JULY/AUGUST 2021 # 55

the Ophthalmologist™

A Feast for the Eyes

Welcome to 2021's gallery of inspiring, provoking, and compelling ophthalmic images

WHAT COULD SHE SEE THIS YEAR?

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

Inspired by a real patient with DME.

375 MATH TESTS

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.

REGENERON

777 Old Saw Mill River Road, Tarrytown, NY 10591

EYLEA ACHIEVED RAPID, SUSTAINED OUTCOMES IN DME

Demonstrated efficacy outcomes in VISTA and VIVID, phase 3 anti-VEGF trials in DME (N=862)[1]

Mean change in BCVA (ETDRS letters) at Year 1 from baseline[1-5,*]

	Initial Gains (Month 5)		Primary Endpoint (Year 1)		Prespecified Exploratory Endpoint (Year 3)	
	VISTA	VIVID	VISTA	VIVID	VISTA	VIVID
EYLEA Q4	+10.3 (n=154)	+9.3 (n=136)	+12.5 (n=154)	+10.5 (n=136)	+10.4 (n=154)	+10.3 (n=136)
EYLEA Q8†	+9.9 (n=151)	+9.3 (n=135)	+10.7 (n=151)	+10.7 (n=135)	+10.5 (n=151)	+11.7 (n=135)
Control	+1.8 (n=154)	+1.8 (n=132)	+0.2 (n=154)	+1.2 (n=132)	+1.4 (n=154)	+1.6 (n=132)

P<0.01 vs control at Year 1.

The analyses of these exploratory endpoints were not multiplicity protected and are descriptive only.

Year 2 data was consistent with results seen in Year 1.[5]

VISTA and VIVID study designs: Two randomized, multicenter, double-masked, controlled clinical studies in which patients with DME (N=862; age range: 23-87 years, with a mean of 63 years) were randomized and received: 1) EYLEA 2 mg Q8 following 5 initial monthly doses; 2) EYLEA 2 mg Q4; or 3) macular laser photocoagulation (control) at baseline and then as needed. From Week 100, laser control patients who had not received EYLEA rescue treatment received EYLEA as needed per re-treatment criteria. Protocol-specified visits occurred every 28 (±7) days.[1]

In both clinical studies, the primary efficacy endpoint was the mean change from baseline in BCVA at Week 52, as measured by ETDRS letter score.[1]

*Last observation carried forward; full analysis set.
†Following 5 initial monthly doses.

SEE WHAT EYLEA COULD DO FOR YOUR PATIENTS WITH DME AT HCP.EYLEA.US

anti-VEGF, anti–vascular endothelial growth factor; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; Q4, every 4 weeks; Q8, every 8 weeks.

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).

References: 1. EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. August 2019. **2.** Korobelnik JF, Do DV, Schmidt-Erfurth U, et al. Intravitreal aflibercept for diabetic macular edema. *Ophthalmology.* 2014;121(11):2247-2254. doi:10.1016/j.ophtha.2014.05.006 **3.** Brown DM, Schmidt-Erfurth U, Do DV, et al. Intravitreal aflibercept for diabetic macular edema: 100-week results from the VISTA and VIVID studies. *Ophthalmology.* 2015;122(10):2044-2052. doi:10.1016/j.ophtha.2015.06.017 **4.** Data on file. Regeneron Pharmaceuticals, Inc. **5.** Heier JS, Korobelnik JF, Brown DM, et al. Intravitreal aflibercept for diabetic macular edema: 148-week results from the VISTA and VIVID studies. *Ophthalmology.* 2016;123(11):2376-2385. doi:10.1016/j.ophtha.2016.07.032

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

04/2021
EYL.21.03.0211

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.

5.3 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 (5.3)*]

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 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).

6.2 Immunogenicity
As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.
In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

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 humans 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 humans 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 in pediatric patients have not been established.

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.

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: 08/2019
Initial U.S. Approval: 2011

Based on the August 2019 EYLEA® (aflibercept) Injection full Prescribing Information.

EYL.20.09.0052

The Beauty of Imperfection

People with disabilities have long been expressing themselves through art, but can art and culture even exist without disability?

I recently took part in an enlightening workshop focused on bringing inclusive practice into various communication initiatives; one strong theme seemed to permeate the event: most of us are not doing enough. Yes, we are increasingly aware of the need for diversity (gender and ethnic) in our various endeavors – an attitude The Ophthalmologist has actively adopted and strived to maintain – but inclusivity, especially of disabled communities, is often lagging behind.

This reality was fresh in my mind as I began collecting artwork for this year's Images of Ophthalmology feature (see pages 14-30). Art has always had a connection to impairment; for centuries (possibly millennia), people with disabilities have been expressing themselves through various cultural forms and genres, including painting, music, and dance – sometimes as an expression of struggle, developing group consciousness, or seeking solidarity.

Impairment and suffering, whether physical or mental, is also evident in the biographies of many famous artists. More specifically, Patrick Trevor-Roper, whose biography we share on page 10, explored how vision impairment influenced not only the artistry – the style and technique – but also the personality of the most famous artists in *The World Through Blunted Sight: An Inquiry into the Influence of Defective Vision on Art and Character.* He claims that art is influenced not only by physical changes – the distorted retinal image, blurred vision, visual field defects, or imperfect color perception – but also by the subtle and complex changes in the artist's personality caused by loss of vision (1).

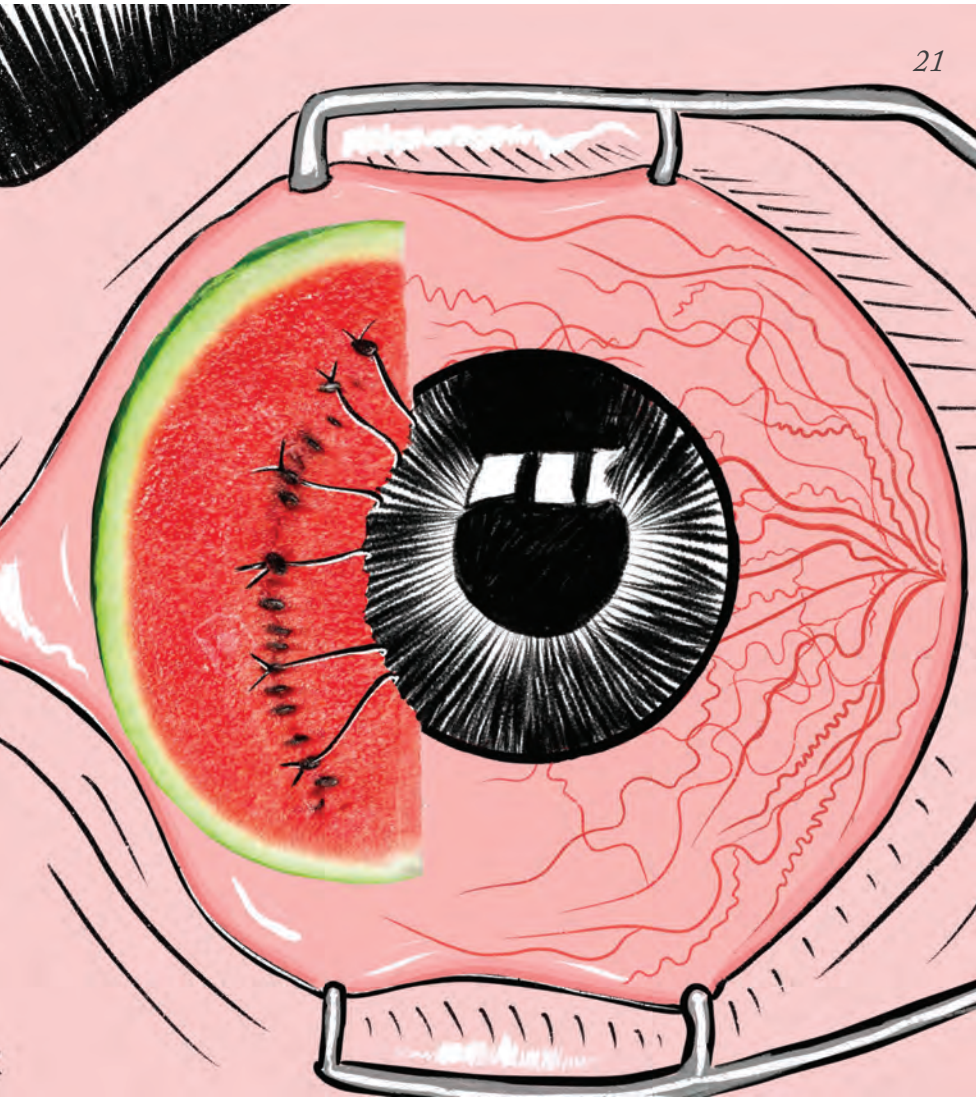
So, dear ophthalmologists, with your extensive knowledge of all possible conditions affecting sight, you are likely better qualified than most to try to answer my question: Would our artistic and cultural heritage be stripped of its finest works if the world was free of vision impairment?

Aleksandra Jones
Editor

Reference

1. *P Trevor-Roper, 3rd edition. Souvenir Press: 2012.*

Contents



On The Cover

Image by Jui Telavane, ophthalmology resident at Pravara Institute of Medical Sciences in Ahmednagar, India

In Practice

NextGen

Profession

Sitting Down With...

the Ophthalmologist

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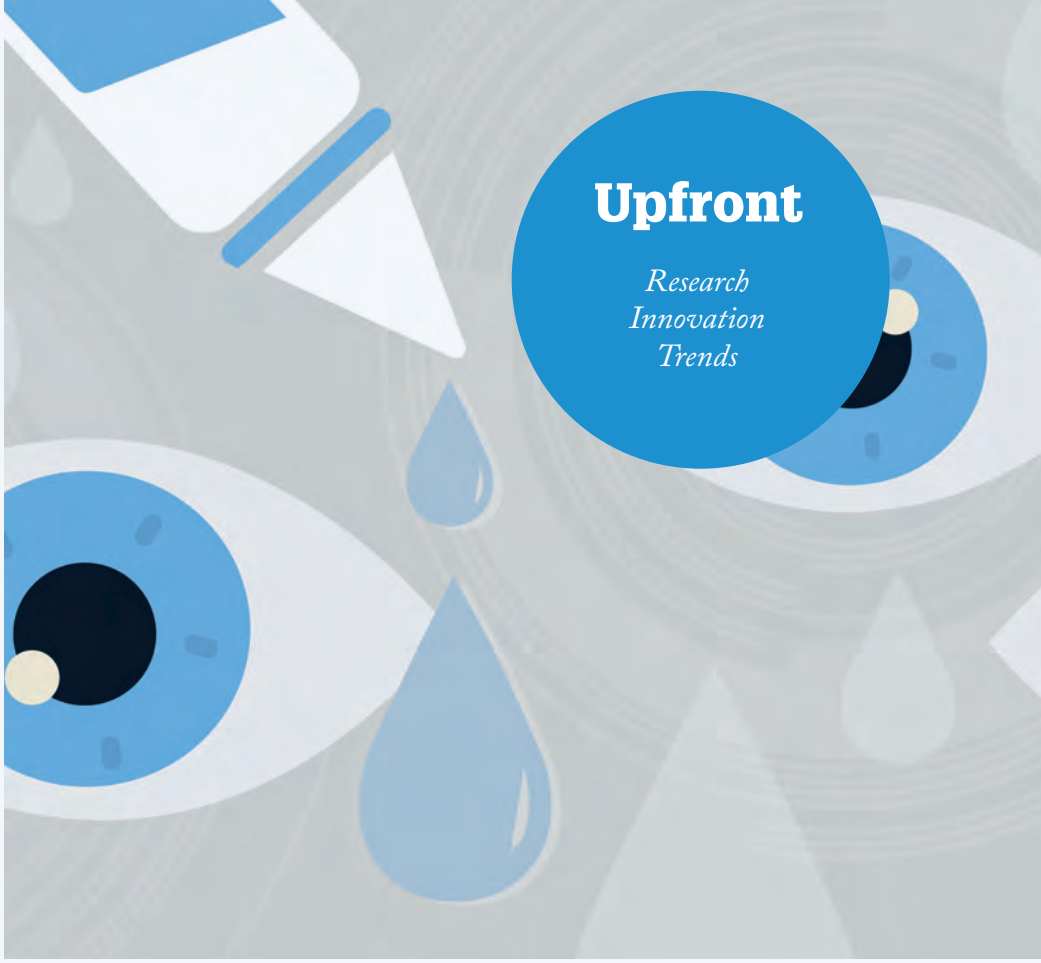


Come Gel or Eye Water

Fluid-gel eye drops improve drug retention at the eye surface and reduce corneal scarring

Eye drops are a notorious challenge to ophthalmic patients. Eyelids often sweep drops away from the surface of the eye, reducing effectiveness and resulting in underdosing. To address this problem, researchers from the University of Birmingham, UK, have created a solution in the form of a biocompatible fluid-gel that can ensure a controlled release of drugs – thereby increasing drug retention at the ocular surface and reducing corneal scarring (1).

Liam Grover, Professor in Biomaterials Science and lead researcher, explains, "The fluid-gel has the viscosity of water when the shear force of being extruded from an eyedropper is applied but, upon hitting the surface of the eye, it flows and thickens. Over time, the shear from the eyelid removes the fluid-gel, but this process takes much longer than it does for a normal drop." The material has been tested for efficacy in the lab and in a rodent model, where fluid-gel containing decorin significantly enhanced corneal re-epithelialization within four days.

Recently, another University of Birmingham research group has been working with Grover's team to incorporate a range of drugs that can reduce the issues associated with primary open angle glaucoma (POAG) into the fluid-gel (2, 3). This collaboration could enable POAG therapeutics to be administered at the surface of the eye rather than needing an injection.

Following significant COVID-19-related delays, clinical trials are now imminent. When asked about the possibility of using the fluid-gel with other drugs, Grover states that his team "are looking for partners who may be interested in working on co-development. Our material might improve the efficacy of drugs that are currently limited by poor retention."

References

1. *G Chouhan et al., Biomaterials, 210, 41 (2019). PMID: 31055049.*
2. *LJ Hill et al., NPJ Regenerative Medicine, 6, 3 (2021). PMID: 33414477.*
3. *University of Birmigham (2021). Available at: https://bit.ly/3fBAiQv.*

INFOGRAPHIC

Ebb and Flow

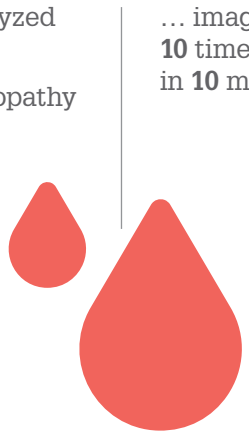
OCT angiography is being used to assess patients with sickle cell retinopathy before the disease progresses to irreversible vision loss

Mount Sinai team analyzed

13 sickle cell retinopathy (SCR) patients

and **14** controls…

… imaging them **10** times in a row in **10** minutes



ARVO 2021

A breakdown of prize-winning posters from the May virtual event

- *Giving the Green Light*
  Different color sensations across the red-green axis can be induced by stimulating single cones with spots of 543 nm light. It has been found that larger and higher-intensity spots increase the likelihood that green is reported and intensify saturation. Whether the spots were stable or drifted across the retina made little difference to color or saturation (1).
- *Lean Mean Gene Screen*
  New rare variants have been identified for refractive error in 43 genes using an exome chip and a large multi-ancestry cohort. This builds on previous genome-wide association studies that have identified over 500 common myopia-causing variants. The newly identified genes are involved in human ocular disease, cell cycle processes, and corneal dystrophies (2).
- *Mind the (Gender) Gap*
  Studies indicate that younger women and older men are more prone to myopia – but why? New research suggests that lifestyle and education changes may be responsible and that future generations should be given guidance on protective behavior (3).
- *Eye-Resolution 3D Glasses*
  Say goodbye to small fields of view and cumbersome systems for OCT. Researchers introduce Adaptive-Glasses Full-Field OCT (FFOCT), which enhances the retinal imaging signal-to-noise ratio by a factor of 10, with high resolution and frame rate and in a compact system similar to eyeglasses. Clinical trials are imminent (4).
- *Mixed Signals*
  Neuronal activity is largely dictated by calcium signaling – but our understanding of how calcium affects retinal ganglion cells (RGCs), especially in glaucoma, is limited. Researchers have discovered that RGCs respond differently to calcium depending on the subtype and subcellular compartment. In glaucoma, they find altered calcium signals indicating impaired cellular homeostasis in vulnerable RGCs (5).

References

1. *J Vanston, Poster presented at ARVO; May 1–7, 2021; Virtual Meeting.*
2. *AEG Haarman, Poster presented at ARVO; May 1–7, 2021; Virtual Meeting.*
3. *C Enthoven, Poster presented at ARVO; May 1–7, 2021; Virtual Meeting.*
4. *P Mecé, Poster presented at ARVO; May 1–7, 2021; Virtual Meeting.*
5. *Y Shiga, Poster presented at ARVO; May 1–7, 2021; Virtual Meeting.*

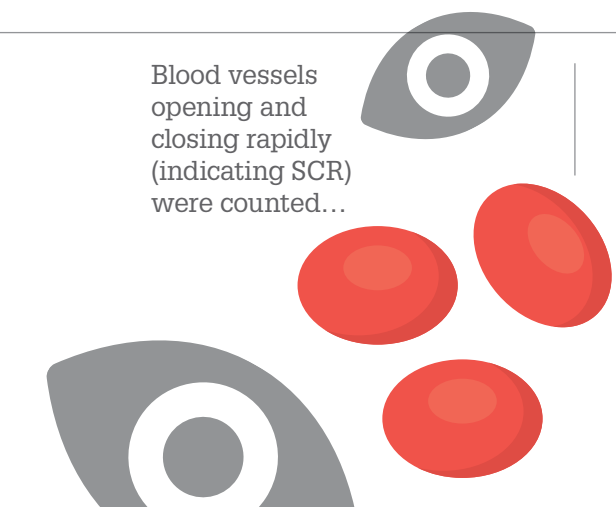
Window of Exclusivity

Using retinal capillary density as a surrogate for Alzheimer's progression and diagnosis

If the brain were a nightclub, it would be filled with A-list celebrities – and you'd probably be refused entry. The only way to get an idea of what's going on (without resorting to extreme measures) would be to peek through the windows. By using OCT angiography to look through the eyes, it is possible to learn how certain Alzheimer's disease (AD) risk genes are affecting the retinal vasculature – as a surrogate measure of disease progression.

