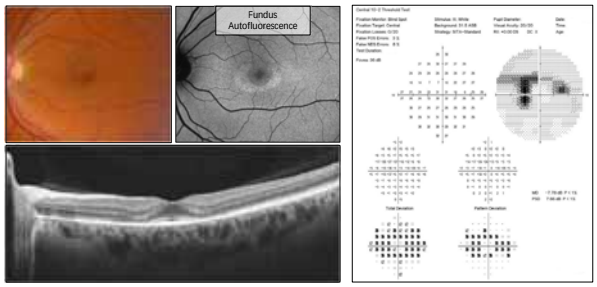
"Wide-pattern" FAF

- Particularly important for the recognition of a pericentral pattern of maculopathy
- Scans should extend beyond the arcades (roughly 30 degrees), and ideally out to 50 or 55 degrees
- Early toxicity involves hyperautofluorescence most often in the inferotemporal quadrant.

* Secondary screening methods: VF (24-2c can screen parafoveal and pericentral regions simultaneously), mfERG

86

Hydroxychloroquine Retinal Toxicity



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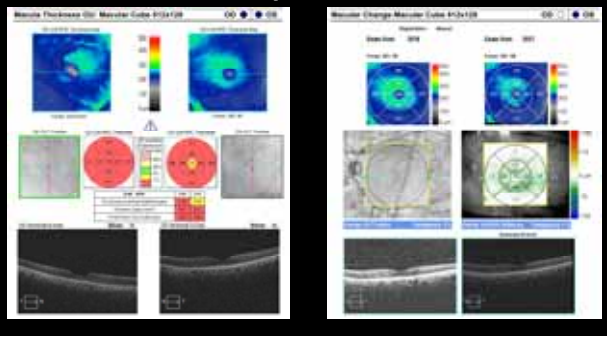
HYDROXYCHLOROQUINE RETINAL TOXICITY



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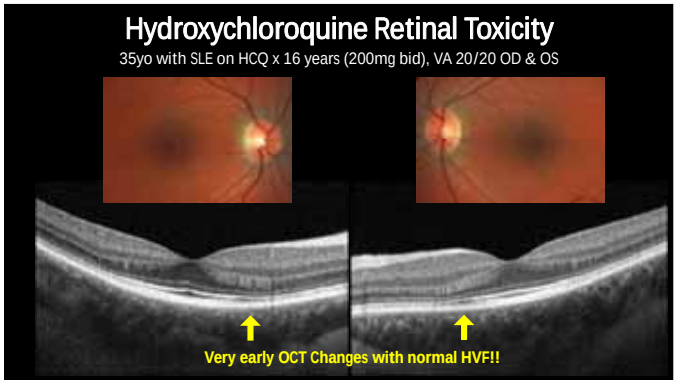
Hydroxychloroquine Retinal Toxicity

35yo with SLE on HCQ x 16 years (200mg bid), VA 20/20 OD & OS



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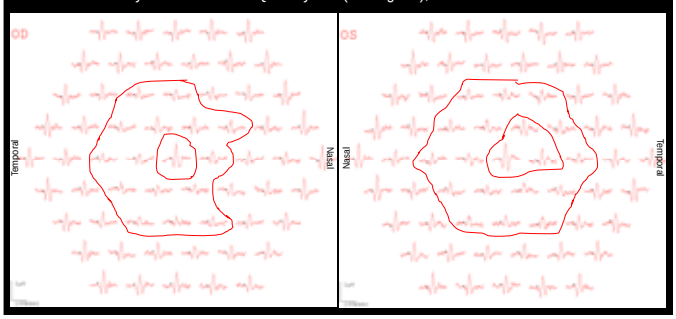
Hydroxychloroquine Retinal Toxicity

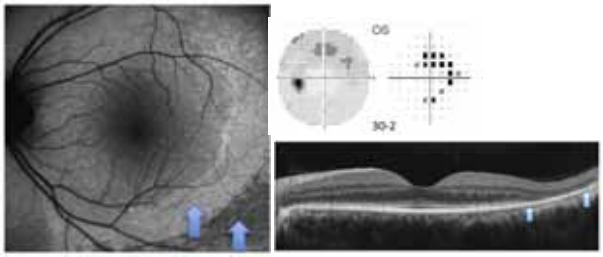
35yo with SLE on HCQ x 16 years (200mg bid), VA 20/20 OD & OS



90

Hydroxychloroquine Retinal Toxicity

Patients of East Asian descent, including both Northeast & Southeast Asia, typically show initial extramacular toxicity near the arcades



AAO. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy 2016.

91

Choroidal Neovascular Membrane

Pathologic Myopia

Jay M. Haynie, OD, FAAO, FORS
Sound Retina
Tacoma Washington, USA
DrJay@soundretina.com

92

CNV secondary to Pathologic Myopia

Incidence of Choroidal Neovascular Membrane is 5-11%

62% of CNV secondary to Myopia occurs before age of 50

3.5% develop CNV in both eyes over lifetime

93

CNV secondary to Pathologic Myopia

Mechanism for CNV not clearly understood

- Inflammatory
- Choroidal Thinning
- Choroidal Hyoperfusion
- Lacquer Cracks

Diagnosis should be considered for any patient with Myopia who presents with ACUTE central vision loss

94

CNV secondary to Pathologic Myopia

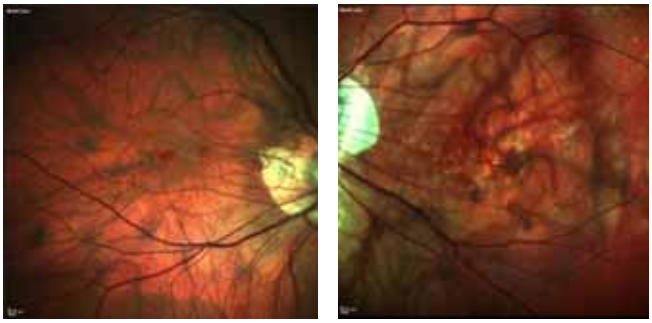
Clinical and Diagnostic testing:

Retinal Photos:

- Not always obvious as CNV is often smaller and not always associated with hemorrhage or obvious retinal edema
- Focal darkened area should raise suspicion

95

CNV secondary to Pathologic Myopia



96

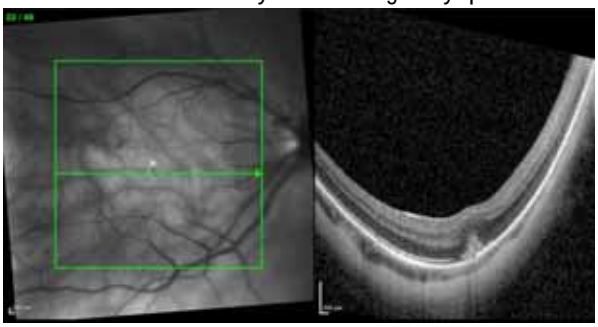
CNV secondary to Pathologic Myopia

Clinical and Diagnostic testing:

- Ocular Coherence Tomography:
  - Focal hyper reflective thickening of the RPE
  - Unlike CNV secondary to AMD you may not see subretinal fluid or intraretinal edema

97

CNV secondary to Pathologic Myopia



98

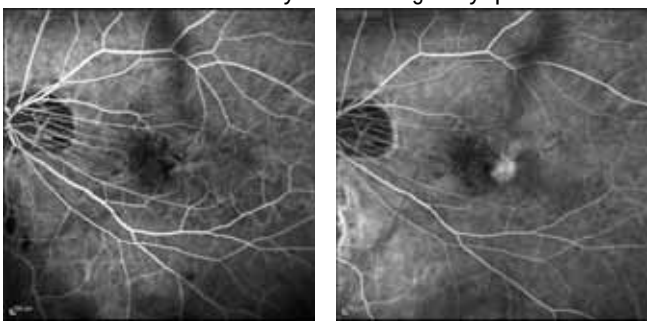
CNV secondary to Pathologic Myopia

Clinical and Diagnostic testing:

- Fluorescein Angiography:
  - Focal hyper reflective well defined lesion (early)
  - Intense leakage (late) – may not leak as much as CNV secondary to AMD

99

CNV secondary to Pathologic Myopia



100

CNV secondary to Pathologic Myopia

Treatment:

- Anti-VEGF compounds
  - Lucentis (Ranibizumab) – only FDA approved compound
  - Avastin (Bevacizumab), Eylea (Aflibercept) and Vabysmo (Faricimab) accepted off label
- Biosimilars
  - Cimerli (Ranibizumab)

101

CNV secondary to Pathologic Myopia

Treatment:

- Anti-VEGF compounds
  - 1+ injection followed by PRN dosing most acceptable
  - Clinical studies favor this treatment compared to 3+ injections followed by treat and extend (TREX) which is typical for CNV secondary to AMD

102

CNV secondary to Pathologic Myopia

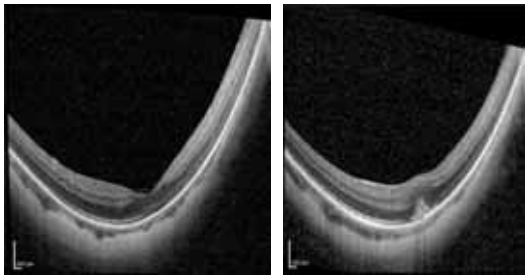
Case 1:

53 YO WM with Myopia
POHx: Retinal Detachment Repair OD 2019
Blurred vision with central distortion OD for 2 months
VA 20/30-2 PH NI

OCT confirmed well defined subfoveal CNV
Treatment: Avastin (Bevacizumab)

103

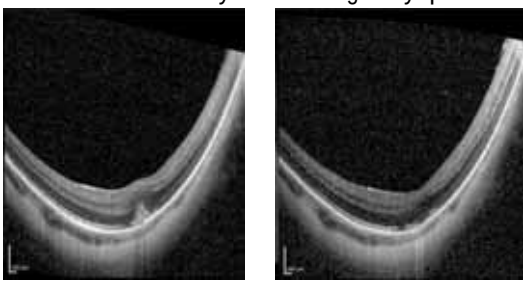
CNV secondary to Pathologic Myopia



OCT 2021 OCT 2024

104

CNV secondary to Pathologic Myopia



Initial OCT and post treatment with Avastin – VA 20/20-1

105

CNV secondary to Pathologic Myopia

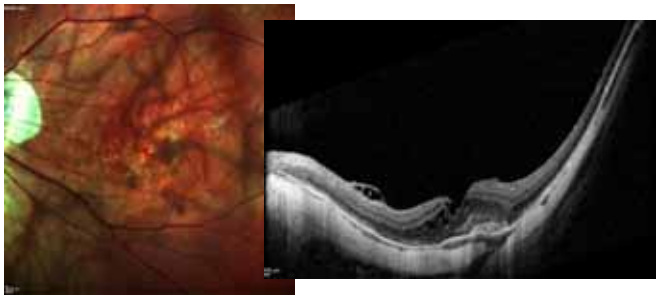
Case 2:

70 YOWF
POHx: ERM with mild foveoschisis
Sudden onset central distortion OS
Referred back for management of ERM
VA OS 20/50-2

OCT confirmed well defined subfoveal CNV
Treatment:

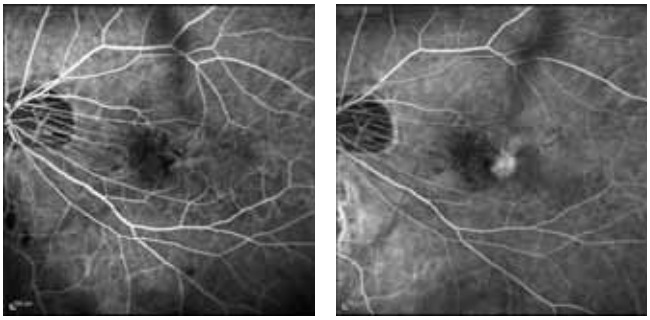
106

CNV secondary to Pathologic Myopia



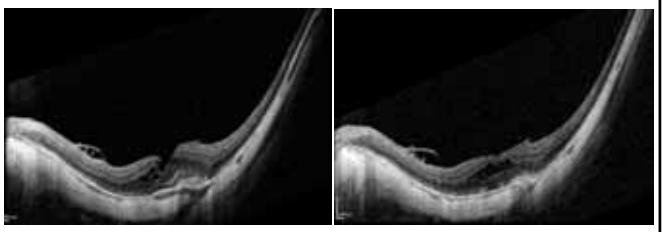
107

CNV secondary to Pathologic Myopia



108

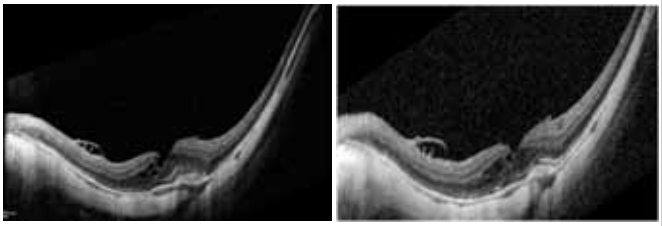
CNV secondary to Pathologic Myopia



Initial OCT Post Vabysmo #1

109

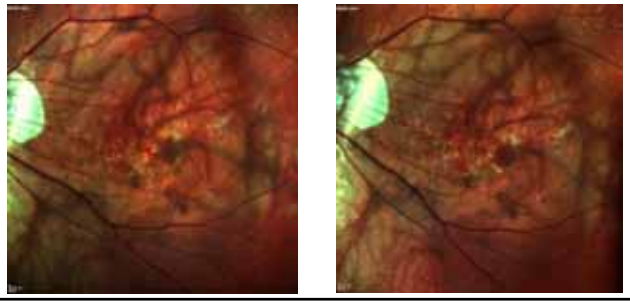
CNV secondary to Pathologic Myopia



Initial OCT Post Vabysmo #3

110

CNV secondary to Pathologic Myopia
Multimodal Imaging Pre and Post Treatment



111

CNV secondary to Pathologic Myopia

Case 3:

71 YOAF
Shadow in central vision of left eye for 3 weeks
VA OS 20/80

OCT confirmed well defined thickening of the RPE
OCT confirmed a well defined vascular CNV
Treatment: Avastin

112

CNV secondary to Pathologic Myopia

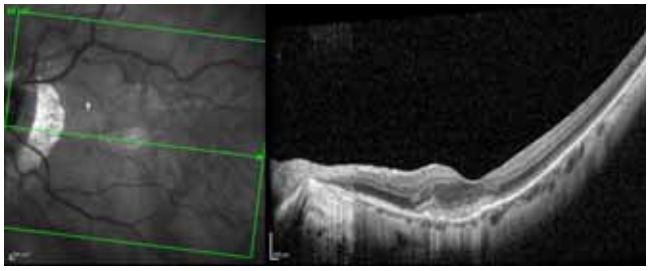
Color Fundus Photography

Tilted ONH with myopic crescent temporal

Subtle Macular hemorrhage with gray thickening subfoveal

113

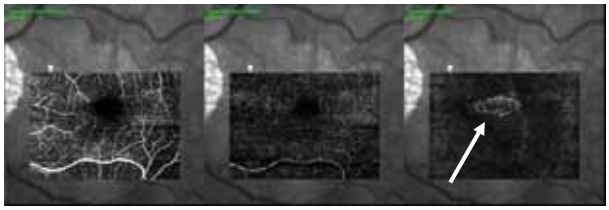
CNV secondary to Pathologic Myopia



OCT confirms a well defined area of subretinal thickening

114

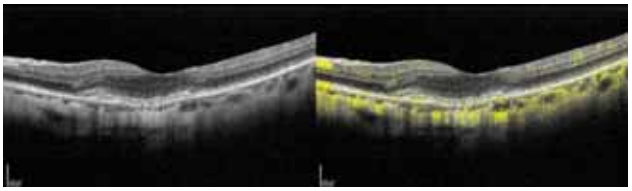
CNV secondary to Pathologic Myopia



OCTA confirms a well defined lesion in the "avascular layer"

