JANUARY / FEBRUARY 2023 # 65

the Ophthalmologist™

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WHAT COULD SHE SEE THIS YEAR?

6,250 PATIENT CHARTS

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

Inspired by a real patient with DME.

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.

TRUST THE #1 PRESCRIBED ANTI-VEGF FDA APPROVED FOR WET AMD, DME, AND MEfRVO*

*IBM Truven MarketScan data: number of injections administered from Q4 2018 through Q3 2019; Data on file.

Proven first-line efficacy

- **Powerful efficacy** and **robust anatomic outcomes** across all indications as shown in phase 3 clinical trials[1-8]
- A broad range of indications and **dosing flexibility** across several FDA-approved indications[1]

Demonstrated safety profile

- **Demonstrated safety** profile across 4 VEGF-driven retinal diseases: Wet AMD, DR, DME, and MEfRVO[1]

A legacy of clinical experience

- **9 years** of extensive real-world experience[1]
- **≈13 million** doses administered to **>1 million** eyes since launch (and counting)[9]

EYLEA® (aflibercept) Injection 4 U℠

A COMPREHENSIVE PATIENT SUPPORT PROGRAM TO HELP FACILITATE ACCESS TO EYLEA

- 82% of payers offer access to EYLEA first line, covering **>272 million** patients[9,†]
- As of June 30, 2020, EYLEA4U® has provided **>4.4 million** total support services to eligible patients prescribed EYLEA[9]

†Data represent payers across the following channels: Medicare Part B, Commercial, Medicare Advantage, and VA. Individual patient coverage is subject to patient's specific plan.

DISCOVER WHAT ELSE YOUR PATIENTS COULD SEE WITH EYLEA AT HCP.EYLEA.US

anti-VEGF, anti–vascular endothelial growth factor.

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.** Heier JS, Brown DM, Chong V, et al; for the VIEW 1 and VIEW 2 Study Groups. Intravitreal aflibercept (VEGF Trap-Eye) in wet age-related macular degeneration. *Ophthalmology.* 2012;119(12):2537-2548. doi:10.1016/j.ophtha.2012.09.006 **3.** Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, et al. Intravitreal aflibercept injection for neovascular age-related macular degeneration: ninety-six-week results of the VIEW studies. *Ophthalmology.* 2014;121(1):193-201. doi:10.1016/j.ophtha.2013.08.011 **4.** 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 **5.** Campochiaro PA, Clark WL, Boyer DS, et al. Intravitreal aflibercept for macular edema following branch retinal vein occlusion: the 24-week results of the VIBRANT study. *Ophthalmology.* 2015;122(3):538-544. doi:10.1016/j.ophtha.2014.08.031 **6.** Boyer D, Heier J, Brown DM, et al. Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase 3 COPERNICUS study. *Ophthalmology.* 2012;119(5):1024-1032. doi:10.1016/j.ophtha.2012.01.042 **7.** Holz FG, Roider J, Ogura Y, et al. VEGF Trap-Eye for macular oedema secondary to central retinal vein occlusion: 6-month results of the phase III GALILEO study. *Br J Ophthalmol.* 2013;97(3):278-284. doi:10.1136/bjophthalmol-2012-301504 **8.** Wykoff CC. Intravitreal aflibercept for moderately severe to severe non-proliferative diabetic retinopathy (NPDR): 2-year outcomes of the phase 3 PANORAMA study. Data presented at: Angiogenesis, Exudation, and Degeneration Annual Meeting; February 8, 2020; Miami, FL. **9.** Data on file. Regeneron Pharmaceuticals, Inc.

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

03/2021
EYL.21.02.0021

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

Looking Forward, Looking Back

Welcome to the New Year – new faces, new plans and new content.

The beginning of a New Year is always a good time to take a moment to look both forward and back, to allow oneself to be both introspective and excited about what is to come. Perhaps you are someone who enjoys the challenge of resolutions, or, setting goals for the future in terms of research and medical practice. Patient groups and doctors often try to encourage their patients into good eye health resolutions – though the continued need for these efforts suggests that even here, patient compliance is still a struggle!

You may notice some new faces here as I'm delighted to be taking over from Aleksandra Jones as Editor and we have Sarah Healey as our new Associate Editor working alongside Associate Editor Oscelle Boye. I hope you will all get to know both Oscelle and Sarah through their outstanding contributions here and through their management of The Ophthalmologist newsletter.

As we bid Aleksandra a fond farewell I wanted to say that she has been a fantastic role model for me, and many other writers, steering The Ophthalmologist through 40 issues and bringing much needed attention to some of the most important stories in ophthalmology. Aleksandra is moving on to take up the editorship of our sister publication The Pathologist and I am sure that readers everywhere will want to join me in wishing her all the best and thank her for her years of incredible work.

As Aleksandra moves on, it is my New Year resolution to ensure that The Ophthalmologist continues to cover the most important stories, news and breakthroughs that make this field so interesting, and to do so with the rigor, human interest and attention to detail that readers expect.

I'm hugely excited about the year to come, and getting to know the wider ophthalmic community. So, if I can ask two things of you for this year, it would be this. First, say hello! We're always keen to hear from our readers via email if you have comments, ideas, suggestions or just want to introduce yourself.

Second: if you have research news, a new breakthrough to share or a strong opinion on the state of the field, we want to publish your work, because the more voices we can bring into dialogue with our readers and the wider ophthalmology community, the better for everyone.

Wherever you are in the world and however you might be spending it, I hope you too can see an exciting and rewarding year ahead.

All the best

Jon Greenaway
Editor

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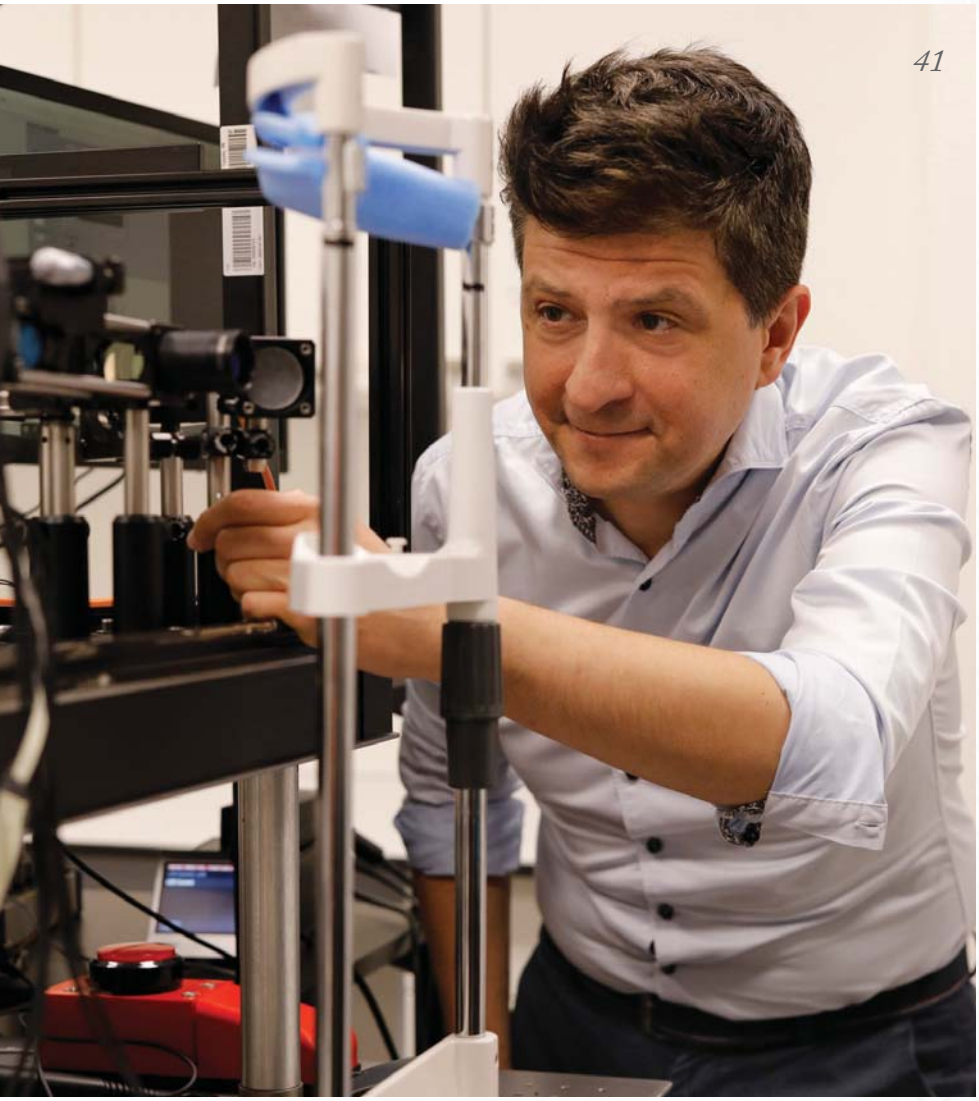

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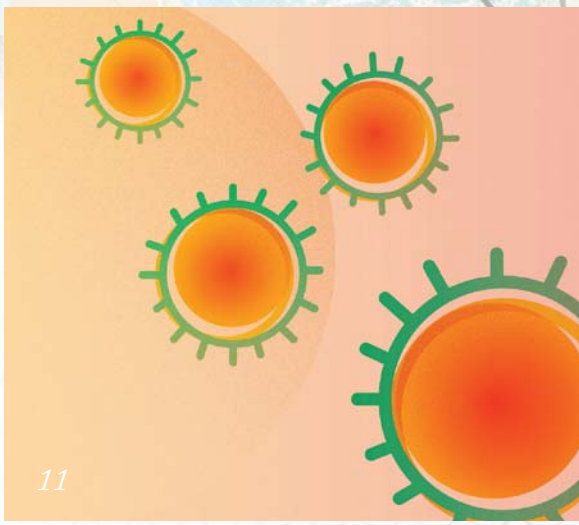

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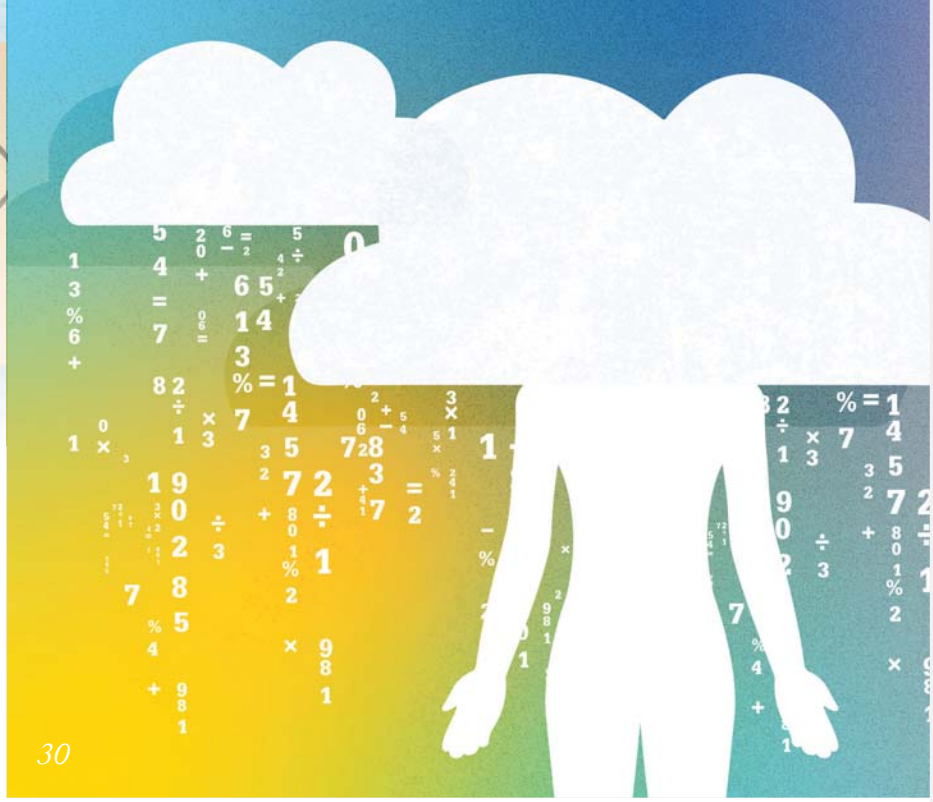

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the Ophthalmologist

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Lowering Lipids – and AMD

Researchers find that lipid-lowering and antidiabetic drugs are associated with lower AMD prevalence

AMD is the leading cause of severe visual impairment and blindness in high-income countries, particularly in the over-55 age group. In Europe alone, 67 million people are affected by AMD (1) and this figure will only increase as the population continues to age. Despite the condition's growing prevalence, few preventative interventions are available.

However, new research offers a promising pathway for the future of AMD treatment. In a meta-analysis of 14 population-based and hospital-based European study cohorts, researchers found an association between the systemic use of lipid-lowering drugs (LLDs) and antidiabetic drugs and lower AMD prevalence. As well as lowering serum levels of low-density lipoprotein and triglycerides, some LLDs also have anti-inflammatory and antioxidant properties that affect AMD pathogenesis (1).

Although previous research has investigated the impact of antidiabetic drugs on AMD, these studies conflicted and were not transferable to the general population because they included diabetic patients whose condition could have interfered with AMD pathophysiology. This new study is the first that meta-analyzes individual-level data, rather than aggregated results.

Despite the study's promising outcomes, the authors stress its limitations and call for further research. The limitations include issues such as cross-sectional data collection that didn't assess causality or risk and the fact the patients involved were taking LLDs or antidiabetic drugs for primary purposes, making it impossible to evaluate the drugs' effects on healthy individuals. Combining these limitations with previous controlled trials that failed to show a causal relationship, it is clear that – although this research paves a new path for the future of AMD treatment – more longitudinal research is needed to better understand the relationship between AMD and systemic medication.

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INFOGRAPHIC

Clearer Skies, Clearer Eyes

The Montreal Protocol has led to an estimated 33 million fewer cataract cases

The Montreal Protocol was enacted in **1987** to protect the ozone layer from ozone-depleting substances (ODSs)

This has been amended since **1987** to expand the list of controlled ODSs and adjust to the phaseout of ODS production

SPOTLIGHT ON ARVO

Keep up to date with the latest research from ARVO journals through our research breakdown

Stair-Gazing

Where do we look when we walk up and down staircases we are familiar with? Researchers conducted a frame-by-frame analysis of 30 participants engaging in a navigation task in their own houses whilst wearing glasses containing a wearable eye tracker and camera (1). Their findings, demonstrate that people often look at familiar steps sequentially, on average directing their gaze at about half of the steps. Their results echo previous studies conducted under constrained lab conditions, whilst also introducing new analysis for better understanding stair climbing gaze behavior.

Food for the Eyes

To determine the associations between fatty acid intake and the prevalence of age-related macular degeneration (AMD) under a population-based cross-sectional study, researchers conducted eye screening on residents of Chikusei City in Japan (2). Although saturated fatty acid intake was inversely associated with the prevalence of AMD in men, only a significant association was observed between the second quartile of linolenic acid intake and the prevalence of any AMD in women.

BKC Breakdown

A new, multi-institutional study screened and compared the proteomic make up of meibomian gland secretions between blepharokeratoconjunctivitis (BKC) patients and healthy individuals to identify target proteins potentially involved in the onset and progression of BKC. BKC patients had significantly lower eyelid margin cleanliness, higher palpebral margin scores, more serious clinical manifestations of secretions, and more damaged meibomian gland morphology compared with the healthy controls (3). S100A8, S100A9, ANXA3, and LCN2 were identified as BKC-associated proteins probably involved in the chronic inflammation of BKC

Dry-Eyed Dogs

New research conducted by researchers from the Department of Oral and Maxillofacial Surgery at Peking University School and Hospital of Stomatology looked to establish a novel Beagle dog model of dry eye disease (DED) (4). They found that a combined type of DED model was established through the removal of the orbital lacrimal gland and resection of the third eyelid. This model is easily accessible and stable over a relatively long time.

See reference online.

VR VFT

Increasing access to glaucoma screening in low income countries

The GlauCUTU – born out of a collaboration between the Department of Ophthalmology at Chulalongkorn University and the Faculty of Engineering at Thammasat University in Thailand – aims to offer a promising new pathway for VFT. Consisting of a VR headset and deep learning algorithms, the new perimetry system provides results clinically comparable to the Humphrey visual field analyser (HFA).

Researchers evaluated the GlauCUTU perimetry system in 31 participants and found that the GlauCUTU effectively differentiated glaucomatous eyes from normal eyes, with a shorter average test duration than HFA (1). Patient comfort was also reported to be greater in the GlauCUTU than HFA.

Visanee Tantisevi, one of the researchers of the study, says, "As accessibility to HFA in low-resource countries is limited, a novel VR technology that is portable and inexpensive has the potential to improve glaucoma care."

See reference online at: top.txp.to/vr/vft

Comparing the adjusted Protocol with a scenario of no controls on ODSs showed the prevention of an estimated

63 MILLION

cataract cases

Adjusting the Montreal Protocol resulted in an estimated

33 MILLION

fewer cataract cases

Skin cancer cases were also estimated to be reduced by

230 MILLION

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Smart(phone) Imaging

How smartphone cameras could be the latest must-have technology both in and out of the exam room

Fundus photography is an essential diagnostic tool, vital for monitoring the posterior segment. Yet, it is often deeply inaccessible in places where it could be most useful – emergency rooms or rural and underserved areas where ophthalmic examinations are needed, but can be expensive or difficult to obtain. Ophthalmic imaging equipment can be costly and take up much-needed space – so the growing demand means that new solutions have to be found. The newest generation of smartphones, with their exceptional cameras, could provide an answer.

Previous research has shown that smartphone based fundoscopy can be effective in diagnosing diseases such as diabetic retinopathy (1), but a new study suggests that phone-based fundus photography can be a great way to reduce the burden on first-point-of-contact healthcare providers and get high-quality images to eye care specialists more efficiently (2).

Images were obtained from 10 eyes with various posterior pathologies and given to 35 reviewers (21 residents and 14 attending physicians) for diagnosis and subsequent comparison with traditional fundus imaging. Posterior segment diseases investigated ranged from retinal detachment to optic nerve avulsion. The results showed that the probability of a correct diagnosis was over 78 percent and there was no difference in accuracy between residents and attending doctors – aside from one case in which residents actually outperformed the more experienced clinicians!

The range of pathologies presented showed that mobile imaging can even be applied in areas such as neuro-ophthalmology and uveitis – particularly important given that delays in diagnosis can lead to serious or even life-threatening illness. Given widespread familiarity with smartphone cameras, integrating their use into healthcare could cut staff training times, too. All of this would allow more doctors to take more images more efficiently. Although more research is needed to evaluate the strategy's long-term performance, the widespread availability of smartphones means they could offer an effective solution to currently underserved ophthalmic imaging needs.