Researchers have found that lower retinal capillary densities occur in cognitively normal APOE ε4 gene carriers, indicating a potential early biomarker for at-risk individuals (1). Specifically, the team collected built a statistical model that measures associations between pathological phenotypes, including retinal vasculature density, and genotype. This enables investigation of the brain vasculature that can illuminate AD mutation pathogenesis, with the ease of an eye test.

See references online at: top.txp.to/window/of/exclusivity



Blood vessels opening and closing rapidly (indicating SCR) were counted…

… and compared for healthy controls and SCR patients on and off treatment

Flow fluctuation measurements were used for an algorithm indicating the best treatment

Reference

1. *DB Zhou et al., Biomedical Optics Express, 12, 2825 (2021). DOI: 10.1364/BOE.418874.*

The World Through Pellucid Lenses

The astonishing life and legacy of Patrick Trevor-Roper, eye surgeon and activist

Born in the midst of World War I, in 1916, the son of a general practitioner in the remote town of Alnwick, UK, Patrick Trevor-Roper was educated at Charterhouse and the University of Cambridge. At school, he was a senior classical scholar, but his plan was to join his father's practice after attending Cambridge and the Westminster Medical School in London. When World War II started, he was 23. He became a captain in the New Zealand Medical Corps in 1943 and served with the Central Mediterranean Forces until 1946.

During an air raid in London, Trevor-Roper found himself sharing a shelter with one of London's leading eye surgeons, E.F. King, who introduced him to Moorfields Eye Hospital and persuaded him to choose ophthalmology as his specialty.

After the war and following his postgraduate training, he became a consultant ophthalmic surgeon at Westminster Hospital (1947–82) and at Moorfields (1961–81), where he established the Westminster-Moorfields Eye-Bank in 1965.

Trevor-Roper was one of the first openly gay men in Britain and instrumental in decriminalizing homosexual activity in 1967. In 1955, he appeared as a witness before the Wolfenden Committee to testify that the majority of gay men had regular lifestyles and posed no threat, and argue that homosexuality was not an illness. He told the Committee about the devastating effects of homophobia and blackmail, which isolated many young gay men, induced depression, and often pushed them to suicide. Trevor-Roper remained active in gay rights activism, co-founding the UK's leading AIDS service organization during the AIDS epidemic in the 1980s.

An important part of his ophthalmic career was the establishment of the Haile Selassie Eye Hospital in Addis Ababa, Ethiopia, and eye hospitals in war-torn Nigeria and Sierra Leone. He also campaigned against drug companies' manipulations and successfully fought to end the monopoly on the sale of reading glasses. He edited Transactions of the Ophthalmological Society UK – later renamed Eye – for 38 years.

Following a hugely successful and influential career, Trevor-Roper was diagnosed with Alzheimer's disease in 2003. He developed cancer in 2004 and died the same year. He was survived by his long-term partner, Herman Chan.

Trevor-Roper left behind many important written works; the most popular is probably *The World Through Blunted Sight*, which explores how common eye conditions influenced the styles of the most famous artists.

See references online at: top.txp.to/trevor/roper

Training Future Daredevils

Using echolocation to better navigate the world as a blind or visually impaired person

Radar sense may not be limited to the Daredevil of Hell's Kitchen anymore. Marvel's favorite blind superhero has used echolocation to scale buildings, duck behind corners to avoid enemies, and take down criminals for many decades – but, in the real world, echolocation training is improving the spatial awareness and navigational skills of those with vision loss.

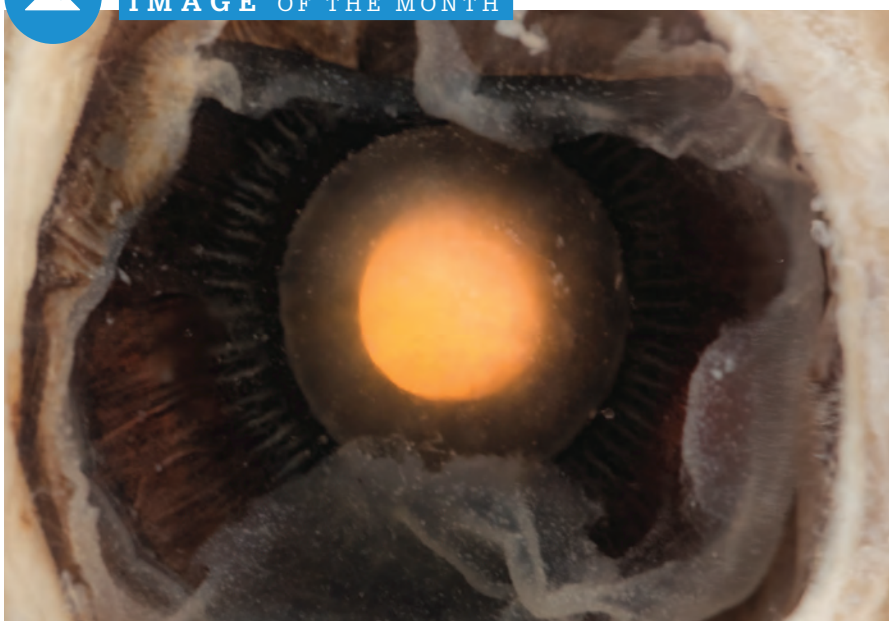
Lore Thaler and her team at Durham University, UK, have been investigating click-based active echolocation and have had excellent results from a 10-week training program Thaler devised. The follow-up surveys for visually impaired participants made the program's success clear: 100 percent reported increased mobility and 83 percent have better independence and wellbeing.

Unlike Daredevil's heightened sense, enhanced echolocation is mostly passive (relying on ambient noise from elsewhere); active echolocation involves spatial awareness from sounds made by the person (such as clicks, cane taps, or footsteps) – with click-based echolocation the most effective technique.

Reference

1. *LJ Norman et al., PLoS One, 16, e0252330 (2021). PMID: 34077457.*

IMAGE OF THE MONTH



From Behind the Lens

This month's image shows a coronal section of an eye from a specimen of the Museum of Anatomy of the Faculty of Medicine of University of Porto, Portugal. The iris and the lens can be seen from a posterior perspective.

Credit: Jose Paulo Andrade, Associate Professor of Anatomy, Faculty of Medicine of University of Porto, Portugal

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

QUOTE OF THE MONTH

"Have my fellow eye docs done surgery on someone [...] blind from cataracts, and when they can see again, [they] completely open up as a person? Happier, more talkative, engaging… It's like they blossom! Such a wonderful thing to witness."

Ashley Brissette, Assistant Professor of Ophthalmology at Weill Cornell Medicine, New York Presbyterian Hospital, New York, USA.

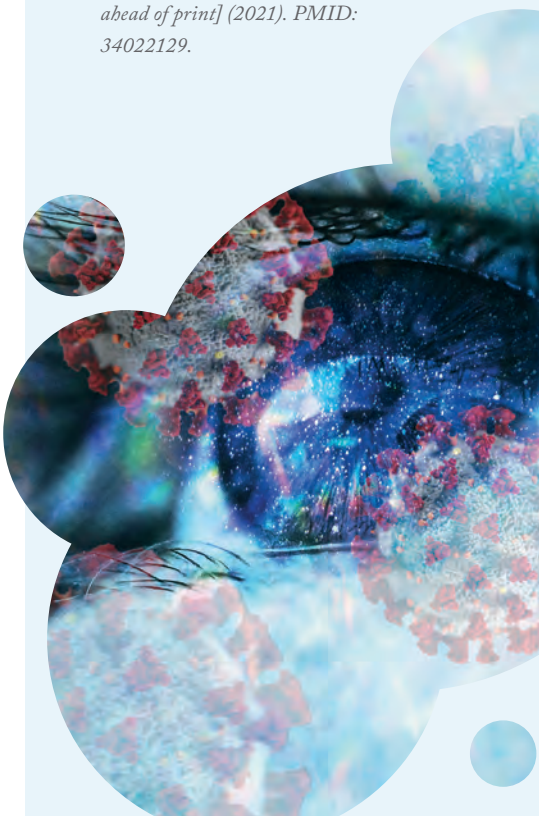
A Limbal Portal

How does SARS-CoV-2 infect ocular tissues?

Aerosol transmission is recognized as the main route of spread of SARS-CoV-2, but viral particles have also been known to penetrate ocular fluid, making the eye a potential point of entry. Now, researchers from the Icahn School of Medicine at Mount Sinai, New York, USA, have confirmed antigen expression in the ocular surface of a COVID-19 patient postmortem and showed that the virus replicates in human ocular tissue samples and eye organoid cultures. The limbus and limbal regions have been identified as the main portal for SARS-CoV-2 entry and the eye has been confirmed to be susceptible to direct infection.

Reference

1. *AZ Eriksen et al., Cell Stem Cell, [Online ahead of print] (2021). PMID: 34022129.*



In My View

Experts from across the world share a single strongly held opinion or key idea.

Those Who Can, Teach Virtually

Virtual training can revolutionize how surgical skills are shared

By Larry Benjamin, Consultant Ophthalmologist, Stoke Mandeville Hospital, Aylesbury, UK

Over the past year, I've been involved in training ophthalmic surgeons from Cameroon with the help of Orbis' virtual training software, Cybersight. A key enabler of this effort? The more reliable, faster broadband that is now almost ubiquitous. You may take this quiet revolution for granted when watching your latest Netflix favorite – but consider how important it is for me to see a clear picture during a training session. Imagine how much better the experience is for all concerned when we can easily interact in real time…

Working with a Cameroonian surgeon, Ted Grimbert Afetane Evina, I can see what he sees through the microscope and talk the team through the procedure in real time. And it's almost like being in the same room – despite being 6,000 miles away. That said, there are differences to working in the same location – for one, I have to think ahead a lot more. And it can be terrifying at times! The fact that I had previously met the surgical team face-to-face definitely helped. I'll admit we've had to overcome a bit of a language barrier; Evina's first language is French and my surgical French is not brilliant...

The Cameroon team has a phaco machine at their hospital and I've been able to teach Evina a new technique that he was keen to learn. He routinely operates on patients, so I am just building on his technique. All in all, it has been a really interesting and fun experience.

Though my experiences are proof that virtual training can work, I believe that teaching the basics of this method wouldn't work remotely. To learn properly, I would advise trainees to first learn the basics live, and do some simulation training before proceeding to virtual real-life surgery training. Even something as simple as how you hold an instrument in your hand can make a massive difference to how you manipulate it during surgery. Using virtual training, I can't take that instrument and place it properly in the trainee's hand, and I can't guide them, other than by showing them my own hand on the screen. Even putting a stitch in a tissue is much more difficult to see and supervise in detail remotely.

But for those surgeons who already have the basics under their belts, I think there are many nuances and techniques that can be taught much more easily remotely.

There is a huge appetite for virtual training right now (if I were cynical, I'd say that's because it's been the only kind of training available for some...). People have realized the clear benefits; you don't have to travel, so it saves huge amounts of time and money. And it gives you instant access to techniques and methods from around the world. People suddenly have a way to broaden their (surgical) horizons without leaving the comfort of their own practice.

"I believe that teaching the basics of this method wouldn't work remotely."

Training schemes in the UK during the pandemic have suffered without access to live surgery and clinics, and online teaching has allowed trainees to continue their learning, rather than putting it on hold for a year. A couple of weeks ago, a group of 10 trainees were doing simulation training on model eyes at the Royal College of Ophthalmologists in London, and – at the same time – I was online supervising a couple of trainees who couldn't get to the session, so they were at home, with some portable microscopes

set up in their front room. People at the college and I could interact with the trainees who were in the building, but also with the two students connecting remotely. It was a pilot to see whether that might work as a way of teaching. It truly does open up new possibilities. Previously, such a session would have required two days of travel (and an overnight stay). But joining the session online is as simple as switching on the microscope.

Consider another benefit: less time spent traveling means more time practicing newly learned skills; as I always say to my trainees: "Those of you who practice the most will be the best surgeons."

Finally, I would like to say to volunteer faculty and eye care teams around the world: "Thank you." Cybersight has blossomed thanks to a fantastic effort from many people. You see people's true nature come to the fore in such difficult times, and the Orbis family has been remarkable.

My message to teams around the world: keep going! Hopefully, the Flying Eye Hospital will take off again soon, and we'll get back to something a bit more akin to normal. Everybody who joins Orbis has a deep-seated belief that sight is super precious. We know that access to eye care is variable around the world, and we are trying to make it more equitable, especially for children and disadvantaged groups – and donations allow us to do this. Certainly, Cybersight from Orbis has given more people access to training during lockdown than would have otherwise been possible. And I think that's really important.

The Real Winners

My thoughts on designing grueling surgical training programs

By George Spaeth, Esposito Research Professor at Wills Eye Hospital, and Professor of Ophthalmology at Sidney Kimmel Medical School, Thomas Jefferson University, Pennsylvania, USA

From the Editor: This is a response to a quote from Judy Melinek on the hardships of surgical training, published in our May issue: "What I love about surgery is its immediacy – the fact that somebody can come in acutely ill and you can fix them. It's gratifying to have that kind of impact on people's lives and to see medicine really work. I love anatomy and physiology. I love the technical aspects of surgery. What I don't like is the hours. I cannot work that many hours – and I don't believe surgical training programs need to abuse the residents the way they do. There are ways of teaching surgery that don't require so many hours of work or create so much mental and physical exhaustion. I don't think that [the current approach] is healthy for surgical residents – or for the patients – or for medicine as a whole."

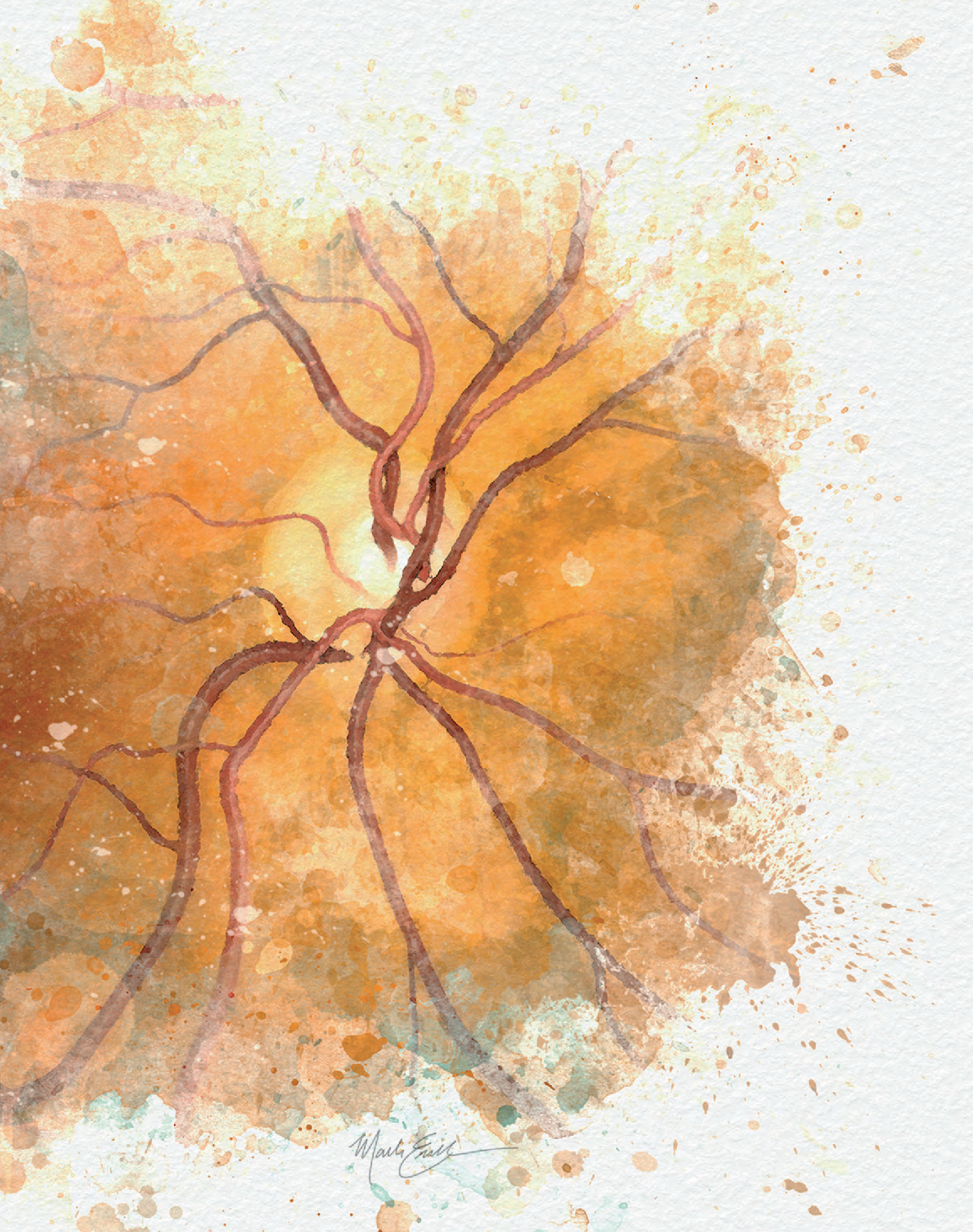
Surgeons like to think they fix things – and, to some extent, they do (take, for instance, cataract surgery). To a greater extent, they simply make it possible for a body to heal itself. Sometimes, they forget their patient's self-healing powers and develop a far higher opinion of themselves than is justified. Great surgeons have to control their movements, their thinking, and their emotions – not to mention their associates, staff, and the surgical environment… and being in control can be a heady experience. Performing a successful surgical procedure conveys a sense of power, often leading to arrogance. The surgeon is handsomely rewarded emotionally and financially for operating and may stop getting rewards from anything else (as happens with many who become skilled at a difficult, highly valued task). The result can make it hard for surgeons to do anything other than surgery.

Skills are learned; some people learn quickly, whereas others take a long time. Even for those who are fast learners, becoming a good surgeon takes a long time – acquiring skills, developing the right attitudes, and learning the appropriate processes. The surgeon who does not devote great effort to acquiring and maintaining skills is almost always a poor surgeon.

Many fine surgeons are terrible teachers, whereas many poor surgeons may have teaching skills, but do not know what to teach. Great surgical mentors know that truly great surgeons are both skilled and humble. In a world that rewards self-promotion and winning, such surgeons do not become the gatekeepers of surgery – teaching included. The situation Judy Melinek describes is the consequence of a culture that rewards those whose goal is to be a winner at any cost – to themselves or others. Their objective is power, not the nature of the outcome. But there is no social value in being the sole winner or being excellent for the sake of it. The true goal is to be a winner while at the same time helping everybody else to win, and that brand has always been rare. Will this ever change?

