SEPTEMBER 2021 # 56

the Ophthalmologist™

Within Reach

Outreach program of retinopathy of prematurity screening in southern India

BVI

Cataract Surgery Streamlined

High contrast and high quality[1] vision.
Seamless, predictable, and efficient preloaded IOL delivery.[2]

Learn More at ipureiol.com

| PURE
ASPHERIC
MONOFOCAL OPTIC

*THIS PRODUCT IS FDA APPROVED AND ONLY SOLD IN THE US.

References
[1]US Patent NO: US8647383. [2]Data on file, BVI, 2019.

ipureiol.com
bvimedical.com

US Tel: 866-906-8080 Fax: 866-906-4304
Email: customersupport@bvimedical.com

1575725-01

Live and Learn

Five personal anecdotes we would never have heard without The Ophthalmologist Power List

Following the publication of our 2021 Power List, which exclusively featured women in ophthalmology, I received a great deal of positive feedback – not only from the female frontrunners but also from their peers. The majority of readers who spoke to me saw the decision to feature only women in the way it was intended: to redress the balance of "power" in the field after years of underrepresentation. Even though it is now easier than ever for women to enter the specialty, certain challenges remain firmly in place, as Tina Felfeli and Yvonne Buys comment on page 10.

Though the 2021 Power List will remain fresh and topical in our minds for some time, we must also look to the future – the 2022 edition. And in case you missed the announcement, nominations are already open: theophthalmologist.com/power-list/2022

I hope that our special focus on equity in 2021 will bear fruit in the form of a strong representation of women and other minorities. So please, go forth and nominate the individuals you feel deserve to be recognized and celebrated. To give you a friendly push in the right direction, I will leave you with five surprising things we learned from previous lists…

1. Serial Power Lister Carol Shields shared the moment she found out the baby she was treating for retinoblastoma lived in her old house in her western Philadelphia hometown
2. Terry Kim (aka DJ Special K) fondly remembered his musical contributions to the biggest ophthalmic meetings in the US – DJing together with Tony Aldave (aka DJ AJA) at major clubs to crowds of over 2,000 AAO and ASCRS attendees
3. David Chang humbly told the story of his young son – a keen baseball player – who suddenly and inexplicably started making mistakes on the court… until a pediatrician suggested the should perhaps check his son's vision
4. Douglas Rhee described how his professional career shifted profoundly when he decided to reassess plans for a clinical fellowship abroad because his cat couldn't travel with him (it all worked out for the best!)
5. And finally, we heard the story of the surprising and timely donation that allowed Sir Peng Tee Khaw to help a key researcher, who then went on to have a rather successful career in cellular regeneration.

What stories will we unearth in 2022? Well, in part, that's up to you (theophthalmologist.com/power-list/2022).

Aleksandra Jones
Editor

CMS Confirmed for continued separate payment in ASCs[1]

Less stress, pure success ...in your O.R. day[2]

OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

The data are compelling and consistent—non-opioid OMIDRIA makes cataract surgery better for you and your patients

Published and presented clinical data and manuscripts report that in post-launch (i.e., not included in current labeling), prospective and retrospective, double-masked and open-label, cohort and case-controlled, single and multi-center studies, the use of OMIDRIA statistically significantly:

- Prevents intraoperative floppy iris syndrome (IFIS)[3]
- Prevents iris prolapse[3]

Compared to steroids*:

- Reduces cystoid macular edema (CME)[4,5]
- Decreases breakthrough iritis[4]
- Reduces pain[4]
- Reduces photophobia[4]

*OMIDRIA used intraoperatively with postoperative NSAIDs (no steroids) when compared to postoperative steroids with or without NSAIDs (no OMIDRIA).

Compared to epinephrine:

- Decreases complication rates[6]
- Decreases use of pupil-expanding devices (PEDs)[6-10]
- Enables performance of surgery and postoperative care without the use of steroids—allowing NSAID-only anti-inflammatory therapy[4,5]
- Shortens surgical times[6,8-10]
- Reduces need for opioids (i.e., fentanyl) during surgery while decreasing VAS pain scores[11]
- Prevents miosis during femtosecond laser-assisted surgery[12]
- Improves uncorrected visual acuity on day after surgery[6]

VAS = visual analog scale

OMIDRIA inhibits the release of inflammation-causing prostaglandins, preventing miosis and reducing postoperative pain[13]

CMS confirmed that OMIDRIA qualifies for separate payment under the non-opioid pain management policy when used in ASCs. Contact your commercial and Medicare Advantage plans to determine OMIDRIA reimbursement. Reach out to your OMIDRIA representative today or visit omidria.com to learn more.†

†Based on currently available information and subject to change without notice. Individual plan coverage, payment, policies, and procedures may vary and should be confirmed by the facility. Omeros does not guarantee coverage or payment.

IMPORTANT SAFETY INFORMATION

INDICATIONS AND USAGE

OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

IMPORTANT SAFETY INFORMATION

OMIDRIA must be added to irrigating solution prior to intraocular use. OMIDRIA is contraindicated in patients with a known hypersensitivity to any of its ingredients.

Systemic exposure to phenylephrine may cause elevations in blood pressure.

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

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

Please see the Full Prescribing Information for OMIDRIA at http://www.omidria.com/prescribinginformation.

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

References: 1. 2020 Medicare Hospital Outpatient Prospective Payment System and Ambulatory Surgical Center Payment System Final Rule (CMS-1736-FC). **2.** Omeros survey data on file. **3.** Silverstein SM, Rana V, Stephens R, et al. Effect of phenylephrine 1.0%-ketorolac 0.3% injection on tamsulosin-associated intraoperative floppy-iris syndrome. *J Cataract Refract Surg.* 2018;44(9):1103-1108. **4.** Visco DM, Bedi R. Effect of intracameral phenylephrine 1.0%-ketorolac 0.3% on postoperative cystoid macular edema, iritis, pain, and photophobia after cataract surgery. *J Cataract Refract Surg.* 2020;46:867–872. **5.** Walter K, Kauffman L, Hess J. Rate of pseudophakic cystoid macular edema using intraoperative and topical nonsteroidal antiinflammatory drugs alone without steroids. *J Cataract Refract Surg.* 2020;46:350–354. **6.** Rosenberg ED, Nattis AS, Alevi D, et al. Visual outcomes, efficacy, and surgical complications associated with intracameral phenylephrine 1.0%/ketorolac 0.3% administered during cataract surgery. *Clin Ophthalmol.* 2018;12:21-28. **7.** Bucci FA Jr, Michalek B, Fluet AT. Comparison of the frequency of use of a pupil expansion device with and without an intracameral phenylephrine and ketorolac injection 1%/0.3% at the time of routine cataract surgery. *Clin Ophthalmol.* 2017;11:1039-1043. **8.** Visco D. Effect of phenylephrine/ketorolac on iris fixation ring use and surgical times in patients at risk of intraoperative miosis. *Clin Ophthalmol.* 2018;12:301-305. **9.** Matossian C. Clinical and economic outcomes in cataract surgery using phenylephrine 1.0%-ketorolac 0.3% in a real-world setting. Presented at: American Society of Cataract and Refractive Surgery – American Society of Ophthalmic Administrators Symposium & Congress (ASCRS-ASOA). April 13-17, 2018. Washington, D.C. **10.** Walter K, Delwadia N, Coben J. Continuous intracameral phenylephrine-ketorolac irrigation for miosis prevention in femtosecond laser-assisted cataract surgery: reduction in surgical time and iris manipulation. *J Cataract Refract Surg.* 2019;45(4):465-469. doi: 10.1016/j.jcrs.2018.11.004 **11.** Donnenfeld ED, Shojaei RD. Effect of intracameral phenylephrine and ketorolac 1.0%/0.3% on intraoperative pain and opioid use during cataract surgery. *Clin Ophthalmol.* 2019;13:2143–2150. **12.** Gayton JL. Effect of early phenylephrine and ketorolac injection 1% / 0.3% (Omidria®) usage on pupil diameter in traditional and femtosecond laser assisted cataract surgery. E-poster presented at: 15th International Congress on Vision Science and Eye; August 10-11, 2017; London, UK. **13.** OMIDRIA [package insert]. Seattle, WA: Omeros Corporation; 2017.

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

Contents

the Ophthalmologist

ISSUE 56 -SEPTEMBER 2021

Change of address info@theophthalmologist.com
Hayley Atiz, The Ophthalmologist, Texere Publishing, 175 Varick St, New York, NY 10014.

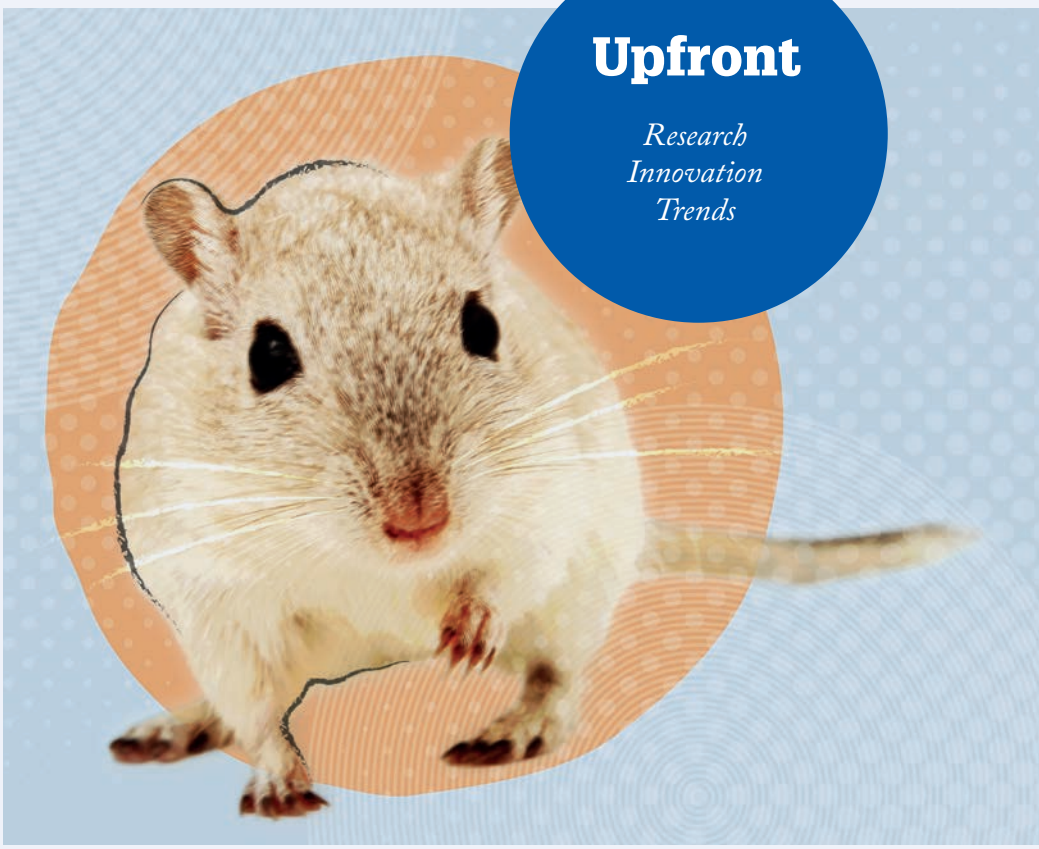
General enquiries
www.texerepublishing.com | info@theophthalmologist.com
+44 (0) 1565 745 200 | sales@texerepublishing.com

Distribution: The Ophthalmologist North America (ISSN 2398-9270), is published monthly by Texere Publishing Inc, 175 Varick St, New York, NY 10014. Single copy sales $15 (plus postage, cost available on request info@info@theophthalmologist.com). Non-qualified annual subscription cost is available on request.

The Ophthalmologist is printed using soy ink

Upfront

Research
Innovation
Trends



Of Mice and Men

The discovery of focea in mice implies that their vision may be more similar to human sight than previously thought

Mice are crucial to research and development in ophthalmology, but how does mouse neuro-ophthalmology compare to that of humans? A recent study has revealed a region of the mouse brain responsible for enhanced spatial resolution – a feature of mouse eyesight not previously seen. Called the focea, this region is named after its closest human counterpart: the fovea, which is located in the retina and specializes in high-resolution vision. Because mice lack a fovea, researchers were unsure as to their spatial resolution capabilities – but the debate could soon be over. "We know that many species, including cats and monkeys, have better resolution in the center of the visual field," explains co-lead researcher Pieter Roelfsema, "and this specialization may be even more widespread than anticipated." Mice actually make compensatory eye movements to keep the region of eyesight that's processed at the focea in front of them – similar to the human saccadic eye movements that focus the fovea on a point of interest.

This finding "increases the potential usage of mouse models as a surrogate for human vision and opens new possibilities for studying how information is brought into the focea," explains co-lead researcher Matthew Self, presenting the possibility of using mouse models to investigate the neural circuitry of high-detail vision.

The discovery of spatial bias in mice visual processing was serendipitous; originally, the group planned to map the mouse visual cortex. "Finding a region with enhanced resolution was a surprise. That is quite often the case in fundamental research; you find something unexpected," states Self.

The next steps for this research are already in place. "We are now studying how mice segregate objects from the background and how this form of vision is influenced by visual experience and learning," says Roelfsema.

Reference

1. *EH van Beest et al., Nat Commun, 12, 4029 (2021). PMID: 34188047.*

INFOGRAPHIC

How Does It Feel Now?

A new survey reveals post-pandemic attitudes to eye care

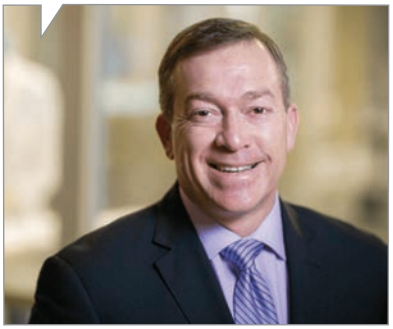
The See Tomorrow initiative surveyed over **1,000 adults** in the US

1 IN 4 respondents is thinking more about their ocular health now than they did before March 2020

BUSINESS IN BRIEF

The latest industry news – in no more than 60 words

- Vance Thompson is appointed Euclid Systems' Chief Medical Officer. Thompson is founder of Vance Thompson Vision in Sioux Falls, South Dakota, and Professor of Ophthalmology at Sanford School of Medicine, at the University of South Dakota, Vermillion, USA. Euclid is a global leader in orthokeratology and myopia management
- Monty Montoya has been appointed the CEO of TherOptix. Montoya is a founder and CEO of CorneaGen and founder of Aurion Biotech – previously known as the CEO of SightLife. TherOptix develops a drug-eluting contact lens system to deliver therapeutics to the eye. It has received orphan drug designation on a lead candidate for prevention of proliferative vitreoretinopathy.
- NovaBay and ImprimisRX have partnered up to promote prescription of Avenova, an antimicrobial lid and lash solution used for managing numerous eye conditions. ImprimisRx is a leading ophthalmology-focused pharmaceutical business that will promote Avenova, and NovaBay Pharmaceuticals is focused on Avenova commercialization for the eye care market.