See reference online at: top.txp.to/smartphone/imaging

Rapid Rod Recovery

Gene augmentation increases night vision in individuals with congenital blindness

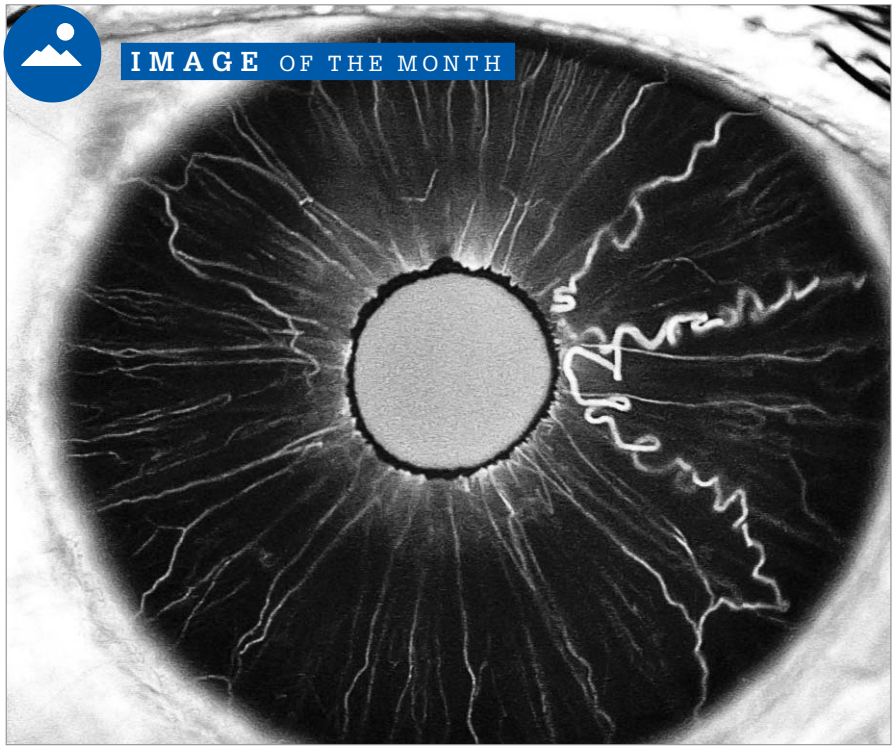
Leber congenital amaurosis (LCA) is a rare retinal dystrophy causing blindness or severe visual impairment at a young age. The condition stems from a GUCY2D gene mutation that causes a molecular defect in cyclic GMP production. LCA has long been considered untreatable and incurable – factors leading researchers from the University of Pennsylvania's Scheie Eye Institute to use adeno-associated virus (AAV) gene therapy in a revolutionary study that restored the night vision of two individuals with LCA, increasing their functional vision 1000-fold in a matter of days (1).

Samuel G. Jacobson, coauthor of the paper, said, "These exciting results demonstrate that the basic molecular machinery of phototransduction remains largely intact in some cases of LCA (2)."

The quick rod photoreceptor recovery indicates that, even after years of dormancy, visual pathways can be functionally restored with the addition of wild-type GUCY2D through gene augmentation.

See reference online at: top.txp.to/rapid/rod/recovery

IMAGE OF THE MONTH



Seeing The Form in The Iris

Iris Fluorescein Angiography using the Heidelberg Spectralis, highlighting Arteriovenous Malformation

Credit: Captured by Luke Carine, Advanced Ophthalmic Science Practitioner.

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

TWEET OF THE ISSUE

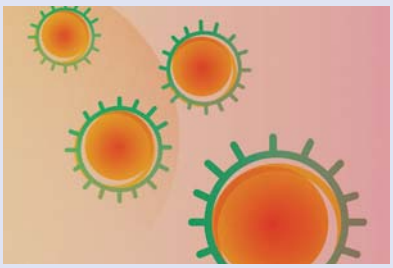
"I don't understand why curable blindness is a thing. Why don't governments step in and help? Even if you're thinking purely from a financial standpoint it's hard to see how they don't roi on taxes from people being able to work again."

Mr Beast - Youtuber

Seeing Through Long COVID

How ophthalmic markers could help with Long COVID diagnostic challenges

The common neurological symptoms of long COVID – brain fog and fatigue – are widely discussed, but a new paper suggests that it can also impact ophthalmic health (1). The study assessed 40 subjects who had recovered from COVID-19 alongside a control group. Each participant was assessed using National Institute for Health and Care Excellence (NICE) long COVID, Douleur Neuropathique 4 (DN4), and Fibromyalgia questionnaires, as well as corneal confocal microscopy to quantify corneal nerve fiber density.



The study highlighted those with long COVID show evidence of small nerve fiber damage that seems to be correlated with the seriousness of the initial infection. This builds on previous research connecting COVID-19 to issues such as Guillain-Barré (2). This new study raises the possibility of using corneal confocal microscopy as an ophthalmic test for long COVID.

See reference online at: top.txp.to/seeing/through/long/covid

THE OPHTHALMOLOGIST'S
TIME MACHINE: CHAPTER 9

One-Eyed Warriors: Federico da Montefeltro

With Stephen G. Schwartz, Christopher T. Leffler, and Andrzej Grzybowski

This is the first in a sub-series of famous one-eyed military leaders.

Figure 1. "Portraits of the Duke and Duchess of Urbino" by Piero della Francesca, Uffizi Gallery in Florence. Image courtesy of Andrzej Grzybowski

The loss of an eye is a highly unfavorable outcome in ophthalmology because it affects stereopsis, visual field, and overall quality of life. So it is perhaps surprising to find that many of history's most celebrated military commanders had monocular vision – typically the result of trauma.

Federico da Montefeltro was born in 1422 and served as the Duke of Urbino from 1474 until his death in 1482. As a condottiero (leader of a mercenary army), he amassed great wealth through repeated military triumphs, which he then spent lavishly as a great patron of the arts, assembling a magnificent library in the Palazzo Ducale. Today, he is probably best remembered as the subject – along with his wife, Battista Sforza – of a famous painting by Piero della Francesca entitled "Portraits of the Duke and Duchess of Urbino," which resides in the Uffizi Gallery in Florence and is shown in Figure 1.

The piece is notable for several reasons. The Duchess is depicted with a very high brow (an ideal at that time) and very pale skin. The light complexion was not only considered beautiful, but also reflected the fact that she died before the painting was completed. The Duke, in contrast, is depicted with a darker complexion – alongside multiple skin lesions, especially on the cheeks in a "warts and all" fashion, suggesting that this is how he really looked, rather than an idealized version. Further, there is an odd shape to his nose, with what seems to be missing tissue superiorly. Notably, the composition not only presented the couple as though they were staring into each other's eyes, but it also had the benefit of capturing the Duke's "better" side. He had no right eye.

Frederico is known to have suffered an eye injury in 1450 during a joust. Jousting-related eye injuries, while unusual, were occasionally reported; perhaps the most famous and historically significant was the injury to the French King Henri II, which ultimately proved fatal (1). What is unknown, and probably lost to history, is how the Duke's nose came to obtain its distinctive shape. It may have been injured at the same time as his eye; however, a more intriguing hypothesis is that the Duke requested nasal surgery to somehow compensate for his lost eye. This theory has been proposed repeatedly by both lay historians and physicians (2). And since we cannot know for certain whether or not the surgery actually happened, a more interesting question is: Would it have helped?

Many individuals will find that, if they close one eye, an inferonasal visual field defect may be detected, especially with the eye turned nasally. The effect might be enhanced when one considers the eye motion visual field (EMVF) or "maximum field of vision," which includes the additional visual field gained with eye movement. A study of normal binocular volunteers reported that mean EMVF measured 37 percent larger than standard binocular visual field measured without eye movement. In addition, EMVF increased with higher exophthalmometry measurements, demonstrating that facial anatomic variation can impact peripheral vision (3).

It is therefore possible that the removal of part of the Duke's nose may have allowed expansion of the EMVF of his remaining left eye – comparable to what might result if the eye could have been made more proptotic. Of course, the additional EMVF would have come at the cost of disfiguring surgery in an era prior to the introduction of anesthesia, antimicrobials, or antisepsis.

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See references online.

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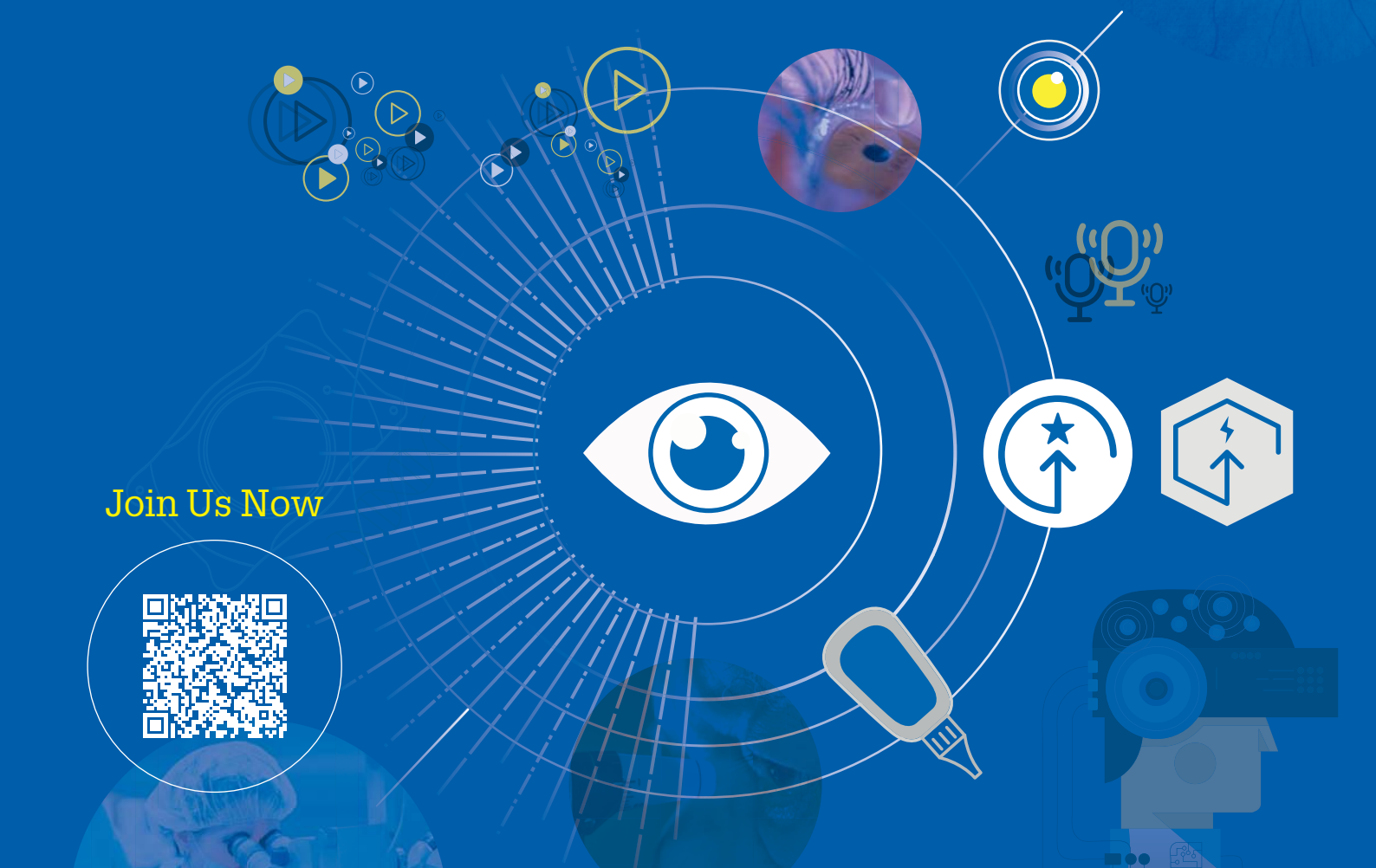

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In My View

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No Shortcuts to Surgery

Why optometric scope expansion bills endanger patient safety

By Rachel Reinhardt, Past-President of the Washington Academy of Eye Physicians and Surgeons and Associate Secretary for State Affairs, American Academy of Ophthalmology

Scope, scope, and more scope. This is a term that we as ophthalmologists have had to incorporate into our daily vocabulary of late – especially those on the front lines of the fight to protect patient safety in state legislatures. At the beginning of 2023, it's important to reflect on legislative wins and losses across the country. Although we lost our patient safety battles in Virginia and Colorado, we celebrated a major win in California with the veto of an optometric scope expansion bill that would have allowed optometrists to perform scalpel and laser surgeries. Nonetheless, the fight for patient safety is far from finished.

It is easy to feel "battle fatigue" from the number of scope battles that come year after year, but it is important to remember that patient safety prevails far more than it fails. In other words, the vast majority of optometry's attempts to expand scope have failed. But it takes an extraordinary amount of advocacy, energy, and money to keep our patients safe.

My hat goes off to all the state societies who, working in conjunction with the American Academy of Ophthalmology State Affairs, have dedicated their evenings and weekends, cancelled clinics to testify, and rallied the troops to stand up for our patients. We all have the same goal: to maintain the current high surgical standards for our patients by ensuring that their eye surgeries are performed by a medical or osteopathic surgeon. As one of my mentors once said, "There are no shortcuts to being a surgeon."

In Washington State, we were successful in defeating an optometry scope of practice bill in the 2022 legislative session, but the Washington Academy of Eye Physicians and Surgeons (WAEPS) expects another scope expansion bill to be introduced in the 2023 session. Like other state ophthalmology societies fighting similar bills, WAEPS will continue to fight the good fight and stand up for patient safety – as many times as necessary.

When patients are informed about the difference between ophthalmology and optometry education, the overwhelming majority want their eye surgeries performed by an ophthalmologist. And when details of these bills make their way outside the halls of the legislature, patients are shocked that these bills are even being considered.

You may ask, "What can we do?" Each and every one of us has a duty to educate our state legislators, the public, and our patients on this topic. Surprisingly few healthcare providers are in state government, so legislators rely on "experts" from their districts to help them understand the nuances of these issues. Become their expert. Become their resource. Reach out to your state senators and representatives today. Let them know you are an ophthalmologist – an MD or DO – who has been to medical school and completed a surgical residency. We all have meaningful relationships with optometrists and work with them on a daily basis, but legislators need to know that there is no such thing as a "half-surgeon."

If you are not already a member of your state society, join today and support the surgical scope fund (1). Ultimately, we have to protect our patients, who may not know the differences in education between optometrists and ophthalmologists. It is our job to make sure patients and legislators know the importance of a medical school education and surgical residency. Join national advocates, WAEPS, and the multitude of other state societies now as we continue to do the right thing – protecting our patients and helping to maintain the highest ocular surgical standards.

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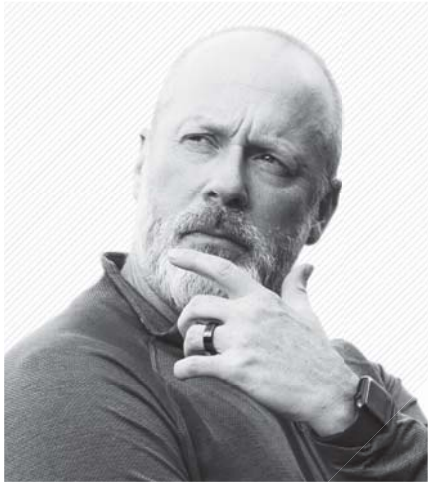
Are We Missing the Big Picture?

Why ultra-widefield imaging is essential for all



By John W. Kitchens is a vitreoretinal surgeon with Retina Associates of Kentucky in Lexington, Kentucky USA

Dilated fundus exams (DFE) are the very foundation of ocular disease evaluation. In fact, we are so accustomed to the DFE that we rarely consider whether we might be missing something significant.

But what if we are?

While chairing an interactive webinar on the applications of single-capture ultra-widefield (UWF) imaging, I polled the attendees (approximately 300 eye doctors) regarding their use of UWF (1). One question provided particularly surprising results. When UWF users were asked if they had ever found unexpected pathology in a patient with no visual complaints, 97 percent responded "Yes."

For those unfamiliar with UWF, this statistic may seem hard to believe. For me, a retina specialist who has used this technology for 12 years, it is not. Indeed, I have this experience almost every week. I suspect that almost any UWF user would have a similar story to tell.

An UWF retinal image, as defined by the International Imaging Study Group, refers to one that encompasses retinal anatomy anterior to the vortex vein ampulla in all four quadrants (2). The Optos technology, which I use in my practice, produces a non-mydriatic 200-degree (80 percent of the retina) single-capture image in less than half of a second.

Though I spend nearly all my clinic days examining retinas, I am continuously surprised by what I find with this technology. On some occasions, I have found something that was missed on a previous exam. On others, it has been unexpected pathology in a patient referred for something else entirely. Using UWF images, I have identified undiagnosed nevi, lattice degeneration, and asymptomatic horseshoe tears – pathologies that often present in the far retinal periphery. I am not an over-tester, but these experiences have led me to order UWF imaging for every patient.

The ability to identify and document retinal pathology is paramount no matter the specialty. As demand for premium IOLs expands, cataract surgeons surely need to know the status of a patient's retina prior to surgery. No one wants to find an undiagnosed epiretinal membrane in a patient with 20/30 or 20/40 vision after a perfect surgery. In the case of a spontaneous post-surgical retinal detachment, a pre-op UWF image documenting a healthy retina can confirm the detachment was not missed by the surgeon.

For general ophthalmologists, the majority of patients may have normal examinations, but for those who do not, the UWF image is incredibly useful for explaining the diagnosis and treatment recommendation, and even illustrating results by comparing pre- and post-treatment images. When a referral is needed, the image can help patients understand why they need to see a specialist.

"Though I spend nearly all my clinic days examining retinas, I am continuously surprised by what I find with this technology.."

When I receive UWF images from referring doctors, I'm able to quickly determine if or how urgently the patient needs to be seen, which also helps ensure efficient care by enabling us to more appropriately prioritize urgent cases. It also supports our referring colleagues by helping them avoid unneeded specialty visits.

One concern I have heard about single-capture UWF imaging is the equipment cost. Given that insurance generally does not cover routine imaging before a patient exam, this concern is understandable – but it is not insurmountable. In our practice, UWF has proven so valuable that we find it well worth writing off. Knowing we are not missing pathology enhances care and gives us peace of mind, and I'd argue that the documentation value of the images is priceless. Some general practices and optometrists build the cost of imaging into the exam fee; others offer it as a patient pay option. These doctors often report that patients ask for their image to be taken each year, despite the incremental cost. In

general, patients are happy to make the investment in their eye health – particularly when they are about to make an even greater investment in something like a premium IOL.

Another common concern is about the time an additional diagnostic test might require. In my experience, using UWF has actually contributed to greater efficiency. Because UWF devices are easy to use and require little training, my staff capture the images in the work-up area (freeing our photographers for more technical work). And that means I have the opportunity to see the macula, optic nerve head, and peripheral retina before I even sit down in front of the patient, thus informing where I need to focus my DFE in advance.