A FEAST for THE Eyes

Eyes are invariably considered objects of beauty, as well as the main instruments through which to perceive it. The scientific world has also been fascinated by these extremely complex organs, allowing our understanding to evolve greatly over time – a process you can observe on page 30. Today, supported by advanced imaging technology, we have more ways of investigating eyes than ever before – and yet they remain mysterious and awe inspiring. If you are here to explore some of the many ways artists, researchers, and clinicians view eyes, you're in for a real treat.



INTO THE SWIM OF THINGS

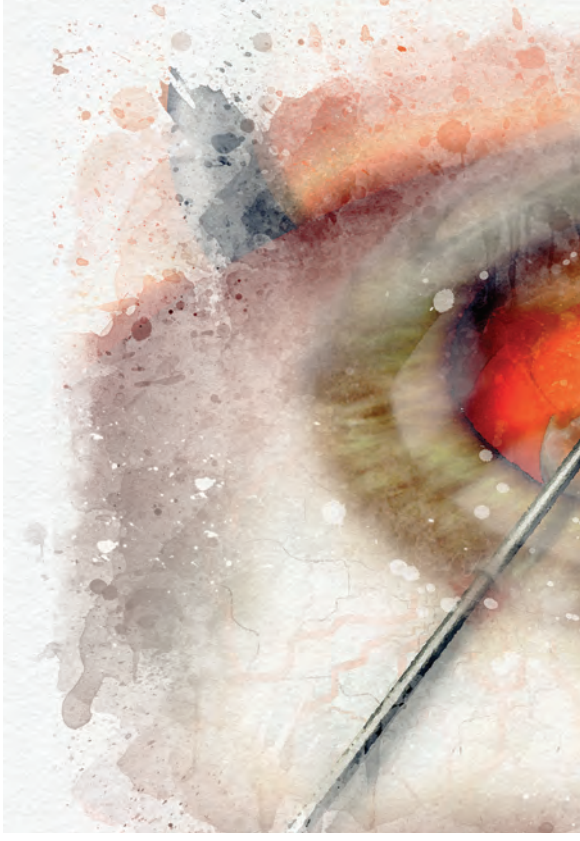
Mark Erickson has been a self-taught ophthalmic illustrator and animator since 1998. All of his art is inspired by his experiences working as an ophthalmic photographer since 1988. He says: "I've been lucky enough to observe, photograph and film the eye's anatomy, diseases and conditions, and surgery, in just about every possible angle or medium! When I'm at a slit lamp or photographing an eye, I can't help but see the subject as a canvas with boundless artistic potential."

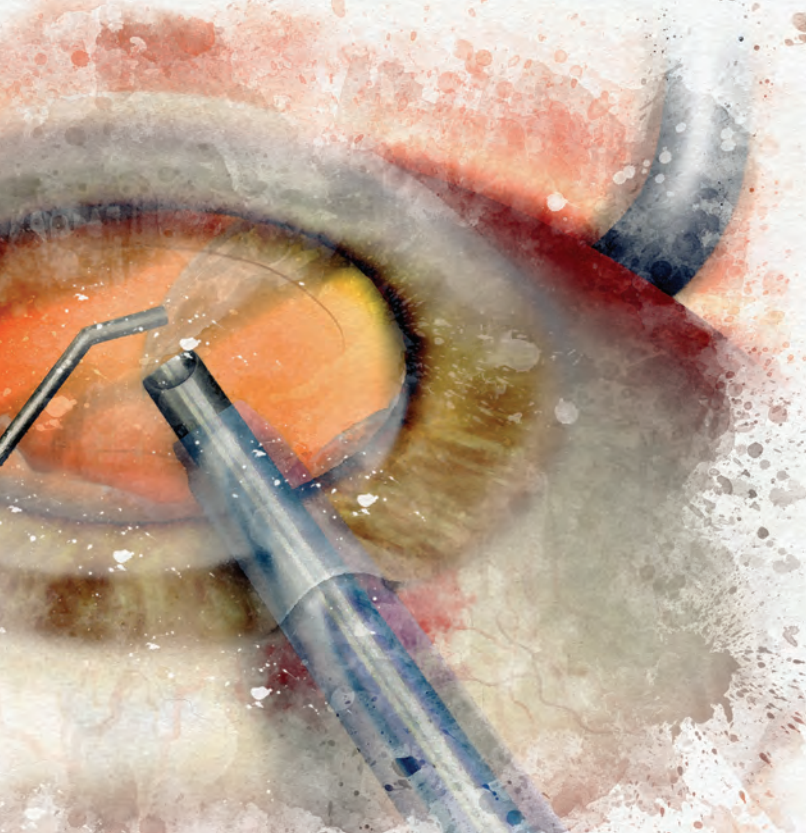
Erickson's artwork starts with a paper pencil sketch, which is then scanned into a digital painting tablet where he creates all his eye illustrations and digital paintings. His work has appeared on more than 50 ophthalmology journal covers and National Geographic books. He has been inspired by the realist style of Andrew Wyeth and the great impressionist, John Singer Sargent.

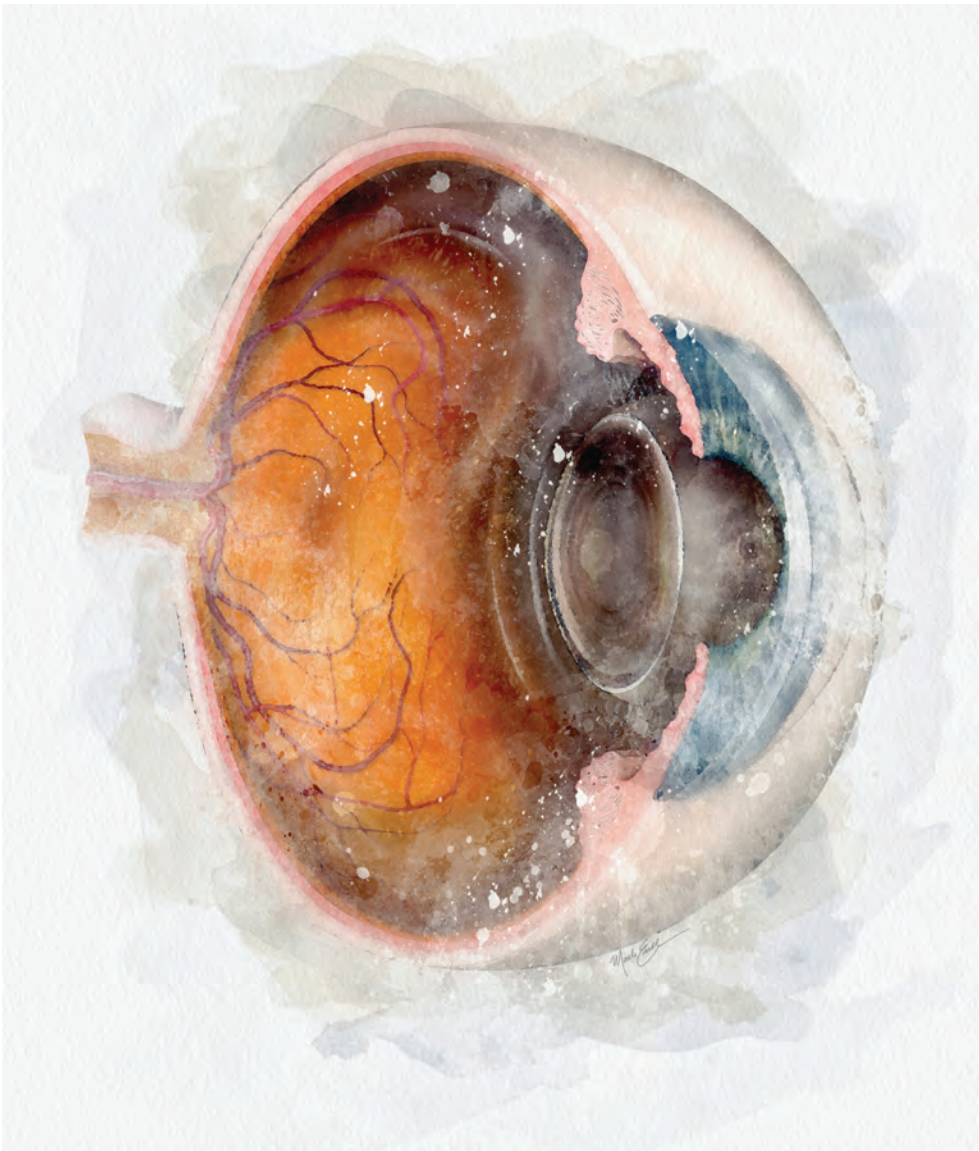
You can see more of his artwork at http://eyeimages.etsy.com and www.JirehDesign.com

Watercolors, clockwise from top left: Cataract Surgery, Ocular Melanoma, Iris and Sunflower, Eyeball Cross-section.

Previous page: Posterior Pole.





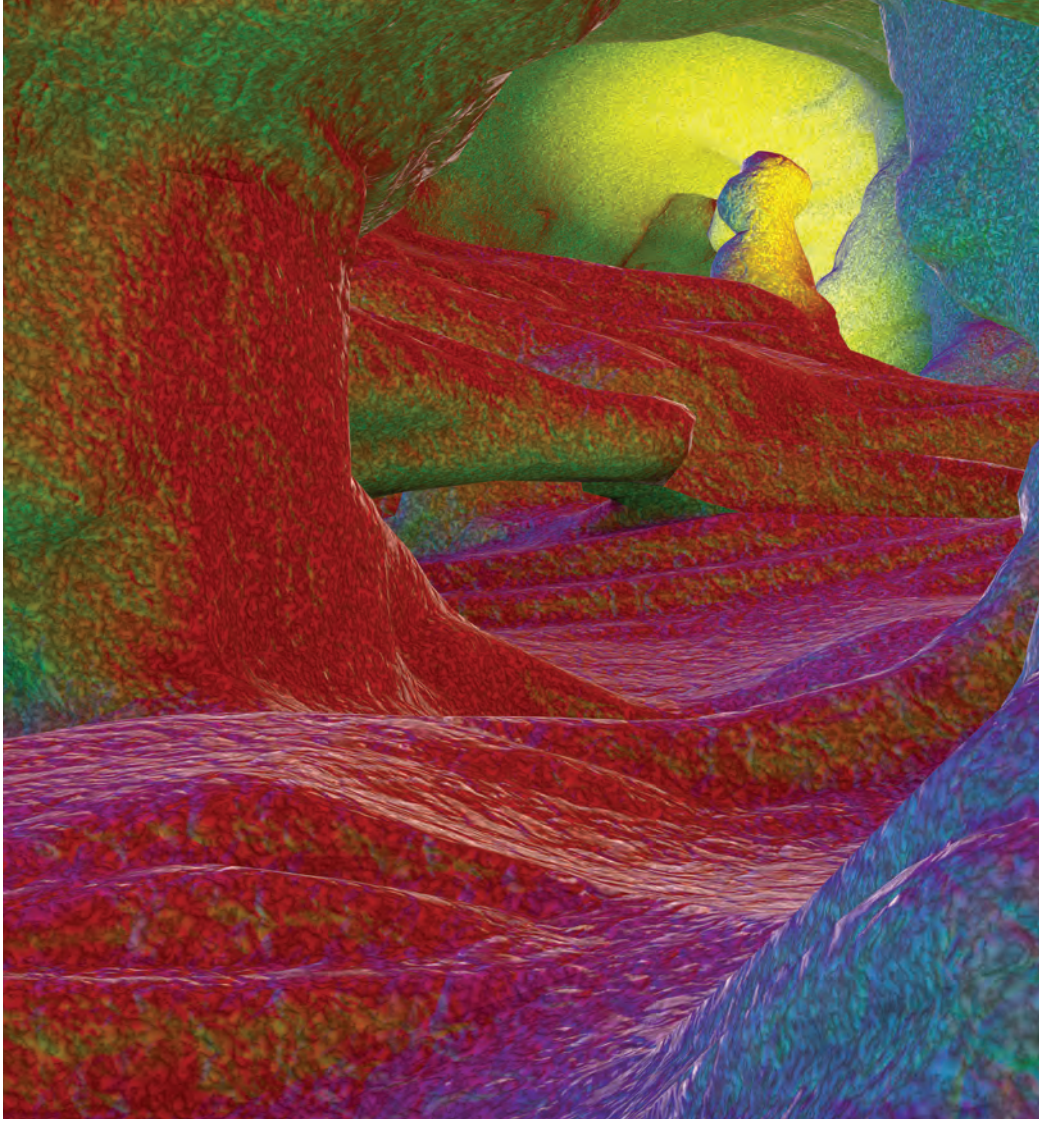


CHOROIDAL SPACES

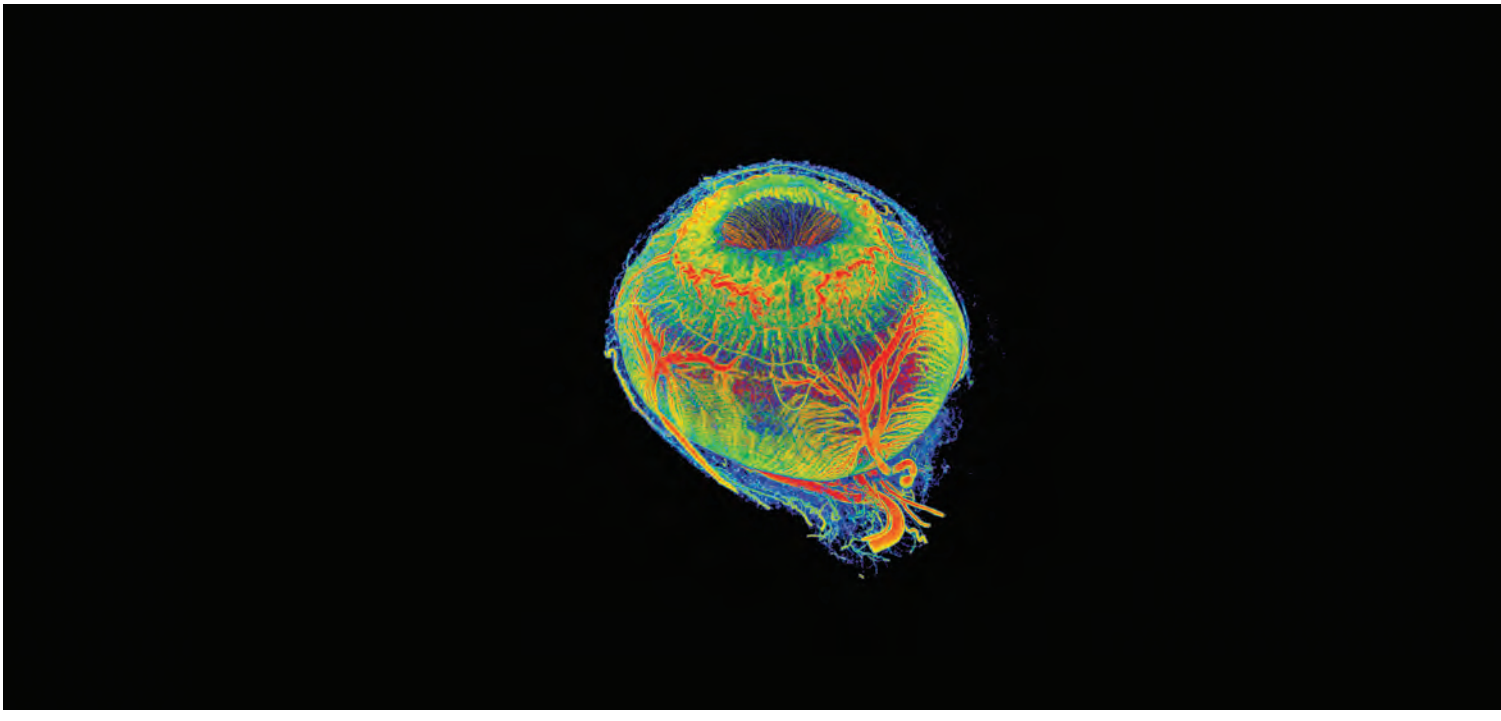
Peter Maloca is a double Wellcome Image Award winner for the best in science image making across the globe. He works as a medical doctor, eye surgeon and is Associate Professor at the University of Basel, Switzerland. He is also Group Leader Ophthalmic Imaging at the Institute of Molecular and Clinical Ophthalmology in Basel and works with Moorfields Eye Hospital in London, UK.

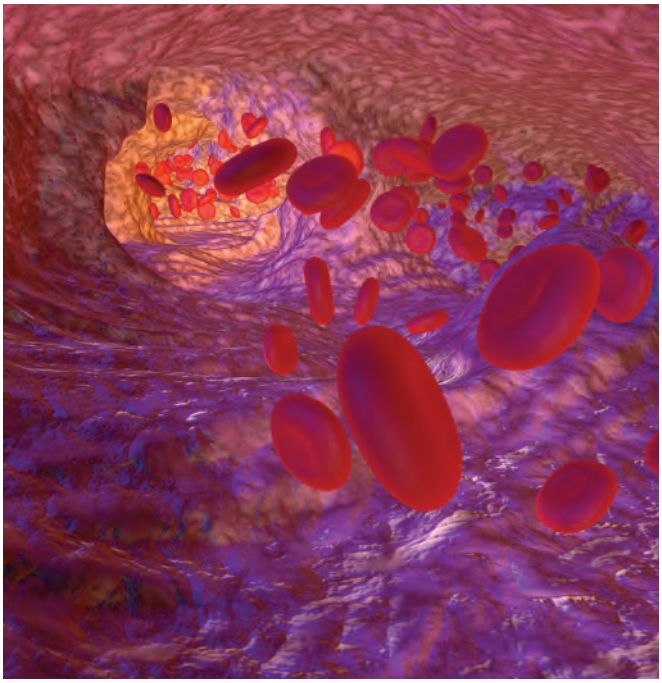
His special focus is medical retina and its fantastic 3D visual displays in modalities such as virtual reality.