- A nine-month preliminary extension pass has been granted to EyePoint Pharmaceuticals to pass through payment status for DEXYCU. EyePoint develops and commercializes therapeutics for serious eye disorders. Without the nine-month extension, pass-through payment status for DEXYCU (a treatment for postoperative inflammation following ocular surgery) would have ended on March 31, 2022.
- The refractive surgery council (RSC) reports very strong H1 laser vision correction (LVC) procedure volume growth – an 82 percent increase on 2020 so far in 2021. "LVC's current momentum is a reflection of consumers' desire to take control of their vision in what has been an uncertain, yet optimistic, moment in time," said RSC Chairman, Jim Wachtman.

The Birds Have (Magnetic) Eyes

Is a light-sensitive eye protein the key to magnetoreception in bird migration?

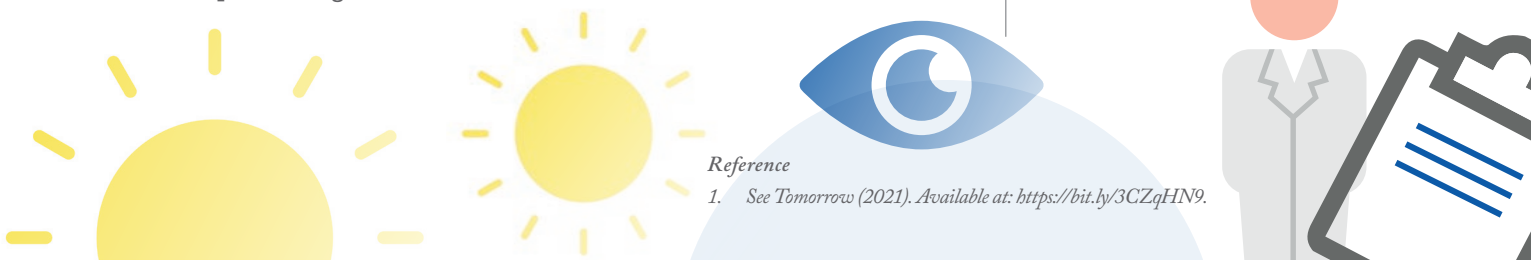
The seasonal migration of birds is fascinating – remarkable distances traveled with a mystifying ability to reach the intended destination. But now, an international collaboration of researchers may have identified the source of magnetoreception – the biological "compass" that guides birds through the Earth's magnetic fields. When isolated and tested in the lab, the team found that the light-sensitive protein cryptochrome 4 (CRY4) from the retina of the European robin is sensitive to magnetic fields (1). Is this the protein responsible for holding the GPS on their seasonal relocation marathon? Study author Peter Hore, Professor at Oxford University, UK, explains: "To establish whether the cryptochrome hypothesis is the correct sensory mechanism, magnetic field effects on cryptochromes need to be measured in vivo to study the magnetic orientation of cryptochrome-deficient birds and/or to measure magnetic field effects on nerve impulses generated in the retina."

See reference online at: top.txp.to/birds

9 out of 10 of respondents indicated their eyesight and eye health were important to the pursuit of a promising future

Compared to before the pandemic, **38 PERCENT** of people are willing to spend more on improving their health

A third of respondents trust their care professional more than they did in early 2020



Reference

1. *See Tomorrow (2021). Available at: https://bit.ly/3CZqHN9.*

A Smoking Gun

How an improved understanding of the genes that drive AMD pathogenesis could lead to new therapeutic options

It's a common story – a disease with a prime suspect, but no smoking gun. Knowing that a gene is likely responsible for AMD pathogenesis isn't enough to show causation of the disease. Hard evidence, like finding the perpetrator at the scene of the crime, is necessary – and researchers at the Sharon Eccles Steele Center for Translational Medicine (SCTM) are on the case. Genes in chromosome 10q26 are associated with AMD, but the prime gene suspects – age-related maculopathy susceptibility 2 *(ARMS2)* and high temperature requirement A serine peptidase 1 *(HTRA1)* – have yet to be caught red handed. Do these genes cause the disease through an active mechanism or is something happening to them to affect their normal function?

Using human eye tissues, the SCTM investigators demonstrated that donors with risk-associated variants had a reduction of *HTRA1* in the retinal pigment epithelium (RPE), within the 10q26 locus, which was not the case in the retina or choroid tissues. The scene of the crime was established. This tissue-specific decrease is caused by the presence of an overlapping sequence of *ARMS2*, which contains a transcription factor binding site that is disrupted by the AMD risk variant rs36212733. Subsequently, HtrA1 protein was found to be reduced at the RPE-Bruch's membrane – a crucial interface where HtrA1 would normally be responsible for driving clearance of waste and general maintenance. Notably, in a regular chromosome 10q26 locus, HtrA1 actually increases with age.

The investigators propose that modulating levels of HtrA1 may offer a new therapeutic avenue for AMD; in the meantime, they're trying to gather more evidence. Translation from association to causation – finding the smoking gun – could be key to understanding and then mitigating RPE-specific and age-dependent drivers of AMD progression, ultimately helping to save the eyesight of those at high genetic risk of developing the disease.

Reference

1. *BL Williams et al., PNAS, 118, e2103617118 (2021). PMID: 34301870.*

Eye-Phone Diagnosis

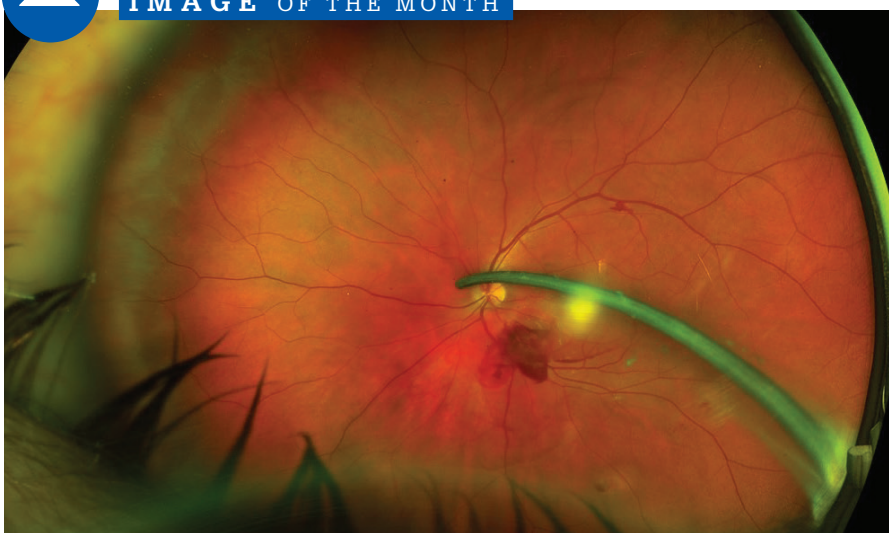
A smartphone app to improve eye health screening and follow-up appointment management

Many low- and middle-income areas of the world have insufficient eye care provisions to meet the minimum requirements set out by WHO, which leads to many people unnecessarily becoming or remaining visually impaired. Now, a smartphone app has almost tripled the number of people attending ophthalmic primary care appointments within the Kenyan Trans Nzoia County community. The Peek Community Eye Health system uses smartphone-based vision screening and referrals – allowing community volunteers to go door-to-door and perform initial eye screenings with the decision-guiding app. Any eye problems identified at this stage result in an automatic referral for follow-up appointments, supported by SMS reminders to maximize patient attendance and treatment. This has improved access to care and maximized the time hospitals have to spend on serious cases – more effectively managing ophthalmologists' limited time.

Reference

1. *H Rono et al., Lancet Digital Health, 3, e414 (2021). PMID: 34167763.*

IMAGE OF THE MONTH



A Foreign Body

This month's image shows a metallic intraocular foreign body very close to the optic nerve. It was removed safely, despite initial immediate postop vitreous inflammation, and the patient recovered completely within three weeks, with unaided visual acuity of 20/20.

Credit: Costas H. Karabatsas, Assistant Professor of Ophthalmology at the Department of Biomedical Sciences of the University of West Attica, Psachna, Greece.

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

QUOTE OF THE MONTH

"The pandemic has given me a chance to reflect, renew, and refocus. It gave me permission to stop and come up for breath, above a life drowning in busyness. This period of reflection has helped me to refocus my priorities. And it will help me to put large rocks into my life's bucket rather than filling it with small pebbles or even grains of sand."

Judy E. Kim, Professor, Ophthalmology and Visual Sciences, Graduate School of Biomedical Sciences, Director of Teleophthalmology and Research at the Medical College of Wisconsin, Wauwatosa, USA

Diagnosis: Glaucoma

Single gene testing may not be sufficient to identify a high risk of glaucoma

A new genetic test that factors in both polygenic and monogenic glaucoma risk variants could result in a 15-fold increase of people being identified as glaucoma suspects (1). Researchers analyzed the association of monogenic and polygenic variants with glaucoma risk – using clinical and genetic data from an Australian/New Zealand glaucoma database (ANZRAG, containing data from 2,507 individuals) and from the UK Biobank (data from 411,337 individuals). Both polygenic and monogenic variants have a comparable risk of developing glaucoma – over a 2.5-fold increase. But high-risk polygenic variants were six times more common than monogenic variants within the ANZRAG database – and more than 15 times more common within the general population (UK Biobank) data.

Although single gene testing is used clinically, a stratified approach of monogenic and polygenic testing will increase opportunities to save patients' sight.

Reference

1. *OM Siggs et al., JAMA Ophthalmol, [Online ahead of print] (2021). PMID: 34264281.*

In My View

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

Equity: Facts and Future

What do we know about the pay and practice disparity amongst male and female ophthalmologists?

By Tina Felfeli, resident physician in the Department of Ophthalmology and Vision Sciences at the University of Toronto, Vanier Scholar and member of the Integrated physician–scientist training program at the Institute of Health Policy, Management and Evaluation, University of Toronto, and Yvonne Buys, clinician investigator at University Health Network's Donald K. Johnson Eye Institute, Professor in the Department of Ophthalmology and Vision Sciences, University of Toronto, and Past President of the Canadian Ophthalmological Society, Toronto, Canada

We recently published a paper in Ophthalmology that featured a population-based evaluation of the differences in remuneration between female and male ophthalmologists compared with other physician specialty groups in Ontario, Canada, over three decades (1). We found that female ophthalmologists in a fee-for-service system had lower median payments than males despite their productivity based on the number of patients in their practice and the number of visits – and after adjusting for age and year of practice. Our results displaced the myth that lower pay is solely the outcome of less work. The same finding was observed amongst other specialty groups, including medical procedural, non-procedural specialties, and surgical – but the sex difference was more pronounced in ophthalmology (1). We are not the first to note these differences in remuneration. In fact, disparity in pay has also been noted for female ophthalmologists in New Zealand, where the pay gap between the sexes remains significant even when adjusted for hours worked (2). Although the true underlying reason for these discrepancies remains to be elucidated, some suggest that the disparity exists even within the first year of starting clinical practice (3).

Another interesting finding from our paper is that female specialists have a smaller representation in ophthalmology than most other surgical and medical specialty groups. And previous studies had already pointed out the under-representation of women in surgical specialties, such as orthopedics, thoracic surgery, and cardiology (4, 5). Again, the reasons remain unknown, but may be related to the lack of mentors and system challenges (6, 7). The finding is particularly alarming when we consider that most medical schools now comprise more women than men (8) – but that the proportion of women in ophthalmology and some other surgical specialties has not increased comparably.

We wondered if the influx of newly graduated female physicians and the delay in the time from graduation to practice may play a role in pay differences, but our age-adjusted model revealed a persistent gap in pay between the two sexes. Some of our previous work has shown that women make up 43 percent of all practicing family physicians in Ontario in 2013 compared with 20 percent in ophthalmology (9). As such, it is apparent that the majority of women are entering non-surgical specialties.

But the big question remains: what is driving the differences in remuneration between women and men? In our study, one striking difference was amongst top paid individuals. Men who were considered to be the most paid (higher than the 60th percentile) in ophthalmology in 2018 (the last year of the study) earned on average 17 percent (US$126,650) more than the top paid female ophthalmologists. In the same year, the top billing male ophthalmologists had a greater number of patient visits than their female colleagues despite having a fewer number of distinct patients. The male ophthalmologists belonging to this group also had 52 percent higher payments than other male ophthalmologists. As such, this cohort of top biller male ophthalmologists has a distinct practice pattern that disproportionately contributes to a large aspect of the healthcare billings in Ontario, Canada.

Some of the temporal trends in practice patterns of ophthalmologists, such as the frequency of patient visits with the rapid

expansion of intravitreal injections after the approval of bevacizumab in 2005, may be driving these differences (10). Gender differences in practice patterns may be related to the inherent variations in subspecialty choices, practice set-up, and billing practices, which warrant further investigation. In a fee-for-service system under the single-payer healthcare system in Canada, those who spend more time on a patient consult for a complex medical or surgical case may be compensated less than those who see multiple routine patient visits during the same period of time. And that's a key concept to bear in mind!

In pursuit of equity in medicine, we must all comprehensively consider the unique challenges and barriers for early-career women in ophthalmology and other specialties (11). Recent studies have suggested that female ophthalmology residents in the US perform fewer cataract operations and total procedures compared with their male counterparts (12). We previously found in a survey of Canadian ophthalmologists that women reported less operating time than men, with 51 percent of women operating less than two days per month compared to 36 percent of males (13). This was later confirmed in a study using billing data of Ontario ophthalmologists, where 68.6 percent of male compared with 57.9 percent of female ophthalmologists performed surgery – and, of those performing cataract surgery, male ophthalmologists had 1.7 times the volume of procedures compared with female ophthalmologists in 2013 (14).

In addition to differences in payments between men and women, disparities have been shown in senior authorship on scientific publications, relationships to the medical industry, and grant opportunities (13, 15, 16, 17). In a survey of Canadian ophthalmologists, women believed that childbearing slowed or markedly slowed career progress, as compared with men (13). Studies on female physicians and surgeons have also noted the challenges they face in terms of delays in childbearing (18) and increased risks of infertility and pregnancy complications (19). Both real and perceived barriers regarding gender-based discrimination, lack of female role models, and challenges in balancing of personal and academic career in surgical specialties may be the major deterrents for recent medical school graduates (20, 21).

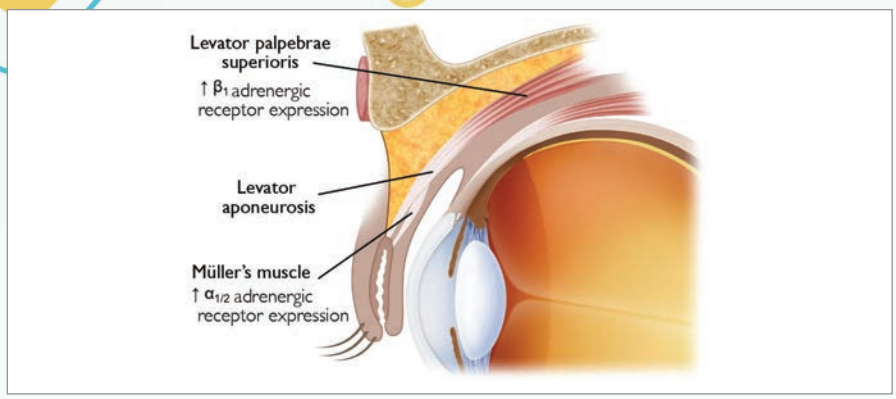
In an era when a growing number of women are choosing to enter medical school, addressing the barriers to progression for female physicians in surgical specialties will likely improve the appeal of ophthalmology as a profession for future generations of women (21).

