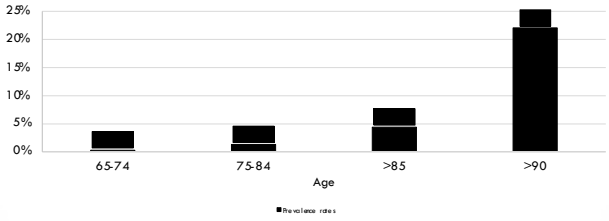
HOT TOPICS IN RETINA!

- STEVEN FERRUCCI OD
  - CHIEF, OPTOMETRY SEPULVEDA VA
  - PROFESSOR, SCCO
- MARK DUNBAR, OD, FAAO
  - BASCOM PALMER EYE INSTITUTE

1

GA CURRENTLY AFFECTS >5 MILLION PEOPLE WORLDWIDE

GLOBAL PREVALENCE OF GA

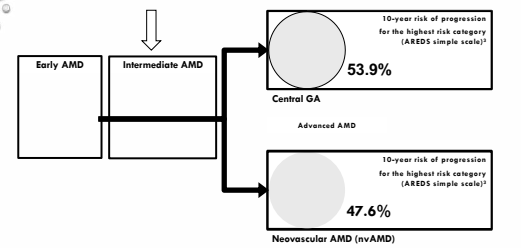


RUDNICKA A, ET AL. OPHTHALMOLOGY. 2012;119:571–80. 2. WONG ET AL, LANCET GLOB HEALTH 2014;2:E106–16.

2

2

STAGING OF AMD



AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study; GA, geographic atrophy; nvAMD, neovascular AMD.
1. Eye Diseases Prevalence Research Group. Arch Ophthalmol. 2004;122(4):477-485. 2. Ferris FL, et al. Ophthalmology. 2013;120(4):844-851. 3. Chew EY, et al. JAMA Ophthalmol. 2014;132(3):272-277. 4. Age-Related Study Disease Study Research Group. Arch Ophthalmol. 2005;123(11):1570-1574.

3

MULTIMODAL IMAGING OF GA

Reprinted with permission from Fleckenstein M, et al. The progression of geographic atrophy secondary to age-related macular degeneration. Ophthalmology. 2018;125(3):369-390. Copyright 2017 by the American Academy of Ophthalmology.

CFP, color fundus photography; FA, fluorescein angiography; FAF, fundus autofluorescence; NIR, near-infrared reflectance.

4

GEOGRAPHIC ATROPHY FEATURES ON OCT

Zone of RPE loss/attenuation & overlying PR degeneration ≥ 250µm in diameter

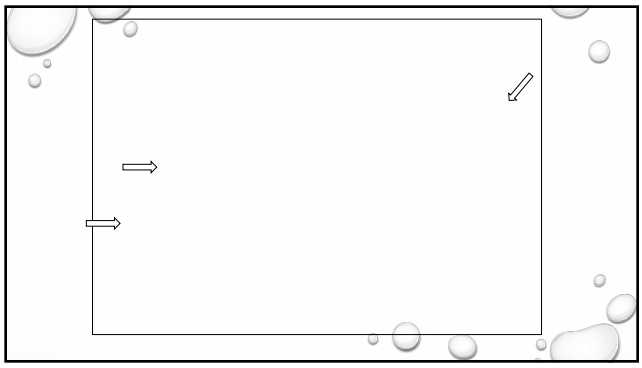
HYPER-TRANSMISSION

5

GEOGRAPHIC ATROPHY

- LESIONS GROW WITH TIME, AT VARIOUS RATES
  - LARGER LESIONS, MULTI-FOCAL LESIONS, EXTRAFOVEAL LESIONS GROW FASTER
- TREATMENT GEARED AT DECREASE IN LESION GROWTH
- GROWTH ASSOCIATED WITH OVER-ACTIVATION OF COMPLEMENT SYSTEM
  - VARIOUS TARGETS BEING INVESTIGATED: C3, C5

6



7

GA TREATMENTS

SYVORE (PEGCETACOPLAN)

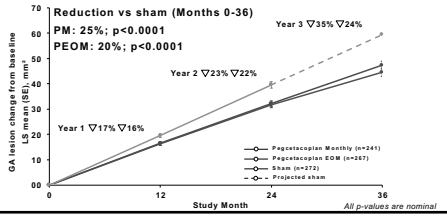
- APELLIS
- BLOCKS C 3
- FDA APPROVED FEB 2023
- DELIVERED INTRAVITREALLY EVERY 25-50 DAYS

IZERVAY (ACP)

- ASTELLAS
- BLOCKS C5
- FDA APPROVED AUGUST 2023
- DELIVERED INTRAVITREALLY EVERY MONTH

8

GALE TOTAL POPULATION (NONSUBFOVEAL + SUBFOVEAL): REDUCTIONS IN GA GROWTH FOLLOWING 36 MONTHS OF **CONTINUOUS** PEGCETACOPLAN INCREASED OVER TIME

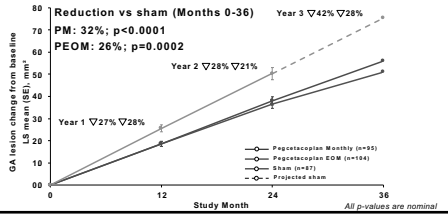


1.49 mm² (PM) & 1.21 mm² (PEOM) of Retinal Tissue Preserved Over 36 Months

LS means estimated from a piecewise linear mixed-effects model that evaluated mean rate of change in GA area between pegcetacoplan arms and sham arm from baseline to Month 36, with knots at Months 12 and 24 allowing for the slope to be linear over each of the 12-month segments but to differ between segments (piecewise slope analysis). Mean rate of change of hypothetical sham from Month 24 to Month 36 was estimated from the mean rate of change in each period from Month 0 to Month 24. The modified full analysis set was used for the analysis, defined as patients who are in OAKS/DERBY antecedent study's ITT set, have not been enrolled in APL2-103, and received ≥1 injection of pegcetacoplan in GALE. Projected sham is shown with a dashed line. Data shown for patients who continued into the GALE trial after OAKS & DERBY. **EOM,** every other month; **GA,** geographic atrophy; **ITT,** intent to treat; **LS,** least-squares; **PEOM,** pegcetacoplan every other month; **PM,** pegcetacoplan monthly; **SE,** standard error.

9

GALE NONSUBFOVEAL SUBGROUP (N=286 EYES): REDUCTIONS IN GA GROWTH WITH 36 MONTHS OF **CONTINUOUS** PEGCETACOPLAN



2.44 mm² (PM) & 1.94 mm² (PEOM) of Retinal Tissue Preserved Over 36 Months

LS means estimated from a piecewise linear mixed-effects model that evaluated mean rate of change in GA area between pegcetacoplan arms and sham arm from baseline to Month 36, with knots at Months 12 and 24 allowing for the slope to be linear over each of the 12-month segments but to differ between segments (piecewise slope analysis). Mean rate of change of hypothetical sham from Month 24 to Month 36 was estimated from the mean rate of change in each period from Month 0 to Month 24. The modified full analysis set was used for the analysis, defined as patients who are in OAKS/DERBY antecedent study's ITT set, have not been enrolled in APL2-103, and received ≥1 injection of pegcetacoplan in GALE. Projected sham is shown with a dashed line. Data shown for patients who continued into the GALE trial after OAKS & DERBY. **EOM,** every other month; **GA,** geographic atrophy; **ITT,** intent to treat; **LS,** least-squares; **PEOM,** pegcetacoplan every other month; **PM,** pegcetacoplan monthly; **SE,** standard error.

10

ACP REDUCED GA GROWTH WHEN DOSED EM AND EOM VS SHAM

11

TREATMENT EFFECT VS SHAM MORE THAN DOUBLED WITH ACP 3 MG EM AND EOM OVER 2 YEARS COMPARED TO THE TREATMENT EFFECT OVER 1 YEAR

12

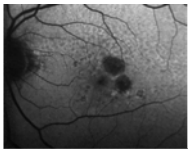
SAFETY

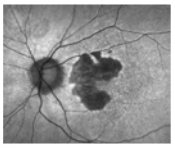
- BOTH AGENTS HAD RELATIVELY GOOD SAFETY PROFILES
- RISK OF ENDOPHTHALMITIS
  - APPROX 1/3000
- RISK OF CONVERSION TO WET AMD
  - 12% WITH SYFOVRE (VS 3% SHAM)
  - 7% WITH IZERVAY
- VASCULITIS/INFLAMMATION REPORTED EARLY ON

13

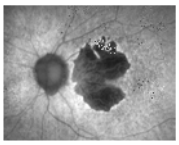
WHEN TO REFER?

- ANY GA THAT IS **THREATENING** CENTRAL VISUAL FUNCTION
- ANY GA THAT ENCROACHING THE FOVEA
- LARGE EXTRAFOVEAL LESIONS
- LESIONS SHOWING PROGRESSION





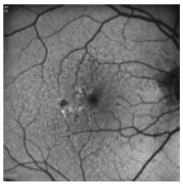
Progression to subfoveal involvement 18 mo

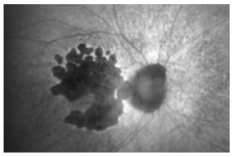


14

WHEN NOT TO REFER?

- EXTRAFOVEAL LESIONS THAT ARE NOT A THREAT TO CENTRAL VA
- CENTRAL GA LESIONS THAT ALREADY HAVE SIG LOSS OF VISUAL FUNCTION





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Valeda® Light Delivery System

VALEDA OVERVIEW

- Valeda treatment delivery very similar to many ophthalmology office diagnostic and treatment devices
- Implementation support available from LumiThera Customer Success Team
- Treatment is simple to learn and easy to train for operators
- No pupil dilation required
- Nine (9) flexible treatment sessions delivered over 3–4 weeks
- 2-3 treatment cycles per annum

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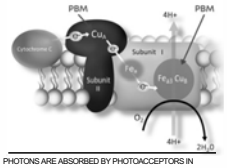
Photobiomodulation (PBM) Approach

PBM uses low-level light to stimulate cells to 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

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.

Valeda Wavelengths (nm)	Cellular Targets	Secondary Effects
590	Stimulates CCO activity, increases nitric oxide (NO) synthesis, inhibits VEGF expression	Vasodilation, Improves local O_2 and nutrient delivery, VEGF reduction
660	Promotes O_2 binding to CCO active Cu_B/Fe_{a3} site	Upregulates Electron Transport Pathway, Increases energy (ATP), Reduces Inflammation and cell death
850	Drives electron transfer at Cu_A site of CCO	Upregulates Electron Transport Pathway, Increases energy (ATP), Reduces Inflammation and cell death

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

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FDA AUTHORIZES BREAKTHROUGH VALEDA THERAPEUTIC FOR DRY AMD TO IMPROVE VISION (NOVEMBER 04, 2024)

Valeda Light Delivery System

- Five successful clinical studies
- US LIGHTSITE III pivotal trial data met BCVA primary endpoint
- Data from two-year LIGHTSITE III trial used to support Valeda FDA submission
- First FDA authorized therapy for Dry AMD Patients to improve vision
- CE marked: Available in Europe and other countries
- Non–invasive, safe therapy for patients

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First FDA treatment for Dry AMD Patients to Improve Vision

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.