115

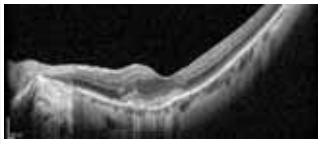
CNV secondary to Pathologic Myopia

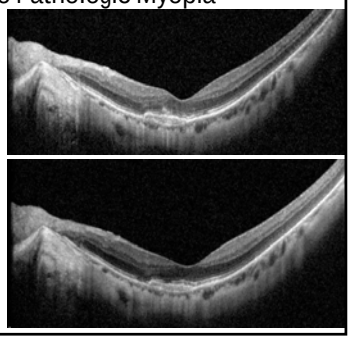


OCTA confirms a "vascular lesion" consistent with CNV

116

CNV secondary to Pathologic Myopia



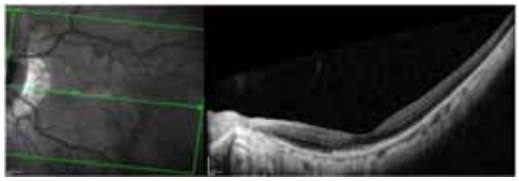


Post treatment with Avastin – regression of CNV noted

117

CNV secondary to Pathologic Myopia

Post treatment with Avastin – regression of CNV noted and stable over 6M



118

CNV secondary to Pathologic Myopia

Summary:

Diagnosis should be considered for any patient with Myopia who presents with ACUTE central vision loss

Clinical features may be subtle on fundoscopic examination
OCT imaging will confirm thickening (hyper reflectivity) of the RPE
May not see hemorrhage on clinical examination or photos
May not see subretinal or intraretinal fluid on OCT

Treatment with Anti-VEGF – 1+ PRN dosing

119

CNV secondary to POHS / Idiopathic

Clinical and Diagnostic testing:

- Ocular Coherence Tomography:
  - Focal hyper reflective thickening of the RPE
  - Unlike CNV secondary to AMD you may not see subretinal fluid or intraretinal edema
- OCT Angiography:
  - Vascular lesion above the retinal pigment epithelium

120

CNV secondary to POHS / Idiopathic

Clinical and Diagnostic testing:

Fluorescein Angiography:

Early Phase typically reveals a well defined lesion

Intense leakage (late) consistent with CNV

121

CNV secondary to POHS / Idiopathic

Treatment:

Anti-VEGF compounds

- No FDA approved compounds – all are used off label

Neovascular AMD (atypical presentation)

122

CNV secondary to POHS / Idiopathic

Treatment:

Anti-VEGF compounds

3+ injection followed by PRN dosing most acceptable

Clinical studies favor this treatment compared to injections followed by treat and extend (TREX) which is typical for CNV secondary to AMD

123

Idiopathic CNV

Case 1:

50 YO AAM

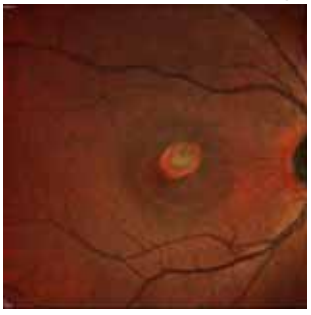
Blurred vision right eye for the past 3 months – described as a smudge or blind spot causing missing letters with reading

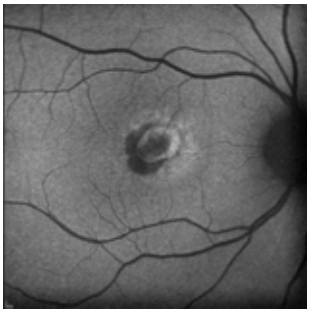
PMHx – unremarkable

VA 20/100-1 OD

124

Idiopathic CNV





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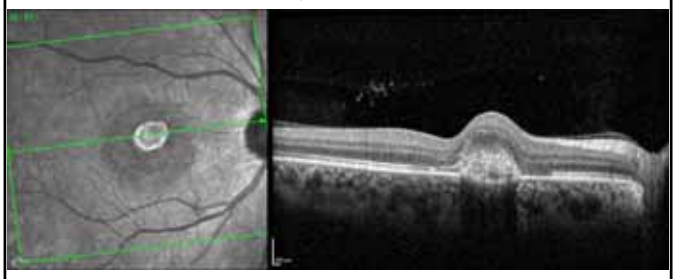
Idiopathic CNV



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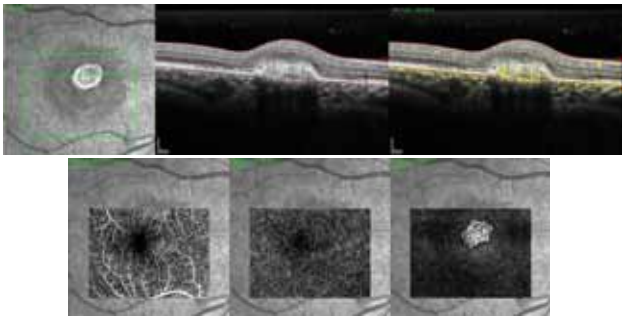
Idiopathic CNV



127

Idiopathic CNV

Case 1:

Treatment with Avastin was advised and recommended a follow up in 4-6 weeks although patient is now LTFU.....

128

CNV secondary to POHS

Case 2:

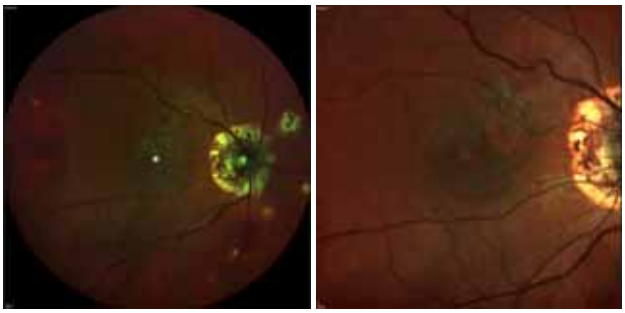
52 YOWF presented for evaluation – She reports blurred vision of right eye for the past 4-5 months – born and raised in OHIO

POHx: Reports prior "injections" in right eye for "edema"
Meds: Hormone Replacement therapy and antidepressants

VA OD 20/30-1

129

CNV secondary to POHS



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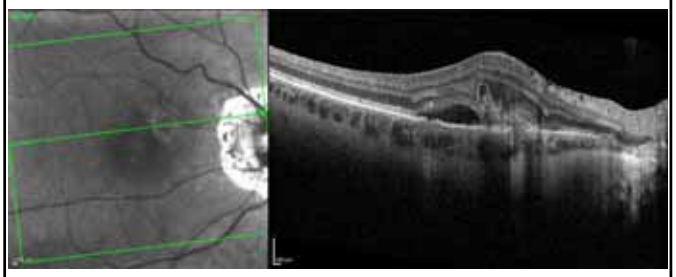
CNV secondary to POHS



