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the Ophthalmologist™

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NOW APPROVED: the first and only FDA-approved treatment for GA secondary to AMD[1]

GA unravels so much
SAVE RETINAL TISSUE BY SLOWING PROGRESSION[1-3]

SYFOVRE achieved continuous reductions in mean lesion growth rate* vs sham pooled from baseline to Month 24[1]

Monthly	Every Other Month (EOM)
OAKS trial (mm^2): (3.11 vs 3.98) **22%**	OAKS trial (mm^2): (3.26 vs 3.98) **18%**
DERBY trial (mm^2): (3.28 vs 4.00) **18%**	DERBY trial (mm^2): (3.31 vs 4.00) **17%**

SE in trials (monthly, EOM, sham pooled): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17.

*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]
Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]

AMD=age-related macular degeneration; GA=geographic atrophy; SE=standard error.

Learn more about the SYFOVRE clinical data at SyfovreECP.com/efficacy

INDICATION

SYFOVRE™ (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- SYFOVRE is contraindicated in patients with ocular or periocular infections, and in patients with active intraocular inflammation

WARNINGS AND PRECAUTIONS

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.
- **Increased Intraocular Pressure**
  - Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥5%) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

Please see Brief Summary of Prescribing Information for SYFOVRE on the adjacent page.

Trial Design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 24–month, Phase 3, randomized, double-masked trials. Patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD were randomly assigned (2:2:1:1) to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly, SYFOVRE EOM, sham monthly, or sham EOM for 24 months. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by fundus autofluorescence (FAF).[1,4]

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. **2.** Pfau M, von der Emde L, de Sisternes L, et al. Progression of photoreceptor degeneration in geographic atrophy secondary to age-related macular degeneration. *JAMA Ophthalmol.* 2020;138(10):1026–1034. **3.** Bird AC, Phillips RL, Hageman GS. Geographic atrophy: a histopathological assessment. *JAMA Ophthalmol.* 2014;132(3):338–345. **4.** Data on file. Apellis Pharmaceuticals, Inc.

SYFOVRE™ (pegcetacoplan injection) 15 mg / 0.1 mL

Apellis

SYFOVRE ™ (pegcetacoplan injection), for intravitreal use
BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see SYFOVRE full Prescribing Information for details.

INDICATIONS AND USAGE

SYFOVRE is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

CONTRAINDICATIONS

Ocular or Periocular Infections
SYFOVRE is contraindicated in patients with ocular or periocular infections.
Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
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Intraocular Inflammation
In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with SYFOVRE.
Increased Intraocular Pressure
Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.
The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

Table 1: Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated with SYFOVRE Through Month 24 in Studies OAKS and DERBY

Adverse Reactions	PM (N = 419) %	PEOM (N = 420) %	Sham Pooled (N = 417) %
Ocular discomfort*	13	10	11
Neovascular age-related macular degeneration*	12	7	3
Vitreous floaters	10	7	1
Conjunctival hemorrhage	8	8	4
Vitreous detachment	4	6	3
Retinal hemorrhage	4	5	3
Punctate keratitis*	5	3	<1
Posterior capsule opacification	4	4	3
Intraocular inflammation*	4	2	<1
Intraocular pressure increased	2	3	<1

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month
*The following reported terms were combined:
Ocular discomfort included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye
Neovascular age-related macular degeneration included: exudative age-related macular degeneration, choroidal neovascularization
Punctate keratitis included: punctate keratitis, keratitis
Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

Endophthalmitis, retinal detachment, hyphema and retinal tears were reported in less than 1% of patients. Optic ischemic neuropathy was reported in 1.7% of patients treated monthly, 0.2% of patients treated every other month and 0.0% of patients assigned to sham. Deaths were reported in 6.7% of patients treated monthly, 3.6% of patients treated every other month and 3.8% of patients assigned to sham. The rates and causes of death were consistent with the elderly study population.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.
Systemic exposure of SYFOVRE following ocular administration is low. Subcutaneous administration of pegcetacoplan to pregnant monkeys from the mid gestation period through birth resulted in increased incidences of abortions and stillbirths at systemic exposures 1040-fold higher than that observed in humans at the maximum recommended human ophthalmic dose (MRHOD) of SYFOVRE (based on the area under the curve (AUC) systemically measured levels). No adverse maternal or fetal effects were observed in monkeys at systemic exposures approximately 470-fold higher than that observed in humans at the MRHOD.
In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
Lactation
Risk Summary
It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.
Females and Males of Reproductive Potential
Contraception
Females: It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits.
Pediatric Use
The safety and effectiveness of SYFOVRE in pediatric patients have not been established.
Geriatric Use
In clinical studies, approximately 97% (813/839) of patients randomized to treatment with SYFOVRE were ≥ 65 years of age and approximately 72% (607/839) were ≥ 75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies. No dosage regimen adjustment is recommended based on age.

PATIENT COUNSELING INFORMATION

Advise patients that following SYFOVRE administration, patients are at risk of developing neovascular AMD, endophthalmitis, and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in vision such as flashing lights, blurred vision or metamorphopsia, instruct the patient to seek immediate care from an ophthalmologist.
Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured for:
Apellis Pharmaceuticals, Inc.
100 Fifth Avenue
Waltham, MA 02451

SYF-PI-17Feb2023-1.0

2/23 US-PEGGA-2200163 v2.0

OMIDRIA SETS THE STAGE FOR YOUR CATARACT SURGERY SUCCESS[1-3]

FDA-APPROVED OMIDRIA:
COUNT ON PERFORMANCE THAT STAYS AHEAD OF THE UNEXPECTED

- **EFFECTIVELY MAINTAINS PUPIL DILATION** and requires less use of PEDs[1,4-8]
- **REDUCES COMPLICATIONS** such as IFIS, CME, and breakthrough iritis[2,3]
- **IMPROVED PATIENT EXPERIENCE** with less pain, greater visual acuity, and fewer drops[1,3,4]

INDICATIONS AND USAGE
OMIDRIA® is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

IMPORTANT SAFETY INFORMATION
OMIDRIA must be added to irrigating solution prior to intraocular use.

OMIDRIA is contraindicated in patients with a known hypersensitivity to any of its ingredients.

Systemic exposure to phenylephrine may cause elevations in blood pressure.

Use OMIDRIA with caution in individuals who have previously exhibited sensitivities to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory drugs (NSAIDs), or have a past medical history of asthma.

The most commonly reported adverse reactions at ≥ 2% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation.

Please see the Full Prescribing Information for OMIDRIA at www.omidriahcp.com/prescribinginformation.

You are encouraged to report Suspected Adverse Reactions to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

OMIDRIA®
(phenylephrine and ketorolac intraocular solution) 1% / 0.3%

VISIT
OMIDRIAHCP.COM

CME=cystoid macular edema; IFIS=intraoperative floppy iris syndrome; PEDs=pupil expansion devices.

References: 1. OMIDRIA [package insert]. Seattle, WA: Omeros Corporation; 2017. **2.** Silverstein SM, Rana VK, Stephens R, et al. Effect of phenylephrine 1.0%–ketorolac 0.3% injection on tamsulosin-associated intraoperative floppy-iris syndrome. *J Cataract Refract Surg*. 2018;44(9):1103-1108. **3.** Visco DM, Bedi R. Effect of intracameral phenylephrine 1.0%–ketorolac 0.3% on postoperative cystoid macular edema, iritis, pain, and photophobia after cataract surgery. *J Cataract Refract Surg*. 2020;46(6):867-872. **4.** Rosenberg ED, Nattis AS, Alevi D, et al. Visual outcomes, efficacy, and surgical complications associated with intracameral phenylephrine 1.0%/ketorolac 0.3% administered during cataract surgery. *Clin Ophthalmol*. 2018;12:21-28. **5.** Al-Hashimi S, Donaldson K, Davidson R, et al. Medical and surgical management of the small pupil during cataract surgery. *J Cataract Refract Surg*. 2018;44(8):1032-1041. **6.** Bucci FA Jr, Michalek B, Fluet AT. Comparison of the frequency of use of a pupil expansion device with and without an intracameral phenylephrine and ketorolac injection 1%/0.3% at the time of routine cataract surgery. *Clin Ophthalmol*. 2017;11:1039-1043. **7.** Walter K, Delwadia N, Coben J. Continuous intracameral phenylephrine–ketorolac irrigation for miosis prevention in femtosecond laser–assisted cataract surgery: reduction in surgical time and iris manipulation. *J Cataract Refract Surg*. 2019;45(4):465-469. **8.** Visco D. Effect of phenylephrine/ketorolac on iris fixation ring use and surgical times in patients at risk of intraoperative miosis. *Clin Ophthalmol*. 2018;12:301-305.

Rayner

Adjusting the Lens

How can we make art accessible for all?

"The Art of Ophthalmology" issue has been running since The Ophthalmologist first opened its eyes in 2014. Showcasing artwork from individuals in the ophthalmic field, the feature bridges the gap between medicine and art – an exciting combination for those interested in both scientific and artistic disciplines, like myself. This year, we have made a concerted effort to feature artwork created by visually impaired (VI) artists, re-focusing the lens on individuals directly affected by the shifting field of ophthalmology.

Putting together this issue – and having the pleasure to sift through a variety of unique artworks created by ophthalmologists and VI artists alike – has really spurred me to think about the scope of accessibility in art. Do galleries do enough to ensure the artwork they display is representative of all creatives? Do museums and galleries do enough to ensure their exhibits are accessible to visitors with disabilities? Although institutions such as The Museum of Modern Art offer touch tours, audio tours, and programs for people with a range of disabilities, this isn't reflective of the art world at large (1). According to audio description (AD) provider, VocalEyes, only three percent of UK museums and galleries mention AD guides on their websites and, where available, they are often infrequent and require advance booking (2).

This opens a door into the wide variety of work created by VI artists – talented individuals who, far from being creatively constrained by their impairments, are instead inspired, using an array of colors, textures, and forms to convey their unique experiences of the world. One such example comes from the legally blind comic book illustrator, Douglas Knight, whose illustration, "The Surge" – displaying a gentleman at a crosswalk gripping a cane – serves as a celebration of Knight's own mobility orientation training.

If museums and galleries can do more to promote artwork created by not just VI artists, but artists with all disabilities, perhaps there will be a shift in how these organizations operate. As stated in a recent article on accessibility, "There is a pressing need to devisualize the museum [...] to move away from the ableist assumption that vision is the primary sense through which heritage and museums should be experienced (2)."

As professionals dedicated to preserving or restoring sight– but with a clear awareness of what it means for people to suddenly or gradually lose their vision – I'm keen to learn your perspective: *sarah.healey@texerepublishing.com*

Sarah Healey
Associate Editor

References

1. *The New York Times, "Making Art Accessible for All" (2023). Available at: https://nyti.ms/3q5KQiT.*
2. *A F Eardley, "Devisualizing the Museum: From Access to Inclusion," Journal of Museum Education, 47, 150 (2022).*

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by Sarah Healey

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Our annual Art of Ophthalmology gallery features works from both visually impaired artists and ophthalmologists

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the Ophthalmologist

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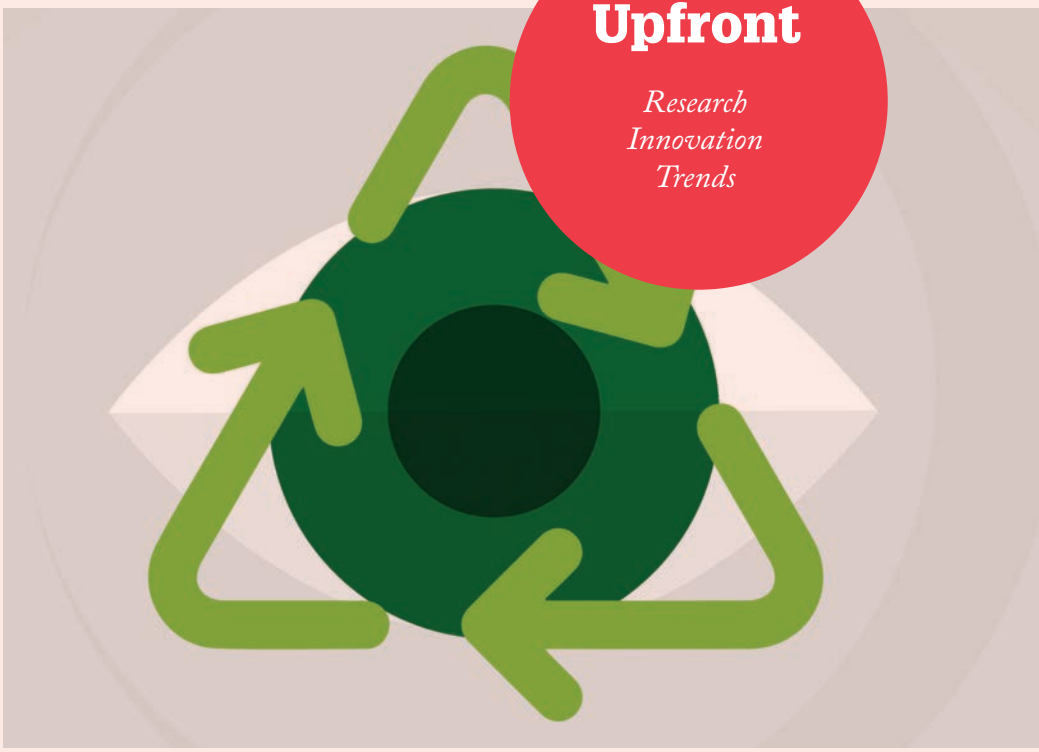
Upfront

Research
Innovation
Trends



Recycling for ROP

Is K604 – a pre-existing drug for Alzheimer's and cancer – a potential new treatment for premature babies with retinopathy of prematurity?

Scientists at the Medical College of Georgia, USA, have discovered a new use for an existing drug that could halt the development of retinopathy of prematurity (ROP) (1). Using an animal model of ROP, researchers found that the small molecule K604 – a drug originally developed to combat excessive cholesterol in atherosclerosis – can block the development of obstructive blood vessels in the retina, reduce inflammation, and enable normal blood vessel growth. K604, which is also used as an Alzheimer's and cancer treatment, achieves the effect by blocking acyl-coenzyme A(CoA):cholesterol acyl transferase 1 (ACAT1) – an enzyme that allows toxic cholesterol to build up in the retina of premature babies, inducing inflammation and retinal injury when left untreated.

The scientists believe that ACAT1 inhibition through K604, which has already been proven to be safe in adults and have no effect on VEGF levels, might help restore the retina to a normal metabolism and prevent pathological neovascularization. However, they suggest further steps must be taken to translate their findings for clinical evaluation of the drug in babies. They also aim to explore the use of K604 for treating diabetic retinopathy, which occurs in around one-third of patients with diabetes.

The researchers concluded, "We have identified a novel mechanism of retinal neovascularization (RNV) that involves a link between the cholesterol pathway (low-density lipoprotein receptor, ACAT1, Cholesteryl ester) and activation of the inflammatory mediators TREM1 and MCSF [...] Systemic inhibition of ACAT1 could represent a new target to treat pathological RNV in ischemic retinopathies without altering levels of VEGF and avoiding the side effects of intravitreal injections."

Reference

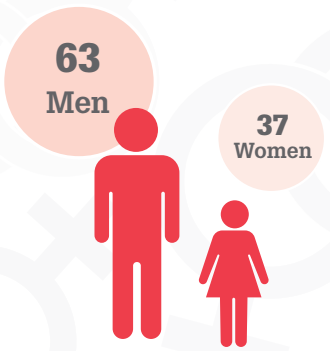
1. *SAH Zaidi et al., J Neuroinflammation 20, 14 (2023). PMID: 36691048.*

INFOGRAPHIC

Power List Numbers

The breakdown of the what, the where, and the how many behind a decade of ophthalmic excellence and impact

The Gender Ratio:



The Winners' Age Range:

YOUNGEST:

Ben LaHood
39 years old

OLDEST:

George L. Spaeth
91 Years Old

SPOTLIGHT ON ARVO

We help you keep up to date with the latest vision research from ARVO's journals

Beauty? Nothing Special
Is judging beauty subject to the same rules as other perceptual judgments? To answer this question, researchers from the Department of Psychology at New York University measured the mutual information of the beauty ratings of everyday images from 50 participants, concluding that beauty judgments had similar values to unidimensional perceptual judgment (M Pombo, DG Pelli, J Vis, 23, 6 (2023). PMID: 37410492).

Deep Learning for DR
Researchers have developed and trained a deep learning-based optical coherence tomography algorithm to detect disorganization of retinal inner layers (DRIL) – an early imaging biomarker for diabetic retinopathy. Their findings demonstrate a classification tool that can be used for the rapid identification of DRIL in both research and clinical settings (R Singh et al., Trans Vis Sci Technol, 12, 6 (2023). PMID: 37410472).

As Easy as Pi
New research conducted by an international, multi-institutional research group presented the development of a rapid and accessible multicolor fluorescence imaging device for the quick and accurate diagnosis of microbial keratitis, the FluroroPi. Researchers evaluated its performance in combination with fluorescent optical reporters, establishing FluoroPi coupled with SmartProbes as an effective, low-cost device for bacterial imaging (S Mohan et al., Trans Vis Sci Technol, 12, 1 (2023). PMID: 37395707).

Glaucoma and Binocular Function
Researchers have found that binocularly asymmetric glaucomatous visual field damage causes widespread loss of disparity sensitivity across both foveal and peripheral regions. However, cortical integration mechanisms appear to be well preserved, suggesting patients with glaucoma "make the best possible use of their remaining binocular function." (G Maiello, M Kwon, Invest Ophthalmol Vis Sci, 64, 2 (2023). PMID: 37129906)

Combating Atrophy
A study found that myofiber in the extraocular muscles is resistant to amyotrophic lateral sclerosis. The researchers hope that these new findings may provide clues to future treatment strategies for strengthening the body's defensive capabilities and decelerating the fatal neuro-degenerative disease. (A Behzadi et al., Invest Ophthalmol Vis Sci, 64, 15 (2023). PMID: 37200039).