Without question a dilated exam is indispensable. However, it requires time, is subject to patient cooperation, and forces us to rely on dictation to a scribe and/or illustration done from memory for documentation. The aging population coupled with a shortage of eye care professionals means that we are all under pressure to see more patients each day, making a thorough DFE even more challenging. In the face of these obstacles, we must remain focused on the big picture: Doing all that we can to ensure we are providing the best possible care for our patients. With this in mind, single-capture UWF imaging has become an invaluable part of my practice. I strongly suspect that at least 97 percent of those who use this technology feel the same.

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A Robotic Revolution

How robotic surgery can improve access to quality eye care worldwide and alleviate surgical difficulty

By Joseph Nathan, President, co-Founder and Chief Medical Officer of ForSight Robotics

Cataract is responsible for 51 percent of blindness worldwide, making it one of the most detrimental eye diseases globally (1). Affecting over 24 million people in the US, nearly five times more that amount in China, and with world wide rates expected to double by 2050, cataracts disease has initiated a global public health emergency (2,3). As the average life expectancy soars, a larger portion of the population is affected by cataracts despite the disease being highly preventable.

As ophthalmologists we have to confront the questions – what is at the core of this global public health emergency? The answer is complex and multifaceted but includes a worldwide shortage in skilled eye surgeons who are able to operate on patients, and a lack of access to quality surgical eye care. Too many patients have simply been abandoned by the global healthcare industry. By neglecting an individual patient, the industry creates an unsustainable cycle that may have disastrous consequences on communities all around the globe.

There are over 28 million cataract surgeries performed every year around the world, placing cataract at the very top of the surgical procedures list (4). Despite the relatively simple surgical fix – a procedure lasting around 20 minutes, during which the clouded cataract lens is removed and a new clear lens inserted – patients are often forced to wait for months and sometimes years as their vision deteriorates before surgery is performed.

The growing gap between ophthalmologists entering the field and leaving is causing significant difficulties. In the US alone, there are at least 100 more surgeons retiring than entering the profession annually (5). Worldwide, an average of 31.7 ophthalmologists treat a population of one million, and when nearly 75 percent of a population is suffering from cataracts – as is the case in India, in adults over the age of 60 – it is clear that the demand for healthcare outweighs the capacity to provide it (6,7).

Beyond impacting a patient's quality of life, cataracts also place a heavy burden on society with estimations showing that the worldwide economic and health burden from visual impairment costs US$3 trillion annually in lost productivity (8). In China, despite approximately 80 percent of potential cataract patients living in rural areas, a shocking 70 percent of cataract surgery resources are located in urban centers (9). This lack of access to ophthalmic treatment leaves patients in a vicious cycle and indefinitely widens socioeconomic inequality.

As both the global shortage in cataract surgeons and the demand for cataract surgeries grow, it is clear that a purely human solution is no longer enough. The key to improving access to cataract surgery

lies in integrating novel technologies like artificial intelligence and automation into surgical eye care. By embracing developments such as robotics, healthcare providers can improve the quality of eyecare, empower surgeons, and raise surgical efficiency and reach.

Implementing robotic surgery into cataract procedures – and other ophthalmic operations – can have a significant impact on both surgeons and patients. Improving both a surgeon's career cycle and a patient's clinical experience, robotics enhances ophthalmic efficiency and success, extending its reach to ensure that millions of patients who currently lack access to treatment are provided quality surgical eye care.

Whether a novice surgeon at the beginning of their career or a veteran physician with thirty years and 15,000 cases of operating experience, a robotic platform's world-class methods can standardize ophthalmic procedures and enable surgeons to provide outstanding surgical care at every step. Robotic platforms – like ForSight Robotics' ORYOM – combine a vast set of analytical data points to implement the finest operation. Observing thousands of procedures and studying the world's leading ophthalmologists' methodology, the robotic platform is built to give every surgeon the ability to perform the most high-quality procedure during every single operation.

More than just a tool, robotic surgery is a source of empowerment, ensuring a more precise and accurate performance than the human hand. Filtering out even a minor hand tremor, robotics can relieve surgeons of unnecessary cognitive stress while providing a streamlined guide during operations. Monitoring, highlighting tools, and alerting when needed are just a number of the ways that AI-based algorithms provide guidance and surgical support during operations.

Today, two-thirds of ophthalmic surgeons experience work-related pain and nearly 15 percent plan to retire early due to poor ergonomics and medical issues that stem from prolonged poor posture (10). Surgical robotic platforms can be designed to alleviate the physical stress endured during surgeries, thus elongating ophthalmic careers and allowing surgeons to practice for a number of years beyond what is possible today.

Enhancing operational performance with robotics begins before a surgeon even steps into an operating room. Robotic surgery allows physicians to learn from, observe, and experience procedures that are happening on the other side of the world. In a leap for the industry, this method of apprenticeship opens new opportunities for surgeons who otherwise would not have access to top-tier ophthalmologists or leading fellowship opportunities. Through increased access to the highest quality resources, surgeons in developing regions or with limited resources can be given a new tool to enhance their practice and serve their patients with the best techniques.

Although promising, the ultimate question is, how can surgical robotics provide a solution for the gap between the increasing number of patients needing surgical eye care and the decreasing number of ophthalmic surgeons? ForSight Robotics' ORYOM is a prime example. Initially targeting cataract procedures, the surgical robotics platform is developed with 14 degrees of freedom, ensuring access to any point within the human eye. Surgical robotics need to pose a solution to more than one condition, and by allowing access to both retinal and subretinal regions, the robotic platform will be able to perform a wide variety of procedures. In turn, instead of focusing on one specific sub-specialty, this model will allow ophthalmic surgeons to expand their practice and treat a broad type of eye conditions and diseases – ultimately reaching a much wider patient population.

Opening up new horizons, robotics surgery allows surgeons to do what they love at the highest possible level with a broader reach than ever before. Early adopters of surgical robotic platforms have an opportunity to impact millions of people worldwide and redefine quality surgical eye care for generations to come. The healthcare industry must act now to promote the development and integration of novel technologies into ophthalmology. By democratizing surgical eye care, robotic surgery has the potential to disrupt the industry and, end today's global public health emergency.

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LANDMARK LITERATURE

Every year, the ophthalmology community takes significant steps towards increased speed, sensitivity, accuracy, accessibility, and more. Here, our experts each share papers that, for them, really stood out from the crowd. Here is the literature and research which has shaped ophthalmology over the last 12 months.


POSTAGE

One of the distinguishing features of ophthalmology as a field of medicine is the speed at which things can change. Innovation is driven by the medical profession but is also powered by high impact research that offers clinicians reliable data. Without research, innovation is unavoidably slowed, new knowledge doesn't come to light as quickly and doctors don't have the latest knowledge at their fingertips.

After another year where the headlines have been full of both news about breakthroughs and problems in healthcare systems worldwide, it is vital to have a clear sense of the state of the field. With that in mind, we gather some of the leading researchers and experts in the world of ophthalmology to offer their thoughts on the landmark literature of the last 12 months. Here's the research which has shaped the field and offers valuable insight into where ophthalmic research might be headed into the year to come. We also spend some time digging into the numbers of how publication data has shifted over the last few years in some of the most popular current areas of ophthalmological research to see where important patterns may emerge.


Jugnoo Rahi

Jugnoo Rahi, Professor of Ophthalmic Epidemiology and Consultant Ophthalmologist, Chair of the Academic and Research Committee of the Royal College of Ophthalmologists (RCOphth) and Director of the Vision and Eyes Group at Great Ormond Street Institute of Child Health

My aim with my choices is to draw readers attention to literature that they might not have noted but which, in my opinion, addresses some of the key issues relating to health in general. These key pieces of academic literature are all reviews or reports of some sort – i.e. the carefully evidenced and rigorously synthesized work that people often forget is critical to changing practice or policy on a large scale.

Landmark paper: P. Rajpurkar, et al., "AI in health and medicine", Nat Med 28, 31, (2022), PMID: 35058619.

This article offers a summary of a two-year long tracking of the developments in medical AI. This is important for ophthalmologists to give some close attention, as there has been much interest in our field about the potential of AI to transform imaging, treatment and diagnostics. However, this paper shows that beyond the hype there is much work to be done to realize the potential to improve healthcare and outcomes for all. Despite the excitement, there remain serious technical and ethical issues from the availability of data to the now well-covered problems of racial bias that still have to be addressed.

Landmark paper: JD Sachs et al., "The Lancet Commission on lessons for the future from the COVID-19 pandemic" Vol 400, 1224, (2022) PMID 36115368.

At this point it may feel like there is little more to say about the impact of the COVID-19 pandemic but the Lancet Commission on the topic is unequivocally correct in describing it as a profound tragedy and a massive global failure on multiple levels. It is impossible to overstate the impact of the COVID-19 pandemic – not just in terms of simple infection numbers but the knock-on effects that go all the way from global healthcare infrastructure to the impact of long COVID. This report sets out the lessons learned that we must not ignore about global health collaboration and pandemic preparedness if we are to avoid repeating the same struggles in the future.

Landmark paper: M. Romanello, et al., "The 2022 report of the Lancet Countdown on health and climate change: health at the mercy of fossil fuels," Vol 400, 1619, (2022) PMID: 36306815.

It's hard to avoid the fact that we are living in a time of multiple crises, all of which impact healthcare in a variety of complex and interlocking ways. This report is detailed and makes the links between anthropogenic climate change and serious consequences for health and wellbeing on a global level painfully clear. Increases in dengue fever, heat related death and the conditions for vibrio pathogens to develop are all directly linked to climate change. There is emerging evidence about the risks to ocular health e.g. associations between air pollution and its impact on specific eye conditions. Furthermore, ophthalmic surgery can often be very resource intensive, producing a lot of waste and previous research has shown the cataract surgery has a relatively high carbon footprint. We all have our part to play, and ophthalmology is no different. One of our biggest challenges is making sure our treatment pathways are getting good outcomes for our patients and helping safeguard the environment.

Landmark paper: N. Halasa, M.D., et al, "Maternal Vaccination and Risk of Hospitalization for Covid-19 among Infants," N Engl J Med, 387, 109, (2022) PMID: 35731908.

Based on a case-control test negative design, this paper assessed the remarkable effectiveness of maternal vaccination during pregnancy against hospitalization for Covid-19 among infants younger than sixmonths of age. This paper reminds us of the importance of the link between mothers and children's health and the often profound impact of antenatal interventions - this applies as much to childhood blindness (one of my own particular research interests) as it does to other areas of health, as exemplified in the World Health Organization's recently published Package of Eye Care Interventions (PECI) which includes a specific module on children.

Landmark paper: World Health Organization, Package of Eye Care Interventions (2022)

Landmark paper: Available at https://bit.ly/3Y3bWmt~

Given our work with the Vision and Eyes Group, this report from the World Health Organization is my final choice. My colleague Dr Lola Solebo and I had the privilege of being the UK members of the international expert group that

Seven of the most read articles from major ophthalmology journals over the past five years.

1. Z. Ling Teo, et al., "Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045," Ophthalmology, 128, 1580, (2021) PMID: 33940045.
2. M. Georgiou et al., "Inherited retinal diseases: Therapeutics, clinical trials and end points—A review" Clin Experiment Ophthalmol, 49, 270, (2021) PMID: 33686777.
3. Z. Li et al., "Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs," Ophthalmology, 125, 1199, (2018) PMID 29506863.
4. M. Phylactou et al., Characteristics of endothelial corneal transplant rejection following immunization with SARS-CoV-2 messenger RNA vaccine," Br J of Ophthalmology, 105, 893 (2021) 105:893-896. PMID: 33910885.
5. P. Dugel et al., "HAWK and HARRIER: Phase 3, Multicenter, Randomized, Double-Masked Trials of Brolucizumab for Neovascular Age-Related Macular Degeneration," Ophthalmology, 126, 72 (2019) PMID: 30986442.
6. Y. Zhou et al., "Ocular Findings and Proportion with Conjunctival SARS-COV-2 in COVID-19 Patients" Ophthalmology, 127, 984 (2020) PMID: 32359840.
7. M. Schlenker et al., "Intermediate Outcomes of a Novel Standalone Ab Externo SIBS Microshunt With Mitomycin C," Am J Ophthal, 215, 141, (2020) PMID: 32173344.

Covering clinical trials, the latest advances in AI, the impact of the COVID-19 pandemic and global data on ophthalmic disease progression these articles show the degree to which ophthalmology has move over the last five years to increasingly focus on widespread health issues – a point made by some of our experts in their own choices of landmark literature.

Papers were selected through searching journal websites for the most read section of the site and cross referencing articles through PubMed, Scopus and CrossRef. This is intended to be a sample of popular work and not in any way an exhaustive list.

developed the pediatric ophthalmology module. The aim of the PECI is to offer advice to policy-makers and technical decision-makers in low- and middle-income countries to integrate eye care into the packages and policies of their health services. The numbers around global vision issues are deeply shocking, with this report estimating a billion people with visual impairment that could be prevented or has yet to be addressed. Service providers within low and middle income countries can use the PECI to plan and implement eye care interventions in their service programs and the donor and development agencies can use it as a blueprint for eye care programs.

Anat Loewenstein, Vice Dean of the Faculty of Medicine and Sidney Fox Chair of Ophthalmology at Tel Aviv University, Chairman of Ophthalmology at Sourasky Medical Center and Director of the department of Ophthalmology at Tel Aviv Medical Centre

When I was asked for the landmark literature of the last year I looked first of all for papers which reported on evidence based level one studies. Namely, on multicenter, randomized clinical trials. It is not that there is not important information in different kinds of trials, or other kinds of academic research but rather, I believe that such information has the potential to change the way we treat patients.

I think that the TENAYA and LUCERNE(1), ALOFT (2), Aflibercept Monotherapy or Bevacizumab First for Diabetic Macular Edema (3) and post hoc analysis of the FILLY study (4) were the most influential studies published this last year.

The common thread in these studies is that they represent advancement for both retina patients and physicians and have the potential to alleviate some of the disease management burden. The TENAYA and LUCERNE studies demonstrate the potential durability of faricimab – a novel treatment for AMD, which can be implemented in the future using the personalized treatment interval regimen – and this is something which can be utilized in our daily clinical practice. Since most patients were fluid free for between two and four months without the need for additional treatment, we are heading towards a more durable and personalized method of care.

As for the ALOFT Study, it shows that monitoring at home can be feasible and also has the potential to alleviate treatment burden by using AI for fluid localization and quantification, thus improving clinical decision making processes. If we implement this model into clinical practice, early diagnosis and treatment for AMD will be within our reach and this can only help patients to manage this all-too-debilitating disease. The study establishes the feasibility of a new digital model for health, with three points of care – the patient's home, the physician's clinic and a monitoring center, for the management of macular degeneration.

Diabetic Macular Edema is another major cause of visual loss. Until today we mainly looked at pivotal trials which investigated the efficacy and safety of one drug given for the duration of the trial, comparing it to the standard of care. In the real world, due to limited resources all over the world, many health systems request initiation of treatment with bevacizuab and then switching to a registered drug only upon non optimal response. This very commonly used regimen was never studied for safety and efficacy. This study

Highly Ranked Journals in Ophthalmology

- *Progress in Retinal and Eye Research*: 2956 citations received in 2021 from articles published in 2018-2020.
- *Ophthalmology*: 374 published articles in 2021
- Annual Review of Vision Science: An average of 7.81 citations per document taken over a two year period.
- *JAMA Ophthalmology*: Has a H-index of 203.
- American Journal of Ophthalmology: 1173 publications over a three year period.
- *Survey of Ophthalmology:* 9990 references in the journal's published articles in 2021.
- *Ophthalmology Retina*: 2049 citations received in 2021 from articles published between 2018-2020.
- *British Journal of Ophthalmology*: The journal was originally established in 1917 after a merger between the Royal London Ophthalmic Hospital Reports with the Ophthalmoscope and the Ophthalmic Record.
- *Ocular Surface*: Has a H-index of 71.
- Current Opinion In Ophthalmology: 1107 citations received in 2021 from articles published 2018-2020.

Details about each journal taken from Scimago Journal and Country rank which is powered by Scopus and has data up to 2021. More recent analysis may give different results.

proves that such a regimen has results similar to those achieved with the regiment studied in the pivotal trial.

As for the post hoc analysis of the FILLY study, results showed that pegcetacoplan has the potential to slow geographic atrophy progression. The progression from iRORA to cRORA is slowed down when using this drug and it gives GA patients much-needed new hope for treatment for this debilitating disease – a hope which was virtually nonexistent since treatment was previously limited to observation.

The studies I chose all offer possible solutions: A digital health model using home monitoring being able to preserve visual acuity at the time of conversion to neovascular disease and at the end of follow up is a new way to manage our patients with possible favorable outcomes, a model that we did not appreciate earlier.

The new trials looking at longer treatment duration offer a reduced burden for the patients, physicians and the system with resultant better compliance and, of course, results. The ability to use bevacizumab and then switch provides reassurance to a regimen commonly used and the ability to lower costs.

The new treatment for GA has been developing rapidly over the last year with several treatment options arising; I look forward to seeing the phase III DERBY and OAKS publications and the revolution in GA care due to these new treatments. In the meantime, the outcomes are being presented at international meetings all over the world along with press releases. Hopefully, phase III outcomes will be published over the year to come.

All of these have the potential to really improve the management of our patients.

"The common thread in these studies is that they represent advancement for both retina patients and physicians and have the potential to alleviate... the disease management burden."

Anat Loewenstein

The state of research in ophthalmology looks promising and the combination of home monitoring and durable therapy has wide ranging possible applications. I am sure that in the future we will see a novel model where patients are treated with durable drugs and monitored from their own home for disease activity. This approach will allow more precise retreatment decisions and longer intervals for those who are suitable for it. In addition to home monitoring among nAMD patients, I can imagine there is a strong possibility of combining home monitoring for GA patients, for instance conversion from iRORA to cRORA from the patient's home thus alleviating management and facilitating the most suitable clinical decisions. I think my choices prove that we are blessed with many new treatment options. We have better, more personalized ways to treat our patients, and I look forward with keen interest to seeing the results of similar trials in other diseases such as RVO.

