MAY / JUNE 2023 # 67

the Ophthalmologist™

Shutting Down Short-Sightedness

How European eye care experts are approaching rising myopia rates

Light Adjustable Lens™

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I believed in the potential of the Light Adjustable Lens™ back when it was only an idea. I treated patients for nearly five decades and am now the chairman of a company that assists practices with streamlining patient care. These experiences let me confidently say this lens will change the industry, and it was an easy decision to choose it for my own cataract surgery.

Read the case study

onlyadjustability.com

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RxSIGHT®

Light Adjustable Lens™

INDICATIONS FOR USE AND IMPORTANT SAFETY INFORMATION

INDICATIONS: The Light Adjustable Lens™ and Light Delivery Device™ system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag in adult patients with preexisting corneal astigmatism of ≥ 0.75 diopters and without preexisting macular disease. The system also reduces the likelihood of clinically significant residual spherical refractive errors.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: The Light Adjustable Lens is contraindicated in patients who are taking systemic medication that may increase sensitivity to ultraviolet (UV) light as the Light Delivery Device (LDD®) treatment may lead to irreversible phototoxic damage to the eye; patients who are taking a systemic medication that is considered toxic to the retina (e.g., tamoxifen) as they may be at increased risk of retinal damage during LDD treatment; patients with a history of ocular herpes simplex virus due to the potential for reactivation from exposure to UV light; patients with nystagmus as they may not be able to maintain steady fixation during LDD treatment; and patients who are unwilling to comply with the postoperative regimen for adjustment and lock-in treatments and wearing of UV protective eyewear. **WARNINGS**: Careful preoperative evaluation and sound clinical judgment should be used by the surgeon to decide the risk/benefit ratio before implanting an IOL in a patient with any of the conditions described in the Light Adjustable Lens and LDD Professional Use Information document. Caution should be used in patients with eyes unable to dilate to a pupil diameter of ≥ 7 mm to ensure that the edge of the Light Adjustable Lens can be visualized during LDD light treatments; patients who the doctor believes will be unable to maintain steady fixation that is necessary for centration of the LDD light treatment; and patients with sufficiently dense cataracts that preclude examination of the macula as patients with preexisting macular disease may be at increased risk for macular disease progression. **PRECAUTIONS**: The long-term effect on vision due to exposure to UV light that causes erythropsia (after LDD treatment) has not been determined. The implanted Light Adjustable Lens MUST undergo a minimum of 2 LDD treatments (1 adjustment procedure plus 1 lock-in treatment) beginning at least 17-21 days post-implantation. All clinical study outcomes were obtained using LDD power adjustments targeted to emmetropia post LDD treatments. The safety and performance of targeting to myopic or hyperopic outcomes have not been evaluated. The safety and effectiveness of the Light Adjustable Lens and LDD have not been substantiated in patients with preexisting ocular conditions and intraoperative complications. Patients must be instructed to wear the RxSight-specified UV protective eyewear during all waking hours after Light Adjustable Lens implantation until 24 hours post final lock-in treatment. Unprotected exposure to UV light during this period can result in unpredictable changes to the Light Adjustable Lens, causing aberrated optics and blurred vision, which might necessitate explantation of the Light Adjustable Lens. **ADVERSE EVENTS**: The most common adverse events (AEs) reported in the randomized pivotal trial included cystoid macular edema (3 eyes, 0.7%), hypopyon (1 eye, 0.2%), and endophthalmitis (1 eye, 0.2%). The rates of AEs did not exceed the rates in the ISO historical control except for the category of secondary surgical interventions (SSI); 1.7% of eyes (7/410) in the Light Adjustable Lens group had an SSI ($p < .05$). AEs related to the UV light from the LDD include phototoxic retinal damage causing temporary loss of best spectacle corrected visual acuity (1 eye, 0.2%), persistent induced tritan color vision anomaly (2 eyes, 0.5%), persistent induced erythropsia (1 eye, 0.3%), reactivation of ocular herpes simplex Infection (1 eye, 0.3%), and persistent unanticipated significant increase in manifest refraction error (≥ 1.0 D cylinder or MRSE) (5 eyes, 1.3%). **CAUTION**: Federal law restricts this device to sale by or on the order of a physician. **Please see the Professional Use Information Document for a complete list of contraindications, warnings, precautions, and adverse events.**

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New AMMC® framework by Kaymak*

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Lenstar Myopia is based on the established Lenstar 900 optical biometer, combined with powerful EyeSuite Myopia software. It boasts a comprehensive toolkit, which now includes the new Age-Matched Myopia Control (AMMC®) framework of Prof. Dr. Hakan Kaymak. It enables you to:

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- Decide on a form of treatment, monitor its progress, adjust where necessary, and control myopia progression.

*AMMC® framework by Prof. Dr. Hakan Kaymak is only available, as standard, in Lenstar Myopia.

www.haag-streit.com/lenstarmyopia

HAAG-STREIT GROUP

Look closer. See further.

Think Globally, Act Locally

On my flight back from ASCRS, I felt compelled to pen a few thoughts on the importance of global ophthalmology…

In May, I attended my first large ophthalmology meeting – ASCRS – held in the city of San Diego, California. It was a hugely exciting few days, meeting people face-to-face, taking in presentations and papers from leading thinkers, and discovering the latest devices and technology. But traveling over 10,000 miles across the Earth was also a great reminder of the fact that ophthalmology is a global field of science and medicine, which got me thinking about the importance of international collaboration.

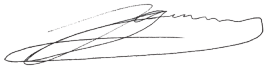
In the aftermath of COVID-19, when so many meetings went virtual, there was something special about being in the same room with so many people all sharing ideas and forging connections.

By forging international partnerships, ophthalmologists can play a crucial role in helping to build healthcare infrastructure and capacity around the world. A great example of this is the World Health Organization's recent Package of Eye Care Interventions developed in consultation with ophthalmologists and experts from across the globe (1).