References

1. *T Felfeli et al., "Pay gap amongst female and male ophthalmologists compared to other specialties," Ophthalmology, [Online ahead of print] (2021). PMID: 34271073.*
2. *HV Danesh-Meyer et al., "Differences in practice and personal profiles between male and female ophthalmologists," Clin Exp Ophthalmol, 35, 318 (2007). PMID: 17539782.*
3. *JS Jia et al., "Gender compensation gap for ophthalmologists in the first year of clinical practice," Ophthalmology, 128, 971 (2021). PMID: 33248156.*
4. *MA Hlatky, LJ Shaw, "Women in cardiology: very few, different work, different pay," J Am Coll Cardiol, 67, 542 (2016). PMID: 26560678.*
5. *TY Wang et al., "Women in interventional cardiology: update in percutaneous coronary intervention practice patterns and outcomes of female operators from the National Cardiovascular Data Registry," Catheter Cardiovasc Interv, 87, 663 (2016). PMID: 26255880.*
6. *LN Trinh et al., "Factors influencing female medical students' decision to pursue surgical specialties: A systematic review," J Surg Educ, 78, 836 (2021). PMID: 32933885.*
7. *A Dixon et al., "Female medical student retention in neurosurgery: A multifaceted approach," World Neurosurg, 122, 245 (2019). PMID: 30391758.*
8. *IA Dhalla et al., "Characteristics of first-year students in Canadian medical schools," CMAJ, 166, 1029 (2002). PMID: 12002979.*
9. *YM Buys et al., "Influence of age, sex, and generation on physician payments and clinical activity in Ontario, Canada: An age–period–cohort analysis," Am J Ophthalmol, 197, 23 (2019). PMID: 30236775.*
10. *RJ Cambpell et al., "Rapid expansion of intravitreal drug injection procedures, 2000 to 2008: a population-based analysis," Arch Ophthalmol, 128, 359 (2010). PMID: 20212208.*
11. *T Bogler, "Female family physicians and the first 5 years: In pursuit of gender equity, work–life integration, and wellness," Can Fam Physician, 65, 585 (2019). PMID: 31413031.*
12. *D Gong et al., "Gender differences in case volume among ophthalmology residents," 137, 1015 (2019). PMID: 31318390.*
13. *R Jagsi et al., "Gender differences in the salaries of physician researchers," 307, 2410 (2012). PMID: 22692173.*
14. *JA Micieli et al., "Gender gap and declining surgical activity among new graduates: cataract surgery in Ontario," Can J Ophthalmol, 51, 154 (2016). PMID: 27316260.*
15. *M Kalavar et al., "Authorship gender composition in the ophthalmology literature from 2015 to 2019," Ophthalmology, 128, 617 (2021). PMID: 32890547.*
16. *JA Eloy et al., "Association of gender with financial relationships between industry and academic otolaryngologists," JAMA Otolaryngol Head Neck Surg, 143, 796 (2017). PMID: 28570741.*
17. *JK Weng et al., "Evaluation of sex distribution of industry payments among radiation oncologists," JAMA Netw Open, 2, e187377 (2019). PMID: 30681710.*
18. *MC Cusimano et al., "Delay of Pregnancy Among Physicians vs Nonphysicians," JAMA Intern Med, 181, 905 (2021). PMID: 33938909.*
19. *EL Rangel et al., "Incidence of Infertility and Pregnancy Complications in US Female Surgeons," JAMA Surg, [Online ahead of print] (2021). PMID: 34319353.J Park et al., "Why are women deterred from general surgery training?" Am J Surg, 190, 141 (2005). PMID: 15972188.*
20. *EL Rangel et al., "Pregnancy and motherhood during surgical training," JAMA Surg, 153, 644 (2018). PMID: 29562068.*
21. *AC Rogers et al., "Gender and specialty influences on personal and professional life among trainees," Ann Surg, 269, 383 (2019). PMID: 29099401.*

Eye-Opening Therapy

A new treatment for acquired ptosis elevates eyelids and improves patients' visual field



Sponsored content by RVL Pharmaceuticals

Michael Korenfeld is the President of the Comprehensive Eye Care in Washington, Missouri, USA, and his practice is as wide ranging as its name suggests. Korenfeld has a special interest in research and innovation, and his practice took part in the clinical trials of Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1% from RVL Pharmaceuticals, a therapy for acquired ptosis in adults, which was approved by the FDA in 2020.

The pathophysiology of ptosis is not always the same. In the presence of ptosis, consideration of potential neurologic or orbital disease is important. Acquired ptosis is often caused by a weakness or stretching of the muscles lifting the eyelid and is broadly recognized as being among the most common disorders of the eyelid encountered in the clinic (1). Its prevalence increases with age, but ocular surgery is also a known risk factor (2). Upneeq activates the α-adrenergic receptors in Müller's muscle, stimulating upper eyelids to contract and elevate (3, 4, 5).

Korenfeld describes the clinical trials for Upneeq that he took part in: "Various tests were used to measure how open patients' eyelids were, down to tenths of a millimeter, with assessments on superior peripheral vision, which can be impaired and functionally troubling for people with ptosis; so both the appearance and visual function were tested before and after administering the medication to the treatment group." A once-daily dose of Upneeq used for 42 days was found to significantly improve both the superior visual field and eyelid elevation with an average eyelid lift of 1.0 mm (6).

Korenfeld's patients range from mild to severe stages of ptosis, although he points out that most people in mild stages will experience better and worse days, and just like with other muscles in their body, their levator function will fluctuate depending on the body's energy reserves. In moderate stages of the condition, the muscle is so dysfunctional that even on good days the eyelid tends to droop, and in the most severe stages, some patients won't be able to open their eyes at all. He comments: "What's great about Upneeq is that patients with mild to moderate ptosis can use the therapy on the days they want to; for some it might be every day, for others – only on weekends or on special occasions." The drop starts working quickly (often within 15 minutes) and the effect lasts for at least six hours. Before the drug became available, clinicians had to rely on a tricky and invasive surgical procedure, shortening the levator muscle with the creation of a pleat. The option to use Upneeq for some patients provides the clinician an effective alternative to this surgical procedure. Nowadays, Korenfeld regularly discusses acquired ptosis with his patients and offers appropriate candidates the option to trial a sample of Upneeq, with his office then handling the prescriptions that follow.

Acquired ptosis is a comorbid condition, which can impede a clinician's access to the cornea and ability to get measurements used to make clinical decisions. This is why Korenfeld has also started discussing acquired ptosis with patients during an examination, when a patient has trouble opening their eyes sufficiently, or has acquired ptosis after years of prostaglandin use to manage glaucoma. "Recognizing that my glaucoma or cataract patients sometimes also suffer from acquired ptosis, and treating them, has made a great difference to my practice," says Korenfeld. "Just two days ago, I had to measure the corneal curvature of a cataract surgery patient, and he couldn't open his eyes effectively. In the past for a patient like this, I would've just reached around and held his eyes open or taped the eyelids, taken measurements and continued my exam without discussing ptosis with the patient. A situation like this has now become a trigger to treat and I take a moment to explain to the patient why their eyelids are drooping into their field of vision. I let them know that there is an eye drop that I want to try to see if it helps them. The patient is administered Upneeq, and after the examination these satisfied patients leave my practice with a prescription."

"When I prescribe Upneeq I also make sure to tell my patients that they may have some adverse reactions and that in the clinical trials, the most common treatment emergent adverse reactions which occurred with an incidence 1 to 5% were: punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache. I also keep in mind that Upneeq may not be right for all patients. Since Upneeq may impact blood pressure, I tell my patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to monitor their condition and seek medical care if it worsens."

Has his evaluation and management of patients changed since the approval of

Upneeq? "Now, when I diagnose a patient with acquired ptosis, I can prescribe them the drug, which creates a more complex interaction. It's a win-win situation, as the visit is of a higher value to the patient, who can now address their condition."

Korenfeld has also received positive reactions from patients: "Many patients who have been using Upneeq are telling me how great it is. Given that I usually see patients annually and that Upneeq was approved relatively recently, I expect these numbers to increase greatly in the coming months. The patients from clinical trials, who I of course saw on a more regular basis, were very happy to have been enrolled. They were able to notice a positive change in the appearance of their eyelids and that they looked more rested, with their friends commenting on the positive change in the appearance of their eyelids. Some patients mentioned how they were able to resume certain activities, such as reading in bed, which was much more difficult before they started the therapy."

What about the rather unusual distribution model that RVL Pharmaceuticals has decided on? Korenfeld is a fan: "If I decide that a patient would benefit from using Upneeq, I give them some samples, and send an electronic prescription to RVL, who ships it directly to the patient. RVL therefore doesn't have the burden to keep stock in every local pharmacy. The patient pays for Upneeq directly outside of the insurance process. I think it's fantastic, and I wish more companies would use a similar model; it's time and cost efficient for the physicians, office staff, and patients."

To other ophthalmologists, he offers these words of wisdom: "I always tell my patients what I can about the drugs I prescribe for them: potential side effects and warnings, what it does, who it is for, what the onset of action is, and how long it lasts. For this purpose, I made a three-minute video that explains these things about Upneeq along with a transcript that the patient gets to take home. I then take any of their questions afterwards. It saves me a lot of time. As I do for all ocular pharmaceuticals, I make sure to tell my Upneeq patients to close their eyes for three minutes after administration, without blinking, so it has time to soak into the eye tissues, and not just stay in the conjunctiva. I also remind patients not to touch the tip of the container to their eye or any other surface to avoid contamination."

Korenfeld concludes: "I have seen this drug have a positive impact for many patients, and I really appreciate the fact that the patients can see the results for themselves, rather than simply taking my word for it."

IMPORTANT SAFETY INFORMATION

INDICATION

UPNEEQ® (oxymetazoline hydrochloride ophthalmic solution), 0.1% is indicated for the treatment of acquired blepharoptosis in adults.

WARNINGS AND PRECAUTIONS

- Ptosis may be associated with neurologic or orbital diseases such as stroke and/or cerebral aneurysm, Horner syndrome, myasthenia gravis, external ophthalmoplegia, orbital infection and orbital masses. Consideration should be given to these conditions in the presence of ptosis with decreased levator muscle function and/or other neurologic signs.
- Alpha-adrenergic agonists as a class may impact blood pressure. Advise UPNEEQ patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens.
- Use UPNEEQ with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome. Advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop.
- UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute narrow angle glaucoma develop. Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

ADVERSE REACTIONS

Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache.

DRUG INTERACTIONS

- Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta-blockers, anti-hypertensives, and/or cardiac glycosides is advised. Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.
- Caution is advised in patients taking monoamine oxidase inhibitors which can affect the metabolism and uptake of circulating amines.

Dr. Michael Korenfeld is a paid consultant of RVL Pharmaceuticals, Inc.

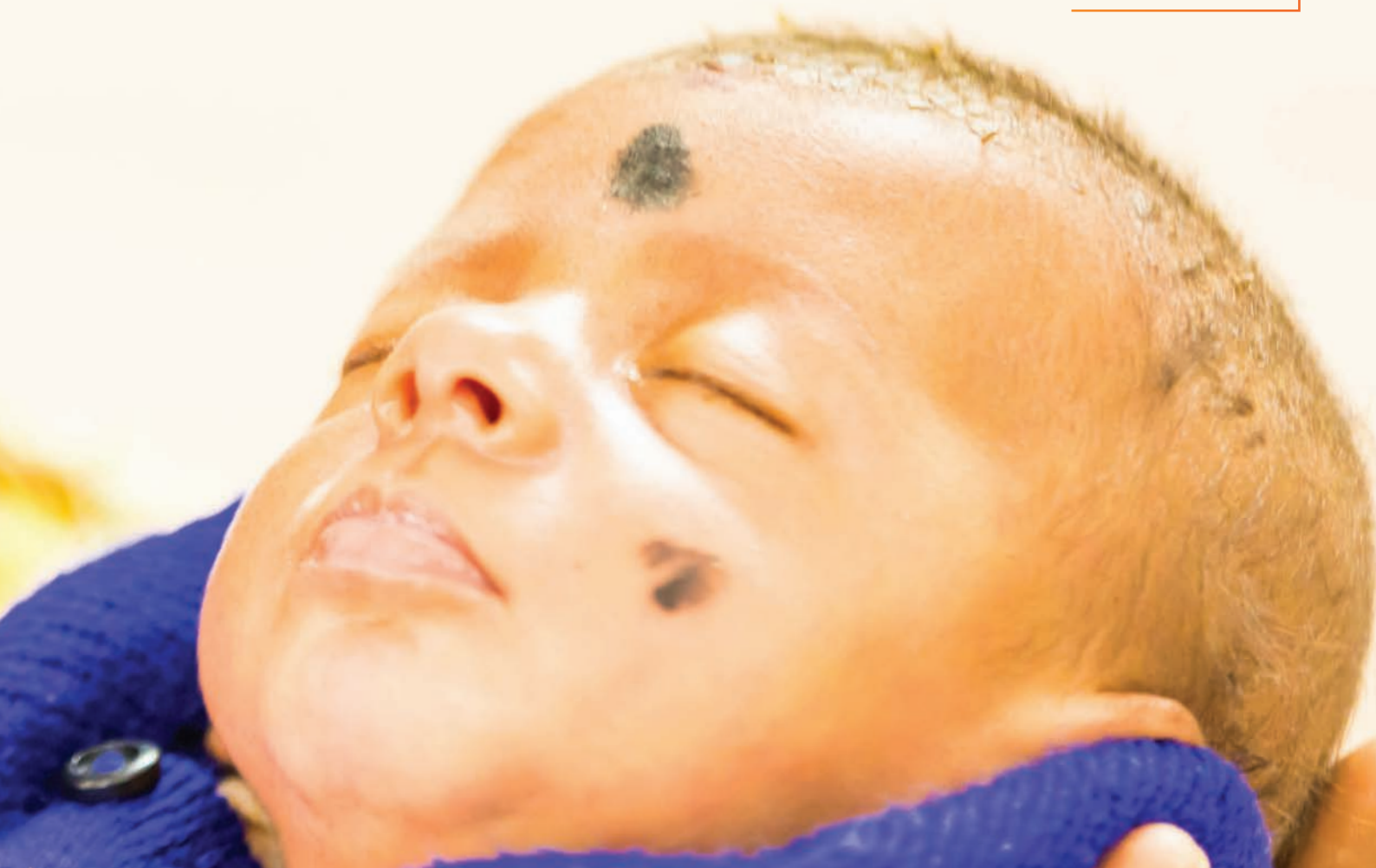
References

1. *J Bacharach et al., Eye (Lond) [Online ahead of print] (2021). PMID: 33927356.*
2. *Y Wang et al., Graefes Arch Clin Exp Ophthalmol, 257, 394 (2018). PMID: 30203103.*
3. *B Esmaeli-Gutstein et al., Ophthalmic Plast Reconstr Surg, 15, 92 (1999). PMID: 10189635.*
4. *BC Skibell et al., Ophthalmic Plast Reconstr Surg, 23, 367 (2007). PMID: 17881986.*
5. *SJ Park et al., Ophthalmic Plast Reconstr Surg, 34, 547 (2018). PMID: 29634605.*
6. *CB Slonim et al., JAMA Ophthalmol, 138, 1168 (2020). PMID: 33001144.*

WITHIN *Reach*

OUTREACH PROGRAM OF RETINOPATHY OF PREMATURITY SCREENING IN MADURAI, INDIA

Images by Terry Cooper




D1300

Just before the Aravind Eye Care System hospitals in southern India closed before the COVID-19 lockdown, Terry Cooper spent time with an outreach team screening for retinopathy of prematurity led by Renu P. Rajan from Aravind Eye Hospital in Madurai, India.