19

LIGHTSITE III: SAFETY SUMMARY

- Similar frequencies of adverse events (AE) (Sham, 25.5%; PBM, 25.8%) and ocular-specific AEs (Sham, 20.0%; PBM, 22.6%) observed between treatment groups
- Three subjects had ocular-specific AEs considered related to the procedure: punctate keratitis (Sham; n = 2; 3.6%), visual perseveration (after image) (Sham; n = 1; 1.8%), and application site warmth (PBM; n = 1; 1.1%). No ocular-specific AEs led to study discontinuation.
- Seven (7.5%) ocular-specific serious adverse events (SAE) of nAMD were reported in the PBM group and three (5.5%) ocular-specific SAEs (2 nAMD, 1 cystoid macular edema) were reported in the Sham group. No SAEs were considered associated to the treatment by the primary investigator.
- Severity of AEs reported were mostly mild/moderate in both treatment groups
- No signs of phototoxicity
- No adverse effect on color vision or perimetry

20

LIGHTSITE III: STUDY SUMMARY

LIGHTSITE III study 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
- 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 treatment groups
- Reduced occurrence of incident GA and other exploratory markers of disease progression
- Reduced macular drusen volume
- Improved QoL in VFQ-25 Composite score and select subscales
- A favorable safety profile was observed 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

21

ANTI-VEGF AGENTS

- THE OG
  - MACUGEN (PEGAPTANIB) 2004
  - LUCENTIS (RANIBIZUMAB)2006
  - EYLEA (AFLIBERCEPT) 2011
  - BEOVU (BROLUCIZUMAB) 2019
  - AVASTIN (BEVACIZUMAB) ≈2005

22

HIGH DOSE AFLIBERCEPT (EYLEA)

- PULSAR (AMD) AND PHOTON (DME) STUDIES
  - LOOKED AT 8 MG VS 2 MG OF EYLEA
  - DEMONSTRATED NON-INFERIOR AND CLINICALLY EQUIVALENT VISION GAINS AT 48 WEEKS WITH 8 MG AT 12 AND 16 WEEK DOSING AFTER 3 INITIAL DOSES COMPARED TO EYLEA EVERY 8 WEEKS AFTER INITIAL DOSING
- EYLEA HD FDA APPROVED 8/18/2023 FOR AMD, DME AND DR
  - RECOMMENDED DOSE 1 INJECTION EVERY 4 WEEKS FOR FIRST 3 MOS FOR ALL INDICATIONS, THEN EVERY 8-16 WEEKS (2-4 MOS) FOR AMD AND DME AND EVERY 8-12 WEEKS (2-3 MOS) FOR DR

23

VABYSMO (FARICIMAB)

- ROCHE/GENENTECH
  - FDA APPROVED JANUARY 3, 2022 FOR AMD AND DME
- FIRST BI-PHASIC ANTIBODY FOR INTRAOCULAR USE
  - ONE ARM: VEGF-A INHIBITOR
  - OTHER ARM: ANGIOPOIETIN-2 (ANG-2)INHIBITOR
    - GROWTH FACTOR THAT PROMOTES VASCULAR DESTABILIZATION AND AND INFLAMMATION
  - DUAL INHIBITION OF VEGF AND ANG-2 HAVE PROVEN MORE EFFECTIVE THAN INHIBITING EITHER TARGET ALONE
- MULTIPLE STUDIES SHOW SIMILAR RESULTS TO MONTHLY LUCENTIS/EYLEA BUT ABLE TO OBJECT LESS FREQUENTLY, MANY PTS Q 16 WEEKS
- MAY BE FDA APPROVED FOR RVO BY END OF YEAR

24

SUSVIMO

- PREVIOUSLY CALLED GENENTECH PORT DELIVERY SYSTEM (PDS)
  - REFILLABLE PORT PLACED UNDER CONJUNCTIVA TO ALLOW STEADY SUPPLY OF LUCENTIS
- STUDIES (LADDER, ARCHWAY) DEMONSTRATED EQUIVALENT RESULTS TO MONTHLY LUCENTIS AT 40 WEEKS
  - LARGE % OF PTS DID NOT NEED REFILL PRIOR TO 6 OR 12 MOS
- FDA APPROVED 10/1
- RECALLED 10/22
  - ISSUE WITH IMPLANTS BREAKING WHEN REFILLED
- REAPPROVED JULY 8, 2024 WITH NEW IMPLANT AND REFILL NEEDLE

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ANTI-VEGF BIOSIMILARS

- 3 FDA APPROVED LUCENTIS (RANIBIZUMAB) BIOSIMILARS
  - BYOOVIZ (SAMSUNG) APPROVED SEPT 2021
  - CIMERLI (COHERUS) APPROVED OCT 2022
  - NUFYMCO (FORMYCON/BIOEQ) DEC 2025
- 6 FDA APPROVED TWO EYLEA (AFLIBERCEPT) BIOSIMILARS
  - YESAFILI (AFLIBERCEPT-JBVF) BIOCON BIOLOGICS; MAY 2024
  - OPUVIZ(AFLIBERCEPT-YSZY) SAMSUNG BIOEPIS/BIOGENMMAY 2024
  - AHZANTIVE (AFLIBERCEPT-MRBB) FORMYCON; JUNE 2024
  - PAVBLU (AFLIBERCEPT-AYYH) AMGEN; AUGUST 2024
  - ENZEEVU (AFLIBERCEPT-ABZV) SANDOZ; DEC 2024
  - EYDENZELT (AFLIBERCEPT-BOAU) CELLTRION; OCT 2025
- MANY OTHERS IN THE WORKS….

26

TKI INHIBITORS

- TYROSINE KINASE INHIBITORS
  - SMALL MOLECULES THAT CAN ACT INTRACELLULARLY TO INHIBIT MULTIPLE PATHWAYS INVOLVED IN THE PATHOGENESIS OR RETINAL DISEASE
  - MAY BE A MORE DURABLE TREATMENT APPROACH, REDUCING TREATMENT BURDEN OVER AVNYI0VEGF
  - EARLY STUDIES SHOW PROMISE
- AIV007 (AIVIVA BIOPHARMA): PHASE 1, SINGLE PERIOCULAR INJECTION FOR DME AND NAMD,
- D-4517.2 (ASHAVATTHA THERAPEUTICS): PHASE 2 TEJAS STUDY, SUBCUTANEOUS OR ORAL FOR DME AND NAMD
- EYP-1901 (EYEPOINT PHARMACEUTICALS): LUGANO ANDCLUCIA TRIALS IN AMD; VERONA IN DME
- OTX-TKI (OCULAR THERAPEUTIX): APAXLI, BIORESORBABLE INTRAVITREAL IMPLANT FOR AMD AND DR
- CLS-AX (CLEARSIDE THERAPEUTICS): SUPRACHOROIDAL INJECTION OF AXITINIB FOR NAMD
- PAN-90806 (ZHAOKE OPHTHALMOLOGY): TOPICAL KI EYE DROP FOR AMD

27

AXPAXLI

- BIORESORBABLE HYDROGEL OF AXITINIB, A TYROSINE KINASE INHIBITOR (TKI) WITH ANTIANGIOGENIC ACTIVITY BY OCULAR THERAPEUTICS
- SOL-1 TRIAL: 344 TREATMENT NAÏVE PTS WITH WET AMD COMPARING SINGLE INJECTION OF AXPAXLI WITH EYLEA 2 MG STANDARD TREATMENT
  - AT WEEK 36, 74.1% AXPAXLI PTS VS 55.8% EYLEA MAINTINED VISUAL ACUITY (PRIMARY ENDPOINT)
  - AT WEEK 52, 65.9% OF AXPAXLI PTS VS 44.2% EYLEA PTS MAINTAINED VISUAL ACUITY
  - ALSO HAD SUPERIOR ANATOMIC OUTCOMES WITH MORE PTS ACHIEVING CST WITHIN 30 U OF BASELINE (55.9% VS 37.8% AT 36 WEEKS)
  - GOOD SAFETY PROFILE WITH NO ENDOPHTHALMITIS, VASCULITIS ECT
- FIRST AND ONLY PRODUCT WITH A NOVEL APPROACH TO SUCCESSFULLY DEMONSTRATE SUPERIORITY TO AN IMPROVED ANTI-VEGF IN WET AMD IN OVER 20 YEARS.

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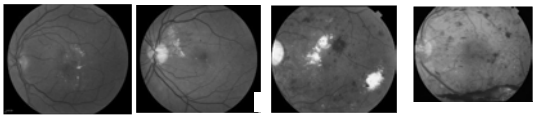
Is our DR Grading Scale Antiquated?

Mild NPDR	Moderate NPDR	Severe NPDR	PDR



Wilkinson CP, Ferris FL, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales *Ophthalmology 2003;110: 1677–1682*

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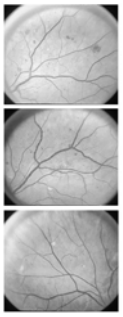
DIABETIC RETINOPATHY GRADING

- DEVELOPED AS A MEANS OF CREATING A **"PROGNOSTIC STANDARD"**
  - RISK OF VISION LOSS IF NOT TREATED
- BASED ON ETDRS/DRS STUDIES THAT WERE DONE IN THE 1980'S
- UTILIZES FUNDUS PHOTOGRAPHY WITH A SET OF "STANDARD SLIDES"
- PHOTOGRAPHS ONLY CAPTURED IMAGES MAINLY OF THE POSTERIOR POLE BETWEEN THE ARCADES
- DOES NOT INCORPORATE CHANGES SEEN IN THE RETINA USING NEWER MODALITIES



Standard Slide 2A

Standard Slide 6A

Standard Slide 8A

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DIABETIC RETINAL NEURODEGENERATION (DRN)

- MAY BE A **"PRECLINICAL MANIFESTATION"** OF DIABETIC RETINAL DISEASE (DRD)
  - DEVELOPS IN THE EARLY STAGES OF DRD
- IDENTIFIED AS **PROGRESSIVE RETINAL THINNING** AND **VISUAL DYSFUNCTION** IN PATIENTS WITH DM BEFORE THE DEVELOPMENT OF DR
- EARLY RETINAL NEURODEGENERATION MAY PRECEDE VASCULAR PATHOLOGY - SUGGESTING THAT NEURONAL DAMAGE MAY CONTRIBUTE TO DISEASE PATHOGENESIS AND REPRESENT AN INDEPENDENT TARGET FOR INTERVENTION
- DRN MAY BE AN INITIAL COMPONENT - ANOTHER STAGE - OF DRD

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NEURODEGENERATIVE MECHANISMS

- GLUTAMATE EXCITOTOXICITY
- OXIDATIVE STRESS
- INFLAMMATION
- RENIN-ANGIOTENSIN SYSTEM ACTIVATION

32

THE LANDSCAPE OF IMAGING MODALITIES

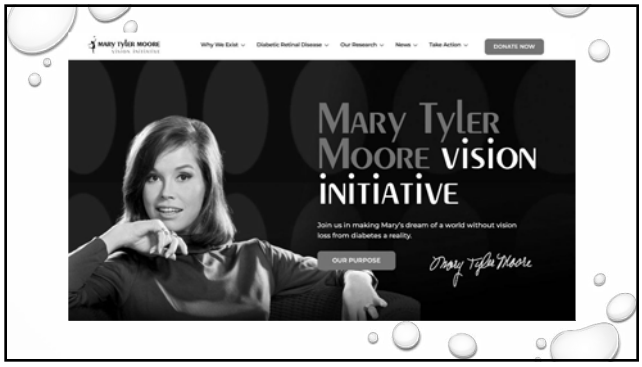
- WIDE-FIELD FUNDUS PHOTOGRAPHY
- SD OCT
- OCT ANGIOGRAPHY
- ADOPTIVE OPTICS
- ERG

33

DIABETIC RETINOPATHY GRADING

- THE **TRADITIONAL END-POINT** FOR DR HAS EVOLVED:
  - LASER PRP (OR VITRECTOMY) ONCE PTS PROGRESSED TO PDR
  - FOCAL/GRID LASER ONCE THEY DEVELOPED CSME
- TO NOW ANTI-VEGF TREATMENTS
  - CI-DME
  - SEVERE NPDR AND PDR
- EARLIER INTERVENTION BEFORE PDR

34



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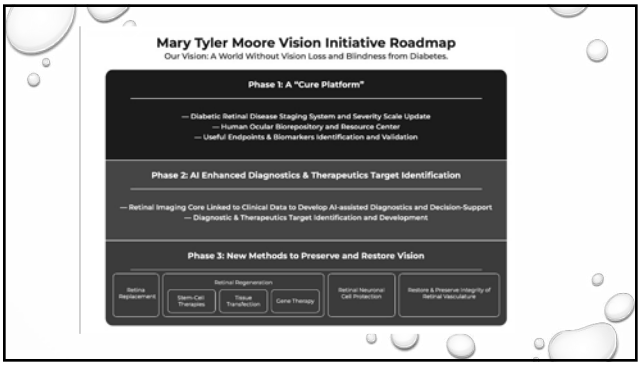

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NEW THINKING

- MUST LOOK IN PERIPHERY
- AS MUCH AS 30% OF HEMES, 27% OF IRMAS, AND 34% OF NVE OUTSIDE EDTRS FIELDS
- 10% OF EYES MISCLASSIFIED LEVEL OF DR UNLESS PERIPHERAL LESION CONSIDERED
- ALSO, PPL (PREDOMINATELY PERIPHERAL LESIONS) AND NPDR HAD 4.7 X INCREASED RISK OF PDR IN 4 YEAR'S
  - 6% TO ALMOST 25%!