By reaching across borders, we have the power to bridge gaps in care and ensure that all individuals, regardless of their geographic location, get the access they need and deserve. A recent academic review of the available literature showed that teleophthalmology has been hugely impactful and will almost certainly continue to be so, especially in light of the aging global population and the colossal unmet needs for retinopathies and glaucoma (2).

But (as my presence at ASCRS emphasized to me) beyond all these tangible benefits, global collaboration cultivates a spirit of camaraderie – a shared purpose. By thinking globally and acting locally, we unlock new possibilities, address healthcare disparities, and transform the landscape of ophthalmology. If you or colleagues are working on global ophthalmology projects – from large-scale research to building healthcare systems – please do get in touch!

Jon Greenaway
Editor



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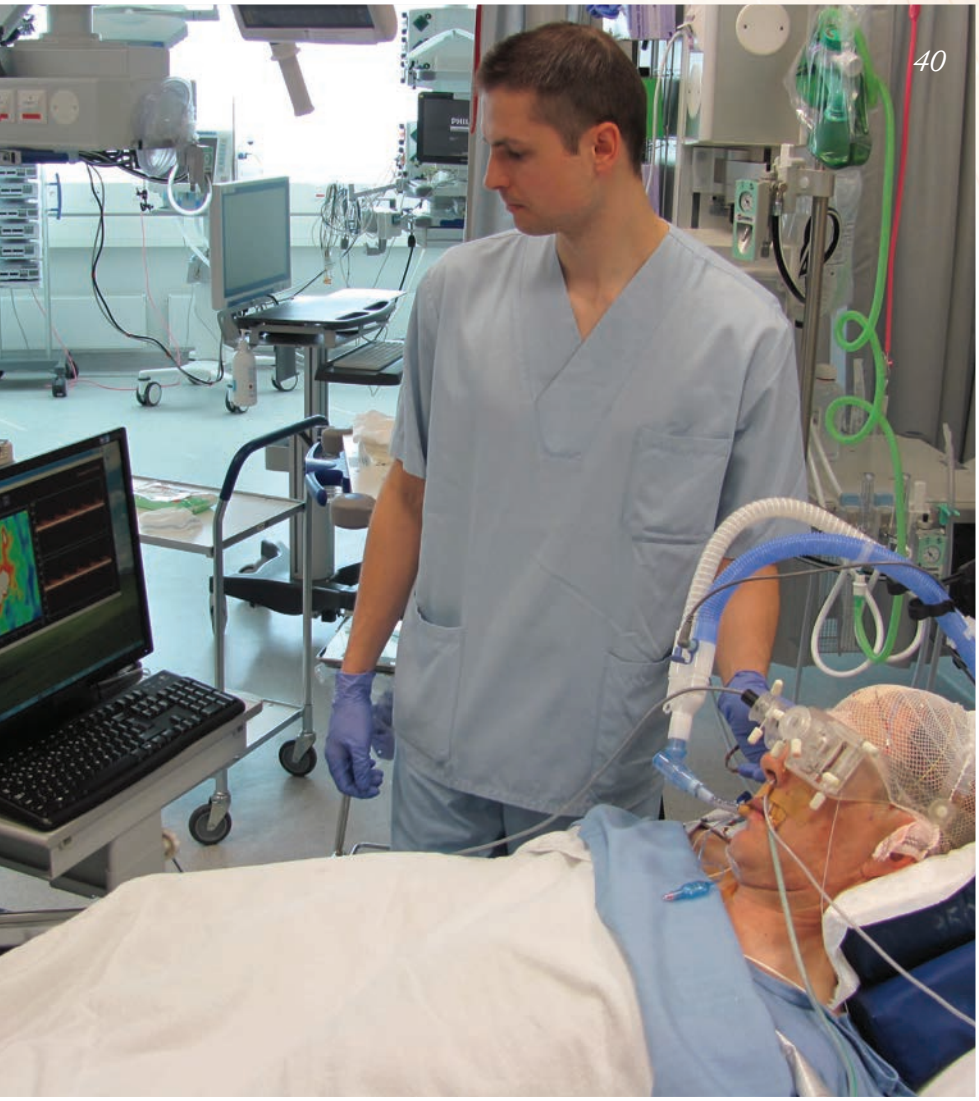
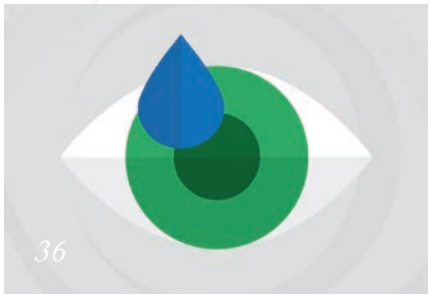




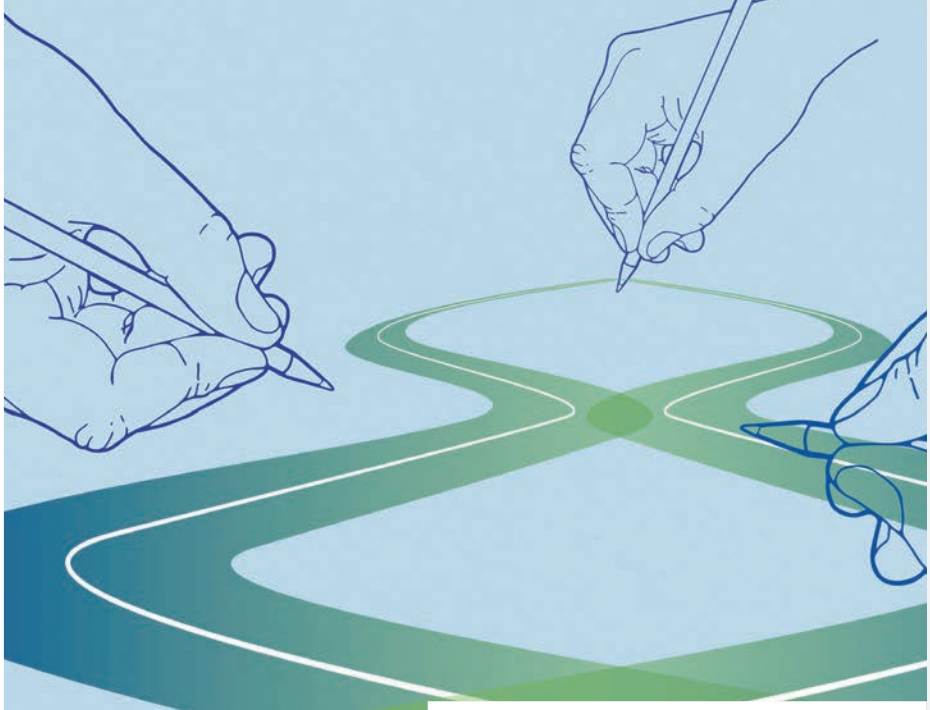
In My View

On The Cover

How are European eyecare professionals responding to increasing myopia rates?