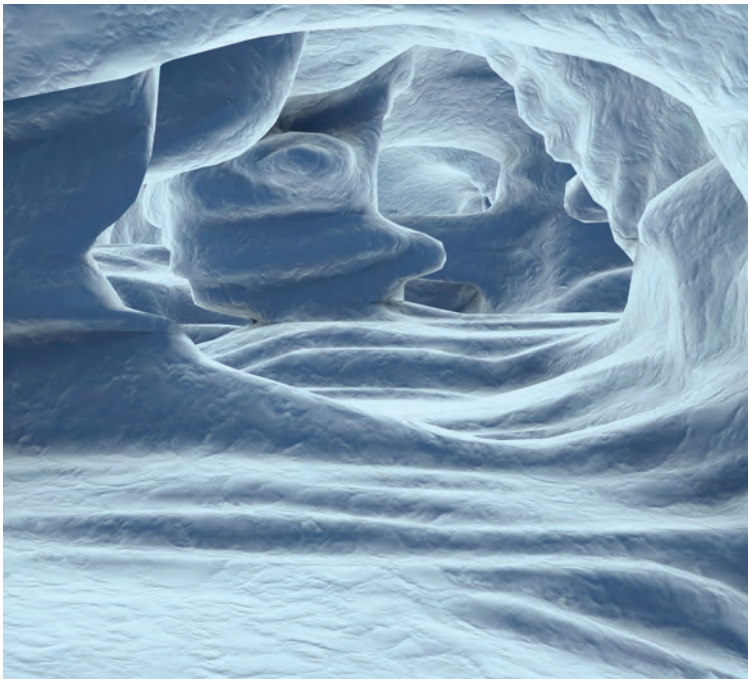
He says: "Nothing is more touching than the inner universe of the eye."

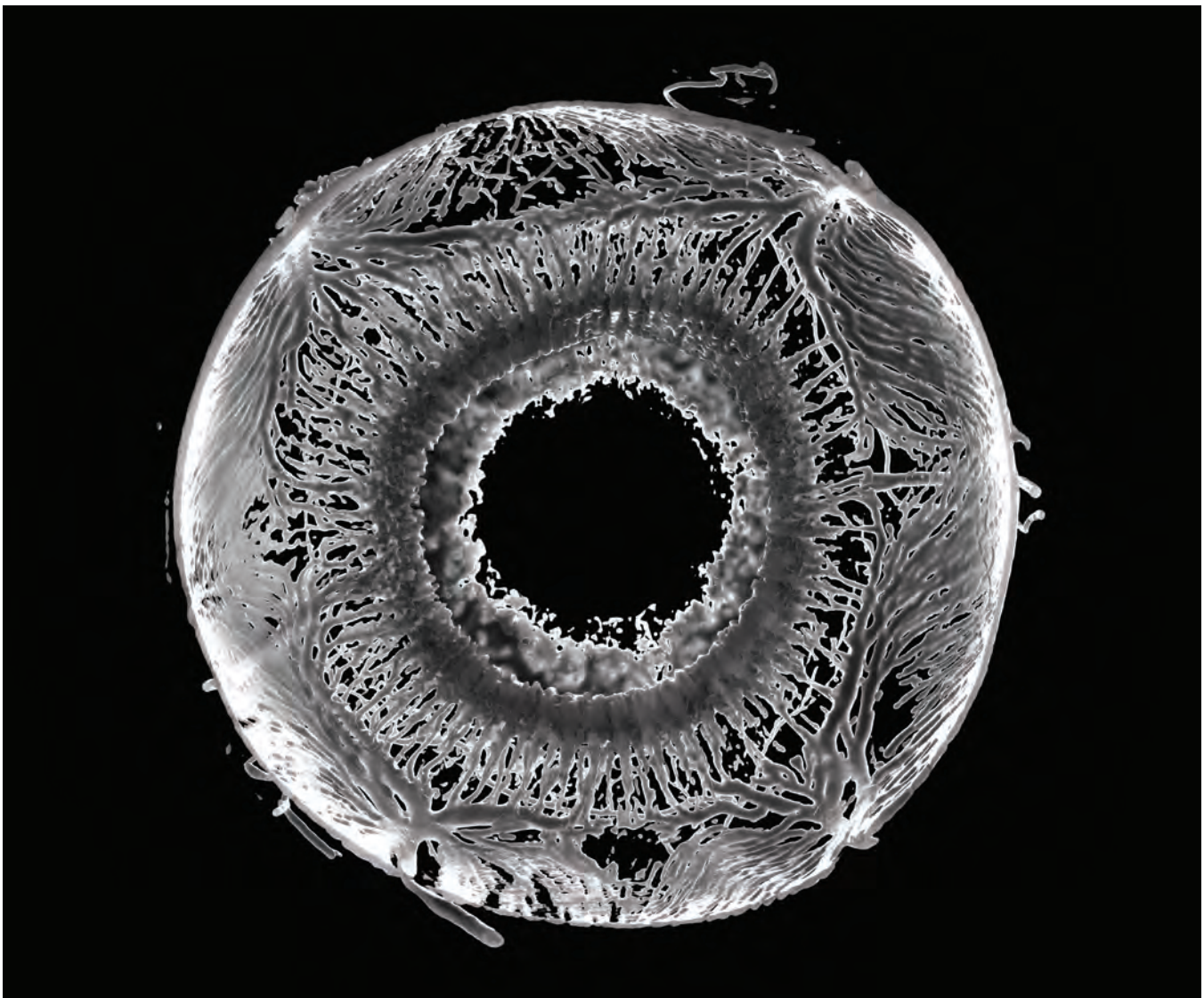


Clockwise from top left: Choroidal space, Choroidal vessels in the human eye with red blood cells, Choroid – zone of Haller, 3D model of a healthy minipig eye from the front, 3D view on vessels of a minipig eye.









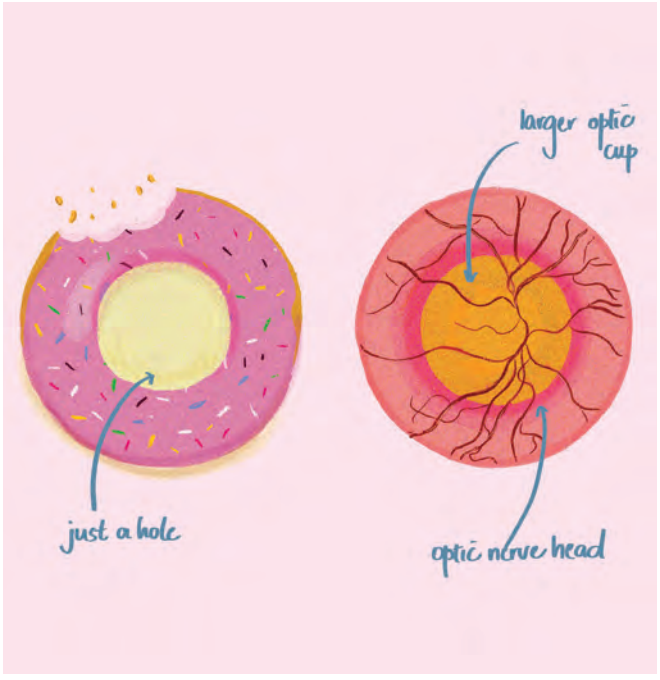
AS SWEET AS EYE

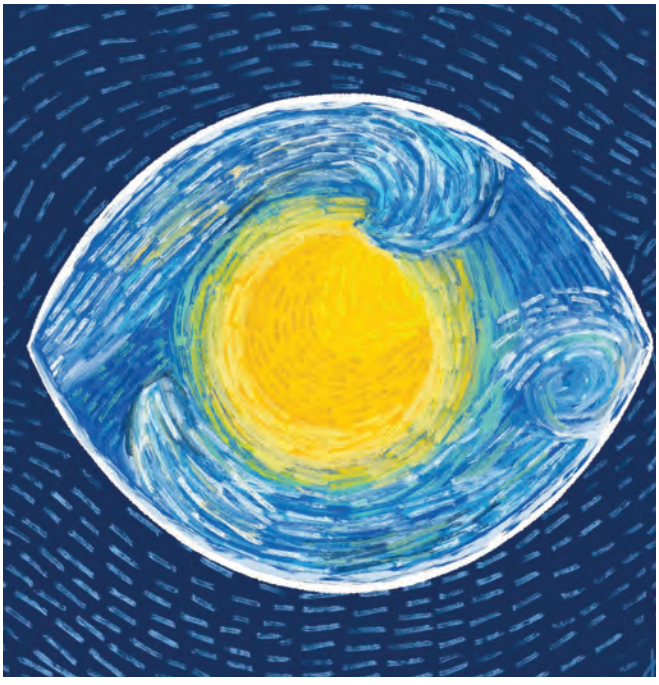
Jui Telavane is a final year ophthalmology resident at Pravara Institute of Medical Sciences in India.

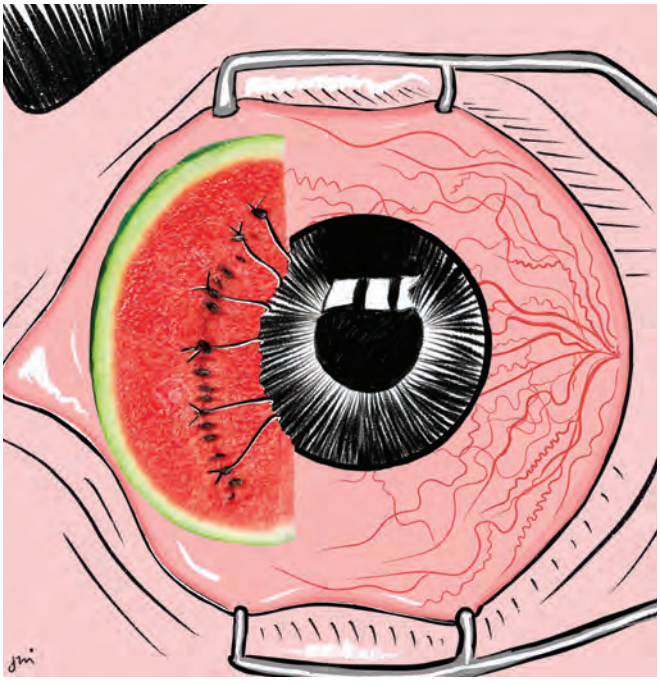
She comments: "I have always had a wacky imagination and I enjoyed art and drawing until I entered medical school, got busy, and lost touch with it. The pandemic slowed down life and drew me back to doodling. I was able to appreciate and connect with nature and indulge in the stillness. It inspired me to draw art that intersected ophthalmology with nature and what I saw around me. I would come across intriguing patient cases, and my mind would instantly imagine them as quirky images, which led me to incorporate them into my doodles.

I often (read: always) struggle remembering the mammoth workings of the petite-sized eye, and these doodles help me integrate and memorise the seemingly impossible task that we all come across as medical students. As I write this, I hope they help you, too!"

Telavane's work can be viewed on Instagram @eye.doodle.


larger optic cup
just a hole
optic nerve head





CHASING RAINBOWS

Sathi Maiti is an ocular surface disease clinical research fellow at the Periman Eye Institute and primary care optometrist in Seattle, Washington, USA. She completed her undergraduate degree in molecular, cellular, and developmental biology at the University of Washington in 2009 and her Doctorate of Optometry at UC Berkeley in 2014. She has done lymphatic and genetics research, taught cell biology and human anatomy, and has always been inspired by the forms found in microscopy, biology and the natural world. While she never formally studied fine art after high school, she has been making art as a hobby for her entire life.

She says: "I enjoy experimenting with different mediums from traditional drawing and painting to collage, embroidery and other fiber art. I gain inspiration from the world around me, and as an eye doctor that has come to include a lot of eyeballs! We are very lucky as eye care practitioners to work with a structure as complex, physiologically fascinating, and aesthetically interesting as the eye."

Maiti shares her art and other eye-related content on her instagram account @dr.maitiseyeballsandstuff

Clockwise, from the left: Refractive errors;, Mushroom retina, monstera iris, poppy vasculature; Eye.

PEAKY BLINDERS

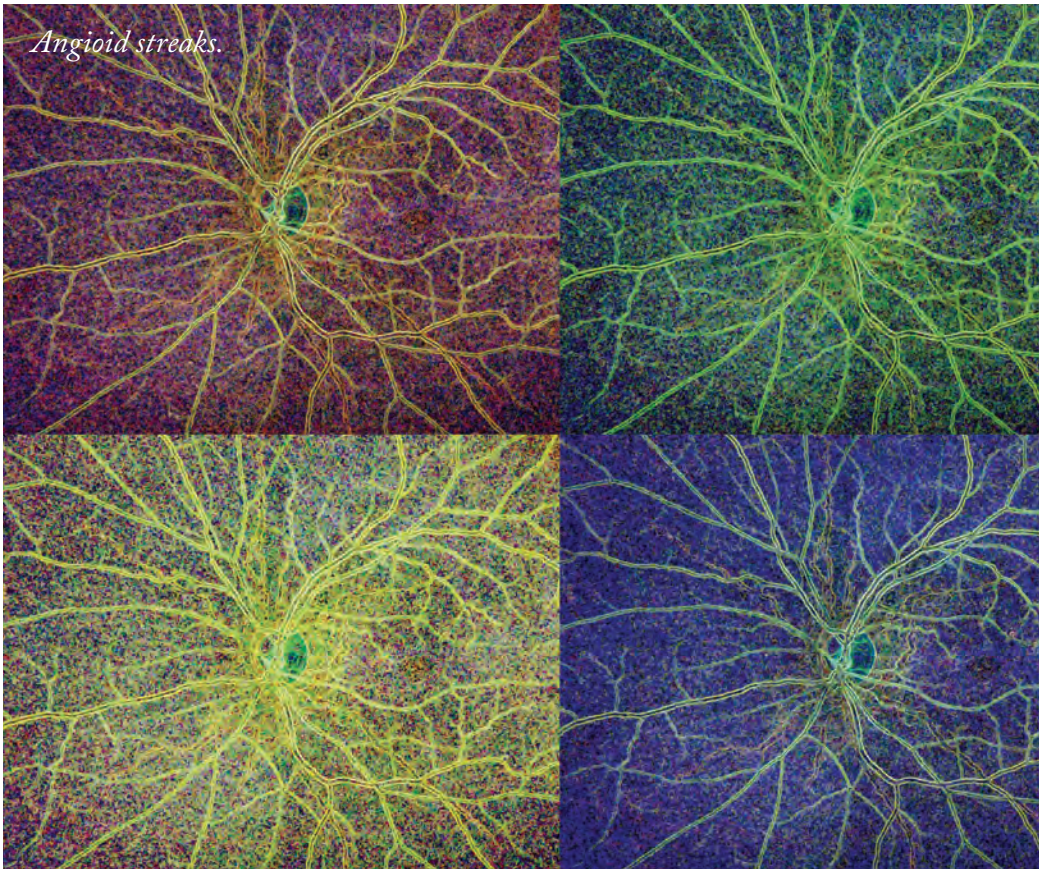
Jennie Jewitt-Harris, featured prominently in last year's Art of Eyes feature, is a CEO of the Transplant Links charity, artist and physician. She has a PhD in Fine Art for her research into the reasons why many people refuse to donate their corneas after death. Her exhibition, "Anything But the Eyes," will be presented at South Hill Park Mirror Gallery in Bracknell, UK, from July 8 to October 2, 2021. This year, she has shared her new work with The Ophthalmologist. Can you tell whose eyes are featured in *Anatomy vs Psychology?*

Anatomy vs Psychology.
Mixed media.