39

JOHNS HOPKINS STUDY

STUDY AIMED TO INVESTIGATE WHETHER THE MANAGEMENT OF PATIENTS WOULD BE ALTERED BY A 200 DEGREE FIELD OF VIEW

☆

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WHAT IS ERG?

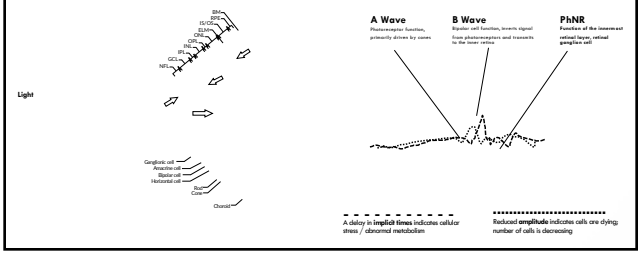
ELECTRORETINOGRAPHY

ERG MEASURES THE ELECTRICAL RESPONSES OF VARIOUS CELL TYPES IN THE RETINA, INCLUDING THE **PHOTORECEPTORS** (RODS AND CONES), **INNER RETINAL CELLS** (BIPOLAR AND AMACRINE CELLS), AND THE **GANGLION CELLS** IN RESPONSE TO A STIMULUS.

41

WHAT IS ERG?

THE ERG WAVEFORM



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PUPILLARY RESPONSE IS ALSO IMPACTED BY DR

DR assessment protocol combines:

IMPLICIT TIME (ERG)
How long it takes the retina to respond

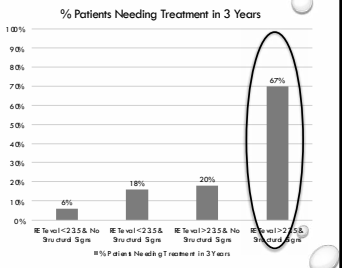
AMPLITUDE (ERG)
How strong the signal from the retina is

PUPIL RESPONSE
Change in pupil diameter–dim vs. bright

PATIENT AGE

A Global DR Score Predicts Who Will Need Tx

- N = 237 in US
- Primary outcome: % receiving laser, IV therapy and/or vitrectomy over 3 yrs
- Clinically observable SEVERE NPDR in tandem with ERG+pupillometry score > 23.5 best predicted Tx



Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. *Trans Vis Sci Tech.* 2020;9(9):40-40.

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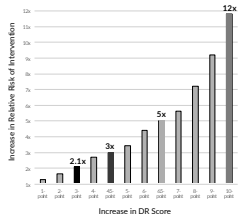
FUNCTION: ASSESS RISK

Each 1-point change in the DR Score increases the probability of ocular intervention over 3 years by 28%

Higher DR Score & change over time dramatically increases risk:

- Risk of intervention more than **doubles** with a 3-point increase in DR Score (e.g. 20 to 23)
- Risk of intervention **triples** with a 4.5-point increase in DR Score (e.g. 20 to 24.5)
- Risk of intervention **increases 5x** with a 6.5-point increase in DR Score (e.g. 20 to 26.5)
- Risk of intervention **increases 12x** with a 10-point increase in DR Score (e.g. 16 to 26)



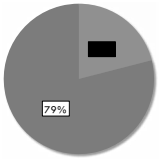
Cox proportional hazards analysis (CI = 1.17 – 1.40, p < 0.0001)

Source: Brigell MG, Chiang B, Maa AY, Davis CQ. Enhancing Risk Assessment in Patients with Diabetic Retinopathy by Combining Measures of Retinal Function and Structure. Trans Vis Sci Tech. 2020;9(9):40-40.

44

DIABETIC RETINOPATHY

NEWEST STUDY SHOWS THE DR SCORE WAS THE STRONGEST PREDICTOR OF PROGRESSION TO VTC



Patients with a DR Score of 26.9 or higher had a 79% chance of progressing to needing treatment in less than 1 year.

- Longitudinal prospective study published in *Ophthalmology Science*, the journal of the American Academy of Ophthalmology
- 48 weeks (~11 months)
- 74 patients with moderate to severe NPDR tested with ERG
- Evaluated 56 parameters at multiple US sites from 4 testing modalities:
  - RETeval DR Assessment (ERG + pupillometry)
  - Color fundus photography (FP)
  - OCT angiography (OCT-A)
  - Ultra-widefield fluorescein angiography (UWF-FA)

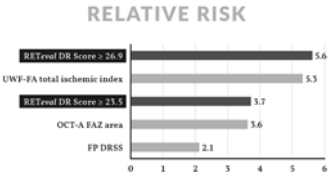
Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859

45

DIABETIC RETINOPATHY

STUDY SHOWS THE DR SCORE WAS THE STRONGEST PREDICTOR OF PROGRESSION TO VTC

RETeval DR Score was the strongest predictor of progression to vision-threatening complications!



Davis, C. Quentin et al. Predicting Progression to Vision-Threatening Complications in Diabetic Retinopathy. Ophthalmology Science, online June 17, 2025, 100859

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DIABETIC RETINOPATHY

WHY THE DR SCORE MATTERS

- **ENABLES RISK STRATIFICATION** TO IDENTIFY PATIENTS WHO NEED CLOSE MONITORING OR EARLY REFERRAL, EVEN WHEN STRUCTURAL IMAGING APPEARS STABLE.
- ALLOWS TARGETED REFERRALS AND/OR RESOURCE PRIORITIZATION, **REDUCING OVERTREATMENT AND MISSED PROGRESSION.**
- CREATES POTENTIAL TO IMPROVE DR STAGING SYSTEMS AND **SUPPORT VALUE-BASED CARE MODELS.**

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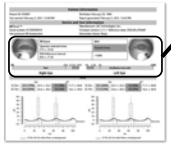
DIABETIC RETINOPATHY

HOW TO USE THE DR SCORE IN PRACTICE → INTERPRETATION GUIDE

PATIENT TEST CONDITIONS
Test is always done un-dilated. Patient is diabetic with suspected retinopathy or diabetic with existing retinopathy.

PROTOCOL
DR Assessment

RESULTS
If the **Operator-selected limit** is marked red with text **Outside limits,** the patient is at risk to develop vision threatening DR within the coming 36 months.



Predicting DR progression

DR SCORE <23.5:
Patient is much less likely to progress to needing treatment in the next few years

DR SCORE ≥23.5:
High chance of requiring treatment in next 3 years

DR SCORE ≥26.9:
Patient is 79% likely to progress to needing treatment in less than 1 year

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DME

- OLD DEFINITIONS BEING REPLACED WITH NEWER ONES BASED ON OCT FINDINGS
  - CENTER INVOLVED
  - NONI-CENTER INVOLVED
  - OCT BEST WAY TO EVALUATE RETINA FOR DME
- DME RESPONSIBLE FOR MORE CASES OF MODERATE VISUAL LOSS IN PTS WITH TYPE 2 DM THAN DR
- NEW TREATMENTS

CSME
1. RT within 500 microns (1/3 DD) from FAZ
2. Hard exudates with associated thickening 500 microns from FAZ
3. RT > 1DD in area any part of which is within 1DD from FAZ

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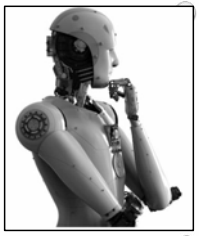
PROTOCOL V

- 702 PTS WITH CI-DME WITH VA 20/25 OR BETTER
- 3 TREATMENT GROUPS
  - EYLEA
  - FML
  - OBSERVATION
- AT END OF 2 YEARS, RATE OF LOSS OF 5 LETTERS OR MORE SIMILAR IN ALL 3 GROUPS
- AVG ACUITY IN ALL 3 GROUPS WAS 20/20
- BOTTOM LINE: PTS WITH CI-DME AND GOOD VA CAN BE OBSERVED

50

Artificial Intelligence

AI is poised to revolutionize medicine.



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ARTIFICIAL INTELLIGENCE (AI)

- AI HOLDS IMMENSE PROMISE IN RESHAPING THE DELIVERY OF HEALTHCARE ON MULTIPLE FRONTS
- IMPROVE PATIENT ACCESS AND CARE OUTCOMES
- POTENTIAL TO BOOST PRODUCTIVITY AND PROVIDER EXPERIENCE
- ADOPTION IS STILL IN ITS INFANCY

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RETINA SPECIALIST

AI for DR screening: Where are we in 2025?

A look at how the algorithms are performing and ways they might be improved.

By Anand E. Rajesh, MD; Aaron Y. Lee, MD, MSCI

APRIL 25, 2025

Take-home points

- There are currently three FDA approved artificial intelligence algorithms for diabetic retinopathy screening in the United States that perform at a sensitivity and specificity of at least 87 and 89 percent, respectively.
- There have been more than 15,000 Medicare claims for AI DR screening algorithms since 2022, mostly in urban areas with academic centers.
- Liability for missed diabetes diagnoses likely falls on the device manufacturers, but it's less clear who's responsible if the model misses other harmful ocular diseases such as a melanoma or retinal detachment.
- There needs to be more studies comparing head-to-head performance of these algorithms across diverse datasets to ensure equitable performance of AI models.

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REIMBURSEMENT STRUCTURE FOR AI SCREENING IN DR 2023

Non-location dependent reimbursement

2022: 15000 MEDICARE CLAIMS FOR AI DR SCREENINGS
MOSTLY AT ACADEMIC UNIVERSITY SETTINGS

- CPT CODE 92229 (REMOTE IMAGING – AUTOMATED ANALYSIS) WAS $40.28
- CPT CODE 92227 (REMOTE IMAGING – STAFF REVIEW) AT $17.35
- CPT CODE 92228 (REMOTE IMAGING – MD INTERPRETATION) AT $29.14

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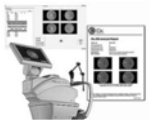
APR 12, 2018

AI device for detecting diabetic retinopathy earns swift FDA approval

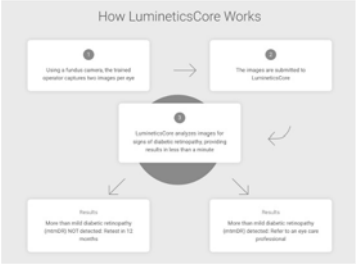
By Kang Jin Lee
FDA



- IMAGES CAPTURED BY TOPCON NW400 NON-MYDRIATIC RETINAL CAMERA
- IMAGES SENT TO A CLOUD-BASED SERVER THAT UTILIZES THE IDX-DR SOFTWARE AND A 'DEEP LEARNING' ALGORITHM
- THE TECHNOLOGY WAS **87% SENSITIVE AND 90% SPECIFIC** FOR DETECTING **MORE THAN MILD** DIABETIC RETINOPATHY
- THE ALGORITHM CORRECTLY IDENTIFIED **100% OF WITH ETDRS LEVEL 43 OR HIGHER (MODERATE NPDR)**

55

LUMINETICSCORE (PREVIOUSLY IDX-DR) BY DIGITAL DIAGNOSTICS



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AUGUST 6, 2020 FDA CLEARS EYEART: AI SYSTEM FOR DIABETIC RETINOPATHY DETECTION

EyeArt is the first FDA cleared AI technology for autonomous detection of both more than mild and vision-threatening diabetic retinopathy. It is the most extensively validated autonomous AI technology, tested in the real-world on more than half million patients and nearly two million retinal images globally..