Upfront

Feature



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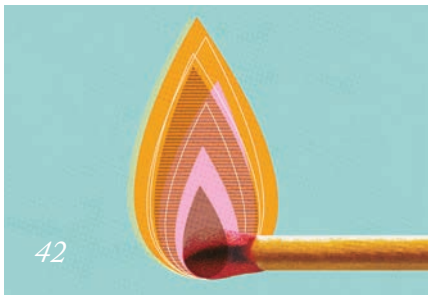

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the Ophthalmologist

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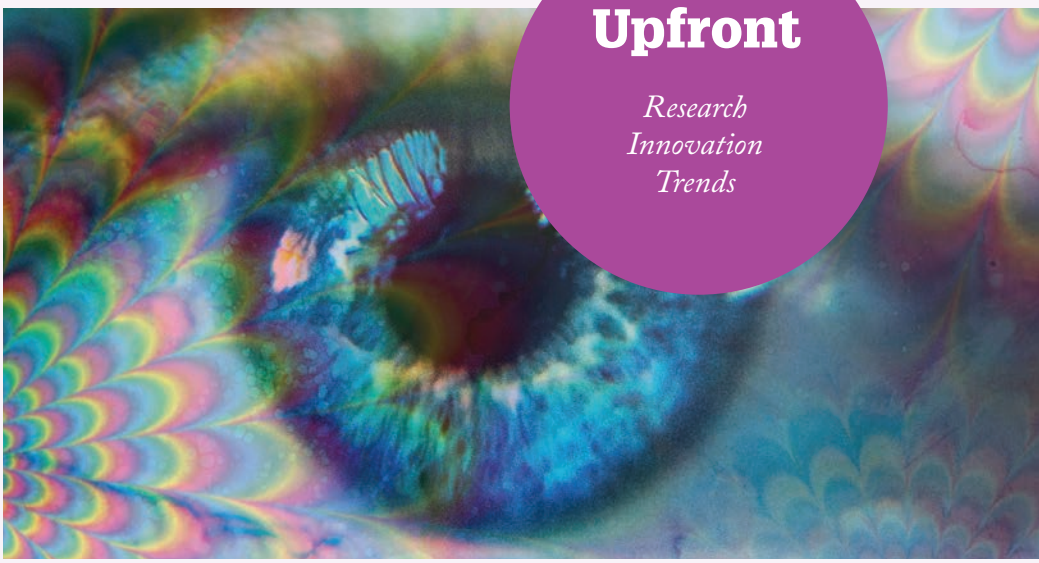
Upfront

Research
Innovation
Trends



Oculomics and Schizophrenia

Is multimodal imaging of retinal features the future of neuropsychiatric disorder detection?

A new paper seeks to better understand the retinal changes observed in schizophrenic individuals (1). Using two deep learning models the paper drew on a database of over 353,157 patients to assess whether schizophrenia could be associated with larger cup-to-disc ratio (CDR), thinner macular ganglion cell-inner plexiform layer (mGC-IPL), and macular retinal nerve fiber layer (RNFL). Here Siegfried Wagner, one of the study's authors, discusses the research.

What initially attracted you to this line of research?

Recognition of the retina as an extension of the central nervous system has motivated much research into neurological disorders, but that focus on psychiatric disease remains relatively limited. Here, retinal imaging may reveal mechanistic insights into the biology of psychiatric disease, particularly the role of neurodegeneration.

Given the confounding impact of comorbidities, how conclusive were the study findings?

I think the direct association between thinner inner retinal sublayers (GCIPL) and schizophrenia is quite convincing – it concurs with previous work, and is robust to adjustment for multiple confounders and subgroup analyses. I agree that the retinovascular differences are indeed attributable to the medical comorbidities – specifically diabetes and hypertension – although I would argue that these retinal vascular markers could still be useful in identifying those with schizophrenia who are at higher risk of developing medical comorbidities.

What were the main limitations of your recent study?

As this study involves data from patients attending a National Health Service ophthalmic hospital, the findings relate to those with eye disease and may not reflect what is seen in all individuals with schizophrenia. Also, there are other possible confounders, such as antipsychotic use, which we could not control for.

What impact would your research have in an ideal world – with no limitations?

I would like to see retinal imaging become part of the standard of care for individuals with schizophrenia and other systemic disorders. Most modalities are non-invasive and increasingly available in community and hospital settings.

See references online at: top.txp.to/oculomics/schizophrenia

INFOGRAPHIC

DR Snapshot

An estimated one in five people with diabetes develop diabetic retinopathy

>400 million

people have diabetes worldwide – and numbers could increase to **~650 million** by 2040

To investigate the progression of DR in the US, researchers explored retinal images of

498 participants

with diabetes

Credit: mages sourced from Unsplash.com and Pixabay.com

SPOTLIGHT ON ARVO

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

The balance of power

How do multifocal spectacle lenses affect accommodative errors – and does this change over time? To answer this, a team in Australia allocated 52 myopes (aged 18–27) to one of two progressive addition lens (PAL) types and measured lags of accommodation over the course of 12 months in three month intervals (1). Results showed that PALs can reduce accommodative lag, if i) additional power is tailored to typical working distances; after the first year, it should be boosted by at least 0.5D to maintain efficiency.