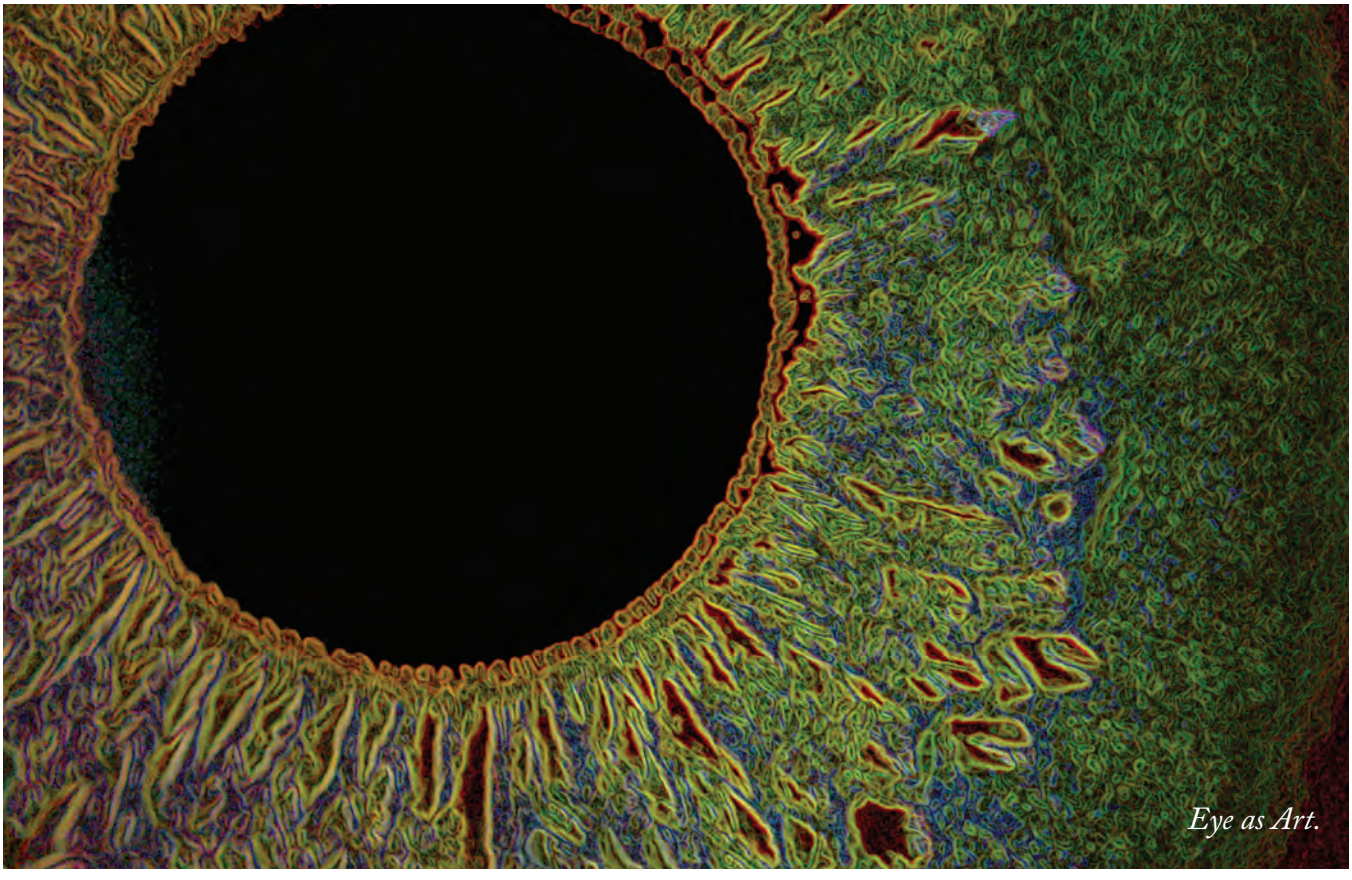

Roze
St. Martin
Ville ès
Gaudins
Faldouet
Gorey
Mont
SETT

DREAM IN TECHNICOLOR

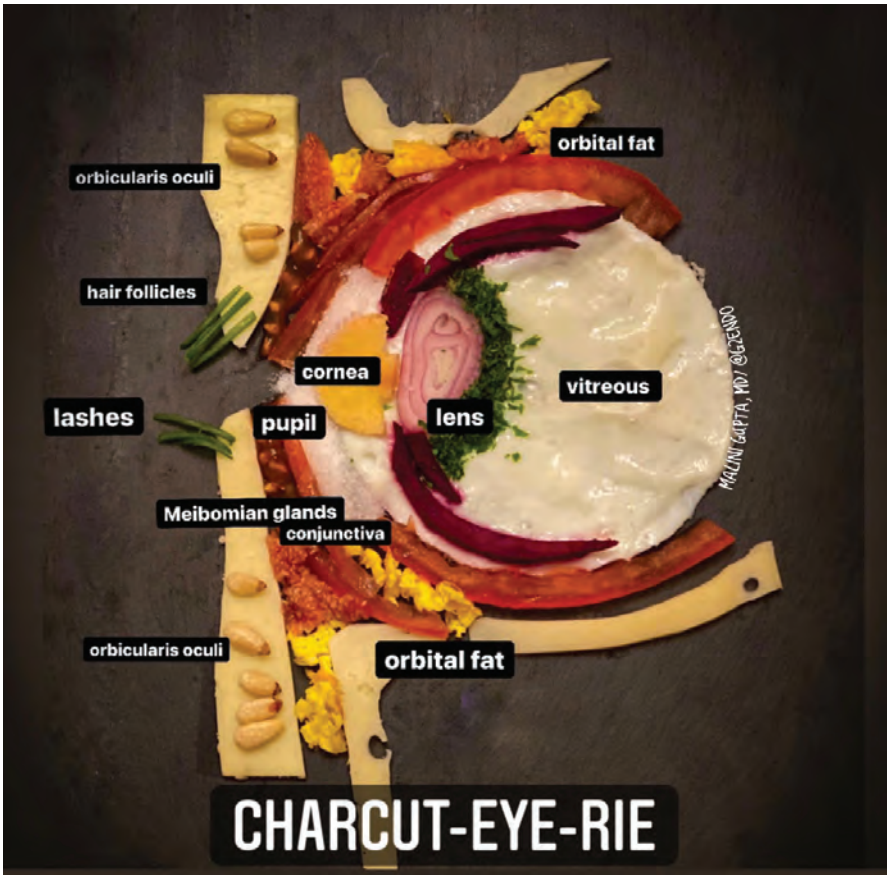
Denice Barsness is Technical Director at the Ophthalmic Diagnostic Center at CPMC Department of Ophthalmology in San Francisco, California, USA. She is very experienced in all aspects of ophthalmic assisting and technology, as well as imaging. She has over 25 years of experience as faculty staff member of ophthalmic imaging education institutions and is Past President of Ophthalmic Photographers' Society.

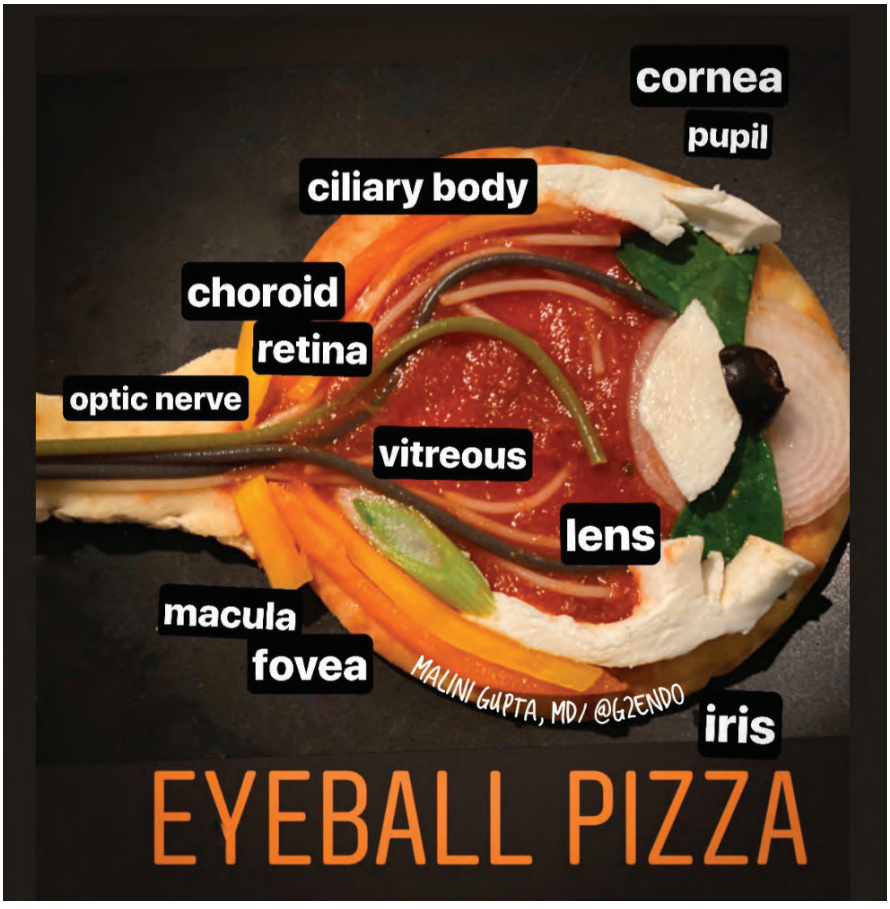


Angioid streaks.



Eye as Art.





HUNGRY FOR KNOWLEDGE

Combining her love of visual art, culinary art, and medicine, Malini Gupta has created a collection of entirely edible medical food art. Gupta graduated from Washington University in St. Louis, Missouri, USA, and attended medical school at the University College Cork in Ireland, with post graduate training in Memphis, Tennessee, and Media & Medicine at Harvard Medical School, Boston, Massachusetts, US. She is a consultant endocrinologist in her private practice, G2Endo. She has had many of her other art pieces on exhibit in the US. All of her artwork has a medical theme or uses medical material.

You can see more of her work on Instagram @G2Endo and @ G2Endo_art and on our website.

MACULAR WINDOW DEFECT

A. David Flug is a board-certified ophthalmologist who has practiced ophthalmology and eye surgery in Forest Hills, New York, USA, since 1978. He is a graduate of the Hahnemann Medical College and did an ophthalmology residency at the Long Island Jewish Medical Center. He is currently on the teaching staff of the North Shore University, Long Island Jewish Medical Center and on staff at Flushing Hospital, and the renowned Mackool Eye Institute.

Caption: Macular window defect

EYE CORKER

Christina Appleman is a Certified Ophthalmic Medical Technologist and an Ophthalmic Research Technician in Rockville, Maryland, USA. Of her art, she says: "My grandfather used to make wine as a hobby so there were always wine corks laying around that were begging to be utilized. I enjoy coming up with creative and unique ways to upcycle the corks."

Appleman's work can be found on Instagram @thewineingtwins.

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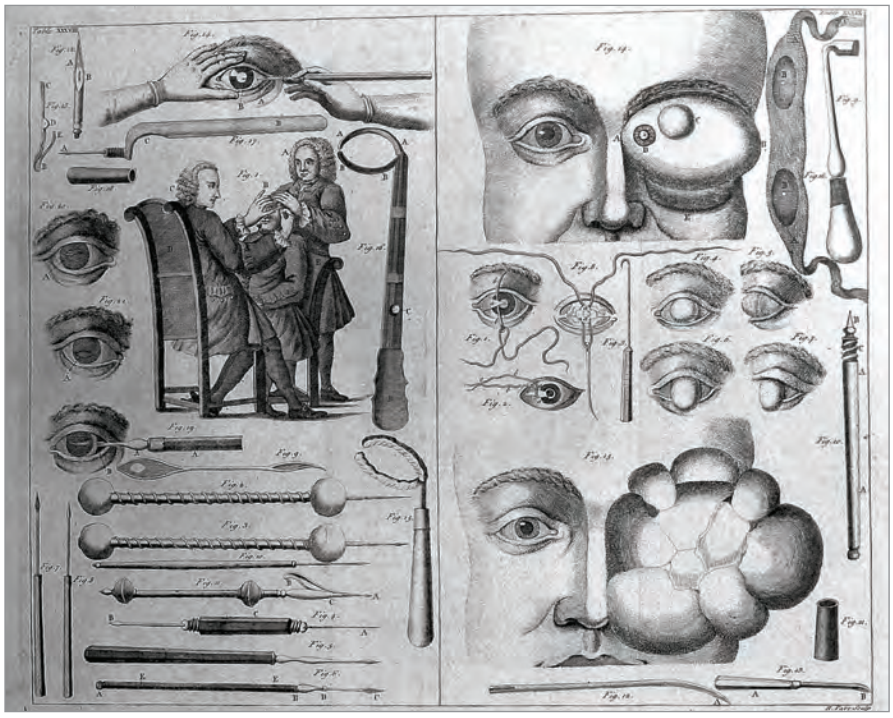
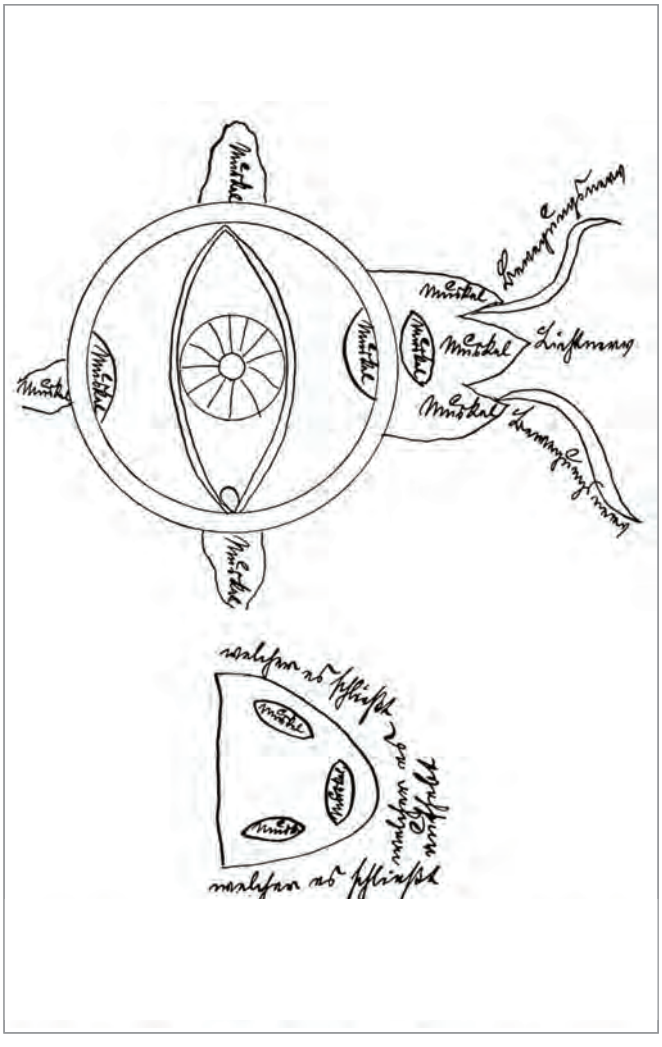
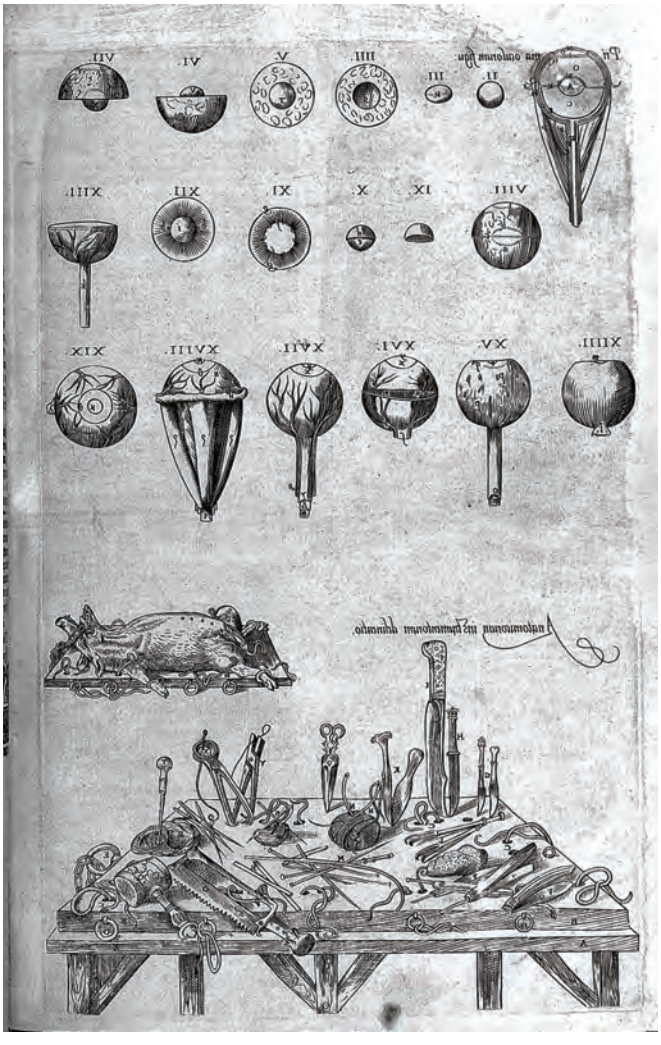
Counterclockwise, from bottom left: Anatomy of the eye: 9th century. From a manuscript of Hunian b. Ishag; Page from Compendiosa totius anatomiae delineation aere exarate by Thomas Geminus, 1545; Eye diseases and surgical instruments. Line engraving by F. Sesone, 1749.







> Learning the day-to-day operations of an eye bank was an incredibly valuable part of my corneal fellowship.

Allison Jarstad, D.O. | SoCal Eye Physicians

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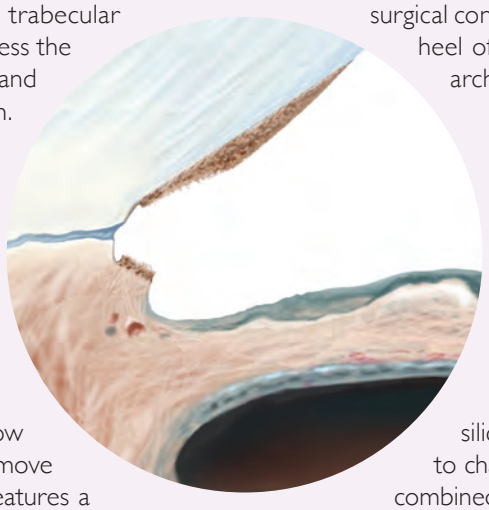
CUTTING IT FINE – IN A GOOD WAY

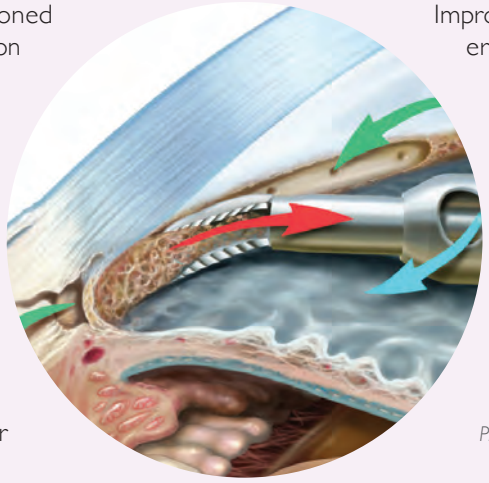
For complete removal of trabecular meshwork – with active irrigation and aspiration – look no further

Meet the TrabEx Pro from MST – an extension to the leading TrabEx line of goniotomy blades from a company continually investing and innovating in the glaucoma space. TrabEx Pro is a surgical instrument designed specifically for the complete removal of diseased trabecular meshwork.

MST's glaucoma focus is to take traditional goniotomy surgery to the next level. In goniotomy, an incision is made in the trabecular meshwork, allowing for aqueous to access the collector channels of Schlemm's canal and drain via the natural outflow system. One concern that surgeons have expressed with goniotomy is that incomplete removal of trabecular meshwork may allow remaining tissue to reactuate and reocclude the aqueous outflow. TrabEx Pro includes innovative features that may facilitate a more complete excision of diseased trabecular meshwork.



What are the unique features that allow the TrabEx Pro to fully and cleanly remove the required tissue? First, the device features a trapezoidal blade head with laser-honed serrated blades. The trapezoidal orientation of the blades allows for a custom cut for each individual patient and each section of tissue, which often varies (1). In narrow sections of trabecular meshwork, the tissue is cut at a narrow section of the blade. In wider sections of trabecular meshwork, the tissue passes further up the graduating blades and is cut at a wider section, leaving minimal amounts of tissue behind. While other blades for goniotomy offer a one-size-fits-all approach, the TrabEx Pro can offer a custom cut for each specific situation.



The TrabEx Pro is also completely polished on the distal end, which can provide gentle contact with tissues that are not intended to be removed. The footplate of the blade is rounded and comes down to 66 microns at the distal end, allowing for high levels of precision and surgical control. What's more, the rounded distal heel of the blade head is contoured to the arch of the eye.

But perhaps the most important aspect of the TrabEx Pro is the way it is compatible with all phacoemulsification platforms. The ergonomic handle is designed to provide comfort and control for the user and features a blade directional indicator that clearly defines the orientation of the device.

Finally, the TrabEx Pro boasts a silicone sleeve that eliminates the need to change incision sizes when performing a combined goniotomy and cataract procedure. Improvements have also been made to the ergonomics of the hand piece, which provide maximum user comfort to every surgeon for every procedure.

The TrabEx Pro is pending 510(k), and not available for sale within the United States.

Reference

1.MH Kuehn et al., "Circumferential trabecular meshwork cell density in the human eye," Exp Eye Res, 205, 108494 (2021). PMID: 33596442.

TWO CONDITIONS – ONE PROCEDURE

With patients suffering from multiple comorbidities – such as cataract and glaucoma – surgeons find it helpful to address their conditions at the same time. Glaukos' iStent *inject*® W is proven to do it safely and effectively (1).