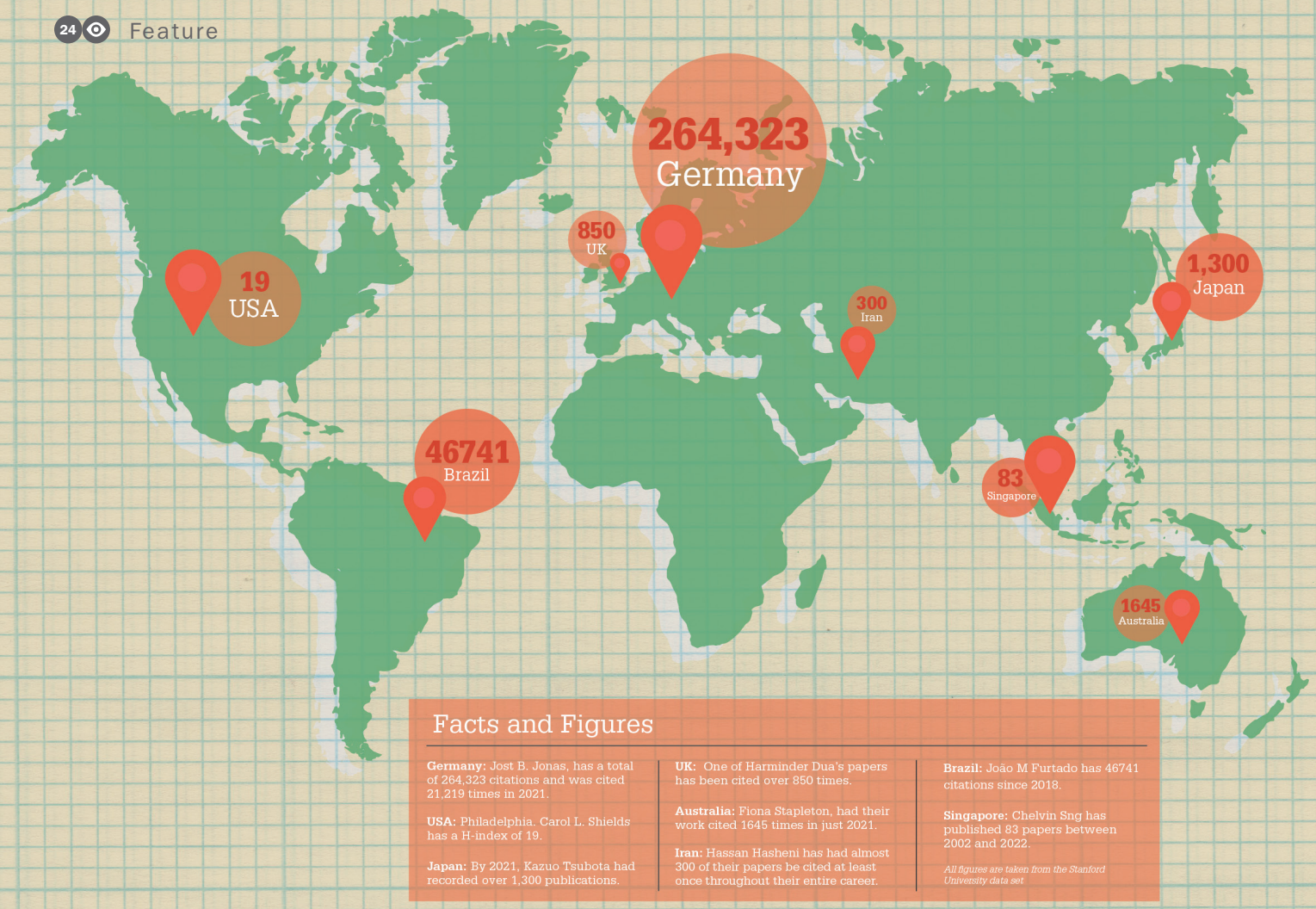


Figure 1: Global Citation Data in Ophthalmology from the Stanford University dataset

The Stanford Data on Ophthalmology

Every year, Stanford University releases a publicly available database of the top cited scientists across the world. The aim of the data set is to provide standardized information on citations, self-citation, numbers of papers and numbers of papers which have been cited at least once – as well as a host of other quantitative measurements. On top of this, the data also collects both career long and individual year impact information. The data set is designed to assess impact rather than just productivity and while all citation data should be used judiciously, it does provide a good visualization of the most impactful papers from the scientific community.

As the authors of the original data set highlight, if a certain figure does not appear on the list it is no reflection on the quality of their work. As the Leiden Manifesto pointed out, quantitative measurement should only ever be used to support qualitative expert assessment. It is undeniably important for ophthalmologists to know the patterns in the web of science, made up as it is of references, citations and publications. For that purpose, these metrics are useful, but the best insight into the state of ophthalmological research comes not just from quantitative measures but when this data meets the qualitative experiences of clinicians, researchers and, of course, patients. While academic science rightly puts serious weight on publication and impact we should not lose sight of how this research translates to the human experience of diagnosis, disease management and – hopefully – better eye health for all.

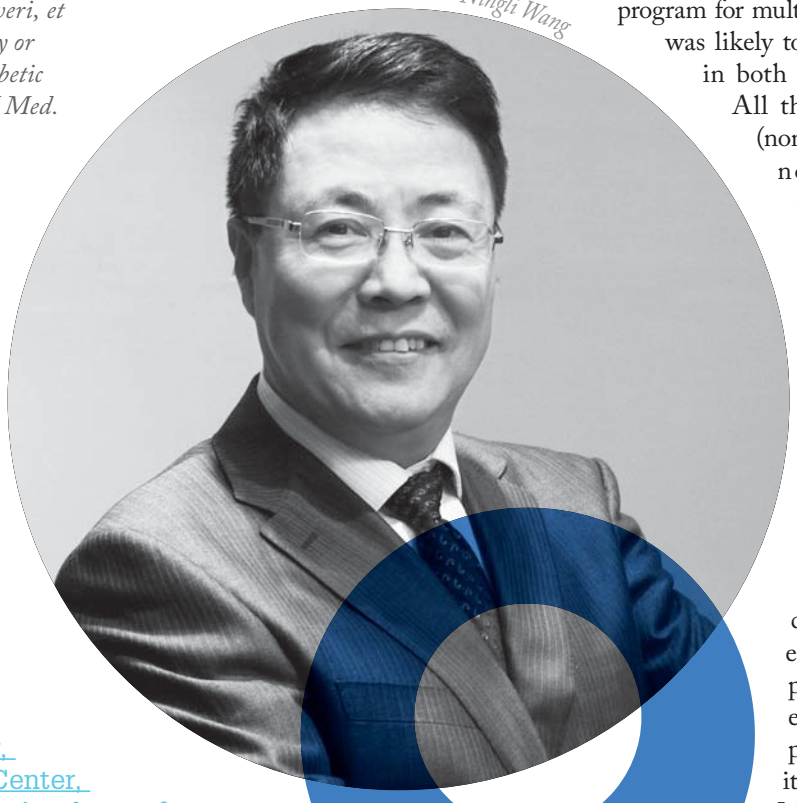
The data on ophthalmology was gathered from the Stanford data set and was compiled by Andrzej Grzybowski, Professor of Ophthalmology, CEO, Foundation for Ophthalmology Development, Poznan, Poland; EVER President-Elect.

Landmark paper: JS. Heier, et al., "Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomized, double-masked, phase 3, non-inferiority trials". Lancet. 2022 Feb PMID: 35085502.

Landmark paper: M. Mathai, et al.," Analysis of the Long-term Visual Outcomes of ForeseeHome Remote Telemonitoring: The ALOFT Study." Ophthalmol Retina (2022) PMID: 35483614.

Landmark paper: CD. Jhaveri, et al.,"Aflibercept Monotherapy or Bevacizumab First for Diabetic Macular Edema," N Engl J Med. PMID: 35833805

Landmark paper: MG. Nittala, et al., "Association of Pegcetacoplan With Progression of Incomplete Retinal Pigment Epithelium and Outer Retinal Atrophy in Age-Related Macular Degeneration: A Post Hoc Analysis of the FILLY Randomized Clinical Trial," JAMA Ophthalmol. 2022 PMID: 35113137.



Ningli Wang

Ningli Wang, Director, Beijing Tongren Eye Center, President of the Asian Academy of Ophthalmology and Dean of the School of Ophthalmology at Capital Medical University.

I have two principal choices for studies that I believe show promising results for a wide range of settings. As global eye care needs increase, ophthalmologists are rightly ever-more concerned with not just treating our individual patients, but in managing health issues on a population level. New technologies and concerted efforts from national health care structures have enormous potential for implementing novel and effective approaches to disease screening, management and prevention.

Landmark paper: L. Hanruo, et al "Economic evaluation of combined population-based screening for multiple blindness-causing eye diseases in China: a cost-effectiveness analysis," Lancet Glob Health. (2023) PMID: 36702141.

This is the first study to analyze the cost-effectiveness of multiple ophthalmic disease screening based on real-world data and a temporally explicit Markov model in a developing country with large economic heterogeneity from a societal perspective. This study showed that a population screening program for multiple blinding eye diseases was likely to be highly cost-effective in both rural and urban China. All three screening strategies (non-telemedicine screening, non-AI telescreening and AI telescreening) met the criterion of a highly cost-effective health intervention. In addition, it revealed that annual AI screening in both rural and urban areas in China was the optimal screening strategy.

The results suggested that routine screening of multiple blinding eye diseases could be highly cost-effective in China, which provides robust economic evidence for informed policymaking regarding its large-scale promotion. Moreover, the results indicated that novel screening strategies, such as utilizing AI-based tools, could achieve even greater cost-effectiveness in population screening. These novel screening approaches could play a unique role in high-quality eye care delivery and improve the equity and accessibility of eye health resources. More importantly, they can serve as a feasible example for other countries, especially LMICs with similar settings or epidemiological features.

Landmark paper: SM Li, et al., "Effect of Text Messaging Parents of School-Aged Children on Outdoor Time to Control Myopia: A Randomized Clinical Trial," JAMA Pediatr, 176, 1077, (2022), PMID: 36155742.

Based on a randomized clinical trial, this paper assessed the remarkable effectiveness of SMS text messages to parents to increase light exposure and time outdoors in school-aged children and provide effective myopia control. This paper reminds us of the importance of school-based increases in time outdoors within the school program, perhaps during lunch breaks, may be necessary to increase time outdoors on school days. The findings suggest that using text message reminders to parents offers improved control of myopia in school-aged children and should be considered as a cost effective tool for use with large populations and over large geographic areas.

Joan W. Miller

Joan W. Miller, Chair of Ophthalmology at Mass Eye and Ear, Massachusetts General Hospital and Ophthalmologist-in-Chief at Brigham and Women's Hospital; and Chair, Department of Ophthalmology at Harvard Medical School.

Given my interests in retinal disease, my choices are designed to bring attention to just a few of the exciting innovations that have occurred in this area of ophthalmic medicine. Our ever increasing knowledge about the genetic roots of so many ophthalmological diseases offers incredible potential not just for early detection and management of disease but unique and targeted therapies for so many patients.

Landmark paper: M. Margeta et al., "Apolipoprotein E4 impairs the response of neurodegenerative retinal microglia and prevents neuronal loss in Glaucoma," Immunity 55, 1627, (2022) PMID: 35977543.

A team of scientists at Mass Eye and Ear and Brigham and Women's Hospital demonstrated that the *APOE4* gene variant—known to increase the risk of Alzheimer's but decrease risk of glaucoma in humans—functions by blocking a disease cascade that leads to the destruction of retinal ganglion cells in glaucoma. Since glaucoma remains a blinding disease for millions of people around the world, these findings provide insight into the role of genetic variants, and the promise of translation to a treatment for patients.

Landmark paper: G. Eraslan et al., Single-nucleus cross-tissue molecular reference maps to decipher disease gene function, Science, 376, 6594, (2022) PMID: 35549429.

This paper is a first-of-its-kind cross-tissue atlas derived from an analysis of nuclei from 25 frozen samples from eight tissue types. As previous research has primarily focused on single-cell atlases derived from one particular healthy or diseased tissue, this cross-tissue atlas has the potential to uncover new clues for specific cell types and genes involved in complex diseases, as these are often caused by dysfunction of more than once cell type or tissue. In ophthalmology, the research team is applying similar approaches to primary open-angle glaucoma, and in the future, age-related macular


Pearse A. Keane

degeneration, with the hope of learning more about these diseases and developing therapies and better strategies for disease prevention.

Landmark paper: H. Fu et al., "Thrombospondin 1 missense alleles induces extracellular matrix protein aggregation and TM dysfunction in congenital glaucoma," J Clin Invest, 132, (2022) PMID: 36453543.

Through advanced genome-sequencing technology, the international team of scientists identified a new genetic mutation in thrombospondin-1 (THBS1) that leads to the development of severe cases of childhood glaucoma, a devastating condition that runs in families and can cause blindness in children by 3 years of age. These findings provide important insights into the causes of childhood glaucoma and offer the prospect of targeted therapy.

Pearse A. Keane, Professor of Artificial Medical Intelligence, Institute of Ophthalmology, UCL and Consultant Ophthalmologist, Moorfields Eye Hospital.

Landmark paper: JS Heier JS, et al., "Efficacy, durability, and safety of intravitreal faricimab up to every 16 weeks for neovascular age-related macular degeneration (TENAYA and LUCERNE): two randomized, double-masked, phase 3, non-inferiority trials," Lancet, (2022) PMID: 35085502

Landmark paper: C. Wykoff et al., Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomized, double-masked, phase 3 trials," Lancet (2022) PMID: 35085503.

Phase III trials are always essential for clinicians to follow, as these trials offer the most potential for directly influencing how we take care of our patients. These are two absolutely pivotal phase III trials showing the efficacy and safety of faricimab in the treatment of wet AMD and diabetic macular edema. These papers have already transformed the care of patients with these conditions all around the world, with faricimab being among the first of the second generation anti-VEGF agents which may be better at eliminating retinal fluid and are thus potentially longer acting.

"Phase three trials are always essential for clinicians to follow, as these trials offer the most potential for directly influencing how we take care of our patients."

The second thing I would like to highlight is the announcement of the DERBY and OAKS phase III trial results. This is top line data which I'm not sure if has been published in a journal yet, but what makes this so important is that the data shows the first potential treatment for patients with geographic atrophy. Over the course of 24 months of treatment the results show a statistically significant improvement in GA lesions along with an excellent safety profile. The three year GALE extension study will extend the research and will hopefully provide more compelling evidence for this new treatment option.

Landmark paper: Available at: http://bit.ly/3I0vL8o

Landmark paper: B. Babenko et al., Detection of signs of disease in external photographs of the eyes via deep learningNature Biomedical Engineering, 6, 1370, (2022) PMID: 35352000.

Finally, I would like to bring some attention to this frankly mind-blowing paper from the Google Brain team. I should stress that the results will need to be independently confirmed but the research team developed a deep learning model to detect the signs of systemic disease just from external photographs of the eye. Focusing on diabetic retinopathy, diabetic macular edema and poor blood glucose control, the initial result showed extremely promising predictive performance and underscores just how much impact the introduction of AI tools can have on disease management.

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[1] Klabe K, et al. 2021 Jul 20. *Clin Ophthalmol*. 15:3121-3129.

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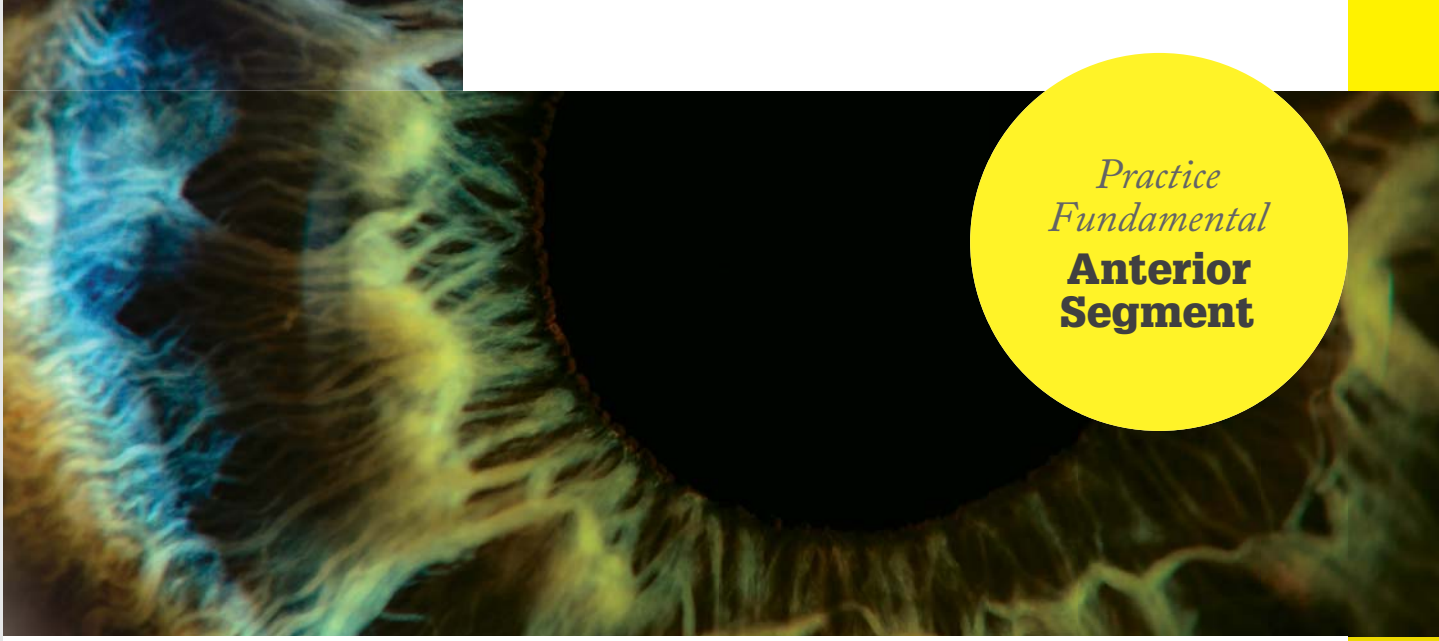
SIGHT SCIENCES



Practice Fundamental

Anterior Segment

Explaining explantation. A new study evaluates the long term corneal endothelial changes and visual outcomes after iris-fixated phakic intraocular lens (pIOL) explantation in patients with endothelial damage. To collate sufficient findings, researchers conducted a retrospective review on patients undergoing pIOL explantation with corneal endothelial cell density (ECD). Including 44 eyes from 28 patients, the study found that although ECD continuously decreased despite pIOL explantation on a long-term follow up, patients did not experience discomfort or decreased visual acuity (1). The findings suggest that a follow-up is required for possible endothelial injury after pIOL explantation.

Lighting the way forward. New research investigates the safety and efficacy of low-level light therapy (LLLT) and intense pulsed light (IPL) for the treatment of meibomian gland dysfunction (MGD). 40 eyes of 40 patients with MGD were randomized to receive either LLLT or IPL over a four-week period. The results showed that although The Standard Patient Evaluation of Eye Dryness score significantly decreased after both LLLT and IPL, this improvement was significantly greater in the LLLT compared with the IPL group (2). Additionally, the LLLT group showed a higher increase in tear meniscus height, securing LLLT as the most effective therapy for treating MGD.