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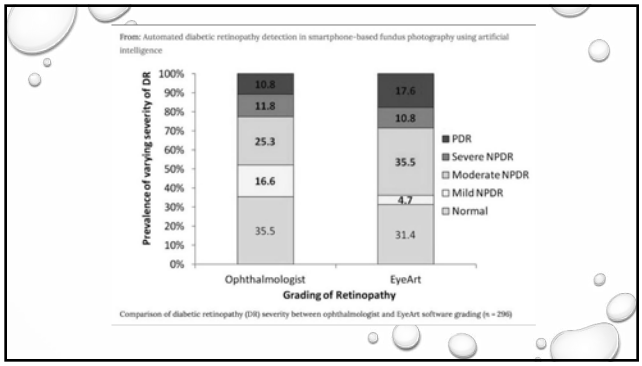

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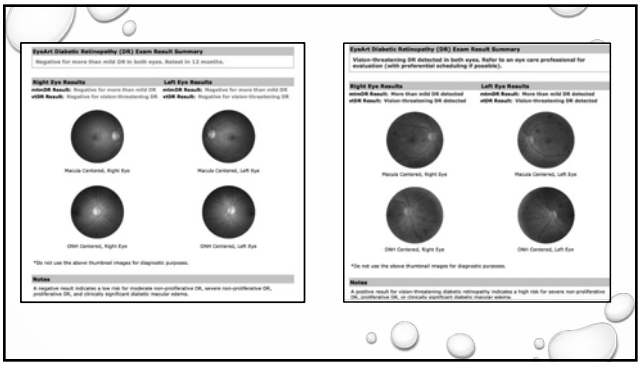

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AEYE FDA CLEARED AI SCREENING FOR DR

Compatible Retinal Cameras

AURORA AEYE

Cost-effective, portable retinal camera with built-in diagnostic screening intelligence

Optomed

92%-93% Sensitivity

89%-94% Specificity

> 99% Success rate

AEYE with Topcon

Robotic tabletop camera for superior ease of use

93% Sensitivity

91% Specificity

> 99% Success rate

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Ophthalmology Science Volume 6, Number 1, January 2026

Autonomous Artificial Intelligence in Diabetic Retinopathy Testing—Lessons Learned on Successful Health System Adoption

Clare W. Ting, MD,[1] Soaeun D. Patel, BS,[1] Andrew J. Barkmeier, MD,[2] T.Y. Alvin Liu, MD,[3] David Myung, MD, PhD,[4] Jeffrey Henderer, MD,[5] James Liu, MD,[3] Eric Hansen, MD,[3] Lama A. Al-Aswad, MD, MPH[1]

Emerging Themes from Early Adoption

Ophthalmology Departments Are Taking the Lead

Table 1. Evidence on Autonomous AI Testing Systems for DR from Clinical Implementations

Institution	AI System	Published Evidence: Sample size (n)	Gradability (nonmydriatic)	Gradability (mydriatic)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Ref.
University of Iowa	LumineticsCore	892	73.4%	96.1%	87.2%	90.7%	76%	96%	15
Mayo Clinic	LumineticsCore	1052	55.1%	91.7%	100%	89.2%	27.5%	100%	40
Johns Hopkins University	LumineticsCore	241	49%	N/A	N/A	N/A	N/A	N/A	43
Stanford University	LumineticsCore	80	71%	N/A	96%	60%	48%	97%	44
Temple University	EyeArt	260	75%	N/A	100%	78%	19%	100%	41

AI = artificial intelligence; DR = diabetic retinopathy; N/A = not applicable.

62

npj Digital Medicine Nov 2019

ARTICLE OPEN

Deep learning algorithm predicts diabetic retinopathy progression in individual patients

In-person expert examinations are impractical and unsustainable given the pandemic size of the diabetic population. As such, AI may offer a solution to this conundrum. DL, and specifically, deep convolutional neural networks (DCNNs), can be used for an end-to-end assessment of raw medical images to produce a target outcome prediction, the authors wrote.

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Algorithm to Predict DR Progression

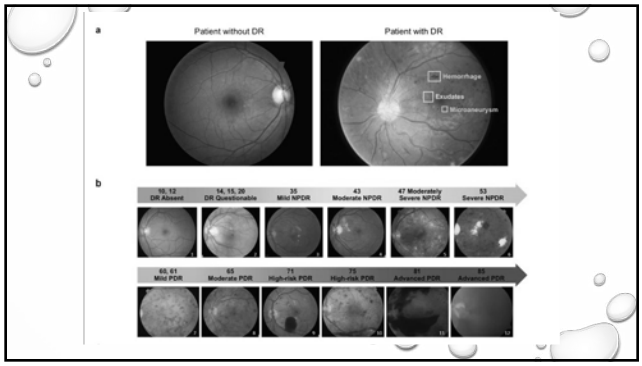
The global burden of diabetic retinopathy (DR) continues to worsen and DR remains a leading cause of vision loss worldwide. Here, we describe an algorithm to predict DR progression by means of deep learning (DL), using as input color fundus photographs (CFPs) acquired at a single visit from a patient with DR. The proposed DL models were designed to predict future DR progression, defined as 2-step worsening on the Early Treatment Diabetic Retinopathy Diabetic Retinopathy Severity Scale, and were trained against DR severity scores assessed after 6, 12, and 24 months from the baseline visit by masked, well-trained, human reading center graders. The performance of one of these models (prediction at month 12) resulted in an area under the curve equal to 0.79. Interestingly, our results highlight the importance of the predictive signal located in the peripheral retinal fields, not routinely collected for DR assessments, and the importance of microvascular abnormalities. Our findings show the feasibility of predicting future DR progression by leveraging CFPs of a patient acquired at a single visit. Upon further development on larger and more diverse datasets, such an algorithm could enable early diagnosis and referral to a retina specialist for more frequent monitoring and even consideration of early intervention. Moreover, it could also improve patient recruitment for clinical trials targeting DR.

npj Digital Medicine (2019)2:92 ; https://doi.org/10.1038/s41746-019-0172-3

Our findings show the feasibility of predicting future DR progression by leveraging Color Fundus Photography of a patient acquired at a single visit.

Upon further development on larger and more diverse datasets, such an algorithm could enable early diagnosis and referral to a retina specialist for more frequent monitoring and even consideration of early intervention.

64



65

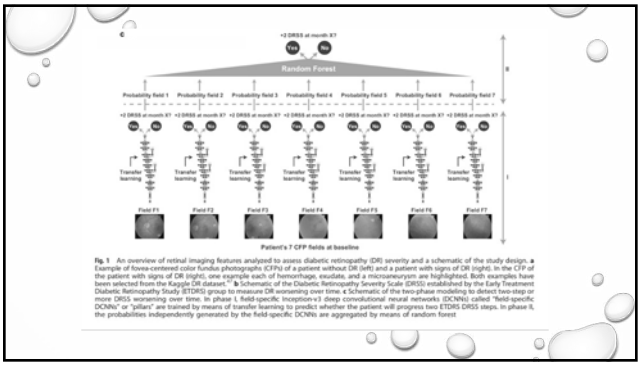


Fig. 1 An overview of retinal imaging features analyzed to assess diabetic retinopathy (DR) severity and a schematic of the study design. a Example of fovea-centered color fundus photographs (CFPs) of a patient without DR (left) and a patient with signs of DR (right). In the CFP of the patient with signs of DR (right), one example each of hemorrhage, exudate, and a microaneurysm are highlighted. Both examples have been selected from the Kaggle DR dataset.[42] b Schematic of the Diabetic Retinopathy Severity Scale (DRSS) established by the Early Treatment Diabetic Retinopathy Study (ETDRS) group to measure DR worsening over time. c Schematic of the two-phase modeling to detect two-step or more DRSS worsening over time. In phase I, field-specific Inception-v3 deep convolutional neural networks (DCNNs) called "field-specific DCNNs" or "pillars" are trained by means of transfer learning to predict whether the patient will progress two ETDRS DRSS steps. In phase II, the probabilities independently generated by the field-specific DCNNs are aggregated by means of random forest

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HOME› SMART HOME

Google Health wants to speed up healthcare with machine learning and smartphones

Accurate results in a flash

BY JULES WANG
PUBLISHED MAR 24, 2022

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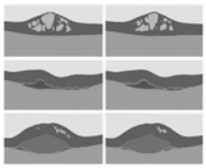
AUG 20, 2018

Google's AI product detects retinal diseases with unprecedented accuracy

By Anni Griswold
DeepMind

Comprehensive Ophthalmology, Retina/Vitreous



K. Widner, S. Virmani, J. Krause, *et al.* Lessons learned from translating AI from development to deployment in healthcare Nat Med, 29 (2023), pp. 1304-1306

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ARTIFICIAL INTELLIGENCE

Google's medical AI was super accurate in a lab. Real life was a different story.

If AI is really going to make a difference to patients we need to know how it works when real humans get their hands on it, in real situations.

MIT Technology Review

April 27, 2020
Will Douglas Heaven

THAILAND STUDY

- MANY OF THE IMAGES REJECTED (20%)
  - POOR LIGHTING
- IMAGES UPLOADED TO THE CLOUD BUT ISSUES WITH INTERNET SPEED
- TIME WASTED RE-TAKING IMAGES
- **WHEN IT DID WORK – IT WORKED WELL**
  - **ONE NURSE WAS ABLE TO SEE > 1000 PTS**
- PATIENTS DIDN'T REALLY CARE THAT IT WAS AN A RATHER THAN A HUMAN READING THEIR IMAGES – JUST WANTED GOOD EXPERIENCE

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AMERICAN ACADEMY OF OPHTHALMOLOGY

Ophthalmology Retina 2017

CrossMark

Deep Learning Is Effective for Classifying Normal versus Age-Related Macular Degeneration OCT Images

Cecilia S. Lee, MD, Doug M. Baughman, BS, Aaron Y. Lee, MD, MSCI

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May/June 2022 | Features

RT Retina Today

Artificial Intelligence in AMD Imaging

Here is a look at what to expect as this tool becomes more ubiquitous in research and the clinic.

AT A GLANCE

- Advances in retinal imaging have led to the identification of biomarkers for AMD progression that may one day shape how we diagnose, treat, and follow patients with AMD.
- Artificial intelligence (AI) algorithms may be able to provide analyses to assist physicians in diagnosing conditions based on specific features extrapolated from large volumes of imaging data.
- Researchers have demonstrated AI's ability to objectively identify, localize, and quantify subretinal fluid and high-risk structural biomarkers on OCT using a fully automated tool.
- AI-based imaging may be particularly useful in the era of personalized medicine, where we may be able to accurately predict outcomes and choose the optimal therapeutic strategies.

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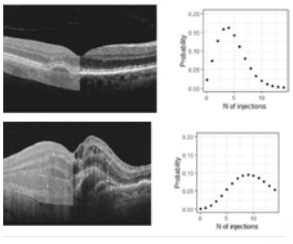
AI APPLICATIONS FOR THE RETINA

- **SCREENING FOR RETINAL DISEASE**
- **ASSESSMENT OF RETINAL ACTIVITY**
- PREDICTING DISEASE PROGRESSION
- ANTI-VEGF TREATMENT REQUIREMENTS
- PREDICTING TREATMENT OUTCOMES
- SURGICAL APPLICATIONS



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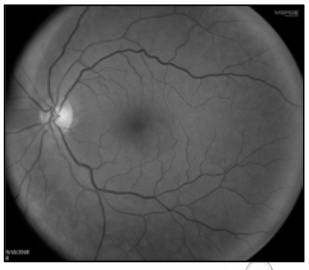
CAN AI DETERMINE METABOLIC HEALTH FROM FUNDUS PHOTOGRAPH?