A point of progress

To assess the performance of geometric deep learning in diagnosing glaucoma, researchers acquired the optic nerve head OCT scans of 77 glaucoma and 2,296 non-glaucoma subjects (2). After each optic nerve head was represented as a 3D point cloud, geometric deep learning (PointNet) was used to provide a glaucoma diagnosis. The results showed that PointNet provided a better diagnosis than that obtained with a convolutional neural network.

Protein Knock-Out

Research by the Department of Ophthalmology of The Hebrew University of Jerusalem, Israel, characterized the centrosome-associated protein CEP250 and its role in causing atypical Usher Syndrome in patients of Iranian Jewish origin (3). A Cep250 KO mouse model showed both retinal degeneration and hearing loss with a relatively late age of onset – results that could aid the development of new gene therapies.

Momentum and Energy

To investigate saccade kinematics in relation to eye-movement, researchers used a horizontal saccade task to compare the saccadic behavior of patients with central vision loss caused by AMD with the behavior of patients with peripheral vision loss caused by retinitis pigmentosa (4). They found that both patient cohorts exhibited impaired saccade reaction times.

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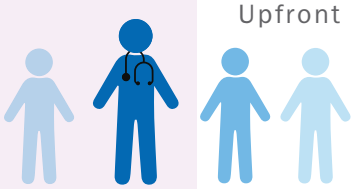

What About the Children?

Disparities in pediatric ophthalmic care have not improved in the last 15 years – they've gotten worse

In an article for the AAO, Daniel Terveen voiced concerns about the shortage of pediatric ophthalmologists in the US. In South Dakota Terveen reports that there is only one pediatric ophthalmologist who provides all of the retinopathy of prematurity (ROP) care and – as a result – has a several month clinical and surgical wait time (1).

Investigating this, researchers from The University of Miami Miller School of Medicine assessed the number and location of pediatric ophthalmologists in the US in relation to US population demographic characteristics (2).

A total of 1056 POs were identified, with men (611) outnumbering women. The states with the most pediatric ophthalmologists were California, New York, Florida, and Texas – also the four most populous states. Counties that had one or more pediatric ophthalmologists had a higher median household income compared with the 90 percent of counties that were found to have zero pediatric ophthalmologists.

See references online at: top.txp.to/what/about/the/children

Over eight years, an estimated

1 in 5

participants **(19.2%)** developed diabetic retinopathy

17.3 percent

experienced DR progression but…

23.3 percent

of those with DR at baseline showed improvement – "possibly reflecting [the improvement of] diabetes care in the US over the last two decades," say the authors

Reference

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THE OPHTHALMOLOGIST'S
TIME MACHINE: CHAPTER 10

How Nelson's eye became part of his legend

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

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

Horatio Nelson (1758–1805) is probably the most celebrated naval commander in history. His most famous victory, which came at the Battle of Trafalgar, was also his last. There, the British Royal Navy defeated the larger combined French and Spanish fleet, preventing a planned invasion of England from Napoleon's forces. Just prior to hostilities, Nelson sent the famous signal to the fleet: "England expects every man will do his duty." Nelson was killed in action shortly thereafter, and is commemorated at Trafalgar Square in London.

Nelson sustained many injuries during his career, including the loss of his right arm at the Battle of Santa Cruz de Tenerife in 1797. Additionally, he is reported to have lost vision in his right eye due to artillery fire at the Siege of Calvi in 1794 – three years prior to the arm injury.

Nelson wrote and spoke frequently of his eye injury, and he appears to have made the most of his monocular status. At Copenhagen in 1801, Vice-Admiral Hyde Parker ordered all ships to retreat. In response, Nelson held his telescope in front of his "blind" eye and remarked, "I really do not see the signal." Defying Parker's order, Nelson attacked and won the battle. Parker was subsequently recalled to England, and Nelson was promoted in his stead. Some say this anecdote popularized the expression "to turn a blind eye."

Despite the injured eye being a memorable detail – one he often spoke of – and despite the stories that incorporated it, historians question the reality.

Outlandish? Well, Nelson's damaged eye may indeed have been fictitious (1). The eye injury was not included in the official reports filed after the Siege of Calvi, where it would have occurred. Nelson was awarded a pension due to the arm injury, which occurred after the eye injury; at this time a blinding eye injury would have been enough to qualify for the pension itself. Perhaps most compelling, sculptures and paintings of Nelson generally feature an apparently normal right eye, although some do depict a scar over the right eyebrow. In general, portraits of other monocular military commanders acknowledge the eye injury in some way – or depict the subject from the side with the uninjured eye, such as the famous painting of the Duke of Urbino in Florence.

Credit: By Lemuel Francis Abbott - National Maritime Museum website. The painting was published as early as 1898 in: Sladen, Douglas (1898).Public Domain, https://commons.wikimedia.org/w/index.php?curid=2833419

It is certainly possible that Nelson suffered a blinding injury that left him with a normal-appearing and non-strabismic right eye; traumatic optic neuropathy, choroidal rupture, or retinal detachment could all have been responsible. But we feel it is all too easy to imagine the flamboyant Nelson exploiting a minor eye injury to burnish his already fearsome reputation.

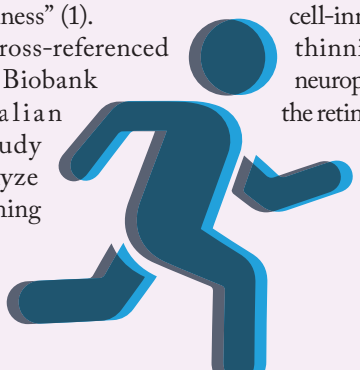
See references online at: top.txp.to/time/machine/10

Let's Get Physical

New study proposes positive correlation between physical exercise and macular thickness in adults living with glaucoma

Epidemiological studies show that daily exercise can lead to lower rates of open-angle glaucoma, AMD, and diabetic retinopathy. Until now no large-scale studies had investigated the relationship between these two variables using spectral-domain optical coherence tomography (SD-OCT), which "offers an objective and reproducible measurement of neuroretinal thickness" (1).