Aravind Eye Hospitals were founded by Govindappa Venkataswamy, better known as Dr V, who started running eye screening camps in early 1970s. He saw too many people needlessly going blind, mostly from cataracts. Rural areas in India have been especially vulnerable, with many locals unable to make the necessary journey to a large city like Madurai to get properly diagnosed and undergo cataract surgery, with costs also being an important consideration.

Venkataswamy organized free outreach campaigns in rural areas, which identified patients who required surgery, arranged their transport in a hospital van the day before the planned surgery, and provided them with free food and accommodation while they waited and recovered; they would be taken back home after the first post-op check-up.

To this day, this is how outreach camps function, with around 2,500 scans being taken annually in Tamil Nadu, the region where the current 14 Aravind Eye Hospitals operate. In the year ending in March 2020, the program screened over 500,000 people, with 92,000 people undergoing surgery as a result. Like in the early days, patients are provided with food and accommodation for the duration of their stay, and one-month follow-up visits are organized for them; in the rare instances of complications, patients are brought back to the hospital to address them.

Community sponsors are found for these events, providing community centers, churches, schools, wedding halls, and other locations free of charge. They also advertise the screening camps locally, posting flyers and making public announcements in the main squares. The sponsors have very strong links within the community, personally knowing all the families, so they can notify the people with existing issues. It is their responsibility to bring as many people as possible to the screening camps.

Depending on the size of the camp, there are usually up to two physicians present, but the team's size is calculated according to the projected turnout. The staff can dispense spectacles for patients with refractive errors, and do whatever is necessary to minimize the numbers of people required to travel to the hospital. Patients usually have to wait one to two hours to receive the right spectacles or prescription, but it saves them the time they would have to spend to travel into the city. Those who need cataract surgery are brought to the hospital for a free-of-charge procedure. Since the COVID-19 pandemic began, restrictions and lockdowns have meant that the outreach camps activity has greatly diminished.

Aravind teams also conduct glaucoma and diabetic retinopathy camps, as well as those specifically aimed at retinopathy of prematurity patients, as you can see in the images accompanying this feature.

Terry Cooper is a photographer based in London, UK. He regularly travels to Uganda, India, and other developing countries, to examine reasons for people going needlessly blind and help find solutions, as well as investigate inequalities in access to healthcare.

In Practice

Surgical Procedures
Diagnosis
New Drugs

A Safer Surgical Glaucoma Algorithm

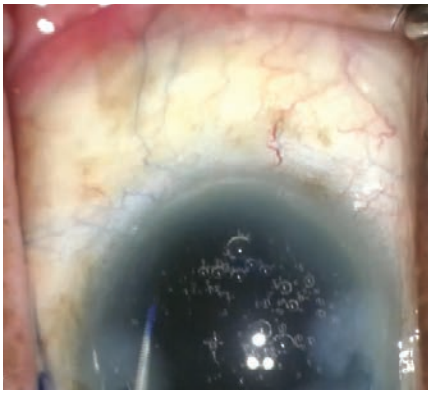
Is earlier – and more aggressive – glaucoma intervention the key to reducing disproportionate blindness in the African-American community?

By Daniel Laroche

Did you know rates of glaucoma are four or five times higher in African Americans? At my practice, in Harlem, New York City, US, an area with a heavy African American population, the cases of glaucoma that present to us are often advanced – -7/-8 DB visual field loss is not uncommon. Unfortunately, in these more advanced patients, eyedrops are less successful as a first line treatment, so my practice has evolved to doing earlier, safer, more aggressive therapies, including earlier cataract surgery and Schlemm's canal surgery.

The reasons African Americans suffer higher rates are complex, but can essentially be attributed to hundreds of years of decreased access to care. Legally, Black people were not allowed to read or write for many years. Only as recently as the 1960s were schools integrating, allowing Black people to go to medical school to become surgeons. And even today, the US only has around 400





Figures: 1. Pigment obstruction of the trabecular meshwork is characterized by dark particles, 2. Hydrus clearly visible within Schlemm's canal with inlet accessing the anterior chamber, 3. Collector system illuminated by injection of trypan blue after placement of Hydrus over the 90-degree span of the device.

African American ophthalmologists. With many residential communities in the US remaining segregated, ophthalmologists often end up practicing in their own racial communities, leaving Black communities with limited options. Decreased access to treatment means many African Americans need earlier intervention – namely, earlier microinvasive trabecular bypass surgery – to bend the curve of blindness, which is what I have been doing in my practice.

"The reasons African Americans suffer higher rates are complex, but can essentially be attributed to hundreds of years of decreased access to care."

We've published papers looking at surgery as a safe, efficacious initial treatment – and we've had excellent results with patients in our practice. It is worth remembering that glaucoma medication is expensive – US$30–50 for prostaglandins and newer combination medications. For some patients, this means having to make a decision between buying food and taking medications; it's no wonder some people don't go to the ophthalmologist at all. Finding another way to lower pressure, improve compliance, and reduce the need for expensive medications would go a long way to reducing this healthcare disparity.

In ophthalmology, we generally make a point of not operating until "necessary" – preferring to treat patients with eyedrops and lasers. This mindset is partly due to the fact that surgical skills are not uniformly distributed, which will prove challenging as the future of glaucoma moves towards earlier surgical intervention. We need to train the next generation of surgeons to be experts in cataract and angle-surgery so they can perform them seamlessly. Cataract surgery is far safer today than it was 20 years ago – and this offers tremendous pressure lowering benefits particularly in combination with microinvasive glaucoma surgery. Trabeculectomy remains the standard of care for surgical glaucoma, despite it having more complications and carrying the potential of losing the patient up to two lines of vision. In glaucoma patients whom receive earlier cataract surgery/lensectomy and microinvasive glaucoma surgery will not need medications nor trabeculectomy.

In my practice, we take a different approach. We have found that in patients over 50 years of age, the cataract – or enlarged lens – is the most common identifiable cause of glaucoma. Trabecular meshwork obstruction and obstruction of Schlemm's canal have an impact on aqueous drainage. Schlemm's canal is compressed by the enlarged lens. The enlarged lens, creates pigment liberation by rubbing against the posterior iris and the pigment becomes trapped in the trabecular meshwork, which further reduces flow and elevates eye pressure. Eye drops do not address this mechanism but only lowers the pressure and can worsen cataract formation.

In the Baltimore Eye Survey, a study investigating the relationship between intraocular pressure and primary open angle glaucoma among White and Black Americans, the mean normal intraocular pressure in individuals without glaucoma was approximately 15 mmHg and the mean intraocular pressure in patients

with untreated glaucoma is 18 mmHg (1). For glaucoma patients with age related cataract, it is essential to perform gonioscopy to identify increased pigment deposition, narrowing of the angle, and compression of the angle structures to identify suitable candidates for potential earlier combination cataract surgery/lensectomy and MIGS glaucoma surgery.

Several randomized clinical studies have shown IOP lowering associated with cataract surgery alone in patients with open angle glaucoma. The addition of a Schlemm's canal based MIGS device can lower IOP even further without changing the safety profile of the procedure. I currently offer patients initial treatment for glaucoma with cataract surgery and the Hydrus Microstent as we know removal of the cataract opens Schlemm's canal and expands the trabecular meshwork. The Hydrus Microstent further enhances aqueous outflow through three mechanisms of action: trabecular meshwork bypass, expansion of Schlemm's canal, and greater access to collector channels (see Figure 4). The bypass feature eliminates resistance to aqueous flow related to the effects of material build up in the trabecular meshwork, while the expansion of the canal over three clock hours of the circumference of the eye allows for optimal access to multiple collector channels.

Despite its complex design, the Hydrus Microstent is approximately the size of an eyelash – small enough that it is typically never felt or seen by the patient. I believe this initial uncomplicated surgical treatment addresses the cause for glaucoma and safely provides the most effective solution currently.

Inserting the Hydrus is an elegant procedure. It is easy to confirm by visual inspection that you are in the right place (see Figure 1). Canal stenting with Hydrus leads to a robust outflow of aqueous to the veins for several clock hours, as may be confirmed. The aqueous veins may be blanched with BSS using the phaco tip. I also use it in advanced glaucoma patients who have not had glaucoma surgery – with very good results.

Two prospective, multicenter, randomized controlled trials supporting the safety and effectiveness of

"We have a responsibility to educate our Black glaucoma patients not only about the need to get checked, but also about the new surgical treatments available."

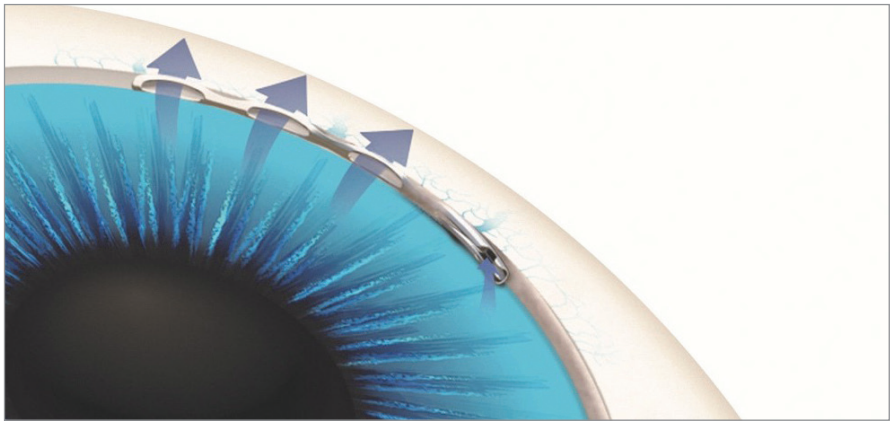


Figure 4. Hydrus mechanism of action: 1. Trabecular Bypass 2. Schlemm's canal dilation 3. 90 degrees of collector channel access.

the device have been published in Ophthalmology (2, 3). In the HORIZON trial, the largest MIGS randomized study conducted to date, the Hydrus demonstrated significant reduction of IOP and medications in a wash out comparison for two years postoperatively. As presented at the recent American Society of Cataract and Refractive Surgery meeting, three-year follow-up has shown that intraocular pressure reductions are maintained, with 73 percent of eyes in the Hydrus group remaining medication-free, with a safety profile similar to phacoemulsification alone, and no significant change in endothelial counts. Additionally, compared with phaco alone, Hydrus with phaco reduced the risk of incisional glaucoma surgery by 80 percent during the follow-up period.

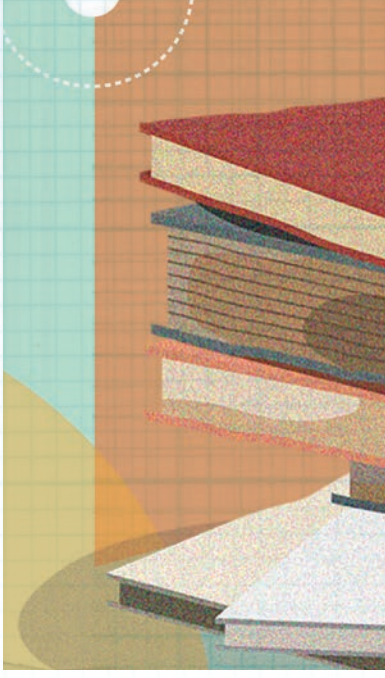
In our published series in Black patients, 74 percent of our patients were medication free at six months – important, as I have mentioned before, considering the financial burden drops put on patients from lower socioeconomic statuses. There was also significant improvement in visual acuity and stabilization of mean deviation on visual field test (baseline -9.2; 6 months -9.1; p = 0.22). In my experience, the Hydrus Microstent is the most powerful MIGS device that can be placed in patients with mild to moderate glaucoma at the time of cataract surgery. Even better, there are no serious risks or complications associated with the procedure. The second generation iStent Inject has been problematic in my hands. At times, it has not been able to penetrate a thickened heavily pigmented trabecular meshwork, or conversely penetrated through both the inner and outer wall of the Schlemm's canal, becoming implanted into the sclera, reducing its efficacy. This has been confirmed by others with AS-OCT imaging of iStent (5). Neither has the Xen subconjunctival stent been foolproof in that the 45µm small lumen can become obstructed subconjunctivally or intraluminally – an obstruction that cannot be overcome with needling or external revision.

Cataract surgery and implanting the Hydrus Microstent at an earlier stage will often serve to preserve the health of the patient's collector channel and provide benefit from the beginning to the end of the disease. Having performed over 2,500 of these procedures in patients with glaucoma, not only can I lower the intraocular pressure and dramatically reduce the number of medications needed, but also improve vision from cataract extraction and refractive lens exchange.

We have a responsibility to educate our Black glaucoma patients not only about the need to get checked, but also to inform them about the new surgical treatments available to them – and that should include earlier cataract surgery and Hydrus Microstent. Finally, to clarify, I've shared here my initial approach to patients with open angle and angle closure glaucoma over the age of 50, but this does not apply to patients with other types of secondary glaucoma, such a neovascular or uveitic glaucoma. This approach should only be used by skilled experienced surgeons able to regularly provide uncomplicated surgery.

Daniel Laroche is the Director of Glaucoma Services and President of Advanced Eyecare of New York and Clinical Assistant Professor of Ophthalmology at The New York Eye and Ear Infirmary of Mount Sinai, New York, USA.

See references online at: top.txp.to/safer-surgical-glaucoma-algorithm



Yamane – Theory to Practice

What is it like to use the Yamane technique for the first time?

By Abha Amin

As Chief of Complex Anterior Segment Surgery at a tertiary referral hospital, I am very used to challenging cases. Surgical complications are our most common patient referrals, with IOL dislocation or retained lens material leaving patients functionally aphakic. Coexisting glaucoma, corneal edema, and iris damage are also frequent, which make case management more difficult. As a result, I often find myself performing secondary IOL implantation. My preferred method for this is iris fixation, which – in my experience – is minimally invasive. But when the iris is damaged, as is often the case, this is no longer a viable option. I have tried Gor-Tex sutures (Gore Medical) as an alternative fixation method, yet this presented other challenges, such as a difficulty in avoiding IOL tilt or rupture of the haptic eyelets.

Although cases can be difficult, improvements in techniques and technologies are constantly making surgeries more effective – and resulting in much improved patient outcomes. The Yamane technique interested me as a solution for cases where iris fixation was not an option. Here, I describe my experience using the technique for the first time.