Crossing the bridge. Although corneal collagen cross-linking (CXL) has been proven to lower high-order aberrations (HOAs) in keratoconus, no evaluation of the effect of the procedure on stereopsis has been performed. A new study changes this by assessing the differences in binocular visual performance in patients with keratoconus before and after CXL. To assess this, 30 patients with keratoconus undergoing standard Dresden protocol epi-off CXL received, among other things, slit lamp examination, corneal tomography and a TNO stereoacuity assessment. The study found that patients with keratoconus showing a reduction of HOAs after CXL also manifest a significant improvement in stereoacuity post treatment (3).

Determining Demographics. To determine the possible associations between demographic and socioeconomic factors and graft survival after penetrating keratoplasty (PK), researchers conducted a retrospective chart review of patients undergoing PK at a tertiary-care corneal practice at Wills Eye Hospital. With a primary focus on measuring graft failure, researchers accounted for demographic and socioeconomic factors, including yearly average adjusted gross income. The results of 822 patients highlighted that individuals who were young, of Black ethnicity, and generated a lower income, were more susceptible to graft failure after PK (4).

See reference online.

IN OTHER NEWS

Caffeine Correlations. *An assessment of the associations between caffeine intake and dry eye disease (DED) in the Netherlands demonstrated that dietary caffeine intake does not seem to be a risk factor for DED in the general population (6).*

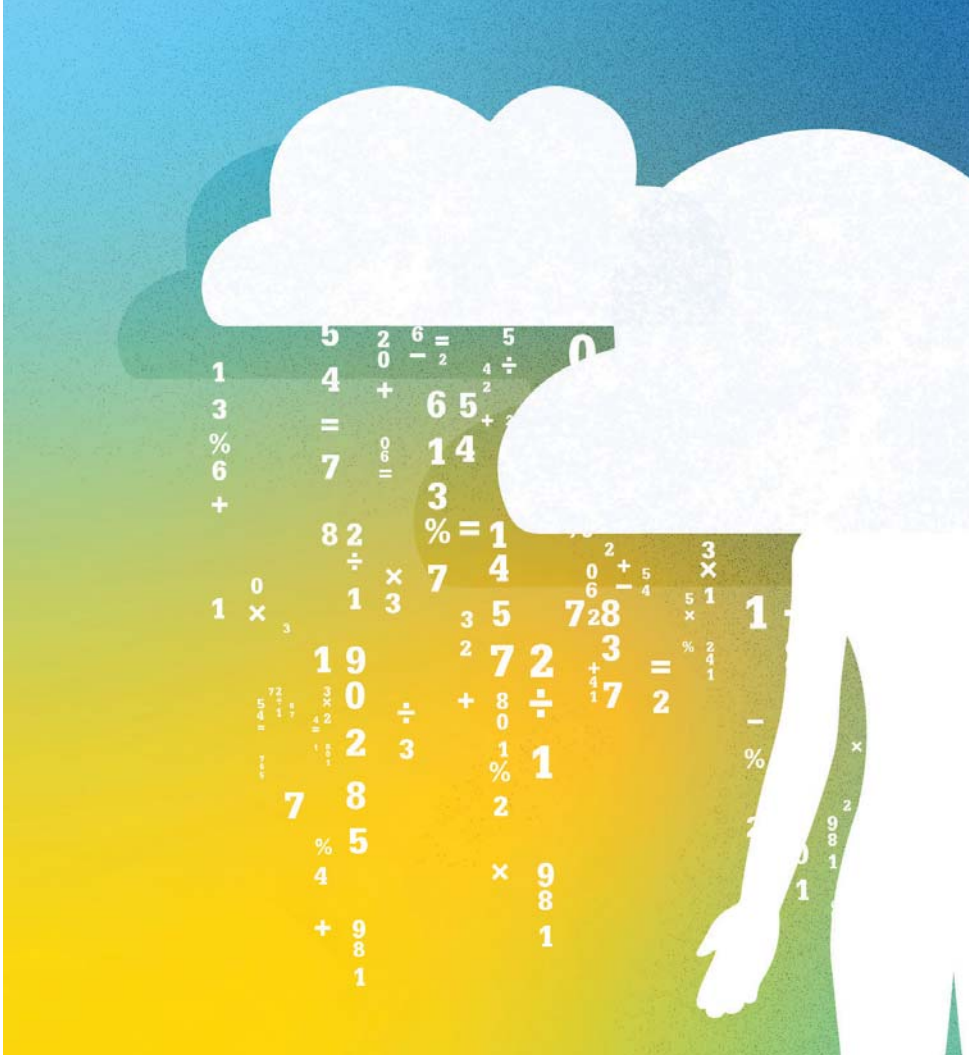
Reclassifying criteria. *Researchers identify the four latent DED subtypes as normal, asymptomatic, symptomatic, and corneal neuropathic pain, enabling refined classification criteria for specific DED subtypes (7).*

Cataract complications. *The IRIS Registry has reported a significantly higher incidence of endophthalmitis in children when compared to adults, however, the associated factors remain largely unknown (8).*

Two good options. *Kahook Dual Blade (KDB) or Trabectome with cataract surgery are both safe and effective at lowering IOP and medication burden with the outcomes being similar, considering the study's limitations (9).*

Seeing Is Believing

When it comes to placing toric IOLs, how true is the "one degree for three percent" rule?



A pervasive adage within cataract and refractive surgery circles is this: for every degree of toric IOL rotation, three percent of the toric effect is lost. At 30˚, the entire effect of the toric IOL is lost, and beyond 30˚, an additional cylinder is induced. The basis for this axiom lies within a landmark study from 1994, which found that the maximum amount of post-operative rotation before a complete negation of the astigmatic effect was 30˚ (1). Though this article provided a guiding principle for rotational tolerance of toric IOLs, there are nuances that are worth discussing.

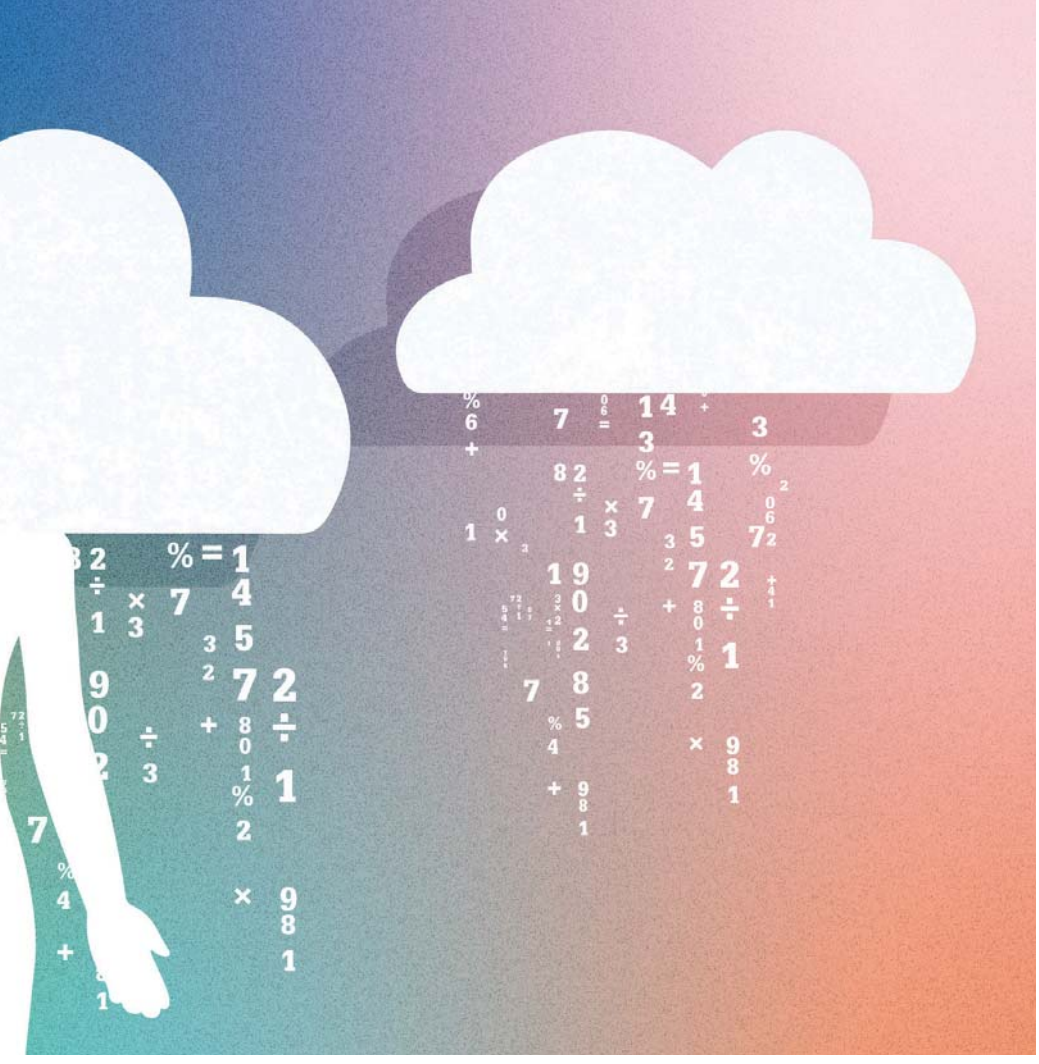
The first thing to consider is that the traditional process of placing a toric IOL introduces a number of opportunities for error. Patients are often marked before surgery by hand, which involves estimating the 0˚, 90˚, and 180˚ positions. Even in the most accurate surgeon's hands, the pen marks span at least 3˚. Next, degree gauge rings are used to mark the toric axis. These rings must line up with the original pre-op marks, and then the surgeon must estimate the exact position of the axis as the rings typically have increments of 5˚ – which again involves making a mark that can also span around 3˚.

When the toric IOL is finally placed, the marks of the toric are compared with the cornea. Like the rest of cataract surgery, this step is subject to parallax distortion. The toric marks on the IOL also must align with the corneal marks. Because the corneal marks may be 3˚ wide, this introduces the possibility of 3˚ of alignment error.

Based on the original adage, given almost 10˚ of potential cumulative error – assuming every step was completed perfectly – we end up with a 30 percent reduction in astigmatic correction from the toric IOL. Clinical experience, however, reveals consistently excellent visual acuity after toric IOL placement, which means either the eye is more tolerant to toric IOL rotation than the study suggests, the relationship is nonlinear, or there are other considerations (2,3). Of course, these problems are addressed by the use of femtosecond technology and a precise toric mark on the capsulorhexis, but studies have shown the visual outcomes for conventional versus femtosecond toric IOL placement in cataract surgery are equivalent (4).

So, what is the missing piece? Maybe the answer is just that it all comes down to the patient's visual experience. "Clinically significant" astigmatism is generally understood as somewhere in the 0.75 D–1.00 D range (5, 6). Therefore, a patient with around 1.50 D of astigmatism should have excellent vision as long as they are at or below that range post-op. If you consider a T3 toric IOL, which corrects 1.50 D of astigmatism at the IOL plane and 1.03 D at the corneal plane. Using the original math of 1˚ for three percent of the effect, the IOL should be able to rotate 20˚ before it loses 60 percent of its corrective power. This would leave 40 percent, or 0.60 D, of the original 1.50 D which would land the eye under the 1.00 D cylinder mark. The conclusion that can be made from this is that the T3 IOL has a 40˚ window of rotation before the eye experiences a "clinically significant" effect. This analysis disregards the vector of astigmatism as with-the-rule astigmatism tends to be the best tolerated and oblique the least. However, studies have demonstrated that the cylinder of any axis minimally impacts visual acuity under a magnitude of 0.75 D (7, 8).

Now consider a T6 IOL, which has 3.75 D of cylinder at the IOL plane and 2.57 D at the corneal plane. To retain 1.75 D of cylinder correction equates to 74 percent of its effect. A T6 then has 26 percent of wiggle



room, or conservatively 8°. Considering both directions, a T6 has around a 16° window before the eye experiences a "clinically significant" effect. By the same math, a T9 would have a 12° window.

It goes without saying that surgeons should always strive for perfection, but if it ever seems that actual outcomes are better than the old "1° for three percent" rule suggests, our thinking above could be the reason why. Even high-powered toric IOLs have more than a 10° window where the outcome likely will be acceptable from a subjective visual perspective. For those without access to femtosecond guided technology, calculating the "window of tolerance" for toric IOLs before surgery may prove to be an interesting exercise and also create additional situation awareness. One easy way to do this is to use the toric Results Analyzer created by John Berdahl and David Hardten. For example, use a T3 and make the current axis, calculated axis, and current refraction plano axis all 90° (basically, input a perfect result). The website graphically demonstrates how much the IOL can rotate and what effect will result. In this case, anywhere from 70° to 110° degrees gives < 0.75 D of residual astigmatism.

Does this mean that surgeons should stop passing the "one for three" rule down to future generations? Not necessarily, especially since it is a principle that looks to instill a mindset of caution and precision when performing conventional toric IOL placement. Instead, this analysis looks to provide an interesting perspective on the real-world tolerances of placing toric IOLs and shines a light on why, when it comes to a patient's sight, their perception is their reality – even when the math might suggest otherwise.

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Peptide Pioneer

Robert Yu discusses the development of a new peptide treatment for dry eye disease

Wonsang "Robert" Yu of Yuyu Pharma talks about his new peptide treatment for dry eye disease. He explores the current market of dry eye disease treatment and discusses the future of his product, which he hopes will be available on the global market.

Robert Yu

Tell us about yourself and your background…

I'm the CEO of Yuyu Pharma. The company was founded by my grandfather over 80 years ago; I am the third generation in the business. Before Yuyu, I was a sales rep in Brooklyn, New York, and then had the opportunity to work for Novartis in Asia. I was based in Singapore and trained sales reps and contract clinical research associates in Singapore, Malaysia, Indonesia, India, Korea, and Japan. That experience gave me the opportunity to understand how Novartis works as a global company. Now, I have aspirations to do the same thing with Yuyu.

What is the current unmet need in dry eye disease?

There are still patients looking for a solution for dry eye disease. From my experience as a sales rep, I know that patients want something that's affordable and that works. If that's not on the market, there's demand. The same is true for dry eye disease; good products already exist, but people are not satisfied with them. Based on preclinical studies, when we discovered that our peptide might have anti-inflammatory properties unlike other treatments on the market, we saw an opportunity – so we decided to develop YP-P10.

Can you explain YP-P10's anti-inflammatory properties?

When we found out through phenotypic screening that this peptide had anti-inflammatory properties, we started to explore potential applications. Dry eye disease took precedence because it had so many unmet needs in terms of drug discovery. So we started to develop our peptides into eye drops.

One of the main challenges of developing dry eye drugs is that they have to be water-soluble for easy application. Fortunately for us, our molecules are highly water-soluble and our studies so far indicate that the peptide has anti-inflammatory properties. We have completed six toxicology studies demonstrating that YP-P10 appears to have a very good safety profile. Now we need to see whether it really works, so we are doing a clinical trial.

We received IND clearance to begin clinical studies from the FDA back in April 2022. We are currently recruiting 240 patients in seven sites across the US. So far, enrollment is going according to plan and we anticipate results in the first half of 2023.

Have you considered using biomaterials such as hydrogels or nanoparticles to enhance YP-P10's effectiveness?

I have explored other technologies that could help the drug stay on the eye longer, but first I need to confirm that it actually works. We have done two in vitro studies and three in vivo studies suggesting that YP-P10 – in various ways – reduces cytokines and chemokines, which is a hypothesis we need to test further. If we see that keeping the drug on the eye longer makes sense, then we will explore options, but I think it's a little early to discuss that.

Could this peptide be useful in other diseases?

We have started looking at other applications for YP-P10. Dry eye treatment is topical and other diseases can require more invasive treatment, so we need additional formulation work. But our *in vitro* and in vivo studies in other inflammatory conditions have shown some encouraging early results. Ultimately, although the possibilities are exciting, we need to get the dry eye drug approved first before we place too much focus on – or investment into – other indications.

"Based on preclinical studies, when we discovered that our peptide might have anti-inflammatory properties unlike other treatments on the market, we saw an opportunity – so we decided to develop YP-P10."

What has been the biggest challenge so far?

It's all about people. Novel drug discovery is tough to begin with; trying to do it from Korea presents an additional challenge because it's hard to find knowledgeable collaborators. I think today's technology makes it easier because you can video-conference with people in other areas to get help. I have great advisors who offer me support, but it's still tricky to find the right people to help move YP-P10 forward and get it approved globally.

As a result, I am developing this drug as though I'm going to launch it myself. I'm already talking to Health Technology Assessment (HTA) and pricing people in the US and Europe. Assuming that the phase II trial comes up positive, what kind of phase III trials do I need to design? The US and European regulators are looking for slightly different things, so I have to think about how to conduct trials that satisfy both. Most importantly, I need to conduct a trial that would convince the HTA and pharmacy benefit managers (PBMs) that this is a valuable drug patients need. I'm thinking about patients, pricing, access, and end results now so that I don't have to worry about it later. I'm not just waiting for my phase II trial; I am actively thinking and planning for success.

What do you most want ophthalmologists to know?

If they haven't heard of Yuyu Pharma, they should know that we are serious about drug discovery, especially in dry eye disease and ophthalmology. We are working on developing a dry eye drug for the global market. Naturally, it will need a lot of support from doctors, so hopefully this interview will let the ophthalmology world know that Yuyu exists.

Some people ask what Yuyu means. Yu is my family name, but it also means "water that flows gently to the vast sea." My grandfather chose an apt name for the company because Yuyu has aspirations in the vast sea beyond Korea. We want to grow – and hopefully getting YP-P10 into the global market will be just the beginning.

Cataract Surgery Is Rush Hour

When it comes to phacoemulsification, are all fluidics systems and phaco tips equal?

By Ivo Silva

Performing cataract surgery – particularly in dense cataracts – is a bit like being Jackie Chan in his highest-grossing Hollywood movie, Rush Hour. Alongside having to fight the Triad leader's henchmen on his own, Chan has to make sure he doesn't damage the priceless Ming vase he's just saved from crashing to the floor. Although we surgeons aren't involved in armed combat, we do adopt similar tactics to Chan – staying acutely aware of the dangers that surround us, prepared to respond to any threat within milliseconds, and handling priceless objects with the utmost care.

Training to take the pressure

Just like Chan, to achieve excellence, we have to train for years. Just like Chan, we need to practice our skills almost daily to stay at the highest level of our game. But while Chan employs the empty hand, the clenched fist, and a swift hip movement to deliver a roundhouse kick to a henchman's torso, we surgeons battle cataracts with a steady hand and phacoemulsification machine: a highly sophisticated instrument that enables us to do what we do, day-in, day-out, safely and effectively.

Like Chan, we cataract surgeons are usually under a lot of pressure. Long to-do lists mean that efficiency is a priority during surgery – without which a patient's vision may be at stake. Although "quick" and "excellent" are not adjectives often used in conjunction, for a cataract surgeon, they are the key to successful outcomes.