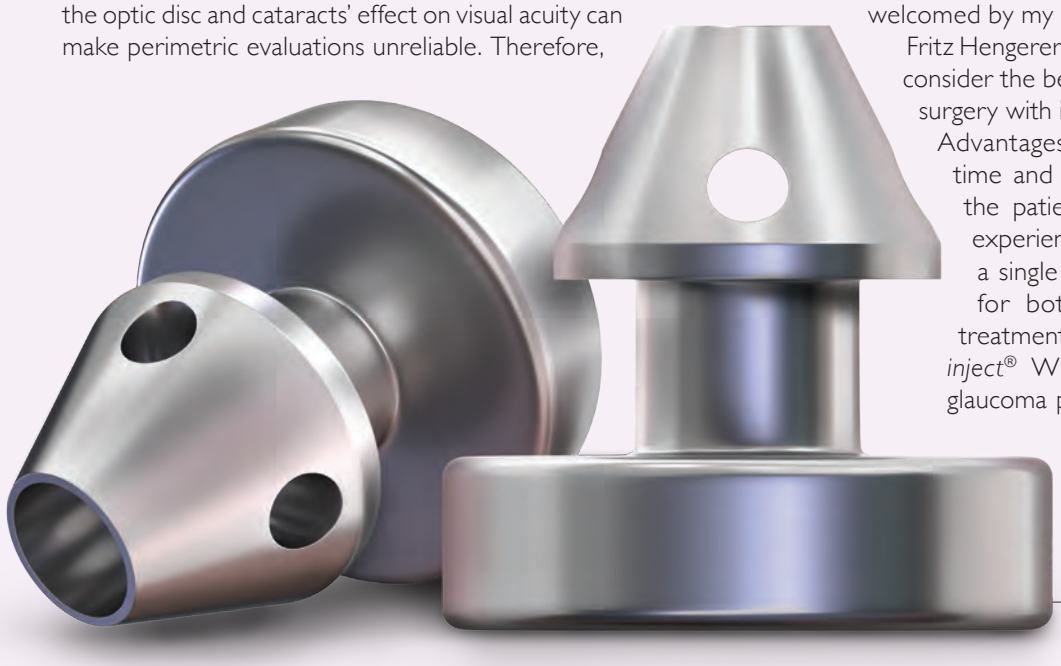
It is common for ophthalmic patients to need input from clinicians specializing in more than one area. When coexisting conditions can be treated by one surgeon in a single procedure, time and money are saved and visual outcomes and IOP lowered at the same time – greatly benefiting patients.

Fritz Hengerer, Director and Chief Medical Officer at the Department of Ophthalmology at Buergerhospital Eye Clinic in Frankfurt, Germany, explains the benefits of linking cataract procedures with glaucoma treatment. "The conditions themselves are often linked in real life: in my own practice, about 15 percent of cataract patients also have glaucoma or ocular hypertension. And in addition, cataracts can interfere with glaucoma diagnosis; for example, lens opacification impedes retinal imaging and ophthalmoscopic evaluation of the optic disc and cataracts' effect on visual acuity can make perimetric evaluations unreliable. Therefore, it is helpful to address both cataracts and glaucoma as part of a single clinical management strategy – and, now that safe and effective trabecular micro-bypass devices (such as iStent *inject*® W) are broadly available, we can do exactly that. If it is possible to address both cataracts and glaucoma symptoms within a single procedure, at a relatively early stage, why not do so? It just makes sense."

Karsten Klabe, ophthalmic surgeon at Breyer, Kaymak & Klabe Augenchirurgie in Düsseldorf, Germany, agrees with this view. "Perhaps the major advantage of iStent technologies is that it allows us to offer both a solution for cataracts and an effective glaucoma treatment within a single surgical episode. iStent *inject*® W combines elegantly with cataract surgery – the only additional requirements are viscoelastic and a gonioprism. You don't need another assistant or additional sophisticated devices – you just put a gonioprism on your operating table and that's it! Also, the time demands of the procedure are acceptable."

Have surgeons noticed any advantages to using the iStent technologies for combined procedures during the COVID-19 pandemic? Imran Masood, Consultant Ophthalmic Surgeon, Birmingham and Midland Eye Centre, UK, offers his perspective. "Some patients whose cataracts might have gotten worse over the first months of the pandemic, when cataract procedures were cancelled, have noticed their visual function deteriorating at a time when they rely on their vision for tasks that keep them occupied at home. Combining cataract and iStent *inject*® surgery has allowed me to improve those patients' vision at the same time as getting their pressure under control, preventing deterioration of their glaucoma and improving their ocular surface, which has been welcomed by my patients."

Fritz Hengerer concludes, "Surgeons should consider the benefits of combining cataract surgery with iStent *inject*® W implantation. Advantages for the surgeon include time and cost savings; advantages for the patient include a single surgery experience, a single anesthesia, and a single postoperative appointment for both glaucoma and cataract treatment. Thus, integration of iStent *inject*® W into cataract surgery for glaucoma patients allows us to kill two birds with one stone."



GLAUKOS

ISTENT *INJECT*® W CASE STUDY

Anshoo Choudhary, glaucoma specialist and Consultant Ophthalmologist at the Royal Liverpool University Hospital, Liverpool, UK, presents a case study of a patient with progression of primary open angle glaucoma despite triple therapy.

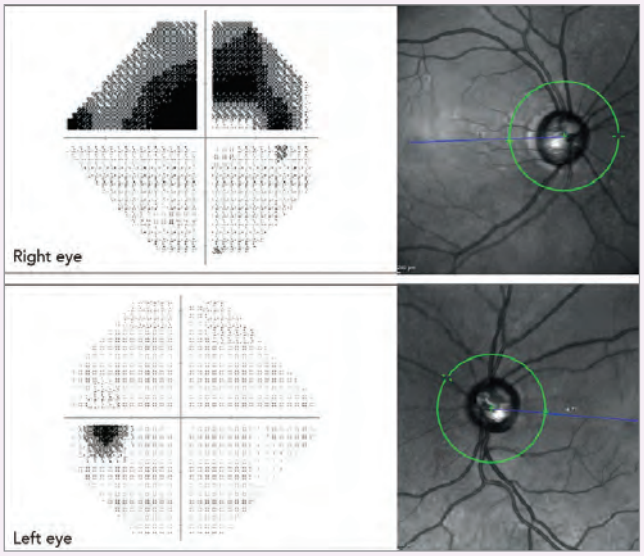
Zhihang Cheng, Ophthalmology specialty trainee at the Mersey Deanery, with an interest in glaucoma and minimally invasive glaucoma surgery research.

Patient
A 72-year-old man referred by a local eye department with open angle glaucoma progression.

Initial examination
Right eye: A significant cataract
Advanced cupping: cup-to-disc ratio 0.9
IOP, with topical therapy: 16 mmHg
Visual field: advanced changes with a mean deviation of -11.89 dB
Left eye: A significant cataract
Moderate glaucoma: cup-to-disc ratio 0.75
IOP, with topical therapy: 15 mmHg
Visual field: early changes with a mean deviation of -1.54 dB

First procedure and subsequent therapy
The patient underwent a cataract surgery and deep sclerectomy (DS) to reduce the IOP in his right eye, which was kept on monotherapy following the surgery to maintain target IOP. His left eye was kept on dual therapy and the IOP remained in the high teens. Eye drop intolerance limited his ability to receive additional ocular hypotensive agents. There were also concerns regarding possible visual field progression.

Combining cataract surgery with iStent inject® W
Two years since the initial referral, the patient reported worsening vision consistent with symptoms of cataract in the left eye. Surgical options discussed with him included a standalone cataract procedure or a combined procedure with iStent *inject*® W to reduce his left-eye IOP. Taking into consideration the potential benefit of better pressure control and reduction of drop burden, the patient opted to have a combined procedure.



Results of the combined procedure
At three months post-op, his IOP was 12 mmHg in the left eye without drops, and disc appearance was stable. Twelve months post-procedure, the patient's left-eye IOP remained stable at 13 mmHg with a stable visual field (mean deviation -0.94).

Conclusion
The iStent *inject*® W is a Trabecular Micro-Bypass glaucoma procedure which is designed to restore outflow of aqueous humour through the physiological outflow pathway. The landmark randomised control trial showed more than 75% of patients achieve a 20% reduction in IOP and in some patients the IOP reduction may be greater. With proven safety and efficacy, it is an attractive option as a combined procedure for patients with mild to moderate glaucoma who are undergoing cataract surgery. Early intervention and improved IOP control might have the added advantage of avoiding filtration surgery in these cases.

Reference

1. *TW Samuelson et al., "Prospective, randomized, controlled pivotal trial of an ab interno implanted trabecular micro-bypass in primary open-angle glaucoma and cataract," Ophthalmology, 126, 811 (2020). PMID: 31973839.*

In Practice

Surgical Procedures
Diagnosis
New Drugs

Analyze This

A timely advance in digital health and mobile perimetry

By Priya Narang and Amar Agarwal

Visual field assessment is integral to the examination and evaluation of glaucoma, and automated perimetry is an essential tool to document visual field defects that may be either glaucomatous or neurological in origin.

Standard automated perimetry (SAP) is a well-accepted test that measures the threshold of each point in the visual field. However, it uses a high-cost, tabletop system with limited mobility. Now, a new device –the Advanced Vision Analyzer (AVA) – meets the global standards for perimetry devices and establishes a usability criterion that expands its utility for adoption by all ophthalmologists and related professionals across the globe. We have found it highly useful in our work, and so we thought we should share it with a wider audience.

The analyzer

The AVA is a battery-powered virtual auto-perimeter that is portable, does not need a dark room to perform the test, and obviates the need to occlude the fellow eye. The device essentially comprises a head-mounted device (for all intents and purposes a virtual reality headset), a handheld device with a patient response button, and a tablet that serves as a controller to perform, record, and analyze the test program. The lightweight head-mounted device allows a high degree of flexibility in patient position and allows testing in the supine position.

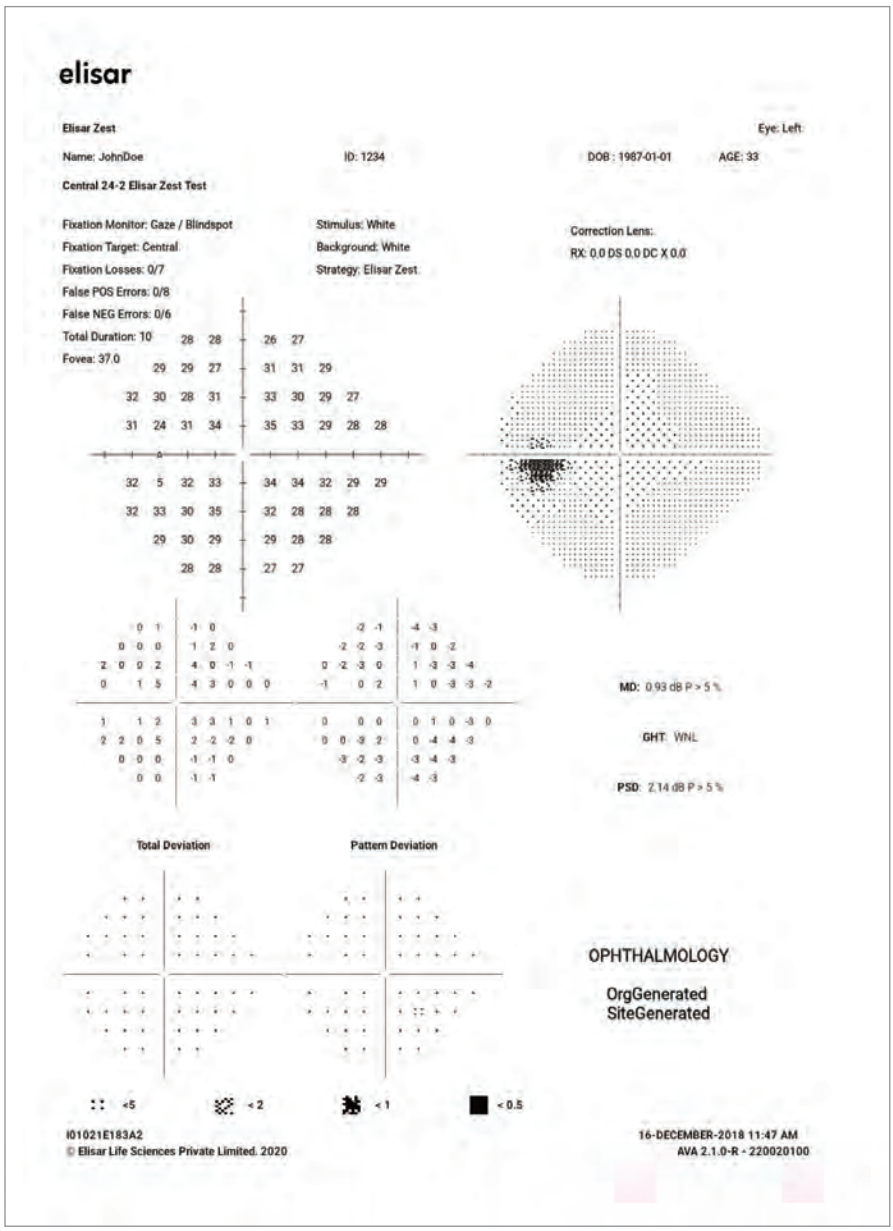
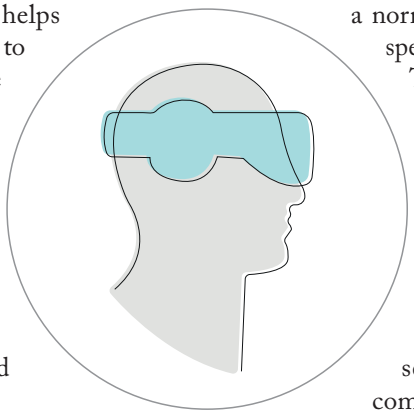


Figure 1. Test report of a case demonstrating Global indices, visual field parameters and the threshold grey-scale chart.

"The report generated by the device meets international standards and adheres to the format that ophthalmologists are accustomed to."

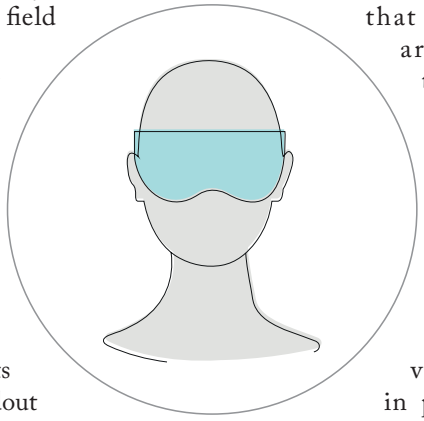
The clinical data on AVA is of course encrypted and therefore secure. But previous test results can be retrieved from cloud storage by entering patient details. The tablet runs cloud-based software that helps keep patient data up to date – and, because it's in the cloud, it also keeps itself up to date with seamless upgrades. The tablet can be connected wirelessly to the printer and the reports can be delivered by email.



The report

AVA offers white-on-white perimetry with stimulus intensity that ranges from 0 to 40 decibels. The test is performed using Goldman III stimulus size and 24-2 and 30-2 patterns; testing strategies include suprathreshold, full threshold, Elisar Zest, and Elisar Fast. Fixation monitoring is done with Heijl-Krakau tests and an integral eye tracker that provides a live feed of the tested eye on the test controller; this advanced infrared tracking technology allows patient monitoring and minimizes fixation loss. The device also possesses an inter-pupillary distance (IPD) adjustment capability that can assure accurate field measurement.

The printed test report consists of: i) patient information, test type, test duration, ii) absolute threshold values and gray scale pattern, iii) gradient plot based on the threshold results obtained, and iv) readout of reliability parameters, such as False Positive, False Negative, and Fixation loss (see Figure 1). The reports include defect significance and global indices that are compared with a normative database built specifically for the device. The global indices (GI) represent a summary of all the sensitivity values produced by the test and are a useful adjunct that provides an overview about the visual field, and sequentially helps to compare the test results for an individual eye in follow-up visits. The GI test-data provided in detail are total deviation, pattern deviation, and glaucoma hemi-field test (GHT). As in SAP, GHT in AVA allows comparison of visual field defects across the horizontal axis, with the response being denoted as i) within normal limits, ii) borderline, and iii) outside normal limits.



For visual field measurement validation, comparative studies between AVA and a conventional auto-perimeter demonstrated equivalent ability to detect all forms of visual field defects. The report generated by the device meets international standards and adheres to the format that ophthalmologists are accustomed to, thereby minimizing the learning curve. Extensive clinical trials have established the utility of this device as an essential tool to detect and analyze visual field defects in patients of all age groups – regardless of them being physically disabled or bedridden.

To summarize our experience: the device is portable, affordable, simple, accurate, and serves as a new portable paradigm to measure and analyze visual field defects concurrently allowing the need to meet global demand for quality eye care in the era of digital health. Particularly in the current COVID-19 pandemic, AVA provides a diagnostic option for patients whose health condition would be threatened by a visit to a central testing site.

Priya Narang is the Director and Chief consultant at Narang Eye Care and Laser Centre in Ahmedabad, India.

Amar Agarwal is Professor and Head of Dr. Agarwal's Eye Hospital and Eye Research Centre, Chennai, India.

The authors report that they have no direct financial interest in the product.

Making Cataract Surgery Child's Play

The FDA's first approved drop for the prevention of intraoperative miosis and reduction of postoperative pain in pediatric patients undergoing cataract surgery has arrived. But is it worth the hype?

By M. Edward Wilson

In children, cataracts are responsible for more visual disability than any other form of treatable blindness. In the US, more than 200,000 children are blind from unoperated cataracts, complications of cataract surgery, or the general effects of cataracts (1). The socioeconomic and quality-of-life costs associated with a lifetime of blindness stemming from untreated visually significant cataracts are huge, and estimates put the cumulative risk of cataract during the growing years as high as 1 per 1,000 (2). Fortunately, not all childhood cataracts require removal.

The complexity of cataract surgery in children demands that the surgeon has a high degree of confidence and competence. Cataract surgeons who specialize in adult surgery often lack training in the techniques specific to pediatric intraocular surgery; therefore, cases should be done by ophthalmic surgeons who perform them on a weekly or biweekly basis to ensure competency. Whenever possible, children should

"Surgery in a pediatric eye is like working inside a squashed grape. The surgeon must maneuver the instruments within a tight space and use copious amounts of fluid."

be referred to regional centers with significant experience (3).

Challenges of the pediatric eye

Cataract surgery in children poses several specific challenges. Anatomically, a child's eye is smaller, softer, and more flexible compared with an adult eye. Performing cataract surgery in an adult is akin to working inside a hard box, because the sclera is firm and holds its shape. Surgery in a pediatric eye, on the other hand, is more like working inside a squashed grape. The surgeon must maneuver the instruments within a tight space and use copious amounts of fluid to ensure that the eye retains its shape.