The new study cross-referenced data from the UK Biobank and the Australian PROGRESSA study cohort (2) to analyze rates of macular thinning with adults living with glaucoma, and the potential neuroprotective benefits of exercise.



The study concluded that moderate/vigorous activity was positively correlated with slower rates of macular ganglion cell-inner plexiform layer (GCIPL) thinning, stressing the potential neuroprotective benefits of exercise on the retina, particularly in an ophthalmic disease-specific cohort.

See references online.

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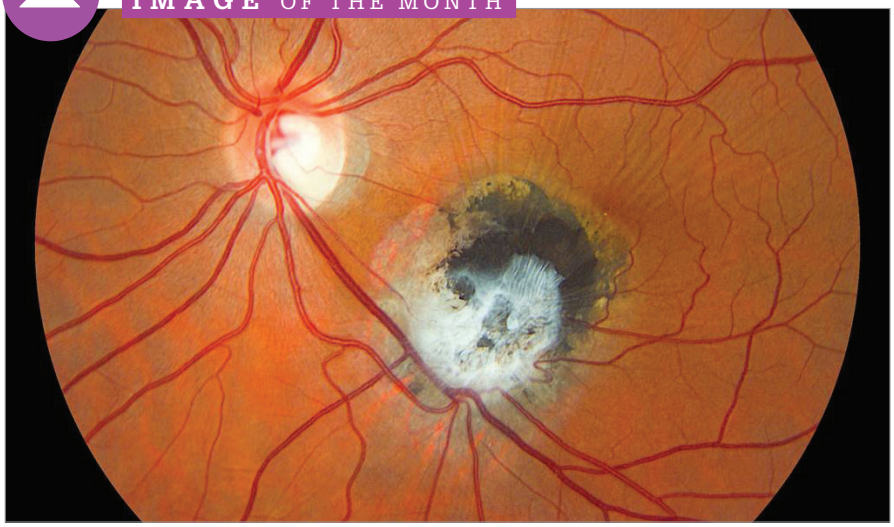
IMAGE OF THE MONTH



Capturing Choroidal Melanoma

This image from the Ophthalmic Photographers' Society Scientific Exhibit Photo Contest was displayed at the American Academy of Ophthalmology (AAO) meeting in 2022. This beautiful fundus photo depicts a Choroidal Melanoma and was taken by Jaime Tesmer from Mayo Clinic in the USA.

Choroidal Melanoma s/p Plaque Brachytherapy courtesy of the Ophthalmic Photographers' Society

Credit: Jaime Tesmer

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

TWEET OF THE ISSUE

"It's so funny when physicians talk about why they sold their practice to private equity. They talk about reimbursement and "the challenging landscape of healthcare" and expansion leading to better patient care. Buddy, you did it for a Scrooge McDuck sized bank vault full of cash."

Dr. Glaucomflecken

Credit: Collage images sourced from Rawpixel.com and Flickr.com

A Helping Hand

How AI models are alleviating the pressure of global healthcare systems

In an exciting follow up to "AI to Interpret," published in The Ophthalmologist back in 2020, the first artificial intelligence (AI) platform for OCT scan analysis has now launched online for public access with FDA clearance currently in process (1). The new Altris AI platform will help alleviate the compounded pressures of the fight against preventable blindness – affecting more than one billion people worldwide – and the global shortage of optometrists (2,3).

Able to detect more than 100 retina pathologies and pathological signs – both widespread and rare – and differentiate between pathological and non-pathological OCT scans within minutes, the new platform provides a promising decision making support tool to help ophthalmologists in their daily practice. Eye care specialists from 140 countries have already registered onto the platform and tested its benefits in clinical practice.

See references online at: top.txp.to/helping/hand

In My View

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

Protecting Veterans' Sight Together

Why the Federal Supremacy Project could negatively affect Veteran Affairs healthcare

By Brandon Kennedy, MD , a PGY-3 Ophthalmology resident

Over the past three years, I have spent a significant amount of time at the Salt Lake City, Utah Veteran Affairs (VA) Medical Center. The VA clinical rotation is one of the most challenging aspects of residency. Every day, it's an all-hands-on-deck approach to get through our high volume, high acuity clinic. Even with our exceptional team, the number of patients we see – and the problems they face – can leave us exhausted. And yet, all that stress melts away each time you call a patient's name and see their familiar face smiling at you from the waiting room.

The patients at our VA are exceptional, and I've been lucky to get to know them. Our interactions often start playfully: "Hey, Dr. Kennedy, ever since you told me you liked the Utah Jazz, they haven't won a game!" However, over the years, those relationships have developed into incredibly meaningful connections. I know who needs extra numbing before their intravitreal injection, who needs a handwritten list of their medications to post on their refrigerator, who is recovering from a recent hospitalization, who recently lost a spouse, and who is expecting a new grandchild. I am honored to be part of the team these patients trust for their eye health.

The burden of responsibility I share to protect our veterans' eyesight is something that became evident almost immediately after starting residency. But one patient in particular has stuck with me as an example of how heavy that burden can be. During an overnight on-call shift in my first year of residency, a veteran presented with sudden vision loss. He was very distraught – not just out of concern for his vision, but also as the sole caretaker of his ailing wife. The thought that he may not be able to care for her brought him to tears. With the help of my attending, I diagnosed him with an acute iris vascular tuft hemorrhage. Blood was pouring from a vessel in his iris and filling his eye, blurring his vision, and raising his intraocular pressure. He had a history of a branch retinal vein occlusion, and I suspected the bleed was from iris neovascularization. We successfully treated him with intravitreal bevacizumab and pressure patched his eye temporarily to stop the bleeding. The hyphema resolved, and his vision and intraocular pressure normalized. I have followed him closely since then and have gotten to know him well as a person. Whenever I need a reminder of why I've chosen this profession, he is the person who comes to mind.

"I fear the Federal Supremacy Project may act as a gateway to lower the standards of eye care veterans receive across the country."