The perils of phacoemulsification

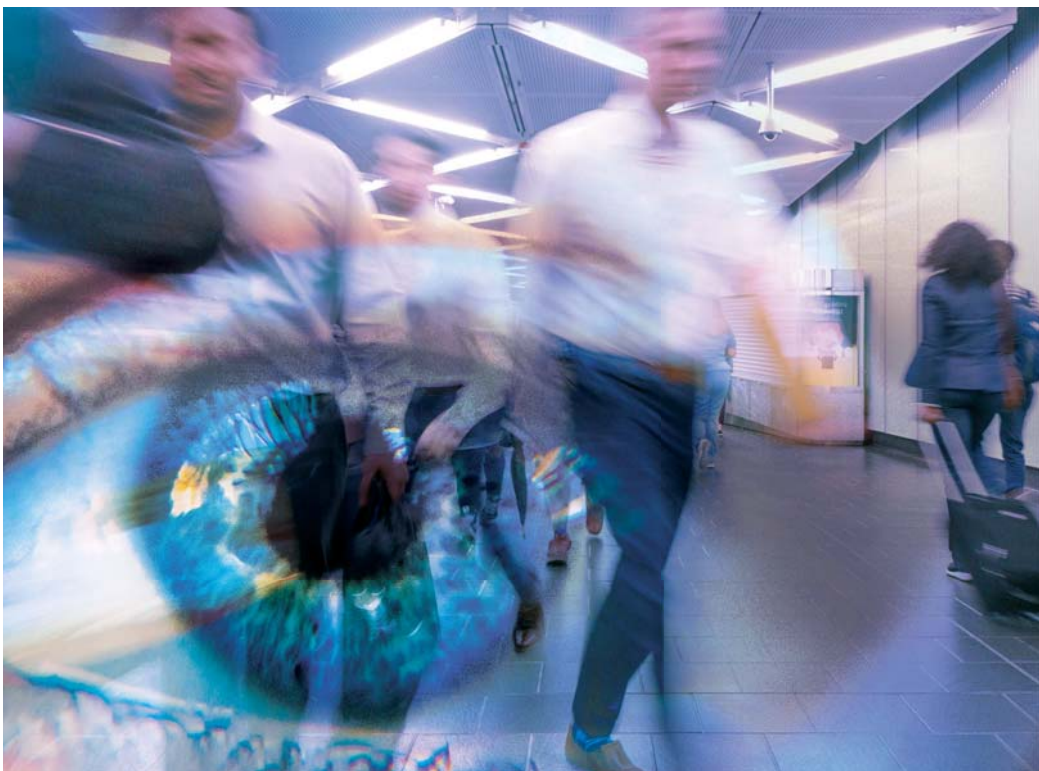
When fighting at the edge of a rooftop, if Chan misjudges a punch and misses the target – or even if he kicks the enemy too hard – the momentum could propel him over the edge. Here, his skill is finessed aggression, where there is a fine line to walk between success and disaster. I view phacoemulsification in much the same way. Although we need to liquefy the lens with ultrasound energy from the phaco tip as quickly and efficiently as possible, we don't want to deliver too much, as this can cause excessive damage to the corneal endothelium as well as causing "shattering" – where the lens fragment "explodes" into many small pieces – each of which needs to be found and removed with care. This is a slow process, but if we miss any of them, we risk focal inflammation, corneal edema, and raised intraocular pressure (IOP).

The lens fragments are removed through aspiration, but this also removes fluid from the anterior chamber, depressurizing the eye, something that can have disastrous consequences. Our partner here isn't Chris Tucker, it's the phaco machine's fluidics system, which tries to keep the IOP constant by adding fluid into the anterior chamber as lens fragments and fluid is being aspirated away.

Fluidics first

Similar to racing drivers boring people with talk about tire compounds, cataract surgeons are mostly occupied with talk of fluidics. Although not as fun as Chris Tucker in the late nineties, keeping IOP within the right range is essential, and a process that has evolved over the years.

Traditionally, we exploited gravity: raise a bag of balanced salt solution (BSS) in the air, and the height determines the pressure inside of the eye. Simple and easy, but not nearly as responsive as it could be. The Alcon Centurion machine took a different approach called "Active Fluidics" – in short, place the BSS in a flexible bag that is acted upon by plates inside the machine to vary the pressure on the BSS – and therefore the eye – to the appropriate level at each step of the surgery. The Alcon Infiniti system



has a peristaltic pump, the Bausch + Lomb Stellaris has a Venturi pump, and the Johnson & Johnson Signature has both Venturi and peristaltic pumps to achieve this (see Table 1). There has been considerable debate regarding which fluidics approach, Venturi or peristaltic, is better. The consensus is that Venturi pumps are faster and more efficient, but peristaltic pumps are safer and more stable – we're almost back to the battle between "quick" and "better" – but in practice, the reality is far more complicated than that. The most recent approach to fluidics is taken by the Zeiss QUATERA 700 system, which uses symmetric pumps. The QUATERA 700 can constantly measure infusion and aspiration volumes (including leakage through the corneal incisions) in real time – a very precise way of maintaining IOP.

Fast feet

One – if not the largest – aspect of being as efficient and excellent as possible during cataract surgery is how familiar and comfortable the surgeon is with the phacoemulsification machine. Why? Most of it comes down to how the phaco machine handles occlusion breaks. We've all been there: there is a fragment of the nucleus in front of the phaco tip, you're deploying phaco energy to liquefy the fragment, and you're aspirating to remove the debris. But while the phaco tip is occluded, a vacuum builds up in the tip and the tubing, and if there's a large pressure difference once the tip clears, ocular fluid can rush in, causing IOP to drop – and with it – a shallowing of the anterior chamber. Further, the iris, or even the posterior capsule, can vault towards the phaco tip, both of which can become damaged if they come into close proximity or contact with the tip. To counter this effect, you tend to lift your foot from the foot pedal as you get close to the point of occlusion break to reduce the amount of vacuum applied, thus minimizing the effect of the occlusion break when it inevitably happens.

Although this caution is completely warranted, if you are too cautious and reduce the vacuum too much, you lose the piece from the tip – and it floats away. You have to go and grab it back again, slowing the process down, and this can happen time after time during the procedure – especially when you're at the start of the cataract surgery learning curve. Suddenly, we're Jackie Chan, fighting on the rooftop again. However, if you feel comfortable that you won't have a big surge after the occlusion break, you don't feel that urge to back off and, subsequently, don't need to have your foot always at the limit, ready to drop the vacuum as fast as your foot-eye coordination permits.

A large market

Clearly, the dynamics of these fluidics systems play an important role in cataract surgery. And so it's interesting to see how manufacturers take different engineering approaches – both to make their fluidics systems work (see Table 1) and to handle the rapid pressure changes during occlusion breaks, which really determines how comfortable a surgeon is using a given system.

Throughout my career as a cataract surgeon, I have used several phacoemulsification machines. I started my training with the AMO (now Johnson & Johnson) Signature system, and since then, I have used the Alcon Infiniti and Centurion platforms, as well as the Bausch + Lomb Stellaris, and, most recently, I have used the Zeiss QUATERA 700 system. I would like to share my experiences with you.

Take your pick

I want to stress that all of them are perfectly fine instruments – all have pros and cons. I tend to use Signature with its peristaltic pump-based fluidics, but this system feels like it is slow to build vacuum to perform aspiration, and is slower to move things around inside than platforms like Infiniti and Stellaris, which use peristaltic and Venturi pump, respectively. Though ultra-rapid vacuum generation might cause anterior chamber instability when my phaco tip is unoccluded, fast vacuum generation is great for when I want to grab the nucleus, cut it, rotate it, and then grab it again. In general terms, I feel that the Centurion keeps IOP more stable than the Stellaris. Although I have had limited experience with the system to date, the Zeiss QUATERA 700 system (with its real-time volume measurement symmetric pump fluidics concept) worked well. Alongside stabilizing IOP, the system also removes surge from the procedure (and some of the drama) and alleviates the need for fast foot action on the foot pedal.

"Although this caution is completely warranted, if you are too cautious and reduce the vacuum too much, you lose the piece from the tip – and it floats away."

The trade-off here is once again between speed and stability – and it can take quite a while for each surgeon to optimize the settings for their own preferences and safety margins.

See full article online.

A Win for Corneal Visionaries

The pioneers of modern corneal science have been awarded the largest visionary prize in the world

Launched in 2006 and supported by the World Health Organization's "Vision 2020 – The Right to Sight" program, the António Champalimaud Vision Award is the largest award of its kind in the world. Boasting an €1,000,000 prize, the achievement celebrates significant contributions to ophthalmology, including far-reaching science and work in the fight against blindness and visual impairment. The 2022 award recognizes two key figures in ophthalmic medicine, Gerrit Melles and Claes Dohlman, both of whom have revolutionized the field of vision.

Claes Dohlman

Now 100 years old, Claes Dohlman is internationally recognized as the "father of modern corneal science" and his work is considered classic literature on corneal biology. Having trained over 200 cornea specialists, his contributions to the field of ophthalmology are indispensable. Over the course of his seven-decade career, Dohlman has spearheaded corneal physiology investigations and laid the foundations for clinical practice in dry eye disease, corneal burns, wound healing, corneal transplantation, and keratoprosthesis.

Alongside finding the first cornea subspecialty clinic in the world (the Massachusetts Eye and Ear clinic), Dohlman's most notable contribution to the field of ophthalmology is the Boston keratoprosthesis (KPro). Having undergone continuous design innovations since its FDA approval in 1992, the Boston KPro is now the most commonly used corneal prosthesis in the world, restoring the sight of more than 11,000 patients in 66 countries (1). Now having also received a European Conformity (CE) mark, the device has been made reimbursable across the European market and is even more accessible.

Reza Dana, Dohlman's successor at Mass Eye and Ear, has said of the Champalimaud Vision award, "Dohlman's indelible contributions to the field of cornea science are evident in his foundational research, which is still highly utilized today in scientific discovery and patient care (2)."

Gerrit Melles

Although Gerrit Melles has not yet been in the ophthalmic field as long as Dohlman, his contributions to ophthalmic research are no less pivotal. As stated by Alan R. Morse, "Melles has revolutionized the field of corneal transplantation and his research is opening new pathways to help people with vision loss lead full and productive lives (3)."

Noticing that there was much to improve in the field of corneal transplantation, Melles made it his mission to treat corneal disorders with minimally invasive techniques that wouldn't damage the ocular surface. Prior approaches to treating corneal disease involved penetrating keratoplasty – removing healthy layers of the cornea alongside diseased layers – that often resulted in unpredictable and unsatisfying visual outcomes. By replacing only the back of the cornea, Melles was able to retain the healthy layers of the cornea while treating the disease.

Melles has since gone on to invent several other advanced lamellar keratoplasty techniques, including Descemet membrane endothelial keratoplasty and Bowman layer transplantation. He has also developed surgical instruments and devices, such as the SurgiCube®, that can be used to execute these techniques.

By developing a range of groundbreaking techniques and technologies, Dohlman and Melles have accelerated the path to treating corneal disease. Their combined research has helped establish a deeper understanding of the cornea and the possibility of a more consistent and cost-effective approach to corneal surgery and transplantation. It goes without saying that the award is well deserved.

See reference online at:
top.txp.to/win/for/corneal/visionaries

Pick an IOL Your Own (Pupil) Size

Mesopic pupil size in an important factor in selecting the best EDoF IOL for your patients

We conducted a prospective single-arm trial of patients undergoing bilateral implantation of a four-point haptic, hydrophilic acrylate, extended depth of field IOL with hydrophobic surface properties, a smooth microphase design, and a diffractive anterior surface design with an optical light bridge to provide satisfactory functional vision over a range of distances. We explored visual outcomes, contrast sensitivity, reading performance, and patient satisfaction. After one year, most patients had an uncorrected distance visual acuity (UDVA) of 20/20 or better and uncorrected near visual acuities (UNVA) of N6 or better (3). The results demonstrate that the EDoF IOL provided good uncorrected near and far visual acuity outcomes.

Evidence suggests visual outcomes depend on several factors, such as coexistent pathology, anterior chamber depth, and zonular stability (4). However, preoperative mesopic pupil size is also important when considering EDoF lenses. To illustrate its potential effect on patient outcomes after EDoF IOL implantation, we have selected two case studies from our research.

The first is a 60-year-old retired male who is overall healthy and leads an active lifestyle. Before surgery, he had grade II nuclear sclerotic cataracts (NS2) and posterior subcapsular cataracts (PSC) in his right eye and NS3 and PSC in his left eye. His preoperative corrected distance visual acuity (CDVA) was 6/9 and 6/18 and his corrected near visual acuity (CNVA), using +2.50 DS, was N6 and N10 for the right and left eye, respectively. The preoperative mesopic sizes of his right and left pupils were relatively large at 5.16 mm and 5.59 mm; the left was the largest pupil in the cohort. Through biometry, we calculated that an IOL power of +19.50 D would achieve emmetropia in both eyes. Our findings one month after surgery included a UDVA of 6/5, UIVA of 6/6 at 60 cm, and UNVA of N8 in both eyes. Binocularly, he had a UDVA of 6/5 and UNVA of N6. He was highly satisfied with his distance vision and satisfied with near and intermediate vision, but found it inconvenient that he still needed glasses to read very small print.

The second case is that of a 62-year-old female, who is also generally healthy and active. She had NS2 and dense PSC with early AMD changes in both eyes. Her preoperative CDVA was 6/9 and 6/12 in the right and left eye, respectively; her CNVA, using +2.50 DS, was N10 in both eyes. The preoperative sizes of her right and left pupils were 2.78 mm and 2.56 mm – smaller than average for her age (5) and among the smallest pupils in the cohort. Biometry suggested that an IOL power of +23.50 DS in both eyes would achieve emmetropia in the right and slight myopia in the left eye. After one month, we observed a UDVA of 6/5, UIVA of 6/6 at 60 cm, and UNVA of N5 in both eyes. Her binocular UDVA was 6/5 and UNVA was N5. At six-month follow-up, the IOL was stable. This patient, who had a much smaller mesopic pupil than the first case, was very happy with her vision, and did not require glasses.

A patient's preoperative mesopic pupil size may be important to keep in mind when considering postoperative UNVA. Patients with large pupils should be told of the possible need for postoperative reading glasses, especially for smaller print. Patients with smaller mesopic pupil sizes may experience improved near vision with EDoF IOLs. Through good surgical planning, accurate biometry, and use of the TK formula, patients can achieve excellent outcomes – the ultimate sign that the right choice was made (6).

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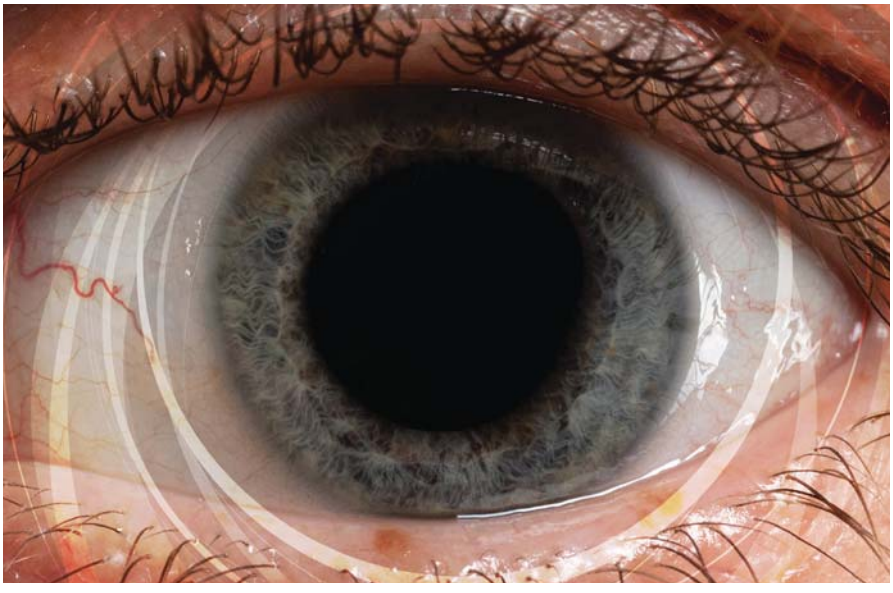

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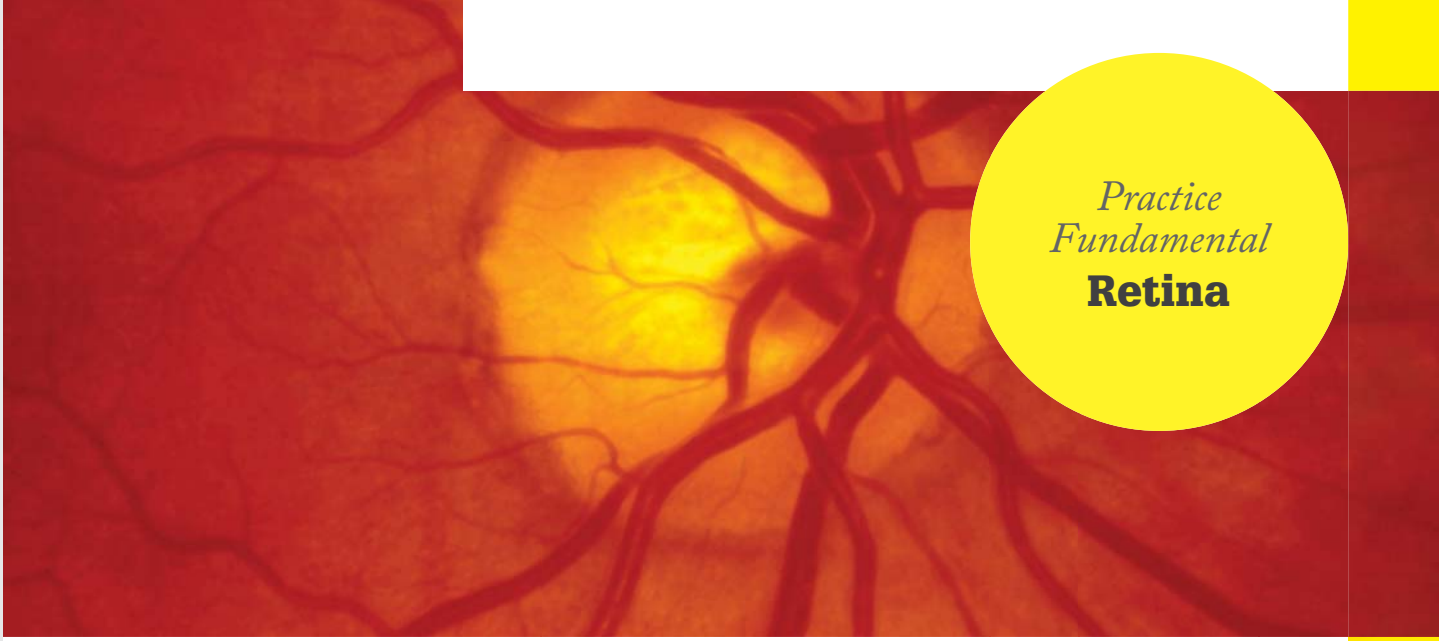

Space plights. An analysis of 36 long-duration crew members assessed the incidence, presentation and progression of chorioretinal fold development during spaceflight missions to the International Space Station. Results found that a sixth developed chorioretinal folds with both macular and peripapillary choroidal folds worsening with flight durations up to a year (1). This indicates that chorioretinal fold progression is a concern for missions to the International Space Station Missions as well as future missions to both the Moon and Mars.