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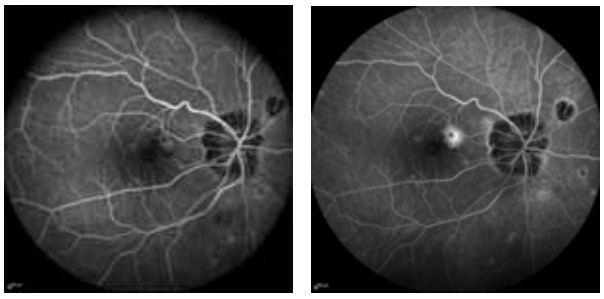
CNV secondary to POHS



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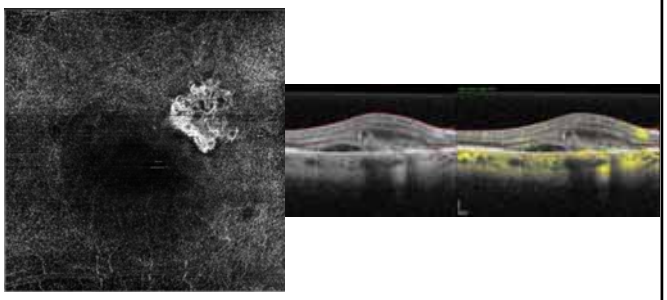
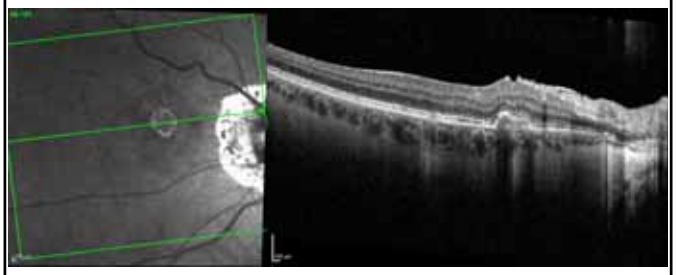
CNV secondary to POHS



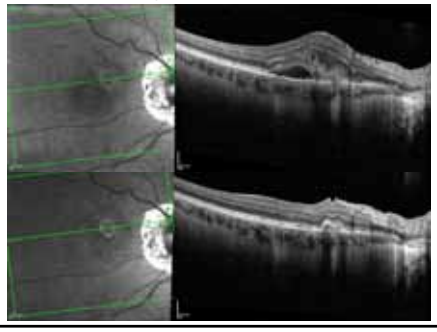
133

CNV secondary to POHS – Post Treatment (IVA 3)



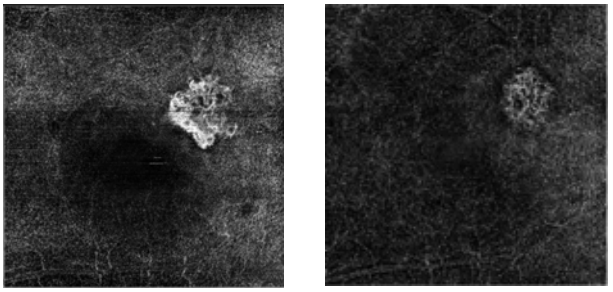
134

CNV secondary to POHS – Post Treatment



135

CNV secondary to POHS – Post Treatment



136

CNV secondary to Macular Telangiectasia

Macular Telangiectasia is seen in about 0.1% of the population with an average age at diagnosis being 63

Progression through stages 1-5 is likely with Stage 5 being secondary neovascularization which can result is irreversible central vision loss

Incidence of CNV secondary to macular telangiectasia is estimated to be up to 13% although limited data is available

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CNV secondary to Macular Telangiectasia

Mechanism for CNV not clearly understood

- Aneurysmal leakage over time triggers release of VEGF and therefore secondary neovascularization develops

Diagnosis should be considered for any patient with Macular Telangiectasia who presents with acute symptoms of vision loss

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CNV secondary to Macular Telangiectasia

Clinical and Diagnostic testing:

- Ocular Coherence Tomography:
  - Focal hyper reflective thickening of the RPE
  - Unlike CNV secondary to AMD you may not see subretinal fluid or intraretinal edema
- OCT Angiography:
  - Vascular lesion above the retinal pigment epithelium

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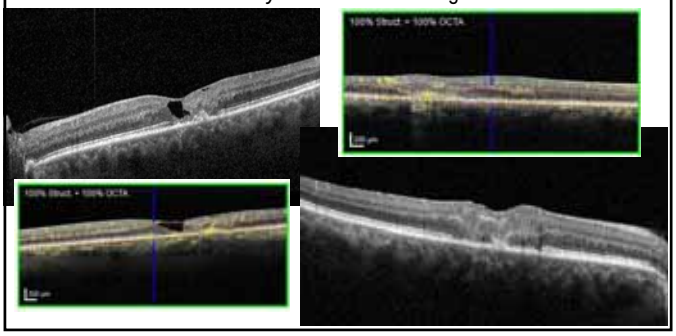
CNV secondary to Macular Telangiectasia



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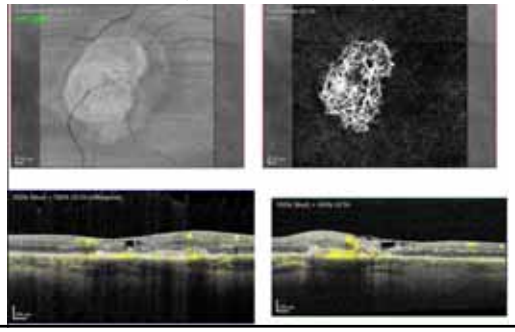
CNV secondary to Macular Telangiectasia



141

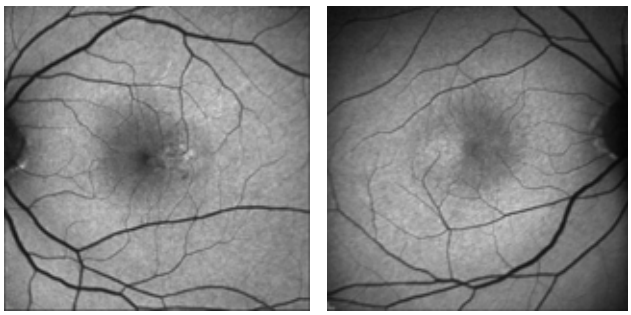
CNV secondary to Macular Telangiectasia

Clinical and Diagnostic testing:

- Fundus Autofluoresence
  - Mixed pattern AF in parafoveal region (temporal)
  - Right angle telangiectasis noted within vasculature

142

CNV secondary to Macular Telangiectasia



143

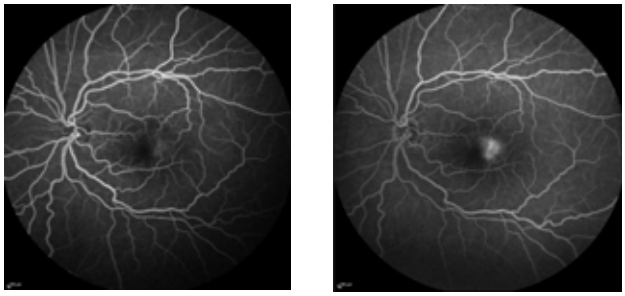
CNV secondary to Macular Telangiectasia

Clinical and Diagnostic testing:

- Fluorescein Angiography:
  - Patchy (parafoveal) hyperfluoresence (early) with telangiectasia
  - Intense leakage (late) – may not leak as much as CNV secondary to AMD