Such commitment to patient care is the beauty of working at the VA, where ophthalmology residents work alongside attending physicians to serve those who have served us. They have earned the best care our medical system can provide. Unfortunately, a recent initiative proposed by the Federal Supremacy Project threatens to jeopardize veteran's medical care and simultaneously impact

residency education nationwide.

Let's go back to 2004, when federal policy was enacted to ensure veterans have the highest standard of eye care – establishing that eye surgery could only be performed by ophthalmologists, regardless of state regulations. Now, the Federal Supremacy Project threatens to challenge these standards and could allow optometrists to perform laser eye surgery. The repercussions of this are far reaching and would allow non-physicians to perform laser eye surgery in every state in the country, regardless of state laws.

Permitting laser eye surgery to be performed by any providers other than trained ophthalmologists unequivocally threatens patient safety. Ophthalmologists are trained to perform these laser procedures under the supervision of an attending physician who has been performing these procedures safely for years. Notably, the clinical decision making that precedes the treatment ultimately influences patient outcomes and safety – even more so than the skill needed to perform them. The decision of who is a good candidate, consideration of less invasive alternatives, weighing the potential complications and how to handle them – and the ability to handle them when they arise – are skills simply not taught in a few lectures. These nuanced decisions, thought processes, and fine motor skills are learned over time with experience, mentorship, and repetition – they are the direct result of the additional years of training that ophthalmology residents undergo.

An example: A patient was referred to me for YAG laser capsulotomy by a non-ophthalmologist. This veteran had multifocal lenses and complained of blurred vision and debilitating dysphotopsias in each eye. Examination demonstrated bilateral minimal, non-central posterior capsule opacification (PCO). It was immediately clear that his PCO was not the cause of his symptoms and a YAG would not be therapeutic. The best solution in this case was an intraocular lens exchange to treat the dysphotopsias and blurred vision. In fact, had the initial YAG laser capsulotomy been performed, as suggested by the referring provider, the definitive treatment with intraocular lens exchange would have made the needed surgery far riskier for the patient.

To put things more directly, I fear the Federal Supremacy Project may act as a gateway to lower the standards of eye care veterans receive across the country.

Ophthalmologists are highly specialized surgeons, with extensive training to ensure the safety and best quality of care for our patients. After four years of medical school, every ophthalmologist completes four years of residency training – and many opt to pursue an additional one to two years of subspecialty training in fellowship. Optometrists attend four years of optometry school. The training any ophthalmologist receives is – at a minimum – four-to-six years longer than the non-ophthalmology providers who might be allowed to perform laser eye procedures under the Federal Supremacy Project.

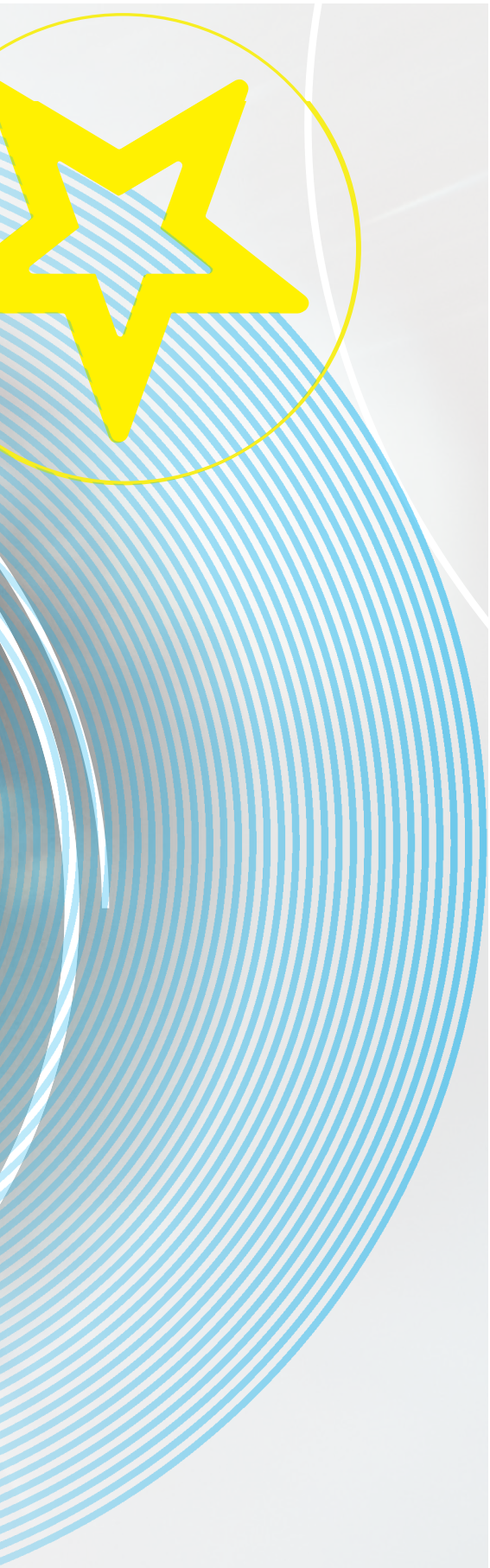
The VA prepares the next generation of ophthalmologists to be safe, reliable, and high-quality clinicians and surgeons and is an integral component of residency training. Much of our required procedure volume comes from experience at veteran hospitals. Learning these skills in a protected setting, with an appropriate balance of autonomy and supervision, optimizes both patient outcomes and resident training. Diluting the volume of procedures and veteran care under the Federal Supremacy Project has the potential to negatively impact residency training, risk patient safety, and confuse leadership of care.

"Every day, it's an all-hands-on-deck approach to get through our high volume, high acuity clinic. Even with our exceptional team, the number of patients we see – and the problems they face – can leave us exhausted."

What can be done to promote the continued safeguarding of procedures? The first steps are education and awareness. And that includes being transparent with both colleagues and patients about potential complications of procedures and how to avoid and manage them.

Ophthalmologists can be involved with their local ophthalmology society, the American Medical Association (AMA), and the American Academy of Ophthalmology (AAO) to advocate for our patients. Local representatives and senators should be contacted with the approach of collaboration to protect veteran sight. We can work together to promote safe care and protect our patients. I am excited to continue to learn, partner, and advocate – and I hope you are too.