73

Japanese Journal of Ophthalmology (2022) 66:499–503
https://doi.org/10.1007/s10384-022-00941-0

THE OFFICIAL INTERNATIONAL JOURNAL OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

EDITORIAL

Featured Article

Japan Ocular Imaging Registry: a national ophthalmology real-world database

- AS OF OCTOBER 2021, 6 FACILITIES ARE CONNECTED TO THE JOI REGISTRY NETWORK
- IT COMPRISES A TOTAL OF 486,189 FUNDUS IMAGES, 25,224 OCT IMAGES, AND 11,565 VISUAL FIELD RESULTS

74

JMA Journal: Volume 8, Issue 1
DOI: 10.31662/jmaj.2024-0139
https://www.jmaj.jp/

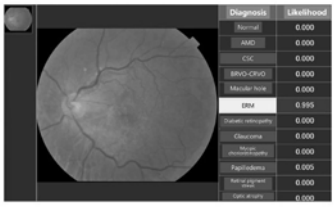


Figure 1. AI application for the differential diagnosis of 11 retinal diseases. This system was generated based on the big data stored in the Japan Ocular Imaging Registry [10].

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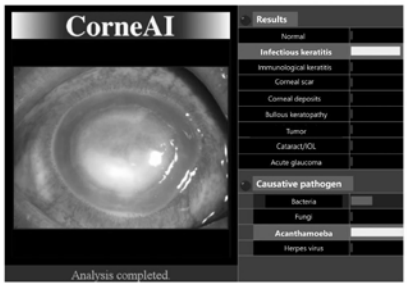

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AI ABLE TO DETERMINE **GENDER** AND **AGE** BASED ON FUNDUS PHOTOS

- JAPANESE OPHTHALMOLOGICAL SOCIETY AND THE NATIONAL INSTITUTE OF INFORMATICS HAS MADE AN ARTIFICIAL INTELLIGENCE (AI) MODEL
- MODEL DEVELOPED USING OVER 131,000 FUNDUS IMAGE FROM JAPAN OCULAR IMAGING REGSISTERY
- **ACCURACY OF PREDICTING BIOLOGICAL SEX WAS 92%**
- **PREDICTING AGE:** THE MEAN ABSOLUTE ERROR (MAE) BETWEEN ACTUAL AGE AND AGE PREDICTED BY THE **AI MODEL WAS 2.39 YEARS**

77

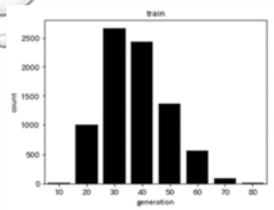

Fig. 1 Age distribution of training data

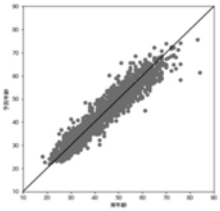

Fig. 3 Relationship between real age and predicted age in test data

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3. Predictive Model for Metabolic Syndrome Parameters from Fundus Images ▲

(1) Overview

This model estimates metabolic syndrome-related parameters (blood pressure, blood glucose levels, abdominal circumference, and BMI) from fundus images using data collected at a health screening facility through the Japan Ocular Imaging Registry. While internal validation has demonstrated the performance described below, there is no guarantee regarding its performance with external datasets. It is intended for use in research related to lifestyle diseases.

(4) Model Performance

Approximately 160,000 fundus images from individuals aged 17 to 94, with ground truth values for systolic and diastolic blood pressure, blood glucose levels, abdominal circumference, and BMI, were used. 80% of the images were used for training, and 20% for evaluation. A deep learning model was developed using TensorFlow 2 in Python 3. The model employed EfficientNet-B7, known for its high performance in fundus image analysis. The input image size for the deep learning model was set to 384×384 pixels. An example input image is shown in

- Systolic blood pressure: 10.34 mmHg
- Diastolic blood pressure: 7.09 mmHg
- Blood glucose: 8.71 mg/dl
- Abdominal circumference: 7.18 cm
- BMI: 2.53

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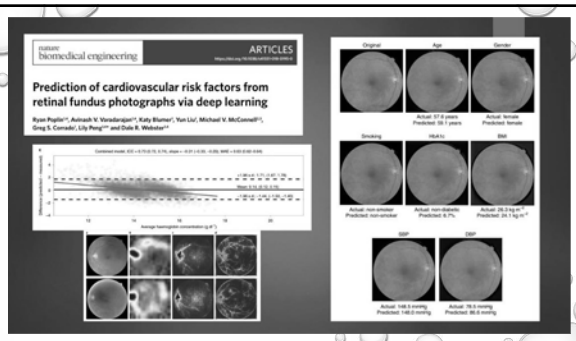

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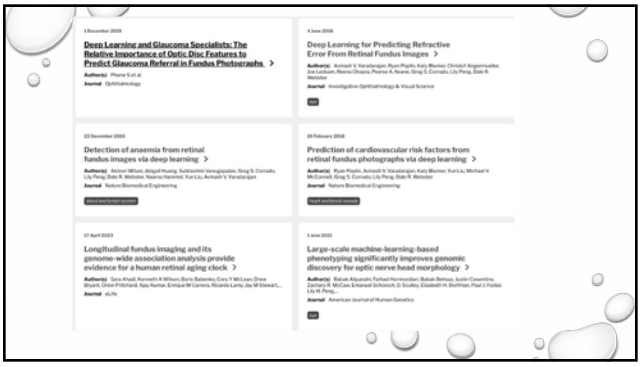
81



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ARTIFICIAL INTELLIGENCE (AI) SUMMARY

- AI HOLDS IMMENSE PROMISE IN RESHAPING THE DELIVERY OF HEALTHCARE ON MULTIPLE FRONTS
- IMPROVE PATIENT ACCESS AND CARE OUTCOMES
- POTENTIAL TO BOOST PRODUCTIVITY AND PROVIDER EXPERIENCE
- ADOPTION IS STILL IN ITS INFANCY

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2024 GLP-I RECEPTOR AGONIST STATISTICS

- 6% OF US ADULTS ACTIVELY TAKING GLP-1RA
- 12% OF US ADULTS HAVE USED GLP-1RA AT SOME POINT
  - 7% FOR CHRONIC DISEASE
  - 5% FOR WEIGHT LOSS ALONE
  - APPROXIMATELY 15 MILLION RXS IN 2024 AND RAPIDLY INCREASING
- OZEMPIC SALES ALONE INCREASED FORM $0.4 B IN 2018 TO $26.4 B IN 2023
- HAVE BEEN ASSOCIATED WITH VARIOUS EYE CONDITIONS, INCLUDING INCREASED RATES OF DR, AMD, AND NAION

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FDA-Approved GLP-1RAs

Generic Name	Brand Name(s)	Approval Year	Dosing	Indications
Exenatide	Byetta, Bydureon BCise	2005/2012/2017	BID/Weekly/Weekly	T2DM adjunct
Liraglutide	Victoza, Saxenda	2010	One time Daily	T2DM, CV risk, Obesity ≥12 y/o
Dulaglutide	Trulicity	2014	One time Weekly	T2DM, CV risk
Lixisenatide	Adlyxin	2016	One time Daily	T2DM adjunct
Semaglutide	Ozempic, Rybelsus, Wegovy	2017-2021	One time Weekly Oral Daily Weekly injection	T2DM, CV risk, Obesity
Tirzepatide	Mounjaro, Zepbound	2022-2023	Weekly injection	T2DM, Obesity, Obstructive Sleep Apnea (OSA)

86

GLP-1RA AND DR

- 2006: SUSTAIN-6
- INCREASED RATE OF DR IN PTS TAKING SEMAGLUTIDE VS CONTROL
  - 3% IN PTS TAKING SEMAGLUTIDE VS 1.8% IN PLACEBO
  - TWICE THE RATE OF PRP: 2.3% VS 1.2%
  - SLIGHTLY MORE ANTI-VEGF INJECTIONS : 1% VS 0.8%
  - MORE VITREOUS HEMES: 1% VS 0.4%
  - MORE DIABETES RELATED BLINDNESS: 0.3% VS 0.1%

87

GLP-1RA AND DR

- 2022: WANG ET AL, CLIN DRUG INVESTIGATION
  - LOOKED AT 23 CLINICAL TRIALS, 22,096 PATIENTS
  - NOT ASSOCIATED WITH INCREASED RISK OF DR
  - INCREASED RATES OF DR IN PATIENTS>60 AND DIABETES DURATIONS > 10 YEARS
- IRIS REGISTRY, AAO MEETING: NOV. 2023
  - 48 K PTS WITH INJECTABLE SEMAGLUTIDE OVER 2 YEARS
  - 2.2% WITH NO OR VERY MILD NPDR HAD INCREASED RETINOPATHY
  - 3.5% WITH MILD TO MODERATE SHOWED WORSENING
  - 60% OF EYES WITH SEVERE NPDR OR WORSE HAD AN IMPROVEMENT IN RETINOPATHY

88

GLP-1RA AND DR

- OCTOBER 2024: ENDOCRINE AND METABOLIC SCIENCE
  - SEMAGLUTIDE NOT ASSOCIATED WITH INCREASED RISK OF DR, VISION LOSS, OR INCREASED NUMBER OF ANTI-VEGF INJECTION OVER 3 YEARS
- NOV 2025 : CLIN DRUG INVESTIGATION
  - NO INCREASED RISK OF PDR OR TREATMENT REQUIRED DR/DME
- SEPT 2025: OPHTHALMOLOGY RETINA
  - PTS ON GLP-1 HAD LOWER RATES OF DME THAN ON OTHER DM MEDS
- SEPT 2025: DIABETES, OBESITY, AND METABOLISM
  - SEMAGLUTIDE SLOWS THE PROGRESSION OF DR BY IMPROVING RETINAL VASCULAR LESIONS AND REDUCING OXIDATIVE STRESS, AND SHOULD FURTHER BE STUDIED AS A POTENTIAL TREATMENT FOR DR

89

GLP-1RA AND AMD

- JUNE 2025: JAMA OPHTH
  - POPULATION BASED CANADIAN STUDY OF 139,002 PATIENTS WITH DM
    - RISK OF NAMD WAS 0.2% IN GLP-1 USERS AND 0.1% IN NON-USERS
    - RELATIVE RISK WAS MORE THAN 2 X
- OCTOBER 2025:JAMA OPHTH
  - LOOKED AT 91,408 PTS TREATED WITH GLP-1FOR OBESITY AND NOT DM
    - REDUCED RISK OF NONEXUDATIVE AMD IN GLP-I USERS
    - NOT ASSOCIATED WITH INCREASED CONVERSION FORM NONEXUDATIVE TO EXUDATIVE AMD
- DEC 2025: RETINA
  - GLP-1 USE MAY REDUCE BOTH THE RISK AND PROGRESSION OF EARLY AND INTERMEDIATE AMD TO ADVANCED AMD IN PATIENTS WITH TYPE 2 DM

90

GLP-1RA AND NAION

- AUG 2024: JAMA OPHTHALMOL
  - FINDINGS *SUGGEST* AN ASSOCIATION BETWEEN NAION AND SEMAGLUTIDE
- JUNE 2025: EUROPEAN MEDICINE AGENCY PHARMACOVIGILANCE ASSESSMENT COMMITTEE CONCLUDED NAION IS A VERY RARE SIDE EFFECT OF SEMAGLUTIDE USE 1/10,000 PATIENTS VS 1/20,000 IN GENERAL
  - DOUBLED THE RISK
  - BUT, ONE ADDITIONAL CASE OVER 10,000

91

CLINICAL RECOMMENDATIONS FOR OPTOMETRIC CARE

- ACCORDING TO THE AOA'S COMPREHENSIVE ADULT EYE AND VISION EXAMINATION, 2ND EDITION, INDIVIDUALS TAKING GLP-1RAS ARE CONSIDERED "AT-RISK" PATIENTS. THESE PATIENTS SHOULD:
  - HAVE BASELINE DILATED EXAMS PRIOR TO OR SHORTLY AFTER INITIATION OF THERAPY
  - FOLLOW MORE FREQUENT REEXAMINATION IF CERTAIN RISK FACTORS
  - RECEIVE INDIVIDUALIZED RISK COUNSELING REGARDING DR, AMD AND NAION RISK, ESPECIALLY IF THEY HAVE A "DISC AT RISK"
  - COLLABORATIVE CARE WITH PROVIDERS MANAGING THE PATIENT'S DIABETIC AND OTHER SYSTEMIC CONDITIONS

92

Risk Factors for the Development of Eye and Vision Problems

Having a personal or family history of ocular disease.	Having functional vision in only one eye.
Belonging to certain racial and ethnic groups.	Wearing contact lenses.
Having systemic health conditions with potential ocular manifestations (e.g., diabetes mellitus, hypertension, obesity, arteriosclerosis).	Undergoing eye surgery or experiencing previous eye injury.
Participating in occupations that are highly demanding visually or have a high potential of being hazardous to the eyes.	Having high or progressive refractive error.
Taking prescription or nonprescription drugs with ocular side effects.	Experiencing other progressive eye-related health concerns or conditions.