144

CNV secondary to Macular Telangiectasia



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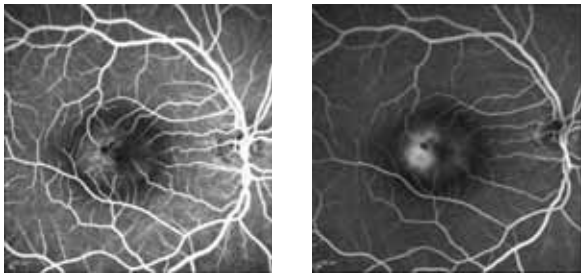
CNV secondary to Macular Telangiectasia



146

CNV secondary to Macular Telangiectasia

Treatment:

Anti-VEGF compounds

- No FDA approved compounds – all are used off label

Neovascular AMD (atypical presentation)

147

CNV secondary to Macular Telangiectasia

Treatment:

Anti-VEGF compounds

3+ injection followed by PRN dosing most acceptable

Clinical studies favor this treatment compared to injections followed by treat and extend (TREX) which is typical for CNV secondary to AMD

148

CNV secondary to Macular Telangiectasia

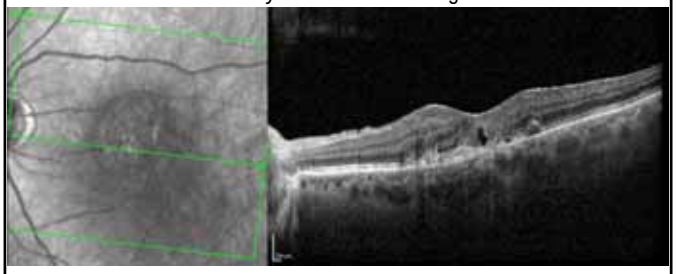
Case 1:

70 YO WM with Macular Telangiectasia

Poor vision in right eye for 10+ years secondary to macular hole
Blurry “spot” in vision of left eye for 6M

149

CNV secondary to Macular Telangiectasia



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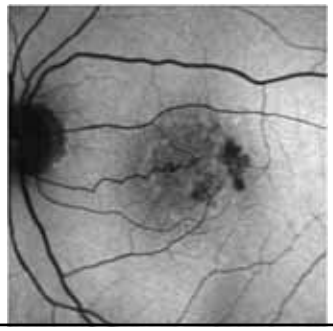
CNV secondary to Macular Telangiectasia

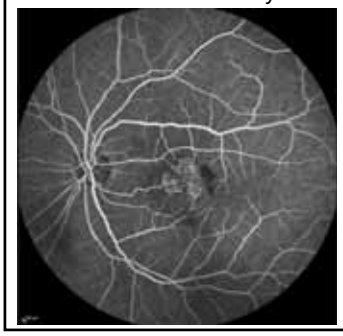


Fundus Autofluoresence

Note right angle vascular changes temporal macula

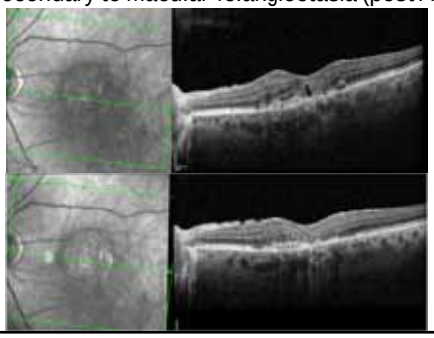
151

CNV secondary to Macular Telangiectasia



152

CNV secondary to Macular Telangiectasia (post Avastin)



153

CNV secondary to Macular Telangiectasia

Case 2:

61 YO WM with Macular Telangiectasia

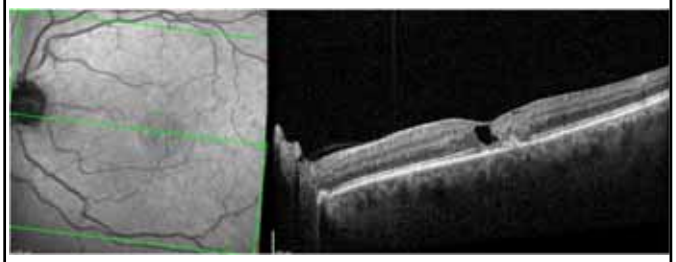
History of treatment OD with "unknown compound" and here as a transfer of care. "Doctor is concerned about a macular hole OS"

Central distortion OS for 6 months

Vision 20/200 OD and 20/25 OS

154

CNV secondary to Macular Telangiectasia



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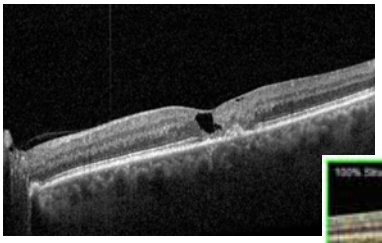
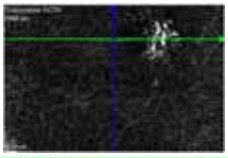
CNV secondary to Macular Telangiectasia





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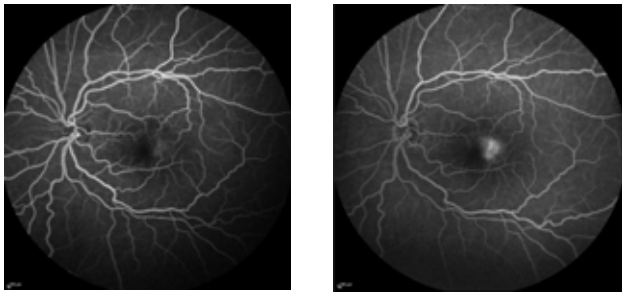
CNV secondary to Macular Telangiectasia



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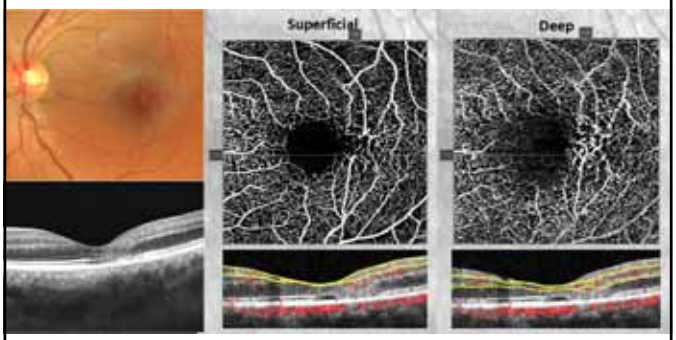

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CNV secondary to Macular Telangiectasia

Summary:

Diagnosis should be considered for any patient with MacTel who presents with central vision loss or metamorphopsia

Clinical features will include parafoveal telangiectasia with gray thickening and often pigment hyperplasia with or without aneurysmal lesions

OCT imaging will confirm thickening (hyper reflectivity) anterior to RPE with or without intra or subretinal fluid

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CNV secondary to Macular Telangiectasia

Summary:

May not see hemorrhage on clinical examination or photos
Look for other features consistent with MACTEL
- right angle vessels (parafoveal)
- ILM draping
- Inner / Outer retinal cavitation (may resemble macular hole)

Treatment with Anti-VEGF – 3+ PRN dosing

160

CNV secondary to NON AMD conditions

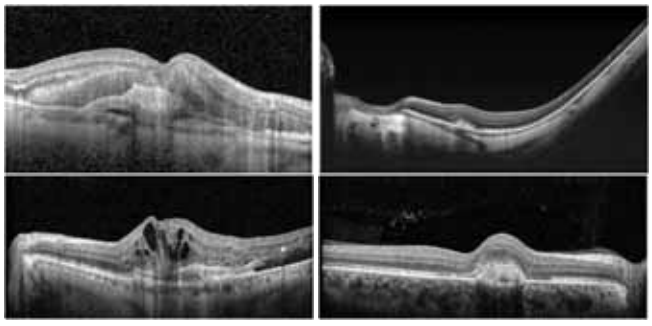
Summary:

May not see hemorrhage on clinical examination or photos
May have minimal to no intraretinal fluid or subretinal fluid
Typically respond better with no need for longer term treatment

Treatment with Anti-VEGF – 3+ PRN dosing

161

CNV secondary to NON AMD conditions differ from that of AMD



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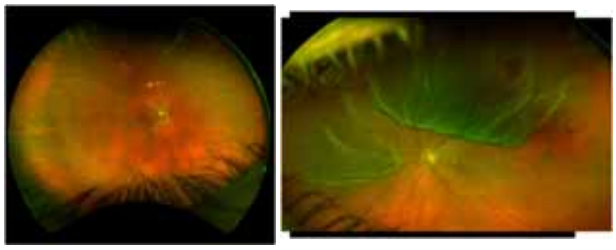
Case Presentation: Friends with Benefits 4/21/2023

- CC: 48 y.o. white female presents with sudden onset of vision loss in the left eye while out of the country. Patient states that she has noticed flashes of lights and the vision coming in and out in the left eye. Patient states that there is no pain, but the left eye feels strain. There are no complaints regarding the right eye.
- Systemic health is negative. Patient is healthy.
- POHx: Phaco/PCIOL OS 11/27/2013
- Family Medical History: No significant family history noted
- VA OD: 20/20 OS: 20/70
- IOP OD:12mmHg OS:13 mmHg

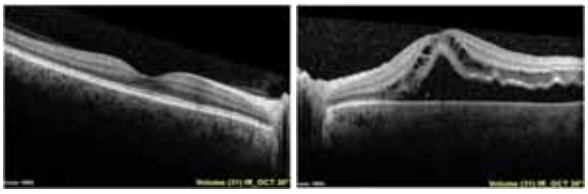
163

And this is the dilated fundus exam:



164

And this is the OCT on 4/21/2023



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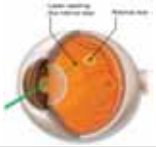
What are the treatment options for retinal tear or hole?

Cryopexy (retinal cryotherapy)

- This procedure uses a probe to *freeze* and damage the tissue surrounding a retinal break, stimulating the development of scar tissue to seal the area and reattach the retina into place.

Laser retinopexy (retinal laser photocoagulation)

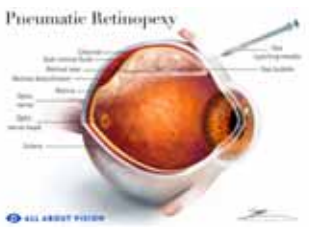
- This procedure uses a laser to generate *heat* and damage the tissue surrounding a retinal break, stimulating the development of scar tissue to seal the area and reattach the retina into place.



166

Sometimes there is a second step to laser…

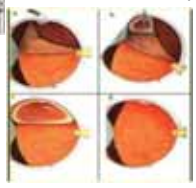
- **Pneumatic Retinopexy (PR):** in-office treatment to repair a rhegmatogenous retinal detachment (RRD). RRD can occur if fluid seeps under the retina, causing it to pull away from the back of the eye. A gas or air bubble is injected into the eye to help hold the retina in place and aid in fluid reabsorption.
- The injected bubble will usually stay in the eye for about two to six weeks. The vision will be blurry during this time. It is important to note that airplane travel is not allowed while the air or gas bubble is in the eye. Higher altitude will cause the bubble to expand, which can cause complications.
- Pneumatic retinopexy is typically done at the same time as laser retinopexy, cryopexy or both.



www.allaboutvision.com/treatments-and-surgery/vision-surgery/other/pneumatic-retinopexy-surgery/

167

Pneumatic Retinopexy: Gas Selection



- The shortest-acting gas that is thought to be adequate should be chosen.
  - SF_6 or C_3F_8 are the most common intraocular gases utilized - these are generally used in their pure (100% concentration) form in PR whereas they are diluted when used in vitrectomy surgery.
    - Pure **SF_6** lasts approximately 2 -3 weeks and expands 2-fold within two days.
    - Pure **C_3F_8** lasts approximately 6-8 weeks and expands 4-fold within four days.

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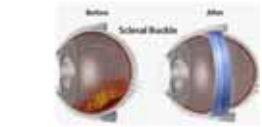
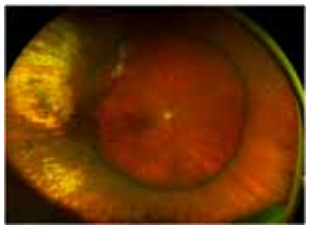
Other RRD repair options: Scleral Buckle

- Scleral Buckle –used to treat RRDs by placing a silicone band around the eye to support the retina from further detachment.
  - The buckle is placed around the eye to indent the sclera which moves the wall of the eye closer to the detached retina-facilitates the drainage of subretinal fluid and promotes reattachment of the retina.
  - Cryo or laser photocoagulation are used to create adhesions around the retinal break-further preventing fluid accumulation and re-detachment





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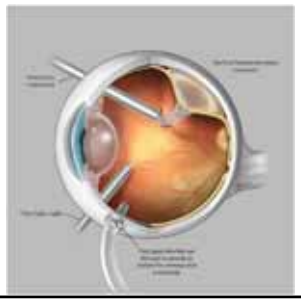
Pars Plana Vitrectomy (PPV)



- PPV is a surgical procedure that removes the vitreous gel form the eye to access the retina
- Indicated for complex retinal detachments which may involve multiple factors:
  - Proliferative vitreoretinopathy "PVR"- presence of fibrous membranes that exert traction on retina
  - Extensive detachment-larger detachments involving multiple quadrants
  - Associated ocular trauma or vitreous heme-PPV helps restore retinal stability and visual function

170

Patient immediately sees the RS for Treatment same day

- Macula off Rhegmatogenous Retinal Detachment left eye
- Pneumatic Retinopexy OS performed in office on 4/21/23
  - 0.4 CC C3F8
  - Cryo x 13
  - Face down x 6 hours, steam roll x 6 hours
  - Then lay on right side with nose to pillow
  - Pred QID, Oflaxacin QID OS
  - S/S of RD discussed
- Patient is seen 1 day after with bubble in place and healing well
- 3 day follow up appears that healing continues to go well, VA is improving to 20/60 OS, and bubble is in place OS. IOP 15 mmHg OS
  - Pigmented lattice is noticed Superior-Temporal on exam, but no new breaks x 360 OS
  - Right side down, nose to pillow; right head tilt
  - Continue current drops: Pred and Oflaxacin QID OS until next visit

171

Why was Cryopexy recommended in this case?

- The location and configuration of the break
  - Retinal break(s) located in the superior 2/3 of the fundus (from 8 to 4 o'clock)
  - No break in the inferior 4 clock hours
  - It may be easier to perform retinal cryopexy for breaks in the peripheral retina or if a laser cannot reach the hole or tear.
- The size of the break(s)
  - Single or multiple breaks within 1 clock hour
- How visible the break is
  - Minimal media opacity
- The patient did not have these other pathologies are in her eye?
  - No PVR grade B or worse
  - No glaucoma history
- Patient is able to maintain positioning for 5-8 days after procedure

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Post Treatment Directions

- The patient should rest after the procedure.
  - This will help the eye to heal and form strong adhesions that will seal the break and reattach the retina.
- After the procedure, the patient may experience a continuing feeling of cold in the eye or a headache caused by the freezing sensation.
  - If the patient experiences a headache or discomfort, take an over-the-counter painkiller such as Tylenol or apply a cold compress.
- For a few days after the procedure, the patient may continue to have increased sensitivity and blurry vision.
- The patient's eye may look red and puffy for a few weeks.
  - This is normal and will go away on its own.
- Recovery takes about one to two weeks, during which the patient should avoid vigorous activity or heavy lifting.
  - The patient may then resume your normal daily activities.