Recognizing non-response. When observing the outcomes of intravitreal bevacizumab treatment of macular edema after retinal vein occlusion following pro re nata regimen found that compared to those who were treatment responsive, the unresponsive group had significantly worse visual best-corrected visual acuity, higher central macular thickness and subfoveal choroidal thickness (SFCT) (2). The researchers concluded that higher baseline SFCT could be considered a predictor for non-response to such therapy.

Knock-on effect. Despite the similar etiologies of AMD and kidney disease, the risk of end-stage renal disease (ESRD) has not been reported. A new population-based cohort data study of over four million patients aged 50 years or older in Korea, determined that AMD was associated with a 33 percent increased risk of ESRD with this risk being higher when accompanied by a visual disability (3).

Solving stability. New research shows that the processes enabling humans to resolve fine details and perceive a stable visual world despite the incessant fixational motion of the eyes relies solely on the visual input to the retina. The visual system has access to high-resolution extra-retinal knowledge of fixational eye movement and uses this to deduce spatial relations (5). From this, the researchers have identified a sensory-motor strategy for encoding space through which oculomotor knowledge is used to interpret fixational input to the retina

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IN OTHER NEWS

Testing torsion. *Ocular torsion within the normal range of cyclofusion affects the horizontal motor fusion of convergent and divergent fusion and stereopsis in normal adults (6).*

Common changes. *Choroidal vascular remodeling is common in both typical neovascular age-related macular degeneration and polypoidal choroidal vasculopathy, but can be driven by differing stimuli (7).*

Interaction inquisition. *Trogocytosis by macaque retinal microglia allows them to present antigens obtained from normal internal retinal cells, promoting antigen-specific tolerance when activated (8).*

Plan of reattachment. *Pars plana vitrectomy is a strategy that is effective in achieving retinal reattachment in patients with tractional retinal detachment, with preoperative VA being the only factor associated with postoperative VA (9).*

H(eye) Definition

STOC-T: a new tomography device that changes the scope for retinal and choroidal imaging

Maciej Wojtkowski and Mounika Rapolu, photographed by Piotr Furman

Although Optical Coherence Tomography (OCT) scans are widely considered the best diagnostic technique for detecting eye conditions, the images they produce are far from perfect. Due to noise and/or limited axial range, OCT scans are unable to capture all the layers of the retina and choroid – resulting in poor quality images, and thus, poorer quality diagnoses.

New research – from The International Centre for Translational Eye Research (ICTER) in Poland – has managed to find a way around these limitations through the development of Spatio-Temporal Optical Coherence Tomography (STOC-T). This new method makes it possible to view the retina and choroid with high resolution at distinct depths in the frontal section – something that has not been achieved previously.

In this article, Maciej Wojtkowski – the lead researcher from the study – speaks about STOC-T's development, the limitations of OCT, and the future of retinal imaging.

What inspired the development of STOC-T?

The particularity of the OCT method is due to the physical property of the light used: the so-called temporal coherence. Unlike microscopy, this property allows 3-D reconstructions to be obtained. An example of something with a small value of temporal coherence would be lasers with very short pulses or so-called superluminescent diodes. There is another property of the emitted light – spatial coherence. Standard lasers have coherences at a high level, while ordinary light bulbs or LEDs have very low coherences. Although it was known that the quality of OCT images – especially those in coronal projection (en-face retinal images) – are not ideal and deviate from what we see under an ordinary ophthalmoscope, until now, no one has controlled the properties of spatial coherence in OCT. Since the first research on the method and the first SDOCT systems in 1999, I had the idea to take advantage of this property of light. However, it was only recently that we came up with a way to control spatial coherence in a low-cost and simple way. For this reason, we called our technique Spatio-Temporal Optical Coherence Tomography (STOC-T).

Another source of inspiration for this work came from feedback from ophthalmologists who have often pointed out to me that they struggle to visualize the choroidal layers well in OCT images. In fact, other than the ICG fluorescence method, there is no good way to know how lesions are progressing in this extremely sensitive tissue. This is especially true for retinal conditions associated with systemic problems such as diabetes, nephritis, parasites, or uveitis.

The last reason is the increasing need among ophthalmologists to introduce functional methods for retinal examination and replace electroretinography (ERG) with optical methods such as OCT. The STOC-T technique we are introducing guarantees very high phase stability and at the same time accelerates 3-D OCT measurements 50 times over.

What are the limitations of OCT – recognized as it is as the current gold standard of clinical imaging?

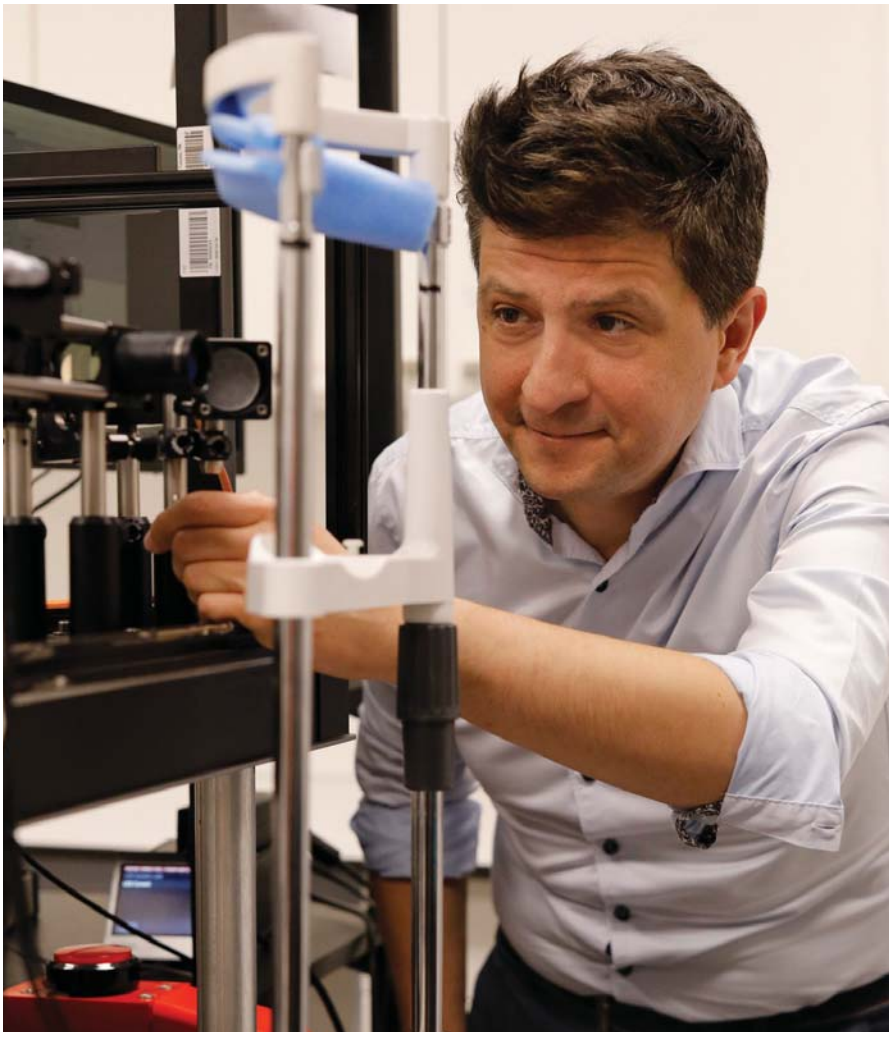
Ophthalmologists have been using ophthalmoscopes or fundus cameras for many decades to view the condition of the retina. Much of the intuition in ocular diagnosis is related precisely to images in the plane of the fundus (coronal projection). While available OCT devices are good at reconstructing cross-sectional images, they unfortunately have limited transverse resolution degrading the quality of retinal images in the fundus plane. Even if the spatial resolution were significantly improved, this unfortunately negatively impacts the depth of imaging – that is, we would only see part of the retina (only the layers of pigment epithelium and photoreceptors or only the layers of neurons). To an even greater extent, it is impossible to penetrate the choroid and see its structure with high resolution. In addition, specific noise – also known as speckles – are present in OCT images of the fundus, further impairing high-resolution imaging and the identification of anatomical details or lesions.

How does the new technology work to provide high quality images of the retina and choroid?

To improve the quality of imaging, we use

a different method of image reconstruction – called full-field registration – that is not found in classic OCT. Unlike OCT, where the laser beam is focused and scanned onto the retina, here the entire fundus image for different wavelengths is collected. In this way, the images are more like a classic microscope or camera, where defocusing does not result in a loss of recorded light, only a blurring of the image. We are able to compensate for this blurring in the computer using appropriate algorithms. In this way, we obtain fundus images in cross sections of five micrometers and resolution of five micrometers collected from any depth of the retina or choroid.

Despite this, registering full-field OCT with a light source like the one used in traditional OCT would end in complete failure: the highly scattered light in the choroid and pigment epithelium would cover all useful structures and all you would see would be fog. To see the details of the choroid and retinal structures through this fog with high contrast, we need a light source with partial spatial coherence. For this, in turn, we used a long multimode optical fiber that generates hundreds of different patterns of illumination of the sample. Each of these patterns – or modes – exits the fiber with a delay relative to the others. These delays are set by the length and type of optical fiber. The presence of delays for different patterns of fundus illumination allows us to average hundreds of interferometric images on the camera and omit scattering effects and speckle noise.



Maciej Wojtkowski, credit: Piotr Furman

What are the limitations for the clinical application of this new technology?

Although we have had successful outcomes measuring several patients, after testing the method in the laboratory, the system was found unsuitable for measurement in a clinical setting. In light of this, in the next stages of our research, the system must be converted to a more portable device and adapted to suit clinical working conditions. For high-resolution measurements from the retinal-vascular complex in a standard field of view, a quarter of a terabyte of data must be collected. Although transferring, analyzing, and storing such a large amount of data presents a huge challenge, it is hoped that analyzing the data at the time of collection will significantly reduce the amount of data to be archived.

What does the development of STOC-T mean for the future of retinal imaging and patient care?

We believe that access to images of the choroid will help ophthalmologists better understand the origins of many eye conditions and more quickly respond to early lesions. It may also enable the diagnosis of systemic conditions by providing a more accurate view of the complex vascular system in this part of the eye. We also hope that the quality of imaging can be further improved by the engineering of the device itself. This will enable us to respond to the needs of monitoring and validating new systemic and eye therapies such as pigment epithelial patch implants, gene therapies to restore vision, and precise surgical interventions.

See reference online.

ON or OFF

New research raises questions around the evolution of vision and the development of retinal circuits

Though it is well known that some photosensitive retinal ganglion cells drive non-image forming vision, there is much we don't know. New research undertaken by the Photoreceptor Physiology group of the National Institute of Health aimed to unlock additional insight into the behaviors of the retinal circuits driving the process. Here, Johan Pahlberg, Senior Scientist and leader of the research group at the National Eye Institute breaks down the main findings.

Could you first provide some context to your research?

Besides the classical photoreceptors in the retina – the rods (which my lab is particularly interested in) and the cones – there are also intrinsically photosensitive retinal ganglion cells that are known to control non-image forming vision, including circadian photoentrainment, the pupillary light response (PLR), mood, and sleep. How they connect to different brain regions is increasingly becoming understood thanks to the efforts and research of many labs – most notably the Hattar Lab, with whom we collaborated on this project.

The outer retinal circuits that drive image-forming vision (that is consciously perceived) have been extensively studied and clearly defined, but the behaviors of the circuits that drive the retinal ganglion cells involved in non-image forming vision remain entirely unknown. With help from our colleagues, we were able to obtain several different mouse lines in which we were able to manipulate different rod and cone retinal pathways, and study how they might influence these behaviors.

What's your elevator pitch for the study?

We observed that the retinal circuits driving image and non-image forming visual behaviors are distinct and mostly non-overlapping (1). Perhaps the most interesting feature of our visual system is the fact that both increases and decreases in light are detected in what are known as the ON and OFF pathways. Remarkably, the ON pathway is dispensable for image-forming vision; the OFF pathway can convey sufficient information to compensate for its absence. In stark contrast to image-forming vision, we found that the OFF pathway does not play any role in non-image forming visual behaviors.

"Remarkably, the ON pathway is dispensable for image-forming vision."

This surprising revelation raises several interesting questions about the evolution of vision and the ON and OFF pathways in the retina, when and how different retinal cell types evolved, and how they connect in the retinal circuitry, and why non-image forming vision completely disregards a major parallel information stream to the brain (the OFF pathway).

Our work could be viewed as a starting blueprint for how to comprehensively dissect neuronal circuits and their function – and thus how to possibly understand deficits in vision.

What are the next steps for your research – and your expectations for the future?

We used a simple vision behavior test (did the mice see or not see a flash of light) and two non-image forming behaviors – the PLR and circadian photoentrainment, so there are several other different behaviors we can use to assess if the retinal circuits are similar or different. Our mouse lines also open up the possibility to comprehensively study and understand how the different rod retinal pathways operate in the retina.

Road asset from unsplash.com

Reference

1. *C Beier, et al., Cell Rep, 39, 111003 (2022). PMID: 35767957.*

Turning Back Time

Does loss of the "youth" protein PEDF drive age-associated visual decline?

It is no secret that eyesight tends to deteriorate with age, but could the decline in secretion of the "youth" protein by the retinal pigment epithelium be the cause? We speak to Patricia Becerra, senior author of a recent study from the National Institutes of Health that aimed to answer this question.

Clock asset form rawpixel.net

How did the study take shape?

Our research team has always wondered if loss of the pigment epithelium-derived factor (PEDF) protein was driven by aging or was driving aging in the eye.

PEDF protects retinal cells against several types of insults known to trigger retinopathies, such as those of photoreceptor degeneration, including AMD and retinitis pigmentosa. PEDF is also colloquially called the "youth" protein because of its abundance in young skin, lung, and retinas, and the fact that it declines with age, occurring with senescence in skin and lung epithelial cells. PEDF also declines in animal models of retinal degeneration. PEDF for photoreceptors is produced and secreted by the retinal pigment epithelium (RPE).

In patients with AMD or certain types of retinal dystrophies, senescence or death of RPE cells leads to vision loss. To address questions of whether PEDF may contribute to aging prevention in the RPE, we used a mouse model lacking the PEDF gene *(Serpinf1)*.

And what were the key findings?

We established that PEDF loss is a cause of senescence-like changes in RPE (1) and highlight PEDF as a regulatory protein of age-related changes.

We found that the deletion of the Serpinf1 gene, which encodes PEDF, increases senescence-associated gene expression. Serpinf1 deletion also increases the senescence-associated β-galactosidase activity in the RPE. The RPE cellular morphology shows enlarged cell nuclei and an increase in the nucleoli number, implying chromatin reorganization when PEDF is missing. Additionally, RPE cells without PEDF have lower levels of unprocessed lipids and photoreceptor outer segments components accumulated in the RPE – likely due to a decline in phagocytic function.

What are the potential implications of your research?

The findings point to applications of PEDF and derivatives as potential therapeutics to counteract the damaging effects of PEDF depletion. One point to consider is that the lack of a macula in the mouse retina means that parallels to some conditions, such as AMD, are not as clear as they might be in species with that structure.

This is the first time that a mouse without PEDF has been used to study senescence and phagocytosis of RPE. Our study provides evidence of the importance of PEDF signaling in age-related disease processes. The decline in the PEDF receptor, PEDF-R, on the surface of RPE cells in the mouse lacking PEDF implies involvement of the PEDF–PEDF-R axis in lipid metabolism. Furthermore, we postulate that PEDF is required to enhance the activity of PEDF-R in the RPE to promote digestion of the phagocytosed photoreceptor outer segments. Therefore, the decline or lack of PEDF can negatively affect the renewal of photoreceptor outer segments – which is vital for the process of vision.

Where next?

The importance of the PEDF protein is clear – we know that its levels decline with age and degenerative diseases; however, we still do not know what causes its loss. Though the retina contains a high content of lipids, the complex role of lipid metabolism in maintaining a healthy retina, especially photoreceptors, has not been fully delineated. Lipid accumulation caused by PEDF loss associates this factor with lipid metabolism in the retina. Our lab will continue exploring ways to use PEDF and PEDF-derivatives or mimics as therapeutics for humans.

Reference

1. *IT Rebustini et al., "PEDF deletion induces senescence and defects in phagocytosis in the RPE," Int J Mol Sci, 23, 7745 (2022). PMID: 35887093.*

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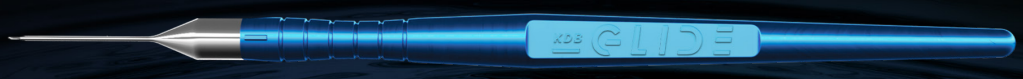

Providing optimal interface with the canal of Schlemm for excisional goniotomy

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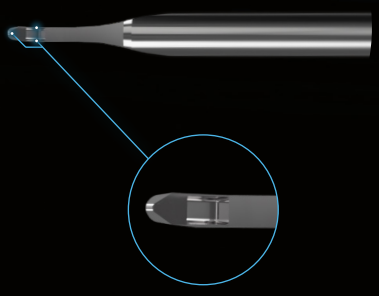
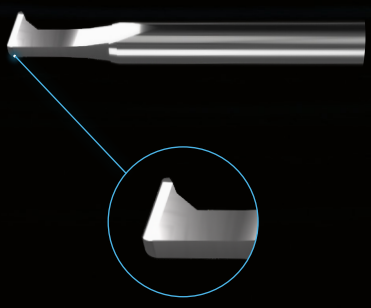


ROUNDED HEEL



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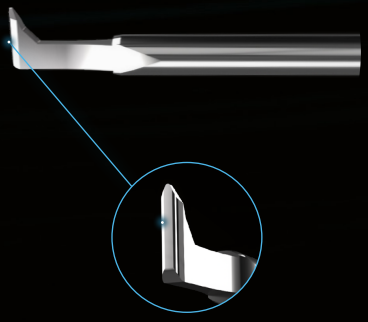

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Assessing ARCA. To test whether the macular and peripapillary structural and vascular alterations in elderly patients with age-related choroidal atrophy (ARCA) mimics glaucomatous degeneration, researchers conducted a cross-sectional, observational study of 95 eyes. The values and fundus autofluorescence images of the peripapillary retinal nerve fiber layer (pRNFL) and macular nerve fiber layer were acquired with spectral domain-optical coherence tomography. The results show that patients with ARCA had decreased pRNFL, inner macular layer thickness, and choroidal vascularity index when compared with healthy, control eyes. (1)

Biomechanics for Glaucoma. A Researchers recently used the Ocular Response Analyzer (ORA) and the Corvis ST (CST) to identify the corneal biomechanical differences between patients with primary open angle glaucoma (POAG) and patients with ocular hypertension (OHT). A total of 31 case-control studies featuring 2462 POAG patients and 345 OHT patients, and 3281 normal controls were included. Among other findings, the results found that the corneal hysteresis (CH), corneal resistance factors, and highest concavity time were all lower in POAG patients than in normal controls. (2)

Curating Contacts. New research, led by Chi Hwan Lee – Associate Professor of Biomedical Engineering in Purdue's Weldon School of Biomedical Engineering and co-founder of BVS Sight – has led to the development of a new wearable biomedical device that continuously monitors intraocular pressure (IOP) in a person's eye. Differing from commercially available options that are often stiff and uncomfortable, Lee's smart contact lenses combine biocompatibility, softness, transparency, wettability, oxygen transmissibility, and overnight wearability, making it a better alternative to current tonometers on the market. (3)

Lost My Nerve. A retrospective analysis investigated the association of mean intraocular pressure (IOP) and IOP variability with the rate of retinal nerve fiber layer thinning over time in patients with glaucoma. The longitudinal cohort included a total of 815 eyes from 508 patients with imaging follow-up for a mean of 6.3 years from December 2008 to October 2020 and found that, even after adjustment for mean IOP, IOP variability was independently associated with structural change in patients with glaucoma, supporting its potential value in clinical management. (4)

See references online.