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PLAQUENIL: HYDROXYCHROLOQUINE (HCQ)

- USED PRIMARILY FOR:
  - SLE
  - RA
  - SARCOID
  - OTHER AUTOINFLAMMATORY AND DERMATOLOGIC DISEASES
- BEING INVESTIGATED FOR:
  - DM
  - HEART DISEASE
  - ADJUNCT CANCER THERAPY
- ASSOCIATED WITH MACULOPATHY

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RISK FACTORS

- ***DAILY HCQ DOSAGE: >5.0 MG/KG (CQ >2.3 MG/KG)***
- ***MAXIMUM 400 MG/DAY IN SEVERE OBESITY***
- ***DURATION OF USE: >5 YEARS***
- ***RENAL DISEASE: SUBNORMAL GLOMERULAR FILTRATION RATE***
- ***CONCOMITANT DRUGS: TAMOXIFEN***
- ***MACULAR DISEASE: IF AFFECTING VISION OR ABILITY TO SCREEN***
- ***OLD AGE: INITIATION OF HCQ AT OLDER AGES***

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BASELINE SCREENING

- ***OBTAIN BASELINE CLOSE TO THE INITIATION OF HCQ***
- ***INCLUDE FUNDUS EXAM, OCT AND WIDE-PATTERN FAF***
- ***ANNUAL SCREENING ON HCQ:***
  - ***ANNUAL SCREENING IS STRONGLY RECOMMENDED***
  - ***CAN DEFER UNTIL AFTER 5 YEARS OF HCQ USE IF NO SIGNIFICANT RISK FACTORS***
- ***BEGIN AT INITIATION OF THERAPY IF SIGNIFICANT RISK FACTORS PRESENT***
- ***ALWAYS INCLUDE OCT AND WIDE-PATTERN FAF***

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ANNUAL SCREENING

- ***PRIMARY TECHNIQUES:***
  - ***SPECTRAL-DOMAIN OCT***
  - ***WIDE-PATTERN FUNDUS AUTOFLUORESCENCE***
- ***SECONDARY OR CONFIRMATORY TECHNIQUES***
  - ***VF (10-2 PLUS 24-2 OR 30-2; OR COMBINED ALGORITHM LIKE 24-2C)***
  - ***MULTIFOCAL ERG (MFERG)***

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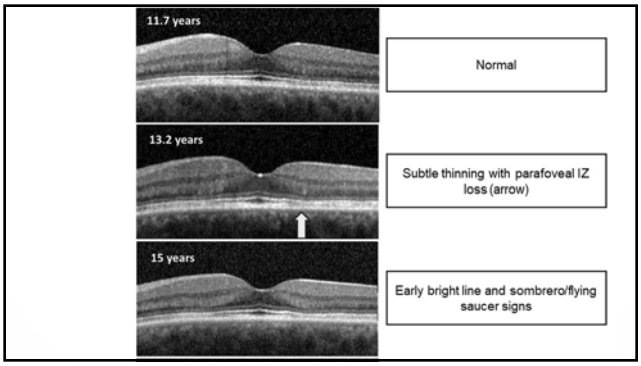
NOT RECOMMENDED FOR ANNUAL SCREENING

- ***FUNDUS EXAMINATION***
- ***TIME-DOMAIN OCT***
- ***OCT-ANGIOGRAPHY (OCT-A)***
- ***FLUORESCEIN ANGIOGRAPHY***
- ***FULL-FIELD ERG***
- ***AMSLER GRID***
- ***COLOR TESTING***
- ***EOG***

98



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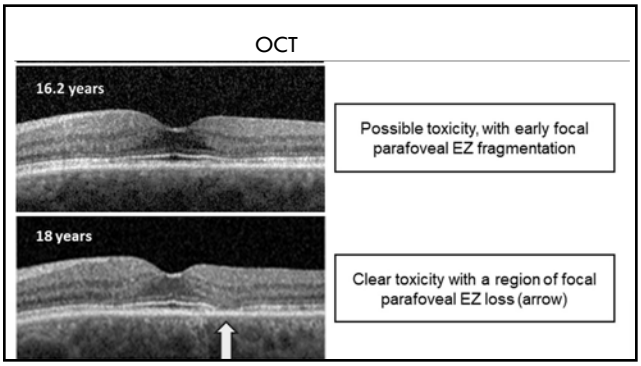

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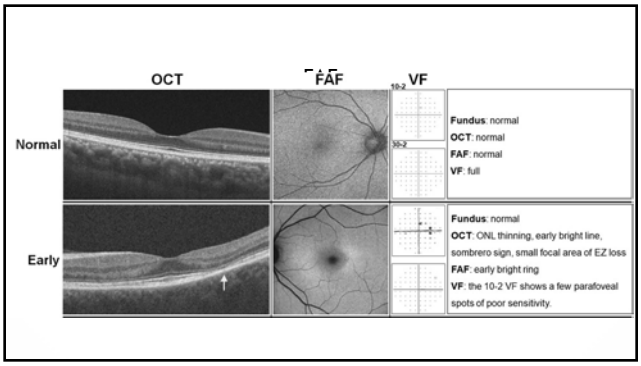

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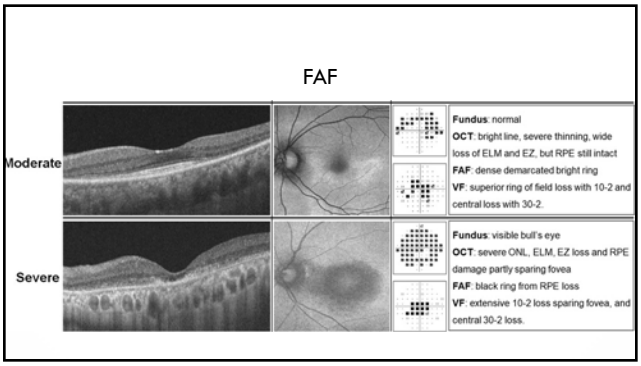

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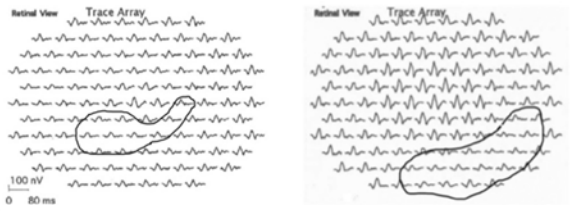
MFERG



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BOTTOM LINE

- 10-2 VF NO LONGER NEEDED FIRST LINE! YAY!!!
- SD-OCT CRUCIAL
- FAF *STRONGLY* SUGGESTED
- FOLLOW YEARLY AFTER 5 YEARS OF USE
- SOONER IN HIGH-RISK PATIENTS
- CONSULT WITH PCP AT FIRST SIGN OF TROUBLE!

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BOTTOM LINE

- GLOBAL OVERALL RISK OF TOXICITY: 7.5%
  - WITH CORRECT DOSAGE:
    - <1% IN 5 YEARS
    - <2% IN 10 YEARS
    - <5% IN 20 YEARS
- MILD MACULOPATHY UNLIKELY TO PROGRESS
- SEVERE MACULOPATHY MAY INCREASE EVEN AFTER DISCONTINUATION FOR YEARS

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PRESERVISION AREDS3: A NEXT-GEN FORMULA THAT COMBINES AREDS2 NUTRIENTS WITH A B-VITAMIN COMPLEX

Nutrient	AREDS 2	AREDS3
Lutein	10 mg	10mg
Zeaxanthin	2 mg	2 mg
Vitamin C	500 mg	500 mg
Vitamin E	180 mg	180 mg
Zinc	80 mg	25 mg
Copper	2 mg	2 mg
Vit B1 (Thiamin)	-	**3.6 mg**
Vit B2 (Riboflavin)	-	**3.9 mg**
Vit B3 (Niacin)	-	**32 mg**
Vit B5 (Pantothenic Acid)	-	**15 mg**
Vit B6	-	**50 mg**
Vit B7 (Biotin)	-	**90 mcg**
Vit B9 (Folate)	-	**1500 mcg DFE**
Vit B12	-	**1000 mcg**

THE PRESERVISION® AREDS3 FORMULA WILL BE STUDIED IN A LONG-TERM TRIAL INCLUDING PATIENTS WITH ALL STAGES OF AMD, FROM EARLY TO GEOGRAPHIC ATROPHY

Adds a B-vitamin complex

Per day amount reflected; take 1 soft gel with a meal 2 times per day

AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study; DFE, Dietary Folate Equivalent; Vit, vitamin

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Why B Vitamins? They Support Essential Functions[1]

B1 (Thiamin)	Energy metabolism
B2 (Riboflavin)	Energy production & antioxidant reactions
B3 (Niacin)	NAD cofactor
B5 (Panothenic acid)	Fat, protein, & carbohydrate metabolism
B6	Homocysteine metabolism
B7 (Biotin)	Fatty acid & glucose metabolism
B9 (Folate)	DNA synthesis, methylation
B12	Myelin & DNA synthesis

Common dietary sources include whole grains, legumes, nuts, dairy, eggs, meat, fish, and leafy greens[1]

Approximately 10–20% of the US population has B-vitamin deficiency[1-3]

NAD, nicotinamide adenine dinucleotide; DNA, deoxyribonucleic acid

1. National Institutes of Health, Office of Dietary Supplements. Vitamin and Mineral Supplement Fact Sheets. 2024. Accessed November 10, 2024. https://ods.od.nih.gov/factsheets/list-vitaminsminerals/ 2. Brown MJ, et al. Vitamin B6 Deficiency. Updated Aug 8, 2022. StatPearls. 2024. 3. Whelan AJ, et al. Clin Med (Lond). 2015;15(2):145-50.