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It is important to educate the patient:

- There is a chance of complications with any surgery.
- In general, since cryotherapy does not require an incision, most people recover fairly quickly, within a week or two.
- There is typically a low risk of complications, such as unexpected damage to the tissue surrounding the treated area.
- However, if the patient notices any of the following symptoms after the procedure, contact a doctor immediately:
  - A dark curtain falling across your vision
  - A total loss of vision or sudden onset of blurry vision
  - A sudden onset of — or increase in — floaters (dark spots appear across your vision)
  - Flashes of light

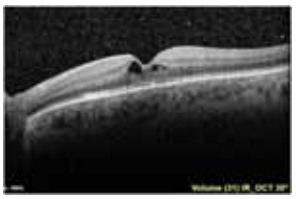
174

Early Signs of a Retinal Tear

175

1 week post op visit

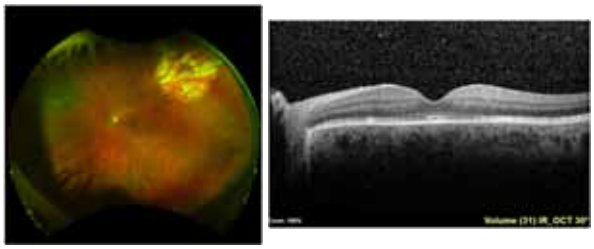
- BCVA: 20/40 OS
- CC: Patient can still see the bubble, but vision is improving
- CME is noted on exam OS
- Bubble is at 30% OS
- Retina is totally attached x 360 OS
- Patient is to continue Pred QID OS, stop Ofloxacin



176

My friend calls again

New flashes and a new blurry spot in the bottom left corner of her left eye. She was at the grocery store when she noticed this. 5/24/23



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Disadvantages of Cryo/PR

- Single-operation success rate is lower than operating room procedures.
  - One survey of the literature revealed a cumulative initial success rate of 75.5%, with a final success rate of 97.4%
    - The initial success rates of pars plana vitrectomy and scleral buckling which are in the 85-88% range.
    - Failure of pneumatic retinopexy is thought to be due to reopening of one of the original breaks, or to missed or new tears.
    - Studies have generally reported higher success rates for pneumatic retinopexy in phakic eyes, likely due to missed or new tears in pseudophakes and aphakes.
- Requires a surgeon highly skilled at retinal examination
- Not all detachments are amenable to repair with pneumatic retinopexy
- Requires significant patient cooperation and positioning
- Surgeon must be able to manage postoperative care and complications

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The RS treats the new break

- Mac on RRD OS
  - New Break at 11:00 OS
  - RD from 9:00-11:30
  - Cryo PR OS for new break
  - CME is resolved, macula is attached
  - Continue Pred QID OS and restart Oflaxacin QID OS
  - Left head tilt with nose down during the day and night
    - Avoid flat on back

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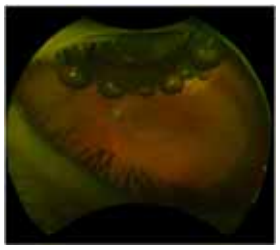
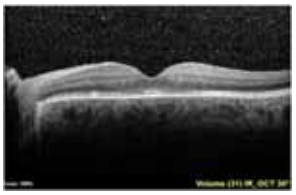
5/25/25 1 day post op
Retina is nicely attached x 360





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Advantages of Cryo/PR

- Outpatient procedure
- Less discomfort than operating room procedures
- No need for MAC or general anesthesia
- No change in refractive error
- No diplopia
- Lower risk of infection
- Faster ocular and systemic recovery
- Lower cost procedure
- Patient can still have operating room procedure without affecting visual prognosis or may have improved prognosis (PIVOT)

181

So far so good: 7/24/25

- Patient states that her vision is stable. Patient states that she still has floaters in the left eye, but no new flashes. Patient denies pain or distortion in either eye.
- BCVA OD: 20/20 and OS 20/20
- IOP: 14mmHg OD and 19mmHg OS
- Exam reveals normal macula and retina is totally attached x 360 OU
- +PVD OS
- Will follow up in 1 year

182

Who is at risk for retinal tear?

- Myopia(nearsighted)
- Having had previous cataract, glaucoma, or other eye surgery
- Taking glaucoma medications that make the pupil small (like pilocarpine)
  - Presbyopia drops?
- Having had a serious eye injury
- Having a retinal tear or detachment in the other eye
- Having family members with retinal detachment
- Having weak areas in the retina (which your ophthalmologist may see during an exam)

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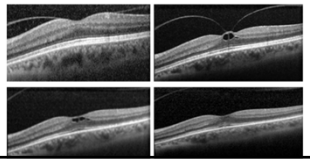
And probably the number one cause for a tear is…

- As we get older, the vitreous in our eyes starts to shrink and get thinner.
- Usually the vitreous moves around on the retina without causing problems.
- But the vitreous may stick to the retina and pull hard enough to tear it.



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FALLING THROUGH THE CRACKS

24yo female – Routine exam

- Oc Hx: unremarkable
- Med Hx: Unremarkable

- BCVAs @dist:
  - OD 20/20, OS 20/20
- Entrance testing: all WNLs
- SLE: WNLs OU
- IOPs: 20 OD/ 22OS
- BP: 122/70

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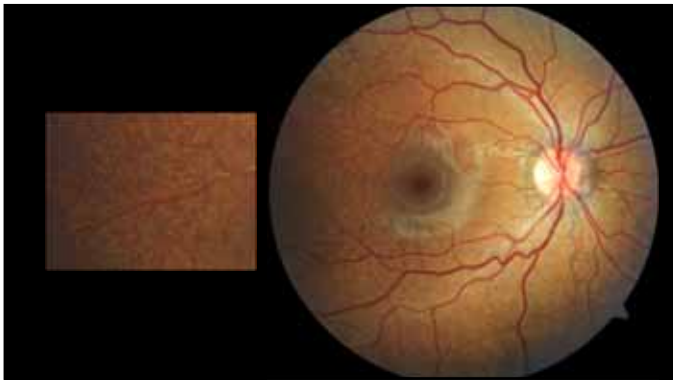

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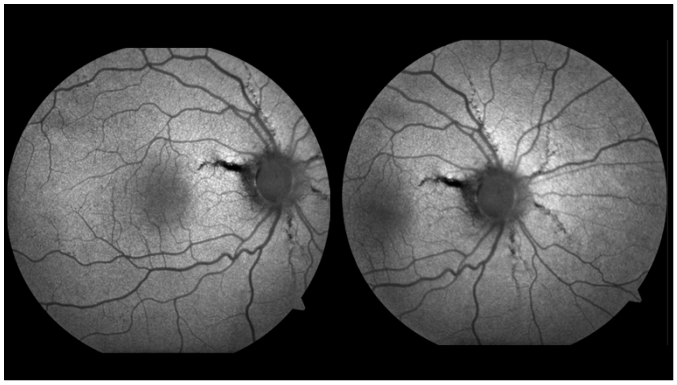