Original eye image from Unsplash.com



Shutting Down *Short-Sightedness*

Experts from across Europe weigh in on the continent's response to increasing rates of myopia

Here, we share the European perspective on myopia, but now we want to hear from you. What's the story in North America? What trends and challenges are emerging? We want to share your views with our global audience in a follow-up article. Get it touch to share your experiences *edit@theophthalmologist.com*.

A 2016 systematic review and meta-analysis of the prevalence of myopia projected that half of the world's population will be myopic by 2050 – a staggering five billion people. It also predicted that one billion would face myopia-related ocular complications and vision loss as a result of high myopia (1). With global organizations, including the International Myopia Institute, reporting that myopia cases worldwide are still rising in accordance with the predictions made eight years ago, the need to take action has never been clearer (2).

Although Europe currently has a lower prevalence of myopia than some of its neighbors (including East Asia and North America at 40 percent), it is no exception to the trend – and the increasing rates are most noticeable in school-aged children (3).

But what is it like to actually observe this increase within the patients you see in your practice? Here, we speak with several eyecare professionals from across Europe to explore current attitudes towards myopia, the limitations of available myopia control measures, and their hopes for the future.

Is myopia a problem in your country? If so, could you share some epidemiological data?

Wolf Alexander Lagrèze – Germany: There is quite a lot of public, scientific, and clinical concern, but I would not term it a "problem." Many ophthalmologists as well as opticians have begun to offer active myopia management over the last few years. It basically all started after the publication of the ATOM2-data in 2012 (4), and the seminal Nature review by Dolgin in 2015 (5). We've seen some competition between pharmacological and optical solutions as well as some potential conflicts of interest – especially when it comes to the latter. We have good quality, national data (from the KIGGS study) that shows that there was not a significant increase in myopia rates over the 11 years from the first baseline study. However, the potential influence of smartphones and other devices are not yet reflected in the data (6). Additionally, the rate of myopic spectacle prescriptions have not changed (7). So, it seems that we are not seeing the often cited "myopia pandemic" in Germany.

Andrzej Grzybowski – Poland: Children in Poland share similar environmental risk factors with other European countries. We have a myopia prevalence between 35–45 percent in teenage and young adult groups, with a tendency to increase. There are a growing number of young myopes who are developing the condition starting between five and six years of age.

Dominique Bremond-Gignac – France: Myopia is definitely a concern in our country as its prevalence has increased to the point that it is now present in between 35–40 percent of our young adult population. The study by Leveziel in a large French population demonstrated the increased frequency of myopia and the need to control it (8, 9, 10).

Paolo Nucci – Italy: Yes, the "myopidemia" is starting to be considered a problem in our country and we, as pediatric ophthalmologists, can be "blamed" for this.

Our frequent presence in both the media and in pediatric congresses all over Italy has contributed to families being more alert about the possible increase in the prevalence of myopic children. As a matter of fact, we face a clear increase of myopia defects in patients under the age of eight in the last five years. In our setting, a university outpatient clinic, in 2014, two out of every 100 myopic patients were under eight years old. In 2022, that figure had risen to nine out of 10 (11, 12)!

This might possibly also be related to the general awareness from ophthalmologists, opticians and pediatricians that low-dose atropine and, more recently, defocus lenses, are effective treatments. Their proactivity is responsible for the increase in referrals.

Carla Lança – Portugal: Myopia is a condition of public health concern in Portugal. A recent systematic review and meta-analysis concluded that the prevalence of refractive error in Portugal is 32 percent (13). Myopia affects between 2–4.5 million Portuguese individuals. Although data on myopia prevalence and myopia progression in Portugal are scarce and heterogeneous, there are some reports that show myopia prevalence to have almost doubled in school children over the last few years. This increasing pattern seems similar to other countries in Europe, although further research is necessary to confirm this trend.

Kathryn Saunders – UK: Myopia is increasing in prevalence in the UK, but not to the same extent as is being seen in East Asian countries. This may be reflective not only of ethnic differences in the susceptibility to myopia, but of the different lifestyle and less intensive early education patterns in the UK compared with many East Asian countries. The Northern Ireland Childhood Errors of Refraction (NICER) study determined prevalence of myopia using robust measures in a population-based study in 2006–2008 as 1.9 percent in six to seven-year-old White children living in the UK, and 16.4 percent in those aged between 12 and 13 years (14). Compared with data published by Sorsby et al. in 1961, using cycloplegic refraction and derived from a population-based, non-clinical cohort, the prevalence of myopia had more than doubled in the intervening 50 years (15) – and this was before the rise of tablets and smartphones!

Olavi Pärssinen – Finland: Myopia is not regarded as a significant problem in Finland. Looking at the historical data, we can see that the prevalence of myopia has increased from World War II. In rural populations, the prevalence of myopia in adults between 41 and 50 years of age, born between 1920–30 was six percent. After the school reform in the 1970s, the length of compulsory education has been between nine and 10 years. Thereafter, the prevalence in the new generation increased to around 25 percent, but has not significantly increased from that since.

According to our data, the prevalence of myopia in first-graders – seven-year olds – is 1–3 percent. With fifth graders (11 and 12 years of age) it is 16 percent. In eighth graders, who are about 15-year-olds, the prevalence is around 20 percent. And in army recruits, aged 18–20-year olds, it is 22–24 percent – without a significant increase over the last two decades.

In the latest study, the prevalence of myopia among ethnically non-Finnish army recruits was about 10 percent higher. The Register of Finnish Visually Impairment cites myopia as being the cause of visual impairment in 1.7 percent of the 17,664 cases in the register in 2021 (16).

Are other doctors or parents aware of myopia – and what educational resources are available?

Wolf Alexander Lagrèze: Our ophthalmologic societies in Germany – DOG, BVA and GSNK – regularly publish and update national guidelines. Optical societies also do this, although sometimes whilst also subtly discrediting atropine. Unfortunately, schools are not currently involved, and health politics does not yet seem to be paying sufficient attention to the issue. However, almost all national newspapers regularly report on myopia.