IN OTHER NEWS

Improving Patient Outcomes. *A A randomized, double-masked, placebo-controlled, cross-over study has found that the use of citicoline oral solution for treating chronic open-angle glaucoma improves the quality of life in glaucoma patients. (5)*

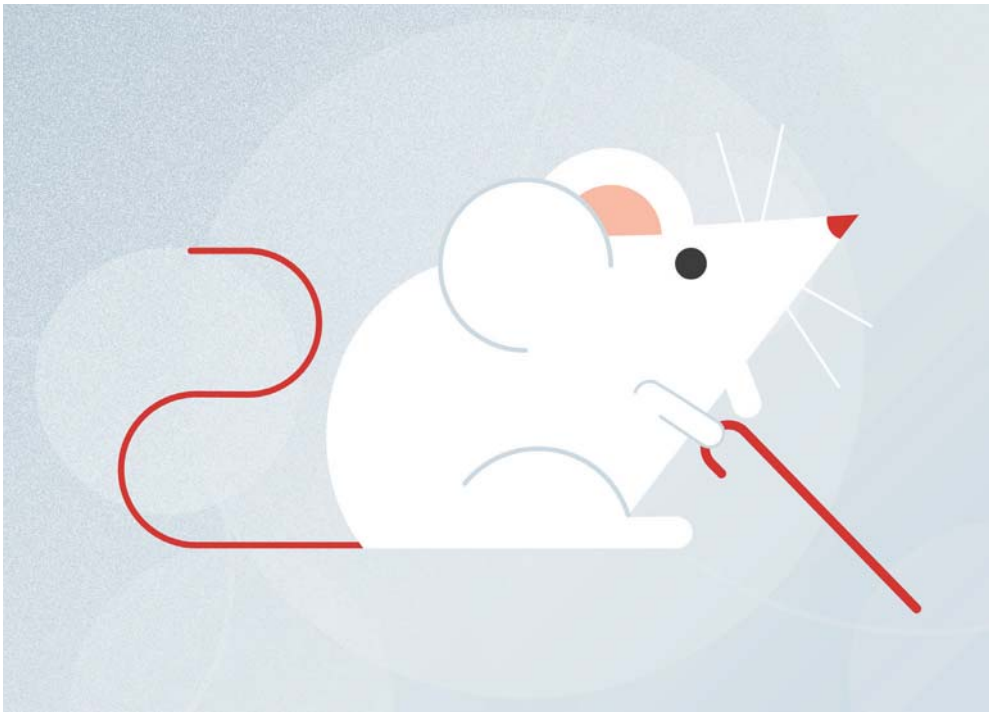
Structural Scanning. *By conducting OCT scans on over 1,000 glaucoma patients, researchers have identified the critical 3D structural features of the optic nerve head for glaucoma diagnosis. (6)*

An Effective Solution. *A new study has found that the aurolab aqueous drainage implant is more effective than the ahmed glaucoma valve for treating refractory glaucoma in both surgical success rate and reducing intraocular pressure. (7)*

Managing Keratopathy. *Research has found that descemet's stripping endothelial keratoplasty combined with retropupillary fixated iris-claw lens is effective management of aphakic/pseudophakic bullous keratopathy in patients who require secondary IOL or IOL exchange.*

Age and Glaucoma

Understanding the molecular effects of aging with a new model of glaucoma



Although glaucoma is complex and affected by several risk factors, including IOP, family history, and high myopia, age is the most predictive factor. Despite this, the molecular impact of aging on the eye remains limited.

Now, researchers at the University of California have developed a new stress-induced aging mouse model to better understand glaucoma progression (1). The team believes their model offers advantages over previous animal models that do not recapitulate all aspects of glaucoma; for instance, some laboratories focus on developing animal models of chronic IOP elevation whereas others use mice who developed natural mutations. The new model allows researchers to capture the specific time span of molecular changes caused by glaucomatous stress and thus provide a clearer picture of how age and stress directly impact the eye.

Most significantly, the team found that susceptibility to stress is pre-conditioned epigenetically and adapts with age. The researchers also noted that the pathways activated upon exposure to IOP elevation included increased inflammation and cell death, as well as the degradation of extracellular matrix integrity. Moreover, when primed with previous instances of mild IOP elevation, strong stress responses were induced in young tissue upon mild hypertension. Finally, the molecular mechanism of aging was shown to be regulated at the level of chromatin modification, meaning that the rate of aging may be modifiable using drug-affecting enzymes involved in chromatin modifications.

The research team says that the multifaceted results highlight the importance of early diagnosis for managing glaucoma. And outside of glaucoma, the study also suggests a potential use of the retina as a model system for studying molecular and functional changes in aging and neurodegeneration.

Reference

1. *Q Xu et al., "Stress induced aging in mouse eye," Aging Cell, [Online ahead of print] (2022). PMID: 36397653.*

THE IMPACT OF AGING

How do you measure the impact of aging on visual functions? In this research, the team used several functional assays. First, quantitative optomotor response measured contrast sensitivity in both day and night time light conditions. To see how the loss of retinal cell ganglion activity is linked to decreased visual acuity, the team used pattern electroretinography responses. To investigate whether the molecular changes in the aging retina can explain the observed functional decline of the visual system, the team undertook whole retina mRNA sequencing to analyze the down-regulation and up-regulation of specific genetic markers.

Digging into Glaucoma's Genetic Roots

Researchers link a newly discovered mutation in the THBS1 gene to congenital glaucoma

Janey Wiggs – Professor of Ophthalmology and Vice Chair for Clinical Research at Harvard Medical School – and her team at Massachusetts Eye and Ear have identified a new mutation of interest in their search for genetic drivers of congenital glaucoma.

Exploring a dataset of more than 34,000 adults with glaucoma, the team found a striking and novel variant in the thrombospondin-1 (THBS1) gene in an American family of European-Caucasian descent (1). Notably, the mutated gene was not found in family members without childhood glaucoma nor in large, population genetic databases. Further research conducted at Flinders University, Australia, found another two families – one of mixed European descent and one Sudanese family originally from Africa – with an alteration in the same amino acid and a history of primary congenital, adding further strength to the correlation. Additionally, a mouse model with the THBS1 mutation was developed by Robert J. D'Amato – the Judah Folkman Chair in Surgery in the Vascular Biology Program at Boston Children's Hospital – to explore pathogenesis.

Here, Wiggs sheds additional light on the research and its potential impact.

What are the implications of finding this new variant?

Identifying genes responsible for inheritable conditions can help define the underlying disease pathogenesis, which can lead to new therapies. Additionally, finding genes that cause these conditions makes it possible to use genetic testing to find mutation carriers who are at high disease risk. Follow up research on a mouse model with the same mutation demonstrated that the thrombospondin mutation caused accumulation of aggregated protein in the trabecular meshwork, resulting in a reduction in intraocular fluid outflow. This novel disease mechanism for congenital glaucoma could potentially impact the development of novel treatments.

How important is collaboration when digging deeper into complex conditions?

Well, this was a very exciting study that involved international collaborations between clinicians, clinician scientists, and basic scientists. Without these collaborations, the project would simply not have been possible.

What does this research mean for the future of childhood glaucoma care?

As noted, adding a new gene for congenital glaucoma improves genetic testing for this condition and also could help identify novel approaches to treatment. Genetic testing is very important for glaucoma; people who have high risk of disease can be identified before the disease becomes manifest, allowing for preemptive treatment.

Where should additional research efforts be directed?

We still need to identify more genes and mutations responsible for early-onset glaucoma. Currently, we have only a few genes known to cause these conditions, so genetic testing using these genes only provides a molecular diagnosis in about 20 percent of individuals. Finding additional genes could help provide useful testing for the remaining 80 percent.

Reference

1. *JL Wiggs et al., "Thrombospondin 1 missense alleles induce extracellular matrix protein aggregation and TM dysfunction in congenital glaucoma," J Clin Invest, [Online ahead of print] (2022). PMID: 36453543.*

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Myopia Management Starts at Home

Noha Ekdawi discusses the growing prevalence of myopia and the importance of outdoor time

By Sarah Healey

Noha Ekdawi is a pediatric ophthalmologist at the Wheaton Eye Clinic in Chicago. Ekdawi's practice focuses on the medical and surgical treatment of various childhood disorders including strabismus, amblyopia, cataract, and glaucoma. Here, Ekdawi discusses the growing prevalence of myopia and the ways in which we can combat this visual impairment at an early age.

Noha Ekdawi

What inspired you to get into pediatric ophthalmology?

I loved pediatrics when I was in medical school. As I was doing my medical rotations, I would always ask to do pediatrics to gain more experience in the subspecialties. As I was doing pediatric ophthalmology, I was working with the famous Marilyn Miller – I didn't realize quite how famous she was at the time! In any case, I walked into her clinic and said to myself, "This is it! This is what I want to do!" In short, I want to help kids. I realized that childhood is the time where you can make a huge difference to the course of someone's life; it is a very positive specialty – you can fix things.

When did you begin to pay particular interest to myopia?

When I came back home from my residency and fellowship at the Mayo Clinic in Minnesota, I found out that all my friends, alongside myself and my father, were near-sighted. There were more nearsighted people in my home city than I was used to seeing at the clinic. When my child was born, research started to come out about how the rates of nearsightedness in Minnesota weren't as bad as they were in Chicago. I wanted to identify the reason why and started researching myopia. Since then, I've started using low dose atropine to treat nearsightedness and, although I have been pleased with the results, I appreciate that it doesn't work for everyone. It is now important to look for other alternatives.

What factors determine myopia?

I think there are many factors that determine myopia – genetics being one. If you live in an area where the gene pool is myopic, you are likely to develop myopia. I grew up in Chicago, and moved back here after my residencies – and I am now myopic; this is no coincidence. Outdoor time is really interesting too. You would think that people in the suburbs would be outside more – but the reality is that people watch a lot of TV and everyone has a Nintendo. It's going to be interesting to see studies on the impact of screen time on myopic progression in the aftermath of COVID….

How have you tried to prevent the onset of myopia in your children?

Ultimately, it starts in the home. The choices we make as parents make a difference. My children didn't get given technology when they were younger and I picked childcare options that instilled more outdoor time in their day. When we moved to a house that didn't have a park nearby, I had a swing set built in the backyard in the first week. Notably, being outdoors is not only good for preventing myopia, it has also been found to decrease ADHD symptoms and depression rates. If we push children to go outside more, even in inclement weather, their eyesight would be much better off.

What does the future of myopia management look like?

Some technologies, such as MiSight contact lenses and Ortho-k lenses, have been circulating for a long time – and I suspect they will continue to do so. New research into red light therapy looks particularly promising, but it requires a machine, making it more difficult to implement in everyday clinics. There is also a great deal of genetics research that needs to be explored. I believe some really high myopes have genetic disorders; I had an adopted child who was progressing no matter what I did. After conducting some genetic testing, I discovered that she had a gene that made it very likely that she would suffer from retinitis pigmentosa.

As for the actions I am going to take as a pediatric ophthalmologist, I want to try and educate my area of school nurses and principals about the importance of increasing outdoor time and outdoor education. I have personally seen the benefits; my kids should be myopic but little changes have changed their sight. Myopia is not the devil – but when you hit a minus six prescription and lower, problems like retinal tears and glaucoma start to occur.

It is clear that much more research is needed to combat the growing prevalence of myopia in children. Although health economic policies and school settings contribute to the factors that can determine myopia, ultimately the prevention of nearsightedness starts in the home. Small steps can lead to big differences.

"Being outdoors is not only good for preventing myopia, it has also been found to decrease ADHD symptoms and depression rates. If we push children to go outside more, even in inclement weather, their eyesight would be much better off.."

What can be done to ensure that children in low income countries get access to the eye care they need?

One initiative striving to make a small difference comes from the aforementioned Marilyn Miller, who developed a program that allows ophthalmologists from outside of America to attend the American Academy of Pediatric Ophthalmology and Strabismus meetings (1). The program aims to provide ophthalmologists from around the world with information about current innovations and practices in ophthalmology that can be taken back to their home countries. I have recently joined the travel fund myself to help support this important initiative. Although it's a step in the right direction, there is a great deal that needs to be done. Education is my only answer right now.

Inspiring Innovation

Sitting Down With… George Magrath,
CEO of LexitasPharma Services, and Ophthalmologist at the Medical University of South Carolina, Charleston, South Carolina, USA

Can you tell us a little about your career journey so far?

My career journey has been rather unorthodox! During my ophthalmology residency, one of the things that I noticed in our area of South Carolina – there was very little care for people with ocular cancer – so I went to Wills Eye Hospital for a couple of years of training in ocular oncology, then came back six years ago to create an ocular oncology practice where I also do some medical retina work.

In parallel with that, I earned two degrees – one a Master's of Business Administration, the other a Master's of Applied Economics. Together, they ultimately led to my role at Lexitas, a contract research organization solely dedicated to ophthalmology. I began there as Chief Medical Officer, but about six months in, I became CEO, a position I've held for over two years now.

What are your thoughts on the relationship between ophthalmology patient care and industry?

I think everybody's goal is to develop new medicines to change the lives of our patients and, to do that, you need a sustainable business model. Without industry, there would be significantly slower development of new products. Just look at what Eylea and Lucentis have done. They have been transformational! Solutions to those problems would not have happened as rapidly or effectively without industry support.

After all, as a doctor, if I don't have medicines to give to patients, I can't do much. There's no treatment for geographic atrophy right now – but, because of industry working with academia, there may be in the future. I think that industry is fantastic at identifying good science and putting significant resources behind it. We (rightfully) must run extremely rigorous trials to prove that medicines are safe and effective before they reach patients, but that's a risky, expensive, and time-consuming process that is very hard to be done without industry support.

What do you think of the current models for drug financing in ophthalmology?

We're fortunate in ophthalmology that early-stage venture capital funds, such as Ex-Sight Ventures or Infocus Ventures, come in to help fill gaps in the development process. Funds like these fulfill a critical role by providing Series A capital to companies that have a great idea, but need a funding boost to finish their first study. It's an incredibly high-risk scenario – most drugs never reach the approval stage. The availability of early stage capital has been a game-changer in ophthalmology over the past couple of years and we are very fortunate to have amazing early stage venture capitalists willing to invest in our area.

The next step in the process comes with a bigger check, usually from venture funds that have identified ophthalmology as a key investment area. These are critical for getting proof-of-concept data. After that, you're looking at funding phase three, at which point the risk is generally lower and more around the commercialization of the product. Traditionally, this has been done in ophthalmology by either a strategic acquisition or the public markets – going into an IPO. Unfortunately, the IPO market has had a hard time over the past year and that situation will likely continue for another year or more. This has created a gap that will inevitably be filled by strategic acquisitions. We know, for a host of reasons, that large, publicly traded pharma companies have healthy balance sheets, giving them the ability to engage in strategic mergers and acquisitions as the valuations in the IPO market have fallen.

I think that, for the investment community, ophthalmology is interesting because we are a niche investment area. I mentioned Eylea and Lucentis earlier; another example would be Spark Therapeutics' LUXTURNA or Horizon's TEPEZZA. For a small specialty, we have a lot of great success stories.

What have been the biggest ophthalmology innovations in recent years – and what's on the horizon?

We're moving away from some broad treatments, such as steroids, and toward precise treatments that address the underlying pathophysiology of a disease. For example, we have multiple steroid-sparing immunomodulating drugs in trial now. Immunology has been an amazing field for oncology and rheumatology over the past decade or so, and ophthalmology is next. The immune system plays a role in almost every retinal disease, so why not see what we can gain by targeting it?

What do you think is the best thing about working in ophthalmology?

The best thing about being an ophthalmologist is the amazing impact you can make on patients. Our patients come to us because they're going blind. It's an incredibly serious thing – I consider myself doubly privileged because I not only see the patients and the impact treatment has on their lives, but also get to be involved in a small way in developing treatments.

What was the moment that made you realize, "Ophthalmology is for me?"

When I was rotating through the ophthalmology clinics at the Medical University of South Carolina (MUSC), there were two physicians, Charles Beischel and Joe Lally, working in general ophthalmology at MUSC. Working with them, I saw first hand how they impacted people in a really deep way. They, along with many others, taught me what it meant to be a surgeon. The precision, focus, repetition, and constant refinement you need to foster in order to achieve excellent, consistent results. I've watched them, and many others, truly change people's lives with their care. Those two people and their clinics were all it took to make me go all in on ophthalmology.

When my patients don't have time for downtime, I recommend

MicroPulse® Transscleral Laser Therapy for Glaucoma

"MicroPulse TLT is very patient and lifestyle friendly. With a good safety profile and minimal downtime, the procedure doesn't impact quality of life. It's a non-incisional option that I use for all types and stages of glaucoma and for those who don't have time for post-op limitations.

My active working patient

My 78-year-old patient presented with uncontrolled secondary glaucoma on maximum medical therapy following multiple retinal detachment surgeries. He owns a body shop and did not want to be away from his business. Following MicroPulse TLT, his pressure fell from 18 OS on three drops to 13 OS on two drops, and his vision was stable. He is happy and continues to work.

Ye Elaine Wang, MD
Harvard Eye Associates
& Clinical Instructor
UCLA Stein Eye Institute
Laguna Hills, California

Scan QR to learn how Dr. Ye Elaine Wang uses MicroPulse® Technology in her practice.

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