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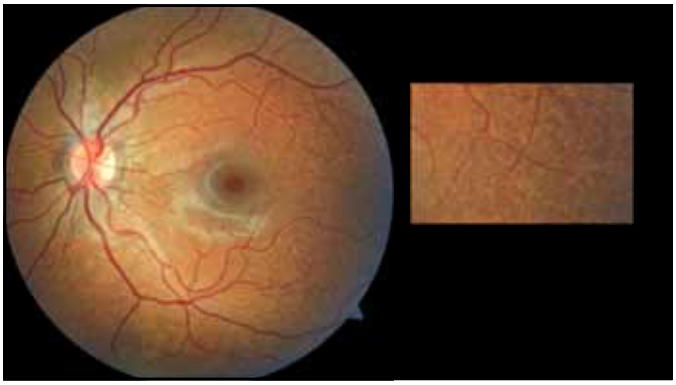

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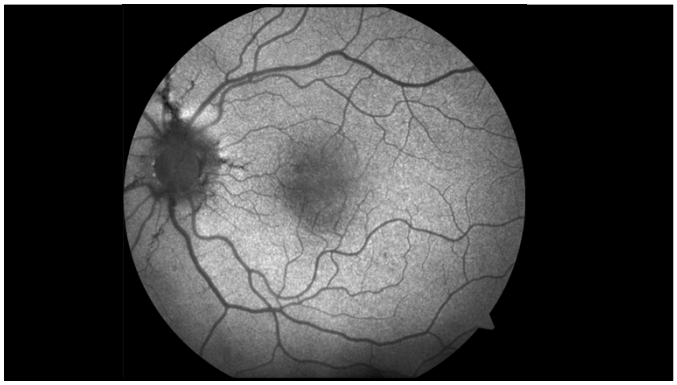

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Genetic testing results

SUMMARY OF RESULTS

PRIMARY FINDINGS

The patient is heterozygous for *ABCC6* c.2787+1G>T, which is pathogenic.
The patient is heterozygous for *ABCC6* c.1674del, p.(Glu559Argfs*4), which is likely pathogenic.

PRIMARY FINDINGS: SEQUENCE ALTERATIONS

GENE	TRANSCRIPT	NOMENCLATURE	GENOTYPE	CONSEQUENCE	INHERITANCE	CLASSIFICATION
ABCC6	NM_001171.5	c.2787+1G>T	HET	splice_donor_variant	AR	Pathogenic
	ID	ASSEMBLY	POS	REF/ALT		
	rs72644209	GRCh37/hg19	16:16287140	G/A		
	gnomAD AC/AN	POLYPHEN	SIFT	MUTTASTER	PHENOTYPE	
	33/282394	N/A	N/A	disease causing	Pseudoxanthoma elasticum	
GENE	TRANSCRIPT	NOMENCLATURE	GENOTYPE	CONSEQUENCE	INHERITANCE	CLASSIFICATION
ABCC6	NM_001171.5	c.1674del, p.(Glu559Argfs*4)	HET	frameshift_variant	AR	Likely pathogenic
	ID	ASSEMBLY	POS	REF/ALT		
		GRCh37/hg19	16:16282792	CGTC		
	gnomAD AC/AN	POLYPHEN	SIFT	MUTTASTER	PHENOTYPE	
	0/0	N/A	N/A	N/A	Pseudoxanthoma elasticum	

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ANGIOID STREAKS

- Diff Dx includes choroidal rupture, lacquer cracks, laser injury, ocular parasite
- Breaks in a thickened, calcified Bruch membrane
- Irregular lines 50-500 um wide
  - Reddish to brownish
  - Radiate from or concentrically surround optic disc
  - Can increase in length and width over time
- RPE thinning and clumping
  - Mixed autofluorescence pattern
  - Irregular hyperfluorescence on FA
- Risk of CNV

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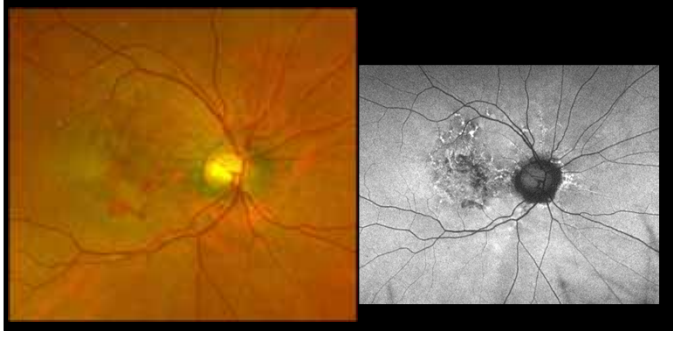
May be complicated by CNVM requiring anti-VEGF



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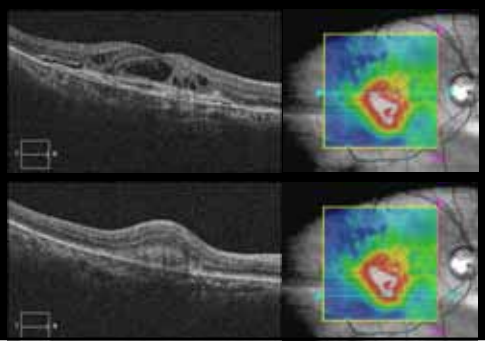
May be complicated by CNVM requiring anti-VEGF



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ANGIOID STREAKS

- **P**seudoxanthoma elasticum (PXE)
- **E**hlers-Danlos syndrome
- **P**aget's disease
- **S**ickle cell retinopathy
- **I**diopathic
- Other conditions, especially hematologic and metabolic

- **Workup:** Most cases due to PXE: Obtain free genetic testing
- If genetic testing neg & no associated systemic disease evident on history/exam obtain hemoglobin electrophoresis, serum alkaline phosphatase

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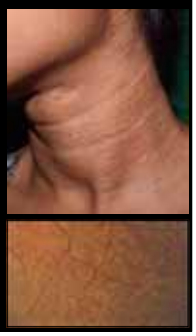
PSEUDOXANTHOMA ELASTICUM (PXE)

- Progressive calcification & fragmentation of elastic fibers
  - Especially in skin, fundus, and cardiovascular sys
- Rare, usually autosomal recessive, ABCC6 gene
- F:M 2:1, all ethnicities, avg age 13 (wide range)
- Eye findings besides angioid streaks
  - "Peau d'orange" fundus: subtle pigmentary mottling esp in temporal periphery
  - Pattern dystrophy-like macula
  - Progressive geographic atrophy and/or subretinal fibrosis
  - Temporal comet-shaped lesions of RPE atrophy
  - Disc drusen
- Systemic: early atherosclerosis, skin plaques & laxity, rarely GI or cerebral hemorrhages



Singh A, et al. Dermoscopy of PXE. Case Reports 2017.

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MANAGEMENT OF ANGIOID STREAKS & PXE

- Angioid streaks:
  - Evaluate for systemic disease
  - Monitor for CNV as in intermediate AMD
    - Treat CNV with anti-VEGF injections
    - Amlser grid
  - Counsel patients regarding the importance of protective eyewear
    - Minor eye trauma can cause hemorrhage
- PXE:
  - Send to PCP and/or cardiologist
    - May need prophylaxis against MI/stroke, such as statin
    - Monitor for HTN

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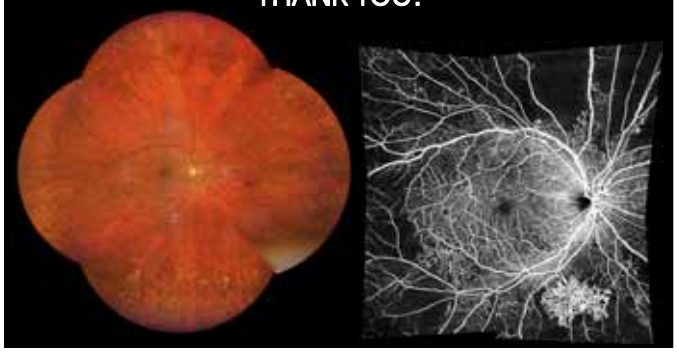
THANK YOU!



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