Credit: Seed Image sourced from Rawpixel.com

Sowing the Stem Cells

Novel stem cell method for replacing degenerated photoreceptors shows potential breakthrough for inherited retinal diseases

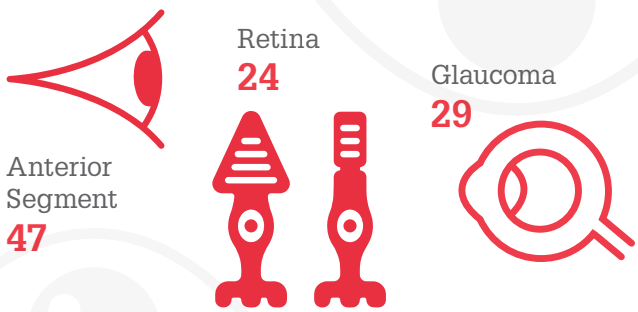
An international preclinical study has developed a novel stem cell technique that produces photoreceptor progenitor cells closely resembling those found in the human retina. "We saw an unmet clinical need for blindness caused by photoreceptor loss in patients with advanced stages of inherited retinal diseases," explains Tay Hwee Goon, lead author of the study. "There is no effective treatment for these diseases, and replacement of functional photoreceptors appeared to be the most promising route towards retina regeneration." The novel protocol has now been licensed to Alder Therapeutics. "These cells will subsequently be tested for safety and efficacy before advancing to the next stage," Goon says. "By the end of this period, our lab hopes to see vision being restored in patients with vision loss."

Reference

1. *TH Goon, et al., Mol Ther, 31, 825 (2023). PMID: 36638800.*

Continent Breakdown:

Subspecialties represented:



Time to Talk Time Off

Responses to a study on parental leave indicate the need for more communication on workplace options

Although many ophthalmologists will take parental leave at some point in their careers, little is known about the perceptions and potential impact of doing so. This gap in the literature prompted Lora Glass' lab to put the issue under a much-needed spotlight. As Glass explains, "We set out to gain a better understanding of perceptions toward stop-the-clock policies, workplace culture, and stressors involved in taking parental leave amongst this population. We also [looked] at the association between demographic factors such as sex, years out of training, parental status, and type of employment (private practice versus academic)."

Glass' lab conducted a non-validated survey through an online questionnaire that was completed by 186 self-identified North American-based ophthalmologists. According to lead author Kisha Kalra, the results were varied (1). "Interestingly, attitudes towards stop-the-clock policies were mixed, even when stratified by demographic factors – no particular group was more opinionated about these policies than another. This might reflect that policy awareness is limited across the board, and/or that these policies vary considerably from one place of work to another." Another notable trend, says Kalra, was that those graduating more recently were more comfortable taking leave. "This may imply a generational shift in both expectations and attitudes to work-life balance."

Addressing the concerns found in the study will likely need to begin with increased communication. As many physicians lack full awareness of their current workplace policy and options, certain concerns – such as coverage and salary – may need to be more transparently and smoothly addressed in larger groups and departments. As for future research, Glass' team wants to take a deeper dive. Glass explains, "There are still so many questions to answer in this area. For instance, what is the effect of leave duration and total number of leaves? Does parental vs. non-parental (for example medical) leave alter responses? By opening up conversation about the nuances of taking leave, we hope policy can adapt to suit the needs of ophthalmologists over time and in all practice settings."

Reference

1. *K Kalra et al., "Perceptions of Parental Leave Among Ophthalmologists," JAMA Ophthalmol, 141, 24 (2023). PMID: 36480180.*

Probiotics Are DED Friendly

Dry eye disease treatment uses bacteria found in the human gastrointestinal tract

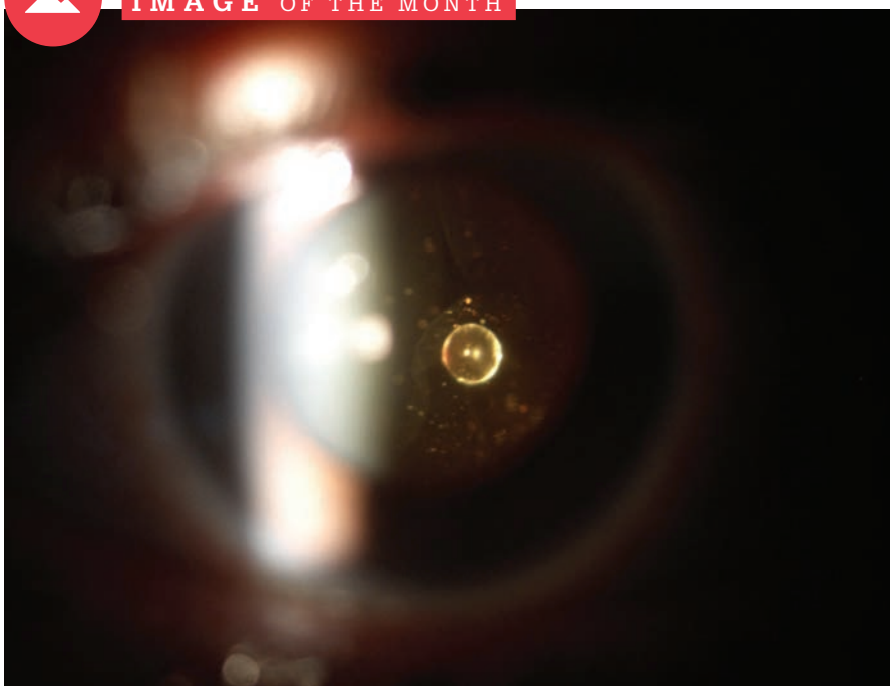
An unconventional dry eye disease (DED) treatment has been developed using "friendly" bacteria – Limosilactobacillus reuteri DSM 17938 – commonly found in the human gastrointestinal tract (1). Previous literature has shown that human-derived, commercially available bacteria to be beneficial to human health, but this is one of the first studies to examine how the bacteria behaves in the context of eye health.

"Despite the prevalence of dry eye (approximately 1 in 20 people in the US), there are only a handful of drugs currently available, and for some patients these drugs do not work very well to improve symptoms," says Laura Schaefer, first author of the study. "These findings show that bacteria with anti-inflammatory effects in the gut can also reduce inflammatory conditions in the eye."

Reference

1. *L Schaefer et al., "Probiotic Limosilactobacillus reuteri DSM 17938 suppresses corneal barrier dysfunction and conjunctival goblet cell reduction in mice subjected to desiccating stress", Invest Ophthalmol Vis Sci, 64, 697 (2023).*

IMAGE OF THE MONTH



You've Only Got One Drop

This month's image shows a silicone drop seen in the anterior vitreous of a 76-year-old female patient who has received 54 ranibizumab (Lucentis) injections for wet AMD.

Credit: Costas H. Karabatsas

Would you like your photo featured in Image of the Month? Send it to edit@theophthalmologist.com

QUOTE OF THE MONTH

"We believe working on inclusion is key to delivering the level of representation we not only desire but actually require."

C Dinah and colleagues write in "Inclusive research in ophthalmology is mission critical! The 10-point action plan," Eye, [Online ahead of print] (2023). PMID: 37488232.

Presbyopia Possibility

Preservative-free ophthalmic treatment for presbyopia passes phase III trial

A new presbyopia-correcting drop, Brimochol PF, has passed the first phase III trials required by the FDA. Manufactured by Visus Therapeutics, Brimochol PF is a preservative-free, fixed-dose combination of carbachol 2.75 percent and brimonidine tartrate 0.1 percent, it is designed to be used once-daily.

The crossover study design enrolled 182 emmetropic patients aged 45–80; visual acuity and pupil size was measured repeatedly throughout the trial. Investigators found a statistically significant reduction in pupil size when using Brimochol PF, compared with the active controls (carbachol and brimonidine) at each time point. During the trial, Brimochol PF met primary FDA endpoints for presbyopia-correcting drops, as well as prespecified EU and UK endpoints. There were no treatment-related serious adverse events. A second phase III study, comparing the drug to a vehicle control, is currently underway.

The ART of EYES

Eyes have long been associated with beauty, serving as the inspiration for countless works of art. In this feature, we present this year's best ophthalmic images, illustrations, and mixed media created by both ophthalmologists and visually impaired artists. Our take? You're in for a real treat!

WINDOW TO THE SOUL

Kathleen Ho's study, "Abyss," aims to capture the boundless details of the iris on a large scale canvas to allow for a greater appreciation of its complexities. As a third-year medical student with an interest in pursuing a career in ophthalmology, Ho aims to continue the practice of her art alongside her medical endeavors.

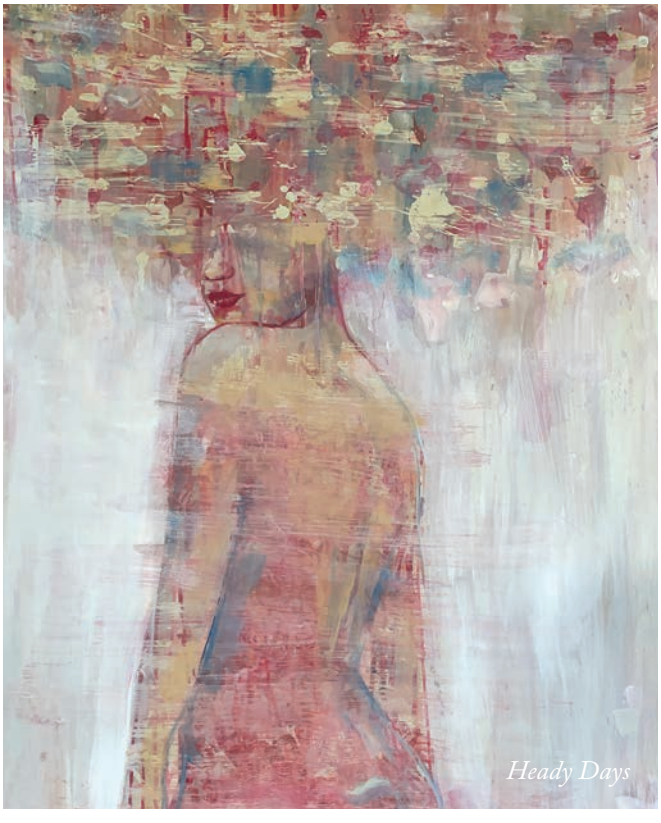
PATTERNED WORLDS

Abi Jameson is a partially sighted, award-winning contemporary artist. Her work – inspired by wisdom, inner-strength, and human connectivity – has been published and exhibited throughout Europe, and is due to exhibit in London at the end of 2023.

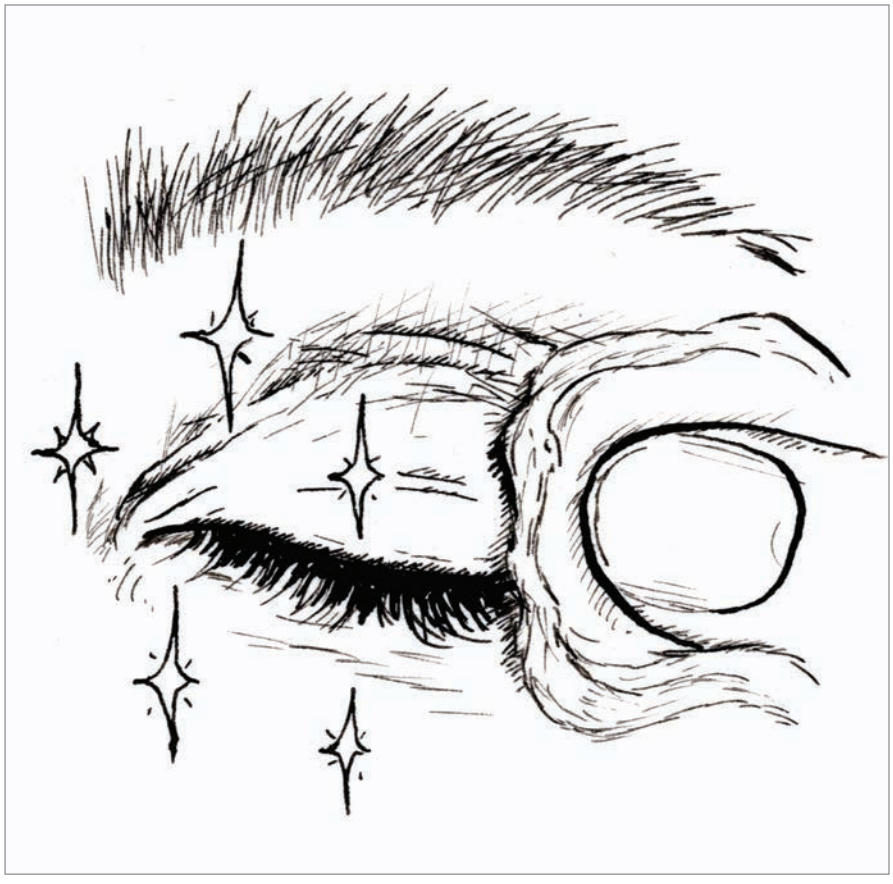
After painting and exhibiting for 10 years in 2013, Abi lost her sight in one eye and half the sight in the other. Since this event, the way she sees the world has changed, which is reflected in her artwork: colors are brighter and messages are stronger. They are a small insight into her world of patterns, random marks, merging foregrounds and backgrounds, and missing information shown through the female portrait.

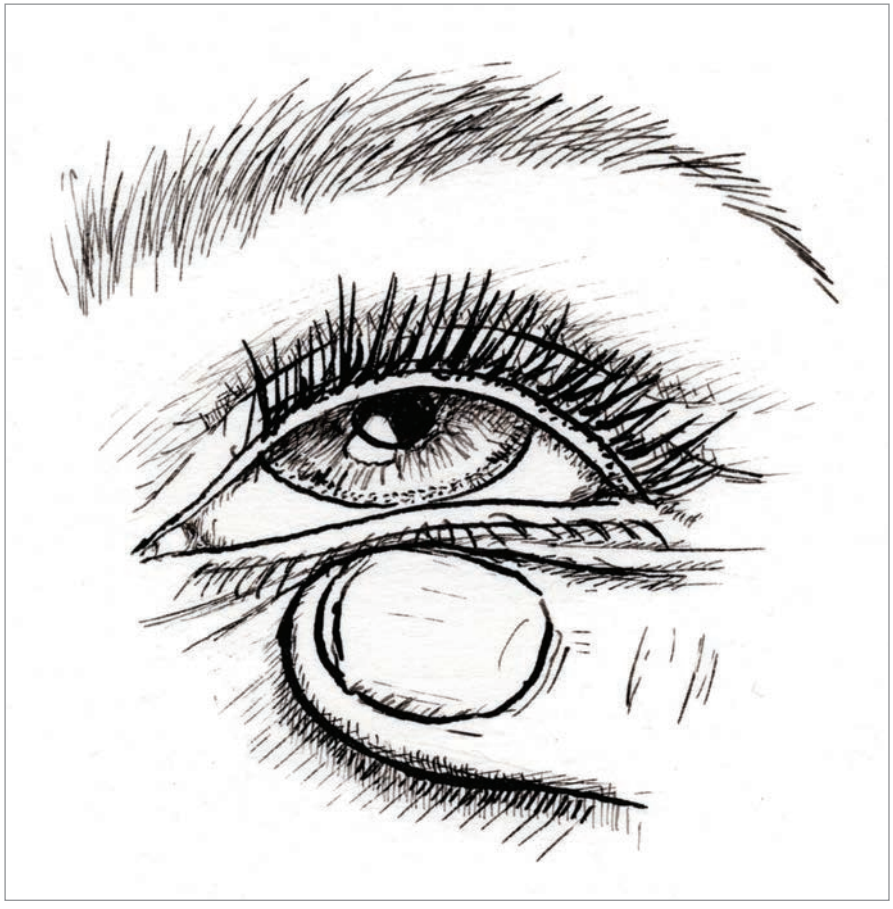
The Flowers Whisper

Sunrise Whisper



Heady Days





ILLUSTRATIONS FOR INSTRUCTION

Dorothea Laurence is a second year ophthalmology resident from Braunschweig, Germany. She completed her medical studies as well as her doctorate at the Georg-August-University of Göttingen, Germany.

Laurence is delighted that she can connect her hobbies with her profession. Aside from creating cartoons – such as her beloved 'Dr Lizard' featured in last year's issue – Laurence enjoys illustrating to help her patients. Studies suggest that patients retain only 14 percent of the information given to them in their appointments; these illustrations aim to provide Laurence's patients with visual instructions that they can retain. Laurence wanted to create something that could be easily printed, so she sketched the illustrations with a drawing nib and black ink.

www.dorothealaurence.com.

**Illustrations may not be reused without permission*

SHEDDING LIGHT ON THE ABSTRACT

Fae Kilburn is a Birmingham-based multidisciplinary artist and arts facilitator, with a Master's in Fine Art. She has a passion for printmaking and uses a variety of techniques, including monoprint, silkscreen, collagraph, and etching.