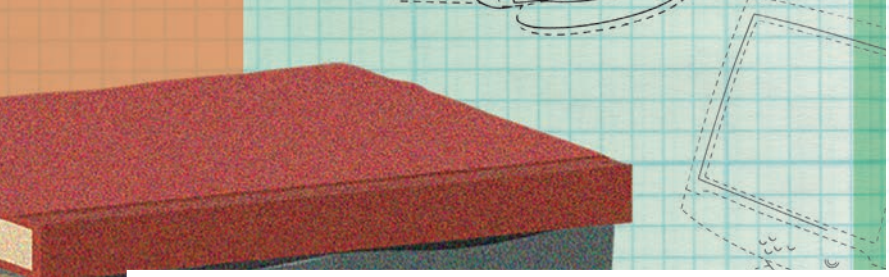
Preparation is key

Though the Yamane technique has great potential, making it efficient demands a great deal of work and preparation. For me, that meant hitting the books, watching surgical videos, and, most importantly, doing extensive training in two separate wet labs. Training sessions included the disassembly of an eye model to gain an inside out view – crucial to understanding the technique as it allowed me to see haptic fixation points inside the eye, and where I had entered when penetrating the globe. Interestingly, the haptic fixation points do not have the classic C shape that you would imagine; on the contrary, they are stretched out and very straight. This highlighted and underscored how important IOL model selection is in surgical success; the ability to open the model eye after completing the wet lab confirms your internal fixation and IOL placement, and shows whether your entry is through the sulcus or ciliary body.

Off the bench and into the operating room

Feeling as prepared as I could be, it was time to put what I had learned into practice. The opportunity to use the technique arose from a patient who had a complication during cataract surgery. The surgeon called from the operating room to inform me that part of the cataract had fallen posteriorly and there was a vitreous prolapse – I told him to not implant the IOL and to send the patient to me the next day. The patient was diabetic and on dialysis, and had lost his other eye a few months ago due to an infection whilst in hospital. He was aphakic and had insufficient capsular or iris support

"Though the Yamane technique has great potential, making it efficient demands a great deal of work and preparation."



as the iris was traumatized and stuck to the wound. After examination by the retina service, it was decided to proceed with scleral fixation of the IOL using the Yamane technique. I proceeded immediately after an accompanying retinal surgeon removed the nuclear fragments through a pars plana vitrectomy and lensectomy. I used the CT Lucia IOL (Zeiss) with PVDF haptics, which, in my opinion, are the only haptics that would resist breaking, and the Scleral IOL Solutions Pack (MicroSurgical Technology) that provides the essential materials for the technique, including specialty needles with holders that provided optimum precision during the case.

I'll be honest: the procedure was stressful, but my thorough preparation resulted in successful surgery.

Yamane case takeaways

- *Letting the needle go*

In the beginning, I was so fixated with the entry point of the needle that I did not let the first needle go – after incarcerating the leading haptic into the lumen of the needle, I went ahead and externalized the haptic. The IOL with the trailing haptic rotated, which made the next few steps more challenging. It is best to release the needle at the hub with the captured haptic deep into the anterior vitreous – then take a deep breath before continuing. It still worked out, although capturing the trailing haptic was more difficult than it needed to be. The needle holders in the Scleral IOL Solutions Pack allow for easy release and recapture of the needles.

- *Opening the conjunctiva for enhanced visualization*

The online surgical videos demonstrate needle penetration directly through the conjunctiva. Nevertheless, I personally wanted to see exactly where and how deep I was entering as I was creating the scleral tunnel before making the sharp turn and deep dive at the 2 mm point. I have no hesitation opening the conjunctiva to see what I am doing and then closing it, as it only takes a few more minutes.

The ultimate measure of success

The main indicator of a successful procedure is, of course, the patient's outcome. The patient is doing very well post operation with a refractive error of -0.5 D and corrected visual acuity of 20/40 with no IOL tilt. His vision is still affected by mild macular edema from his diabetic retinopathy, so I will continue to monitor him to see how he progresses. All things considered, he looks very good and is functioning much better than before. I learned a lot from this first case, but it also reinforced how important it is to have the right equipment and preparation – especially the wet lab training.

Abha Amin is the Chief of Complex Anterior Segment Surgery at the Westchester Medical Center in Valhalla, New York, USA.

To watch a video of Amin's case, go to top.txp.to/theory-to-practice

Enter the Fast Lane for Dry Eye Flare-Ups

How a short-term treatment quickly quells dry-eye symptoms – including those associated with prolonged mask wear

By Cynthia Matossian

Dry eye disease (DED) is ubiquitous in our practices, and it may come as no surprise that it is becoming even more common in work-from-home environments, where patients are spending increased time in front of screens. Moreover, after prolonged wearing of masks – essential to stem the spread of COVID-19 – many of us have become aware of a new phenomenon: mask-associated dry eye or MADE (1). MADE occurs when exhaled air is funneled upward and across the surface of the eyes – typically, when the wearer's mask is not tightly fitted. A recent review concluded that eye dryness and irritation from mask wear may become a problem for a large percentage of the population (2). In short, the convergence of several factors is increasing patients' symptoms – and driving more of them into our offices as they seek relief.

Often considered a chronic condition, DED can also be episodic in nature; not all patients experience consistent symptoms; rather, they experience dry eye flares of varying levels of discomfort – the result of a variety of potential triggers. Though 80–90 percent of patients who receive a diagnosis of DED will also have periods of inflammatory exacerbations or flares, surveys also reveal that nearly half of patients report suffering from flares alone (3, 4). The triggers can include seasonal and indoor allergies, screen time, environmental factors (such as fan use and exposure to forced air associated with heat and air conditioning), contact lens wear, as well as cataract and refractive surgery (5).

With last year's FDA approval of Eysuvis (loteprednol etabonate ophthalmic suspension 0.25%; Kala Pharmaceuticals), we now have a novel prescription steroid option specifically indicated for the short-term treatment (up to two weeks) of the signs and symptoms of DED, including those who may suffer dry eye flares (see Box "After the trials").

Practice experience

Having recently incorporated Eysuvis into my practice with excellent results, I can distinguish four different categories of patients for whom I prescribe this short-term agent. When I see someone who is very symptomatic or extremely uncomfortable, I consider it a first-line therapy. These are typically patients who are new to our practice or those who have not kept their follow-up appointments, now complaining that their dry eye symptoms have escalated to a palpable flare. By the time they are in my office, these patients are desperate for relief. Once I rule out an infectious process, I prescribe Eysuvis to calm their ocular surface inflammation. After the recommended 14 days of therapy, I bring these patients back for their dry eye workup. Patients are relieved to have a drop that works effectively and quickly; the success of the treatment helps them gain my trust.

The second group for whom I prescribe Eysuvis is made up of established DED patients on chronic maintenance therapy who are having an uptick in their symptoms. Each patient's treatment regimen is personalized to their level of disease. It consists of a combination of at-home remedies, such as the heated Bruder mask, NuLids cleanser (NuSight Medical), and oral omega-3 supplement, coupled with immunomodulators like Xiidra (lifitegrast ophthalmic solution 5%; Novartis), Cequa (cyclosporine ophthalmic solution 0.09%; Sun Ophthalmics), Restasis (cyclosporine ophthalmic emulsion 0.05%; Allergan), or Klarity-C (cyclosporine 0.1% ophthalmic emulsion PF; Imprimis). Many of these patients also receive annual or semi-annual in-office procedures; for example, LipiFlow

After the trials

The FDA approval of Eysuvis was based on data from phase 2 and three phase 3 trials that included almost 2,900 patients (6). In the largest-ever clinical development program conducted for DED, researchers observed improvement in the measures of conjunctival hyperemia, corneal fluorescein staining, and patient-reported ocular discomfort severity score. Patients assigned to treatment with Eysuvis experienced symptom improvement as early as day 2 in a phase 3 trial when dosed q.i.d. for 15 days (6). Eysuvis demonstrated a beneficial safety profile: IOP was similar among the vehicle and the Eysuvis arm. In treatment and vehicle groups, respectively, 0.6% and 0.2% of patients experienced an increase of over 5 mm Hg from baseline resulting in an IOP measurement of 21 or more mm Hg in one or both eyes at any post-baseline visit (7).

Eysuvis is formulated with AMPPLIFY – a proprietary mucus-penetrating nanoparticle technology. These nanoparticles (approximately 300 nm in diameter) are coated to facilitate their mucus barrier penetration, which allows the drug to spread more uniformly on the ocular surface to achieve longer retention (8, 9).

(Johnson & Johnson Vision), TearCare (Sight Sciences), Systane iLux (Alcon), BlephEx (BlephEx LLC), or intense pulsed light (IPL, such as with systems like those from Lumenis and Quantel Medical).

But despite the management of their condition, these DED patients can have symptom exacerbation at any time, depending on individual triggers. During a flare, they are more uncomfortable, becoming more aware of their eyes. Here, again, I prescribe Eysuvis to deliver rapid relief. Depending on the severity of their symptoms, they take the drop up to four times a day, for a maximum of 14 days.

A third group of patients are those who are starting immunomodulation therapy. When I start them on one of these agents, I know that it can take several weeks to months for patients to experience relief. Therefore, I prescribe Eysuvis as a concurrent two-week therapy during the induction period. I want to jumpstart their symptomatic improvement and provide fast relief while the immunomodulator takes effect.

The fourth category includes patients who are completely asymptomatic most of the year; however, suffer from periodic dry eye flares. The number of episodes can vary – perhaps four to six times a year with short bouts. These individuals have likely tried artificial tears to self-treat their underlying ocular inflammation – without success. They swear to me they will not be compliant with BID dosed drops. They are adamant that their symptoms do not warrant chronic treatment; they are seeking relief for episodic flare-ups. I appreciate this honesty, since prescribing an immunomodulator will not be effective if only used sporadically. For these patients, I prescribe Eysuvis to be instilled four times a day for two weeks.

In the short run

When it comes to safety, I emphasize to patients that Eysuvis is a low concentration steroid to be used as intermittent therapy for the treatment of their dry eye exacerbations. As part of my consultation, I ensure patients understand that the prescribed drug is approved for no more than 14-day use per treatment cycle while I inform them about the known side effects associated with steroidal medications.

My patients have reported feeling relief within a couple of days without any stinging, burning, or blurred vision. None of my patients have discontinued the medication.

Eysuvis is the first and only prescription therapy approved specifically for short-term treatment of the signs and symptoms of dry eye disease. This innovative treatment option fills a gap in our practices for patients who are experiencing exacerbations of ocular surface symptoms by empowering them to take back control of their condition.

Cynthia Matossian is the Founder and Medical Director of Matossian Eye Associates, an affiliate of Prism Vision Group with offices in Pennsylvania and New Jersey, USA.

The author discloses that she is a consultant to Kala Pharmaceuticals, Johnson & Johnson, Alcon, Allergan, Novartis, Sight Sciences, Sun Pharma, NuSight, Bruder, Imprimis, BlephEx, Lumenis, and PRN.

See references online at: top.txp.to/fast-lane

DRY EYELAND

Journey to a world

WHERE A LOSS OF TEAR FILM HOMEOSTASIS LEADS TO DRY EYE[1]

When it comes to dry eye disease and the loss of tear film homeostasis, there's a broader integrated system that needs exploring. We call it Dry Eyeland.[2,3]

Come travel this anatomical landscape, where:

- Loss of tear film homeostasis is the unifying characteristic of all dry eye[1]
- The parasympathetic nervous system plays a major role in tear film homeostasis[2]
- The lacrimal functional unit (LFU) is far more than just the lacrimal gland[3]

Allow us to be your guide to dry eye—visit DryEyeland.com to see the sights.

Because a whole world awaits beyond the ocular surface.

OYSTER POINT™

References: 1. Craig JP, Nelson JD, Azar DT, et al. *Ocul Surf.* 2017;15(4):802-812. **2.** Efron N, Jones L, Bron AJ, et al. *Invest Ophthalmol Vis Sci.* 2013;54(11):TFOS98-TFOS122. **3.** *Ocul Surf.* 2007;5(2):75-92.

NextGen

Research advances
Experimental treatments
Drug/device pipelines

Serving One's (Re)Purpose

Repurposing HIV drugs may be an effective and time-efficient route to treating dry AMD

By Jayakrishna Ambati

Dry AMD and geographic atrophy (GA) are subsequent stages of the same condition, with no current therapeutics available to stop the irreversible progression to blindness. For patients, it is an arduous wait in the hope that an effective treatment will be approved and save their eyesight. So how can we identify a treatment for this disease before it's too late? Could the answer be a drug that already exists – but has not yet been applied to this condition?

Repurposing drugs that are already approved for other applications could knock years off the drug development pipeline – and millions of dollars off the cost of early-stage pre-clinical and clinical trials. My team and I have discovered that dry AMD and GA can be treated by repurposing the HIV drug class nucleoside reverse transcriptase inhibitors (NRTIs) (1) and we will be performing clinical trials for this purpose. This ties in with our discovery that Alu DNA causes death of the retinal pigment epithelium (RPE) and – crucially – is not produced when NRTIs are administered.

Digging for answers

This discovery tracks back to 2014, when we originally published research showing that NRTIs can block a mouse model of dry AMD in mice (2) – a completely different application to NRTIs' original purpose.

"When starting from scratch, drug development may take 12 to 15 years and cost anywhere from US$2–3 billion to bring to market."

All we knew at the time, in terms of the mechanism of action, was that these drugs inhibit inflammatory activity, which led us to investigate them further and decipher more details. Fortunately, the advent of big data archeology – which mines large databases of patient records for drug-disease associations – enabled us to test our hypothesis. The analysis of four distinctly different databases from both public and private health insurance carriers supported our notion that NRTIs are beneficial to treatment of dry AMD. We also identified (through big data archaeology) that Alu DNA, which we had previously identified as present in high levels in dry AMD eyes, was made in the cytoplasm. These findings are the culmination of work that started a decade ago and drove us to seek a deeper understanding of the biology of the disease.

NRTIs work by two mechanisms: blocking reverse transcriptase and blocking the inflammasome of the immune system. Blocking reverse transcriptase is beneficial to dry AMD because it stops the conversion of Alu RNA to Alu cDNA, preventing the toxic Alu effect that causes RPE death in GA. The second mechanism of action, blocking the inflammasome, reduces the damage caused by the immune response to the disease – further increasing retinal protection. The combination of these two mechanisms helps to explain NRTIs' tremendous beneficial effects against dry AMD.

NRTIs are not perfect; they can be pretty nasty drugs, especially the early versions. Newer generations have been more tolerable, but still feature side effects that HIV patients tolerate due to the drugs' survival benefits. Dry AMD patients are mostly middle-aged or elderly and may stand to lose their sight – but not their lives – so may be less tolerant of side effects. This led us to create NRTI derivatives – called Kamuvudines – that retains the beneficial aspects of the drug, but lacks its toxicity. It is these derivative drugs that we are now taking forward into clinical trials.

Looking to the future

There are multiple benefits to repurposing a well-classified drug class with copious amounts of real-world data. When starting from scratch, drug development may take 12 to 15 years and cost anywhere from US$2–3 billion to bring to market. This takes into account the immense failures inherent in this process; many drugs fail the expensive tests along the development pipeline, sometimes even when they are potentially beneficial, but may cause adverse effects. Repurposed drugs have already achieved this extensive, expensive, and time-consuming stamp of approval. Because they are already used in patients, we know that they meet reasonable safety and tolerability standards. We know the dosing regimen and pharmacokinetics of the drug. All of these factors shorten the runway for launching a clinical trial and may allow researchers to skip phase I and II clinical trials (designed to establish safety) and initiate phase III trials as a first step.