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Multiple Studies Support the Role of B Vitamins in Reducing Incidence & Progression of AMD

› **These study points helped inform the ingredient profile for the AREDS3 formulation**

	Dietary Intake	Risk Level
B1	↑	↓ by ~45-60% for late AMD[1]
B6	↑	↓ for wet AMD[2]
B9	↑	↓ for developing GA and large drusen[2,3]
B12	↑	↓ for AMD by 42%[4]
B5, B6	↑	↓ by ~28% for advanced AMD[5]
B6, B9	↑	↓ for late AMD[2]
B1, B2, B3, B5, B6, B9, B12	↓	Observed in patients with AMD vs without AMD[6,7]

Daily Supplement	
B2 + 13 other ingredients	Stabilized atrophic AMD[8,9]
B3 + 2 other ingredients	Improved a measure of retinal function (FERG)[10]
B12 + 11 other ingredients	Functional improvement of preganglionic retinal elements[11]
B6, B9, & B12	↓ risk of AMD vs placebo by ~41%[12]

B vitamin supplementation has been found to lower levels of homocysteine, a potential contributor to AMD[13]

AMD, age-related macular degeneration; AREDS, Age-related Eye Disease Study; FERG, focal electroretinogram; GA, geographic atrophy

1. Zhang Q, et al. Ophthalmol Ther. 2022;Jan13:1-21. 2. Agrón E, et al. Ophthalmology. 2021;128:435-42. 3. Merle BMJ, et al. Am J Clin Nutr. 2016;103:1135-44. 4. Gopinath B, et al. Am J Clin Nutr. 2013;98:129-35. 5. Merle BMJ, et al. Nutrients. 2022;14:2831. 6. Šoltésová Prnová J, et al. Cent Eur J Public Health. 2020;28:1-40. 7. Liu Z, et al. Front Nutr. 2024;11:1504581. 8. Age-Related Macular Degeneration Study Group. J Am Optom Assoc. 1996; 67:12-26. 9. Bolton S, et al. Am Optom Assoc. 1996; 67:30-49. 10. Fisher R, et al. Ophthalmology. 2005; 112:61-80. 11. Parravano M, et al. Adv Ther. 2019; 36:2492-502. 12. Christen WG, et al. Arch Intern Med. 2009; 169:335-41.

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PUBLISHED STUDIES SUGGEST A WIDER RANGE OF PATIENTS MAY BENEFIT FROM ADDING B-VITAMIN SUPPLEMENTATION

Studies show that intake of certain **B vitamins** are associated with reduced risk of early and visually significant AMD[2,3]

AREDS 2 formula may reduce risk of progression to advanced AMD and slow GA spread toward the macula[4,5]

AMD, age-related macular degeneration; AREDS, Age-Related Eye Disease Study; GA, geographic atrophy

2. Gopinath B, et al. *Am J Clin Nutr.* 2013;98(1):129–1351. 3. Christen WG, et al. *Ophthalmic Epidemiol.* 2016;23(1):22–39. 4. Age-Related Eye Disease Study Research Group. AREDS report no. 7. *ArchOphthalmol.* 2001. 5. Keenan TDL, et al. *Ophthalmology.* 2022;129(2):214-29.

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B VITAMINS MAY BE SUPPORTIVE IN OCULAR DISEASE BEYOND AMD

Condition	B Vitamins	Mechanism
Dry Eye/OSD[1,2]	B2, B6	• Promote tear secretion • Reduce inflammation via cytokine modulation
Diabetic Retinopathy[3,4]	B1, B6, B12	• Protect against oxidative stress • Neuroprotection of RGC and pericytes
Optic Neuropathy[5,6]	B12	• Neuroprotection of RGC • Reduce homocysteine levels • Myelin sheath synthesis and maintenance
Glaucoma[6]	B6, B9, B12	• Neuroprotection of RGC • Reduce homocysteine levels • Maintain ONH vascular perfusion

AMD, age-related macular degeneration; ONH, optic nerve head; OSD, ocular surface disease; RGC, retinal ganglion cells

1. Hyon JY, Han SB. *Applied Sciences.* 2022; 12(5):2541. 2. Hu J, et al. *Biomedicines.* 2025;13(1):541. 3. Sekhonia E, et al. *Acta Diabetol.* 2021;58(11):1433-1439. 4. Ola MS, et al. *Int J Mol Sci.* 2013;14(2):2559-72. 5. Garg P, et al. *The Pan-American Journal of Ophthalmology.* 2020;7(1):165.
6. Tribble JR, et al. *Cell Rep Med.* 2025;6(5):102127.

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MANY ARE AT RISK OF B-VITAMIN DEFICIENCY

Older adults
- Up to 20% may have subclinical B12 deficiency[1,2]
- B12 deficiency raises homocysteine levels, associated with microvascular injury in the eye[3]

Plant-based diets
- Vitamin B12 primarily obtained from animal-based sources[4]
- Vitamin B12 not naturally found in plant foods, but can be added to some (eg, cereals and nutritional yeast)[5]

Metformin-induced deficiency[6]
- Evidence suggests that long-term and high-dose metformin therapy impairs vitamin B12 (cobalamin) status

Bariatric surgery[7]
- Contributes to deficiency via lower intake and malabsorption
- Even preoperatively, 20-30% of candidates may have B-vitamin deficiency

1. Allen LH. *Am J Clin Nutr.* 2009;89(2):693S-6S. 2. O'Leary F, et al. *Nutrients.* 2010;2(3):299-316. 3. Satyanarayana A, et al. *PLoS One.* 2011;6(1):e26747. 4. Niklewicz A, et al. *Eur J Nutr.* 2023 ;62(2):1551-1559. 5. National Institutes of Health, Office of Dietary Supplements. Vitamin and Mineral Supplement Fact Sheets. 2024. Accessed November 10, 2025. https://ods.od.nih.gov/factsheets/list-all/. 6. Alharbi N, et al. *World J Diabetes.* 2021;12(7):916-931. 7. Al-Mansoori A, et al. *Nutrients.* 2021;13(6):2383.

111

WHAT ABOUT THE SAFETY OF B VITAMINS?

B vitamins are water-soluble and generally deemed safe, especially for ocular health

Clinical Adverse Events
- Five trials: No ocular adverse events with supplementation[1-6]

At-Risk Populations
- Liver disease → higher risk of niacin toxicity[7]
- Neuropathy → vulnerable to chronic high-dose B6 toxicity[8]

1. Falsini B, et al. *Ophthalmology.* 2003;110:51-60. 2. Parravano M, et al. *Adv Ther.* 2019;36:2493-505. 3. Christen WG, et al. *Arch Intern Med.* 2009;169:335-41.
4. Richer S, et al. *Optometry.* 2004;75:216-30. 5. Richer S, et al. *Optometry.* 2007; 78:213-9. 6. Azer G, et al. *J Ft Ophthalmol.* 2017;40:303-13.
7. Duffy M, et al. *Cureus.* 2024;16(9):e68018. 8. Patsoukis A, et al. *Cureus.* 2022;15(11):e48792.

112

WOULD YOU RECOMMEND SURGICAL INTERVENTION FOR PATIENTS WITH INTRACTABLE SYMPTOMS OF FLOATERS?

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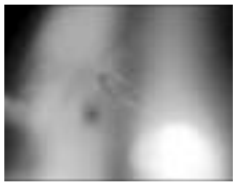
FLOATERECTOMY?

- IS IT TOO DANGEROUS OR A REASONABLE OPTION?



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THE BURDON OF FLOATERS

RETROSPECTIVE STUDY BASCOM PALMER EYE INSTITUTE 2008-2011

- 7.2% OF PATIENTS REFERRED TO A RETINAL SPECIALIST HAD FLOATERS
- 5TH MOST COMMON DIAGNOSIS OVER THAT TIME
  - > 60 YO 3RD MOST COMMON DX
- VITRECTOMY: VERY SUCCESSFUL, TECHNICALLY SIMPLE, WITH LOW SIDE-EFFECT PROFILE
  - RISK OF CATARACT, ERM, AND RETINAL TEARS/DETACHMENTS

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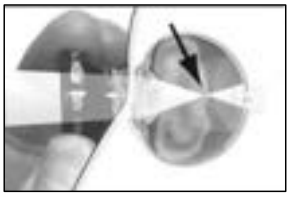
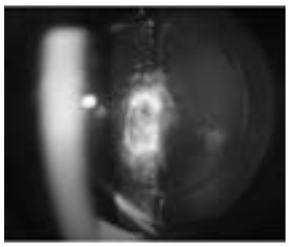
OPTIONS FOR TREATMENT OF FLOATERS

- YAG VITREOLOYSIS
- PARS PLANA VITRECTOMY





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IMPORTANT CONSIDERATIONS IN PATIENTS WITH FLOATERS

ARE THEY ACUTE OR CHRONIC?

- ACUTE FLOATERS – OFTEN FROM PVD
  - USUALLY RESOLVE
- CHRONIC FLOATERS THAT IMPACT DAILY ACTIVITIES

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REASONS FOR SURGERY FOR FLOATERS

SYMPTOMS THAT IMPACT THE QUALITY OF LIFE

- UNABLE TO READ CONTINUOUSLY
- UNABLE TO SAFELY DRIVE A CAR
  - THE FLOATERS/CLOUD MOVES IN FRONT OF THEIR VISION AND THEY NEARLY HAVE TO PULL OVER FOR FEAR OF HAVING AN ACCIDENT
- AFFECTS ABILITY TO PERFORM YOUR JOB

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THE IDEAL CANDIDATE FOR TREATMENT OF FLOATERS

- SYMPTOMATIC
- PSEUDOPHAKIC
- PVD

The **NOT** Ideal Candidate for Treatment of Floaters

- Young
- Phakic
- Attached vitreous
- High myope

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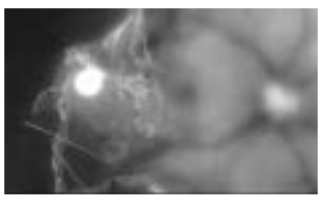
LASER VITREOLYSIS FOR FLOATERS

- DONE WITH A YAG
- HIGHLY VARIABLE RESULTS
- COMPLICATIONS:
  - CATARACT (HITTING THE LENS)
  - POSTERIOR CAPSULE TEARS
  - RETINAL BURNS
  - FOVEAL BURNS
  - CHOROIDAL RUPTURE
  - CHOROIDAL HEMORRHAGES
  - RETINAL TEAR



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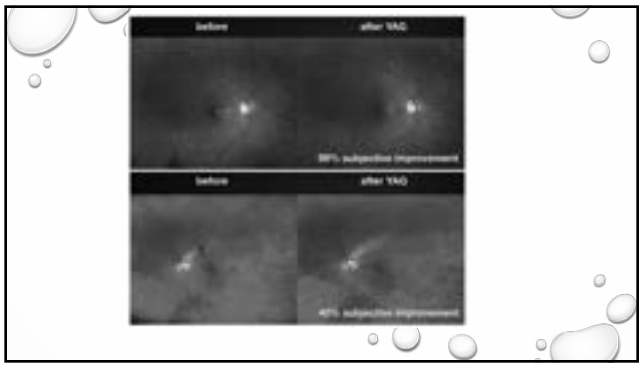

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Long-Term Follow-Up of Efficacy and Safety of YAG Vitreolysis for Symptomatic Weiss Ring Floaters

Chirag P. Shah, MD, MPH; Jeffrey S. Heier, MD

- 35 OF 52 PATIENTS RANDOMIZED TO YAG VITREOLYSIS OR CONTROL FOLLOWED FOR 2.3 YEARS
- 50% FELT THEIR SYMPTOMS WERE SIGNIFICANTLY OR COMPLETELY BETTER AT 6 MONTHS
  - ~60% OVERALL IMPROVEMENT IN SYMPTOMS
- 3 PATIENTS DEVELOPED RETINAL TEARS AFTER 6 MONTHS (NOT SYMPTOMATIC)

Ophthalmic Surg Lasers Imaging Retina 2020

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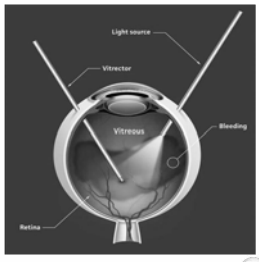
IS VITRECTOMY A BETTER OPTION?



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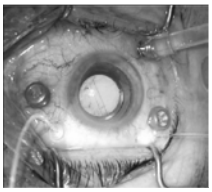
VITRECTOMY 2023

- SMALLER-GAUGE INSTRUMENTS (25 OR 27) COMPARED WITH THE 20-GAUGE NEEDLES USED LESS THAN 15 YEARS AG
- SMALLER VITRECTOMY INSTRUMENTS ALLOW FOR SUTURELESS PROCEDURES
  - SMALLER SCLEROTOMY
  - TROCARS ALLOW FOR SMALL, THIN-WALL CANNULA
- LESS INFLAMMATION
- FEWER COMPLICATIONS
- MUCH GREATER SUCCESS RATE



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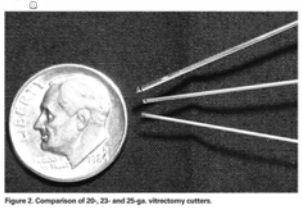

Figure 2. Comparison of 20-, 23- and 25-ga. vitrectomy cutters.