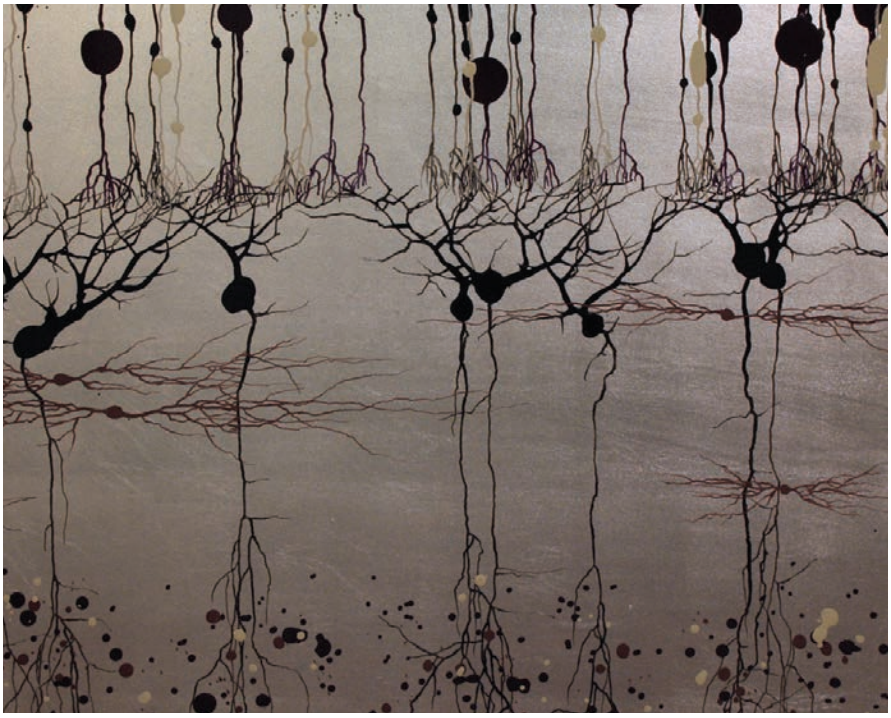
Her recent body of work is "Transient Moments," a series of print installations that creatively document Fae's transition from partial-sight to blindness as an artist, and challenge others' understanding of sight-loss. Creating disability awareness through art is an important part of her practice – as is making workshops and participatory events accessible and inclusive. Fae has successfully created commissions for several organizations and has been exhibiting consistently since 2015.

www.faekilburn.co.uk

NEURAL FORMATIONS

Greg Dunn is an artist who received his PhD in neuroscience from the University of Pennsylvania in 2011. Dunn is now a full time artist based in Philadelphia. He works to incorporate his knowledge of neuroscience, physics, and biology into the artistic process through both imagery and technique. Together with Brian Edwards, a collaborating artist and electrical engineer at Penn, Greg invented a revolutionary technique called reflective microetching that allows dynamic control of imagery and color in reflective gold surfaces.

www.gregadunn.com



THE SWEET SPOT

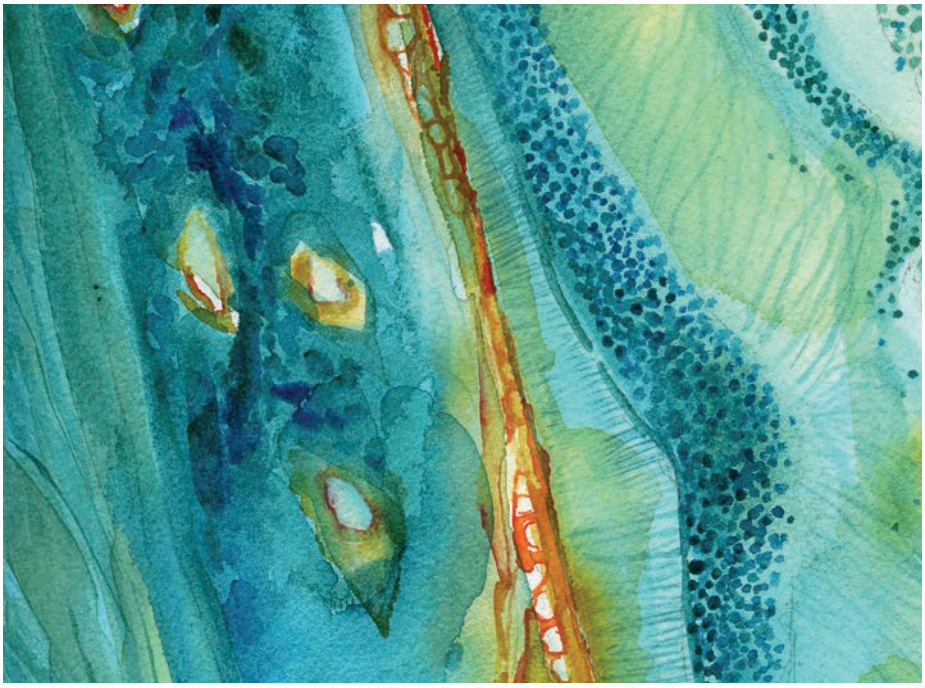
Jui Telavane is a recently graduated ophthalmologist from India, currently undertaking a medical retina fellowship. Since COVID-19, Telavane has been incorporating ophthalmology into her art, re-imagining the eye using various unusual objects. For Telavane, doodling is like therapy, and she now hopes to intersect retinal pathologies within her doodles.

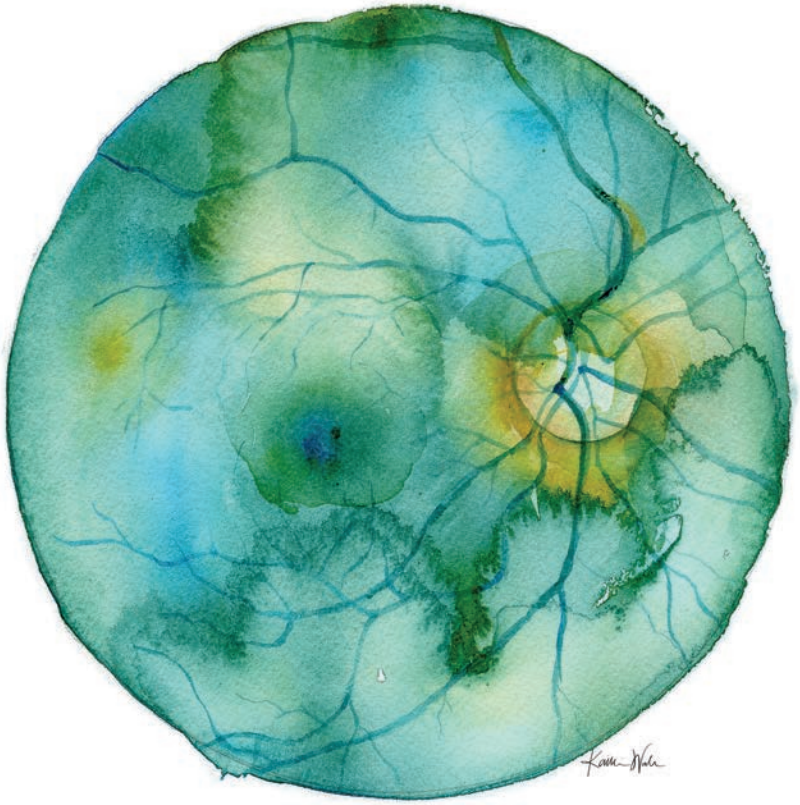
You can see more of Jui's work on Instagram @eye.dooodle

WATERCOLOR VISIONS

Kaitlin Walsh is an independent artist specializing in abstract anatomical watercolor and oil paintings. From a young age, she exhibited an immense fascination with both art and medicine. She focused her studies on both disciplines, eventually receiving a graduate degree in Biomedical Visualization at the University of Illinois at Chicago, where she took a combination of fine art and medical school courses. After graduating, Kaitlin gave birth to her first child, who sadly, after experiencing severe prenatal complications, had to spend several months in hospital. The experience inspired Kaitlin to focus her career on portraying the beauty and complexity of the human body through painting. After spending some time honing her craft and increasing her inventory, she launched her studio, Lyon Road Art, in 2015. She has now sold over 5,000 prints of her work and is a well-known name in the anatomical art community.

Kaitlin shares her art on her website www.kaitlinwalshart.com





Clockwise, from the top left: Rods and Cones;, The Retina, The Fovea

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A COLORFUL MESSAGE

Clarke Reynolds is registered as severely sighted, but is also a visual artist. Reynolds uses Braille – the tactile coding system made up of a six dot cell – as a vessel to hold a word through the shape, color, and size of the dot. Over the past three years Reynolds has been exploring Braille as a visual language, and his work has been displayed in multiple solo exhibitions, including his first solo show at the capital in Quantus gallery. Reynolds' aim is to bring Braille into the 21st century through workshops, exhibitions, and public art, and to be a role model for people of all ages with visual impairment. Reynolds is also the patron for the charity VICTA, for visually impaired children and young adults.

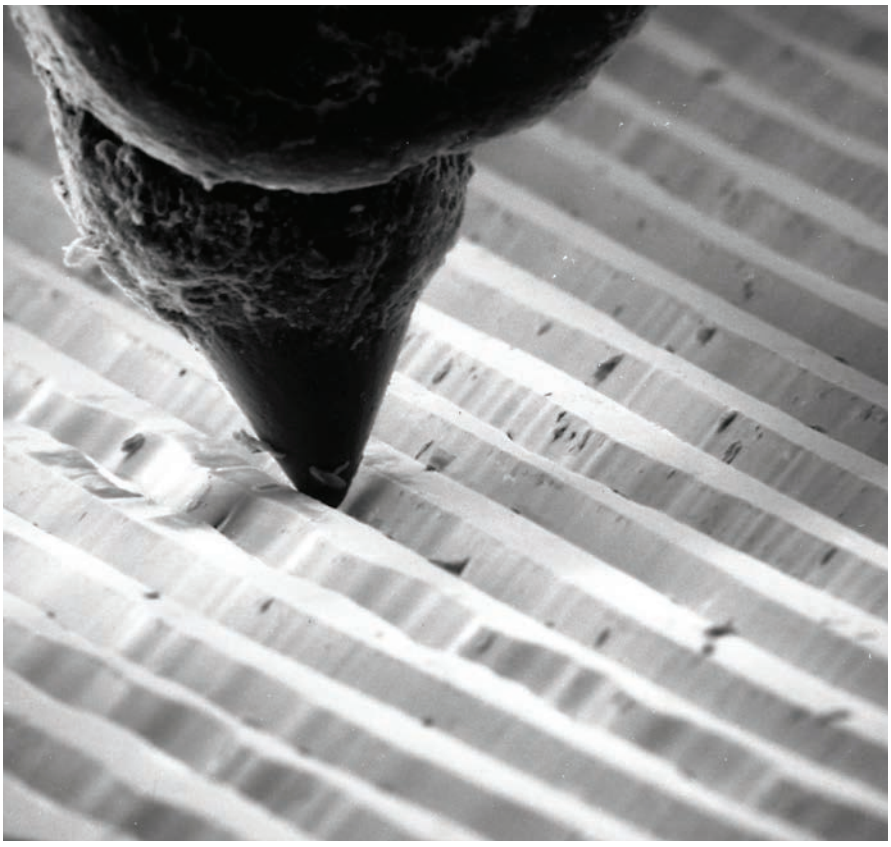
www.seeingwithoutseeing.com
Instagram: @blind.braille.artist

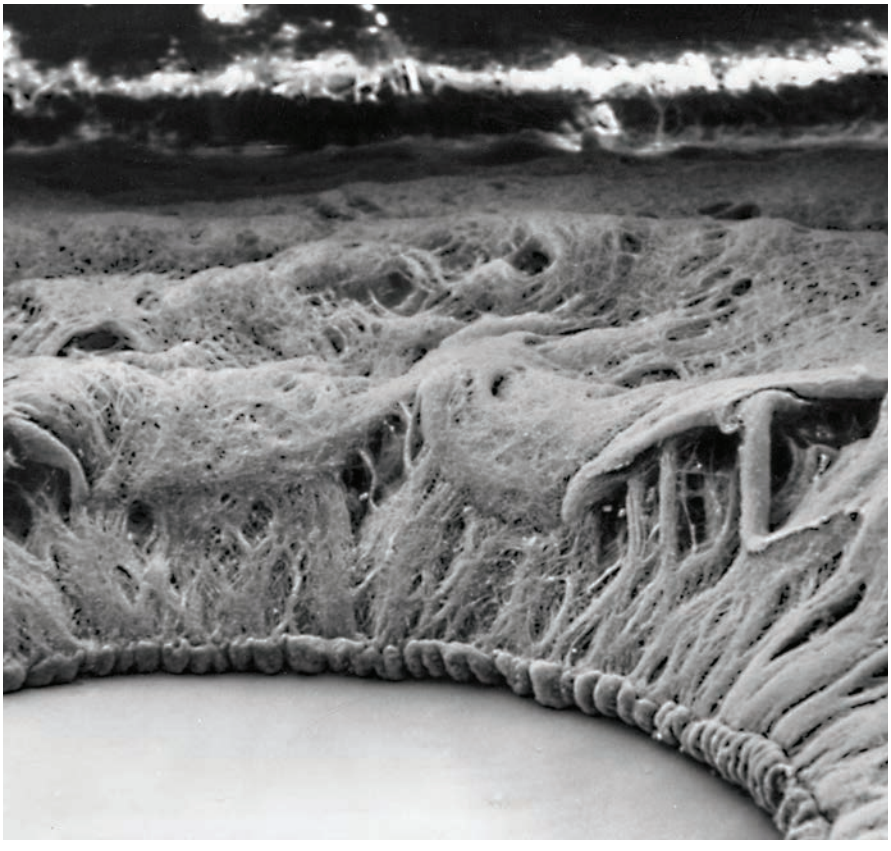
**All images credited: 'Clark Reynolds/Quantus Gallery'*

DREAMING IN COMICS

At the age of four, Douglas Knight was diagnosed with a brain tumor located on his optic chiasm. Although the tumor was treated with chemotherapy, Knight was left legally blind. While his chances of becoming a jet pilot or F1 driver were over, he developed a passion for the visual arts. He has now become an accomplished visual artist, a professional tattoo artist, and an Indie Comic book creator who is making big splashes in all the right places.

www.crosseyecomics.com
Instagram and Twitter: @crosseyecomics





FOCUSING THE LENS

Ralph Eagle has been interested in art all his life. Owing to both his father and maternal grandfather being avid photographers, Eagle has owned a 35 mm Nikon camera since high school. Eagle's subspecialty, ophthalmic pathology, emphasizes visual pattern recognition and imagery. Eagle is known best for the quality of his macro and microscopic images of eye disease. Eagle has won numerous awards for gross and microphotography in the Ophthalmic Photographer's Society's exhibits at the American Academy of Ophthalmology's annual meeting, and has been the official archivist-photographer of the American Ophthalmological Society for more than 25 years. Alongside medical photography, Eagle likes to travel and has recently begun to photograph birds. He also enjoys designing neckties.

Top: Phonograph needle
Bottom: Lake of the rainbow

Building A Sustainable Future

How Alcon is meeting the challenge of protecting the environment without compromising patient care

The impact of ophthalmology on our shared environment is profound, but can be changed for the better through individual actions as well as large scale changes from ophthalmology industry leaders. To find out more about how Alcon is building sustainable practices into every aspect of their surgical franchise, we sat down with Jeannette Bankes, President and General Manager for Alcon's Global Surgical Franchise.

What are some of the unique challenges of sustainable practice in ophthalmology?

We're facing the challenge of balancing single-use versus reusable medical devices while always prioritizing patient safety. We know that single-use materials have a greater environmental impact, so we focus on creating disposables that are environmentally friendly and reusables that are effective and safe. At Alcon, we have well-established, rigorous safety procedures from product innovation to distribution to clinical trials that have allowed us to seamlessly integrate sustainable practices across our surgical franchise. We know we can also move the needle on sustainability by minimizing energy use, reducing packaging and post-consumer waste, and increasing the use of recycled materials, while never compromising on patient safety.

What is the value of sustainability for Alcon?

The value of sustainability is paramount at Alcon. We recognize that our health is intrinsically tied to the health of our planet and environment. One of our pillar areas for social impact and sustainability is Brilliant Lives. Through our Brilliant Lives initiatives, we've committed to help improve vision for five million people afflicted with untreated cataracts in low- and middle-income countries and provide 150,000 vision screenings to children by our associates. These commitments are examples of how sustainability drives measurable value for our business, partners and associates.

How is Alcon focusing on sustainability at the moment?

We prioritize three focus areas: Incorporating Sustainability into Product Development, Reducing Product-Related Environmental Impact, and Reducing Operational Environmental Impact. While we are always working against these areas, most recently, we announced the expansion of our Plastic Bank partnership. The idea is simple – for each ton of plastic introduced in the marketplace with UltraSert and AutonoMe, Plastic Bank, an organization that builds recycling ecosystems in under-developed communities to fight plastic pollution, will collect an equivalent amount of ocean-bound plastic in vulnerable coastal communities.

Can you tell us about the Green Innovations Surgical Team – what are its aims, and what's new with its 2023 program?

We formed the Green Innovations Surgical Team (GreenIST) in 2021 to identify opportunities to increase sustainability measures and reduce waste for commercialized products within our Surgical franchise globally. Some of the changes led by GreenIST include removing the plastic tray from our Centurion® Fluid Management System (FMS) pack, resulting in a ~90 percent reduction in material waste. We also implemented the removal of printed Directions for Use (DFU) booklets, reducing paper and carbon dioxide (CO_2) usage and decreasing the weight of IOL packages by 53 percent. In 2023, we are continuing to expand our efforts bringing these changes to even more countries and looking across our portfolio of products for new ways we can remove waste.

What are some of Alcon's sustainability goals for the future?

In addition to the Brilliant Lives goals, we are pursuing a pathway to be carbon neutral across global operations by 2030 (Scope 1 and Scope 2 emissions). We've also committed to diverting 100 percent of non-hazardous waste generated at manufacturing sites and distribution centers from landfill and sourcing 100 percent renewable energy by improving energy efficiency across our operations through renewable energy and energy-saving projects.

Is there anything else you would like to pass on about this to the eyecare world?

At Alcon, we believe we can improve lives and strengthen communities through innovative eye care to help everyone See Brilliantly. Safe and equitable eye health treatment can be possible while we care for our planet too. More details about all our social impact and sustainability efforts and our progress toward these goals can be found in our annual Social Impact & Sustainability Report.

References

1. *Alcon Data on file,2021.*
2. *Alcon Data on File, 2022.*
3. *Alcon Data on file, 2022.*

Alcon

 www.alcon.com

the Ophthalmologist

POWER *List*

HALL *of* FAME

Over the past decade, The Ophthalmologist Power List has championed and celebrated innovation, leadership, and excellence across ophthalmology – from those fighting against preventable blindness globally, to the surgical and clinical pioneers who, through their research and innovation, revolutionize treatment and introduce ground-breaking new procedures.

Here, we are proud to introduce a new element to the Power List: the Hall of Fame.