The discovery of DNA synthesis in the cytoplasm also opens up a new chapter in biology and disease, teaching us that DNA is not produced in the nucleus alone. Our new understanding of Alu is similarly enlightening – with evidence that Alu is involved in the pathology of Alzheimer's disease, multiple sclerosis, lupus, and several other diseases, it is perfectly reasonable to hypothesize that these diseases may see a similar benefit from Alu-targeting treatments. In fact, we are actively looking at wider disease applications in addition to dry AMD – and our early results are intriguing.

In addition to this work, I've formed a company called Inflammasome Therapeutics that has licensed this technology. Our next step is to run clinical trials through the company for dry AMD and some other diseases, including systemic conditions, to bring this drug into use. As the world slowly begins to move past COVID-19, we hope to advance our clinical trials as soon as possible.

Jayakrishna Ambati is Professor and Vice Chair for Research, and Founding Director of the Center for Advanced Vision Science at the University of Virginia, Charlottesville, Virginia, USA.

Disclosures: Jayakrishna Ambati is a co-founder of Inflammasome Therapeutics, iVeena Holdings, iVeena Delivery Systems, and DiceRx, and has been a consultant for Allergan, Boehringer-Ingelheim, Olix Pharmaceuticals, Retinal Solutions, and Saksin LifeSciences unrelated to this work.

See references online at: top.txp.to/repurpose

Structurally Sound

How photoacoustic imaging may revolutionize ophthalmic imaging and diagnosis

By Parsin Haji Reza

What could you do with better imaging? With better information at your fingertips, how many more ocular diseases would be diagnosed earlier – before damage became irreversible? I hope to help you find answers to these questions with the photoacoustic remote sensing microscopy (PARS) technology developed in my lab; PARS enables structural and functional imaging of the eye – with high resolution.

Given its strengths, there is virtually no limit to the potential applications of PARS in ophthalmology. We can use it for early diagnosis of most blinding diseases and anything else that can be detected based on functional information, oxygen saturation, oxygen metabolism, and blood flow. And we can measure this information accurately down to a single capillary or – in some cases – down to a single red blood cell. This ability may extend to measuring the thickness of the RPE layer and melanin concentrations. We are also able to take advantage of the various optical absorptions of different contrast agents and drugs – thereby enabling measurement of drug concentrations in the eye, which could open a new field in pharmaceutical development.

Making waves

Photoacoustic imaging, in general, uses light energy to generate ultrasonic sound waves in a sample – the waves can be translated into an image – much like the ultrasound technology we're all familiar with.

So why isn't it already being used for eye imaging? Probably the biggest issue is the need for direct contact, with both gel and transducer touching the eye; needless to say, this is not ideal – both because of patient discomfort and the increased risk of infection from the physical contact. Furthermore, contact-based imaging directly affects the balance of vascular function and oxygen diffusion from the pressure applied to the eye, which means we are unable to study dynamic processes under conditions that are close to normality.

PARS uses an excitation laser to generate sound waves that are collected by a novel remote laser sensor that completely avoids physical contact, and collects the initial pressure right at the source. A traditional ultrasound transducer can only collect sound waves that travel to the surface of the tissue, requiring constant physical contact. To put the process in other words, when you throw a stone into a lake, shockwaves or initial pressures are generated from the moment that the stone hits the water, and these waves travel to the shore. The further you are from the place of impact, the less pressure you detect in the waves – as is the case with some transducer and traditional photoacoustic imaging. In PARS, instead of collecting the waves that have travelled to the shore, we only collect the initial pressures – the immediate pressure in the first few hundred nanoseconds after the stone (laser) hits the water (eye).

In short, PARS gives us a non-contact imaging method that, in addition to optical absorption, can provide additional imaging contrast, including scattering.

Better together

PARS is a powerful technique but, by harmonizing it with OCT, we are able to access the best of both worlds. PARS provides accurate measurements directly from optical absorption and OCT provides optical scattering, so they work in concert with each other. PARS can also provide optical scattering (and a few other light-matter interactions), but OCT is the gold standard in the field of ophthalmology – and the images are easy to understand – so we wanted to make sure that PARS images were collected from the same exact location to provide verification for what we are imaging and how we are imaging it. In future, PARS will be able to function as a stand-alone technology and for many applications OCT won't be needed.

The imaging penetration depth is related to the wavelength and the tissue type we are looking at – which makes the eye especially advantageous. With visible wavelengths, we cannot penetrate more than two or three millimeters into scattering tissues. As the eye is transparent to most of the wavelengths we use, there is no limit to the depth we can achieve. We can look at the retina and the structures at the back of the eye easily. The RPE layer may bring a unique challenge given that the role of this tissue is to absorb light – and that may limit the ability to image the choroid and beyond. As most of the light will be absorbed by the RPE layer, not enough photons will get through to generate the photoacoustic waves that create the image; however, we are actively working on techniques to overcome this.

One of the major advantages of PARS is the ability to measure optical absorption directly and accurately. Almost everything absorbs light: RNA, DNA, melanin, lipids, hemoglobin, and more. With PARS, we can directly pick up this information – and that results in high-resolution imaging; if needed, we can see right down to a single red blood cell and even gain functional details down to the capillary level. And we can use any wavelength in the visible light range and even the infrared range to visualize what we want to see.

Right now, the opportunities seem limitless. But we need to do more investigations and run clinical studies to discover the true potential of PARS. I suspect that PARS will give access to biomarkers we're not currently able to see – biomarkers that will become critical prognostic indicators for disease activity.

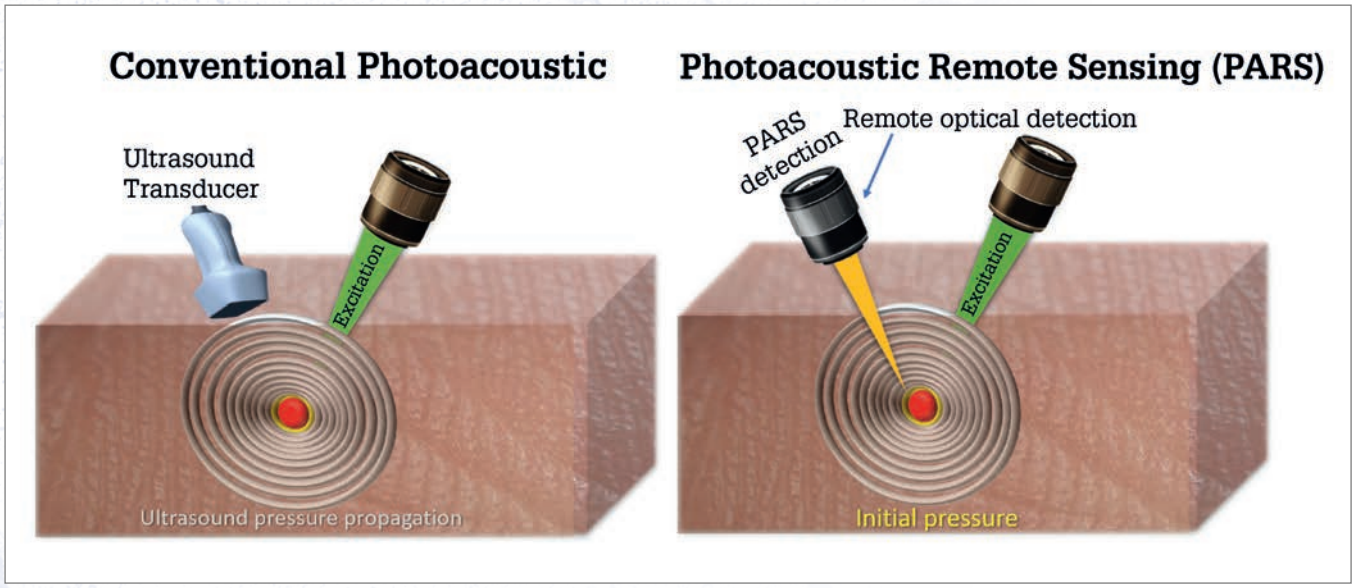
Tackling translation

We are optimistic but we are also perfectionists and realists – and we

The Sweet Sound of Serendipity

I actually discovered the PARS method by accident during my PhD. Whilst working on a completely different project, I noticed that it was possible to collect pressure or photoacoustic signals that were generated through the air. From that point onwards, I have focused my career on further developing the physics behind PARS – and translating that knowledge into a new optical imaging modality.

When it comes to light and optical imaging methods, one natural application is ophthalmology; after all, our eyes have evolved to collect light. We were also aware that there is a continuous drive to better understand the function of the eye – and that demands increasingly sophisticated imaging modalities, which inspired to use the physics behind PARS to work on an ophthalmic device.



General principle of photoacoustic imaging (left) and PARS remote optical imaging (right).

"We can use PARS for early diagnosis of most blinding diseases and anything else that can be detected based on functional information."

are actively working to address any (current and potential) limitations in a bid to further improve the technique. For example, we do not have fast 3D imaging capabilities – yet (though we have patented a method…). Perhaps the biggest barrier to successful implementation of PARS is the fact that it takes time to introduce a brand new technology that provides unique information into the clinic.

I think PARS will have a revolutionary impact on a number of clinical settings outside of ophthalmology. For example, we hope to have an impact in surgical oncology by providing real-time information with the aid of a surgical microscope. PARS is already being integrated into the first histology device for either in situ assessment of cancer margins during surgery or as a stand-alone tabletop device to reduce the time it takes to do histological analysis; in fact, that has been my main focus for the last two years. We can also reduce the size of the technology down to a single-mode fiber, which could be used in endoscopic applications.

I believe that, in a year or so, our first products for histology imaging should be commercially available. To get there, we've built a highly skilled team and developed a comprehensive plan. From a list of 50 possible applications in my office, ophthalmology has high priority!

My dream is to see PARS as a gold standard in optical imaging in many applications –especially in ophthalmology. Like any scientist, I want to see my findings making impact in our society.

Most of our work on PARS– and its translation to a clinical setting – is supported by my company illumisonics, which was established specifically to patent and commercialize PARS applications. I've always believed that academia and industry need to work together side by side because they complement one another so well. And now, wearing two hats, I know that to be true. The real philosophy behind my research is to deliver real-world impact – and that is exactly what I intend to do.

Parsin Haji Reza is an Assistant Professor in Biomedical Engineering within the Department of Systems Design Engineering and director of PhotoMedicine Labs at the University of Waterloo, Ontario, Canada.

Reference

1. *Z Hosseinaee et al., "Functional and structural ophthalmic imaging using noncontact multimodal photoacoustic remote sensing microscopy and optical coherence tomography,", Scientific Reports 11, 11466 (2021). PMID: 34075105.*

Finding Ocular Surface Inflammation

InflammaDry® – the first commercially available, rapid result, in-office test that detects elevated levels of inflammatory marker MMP-9 – helps document ocular surface inflammation

Robert J. Noecker is an internationally known glaucoma expert who specializes in cataract and micro-invasive glaucoma surgery. He is Assistant Clinical Professor of Ophthalmology at the Yale University School of Medicine, Clinical Professor of Surgery at the Frank Netter School of Medicine of Quinnipiac University, and practices at Ophthalmic Consultants of Connecticut, USA.

Noecker presents this third case study in the InflammaDry® series.

Background

The patient is a 67-year-old woman with moderate primary open angle glaucoma and a history of numerous glaucoma treatments over the past few decades. She had undergone surgery with a Xen gel stent in the left eye approximately three months prior to the consultation, and was using difluprednate once a day. Her IOP was 12 mm Hg.

She presented with increased eye redness and complained of unstable vision while reading, as well as a foreign body sensation – all symptoms were worse in the right eye than the left.

Diagnosis

The patient had superior nasal step visual field loss in both eyes with corresponding optic nerve and RNFL thinning. On brimonidine, bimatoprost and dorzolamide, her right eye IOP was 18 mm Hg.

She had significant ocular surface disease in both eyes, with the right being significantly worse than the left. After her previous surgery, she had continued using glaucoma medications in the right eye while not using them in the left eye. This corresponded to a more inflamed tear film and confirmed the cause of the patient's symptoms.

The pro-inflammatory effect of glaucoma medications on the ocular surface is well documented. Benzalkonium chloride (BAK) is the agent most commonly implicated, but the active ingredient, pH and other excipients, as well as duration and frequency of application, have been linked to increased inflammation in ocular surface tissues. The changes are reversible with the use of tropical anti-inflammatory agents, but the longer the inflammatory changes have been present, the longer they take to dissipate.

Intervention and treatment

MMP-9 testing helped to confirm that the glaucoma medications significantly contributed to this patient's ocular surface problems; approximately six months before, she had tested highly positive for the presence of MMP-9 in both eyes.

After a review of both ocular surface and glaucoma status, the patient was scheduled for surgery in her right eye with the goal of controlling her IOP without the further use of glaucoma medications.

The role of MMP-9

A baseline evaluation for the presence of MMP-9 in our glaucoma patients is standard protocol – and can be performed using the InflammaDry® MMP-9 rapid point-0f-care diagnostic test (Quidel Corporation, San Diego, CA, USA). In my experience, most glaucoma patients suffer from ocular surface disease, which often bothers them more than the glaucoma.

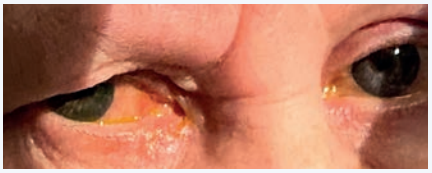


Figure 1. The patient's right eye.

Figure 2. MMP-9 testing of right and left eye.

Figure 3. Right eye (lower test) shows much higher presence of MMP-9 than in the left eye, which is negative with no strong pink line.

MMP-9 testing in all patients helps to guide therapeutic decisions, and objectively documenting ocular surface inflammation helps with patient education on available therapy options.

Patient outcome

MMP-9 testing in this patient corroborated the clinical findings. By eliminating the glaucoma medications and using anti-inflammatory therapy in the form of corticosteroids, the changes were reversed through surgical intervention.

The patient was operated on successfully and is doing well off glaucoma medications, with an improving ocular surface status.

Profession

Your career
Your business
Your life

Ain't No Mountain High Enough

Simon Prosser developed a unique model of helping to improve quality of life of AMD sufferers by climbing the world's highest peaks

By Aleksandra Jones, with Simon Prosser

Does the name Summits4Sight sound familiar to you? If it does, it might be because recently a foundation of this name has been making some noise, with more and more people within the ophthalmic community – and beyond – becoming aware of its goals. The man behind it, Simon Prosser, has had the vision of Summits4Sight in his head for a long time, and over the past few months, he has been busy training and then putting it into practice climbing some the highest mountains in the world, all with a view to help improve lives of people with vision loss caused by AMD. But where did the idea come from, what is involved, and what are Prosser's plans for the future of Summits4Sight?