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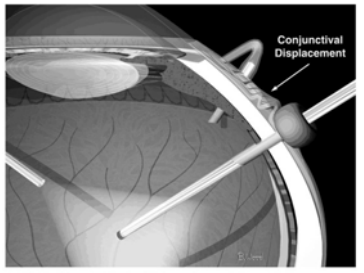

Figure 9.2 ■ Wound leaks are prevented by conjunctival displacement with respect to the 0.5-mm scleral incision.

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RISK FACTORS FOR VITRECTOMY

- CATARACT
- RETINAL TEAR OR DETACHMENT
- ERM/MACULAR PUCKER
- MACULAR EDEMA
- ENDOPHTHALMITIS

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INDUCE A PVD….OR NOT

- RISK OF DEVELOPING A RETINAL TEAR BY INDUCING PVD
- REDUCED RISK/TIME OF DEVELOPING CATARACT WITH PARTIAL VITRECTOMY

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BASCOM PALMER VITRECTOMY FOR FLOATERS STUDY

- RETROSPECTIVE CHART REVIEW
- PPV FOR SYMPTOMATIC PRIMARY VITREOUS FLOATERS
- **150 PATIENTS** EVALUATED BETWEEN 1/1/2012– 1/1/2023
- AGE OF ONSET 66/67
- GENDER: 65 FEMALE, 85 MALE
- **# OF EYES: 208**
- SYMPTOMS DURATION **12.3 MO ± 8 MO**
- 74% PSEUDOPHAKIA

Ocular Disease
- 4 eyes treated tears
- 2 asteroid hyalosis
- 5 eyes glaucoma
- 10 high myopia
- 10 eyes refractive surgery

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COMPLICATIONS

Post Op Complications	# Eyes	Mean Time of Dx following Surgery
Cataract	18 (53%)	9.13 ± 6 months
Steroid induced Increase in IOP	10 (4.8%)	1 moth
Vit Heme	8 (3.9%)	4 ± 4 days
Retinal Detachment	7 (3.4%)	20 ± 37 months
Symptomatic CME	4 (1.9%)	16.8 ± months
ERM	3 (1.4%)	15 ± months
Endophthalmitis	1 (0.5%)	1 day
Hyphema	1 (0.5%)	1 day
Symptomatic floats	1 (0.5)	6 months

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RATE OF COMPLICATIONS FOR VITRECTOMY FOR VITREOUS FLOATERS IS "LOW"

NEEDS TO BE DISCUSSED WITH THE PATIENT

- RRD: 7 EYES (3.4%)
- VH: 7 EYES (3.4%): ALL CLEARED
- OTHER
  - ENDOPHTHALMITIS 1 EYE
  - REDO SURGERY 1 EYE

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ARVO Annual Meeting Abstract | June 2013

Long-term Safety of Vitrectomy for Patients with Floaters

Christianne Wa; Kenneth Yee; Laura Huang; Alfredo Sadun; J Sebag

- 66 EYES IN 52 PATIENTS (AGE = 63 ± 12 YEARS) WERE INCLUDED
- 36/66 (**54.5%**) EYES WERE **PHAKIC**
- AVERAGE DURATION OF COPING WAS 30 MONTHS
- ETIOLOGY OF FLOATERS WAS **PVD IN 44/66 (67%),** MYOPIA IN 19/66 (28%), ASTEROID HYALOSIS IN 8/66 (12%)
- RETINOPEXY FOR RETINAL BREAKS OCCURRING AT THE TIME OF PVD WAS PERFORMED IN 16 EYES (36% OF ALL EYES WITH PVD; 24% OF ALL EYES), A **MINIMUM OF 3 MONTHS PRIOR TO VITRECTOMY**
- **22 EYES WITHOUT PVD: PVD NOT INDUCED AND VITREOUS REMAINED INTACT PERIPHERALLY.**
- MAIN OUTCOME: INCIDENCE OF RET TEARS/DETACHMENTS AND CATARACT REQUIRING SURGERY

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ARVO Annual Meeting Abstract | June 2013

Long-term Safety of Vitrectomy for Patients with Floaters

Christianne Wu; Kenneth Yee; Laura Huang; Alfredo Sadun; J Sebag

- **FLOATER SYMPTOMS RESOLVED IN 65 OF 66 EYES (98.5%)**
- NO PATIENTS (0/66; 0%) DEVELOPED RETINAL BREAKS, HEMORRHAGE, INFECTION, OR GLAUCOMA (3 MONTH – 3 YEARS)
- **NO RETINAL BREAKS/ DETACHMENTS IN THE 22 PATIENTS WITHOUT PVD PRE-OPERATIVELY (0/22 VS 9/30)**
- ONLY **7/36 (19%) PHAKIC EYES DEVELOPED CATARACTS** REQUIRING SURGERY, AN AVERAGE OF 16.5 MONTHS POST-VITRECTOMY (7/36 VS 18/36 (50%)

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Ophthalmology Retina

2018

Long-Term Safety and Efficacy of Limited Vitrectomy for Vision Degrading Vitreopathy Resulting from Vitreous Floaters

J. Sebag, MD, FARVO • Kenneth M.P. Yee, BS • Justin H. Nguyen, BA • Jeannie Nguyen-Cuu, BS

Published: May 11, 2018 • DOI: https://doi.org/10.1016/j.oret.2018.03.011 • Check for updates

Methods

195 Eyes

Limited vitrectomy with 25-gauge instruments was performed without surgical PVD induction, preserving 3 to 4 mm of retrolental vitreous in phakic eyes. Follow-up averaged 32.6 ± 23.5 months (range, 3–115 months), with 2 years or more in 144 eyes, 3 years or more in 69 eyes, 4 years or more in 51 eyes, and 5 years or more in 24 eyes.

Conclusions

Limited vitrectomy for Vision Degrading Vitreopathy decreases vitreous echodensity, improves patient well-being, improves VA, and normalizes CSF. The long-term efficacy and safety profiles suggest this may be a safe and effective treatment for clinically significant vitreous floaters, warranting a prospective randomized trial.

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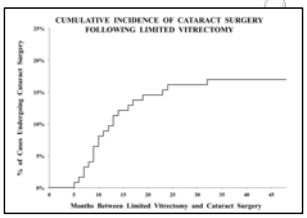
Table 2. Postoperative Complications

Complication	No. (n = 195 Eyes)	%
Vitreous hemorrhage	2	1.0
Retinal detachment	3	1.5
Retinal tear	3	1.5
BRVO	3	1.5
CRAO	2	1.0
Endophthalmitis	0	0.0
Glaucoma	1	0.5
Cataract surgery (124 phakic eyes)	21/124	16.9
PVD (43 without PVD before surgery)	4/43	9.3
Macular pucker	2	1.0

BRVO = branch retinal vein occlusion; CRAO = central retinal artery occlusion; PVD = posterior vitreous detachment.



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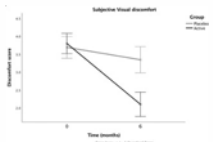
Dietary Intervention With a Targeted Micronutrient Formulation Reduces the Visual Discomfort Associated With Vitreous Degeneration

Emmanuel Ankamah, Marina Green-Gomez, Warren Roche, Eugene Ng, Ulrich Welge-Lüßen, Thomas Kaercher, and John M. Nolan

- 61 PTS FOLLOWED FOR 60 DAYS
- LESS DISCOMFORT FROM FLOATERS IN TREATED PTS FROM INITIAL VISIT TO FINAL VISIT
- LESS EFFECT OF FLOATERS ON DAILY LIFE IN TREATED PTS FROM INITIAL VISIT TO FINAL VISIT
- DECREASE IN VITREOUS OPACITES IN 20/26 (76.9%) OF TREATED PTS VS 28.6% IN PLACEBO
- INCREASE IN CONTRAST SENSITIVITY IN TREATED PTS
- OVERALL, 66.6% OF TREATED PTS EXPERIENCE AN IMPROVEMENT IN VISUAL COMFORT



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MACULAR HOLE SURGERY

- VITRECTOMY AND MEMBRANE PEEL
- FILLED WITH GAS WHICH DISSIPATES OVER 4-6 WEEKS
- FACE DOWN POSITIONING
  - 14 DAYS TRADITIONAL
  - NEWER STUDIES EVALUATING LESS VS NONE
- 95% SUCCESS RATE IF OPERATED WITHIN 1 YR
- RISKS
  - ENDOPHTHALMITIS: 1:1000
  - RD: 5%
  - CATARACT FORMATION: MANY PTS NEED CATARACT SURGERY WITHIN 1 YEAR OF VITRECTOMY

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MACULAR HOLE MEDICAL THERAPY

- 49 PTS WITH FTMH STARTED ON PF, NSAID, CAI
- 18/49 (36.7%) ACHIEVED CLOSURE WITH DROPS
  - HIGHER % IN SMALL HOLES AND THOSE WITHOUT VMT
- HOLE SIZE DIRECTLY RELATED TO CHANCE OF CLOSURE
  - EVERY 10 UM DECREASE IN SIZE INCREASED ODDS FOR CLOSURE BY 1.2X
  - BEST RESULTS LESS THAN 200UM
  - 200-300UM ≅ 25% CLOSURE
  - NO FTMH OVER 300 UM HAD CLOSURE
- AVG TIME TO CLOSURE WAS 107.2 DAYS (RANGE 20-512 DAYS)
- IF NO RESPONSE AT ALL WITHIN FIRST 1-3 MOS RESPONSE UNLIKELY AND SURGICAL CANDIDATE

Wang J, et al. Full-thickness macular hole closure with topical medical therapy. Retina 44:392.399, 2024.

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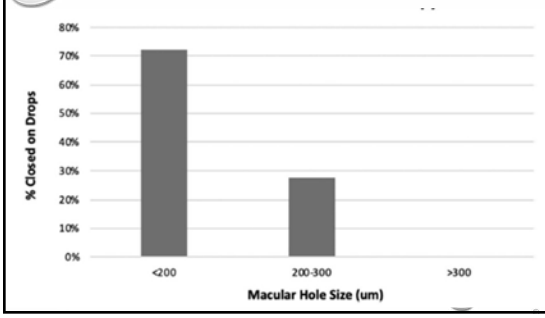
RATE OF FTMH CLOSURE ON MEDICAL THERAPY



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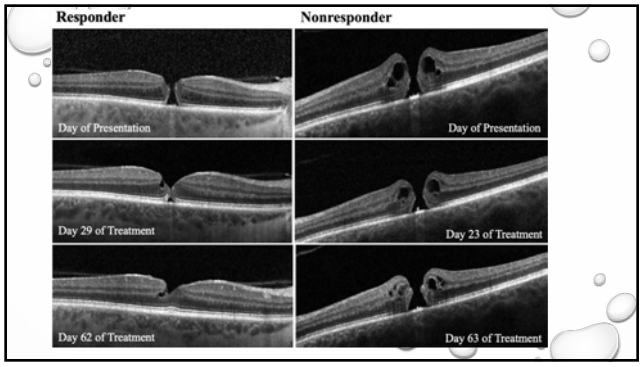

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TAKE HOME

- MY TAKE HOME:
  - IF < 300 UM, TRY CONSIDER TRYING
    - PF QID
    - NSAID (VOLTAREN, ACULAR) QID
    - CAI (TRUSOPT) BID UTIL SEES RETINA
  - REFER TO RETINA 1 MOS
  - SEND OCT TO COMPARE
  - IF NO IMPROVEMENT IN 1 MOS, UNLIKELY TO HAVE CHANGE SO SURGICAL CANDIDATE
  - IF IMPROVEMENT, TRY FOR 3 MOS THEN DECIDE ON SURGERY

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