The Hall of Fame is our way of honoring some of the giants of ophthalmology whose contributions to the field over the course of their distinguished careers have been truly transformative. The great figures inducted into the Hall of Fame will no longer be eligible for the yearly Power List, instead having their legacy cemented within this prestigious and ongoing commemoration of the true brilliance of the field, as each year we induct more ophthalmic leaders, expanding the Hall of Fame.

In this, the Hall of Fame's maiden year, we are delighted to present our 10 inaugural inductees, whose contributions to the field, across a diverse range of subspecialties, have had a seismic impact and improved outcomes for countless patients worldwide.

Welcome to the Hall of Fame.

See the full profiles in all their glory online: ***top.txp.to/power-list-hof***

Anat Loewenstein

Chairman of Ophthalmology, Sourasky Medical Center, Vice Dean, Faculty of Medicine, Tel Aviv University, Sidney Fox Chair of Ophthalmology, Tel Aviv University, Israel

Anat Loewenstein is perhaps best recognized as one of the leading forces behind the development of model technology used for the early detection of macular degeneration, as well as the coordinating investigator in the multicenter studies which helped prove the importance of this technology. She's also been heavily invested in the research and development of automated technology for the detection of retinal disease activity, as well as looking at ways in which augmented virtual reality might be used to replace the traditional operating microscope.

She has presented at hundreds of meetings as a guest professor, and published more than 460 papers in peer-reviewed journals. Loewenstein now spends her time between clinical work, academia, education, and research. At Tel Aviv University, she prioritizes teaching and mentoring young ophthalmologists on retinal disease and their own career goals. For a variety of different international groups, including ARVO, she mentors other aspiring ophthalmologists.

Regarded as one of the top retina specialists and surgeons worldwide, Anat Loewenstein's place in The Ophthalmologist Power List Hall of Fame will come as no surprise.

Carol Shields

Chief, Ocular Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Since 1984, Carol Shields has been at Wills Eye Hospital in Philadelphia, USA. First arriving as a resident and staying there ever since, Carol Shields has been involved in the development of the Wills Eye Ocular Oncology Service, widely believed to be one of the leading centers for ocular oncology in the world. She is the author of hundreds of scientific articles and textbooks, many of which were co-written with her husband, Jerry Shields.

What is particularly striking about Shields' career is the extent to which, through her efforts (alongside her husband and their many students and fellows), ocular oncology has been placed upon a foundation of rigorous evidentiary authentication. Her publications, which often detail years of painstaking experience and experimentation on the ground, have been of colossal benefit to ophthalmologists and have helped save the sight – and lives – of innumerable patients. Beyond her staggering professional contributions, her tireless commitment to her fellows, ocular oncologists worldwide, and, above all, to her patients, have all been mentioned in her multiple Power List nominations. It is for these reasons – and so many others – that we induct Carol L. Shields into The Ophthalmologist Power List Hall of Fame.

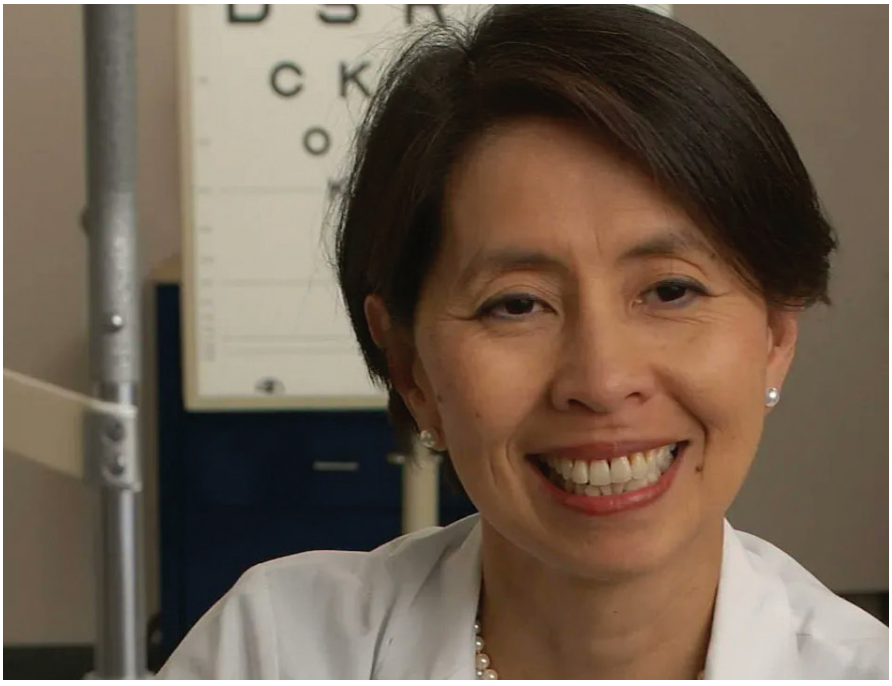
David (Ted) Garway-Heath

Professor, Ophthalmology for Glaucoma and Allied Studies, UCL; Consultant Ophthalmic Surgeon, Moorfields Eye Hospital NHS Foundation Trust London, UK

From the time he joined Moorfields Eye Hospital in 1991, Ted Garway-Heath has forged an impressive career in ophthalmology and the world of glaucoma research. Within this research field, he is perhaps most well-known as the inventor of the Garway-Heath sectorization map and the Moorfields Regression Analysis algorithm, which was used worldwide, revolutionizing how imaging is employed in the clinical management of glaucoma.

Though Garway-Heath has authored over 200 research papers, one in particular propelled his career forward. After being asked to design a clinical trial by Pfizer at ARVO 2006, in just six weeks, Garway-Heath devised the UKGTS which, under his leadership as principal investigator, became a landmark trial in glaucoma management.

Garway-Heath served as President of the European Glaucoma Society between 2017 and 2021. In addition to this esteemed role – and many other memberships of professional bodies – he continues to work as honorary consultant ophthalmic surgeon at Moorfields Eye Hospital. For all these achievements and more – and his continued dedication to tackling vision loss – David (Ted) Garway-Heath has been inducted into The Ophthalmologist Power List Hall of Fame.



Emily Y. Chew

Director of the Division of Epidemiology and Clinical Applications; Chief of the Clinical Trials Branch, National Eye Institute, National Institutes of Health, Bethesda, Maryland, USA

At the heart of Emily Chew's incredible career has always been the desire to have a meaningful and long-lasting impact on her patients and their families. In fact, that same desire led her to ophthalmology and the retina subspeciality, which she discovered during an elective period working with Brenda Gallie. Notably, it was Gallie who impressed upon Chew the importance of research and its potential to multiply a clinician's impact.

Today, with that lesson clearly learned, Emily Chew stands as a giant of retinal research with a long list of field-changing work, including the Early Treatment Diabetic Retinopathy Study (ETDRS), the Age-Related Eye Disease Study (AREDS), and the Age-Related Eye Disease Study 2 (AREDS2), which she chairs.

Alongside the strides she has made in adding to the ophthalmology literature, Chew has also paid forward the gift of mentorship that she received from Gallie and her other mentors; she has served as a mentor to over 70 medical retinal fellows and medical students. Additionally, Chew has served the ophthalmology community by sitting on numerous committees, including the ARVO Awards Committee, the NIH Equity Committee, the Helen Keller Award Committee. She also served as the Co-Chair of the Women's Leadership Development Program for ARVO.

With such a career, it is no surprise that Chew has become a well known face not only in the retinal subspecialty, but within the wider ophthalmology and medical communities. Her achievements have consistently been recognized by her peers; she has appeared on The Ophthalmologist Power List a record eight times, and has received a plethora of other awards and honors, including the American Academy of Ophthalmology's Secretariat, Guest and Lifetime Achievement awards, the American Medical Association's Inspirational Physician Recognition honor, and ARVO's Distinguished Service Awards as well as the Proctor Medal. Now in 2023, we at The Ophthalmologist are delighted to induct Emily Chew into the Power List Hall of Fame.

George L. Spaeth
Director Emeritus, Glaucoma Service, Wills Eye Hospital Sidney Kimmel Medical College and Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Despite his father establishing an internationally recognized department of ophthalmology at Walter Reed, George Spaeth only became interested in ophthalmology during a rotating internship at the University of Michigan. Finding it to be a rewarding and "clean" specialty, Spaeth became a resident at Wills Eye Hospital in 1961. Here he both discovered homocystinuria and became the first person to treat a severe trichinosis patient with thiabendazole. At this point, Spaeth also discovered the importance of listening to patients and asking relevant questions to identify the best cause of action. More than 60 years later, this ethos remains particularly important for Spaeth.

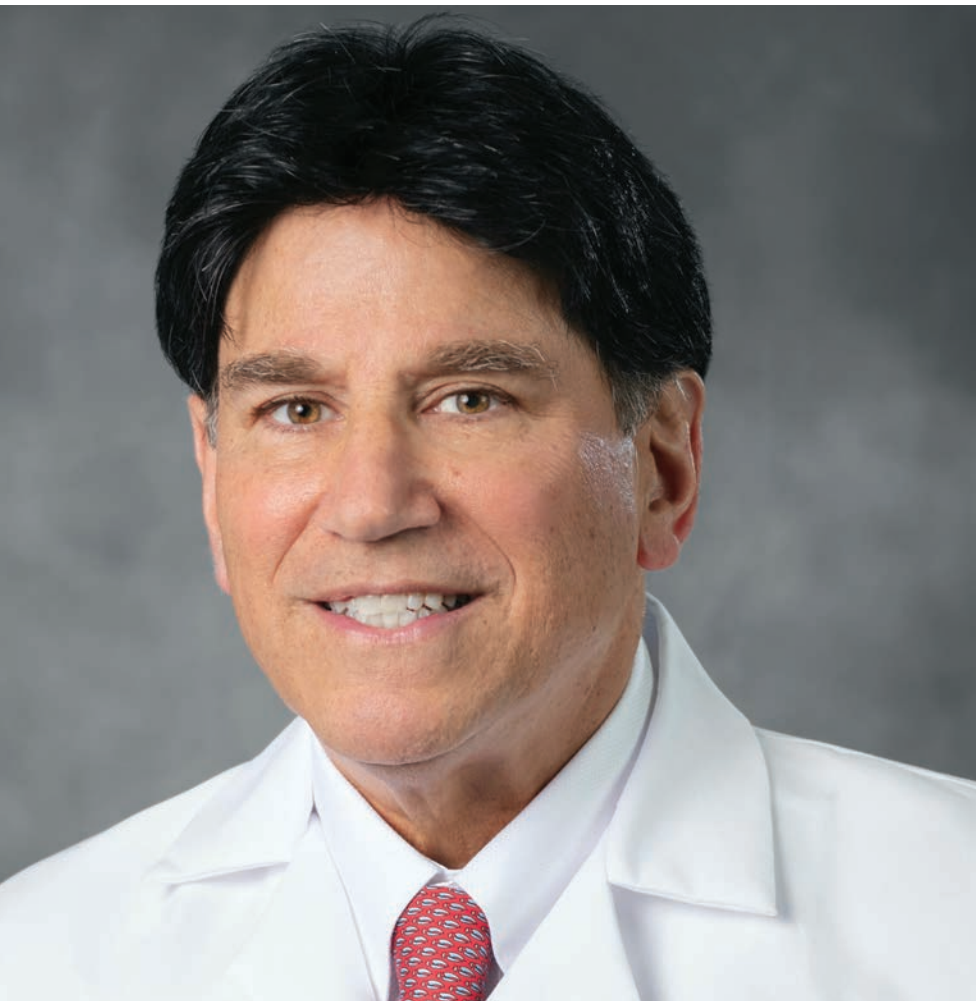
Throughout his career, Spaeth has become as an internationally recognized figure in ophthalmology. With over 400 papers, 200 editorials, and 23 books published, Spaeth's influence over the field is unequivocal. Alongside this, Spaeth has presented over 30 named lectures, famously set up a practice specializing in glaucoma at Wills Eye Hospital, and founded – and was the first president of – the American Glaucoma Society. Amidst all of these groundbreaking accomplishments, Spaeth continues to stress that the most important thing is not our career by any stretch – "It's what kind of people we are." We are delighted to induct George Spaeth into The Ophthalmologist Power List Hall of Fame not only for his many achievements – but also for his inspirational attitude to medicine and life.

Graham D. Barrett
Consultant Ophthalmologist, Sir Charles Gairdner Hospital, and Lions Eye Institute; Clinical Professor, Centre for Ophthalmology and Visual Science, University of Western Australia

From the moment he set his sights on completing his ophthalmology residency, Graham David Barrett has made extensive and varied contributions to the field. A pioneer and leader both within his home country of Australia and internationally, throughout his career, Barrett has served on the boards of several international and highly-regarded ophthalmology societies and sat on several industry editorial boards.

Of particular note, Barrett co-founded the Australasian Society of Cataract and Refractive Surgeons (AUSCRS) in 1995, serving as its President for over 25 years. Over this period, the society developed a thriving community of professionals committed to analyzing how cataract and refractive surgery could continue to improve. This commitment has not only been a mainstay of Barrett's career but also the driving force behind his development of numerous pioneering instruments and innovations, including the development of the world's first foldable IOL implanted in 1983, popular Barrett Toric Formula and Calculator and the first, and only, available IOL optimized for use with Monovision.

With such an impact, it is no surprise that Barrett has received recognition through several awards and honors – even in this arena, Barrett broke new ground, becoming the first Australian ophthalmologist to win, in the same year, the prestigious Binkhorst, Choyce, Ridley and Susruta awards. This culminated in Barrett's recognization in the 2022 Queen's Birthday Honors for Australia, for his significant service to ophthalmology and to professional organizations. In 2023, it seems only right that we honor Graham Barrett's incredible career and service further through his induction into The Ophthalmologist Power List Hall of Fame.



Robert N. Weinreb

Distinguished Professor and Chair, Ophthalmology; Director, Shiley Eye Institute; Morris Gleich MD Chair of Glaucoma; University of California, USA

Following his medical degree from Harvard Medical School and a degree in electrical engineering from the Massachusetts Institute of Technology, Robert N. Weinreb has gone on to become a world-renowned clinician, surgeon, and scientist. Now the Director of the Shiley Eye Institute and the Director of the Hamilton Glaucoma Center, Weinreb has the responsibility of overseeing all activities, devoting himself not only to the development of better glaucoma treatment, but also to the development of enhanced, patient-centered care.

Throughout the years, Weinreb's research has covered all aspects of the eye, exploring what role each structure plays in the development of glaucoma. He has developed and investigated novel imaging technology, functional tests, IOP sensors for continual testing, and, more recently, medication adherence monitors. It is inspiring that, amidst all of his success and pioneering efforts, Weinreb has a plaque in his office with a Michelangelo quote reading, "I am still learning."

Thanks to his enduring contributions to ophthalmology, Weinreb has received numerous prestigious awards world-over. Having delivered more than 140 named lectures, while serving on multiple editorial boards and training more than 150 post-doctoral fellows in glaucoma, it is abundantly clear that Weinreb's position in the Hall of Fame is fully deserved.

Shigeru Kinoshita

Professor and Chair, Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Japan

Shigeru Kinoshita has consistently led the charge in the advancement of corneal knowledge, making a huge impact through his development of new corneal therapeutic modalities. One of his earliest contributions in this regard came in the early 1980s when he co-established the concept of the centripetal movement of the corneal epithelium, which played a large part in the later development of corneal stem cell theory.

Over the following 40 years, Kinoshita continued to add to the ophthalmic literature, publishing over 670 articles with an H-index of 98, also holding more than 39 patents worldwide. Kinoshita's reputation as a pioneer and innovative researcher has only been strengthened by his instrumental role in the formation of the Eye Research Program at Kyoto Prefectural University of Medicine, where he has also held the titles of Professor and Chairman since 1992.

Though it is an incredible task to recognize the true impact of Kinoshita's career, a look at some of the honors he has received provides some insight. The recipient of the Alcon Research Institute Awards, The Cornea Society's Castroviejo Medal, and ARVO's Friedenwald Award, amongst many others, in 2023, we recognize Shigeru Kinoshita's contribution to ophthalmology through his induction into the Hall of Fame.

Sir Peng Tee Khaw

Director, Research & Development, Moorfields Eye Hospital NHS Foundation Trust; Co-Director, NIHR Biomedical Research Centre (BRC), Moorfields Eye Hospital, and UCL Institute of Ophthalmology, Professor and Consultant Eye Surgeon. NIHR Emeritus Senior Investigator, London, UK

Sir Peng Tee Khaw has amassed a wealth of awards, and worldwide recognition for his clinical work, research experience, education and fundraising since he joined Moorfields Eye Hospital in 1987. He became the director of the National ophthalmology translation centre, the NIHR Biomedical Research Centre (BRC) at Moorfields Eye Hospital and UCL Institute of Ophthalmology in 2007, leading advances in genomic discovery, cell, gene and new device therapies. Alongside this, Sir Peng has also been extensively involved in innovations in glaucoma surgery, wound healing, new instruments, ocular pharmacology and stem cell discovery, and the development of treatments for glaucoma. To date, he has published over 600 papers, chapters, and books, whilst also training, supervising, and mentoring 42 PhD students and 11 MD students and many more clinical fellows.

Sir Peng has been on the Times List of Britain's Top 100 Doctors for adults and children, was elected to the British Academy of Medical Sciences in 2003, and appointed as one of 200 UK NIHR Senior Investigators in all specialties. He achieved a Platinum Clinical Excellence Award, the highest level from the NHS and was knighted by Her Majesty Queen Elizabeth II in 2013, only the second person in the last century for services to ophthalmology.

Looking at the scope of Sir Peng's career, one major theme that binds all of his work is the sustained belief that we can have a significant clinical impact on glaucoma. We are delighted to welcome Sir Peng Tee Khaw into The Ophthalmologist Power List Hall of Fame.