The beginnings

Originally from the UK, Simon Prosser spent his formative years in Germany, before moving back to Britain to work as an application engineer for an automotive business. After a couple of further career changes, he was offered an opportunity of entering the ophthalmic field, working for Synergetics, now part of the Bausch + Lomb group. He successfully set up the company's European office and helped build its business. He then began working for

DORC – Dutch Ophthalmic Research Center International – in Germany; he spearheaded the company's US operations in Dallas, and worked in South America ahead of and immediately after the company's sale to Montagu. After a stint at Vitrek, the time came for him to look for something he felt really passionate about. He began working for Eye Tech, a company developing eye tracking systems for people with disabilities, which at the time started to branch out into ophthalmology and neurology – two areas he was familiar with – where he met Michael Freeman, the CEO and Founder of Ocutrx, a company Prosser now works for.

At Ocutrx, he became involved in the company's project using a wearable augmented reality (AR) device to help people with severe central vision loss due to AMD. Freeman, whose father had suffered from AMD at a time when no treatment was available, was inspired to try to develop new capabilities for people afflicted with the condition. He sought Prosser out thanks to his experience with eye tracking systems, as well as retinal surgery, and asked for his help in bringing the AR vision aid to market, and designing a surgical platform.

As Prosser had already had an idea to found a non-profit that would fundraise money to help people by climbing peaks, making Ocutrx's AR technology available to as many AMD sufferers as possible seemed like the perfect cause to focus on. He became the company's Global Director, working on developing its surgical platform, and he has also been working on developing the foundation to distribute the Ocutrx platform widely to people who need it – Summits4Sight, a foundation that Ocutrx is now also supporting financially.

The cause

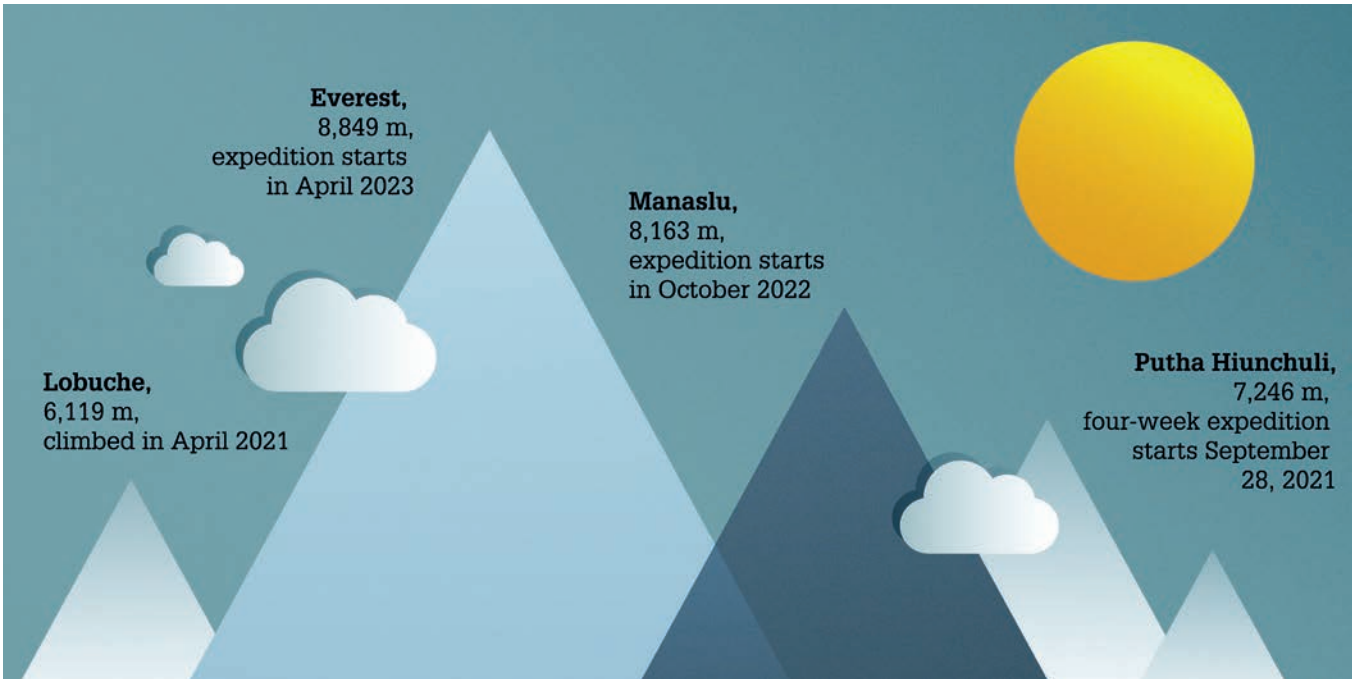
Prosser began to look into "giving back" and setting up a charitable foundation a while ago, and over the months and years the idea started to take shape in his head. While he saw many organizations and foundations focused on funding research in the field of retina, there wasn't much that focused directly on patients, and improving their quality of life immediately. The latest technologies improving quality of life for people with vision loss are not usually commercially available to all those who need them. Selected few wealthy individuals can access certain resources, but most useful innovations are not available to most people as they are not affordable and/or not covered by insurance.

Prosser saw an opportunity in bringing together existing low vision centers and groups, and developing criteria to select people who would benefit from using the technology Ocutrx has been working on, at no cost to themselves. This is still work in progress, and for now, Prosser is focusing on raising awareness of the cause in order to raise funds to purchase the needed technology from interested, relevant vendors – including Ocutrx – at production cost, to maximize the technology's future reach and availability. The idea is to fund real-life solutions that improve quality of life, which low vision centers and groups will be able to distribute among their members, according to their needs.

"Prosser saw an opportunity in bringing together existing low vision centers and groups."

The fundraising

Prosser is looking for the ophthalmic industry's wide support, with many companies already helping out with donation. His network, built up over 20 years or more, includes many physicians and leading industry figures. What's more, some automotive and engineering companies he worked with at the beginning of his career are also involved in supporting the foundation, without the perspective of gains in the ophthalmic field. Some wealthy individuals in the US and in Europe are throwing their weight behind him, so the initial goal of raising US$ 1 million seems well within reach in the first several months of the fundraising efforts.



The peaks Prosser is planning to climb as part of this fundraising campaign.

This could help hundreds of people, with many more that could be supported over the coming years.

For now, it has been a tough job of navigating the legal and administrative issues between intensive daily workouts, and climbing training t weekends. It would be made easier with extra paid help, but Prosser is determined for that not to impact the fundraising total before absolutely necessary. The four climbs are already fully-funded, and Prosser has made sure that the necessary funds to begin the distribution of the device to AMD groups in the fourth quarter of 2021 are in place.

The preparations

The ambitious plan of conquering the "summits" of Summits4Sight means that when Prosser completes it, having climbed the four mountains he is attacking, he will have climbed twice the height that he has ever climbed before – and he has already done his fair share. As the mountain heights increase, so do the demands and dangers of the climbs.

Prosser first came to contact with rock and mountain climbing as a young child, through his father, although he didn't enjoy it to begin with. He then became a semi-professional skier, and fell in love with mountains and hiking, climbing Alpine peaks when living in Europe. In the last decade or so, he has turned it into a real passion, and traveling with work allowed him to explore mountains in different parts of the world, including South America, in his free time. As a result, he had a few close calls, and has become accustomed to pushing his limits.

To develop his Summits4Sight plan, he got in touch with the International Mountain Guides (IMG) who helped him come up with an appropriate training schedule and advice on staggering the climbs, so that the whole idea of reaching the four peaks became realistic. As he points out, he has never been a professional alpinist and spent most of his life in an office or an OR, so this project is way out of his comfort zone and requires a lot of preparation.

In September 2020, Prosser embarked on a strict training and diet regimen. He has been very active throughout his life – apart from skiing, he is also a keen diver, and he got involved in bodybuilding, so he already had the knowledge of nutrition, appropriate training, and the discipline required. He typically trains three to four hours a day, shared between treadmills, cross trainers, stairs, and bicycles, and when he's not on the machines, he's training in the mountains, both in the US (in Arizona and Colorado) and in Switzerland. The pandemic has occasionally put a spanner in the works with imposed quarantines – and Prosser, who only takes a day off every week from his training, gets a bit anxious if he misses any more of it – but it also allowed him to focus on his training while staying at home for months, without the feeling of missing out on much happening outside.

The first climb

Following this intense training, which luckily didn't result in any injuries, in April 2021, Prosser made his first trip to Nepal, to climb Lobuche. He was prepared to have to quarantine for 10 days upon his arrival, but the requirement was dropped 24 hours before his planned arrival, which really helped keep

his fitness levels up. He made it to the base camp three days ahead of schedule and didn't experience any altitude sickness – a success he ascribes to his training in high peaks of Arizona ahead of the Nepal trip. As the weather window was coming to an end, with a storm coming, it was the last opportunity to reach the summit. On April 21, at 7.30 am, after a record ascent time, Prosser and his team reached the summit of Lobuche. He says: "It was a fantastic experience. I wanted to prove to myself that I could live up to the expectations of all the people who have supported me, trusted me, and made this climb happen, so to get to the top without a struggle meant a lot to me. On the way down, I saw people using Lobuche as training ahead of climbing Everest, and even though they were struggling, they were still planning to attempt the world's highest peak in a few weeks' time – something that shocked me, as I don't consider it to be a responsible approach." It took the team around 3.5 hours to get down to the high camp, where they were going to rest for a few hours and "charge the batteries," but the guides, seeing the rapid change in the weather, insisted on coming down much faster. Prosser continues: "Immediately after leaving the camp, snow started coming in from all directions. I was wearing all my hard-shell protective clothing, with just a little gap for my eyes, but the snow still found its way in and crammed in my eyes. I had no clue where the path was, and there were huge drops on either side. Luckily, with the Sherpa guides' experience, we made our way down, although it took us two days to make the descent." Having gained five days on his original schedule, Prosser then had a wait for his return flight from Kathmandu, with the added difficulty of having to get PCR test results ahead of flying home at a time when the city was going into a new lockdown.

Most of the corporate sponsors who have already agreed to support the foundation have guaranteed a base sponsorship, but they are also reserving bonus sponsorships for reaching the summits, which is a real incentive for Prosser to push to his absolute

limits, as he knows that not making the summit will cost the foundation money, which would ultimately limit the number of people he can help. This pressure keeps him going, both during his training, and during the climbs, and ensures that he plans things well. He trusts the IMG's guidance – the guides have helped hundreds of people get to the top of Everest and have never lost anyone, and even though the risks that high up the mountain are always substantial, they can be mitigated with good preparation, team work, and knowing how hard one can and should push themselves.

As Prosser says himself, the biggest challenge for him are not the climbs itself: it is getting enough people on board to make Summits4Sight as successful as it can be, and exceed everyone's expectations. He has been off to a great start, having already secured good funding to see the project through, and being able to stick to his climbing schedule, so he is convinced that the foundation is going to make a big difference.

Still, he does have a level of fear of the climbing itself – healthy fear, as he says. At any point during a climb, many things can go wrong, and the threat to life is constantly present. Only a naïve person would go into these circumstances with no fear, and it is necessary to make sure you don't make a mistake that could cost your or somebody else's life.

The future

For now, between Arizona and Switzerland, Prosser is busy training for the next scheduled climb – Putha Hiunchuli, for which the expedition will begin at the end of September. For this, together with his guide, he decided to make his own team, rather than attach himself to an existing one. This means having to organize and fund the logistics – down to booking and paying for eight yaks. The normal time to climb the peak is 31-34 days, and Prosser will attempt to do it in 24 days, trying to break another speed record.

Once he's done all the four climbs (see the graph below) he has planned, is that going to be it for Prosser's work on Summits4Sight? It seems very unlikely, as he already has fresh ideas, such as going to Antarctica, and perhaps writing a book about his experiences, to raise even more funds. It seems obvious that after this chapter, Summits4Sight will carry on helping the AMD patients with vision loss, but, as Prosser comments, he is focusing on his current goals and not looking too far ahead – the plan is ambitious in both the climbing scope, and financial targets, and it needs his full attention to come to fruition.

Zambia's Fight Against Blindness

ORBIS International is working to combat unnecessary blindness across Zambia

By Lucia Nadaf

In Zambia, we have a blindness prevalence of two percent. One person's preventable blindness is a big problem – so the Zambian figure is a massive problem and a clear unmet need. The biggest reason for this is a lack of trained eye care staff in the country, which often results in waits of months or years before treatment becomes available. Although the government can sponsor a patient's travel to another country for treatment, this is expensive – and money is not always available. Other barriers include myths and misconceptions regarding eye health, with education and poverty the major limiting factors in people's looking after their own eye health and seeking medical treatment when necessary.

I work at ORBIS International as country director for Zambia. The role consists of managing our work portfolio in comprehensive and pediatric eye health, with a focus on adult cataracts and glaucoma prevention. ORBIS is an international non-profit organization that aims to treat and prevent avoidable blindness and has been working in Zambia for just over a decade now – with our work located in three of the country's 10 provinces. This started in the northern area on the copper belt, working out of a tertiary facility that has grown from

"Keeping our staff, partners, and communities safe has been important, but it has also meant that we haven't been able to see patients as usual."

a single unit to an entire eye hospital. Initially providing pediatric eye health services, it then became a training facility for upcoming ophthalmologists, as well as strengthening the faculty through quality ophthalmic training and providing free treatment for children. Now, its focus has grown to include strengthening existing centers – with equipment, supplies, and training referrals for staff, – and setting up new ones. These improvements have enabled centers to work at full capacity, rather than opening only one or a few days a week. General physicians and nurses at primary health care centers have also been trained in basic eye health, so that eye conditions can be recognized in their early stages and either treated there or referred to a center that can assess further or treat the patient. District health facilities and community volunteers have also been trained to identify cases so that they can refer children to eye care centers if they see an issue. Community outreach is very important to ORBIS. We do this in several ways, but we try never to lecture, because we don't want to be "in charge"; we want to form partnerships and work with the community for the betterment of eye health. Eyesight is crucial to education and people's ability to provide for their families – so the work we do is important.

My work at ORBIS centers on treating and preventing blindness. Working with the ministries of health in multiple countries, we aim to build their capacity to provide quality eye care – through training, equipment, and medical supplies. Additionally, we work with these communities directly; the figures that appear in reports and the eyes that we treat are people and families, so our work needs this interaction and engagement.

Pandemic eye care

Ophthalmology was hit hard by COVID-19 (as we're all aware), but what about countries who already had a disproportionately high rate of blindness and eye health issues before the pandemic hit? Working through COVID-19 has required lots of adaptation in our processes. Keeping our staff, partners, and communities safe has been important, but it has also meant that we haven't been able to see patients as usual – especially during the first and second waves, when we were only able to address emergency cases. This has had a major impact on our previous work to increase awareness of eye health in Zambian communities, with many reverting back to old habits – not looking after their eyes and avoiding coming into the clinic if issues arose.

The pandemic has forced us to be more innovative with our work. Because we can't be in the communities, we've had to ride with ongoing government programs along the copper belt – often using COVID-19 programs as a vehicle to do our eye care work. In parts of northern Zambia, for instance, COVID-19 and eye health screening have been added to the standard child health activity programs. This has extended to training midwives and general nurses in basic eye health so that they can identify cases or risks in a child or mother. Another way we've adapted to the situation is by taking advantage of Zambia's widespread radio to broadcast our messaging about eye health and COVID-19. We have also produced educational material on handwashing and what to look for in terms of eye health; this has enabled us to educate the community indirectly on eye care and the link between COVID-19 and conjunctivitis.