Another challenge in pediatric eyes is maintaining adequate intraoperative mydriasis – partly because of the lack of development of the pupil dilator muscle. Stromal rigidity is also reduced, causing the iris to constrict in response to even mild amounts of trauma during the surgery. Such features are consistent with adult intraoperative floppy-iris syndrome. Preservative-free epinephrine may be used intraoperatively in the irrigating solution – a step that has been routine in children long before it was seen as a need in even the most unusual adult cases.

Tools for more predictable surgeries

Following the approval of Omidria (phenylephrine and ketorolac intraocular solution, 1%/0.3%; Omeros Corporation) for maintaining pupil size by preventing intraoperative miosis and for reducing postoperative ocular pain in adult cataract surgery, the company conducted a study in pediatric patients (4); I was an investigator. It was not possible to use a control arm that did not include treatment (in other words, no additive to the BSS) in this patient population; therefore, we randomized subjects to phenylephrine plus ketorolac or phenylephrine alone. As a result, we were also able to evaluate the effect of the nonsteroidal anti-inflammatory agent (ketorolac) on pain. Because the use of phenylephrine is off-label in pediatric cataract surgery, the manufacturer provided both the phenylephrine plus ketorolac product and the phenylephrine for the purposes of the study.

The multicenter, double-masked Phase 3 registration trial was conducted at 17 US sites to compare the safety of phenylephrine and ketorolac 1.0%/0.3% (PE/K 1.0%/0.3%) with phenylephrine 1.0% (PE 1.0%) in children undergoing cataract surgery who were aged from birth to three years old – a notoriously difficult age group for surgery. We also measured intraoperative pupil diameter and postoperative pain. The safety endpoints were evaluated up to 90 days postoperatively. A masked central reader looking at surgical videos measured change in pupil diameter from immediately prior to incision to wound closure. Postoperative pain was measured using the Alder Hey Triage Pain Score at 3, 6, 9, and 24 hours following wound closure. The parent/caregiver recorded the results.

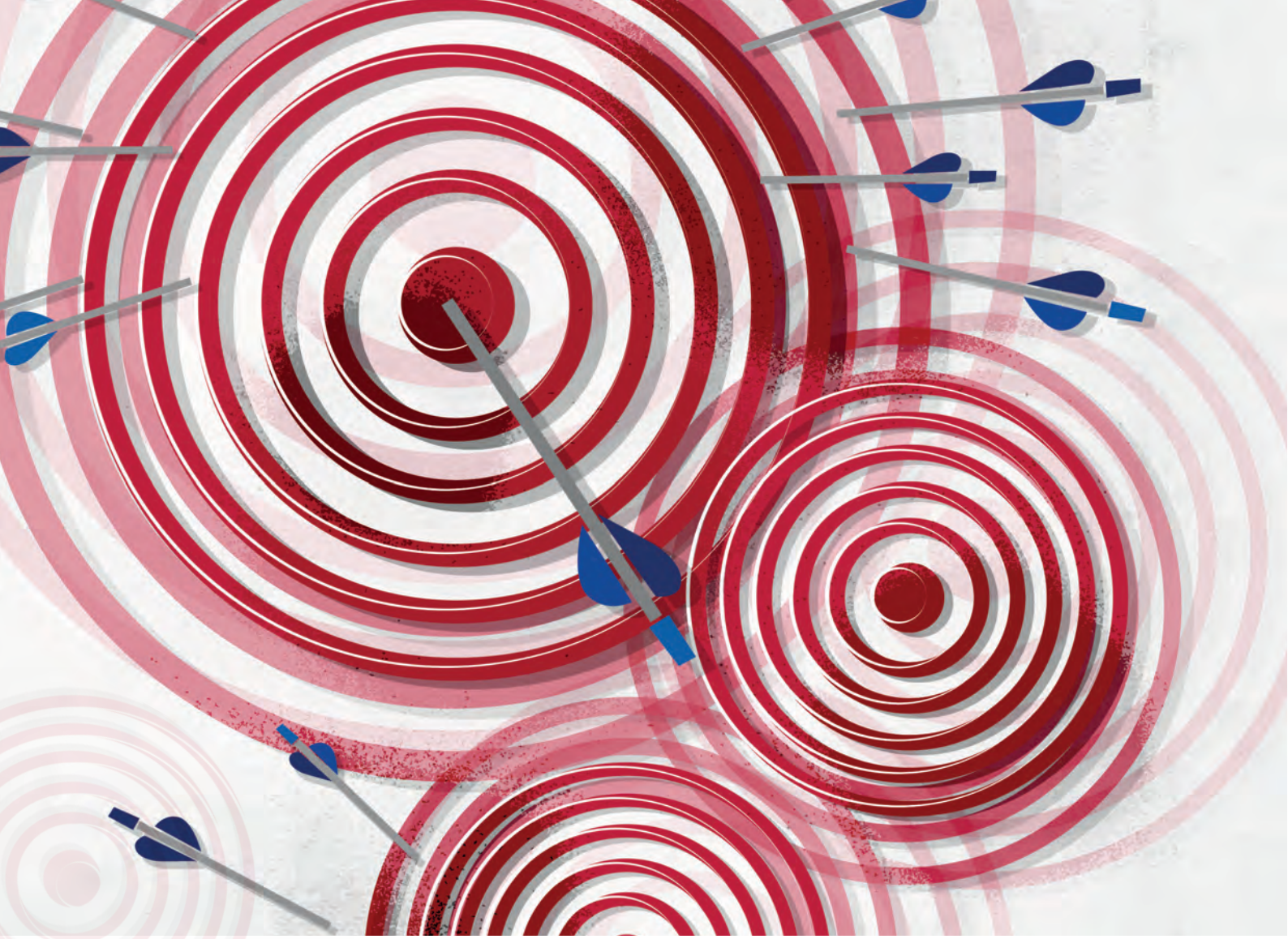
It is important to note that this study was powered to assess safety only as the FDA indicated that efficacy could be extrapolated from the prior pivotal trial results that were the basis for FDA approval in the adult population. Consistent with the primary objective of assessing safety, enrollment was limited to 78 patients of whom 72 patients were ultimately randomized; no notable changes in vital signs or ophthalmological complications were observed in either group. The mean change in pupil diameter was similar between PE/K 1.0%/0.3% and PE 1.0% (mean difference in AUC -0.071; P = .599). Despite the study design's relatively limited sample size, the postoperative ocular pain scores and overall mean scores were lower in the PE/K group at all individual time points, and differences in overall mean scores were statistically significant at 6 and 24 hours (P = 0.029 and 0.021, respectively).

In short, the study demonstrated that PE/K 1.0%/0.3% was safe for use in children and maintained mydriasis during cataract surgery. And showed that postoperative pain levels were lower in the PE/K 1.0%/0.3% group. The results of which were published in the Journal of Cataract and Refractive Surgery (4)

Addressing a moving target

Removing the cataract in a pediatric eye is only part of the procedure; a child's eye is still growing, so implant choice is critically important. Indeed, the growing eye represents a moving target – with the surgeon attempting to predict the development of the eye's future refractive error.

When an adult has cataract surgery, refractive error is corrected at the same time, making cataract surgery a truly refractive procedure. In a pediatric eye,



"Pediatric cataract surgery is exceedingly challenging but not impossible."

it is the opposite. When the cataract is removed, so too is an essential regulator of refractive error in the growing eye. The lens is replaced with an implant that does not change, thereby derailing the process of emmetropization. And that's why the procedure is only performed when absolutely necessary.

To summarize, pediatric cataract surgery is exceedingly challenging but not impossible. In such cases, it is helpful to remove the unknowns and create a process for as much of the surgery as possible to ensure a good outcome. With Omidria now FDA-approved for preventing intraoperative miosis and reducing postoperative ocular pain in children, pediatric surgeons can have added confidence and greater predictability of outcomes while performing these complex procedures.

M. Edward Wilson is the N. Edgar Miles Professor of Ophthalmology and Pediatrics and Director of Fellowship training at the Storm Eye Institute, Medical University of South Carolina Charleston, SC, USA.

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NextGen

Research advances
Experimental treatments
Drug/device pipelines

Off the Beaten Pathway

The development of a geographic atrophy therapeutic may be one step closer

By Peter K. Kaiser

The drug development process is long and arduous, which can be exasperating for both patients in need of a treatment – and the physicians charged with their care. But patients in the advanced stages of dry AMD known as geographic atrophy (GA) are more than frustrated by the lack of approved treatments, as the progressive and irreversible loss of retinal photoreceptor cells leads to blindness.

And that's why I was so excited to take part in the ARCHER clinical trial (1). Phase II has just begun and will assess both the efficacy and safety of the anti-C1q ANX007 treatment, assessing GA reduction through non-invasive fundus autofluorescence (FAF).

A steep descent

So how does ANX007 work? It inhibits C1q, thereby inhibiting the immune pathway that is believed to be causing most of the damage – the complement cascade. Typically, the complement cascade pathways should aid the clearance of any pathogens. However, certain genetic mutations can lead the complement cascade to cause intrinsic damage; if left unchecked, this can lead to GA.

At present, the complement cascade is

"The future also looks bright for expansion of trials to other countries outside of the US – most likely focusing on regions with high GA prevalence, such as Europe."

known to be involved in GA, but this was not always the case – even though some of the earliest mutations discovered were known as complement cascade factors; each mutation increasing the risk of developing dry AMD. Some of the early genome wide association studies (GWAS) exposed different complement factors – related to mutations – deposited in drusen around GA lesions. And that has paved the way to a much clearer knowledge of GA pathology.

Better understanding of GA pathology has led to the idea of targeting this system to override the effects of the damaging mutations – preventing the degradation of retinal neurons. With C1q as an activator of a facet of the complement cascade, being localized in both drusen and around GA lesions, it makes sense to look at using a C1q inhibitor to potentially prevent damage to photoreceptors and other neurons in the retina.

Which pathway to choose?

There are three different pathways to activate the complement cascade: classic, alternative, and lectin. The anti-C1q treatment selectively blocks the classic complement pathway, leaving the two other pathways to maintain their normal function. Although the complement cascade is clearly causing damage in GA, it has extremely important responsibilities for immune function elsewhere. Therefore, inhibiting all three complement pathways would be inviting a high risk of infection and other complications. Another advantage of this single-pathway approach is reduced risk of off-target effects. In my words: it's better to use a sniper rifle to target what's really important, instead of using a bazooka to blow the whole thing up.

The path to targeting the complement cascade for GA has not previously been filled with success. There have been high profile clinical trials of therapeutics, aiming to inhibit the alternative pathway, which failed in both Phase II and Phase III; C3 and C5 inhibitors, which block alternative and lectin pathways respectively have proven to be ineffective. Luckily, researchers have learned from those failures and instead chosen to target the classic pathway – potentially, with much better results.

Although we are at an early stage of our clinical studies, there have been no indications of drawbacks or safety concerns; intravitreal ANX007 was well tolerated and fully inhibited C1q in Phase I. These results obviously follow on from strong preclinical studies that, very excitingly, improved the health of neurons, protecting against photoreceptor loss – a major pathological feature of GA. Though the treatment has had fantastic results so far in both preclinical and Phase I studies, expectations must of course be checked; after all, we are talking about a new treatment and a new target. Though I'm unable to guarantee that this treatment is the best new thing out there, I can say that it has been shown to prevent the off-target effects that blocking everything – the "bazooka approach" – may cause, which I find very exciting.

New paths?

The promise of precisely targeting one complement pathway has also brought enthusiasm from other ophthalmologists. The neuroprotective effect observed has been exclusive to C1q complement cascade inhibition, and has translated into neurodegenerative disease models – giving insight into neurodegeneration pathology, and possibly an additional avenue for ANX007. This shared neuroprotection between anti-C1q in the eye and in the brain is exciting; what happens in Alzheimer's disease is scarily mirrored in dry AMD – the parallel systems of pathology are fascinating.

What's next for this therapeutic? Due to the slow progression of disease and regulatory requirements, it is likely to take 5–7 years before ANX007 can be brought into clinical practice. Although this wait will seem far too long for many, it should be worth it in the end. As GA prevention is one of the biggest unmet needs in ophthalmology, filling clinical trials with patients is extremely easy; they are desperate for anything that we as ophthalmologists can do to reduce their risk of going blind.

The future also looks bright for expansion of trials to other countries outside of the US – most likely focusing on regions with high GA prevalence, such as Europe. GA is a huge problem across the globe, and with the absence of any therapeutics to combat the disease, any breakthrough would be welcomed.

Peter K. Kaiser is Professor of Ophthalmology at the Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, USA.

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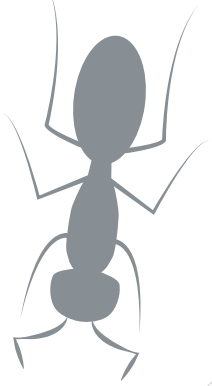

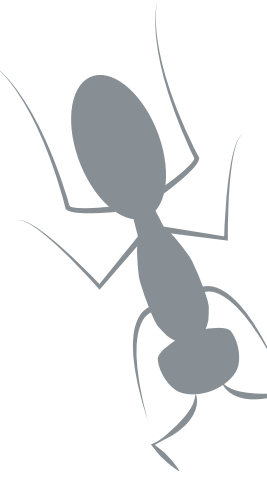

Not So Alien Ant Farm

A fully synthetic corneal implant improves accessibility and outcomes in corneal transplant surgery

By Gilad Litvin

Corneal transplants are currently limited by multiple factors; one of them is the fact that 50 percent of the world's population doesn't have access to corneal tissue, another is that 20 percent of patients are not suited for a transplant due to medical reasons. A completely synthetic alternative that can be stored on the shelf and implanted in a simple procedure when needed can solve this issue. This is where the CorNeat KPro artificial corneal implant I invented enters the fray. As the implant is fully synthetic, it does not require sourcing of corneal tissue harvested from either humans or animals, and has the potential to enhance accessibility of corneal transplants. A hurdle to success when implanting an artificial corneal implant into the body is to fool the cells into accepting the synthetic materials as part of the native tissue – so a biomimetic material that stimulates cellular proliferation, leading to tissue integration, is needed.

This is like when a child buys an ant farm. When they introduce ants to the farm, the ants don't know that they're not in the wild, so they carry on farming and making their home as good as ants will – the cells are similarly fooled and grow into the synthetic matrix we've provided by embedding the CorNeat KPro into the body.

How it started… and how it's going

Following my residency and subspecialty training in retina, I followed a career in developing medical devices, and drafted my first patent during my last years working for the public healthcare system. Since then, I've devoted most of my time to developing these devices, and much less to practicing ophthalmology. Currently, I see patients and perform surgical procedures one day a week, with the rest of my time spent on innovating.

I drafted the patent for the CorNeat KPro around 2015. It then took five years, using my experience in chemical engineering and biology, to create this synthetic cornea that integrates into and is biocompatible with the eye wall – with no signs of inflammation or infection. It is now in clinical trials and has already been successful in restoring the sight of a 78-year-old man who had been legally blind for a decade. This patient has had stable visual acuity for over three months now. This has allowed him to see his grandchildren for the first time, use the dials on his phone, and make his own coffee among other things – which may seem small, but make a huge difference to his quality of life and independence.

The success of this surgical procedure may be due to the engineering perspective used, with the implant being integrated into the vascularized white part of the eye. All previous attempts at corneal transplants have focused solely on the transparent, non-vascular, and mostly acellular cornea, but implanting in that location can reduce the ability for the new tissue to integrate with the eye as a whole organ. CorNeat KPro benefits from being implanted into the vascularized white part of the eye, where even small inflammation can be seen due to the blood vessels' presence, and the result is long-term and robust integration.

"The success of this surgical procedure may be due to the engineering perspective used."

Apart from filling the gap of inaccessibility to corneal transplants, CorNeat KPro also showed immediate improvements on the outcomes of patient vision when compared to current standards. The synthetic nature of the implant means that it can be tailored to the specifications of the eye, whereas when using human or animal corneal tissue, the sutures must be made precisely and there are always optical distortions.

First in human

Renowned corneal surgeon Irit Bahar,

Gilad Litvin and Irit Bahar.

Clinical Professor of Ophthalmology at Tel Aviv University and Chief Physician of the Department of Adult and Pediatric Ophthalmology at the Rabin Medical Center in Petah Tikva, Israel, is the principal investigator for the Phase I clinical trial, and she's been heavily involved in patient selection and recruitment. This collaborative involvement has been very important to arranging the best selection criteria possible – as any disagreements led to discussion, which in turn led to establishing the final protocol. Bahar and an experienced assistant trained with me a couple of times prior to the surgery, and I was granted special disposition by the Ministry of Health to attend and advise during the surgery to ensure the technique was implemented correctly – I looked down the microscope every few minutes to check how it was going. In the end, it was a very straightforward, hour-long surgery. The next day, the patient told us he slept well and had no pain. He compared it with his previous experiences of corneal implantation, which were very painful for him. We hadn't planned for our method to be less painful, but it turned out to be an additional advantage.

The moment when the patient's bandages were removed was very moving, with a mixture of anxiety and excitement. It was a culmination of five years of hard work on an ambitious project. The realization that our previously blind patient could now read digits on a board brought tears to our eyes, and it seemed like the patient was the calmest one in the room – in reality he was quite shocked and it actually took him a couple of hours to fully grasp what had happened. When I talked to him later, he was very excited.

Looking ahead

We have received approval in Canada for CorNeat KPro, and we are starting trials at centers in Vancouver and Toronto. These trials are being led by local professors, all of whom are worldwide leaders in the field. We have further implantations planned in Israel. We have submitted requests for approval in The Netherlands, France, and with the FDA in the US. Altogether, we have submitted applications for implantations in 50 patients. Once we have completed 30 of them, the plan is to stop the trial, follow the patients up for a year, and submit the final request for FDA approval.

Once approved, the primary indications will be in patients whose previous corneal transplantations failed or who are not suitable for them, before we can fully test safety and efficacy in a larger trial.

CorNeat KPro is only one of many patents for medical devices that I have developed over the years, and there are more projects on the way. One of them is using advanced chemical engineering, similar to the CorNeat KPro, to try and imitate the natural drainage pathways in the eye using fully synthetic means. This also involves tricking the body into believing the synthetic component is biological so that it can be accepted and integrated into the tissue. The glaucoma drainage device imitates the apparatus and physiological pressure of the eye to make this possible.

The concept of using biocompatible and fully synthetic devices has also enabled our expansion into other areas of medicine. For example, there are initial steps to use them in periodontology for gingival recession, and we've been approached by orthopedic surgeons and gynecologists, among others.

The surgical team.

This has been our core competency, enabled by the creation of an artificial extracellular matrix, or micro-tissue skeleton, which – when placed within the body – fools the cells into growing and regenerating the tissue like they would normally, just like ants make their home in an artificial ant farm.