Theo Seiler

Founder of the Institute of Refractive and Ophthalmic Surgery (IROC), Zürich, Switzerland

After completing his PhD in Experimental Physics at the Free University of Berlin in 1974, Theo Seiler went on to complete a residency and PhD in the university's Department of Ophthalmology, where he rose to senior assistant and lecturer in 1985. One year later, Seiler became the first person to perform laser surgery on a human eye, laying the foundations for the development of LASIK surgery. Alongside this, Seiler is recognized for his research in corneal crosslinking through his idea of crosslinking collagen in the cornea to prevent keratoconus progression. Following a 1999 pilot study which confirmed clinical feasibility, it became, and has remained, the gold standard approach.

In 2002, Seiler founded The Institute for Refractive and Ophthalmic Surgery (IROC) in Zurich. Offering an entire spectrum of eye care but specializing in laser eye and cataract surgery, IROC not only serves its patients but serves as a reminder of Seiler's enduring contributions to laser eye treatment. Seiler now spends 80 percent of his time at IROC, with the rest being dedicated to research, training the next generation of doctors, and performing surgery in developing countries. Helping people – especially those who may struggle to afford eye treatment and surgery – is what motivates him to achieve at such a high level.

Thanks to his pioneering feats that have paved the way for modern ophthalmology, Seiler's spot in The Hall of Fame is both expected and thoroughly deserved.

EMPOWERMENT THROUGH SIMPLICITY: DON'T OVERLOOK THE OBVIOUS

Bruder Healthcare's range of hygiene, heat, and hydration products makes it easy for patients to participate in their eye health as well as help to improve surgical outcomes.

Of all the five senses, vision is the one that patients value most, yet they don't act accordingly when they neglect their eye health. The result: dry eye and other forms of ocular surface and lid disease continue to diminish quality of life for tens of millions of patients. So, why do patients pay so little attention to something of such personal value and significance? "Part of the answer is that patients don't know how to do their part when it comes to caring for their eyes and vision," says Cynthia Matossian, MD, FACS. "Proper hydration and daily lid hygiene is very simple and is recommended for everyone."

A basic self-care routine for the eyes should be as fundamental as brushing and flossing teeth. Three easy steps – hygiene, heat, hydration – are considered foundational and are useful alone or in combination with other technologies to provide relief to dry eye patients – or prevent signs and symptoms before they emerge. So, why isn't every eye doctor recommending this approach at every patient visit? Much of the hesitation stems from a common misconception that patients won't engage in a daily eye care routine, even though research shows the exact opposite – patients would do it, if only their doctors would ask (1).

Empower patients in their hygiene routine

"Research has also shown eyelid wipes as a beneficial tool pre and post cataract surgery," says P Dee G. Stephenson, MD. Gently wiping a Bruder Hygienic Eyelid Cleansing Wipe across the eyelids and lashes is the optimal first step in a lid hygiene regimen. Bruder Eyelid Cleansing Wipes are easy-to-use and feature a leave-on, no-rinse formula that helps dissolve and remove excessive oils and debris from eyelids and lashes. The premoistened wipes are hypo-allergenic and free of harsh chemicals. Importantly, they don't sting or burn and are gentle enough for daily use. Wipes with tea tree oil are also available for patients with moderate-to-severe eye irritation, such as those who have *Demodex*.

"After cleaning with the wipes, it's advisable for patients to apply one to two sprays of Bruder Hygienic Eyelid Solution to closed eyes to reduce bacterial growth," says Dr. Stephenson. The spray contains 0.02% pure hypochlorous acid, a commonly used ingredient in lid hygiene sprays because it's so effective against a wide range of microorganisms. It helps to fight infection, reduce inflammation, control the body's response to injury, and enhance its natural ability to heal. Hypochlorous acid works to support rapid and effective relief from dry eyes, styes, and red, itchy eyelids associated with conditions like blepharitis and meibomian gland dysfunction (MGD). In contrast to other lid sprays, the Bruder solution contains no preservatives, alcohol, oil, sulfates, parabens or added fragrance.

Patient education is fast and simple with support material developed by Bruder Healthcare

83% of patients said they would use a hygiene kit if they were asked to buy one.[1]

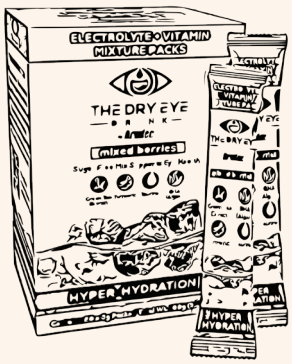
Empower patients to add moist heat

"Heat therapy has shown significant benefits in improving tear film stability," says Dr. Matossian. When selecting a mask, it's worth noting that the Bruder Moist Heat Eye Compress is not like other eye masks, as it features patented MediBeads technology providing the moist, uniform, extended heat required to effectively liquify oil in the meibomian glands and release the eye's natural hydration. Traditional compresses rely on silica gel beads, gel, or grains that can dry out and deliver uneven heat, causing hot spots that are dangerous and reduce product performance. The Bruder MediBead honeycomb molecular structure encourages complete absorption of water molecules and, when microwaved, releases moist heat in a controlled and consistent manner for eight to 12 minutes.

MediBeads are also infused with silver to repel bacteria and reduce the risk of infection. Importantly, the compress withstands the rigors of daily use and regular washing , and will not break down like inferior materials found in other compresses.

Empower patients to hydrate

Water is a major constituent of the eye (2), so, naturally, hydration is important. Hydration affects the ocular physiology, morphology, ocular pathophysiologic processes, and disease states found in both the front and back of the eye (3). Specifically, whole-body hydration is an important consideration in dry eye etiology and management (4). Unfortunately, average water intake falls far below recommendations. To make adequate hydration easier for patients, Bruder Healthcare has introduced Dry Eye Drink by Bruder. "This hyper-hydration drink was developed by optometrists and ophthalmologists specifically looking to help patients defend against dry eye signs and symptoms," notes Joshua Davidson, OD, who helped spearhead the development and research of the drink. "It is specially formulated with anti-inflammatory ingredients, vitamins, and electrolytes to nourish and hydrate the eyes and the body," he adds. By addressing the underlying causes of dry eye disease, the hydration drink helps maintain optimal ocular health, and it does so without sugar and without significant amounts of sodium. In short, proper hydration therapy with Dry Eye Drink treats the eyes from the inside out.



Some of the time beats none of the time

Whether a patient's eyes are currently uncomfortable or not, empower them to care for their lids and lashes. Indeed, a daily routine with the Bruder system of products is as natural and necessary as facial cleansing and moisturizing, exercising and stretching, or brushing one's teeth. "Sure, patients sometimes skip flossing or exercising, but falling short occasionally doesn't diminish the importance of the routine – or how easy it is to pick up again," says Dr. Matossian.

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Doctor-developed Dry Eye Drink enables patients to treat eyes from the inside out, with anti-inflammatory ingredients, vitamins, and electrolytes to nourish and hydrate the eyes and the body.

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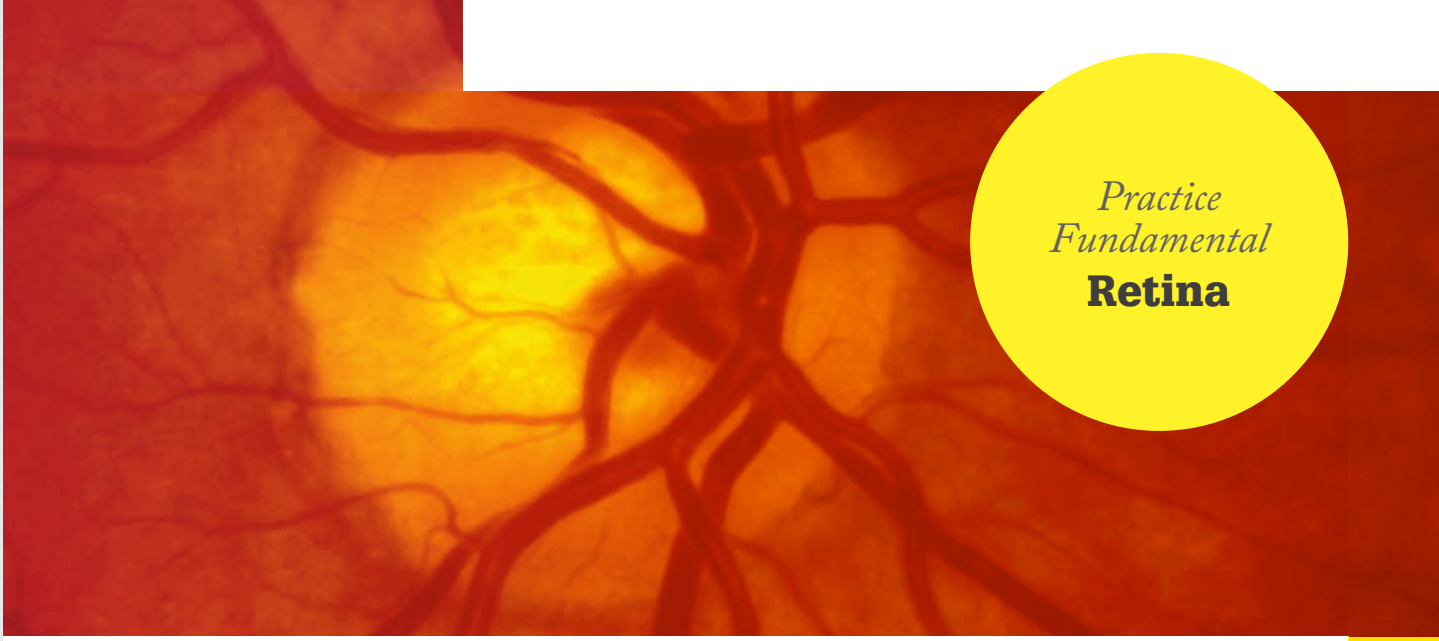

Elucidating effects. New research aiming to clarify the effects of sildenafil citrate (SC) on diabetic retinopathy (DR) tested the effect of the drug on a murine model of the condition by measuring the DR mediator, vascular endothelial growth factor (VEGF). They found that there was a significant decrease in VEGF following chronic oral SC treatment, indicating that it may have a modifying or attenuating effect on DR; further studies are needed to evaluate its use as an adjunctive therapeutic (OA Sorour et al., Int J Retina Vitreous; PMID: 37460929).

Damaging data. Building on previous research highlighting tumor necrosis factor-alpha-induced protein 8 (TNFAIP8) as being elevated in the plasma extracellular vesicles and vitreous humor in DR, researchers have now shown TNFAIP8 to significantly decrease a/b-wave amplitude and retinal thickness in diabetic mice, as well as aggravating pathological abnormalities with distorted organization of the retina. TNFAIP8 also increases the avascular area, leukostasis, and the expression of inflammatory factors in the retina (F Yang et al., Exp Eye Res, [Online ahead of print]; PMID: 37451566).

You eye what you eat. What are the dietary habits of patients with AMD compared to those without? A study of 161 Czech patients found that, although the dietary habits of patients with AMD and control patients were similar, men in the AMD case group consumed alcoholic beverages more frequently than those in the control group. The control group also achieved recommended dietary intakes and had significantly higher dietary intakes of key macronutrients (JS Kráľová et al., Cent Eur J Public Health; PMID: 37451248).

Surveying the landscape. From current treatments available on the market to prospective treatments in or about to enter clinical trials, researchers outlined their findings following an analysis of the current landscape of retinal therapeutics. They also highlight novel investigation methods of identifying several retinopathies for a more "precise medicine" approach, tailoring dedicated treatments to the identification of the specific molecular pathways behind an individual's retinopathy (R Marino et al., Neural Regen Res; PMID: 37449599).

(Cut) off from work. Looking to better understand the relationship between AMD and workplace productivity, researchers conducted a meta-analysis of economic studies, comparative studies, observational studies, cohort studies, case series, randomized control trials, clinical trials, multicenter studies from MEDLINE, EMBASE, and CINHAL, as well as gray literature. They found that AMD patients had a significant unemployment rate and experienced impaired work productivity, which was demonstrated by wages lost (E Tran et al., Eur J Ophthalmol, [Online ahead of print]; PMID: 37448315).

IN OTHER NEWS

Two new targets. *Rho-ROCK and GPR84 signaling may be potential therapeutic targets to prevent the neurotoxic microglial phenotype induced by optic nerve damage (K Sato et al., Glia, [Online ahead of print]; PMID: 37470163).*

Low vision, high QoL. *Low vision patients with AMD-related geographic atrophy should consider low vision aids as soon as possible and should be included in low vision rehabilitation programs (DE Acar, et al., J Ophthalmol; PMID: 37455795).*

Easily predictable. *Bimanual technique using a soft tip cannula under direct visualization is safe and efficient, making membrane retrieval a predictable process (P Agarwal, et al., Retina; PMID: 32649490).*

Synthetic segmentatione. *Multimodal deep learning networks to segment geographic atrophy lesions can produce accurate results comparable with those of expert graders (T Spaide, et al., Transl Vis Sci Technol; PMID: 37428131).*

Watching from a Distance

ARVO 2023: Jennifer Jacobs discusses a teleophthalmology model that could revolutionize AMD monitoring and treatment

The disruption caused by the pandemic, particularly to ophthalmic practices, saw an inevitable increase in (and development of) teleophthalmology practices to ensure continuity of care for patients affected by long-term conditions. Here, Jennifer Jacobs, an ophthalmologist specializing in remote AMD monitoring, speaks to The Ophthalmologist about her own research, presented at ARVO 2023, that explores how teleophthalmology can be best applied to remote monitoring for patients living with age-related macular degeneration (AMD).

What is the current state of AMD treatment?

When it comes to AMD treatment, there's always research being done. We know that we have very effective treatments for wet AMD – we've had those for two decades or so. But we also know that macular degeneration is a leading cause of blindness in the US. Even though we have effective treatments, there's still a diagnostic gap – one we can help meet with remote monitoring. Around 10–15 percent of patients with dry AMD will convert to the more severe, vision-threatening wet AMD. The average visual acuity at wet AMD diagnosis is around 20/83. Studies have shown that patients who receive remote monitoring in addition to their standard care are diagnosed with better visual acuity than those who do not, and in fact, the average visual acuity of the monitored patient at wet AMD diagnosis is better than or equal to 20/40. The ALOFT study was a study that showed that even long-term, after diagnosis and treatment of wet AMD in the monitored patient, good visual acuity is maintained because advancing disease in these patients has been caught earlier (3). We also know that the best predictor of long-term visual outcome is the visual acuity at diagnosis and start of treatment. There is definitely a need for remote monitoring that can help catch patients when they convert from dry to wet AMD as early as possible. There's also a need in neovascular AMD for monitoring patients with home-based OCT; with this heterogeneous disease, being able to personalize treatment, to some extent, could be great for patients. Through home-based OCT, we monitor patients remotely so doctors have the ability to determine remotely if patients are responding to anti-VEGF treatments – and if they would like to bring them in sooner for further treatment.

What did you share at ARVO 2023

The model I presented includes three basic components – one of which is the monitoring center. We wanted to assess patient compliance, patient retention, and also look at patient experience – if patients have a good experience of monitoring, they will continue with it. The performance metrics of the model have been demonstrated in peer-reviewed studies. One retrospective study looked at over 2,000 intermediate AMD patients on the ForeseeHome AMD Monitoring

Program, with compliance determined by the number of tests patients performed per week. The study found that patients performed a mean of 5.2 tests per week. In looking at longitudinal compliance over a period of 10 years, it was discovered that patients continued to test between 4.8 to 6.9 tests per week, indicating that there isn't really a dip in compliance over time. In terms of neovascular AMD, a study looking at patients who were monitored using the home-based OCT showed that compliance was also very good (5.7 times per week) (4).

"When patients understand their disease process, they're more likely to take an active role in monitoring their condition."

These results show that compliance is not a problem and suggest our monitoring center model is really helping patients. We also saw this in the positive responses to a patient survey that assessed the device's user-friendliness the patients' experience with monitoring center service calls, and whether patients wanted to continue using the device. The monitoring center also gives out general information and education for patients about macular degeneration. When patients understand their disease process, they're more likely to be compliant and want to take an active role in the monitoring of their condition.

How will teleophthalmology change how clinicians practice?

In terms of monitoring intermediate AMD patients, it certainly has made a mark in helping doctors diagnose conversion from dry to wet AMD earlier. The ForeseeHome preferential hyperacuity perimetry device is approved for patients with intermediate AMD because they are high-risk. I think it will be very helpful in terms of preserving vision, as doctors catching the conversion can do so while visual acuity is good.

I think home-based OCT on the other hand will be instrumental in how doctors manage patients on therapy. Now, doctors use in-office OCT and OCT-A to help evaluate if patients have converted, help determine whether they have subretinal or intraretinal fluid, and to assess what kind of treatment they require. Home-based OCT will also enable doctors to see if patients are responding to treatment, and if the patient has developed more fluid and regressed. With the home-based OCT, doctors can specify when they want to be alerted (based on how much fluid is in or under the retina). I don't think it's bold to say that it's going to better personalize medicine for wet AMD patients, which will help both the patient and the doctor.

What's the take-home from your work?

The results of this model are important because patient compliance is a big issue, not just for macular degeneration or glaucoma, but across all aspects of medicine. The monitoring center makes a huge difference. We didn't have the center when we first began our monitoring program; over the years, the program has been developed. Now there's a clinical partner at the monitoring center, assigned to the patient, who walks them through the monitoring process, helps them set up the equipment, and gives them testing tips.

MEET JENNIFER JACOBS

I'm Jennifer Jacobs, an ophthalmologist based in Virginia. I have a practice where I see patients, but I'm also a medical director for the Notal Vision Monitoring Center, a Medicare accredited digital healthcare provider specializing in remote patient monitoring services. My interests are primarily based around helping patients maintain functional vision at wet AMD diagnosis through effective home monitoring. Studies have shown how our monitoring center model is helping in terms of visual acuity (1).

The center certainly helps patients to understand the importance of monitoring. We didn't know that the compliance would turn out to be so great – but it is, and we're pretty happy about that. From what we've seen, the model works!