The work also stretches out to communities with no access to health services, where people would go needlessly blind without our help. One such community is an older population, mainly farmers who only grow food for their own consumption and therefore don't earn an income. For them, travel isn't an option, so we developed a project to allow an ophthalmic professional to meet them and educate the community on eye health through screenings and treatment, including surgery.

We also have staff working on the frontlines. Two ophthalmic clinical officers working on the copper belt border between Zambia and the Democratic Republic of the Congo (DRC) have been screening truck drivers for both COVID-19 and eye conditions. There is also an eye health center on the copper belt where both COVID-19 and eye health are being screened.

We have worked hard to provide education (to both local communities and healthcare professionals), eye screening, and treatment to the people of Zambia – it is my hope that this eventually translates to the eradication of unnecessary blindness for the country's population.

Lucia Nadaf, Orbis International Country Director for Zambia, Lusaka, Zambia.

First Things First

A review of the Royal College of Ophthalmologists' Introduction to Ophthalmic Surgery course

By Teerajet Taechameekietichai

In 2019, the UK's immensely popular Microsurgical Skills (MSS) course was replaced with Introduction to Ophthalmic Surgery for non-ophthalmology trainees. The three-day MSS training had ranked among the most successful courses provided by the Royal College of Ophthalmologists (RCOphth) and, though held in the UK, it was open to international attendees and easily accessible thanks to its London location. The course provided an excellent foundation for ophthalmology trainees to develop good microsurgical skills. In the last few years, there was a clear trend toward doctors' attending the course early in their careers.

One of the reasons behind the high demand for the MSS course was that it helped Specialist Training candidates secure a point in the Training and Experience section of their recruitment portfolios – but trainees often forgot the knowledge and skills they gained through the MSS course when they started their posts a year later (1). This is why RCOphth decided to replace MSS with the Introduction to Ophthalmic Surgery and Introduction to Phacoemulsification courses for non-ophthalmology trainees and Special Training candidates, respectively. The former presents an opportunity for non-ophthalmology trainees to learn the fundamental skills of ophthalmic surgery.

Who is the course for?

The course is aimed at Foundation Doctors (who are completing a postgraduate medical training course in the UK), medical students, overseas doctors, and anyone who wishes to pursue a career in ophthalmology. Although it is not compulsory, attendees are awarded an extra point in the recruitment section of their portfolio. In October 2019, when I attended, the majority of participants were current Foundation Program Year 2 Doctors.

I decided to sign up for the RCOphth Introduction to Ophthalmic Surgery course for several reasons. First of all, like many medical students, I found that my medical school did not offer much exposure to ophthalmology and I believed that the course would reinforce my own understanding of surgical procedures for different ophthalmic conditions. I was also genuinely fascinated by the complexity of microsurgery and impressed by the high level of manual dexterity required.

Theory and practice

The course includes a short lecture before moving on to practical skills, which familiarized me with different types of ophthalmic surgery. I had around five hours to practice different practical skills on an eye model.

Before the course, students are given a link to an e-learning resource. This allows those with no surgical experience to learn the basic suture types and surgical instruments. Additionally, it provides multiple videos demonstrating different suturing and knot tying techniques; some on real patients.

"By the end of the first session, I felt I'd developed a good basic suturing skill that would be useful for all kinds of surgical jobs."

The course itself was very well organized and I felt that I had sufficient time to go through each skill before moving on to the next one. We were taught how to correctly handle different surgical instruments, as well as the basics of knot tying and suturing, and we had the opportunity to practice these techniques on foam boards. Even my minimal surgical experience allowed me to take full advantage of the training and, by the end of the first session, I felt I'd developed a good basic suturing skill that would be useful for all kinds of surgical jobs.

The session continued with a demonstration and practice of scleral and rectus muscle suturing, with an introduction to basic muscle surgery concepts such as muscle resection and recession. Each student got a chance to spend around 15 minutes on the Eyesi Ophthalmic Surgical Simulator, using the first setting of the basic anterior chamber navigation module, and we each got an account that allowed us EyeSi access at the RCOphth. We carried on with an eyelid suturing demonstration and were then introduced to using an operating microscope for corneal incision and suturing. I found using the microscope quite realistic, but suturing under it proved a lot more challenging than I had expected, with my field of view considerably restricted. Nevertheless, I felt that the session was well-supervised and the consultants were willing to help with any challenges I encountered.

Was it worth it?

I think that this course hugely improved my surgical skills and I would definitely recommend it to anyone thinking of pursuing a career in ophthalmology. Additionally, the course gave me insight into what it is like to perform an ophthalmic procedure. The course is definitely worth its (inexpensive) price, but it is in high demand, so for those interested – book early!

Teerajet (Chris) Taechameekietichai is a Foundation Doctor at the University Hospital of North Tees, Stockton, UK.

Reference

1. *The Royal College of Ophthalmologists, "Microsurgical Skills Course Changes for 2019" (2019). Available at: https://bit.ly/3jKMAbB.*

The Happiness Equation

Sitting Down With… Judy E. Kim, Professor, Ophthalmology and Visual Sciences, Graduate School of Biomedical Sciences, Director of Teleophthalmology and Research at the Medical College of Wisconsin, Milwaukee, Wisconsin, USA

Which traits of your character have brought you to where you are?

Creativity and curiosity have been strong traits in me since I was a child. As I got older, I found the importance of spirituality and developed a strong desire to help others, reduce suffering, and improve our current state of being. While I was born in South Korea, my family lived in Japan briefly and then immigrated to the United States when I was 11 years old, not speaking a word of English. My parents always told me and my siblings that their inheritance to us are education and faith. Perhaps because I have lived in the East as well as the West, I tend to have a global view and a desire to bridge the two cultures. I am curious about people, love to learn about others and their experiences, and have an open mind, wanting to understand rather than to judge.

When I was younger, I wanted to be a teacher and then a scientist – to pursue intellectual endeavors and find answers that I may be able to impart to others to improve their lives. I must admit, there was also a brief moment when I entertained the thought of becoming a nun – and I'm not even a Catholic! While assisting in research as a college student at the University of Chicago, Lawrence Berkeley Laboratory, and National Institutes of Health (NIH), as a medical student at Johns Hopkins University School of Medicine, and as a Howard-Hughes Research Scholar at NIH, I thrived on scientific inquiry and exploring the unknown. It has been this quest for knowledge that demanded creative methods to find answers and to translate scientific findings from the bench to the bedside to improve people's lives. While working alongside many students, post-docs, and mentors in the laboratories as a college student, I realized that a career in medicine possessed even greater options. All the qualities that I found to be meaningful – especially relieving suffering – are required in this profession on an immediate and daily basis. Therefore, I became a medical doctor to provide compassionate care. Furthermore, working in academic medicine has allowed me to combine patient care, teaching, researching, and serving – all the things that fulfil me.

I believe being a physician is not a job, but a calling. Though becoming a physician is a long and rough road, and being a physician requires much personal sacrifice, I feel so fortunate to have found a calling that excites me and makes me want to get up each day. I am also humbled each day by my patients and research subjects who open up their lives to me, entrust their sight to me, and allow me to be a part of their life's journey.

What inspired you to choose ophthalmology?

I fell into ophthalmology by chance. When I returned from researching at the NIH between second and third year of medical school, l took ophthalmology elective as an "easy" rotation to ease into clinical training. However, when I realized the importance of sight in people's lives, the delicate nature of ophthalmic surgery, and the intricacies of the ocular tissues and their function, I changed my goal from becoming an immunologist to an ophthalmologist.

Of all the senses we possess, I believe sight is the most important. It overwhelmingly contributes to our sense of reality and perspective, which in turn makes up who we are, how we think, and how we interact with the world around us. Furthermore, through our eyes, we can tell what is going on inside our body… How cool is that?

And how did you come to choose your subspecialty?

During my residency at Bascom Palmer Eye Institute, I fell in love with retina. Even to this day, I find it to be so beautiful and complex, something I want to know more about. However, I initially hesitated from pursuing retina as a subspecialty, as it is known for its rigor and the reality of an unpredictable lifestyle. I did not think it would be ideal for a married female ophthalmologist with a toddler, possibly because there were very few female vitreoretinal surgeons at the time – and even fewer who were married with children. However, I was fortunate to have learned from many giants of retina, such as Don Gass, who was not only considered the father of medical retina, but also the one who staffed my first scleral buckling procedure! While doing research with Harry Flynn, a superb retina specialist with a family who loved to mentor, and Stephen Pflugfelder, a cornea specialist who gave me confidence in my surgical skills, I chose to pursue retina. I have never looked back!

What has kept you fascinated with the retina field?

The field of retina has kept me fulfilled, entertained, excited, curious, and challenged – and it has propelled me forward right from the beginning of my ophthalmic career. Retina had the greatest promise for innovation, both surgically and medically. Over the years, the advances made in retina, such as pharmacologic treatments, ophthalmic imaging, surgical instruments, and gene therapy, among others, have confirmed that my initial impressions were correct. I also love being in the operating room. Due to the complexity of the surgeries, we often have to go into the battlefield with a clear battle plan in our heads, sometimes with two or three alternative plans, and even have to think quickly and improvise as the battle takes unexpected turns. While those who like routine procedures may be stressed under these situations, I find these moments to be thrilling, and they allow me to be creative. But, thankfully, these "thrills" are not common. The biggest thrill I get, even to this day, is seeing a closed macular hole or attached retina post-operatively, or a swollen retina return to normal anatomy after intravitreal injections. The most significant source of satisfaction is hearing my patients tell me how much the restoration of sight

has meant to them and their families. Satisfaction also comes from clinical trials and research that I have helped lead, which has resulted in life-altering treatments around the world. Educating the next generation of physicians, seeing my students flourish in their chosen field, being able to serve my community and organizations with my skills – all of these things keep me fascinated with my chosen field. Perhaps others have observed my love and passion for the field and gave me the honor to serve on various leadership roles, such as the American Academy of Ophthalmology Board of Trustee, executive committees of American Society of Retina Specialists, Macula Society, Women in Retina, National Eye Health Education Program, NAEVR/AEVR, and DRCRnet, among others. Service to these organizations are yet another way to make a difference in my field and to pay forward for the next generation.

What impact has the COVID-19 pandemic had on your life?

The pandemic has given me a chance to reflect, renew, and refocus. And that's been a huge change, as my head is usually like New York's Times Square ticker tape: constantly running! It gave me permission to stop and come up for breath, above a life drowning in "busyness." For some uncanny reason, I have always been acutely aware of our limited time on this earth. All of us are born with a time limit. Even if we live to be 80 years old, that's only 4,160 weeks! This realization of brevity of time has driven me to accomplish as much as possible and take on more than I should at times. The pandemic period of reflection has helped me to refocus my priorities. And it will help me to put large rocks into my life's bucket rather than filling it with small pebbles or even grains of sand.

I have a Happiness Equation: Happiness = (Reality - Expectations) x Gratitude. During the pandemic, I have exercised the act of Gratitude much more than before – being thankful for my family, friends, colleagues, health, another sunrise, rose bushes in my garden, among other things – while decreasing Expectations – learning to accept the uncertainty, letting go, going with the flow. I have been trying to elevate the state of Reality – seemingly bleak, terrible, and depressing not only from the pandemic with so many lives lost and sickened but also from social, economic, and health inequities and political unrest around the world – with love, kindness, and compassion for others and myself. After all, living is about relationships. The pandemic has reaffirmed my desire to be His instrument to improve people's lives to the best of my abilities until my expiration date.

YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection
Initial U.S. Approval: 1963

BRIEF SUMMARY: Please see package insert for full prescribing information.

1. INDICATIONS AND USAGE. YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

4. CONTRAINDICATIONS. 4.1. Ocular or Periocular Infections. YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases. **4.2. Hypersensitivity.** YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

5. WARNINGS AND PRECAUTIONS. 5.1. Intravitreal Injection-related Effects. Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection *[see Patient Counseling Information (17) in the full prescribing information]*. **5.2. Steroid-related Effects.** Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. **5.3. Risk of Implant Migration.** Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

6. ADVERSE REACTIONS. 6.1. Clinical Studies Experience. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study. Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)

(continued)

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

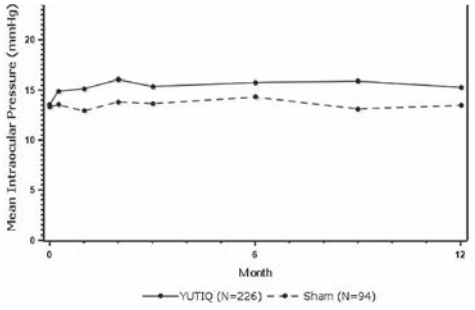
Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS. 8.1 Pregnancy. Risk Summary. Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. **8.2 Lactation.** Risk Summary. Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ. **8.4 Pediatric Use.** Safety and effectiveness of YUTIQ in pediatric patients have not been established. **8.5 Geriatric Use.** No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Manufactured by:
EyePoint Pharmaceuticals US, Inc., 480 Pleasant Street, Watertown, MA 02472 USA
Patented.

0.18 mg
YUTIQ®
(fluocinolone acetonide intravitreal implant) 0.18 mg

Discover continuous calm in uveitis

YUTIQ® (fluocinolone acetonide intravitreal implant) **0.18 mg:**

- **Proven to reduce uveitis recurrence at 6 and 12 months[1]***
  [At 6 months–18% for YUTIQ and 79% for sham for study 1 and 22% for YUTIQ and 54% for sham for study 2 (*P*<.01). At 12 months–28% for YUTIQ and 86% for sham for study 1 and 33% for YUTIQ and 60% for sham for study 2.]
- **Innovative Durasert® technology is designed for a sustained release of fluocinolone acetonide for up to 36 months with just 1 YUTIQ implant[2]**

For more information, visit **YUTIQ.com**

J code: J7314

Now With a Siliconized Needle

*Study design: The efficacy of YUTIQ was assessed in 2 randomized, multicenter, sham-controlled, double-masked, phase 3 studies in adult patients (N=282) with noninfectious uveitis affecting the posterior segment of the eye. The primary endpoint in both studies was the proportion of patients who experienced recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to noninfectious uveitis, or the use of prohibited medications.[1,3]

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Ocular or Periocular Infections: YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

Hypersensitivity: YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Risk of Implant Migration: Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

Please see next page for Brief Summary of full Prescribing Information.

References: 1. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. October 2018. **2.** EyePoint Pharmaceuticals Receives FDA Approval of YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg. Global Newswire. https://www.globenewswire.com/news-release/2018/10/15/1621023/0/en/EyePoint-Pharmaceuticals-Receives-FDA-Approval-of-YUTIQ-fluocinolone-acetonide-intravitreal-implant-0-18-mg.html. Accessed February 7, 2020. **3.** Data on file.

EyePoint PHARMACEUTICALS

480 Pleasant Street, Suite B300, Watertown, MA 02472

2/2021
US-YUT-2100009