Gilad Litvin is the Founder, Chairman and Chief Medical Officer of CorNeat Vision, based in Sde Warburg, Israel.

Profession

Your career
Your business
Your life

The Aspiring Eye Doctor's Guide to the Galaxy

Sohaib Rufai offers crucial advice on how to secure an ophthalmic specialist training (OST) post

Interview by Geoffrey Potjewyd

What inspired you to write your book: A Practical Guide for Aspiring Ophthalmologists?

I have always loved teaching. In recent years, I have enjoyed teaching aspiring ophthalmologists and, to my delight, many have successfully secured their ophthalmic specialist training posts, which is our British equivalent of "matching" to an ophthalmology residency! These residents, along with my peers, strongly encouraged me to write this book so that this teaching and advice is more widely accessible.

It was a long and challenging process, taking one year from inception to publication, but I am thrilled to see the book published at last, and already ranking top of the Amazon ophthalmology bestseller list! I hope it helps many more aspiring ophthalmologists achieve a brilliant and fulfilling career.

What was your personal experience of the ophthalmology training application process? Would you make any improvements to the current system?

Given the immense popularity of ophthalmology as a specialty, the

Sohaib Rufai

application process is extremely competitive. I was most fortunate to discover ophthalmology as a career option relatively early on in medical school, which gave me a head start. I learned the fundamentals of clinical ophthalmology by spending a lot of time in the department. I showed a lot of enthusiasm to learn more, so a number of consultants offered me many opportunities such as audits, research projects, teaching sessions to organize, all of which earned a lot of "points" for my future application. In essence, I brought extra enthusiasm and a "Completer-Finisher" attitude! However, even if the decision to pursue ophthalmology is made later on, it is still possible to secure a training post – provided one takes the right steps and prepares well.

I encountered both direct and indirect challenges during this process. Direct challenges included the highly competitive scoring system for the portfolio, the Multi-Specialty Recruitment Assessment (MSRA), which tests general medical knowledge not limited to ophthalmology, and the unpredictability of interview station topics. Indirect challenges included balancing my medical studies and foundation training with my interest for ophthalmology, seeking ethical approval for projects, securing funding to attend conferences, finding time to meet busy supervisors, and maintaining a good work-life balance.

In an ideal world, I would like to see more ophthalmology training posts created. This would enable more aspiring ophthalmologists to enter this fantastic specialty and help to meet the growing demand for eye care provision, particularly due to our aging population with increasingly complex care needs.

What is the best way to boost your score across all sections?

I would say the best thing you can do is develop a genuine enthusiasm for ophthalmology – and then get organized, work smart, and spend time with an ophthalmologist or ophthalmology department. Working smart involves being strategic with your time, setting realistic timelines, and communicating effectively. Make lists of the portfolio sections, interview scenarios, revision topics, and work through things systematically and well in advance to boost your chances of success.

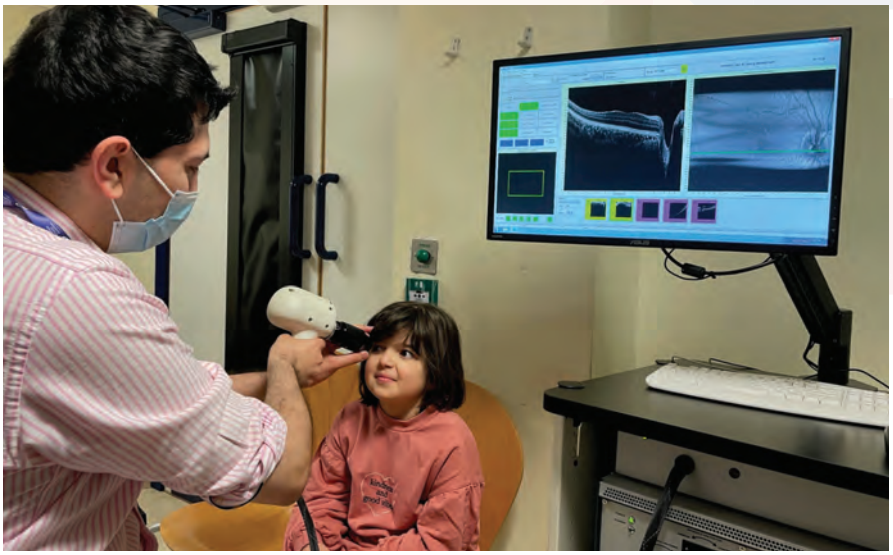

Figure 1. Rufai examines a patient with handheld OCT – 3D imaging of the retina and optic nerve (image taken and shared with parental consent).

"In an ideal world, I would like to see more ophthalmology training posts created."

Most ophthalmologists tend to be friendly people and will do what they can to help you. A small number may go the extra mile and offer to take you under their wing, mentor you, and really help you flourish. That's how you can unlock the majority of the "points" in the application – but you will only get all these opportunities by being organized, showing up, and making your face known.

Ophthalmologists can be found in the eye department, via their secretaries, in their offices, at local or regional ophthalmology teaching sessions, or at ophthalmology conferences. They are more likely to respond to emails if they have met you face-to-face beforehand – even briefly – and if your email lands in their inbox at the right time, such as during their admin sessions. Secretaries can be extremely helpful with this sort of advice, so aim to build good relationships with them. I appreciate this is all challenging with the current COVID-19 restrictions, but even if your only initial opportunities include attending the ophthalmology departmental virtual teaching sessions or local conferences, make sure you have your camera on to at least make your face known.

In summary, prepare early, reach out to people who can help you, show genuine enthusiasm, and the opportunities will come your way. And don't forget to enjoy the journey!

Figure 2. Rufai's best Rocky impressions: 2009 (left) just prior to entering medical school; 2019 (right) as a Visiting Scholar to the Children's Hospital of Philadelphia, Pennsylvania, USA.

Why is ophthalmology one of the most popular and rewarding specialties in medicine?

Ophthalmology continues to deliver incredibly high patient and doctor satisfaction. It offers an exciting mix of medicine and surgery, with a favorable work-life balance.

The eye is a fascinating organ which, uniquely, can be directly examined without breaching its integrity. It can also provide vital information about a patient's general health – indeed, the developing field of oculomics involves identifying ocular biomarkers of systemic disease, with particular use of non-invasive imaging methods, such as optical coherence tomography (see Figure 1). Ophthalmology is also at the forefront of health research across many disciplines, including artificial intelligence, gene therapy, stem cell research, and more.

In the UK, I have found the ophthalmology community to be warm, welcoming, and tightly knit, with pleasant colleagues and working conditions. Although the clinics tend to be heavily booked, ophthalmologists are well supported by the wider team and advanced technology. Due to the sessional nature of the work, ophthalmologists have opportunities to divide their time to pursue other interests such as teaching, research, management, private and voluntary work, among other things. With a huge variety of sub-specialist interests within ophthalmology, there really is something for everyone.

Does the book include advice or opinions from other ophthalmologists with different experiences?

Yes – I have sought advice from peers and seniors throughout my journey, from getting into ophthalmology myself to writing this book. And my colleagues provided their valuable opinions on my book prior to its publication. I must especially thank I. Christopher Lloyd, Head of Ophthalmology at GOSH, for reviewing the book and writing the foreword, plus Hussein

"It takes much longer than you might imagine to prepare a competitive application."

Almuhtaseb for his stunning fundus images.

I also consulted the Royal College of Ophthalmologists' official guidance available online, but I must note that my book does not represent nor is it affiliated with the Royal College of Ophthalmologists – it is simply my humble attempt to support aspiring ophthalmologists. The book does not contain any shortcuts or secret inside information, rather it provides guidance and strategies to prepare a competitive application using a systematic approach.

What is the most important thing to know when securing an ophthalmic specialist training post?

It takes much longer than you might imagine to prepare a competitive application. This applies to all aspects of the recruitment process, from the MSRA to the portfolio and interview. Therefore, it is important to prepare early and prepare well.

In recent years, the UK's Royal College of Ophthalmologists has put more emphasis on the MSRA. Ample time should be invested in preparation for it to achieve a strong score, as this determines whether a candidate is shortlisted for interview, and contributes to their overall score for ranking.

Depending on the candidate and their career background, it can take more than a year to develop a strong portfolio covering all the sections, including commitment to specialty, presentations, and publications. The interview also requires ample time for preparation, as so many possible scenarios could come up. It is always better to be overprepared!

Who can benefit from the advice given in the book?

It is primarily written for applicants to UK-based ophthalmology training; however, a lot of the content is broadly applicable and helpful for med students/doctors from other countries who are interested in an ophthalmic career. For example, the book contains clinical knowledge exercises covering common and important ophthalmic conditions and systemic conditions manifesting in the eye, ophthalmic CV boosting and careers advice, critical appraisal, communication skills, audit and quality improvement, presenting, publishing, prizes, and more.

My book hopefully fills a gap in the UK market for an up-to-date print book for aspiring ophthalmologists – a systematic approach to the application and interview is provided with practice stations and solutions, plus high-quality clinical images. To my delight, it is already proving popular amongst aspiring ophthalmologists. Of course, there are countless other fantastic print books and e-books in the field of ophthalmology and all its subspecialties..

Which movie provides the best analogy for your book? Is the application process described within its pages more like The Lord of The Rings (extended cut), The Revenant, or Rocky – or does it have a more coming of age feeling like Star Wars: The Force Awakens or A Star Is Born?

It's funny you should mention this. Back in 2009, I was on holiday in Philadelphia, US, which is where I found out I was going to medical school at the University of Southampton. To live out my childhood dream, I ran up the Rocky steps outside the Philadelphia Art Museum, and did my own Rocky celebration. Ten years on, in 2019, I was invited to deliver the Grands Rounds lecture as a Visiting Scholar to the Children's Hospital of Philadelphia. As you can see in the photos (see Figure 2), not much has changed! It's difficult to say which movie analogy best describes my book, but Rocky clearly played a part in my overall journey!

If you could give your younger self one piece of advice, what would it be?

Don't be afraid to reach out and ask for help. Ophthalmologists tend to be friendly people who are usually willing to help any enthusiastic student or junior doctor expressing genuine enthusiasm for ophthalmology. What's the worst that could happen? They say no, the project doesn't work out, or your paper gets rejected. Realize that every experience is a lesson – reflect, stay positive, and learn to bounce back. What's the best that could happen? You build good relationships with the right people who want to see you succeed, and you enter a positive cycle of positive thinking, positive results, experiential learning, and achievement. The sky's the limit!

And if you could distil the book down to one key message?

By taking the right steps and preparing well, you too can achieve a fantastic and fulfilling career in ophthalmology.

Sohaib Rufai is NIHR Doctoral Fellow and Specialist Registrar in Ophthalmology, Great Ormond Street Hospital, London, and the University of Leicester Ulverscroft Eye Unit, Leicester, UK.

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A Vision for Ophthalmic Pathology

Sitting Down With… Sarah Coupland, Professor and George Holt Chair of Pathology at the University of Liverpool, leader of the Liverpool Ocular Oncology Research Group, and Honorary Consultant Histopathologist at Royal Liverpool and Broadgreen University Hospitals NHS Trust, UK

What inspired you to the ophthalmic field?

My father was a medical oncologist and my mother was a nurse, so I grew up with "medical speak" over the dinner table – it became second nature to me. After graduating from medicine in Sydney, Australia, I moved to Berlin, Germany, and began a PhD in ophthalmology. I examined the immune mechanisms involved in corneal rejection, which meant performing corneal transplants in rats followed by histological and immunohistological examination of their eyes. And that's how I rediscovered my enthusiasm for the morphological understanding of disease mechanisms.

After completing my PhD, I did a three-month elective with William Lee in Glasgow, UK – a period during which I finally made the decision to specialize in histopathology. I then spent seven years training in general pathology with Harald Stein at the Charité Benjamin Franklin in Berlin – at that time a referral center for lymphomas, head and neck surgery and ophthalmic tumors – and emerged with a number of pathology subspecialties under my belt.

You make it sound straightforward, but there were a few "bumps in the road…"

I've not encountered what I would consider true adversity, but I have experienced a number of challenges along the way. Learning German in my mid-twenties to a sufficient standard to work as a pathologist, write complicated medical reports, and teach students was particularly demanding. To complicate things further, human anatomy in the German medical system is still described in Latin, so I had to learn that as well!

The most dramatic (and literal) bump in the road was my pregnancy with triplets near the end of my pathology training. Unfortunately, my contract was due to end during my maternity leave, and there was a strong prevailing opinion that I was unlikely to return to work – so there was considerable doubt that I would have a job to return to at all! Luckily, I was able to organize a phased return to work. I completed my training two years after the children's birth (despite the complication of HELLP syndrome, which put us all in intensive care for a few weeks!) and then submitted my Associate Professor thesis, becoming the first female "Privat Dozent" from the Stein lab.

What is unique about ophthalmic pathology?

As an ophthalmic pathologist concentrating on ocular oncology, I interact closely with clinical teams. Ophthalmological diagnoses are very reliant on morphology and images. The beauty of the eye – and the surrounding structures – is the ability to see many pathologies in situ in the patient, which can allow for easier interpretation of the samples. That being said, many cases are difficult because the samples are tiny! For example, intraocular biopsies of the choroid or vitreous can be very demanding; one is expected to squeeze out as much information as possible: morphology, immunophenotype, and genotype.

My favorite aspect of the work is making a difficult diagnosis in a timely manner to improve a patient's outcome. The typical scenario would be a vitreous biopsy for suspected vitreoretinal lymphoma. These are notorious for the fragility of the tumor cells and the relatively high rate of non-diagnostic samples. By working closely with the vitreoretinal surgeons, we have been able to make recommendations with respect to how the sample is taken, transported, and processed in the lab to improve the diagnostic yield. And that is essential because vitreoretinal lymphomas are high-grade tumors where diagnostic delays must be avoided.

"The pandemic has actually brought me closer to my research team."

What is your proudest professional achievement?

Receiving the ICO's Award for Ophthalmic Pathology in 2018 at the World Ophthalmological Congress in Barcelona. This award is given out only every four years to someone who has consistently supported training and research in Eye Pathology. It was instigated by Gottfried and Lieselotte Naumann of Erlangen, Germany, and involves an international competitive selection process. Together with William Lee from Glasgow, Naumann was one of my mentors during my training as an eye pathologist. To be chosen amongst the previous awardees was a great honour for me.

How has your life changed during the COVID-19 pandemic?

The pandemic has actually brought me closer to my research team. I used to rush between buildings, cities, and countries – but a lot of time can be saved through virtual platforms.

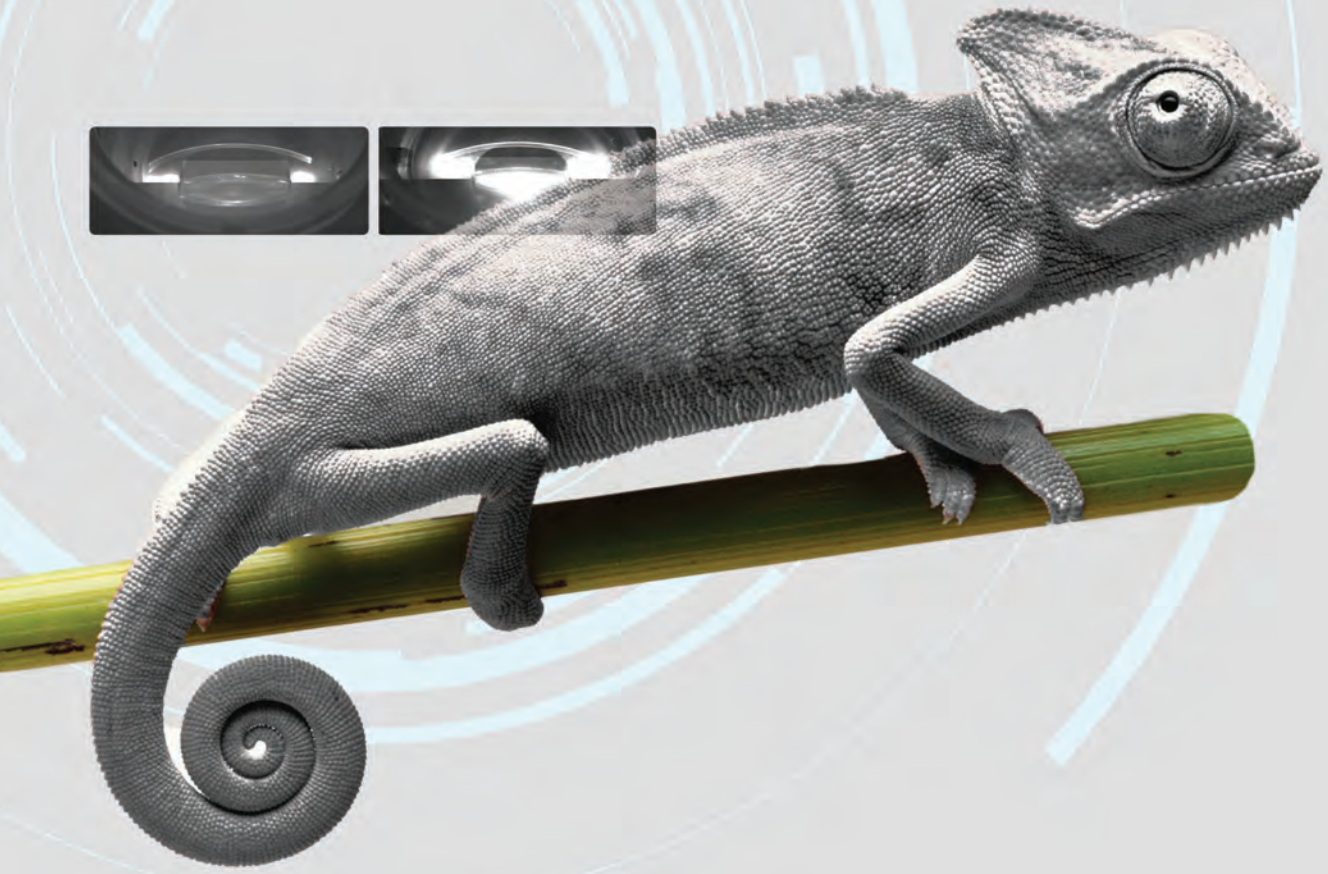
If you could go back in time to give yourself some advice, what would you say?

Pick your battles. Don't waste time on things that take you away from science. And don't spend too much time writing long emails!

Outside of work, what makes you happy?

My three children make me very happy and proud, and beyond them, I very much enjoy cycling, walking, photography, music, and delicious seafood!

Cataract technology that adapts?



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