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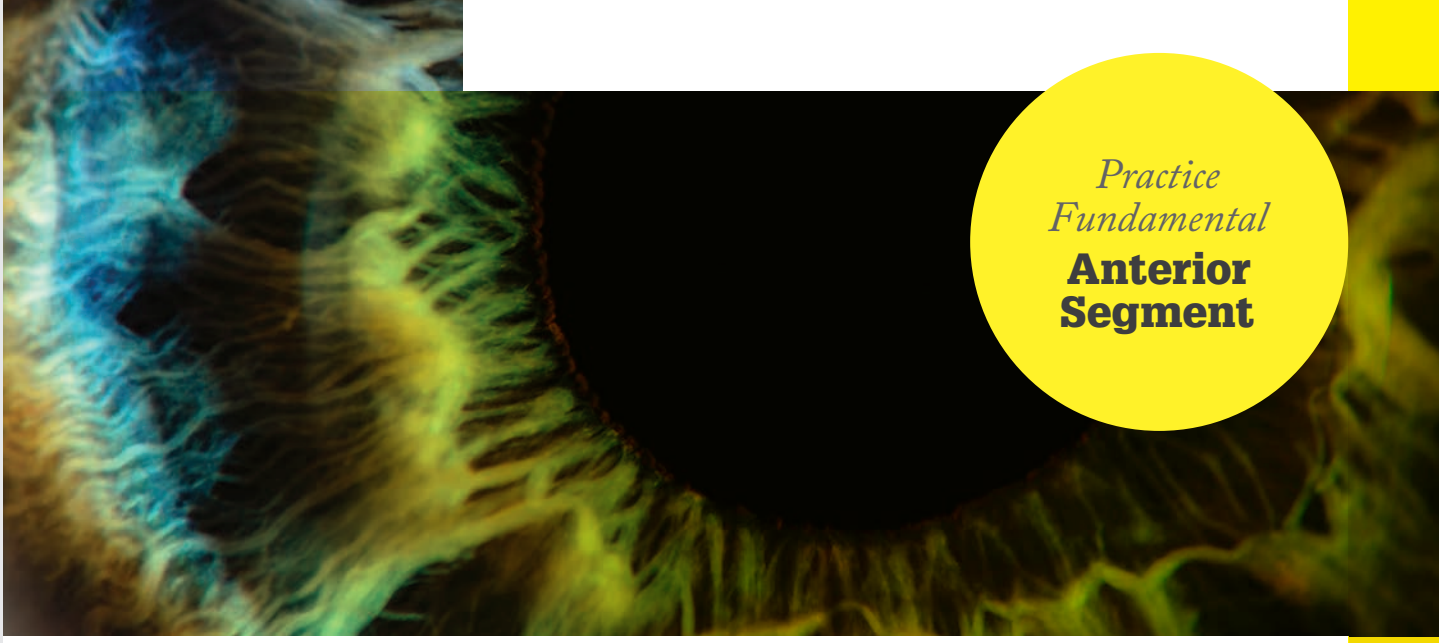

Medium-rare. A German study of 10,000 participants found the prevalence of keratoconus to be approximately 10 times higher than previously reported (0.49 percent of those involved in the study). The researchers used Scheimpflug imaging, a diagnostic technology that allows for greater sensitivity when detecting keratoconus, and, in contradiction with existing literature, found no associations between keratoconus and diabetes, smoking, sleep apnea, or depression (S Marx-Gross et al., Graefes Arch Clin Exp Ophthalmol; PMID: 37314521).

Blinking after Botox. A new Journal of Neuro-Ophthalmology study looking into how patients with blepharospasm or hemifacial spasm respond to botulinum toxin injections has gathered data evidencing reduced rates of blinking (in terms of amplitude and velocity) in both disorders. The authors measured blinking metrics using a high-speed camera and microlight-emitting diodes to conclude that post-botox blinking does not generally normalize in patients (GR Gameiro et al., J Neuroophthalmol; PMID: 37307066).

Time and motion. Researchers used time and motion studies to compare the productivity of the UK National Health Service cataract lists performing unilateral cataract surgery versus immediate sequential bilateral cataract surgery (ISBCS). The results found that performing consecutive ISBCS cases under local anesthesia on routine cataract surgery lists can increase surgical efficiency (K Naderi et al., Eye; PMID: 37277612).

SS upregulation. Sjögren's syndrome (SS), an autoimmune disease affecting the lacrimal glands, is already known to cause severe dry eye disease (DED) and other ocular surface diseases. Now, a new study has compared the tear protein concentration of those suffering from the syndrome with healthy individuals. Using Schirmer strips to collect tear samples, the researchers uncovered results suggesting tear protein concentration was altered in those with SS, with 241 upregulated tear proteins linked to DED symptoms and severity (SP Yoon et al., Transl Vis Sci Technol; PMID: 37310735).

Diabetic discoveries. Twenty-four diabetic patients with cataracts (group D) and 14 sex- and age-matched patients with age-related cataracts (group N) were recruited for a study aiming to investigate differences in the ocular surface bacterial composition in cataract patients with and without type II diabetes (T2D). The results found that the bacterial composition was similar between group D and group N, but several bacterial strains that were reported beneficial in the gut were decreased while pathogenic bacteria were increased in T2D (Z Shao et al., Transl Vis Sci Technol; PMID: 37261381).

IN OTHER NEWS

Name drop. *A recent study including 312 participants has found that perfluorohexyloctane eye drops significantly improve the signs and symptoms of meibomian gland dysfunction–associated dry eye disease in Chinese patients (L Tian et al., JAMA Ophthalmol; PMID: 36929413).*

A better SMILE. *Research conducted by a global, multi-institutional research group compared the change in corneal stiffness after small incision lenticule extraction, femtosecond laser–assisted in situ keratomileusis, and photorefractive keratectomy (A Abu-Diab et al., Transl Vis Sci Technol; PMID: 36857066.).*

Hot and cold. *To determine the sensitivity of phase-decorrelation optical coherence tomography to protein aggregation associated with cataracts in the ocular lens, researchers held six fresh porcine globes at 4 °C until cold cataracts developed (BJ Blackburn et al., Transl Vis Sci Technol; PMID: 36971678).*

CFS: It's a Numbers Game

The evolution of the NEI corneal sodium fluorescein staining scale

By Andrew D. Pucker and George Magrath

First popularized in the mid-1990s, ocular image grading scales have long been established as valuable tools for judging the severity of ocular disease. But how do they work? The most commonly-used grading scales contain images (photographs or illustrations) that practitioners use to compare against their patient's eye. The practitioner then determines the severity based upon the defined scale, with higher numbers typically representing more serious disease. Although an initial study (2) suggested that using grading scales with finer increments (for example, 0.1 units) would improve the sensitivity of a scale, a later study found that investigators had a tendency to grade in whole and half unit increments, even when given the opportunity to use smaller units (3).

Corneal fluorescein staining (CFS) is a key clinical sign of corneal surface integrity and clinical trial endpoint for patients with conditions such as dry eye disease (DED). Although numerous CFS grading scales exist, the NEI corneal grading scale provides additional grading detail, evaluating five regions of the cornea as opposed to just one. And that has cemented the NEI corneal grading scale as the most frequently used CFS scale in DED clinical trials (7).

The NEI corneal staining scale was introduced in 1995 as a product of the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eye (4). This workshop included a group of international experts who wrote a consensus report on the topic to help standardize the first definition of DED and the metrics used to evaluate it. The original NEI corneal grading scale uses a 0 to 3 integer grading scale for each eye across five corneal regions (central, inferior, superior, temporal, nasal); the width of each of these regions is about one third of the corneal diameter. A total NEI corneal staining scale score is obtained by adding the five regions together, resulting in a 0 to 15 scale – with 15 being the worst possible grade (4). Clinical trials frequently use a score of ≥2 units in any corneal region as a trial inclusion criteria (5). When performing this evaluation, sodium fluorescein should not be applied in excess because dye quenching may occur (reduction in fluorescent efficiency/brightness) (6), and grading should happen at a defined time point (for example, two-minute post-application) to decrease test-to-test variability (7). Although the original NEI corneal staining grading scale was an advancement for the field, it was graded based upon gestalt, which is challenging for multicenter clinical trials that include numerous investigators.

With this known issue, investigators have since developed more descriptive

Grade (Units)	Description
0	0 dots
0.5	1-7 dots
1.0	8-15 dots
1.5	16-22 dots
2.0	23-30 dots
2.5	31-37 dots
3.0	≥38 dots/too numerous to count and must be less than half of the area of the region. May have confluence (closely adjacent dots) but not coalescence (merging dots).
3.5	≥38 dots/too numerous to count and must be ≥half of the area of the region. May have confluence (closely adjacent dots) but not coalescence (merging dots).
4.0	≥38 dots/too numerous to count and must have an area of coalescence (merging dots).

Table 1. Lexitas Modified NEI Staining Scale (10)

grading options, which include the Dot Count NEI staining scale and the Lexitas modified NEI staining scale (8). The Dot Count NEI staining scale still uses a 0 to 3 grading scale, though scores of 0, 1, 2, and 3 correspond to 0, 1-15, 16-30, and ≥31 dots while the Lexitas modified NEI staining scale breaks the Dot Count NEI staining scale system into half step increments and expands this scale to a 0 to 4 scale (see Table 1). The Lexitas modified NEI staining scale furthermore provides additional grading details. The Lexitas modified NEI staining scale subsequently allows greater grade granularity while also likely making it easier for multiple investigators to arrive at consistent grades across sites and over the life of a clinical trial.

A recent study validated the repeatability of the Lexitas modified NEI staining scale in conjunction with the other two noted versions of the NEI staining scale (8). The researchers determined that there was a high degree of inter- and intra-examiner repeatability for all three of the NEI staining scales evaluated. The same result was established when the investigators were asked to grade illustrations or clinic sourced images. Despite these findings, one caveat of this study was that it only used trained expert practitioners for grading. As highlighted in previous studies, trained eye care practitioners provide more reliable grades than non-eye care practitioners (9).

"Though there exists a plethora of ocular surface grading scales, the NEI staining scale is one of the most accepted options available for evaluating the cornea."

Though there exists a plethora of ocular surface grading scales, the NEI staining scale is one of the most accepted options available for evaluating the cornea. Although the most used versions of the NEI staining scale are all highly repeatable, the Lexitas modified NEI staining scale is arguably the best option currently available because of its highly descriptive grading instructions and because of its expanded grading scale. We would suggest it should be seriously considered for use in future studies.

Andrew D. Pucker, OD, PhD, is Senior Director of Clinical and Medical Science, at Lexitas Pharma Services.

George Magrath is Chief Executive Officer at Lexitas Pharma Services.

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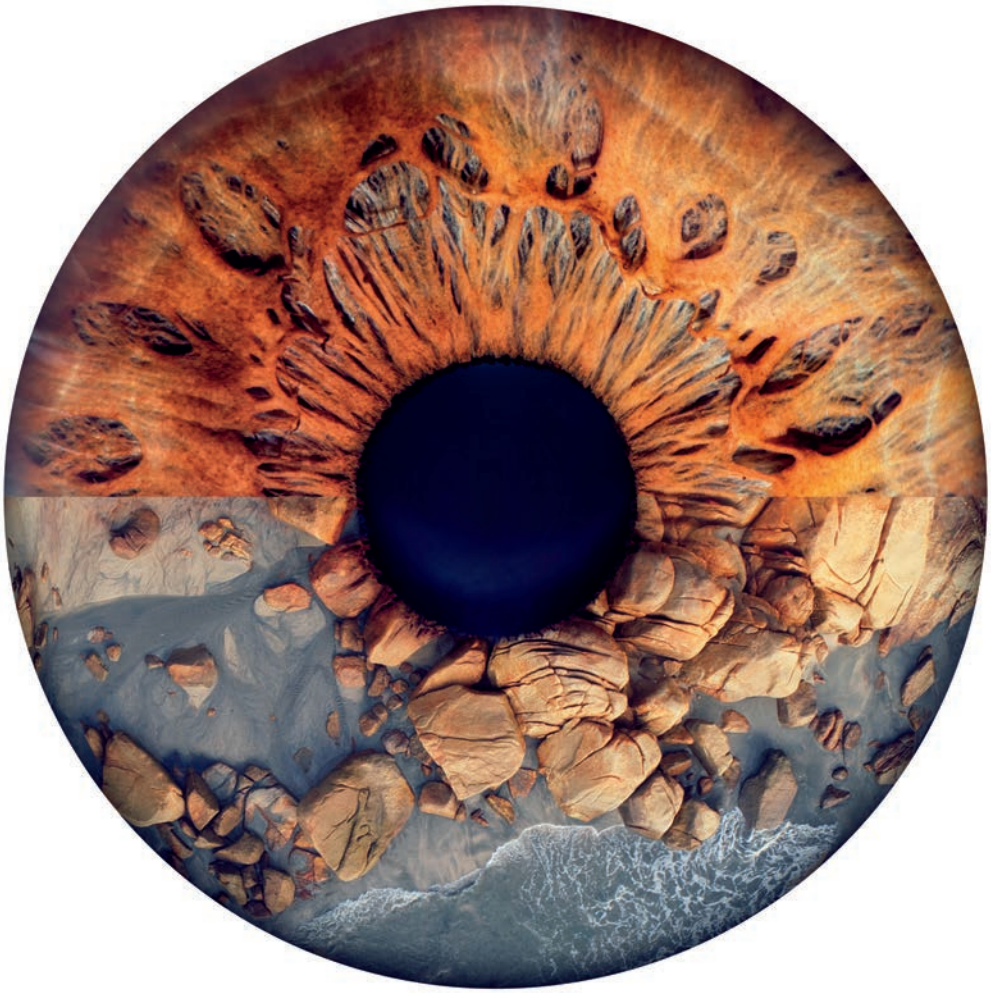

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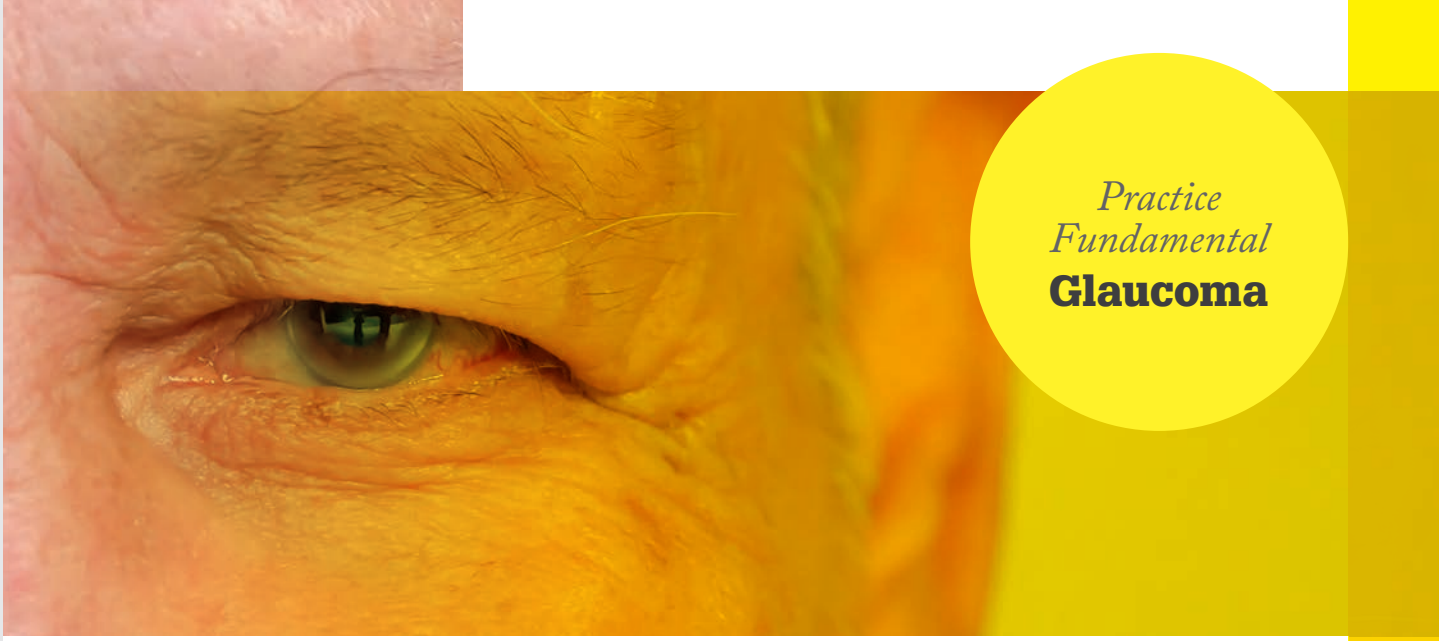


Myopic links. Investigating the relatively unknown association between myopia and glaucoma, scientists from the University of Alabama at Birmingham (US) and Menoufia University (Egypt) examined the positional changes that occur in Bruch's membrane opening and the anterior scleral canal opening. The study concluded that the asymmetrical changes caused by experimental high myopia development, through contribution to pathological optic nerve head remodeling, may increase the risk of glaucoma in later life (M T KhalafAllah, et al., Invest Ophthalmol Vis Sci; PMID: 37010856).

Ratifying reports. Looking to provide direct clinical evidence to support the implication of heat shock protein (HSP)-specific T-cell responses in glaucoma pathogenesis by previous laboratory reports, a research team conducted a cross-sectional case-control study. The study involved 32 adult patients with primary open-angle glaucoma and 38 controls, all of whom were subjected to blood draw and optic nerve imaging. The research team found that higher levels of HSP-specific Th1 cells are associated with thinner retinal nerve fiber layer thickness, a significant inverse relationship that supports these T cells in glaucomatous neurodegeneration (C Saini, et al., Ophthalmol Sci; PMID: 37197701).

Calculated G-RISK. Aiming to overcome the issue of glaucoma classification models struggling to replicate their impressive internal performance on external datasets, a research team tested and confirmed that the previously described G-RISK regression network for glaucoma can obtain excellent results in a number of challenging settings. The network was tested on 13 different data sources of labeled fundus images and surpassed the minimum sensitivity criteria recommended by Prevent Blindness America (R Hemelings, et al., NPJ Digit Med; PMID: 37311940).

SLT discovery. A study in the Philippines aimed to compare the economic viability of initial medical therapy with topical prostaglandin analogues (PGAs) versus selective laser trabeculoplasty (SLT) in the treatment of primary open-angle glaucoma (POAG). Researchers conducted a socioeconomic and demographic survey among 31 POAG patients at the Department of Health Eye Center of the East Avenue Medical Center in the Philippines, and found that SLT was more cost effective compared with PGAS in POAG patients in a low-resource, public hospital setting. The authors write, "Cost-effective health care attempting to reduce the disease burden of visual loss is the priority of all nations but notably in the developing world since this may pose an economic burden to society." They believe that SLT could be offered as an initial therapy for POAG to decrease the economic burden both for patients and the healthcare system. (JMD Jacomina, et al., Philippine Journal of Ophthalmology, 48).

IN OTHER NEWS

Translated results. *Researchers have found the Moroccan Arabic dialect version of the Glaucoma Quality of Life-15 questionnaire to be a valid and reliable tool (M Maiouak, et al., J Fr Ophtalmol; PMID: 37225606).*

Cannabis characterizations. *A cross-sectional study found that nearly half of patients with open-angle glaucoma were cannabis ever-users, with diversity in ethnicity and socioeconomic characteristics (J H Wu, et al., Heliyon; PMID: 37215923).*

Clean data. *Researchers find that anterior chamber washout during Ahmed valve glaucoma surgery decreases the likelihood of hypertensive phase compared with controls (MM Chang, et al., J Glaucoma; PMID: 36946974).*

Two parts of the same coin. *Efficacy outcomes of selective laser trabeculoplasty are found to be comparable between eyes treated by optometrists and ophthalmologists (CN Lee, et al., Invest Ophthalmol Vis Sci; 64).*

Glaucoma Under Pressure

Serial entrepreneur Barbara Wirostko walks us through a novel therapeutic approach that tackles EVP

The last two decades have seen an explosion in treatment options for glaucoma – from new pharmacotherapies to the increasingly popular (minimally invasive) surgical intervention. But despite all the exciting developments, there is still more to do, attracting the attention of savvy clinician-researchers and business innovators who know the need and potential market. Here, ophthalmologist and entrepreneur Barbara Wirostko explains how episcleral venous pressure (EVP) could expand the glaucoma armamentarium.

What are your company's aims?

When I co-founded Qlaris Bio in August 2019 with Thurein Htoo – a former colleague from Pfizer we had a singular premise in mind: To develop better solutions for patients suffering from debilitating ophthalmic diseases.

We started the company based on the innovative research of Michael Fautsch, of Mayo Clinic, who had been working on ATP-sensitive potassium channel openers as vasodilatory agents for lowering intraocular pressure (IOP). He discovered that these agents worked on a very unique portion of the Goldmann equation – EVP. Since the introduction of MIGS, the field has been running into a problem, we can lower IOP, but it seems like we can only lower it so much. This pressure floor is likely due to EVP's impact on the outflow system, which is exactly what the potassium channel openers target. Our developmental compound QLS-111 specifically targets EVP to treat various forms of glaucoma.

Could you share a few more details about your novel compound?

What is unique about this compound is that it works with physiology and doesn't disrupt the normal tight junctions of the vasculature. As a result, we have a great safety profile – we don't see any clinically relevant hyperemia – and the results on efficacy are extremely promising. We are currently entering phase II trials for normal-tension glaucoma (NTG) and primary open-angle glaucoma (POAG).

Beyond QLS-111, what other avenues are you exploring with Qlaris Bio?

We have known that EVP played a role in the progression of diseases like Sturge-Weber syndrome, but we didn't appreciate to what extent EVP also plays a role in the progression experienced by POAG and NTG patients. It wasn't until we had the breakthrough of MIGS – when we really did expect the pressure to be lower than what was achieved – that the picture became clearer that the limiting factor was EVP. And that's a good lesson; every time we take a step forward in treatment options, we have to confront the fact that new problems and learnings may be encountered.

What does the future of glaucoma treatment hold?

I would love to be able to offer patients continual IOP-lowering therapeutics – whether that's laser, surgery, or medication. I think it all has a place.

MEET BARBARA WIROSTKO

I'm Barbara Wirostko – a fellowship trained glaucoma specialist, board-certified by the American Academy of Ophthalmology (AAO). I'm also a Gold Fellow with the Association for Research in Vision and Ophthalmology (ARVO), and I serve as an adjunct professor of ophthalmology and biomedical engineering at the John A. Moran Eye Center at the University of Utah.

I describe myself as a clinician-researcher as well as a serial entrepreneur, and I am currently the co-founder and chief medical officer (CMO) of Qlaris Bio – a biotechnology company that targets high unmet needs in debilitating ophthalmic diseases. I'm also the co-founder and CMO of a start-up called MyEyes, which aims to help patients get access to an at-home tonometer.

I see patients at my clinical practice in Park City, Utah, and work at the Salt Lake City Veterans Administration Hospital as an attending physician at the glaucoma clinic, where I teach fellows, residents, and medical students.

When it comes to my business activities, what unites all my projects is a love for being creative, innovative, and building teams that have the freedom to tackle big problems. If you build a team with that aim, you get to see people develop – and watch them conceive exciting ideas.

"What is unique about this compound is that it works with physiology and doesn't disrupt the normal tight junctions of the vasculature."

When it comes to medication, tolerability and compliance are problems for multiple reasons. Patients can and do really struggle with a multi-drop regimen and often end up with ocular surface irritation and hyperemia, leading to non-adherence.

In the next 5–10 years, I believe we will be moving toward continuous IOP control. Whether that be longitudinal across months/years or simply better 24-hour IOP lowering therapeutics, we need less fluctuation and far better control. The other important area will be understanding not only the unmet needs associated with EVP, but also the genetics, so we can treat or even cure glaucoma. Of course, these efforts will develop alongside other areas, such as neuroprotection or neuroregeneration.

I think those three: continuous and sustained IOP control, genetic identification and approach, and neuro regeneration/protection are the three holy grails of glaucoma in the coming decade, and I can't wait to see what we come up with next!

Ophthalmology has several good examples of high-profile start-ups shaking up the field. What makes the field so dynamic?

In ophthalmology, we get to draw from every therapeutic area. With antibiotics and anti-infective agents, we draw from the infectious disease space. Timolol, a beta blocker, we drew from cardiology. And for devices, we work with engineering. Just think about anti-VEGF drugs, which have revolutionized how we treat wet AMD – that's ophthalmology borrowing from oncology. It's a unique field that combines surgery and medicine, and given the nature of ocular diseases, we need innovative devices, drugs, and procedures to treat people. I think this inspires people to get creative!

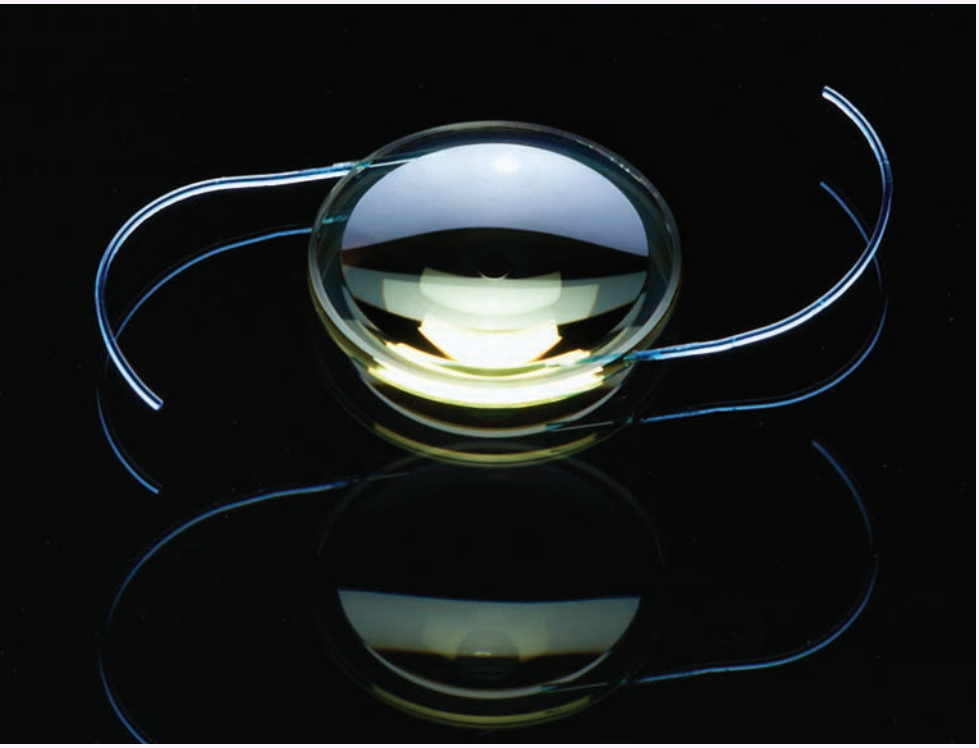
When did you decide that ophthalmology was for you?

I remember the exact moment. My father, Emil Wirostko, a uveitis specialist at Columbia Presbyterian Medical Center, was my biggest role model. I started doing research with him back when I was in high school, so I knew from a young age that I wanted to be a physician. I would later do my training at Columbia, and, during my third year there, I was doing my ophthalmology rotation and we learned how to use an ophthalmoscope. I vividly remember that moment of looking into one of my colleague's eyes and visualizing the retinal blood vessels and the optic nerve in such detail. From that moment on, I fell in love with ophthalmology.

Unleashing the Potential of Blended Vision with the LAL®

The Light Adjustable Lens™ by RxSight® – the first and only lens that can be customized post-cataract surgery

Although there have been many technological advances in cataract surgery since the first extraction was performed by French surgeon Jacques Daviel in 1747, it is still very difficult for surgeons to predict, pre-surgery, how their patients' eyes will eventually heal. Revolutionizing the way cataract surgery is performed, the Light Adjustable Lens (LAL) from RxSight offers patients more control, customization, and confidence in their visual outcomes by allowing doctors to fine tune the lens prescription after surgery, rather than relying only on the choice of IOL power before surgery. The LAL was developed by Robert H. Grubbs, a Nobel Prize-winning scientist, using special photo-sensitive material that responds to UV light. Through a series of noninvasive UV light treatments using the proprietary RxSight Light Delivery Device (LDD™), the technology enables patients to better customize their vision by changing the shape and prescription of the lens post-surgery. This novel approach – the first and only lens that can be customized after cataract surgery – means that patients are effectively able to "test drive" their visual outcomes to determine what tailored approach works best for them.



"The Light Adjustable Lens (LAL) has been a game-changer in my practice," says Priya Mathews, a cataract, refractive, and corneal surgeon based at the Center for Sight in Sarasota, Florida, who has a long-standing interest in addressing corneal blindness on a global scale. "I was initially motivated to use the LAL for two groups of patients in particular: patients with a previous history of refractive surgery and patients with mild-to-moderate corneal or retinal pathology," she adds. "The LAL certainly met my expectations in terms of delivering the best possible outcomes with minimal refractive error in these patients, but I was also pleasantly surprised with how ideal it was for very detail-oriented patients and those who wanted to have some degree of control in their ultimate outcome after cataract surgery."

Blended vision with the aspheric LAL, with refractive adjustments made in the post-surgery period - presents a major benefit to practitioners when compared to the traditional "monovision" route. "Blended vision allows the patient to read without moving their head or the reading material to find the exact focal point," Mathews explains. "Personally, I do not offer a patient traditional monovision unless there's a successful history of monovision in the past, especially if the near target is greater than -1.50 D. Sometimes patients who have done monovision for years can be unhappy after cataract surgery because they can lose some range in their near eye, due to the inability to accommodate after cataract surgery. Blended vision closes this "gap" and gives a wider range of focal points, particularly in the non-dominant eye. A vast majority of patients seem to easily adapt to some degree of difference

RxSIGHT

"A vast majority of patients seem to easily adapt to some degree of difference between the two eyes…and if not, we can always tweak them back! That's the beauty of this lens."

between the two eyes…and if not, we can always tweak them back! That's the beauty of this lens."

While patients should be given the freedom to customize their vision, Mathews believes this freedom shouldn't discourage surgeons from incorporating their own extensive experience into advising against any adjustments they feel are unwarranted. As for the specificities of targeting at surgery, she explains, "For my standard LAL patient, I aim for emmetropia in the dominant eye and -0.75 D in the nondominant eye before cataract surgery. If they have greater than I D of astigmatism, I perform femto LRIs (limbal relaxing incisions) at the time of cataract surgery to debulk the astigmatism and preserve more macromers for spherical adjustments."

Meanwhile, Mathews' strategy for the adjustment process after surgery is generally tailored toward the individual patient. "During the adjustment period, I dive into what the patient's current experience is and what their goals are," she says. "After surgery, patients typically end up about +0.50 D hyperopic of the goal, which is exactly what I want. For the first treatment, I target their initial goal. In addition, in the non-dominant eye, moving from the hyperopic to myopic direction with a goal of -0.50 or more myopia results in a further broadening of the LAL's defocus curve. The secondary LDD treatment (if needed) is different for every patient, depending on what they want. Typically, two-thirds of my patients want more near, while one-third are happy where they are after the first treatment." Then, Mathews adds, "Once the patient is happy and has thoroughly 'tested' their vision in multiple environments, including work, exercise, and home, we lock it in!"

Based on various patient testimonials (1, 2) and other real-world outcomes seen in clinical practice (3), the rate of patient satisfaction with the LAL process is impressive, and the second-generation LAL 2.0 has been reported as being "safe and efficacious even in challenging post-refractive clinical scenarios" (4). Priya Mathews herself confirms these reports: "Overall, I would say that I have a 99 percent satisfaction rate with the LAL. My patients have tailored their visual outcome according to what matters the most to them – therefore, what's not to be happy about?"

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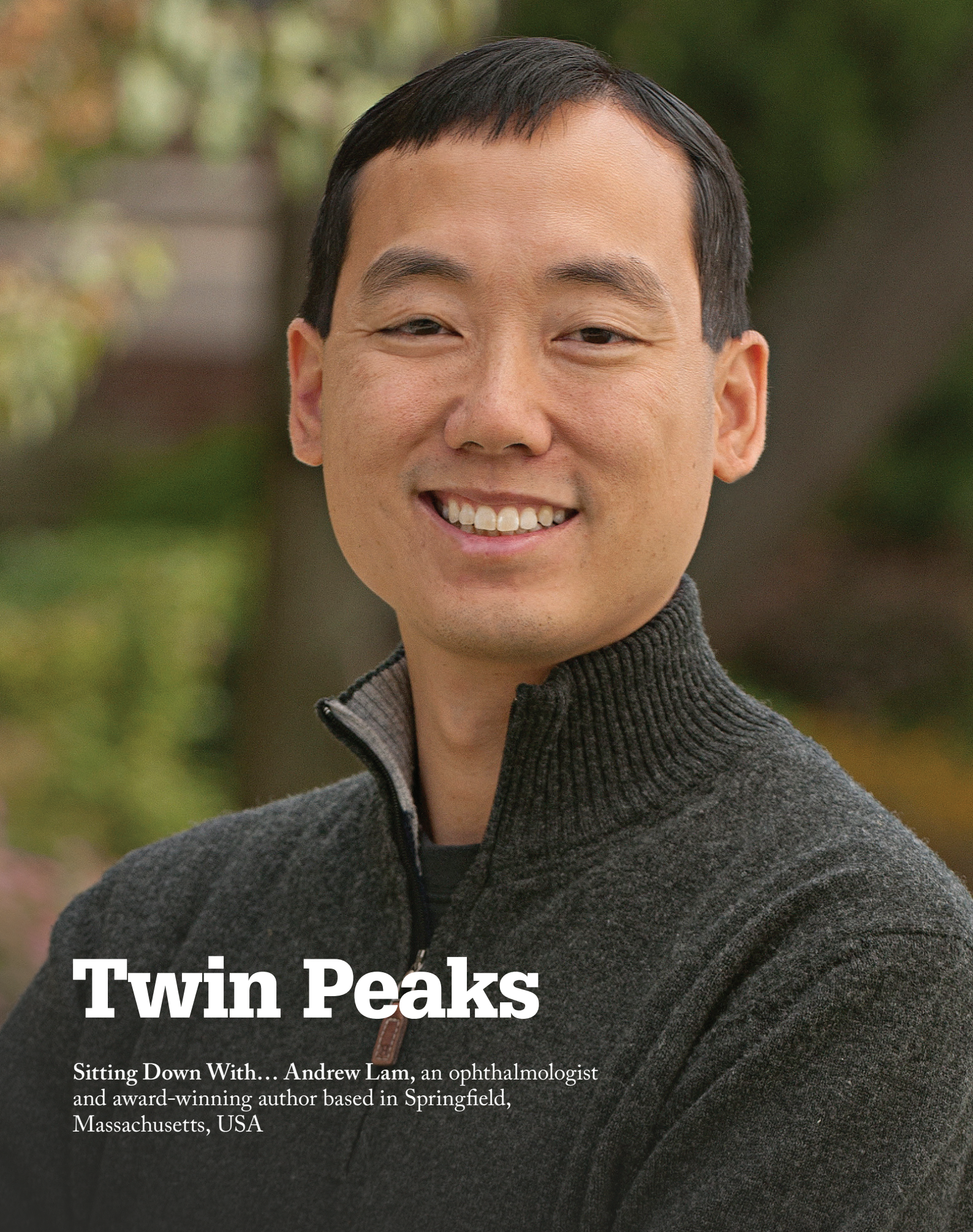

Twin Peaks

Sitting Down With… Andrew Lam, an ophthalmologist and award-winning author based in Springfield, Massachusetts, USA

Can you talk a little about your career journey?

I grew up in Springfield – the capital of Illinois and hometown of Abraham Lincoln. As a kid, I loved reading about history. I studied history at Yale as an undergraduate, but decided to go to medical school because I wanted a career in which I could directly help people. At the University of Pennsylvania, I quickly decided I wanted to choose a surgical subspecialty. I have always been fascinated by vision and the eye – and the ophthalmologists I met seemed happy and fulfilled. After enjoying an ophthalmology elective in my third year of medical school, my mind was made up.

I completed my residency and retina fellowship at Wills Eye Hospital in Philadelphia. I subsequently joined New England Retina Consultants in Massachusetts, where I am now the senior partner. I am also an assistant professor at the University of Massachusetts Medical School.

How did you branch out into writing?

The idea of being a writer occurred to me during residency. I thought, "Isn't it a pity that I can't share all that I learned in college about World War II in China with other people?" I had focused on this topic at Yale and felt that it was an unmined aspect of the war that most people did not know about. I was in a busy residency, with kids, and did not have the time necessary to write a non-fiction book. And then I thought, "What if I wrote a novel?" So, I wrote my first book, *Two Sons of China*, in my spare time over the course of many years. I got an agent and a book deal. That novel came out in 2014 and was a Foreword Reviews Book of the Year.

After that, I wrote *Saving Sight*, an Amazon bestseller that was a memoir of my surgical training, blended with the stories of ophthalmology's greatest heroes (such as Sir Harold Ridley, Charles Kelman, Arnall Patz, and Charles Schepens). These individuals overcame ridicule, setbacks, and innumerable challenges to invent the techniques we use to save sight today. Their stories have touched many readers and I still get emails from people all over the world who tell me the book inspired them to go into ophthalmology, which is very gratifying.

I wrote another novel about WWII called *Repentance*, which highlighted the heroism of Japanese Americans. And my newest book, *The Masters of Medicine*, covers the greatest discoveries in modern medical history. Like many doctors who were having to see patients in the early days of the pandemic, I was quite worried about bringing COVID-19 home to my family. So for weeks, I was semi-quarantined in my home. During that period I had far more time than usual to read. I began to read about the history of cardiology and the numerous mavericks who made serendipitous discoveries, and sometimes risked their own lives to make advances. And then I read about the discovery of insulin, and how the Canadian co-discoverers hated each other so much that one almost refused his Nobel Prize because he was so mad that his co-discoverer was also going to get one! I was hooked. I wanted to write about these unsung medical heroes who deserve to be far more well-known. Their stories were not just inspiring, they were full of human drama and failings, such as envy, arrogance, and self-interest, which often marred their triumphs. So, this effort became *The Masters of Medicine*.

The book shows that medical progress is not inevitable nor guaranteed. It moves forward in fits and starts and depends on brilliant minds who are open to recognizing solutions to questions no one had previously thought to ask. My hope is that it inspires people, that young people will read it and want to go into science or medicine. If only one reader does this and someday makes a discovery that helps us all, the work I put into the book will be entirely worth it.

"If you feel passionate about sharing your insight or expertise on any subject, medical or non-medical, just do it. This could be through writing, blogging, podcasts, or simply being active on social media."

What triggered your interest in writing for the wider public – and what advice would you give to ophthalmologists looking to communicate to a bigger audience?

My love of history and the goal of sharing stories I find fascinating are what spurred me to be a writer. I always encourage my colleagues to write, because I think writing is a beneficial creative outlet. It is also important to pursue our interests outside of medicine; I feel this makes us better doctors and

helps avoid burnout. So my advice is, if you feel passionate about sharing your insight or expertise on any subject, medical or non-medical, just do it. This could be through writing, blogging, podcasts, or simply being active on social media in ways that educate others.

Often the best way to begin building a platform is to start in your local community. It is easy for physicians, as trusted experts, to opine on medical topics. We can also comment on other areas we feel strongly about or have knowledge of. For example, I have written on topics as wide-ranging as affirmative action and WWII history, in publications as varied as The New York Times, The Washington Post, my local newspaper, and ophthalmology publications.

Which mentors have most influenced your ophthalmology career?

In residency and fellowship at Wills Eye Hospital, I had many wonderful teachers and role models. Everyone looked up to William Tasman and William Benson – luminaries who made significant contributions to ophthalmology throughout their careers. And they both shared my love of history. Though they could have rested on their laurels and devoted their time to enjoying retirement, they both clearly enjoyed teaching and spending time with young doctors.

My co-residents and I benefited greatly from the expertise of two top cataract surgeons, Robert Bailey and Mark Blecher. I still remember their patience and assistance as they calmly steered me away from trouble in the operating room and encouraged me as a young surgeon.

I also appreciated the humanism of George Spaeth (glaucoma), the commitment of doctors like Jurij Bilyk (oculoplastics) and Chris Rapuano (cornea), and the expertise of Ralph Eagle (ocular pathology).

I did research and wrote papers with mentors Carl Regillo, Allen Ho, and Carol Shields – all of whom were very kind and served as great role models. Finally, I was fond of two attendings, Joseph Maguire and Arch McNamara, who are no longer with us but were beloved for their talent, kindness, and good humor.

"Everyone looked up to William Tasman and William Benson – luminaries who made significant contributions to ophthalmology throughout their careers."

What are some of the biggest ophthalmology breakthroughs in the last ten years?

There have been several important advances in surgery and medications, including corneal cross-linking for keratoconus, MIGs for glaucoma, Tapezza for thyroid eye disease, improved multifocal IOLs, the femtosecond laser, which has made cataract surgery even safer, progress with the light adjustable lens, low-dose atropine for myopia, and OCT-angiography. Another important advance has been new treatments for geographic atrophy in dry AMD, a condition for which there was no prior treatment.

But perhaps the closest thing to a true breakthrough was Luxturna – the first approved gene therapy in the US and Europe, for retinitis pigmentosa and Lebers congenital amaurosis (caused by mutations in RPE65 gene). This therapy will hopefully be the vanguard of future gene therapies for other inherited retinal diseases; Jean Bennett and Albert Maguire have earned a place in any future book on the history of our field. I met them while in medical school at the University of Pennsylvania and still remember their early presentations on their successful treatment in a dog named Lancelot about 20 years ago…

What do you enjoy doing outside of work?

My wife and I have four kids and raising them has been a fulfilling adventure. For years, my chief function outside of work seemed to be chauffeuring them to their various activities. I love to travel and have a goal of visiting every National Park site in the US. I'm also quite involved in civic activities, have held several positions in municipal government, and am a trustee of a local university.

What future breakthroughs would you like to see in ophthalmology?

I'm hopeful that we will see additional gene therapies for inherited retinal diseases in the next decade. I hope for more effective treatments for geographic atrophy in dry macular degeneration, including possible stem cell therapies. I'm confident AI will prove beneficial for screening of diabetic retinopathy, glaucoma, and macular degeneration. Home OCT monitoring using AI may be beneficial – if it can be done inexpensively. We all share hope for improved accommodating IOLs. And in surgery someday, surgeons may use heads-up displays or visors. In-office vitrectomy for vitreous hemorrhage and floaters may also be realistic future advances.

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

BRIEF SUMMARY—Please see the EYLEA full Prescribing Information available on HCP.EYLEA.US for additional product information.

1 INDICATIONS AND USAGE
EYLEA is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with:

Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections
EYLEA is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation
EYLEA is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity
EYLEA is contraindicated in patients with known hypersensitivity to aflibercept or any of the excipients in EYLEA. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, severe anaphylactic/anaphylactoid reactions, or severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments [*see Adverse Reactions (6.1)*]. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately [*see Patient Counseling Information (17)*].

5.2 Increase in Intraocular Pressure
Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA [*see Adverse Reactions (6.1)*]. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular endothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

5.4 Thromboembolic Events
There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity [*see Contraindications (4.3)*]
- Endophthalmitis and retinal detachments [*see Warnings and Precautions (5.1)*]
- Increase in intraocular pressure [*see Warnings and Precautions (5.2)*]
- Thromboembolic events [*see Warnings and Precautions (5.4)*]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.
A total of 2980 adult patients treated with EYLEA constituted the safety population in eight phase 3 studies. Among those, 2379 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

Neovascular (Wet) Age-Related Macular Degeneration (AMD). The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, controlled clinical studies (VIEW1 and VIEW2) for 24 months (with active control in year 1).
Safety data observed in the EYLEA group in a 52-week, double-masked, Phase 2 study were consistent with these results.

Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies

	Baseline to Week 52		Baseline to Week 96	
Adverse Reactions	**EYLEA (N=1824)**	**Active Control (ranibizumab) (N=595)**	**EYLEA (N=1824)**	**Control (ranibizumab) (N=595)**
Conjunctival hemorrhage	25%	28%	27%	30%
Eye pain	9%	9%	10%	10%
Cataract	7%	7%	13%	10%
Vitreous detachment	6%	6%	8%	8%
Vitreous floaters	6%	7%	8%	10%
Intraocular pressure increased	5%	7%	7%	11%
Ocular hyperemia	4%	8%	5%	10%
Corneal epithelium defect	4%	5%	5%	6%
Detachment of the retinal pigment epithelium	3%	3%	5%	5%
Injection site pain	3%	3%	3%	4%
Foreign body sensation in eyes	3%	4%	4%	4%
Lacrimation increased	3%	1%	4%	2%
Vision blurred	2%	2%	4%	3%
Intraocular inflammation	2%	3%	3%	4%
Retinal pigment epithelium tear	2%	1%	2%	2%
Injection site hemorrhage	1%	2%	2%	2%
Eyelid edema	1%	2%	2%	3%
Corneal edema	1%	1%	1%	1%
Retinal detachment	<1%	<1%	1%	1%

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal tear, and endophthalmitis.

Macular Edema Following Retinal Vein Occlusion (RVO). The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following central retinal vein occlusion (CRVO) in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following branch retinal vein occlusion (BRVO) in one clinical study (VIBRANT).

Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies

	CRVO		BRVO	
Adverse Reactions	**EYLEA (N=218)**	**Control (N=142)**	**EYLEA (N=91)**	**Control (N=92)**
Eye pain	13%	5%	4%	5%
Conjunctival hemorrhage	12%	11%	20%	4%
Intraocular pressure increased	8%	6%	2%	0%
Corneal epithelium defect	5%	4%	2%	0%
Vitreous floaters	5%	1%	1%	0%
Ocular hyperemia	5%	3%	2%	2%
Foreign body sensation in eyes	3%	5%	3%	0%
Vitreous detachment	3%	4%	2%	0%
Lacrimation increased	3%	4%	3%	0%
Injection site pain	3%	1%	1%	0%
Vision blurred	1%	<1%	1%	1%
Intraocular inflammation	1%	1%	0%	0%
Cataract	<1%	1%	5%	0%
Eyelid edema	<1%	1%	1%	0%

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR). The data described below reflect exposure to EYLEA in 578 patients with DME treated with the 2-mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

Table 3: Most Common Adverse Reactions (≥1%) in DME Studies

	Baseline to Week 52		Baseline to Week 100	
Adverse Reactions	**EYLEA (N=578)**	**Control (N=287)**	**EYLEA (N=578)**	**Control (N=287)**
Conjunctival hemorrhage	28%	17%	31%	21%
Eye pain	9%	6%	11%	9%
Cataract	8%	9%	19%	17%
Vitreous floaters	6%	3%	8%	6%
Corneal epithelium defect	5%	3%	7%	5%
Intraocular pressure increased	5%	3%	9%	5%
Ocular hyperemia	5%	6%	5%	6%
Vitreous detachment	3%	3%	8%	6%
Foreign body sensation in eyes	3%	3%	3%	3%
Lacrimation increased	3%	2%	4%	2%
Vision blurred	2%	2%	3%	4%
Intraocular inflammation	2%	<1%	3%	1%
Injection site pain	2%	<1%	2%	<1%
Eyelid edema	<1%	1%	2%	1%

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.
Safety data observed in 269 patients with nonproliferative diabetic retinopathy (NPDR) through week 52 in the PANORAMA trial were consistent with those seen in the phase 3 VIVID and VISTA trials (see Table 3 above).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
Adequate and well-controlled studies with EYLEA have not been conducted in pregnant women. Aflibercept produced adverse embryofetal effects in rabbits, including external, visceral, and skeletal malformations. A fetal No Observed Adverse Effect Level (NOAEL) was not identified. At the lowest dose shown to produce adverse embryofetal effects, systemic exposures (based on AUC for free aflibercept) were approximately 6 times higher than AUC values observed in humans after a single intravitreal treatment at the recommended clinical dose [*see Animal Data*].
Animal reproduction studies are not always predictive of human response, and it is not known whether EYLEA can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for aflibercept, treatment with EYLEA may pose a risk to human embryofetal development. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data
Animal Data
In two embryofetal development studies, aflibercept produced adverse embryofetal effects when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days during organogenesis at subcutaneous doses ≥0.1 mg per kg.
Adverse embryofetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastroschisis, cleft palate, ectrodactyly, intestinal atresia, spina bifida, encephalomeningocele, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternebrae, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal No Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Aflibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was not identified. At the lowest dose shown to produce adverse embryofetal effects in rabbits (0.1 mg per kg), systemic exposure (AUC) of free aflibercept was approximately 6 times higher than systemic exposure (AUC) observed in adult patients after a single intravitreal dose of 2 mg.

8.2 Lactation
Risk Summary
There is no information regarding the presence of aflibercept in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production/excretion. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, EYLEA is not recommended during breastfeeding. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EYLEA and any potential adverse effects on the breastfed child from EYLEA.

8.3 Females and Males of Reproductive Potential
Contraception
Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment, and for at least 3 months after the last intravitreal injection of EYLEA.

Infertility
There are no data regarding the effects of EYLEA on human fertility. Aflibercept adversely affected female and male reproductive systems in cynomolgus monkeys when administered by intravenous injection at a dose approximately 1500 times higher than the systemic level observed in adult patients with an intravitreal dose of 2 mg. A No Observed Adverse Effect Level (NOAEL) was not identified. These findings were reversible within 20 weeks after cessation of treatment.

8.4 Pediatric Use
The safety and effectiveness of EYLEA have been demonstrated in two clinical studies of pre-term infants with ROP. These two studies randomized pre-term infants between initial treatment with EYLEA or laser. Efficacy of each treatment is supported by the demonstration of a clinical course which was better than would have been expected without treatment.

8.5 Geriatric Use
In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.

10 OVERDOSAGE
Overdosing with increased injection volume may increase intraocular pressure. Therefore, in case of overdosage, intraocular pressure should be monitored and if deemed necessary by the treating physician, adequate treatment should be initiated.

17 PATIENT COUNSELING INFORMATION
In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist [*see Warnings and Precautions (5.1)*].
Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations [*see Adverse Reactions (6)*]. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

REGENERON®

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591

Issue Date: 02/2023
Initial U.S. Approval: 2011

Based on the February 2023 EYLEA® (aflibercept) Injection full Prescribing Information.

EYL.23.02.0006

Start With EYLEA From the First Injection in Wet AMD

EYLEA® (aflibercept) Injection
For Intravitreal Injection

Demonstrated maintenance of vision

- **≈95% of patients maintained their vision** (<15 ETDRS letters lost) with EYLEA at Year 1 (primary endpoint)[1]
  – VIEW 1 (n=605); VIEW 2 (n=615)[1,*]

Effective regardless of fluid status

- Vision outcomes in patients **with and without early persistent fluid** (*post hoc* subgroup analysis)[3,†]

Long-term vision outcomes

- EYLEA maintained **+7.1 letters of BCVA gain at Year 4** in the VIEW 1 extension study (n=323)[2]

Broad national coverage

- 75% of lives have access to EYLEA first line, covering **239 million lives nationwide**[4,‡]

When You See Wet AMD, Consider EYLEA First Line

LEARN MORE at hcp.eylea.us

VIEW 1 and VIEW 2 Clinical Trial Designs: Two multicenter, double-masked clinical studies in which patients with Wet AMD (N=2412; age range: 49-99 years, with a mean of 76 years) were randomized to receive: 1) EYLEA 2 mg Q8W following 3 initial monthly doses; 2) EYLEA 2 mg Q4W; 3) EYLEA 0.5 mg Q4W [not an approved dose]; or 4) ranibizumab 0.5 mg Q4W. Protocol-specified visits occurred every 28 (±3) days. In both studies, the primary efficacy endpoint was the proportion of patients with Wet AMD who maintained vision, defined as losing <15 letters of visual acuity at Week 52, compared with baseline.[1]

VIEW 1 Extension Clinical Trial Design: Prospective, open-label, single-arm, multicenter, long-term safety and tolerability study of patients who completed VIEW 1 through Week 96 (n=323; mean age: 79 years). All patients received EYLEA 2 mg on a modified quarterly dosing schedule (maximum treatment interval: Q12W) that was later amended to dosing at least Q8W through Week 212. The primary endpoint was the safety and tolerability of EYLEA.[3]

*Includes patients from both EYLEA Q4W and Q8W treatment arms. EYLEA was clinically equivalent to ranibizumab.
†Early persistent fluid (intraretinal [cystic] or subretinal) was defined as presence of fluid at the first 4 visits (baseline, Week 4, Week 8, and Week 12) after having received 3 initial monthly injections (baseline, Week 4, and Week 8) as seen on TD-OCT.
‡Data represent payers across the following channels as of January 2023: Medicare Part B, Commercial, Medicare Advantage, and VA. Individual patient coverage is subject to patient's specific plan.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
- Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

INDICATIONS

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

Please see Brief Summary of full Prescribing Information on the following page.

References: 1. EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. February 2023. **2.** Kaiser PK, Singer M, Tolentino M, et al. Long-term safety and visual outcome of intravitreal aflibercept in neovascular age-related macular degeneration: VIEW 1 extension study. *Ophthalmol Retina*. 2017;1(4):304-313. doi:10.1016/j.oret.2017.01.004 **3.** Jaffe GJ, Kaiser PK, Thompson D, et al. Differential response to anti-VEGF regimens in age-related macular degeneration patients with early persistent retinal fluid. *Ophthalmology*. 2016;123(9):1856-1864. doi:10.1016/j.ophtha.2016.05.016 **4.** Data on file. Regeneron Pharmaceuticals, Inc.

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; TD-OCT, time domain–optical coherence tomography.

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