Andrzej Grzybowski: The awareness of the problem among general ophthalmologists, other physicians, and parents in Poland is low. The highest profile educational campaigns are organized by the Foundation for Ophthalmology Development in collaboration with other relevant groups – this includes schools and teachers, as they play an important role in the prevention of myopia (17). There are some high-quality materials available at a specialized website that has been co-sponsored by the Polish Ministry of Science and Education. Even with this, there are sadly no national education projects organized by governmental agencies yet.

Dominique Bremond-Gignac: The Myopia National Campaign was developed in 2022 to advise the French population of myopia risks in children. There were TV and radio broadcasts as well as other media efforts that all aimed to relay this information to parents. This private initiative was supported with the financial support of pharmaceutical companies. It will be renewed in 2023. Additionally, paper flyers were distributed and epidemiology and myopia control solutions were presented in numerous meetings for ophthalmologists, opticians and pediatricians. The French Society of Ophthalmology (SFO) is also supportive, as well as eyeglass manufacturers.

Paolo Nucci: The Italian Society of Pediatric Ophthalmology & Strabismus, together with the World Society of Pediatric Ophthalmology and Strabismus, publishes guidelines and informative statements as well as organizing round tables dedicated to the issue of myopia. In the last three years, Hoya and Luxottica-Essilor started a promotional campaign in Italy, and Mostra Internazionale di Ottica (MIDO) implemented media presence with respect to optical treatment. Our Ministry of Health is not involved in any preventive campaign.

The epidemic of myopia has been featured on TV. It has been mentioned on several occasions in the press and at different congresses and meetings for both ophthalmologists and opticians. It is also mentioned in various sponsored meetings arranged by different companies marketing contact lenses. However, there is no national program for myopia prevention.

"Myopia is definitely a concern in our country…it is now present in between 35–40 percent of our young adults."

Carla Lança: The media are aware of the growing problem, and interviews are often published in magazines and newspapers for the general public. The Portuguese Society of Ophthalmology is raising awareness of myopia and its prevention among both parents and the general public. Some Portuguese ophthalmologists also publish information on myopia across social media. There is also a media campaign targeted towards children, with suitable materials explaining myopia and risks factors, and offering lifestyle advice to prevent myopia development. Alongside this, different lens manufacturers have started promotional campaigns on the use of optical treatments.

In Portugal, visual screening of children aged 2–4 targets amblyopia and includes a refractive assessment performed at the primary care level. However, some local and regional screening initiatives that target myopia occur with the support of municipalities, lens manufacturers, and optical shops.

Myopia Control: *A Dynamic Field*

Discussion prepared in collaboration with The European Network for Myopia Prevention and Control

By Andrzej Grzybowski, Poland

Epidemiological studies show an increasing rate of myopia in European populations (1). Although genetic factors play a role in myopia pathogenesis, the recent increase in myopia prevalence worldwide has been attributed to environmental factors, including increasing intensity and duration of education, and global trends related to increased screen time for young children, especially from close distance, especially closer than 30 cm. Indeed, the main risk factors for myopia in children include more near work or near distance activities at a young age – as well as spending less time outdoors and having myopic parents. The major concern related to myopia is that up to 10 percent of children will develop high myopia, a serious risk factor for vision loss related with myopia, macular degeneration, and some serious eye disorders, including retinal detachment, glaucoma, and cataract.

An individual's risk of developing myopic maculopathy, retinal detachment, posterior subcapsular cataract and open-angle glaucoma all increase – by 58 percent, 30 percent, 21 percent and 20 percent respectively – with each additional diopter of myopia. Additionally, children with myopia are also at higher risk of developing depression compared with normally sighted children. Thus, increasing awareness of myopia prevention and controlling myopia progression strategies are becoming more important focuses in our routine ophthalmology practice across Europe. Fortunately, with increasing knowledge about myopia pathophysiology and risk factors, we have more approaches available to control myopia progression. In fact, every year studies presenting new approaches on myopia control are published, giving us an increasing number of options. On the other hand, because of this "dynamic situation," the majority of review articles on this topic published over two years ago are outdated, so staying up to date is becoming more and more difficult.

To that end, we decided to conduct a few analyses, which were recently published (2, 3, 4). The evidence from recent randomized control trials (RCTs) led us to some interesting findings:

- Highly aspheric lenslets (HAL), MiSight contact lenses, low dose atropine 0.05 percent, Biofinity +2.50 D lenses, Defocus Incorporated Multiple Segments (DIMS) eye-glasses, and orthokeratology lenses were all effective in the control of myopia progression.
- Low dose atropine 0.025 percent and extended depth of focus contact lenses have also been found to be effective, but with lower effect sizes.
- Low-dose atropine 0.01 percent was not as effective in reducing axial length progression, according to some studies conducted in Asia.

The recent data on new eye-glasses, including DIMS and HAL, are cause for optimism given their considerable efficacy (5). However, these results need to be confirmed; current knowledge is limited in the length of study periods and number of populations studied. We also analyzed the efficacy and side effects of 0.01 and 0.5 percent atropine eye drops based on the studies conducted in non-Asian countries; we found that 0.01 percent atropine eye drops are effective in non-Asian children, achieving less side effects compared with 0.5 percent atropine eye drops.

Interestingly, the Cochrane systematic review and network meta-analysis was just published (5). The authors highlighted that the effects at one year provided evidence that interventions may slow refractive change and reduce axial elongation, although results were often heterogeneous. Moreover, they noted that much less is known about the effects at two or three years, and it is uncertain if effects are sustained.

See full version and references online:

Kathryn Saunders: There are no educational campaigns directed towards preventing myopia in the UK at present. There is increasing awareness among optometrists and parents, but there is a lot more work to do – particularly with parents and the wider public – to address the issue of why preventing myopia and slowing its progression is important. The College of Optometrists has an award-winning public information website called "Look After Your Eyes" which has some pages dedicated to children's eye health and also to myopia management (18).

What control and management strategies are being used in your country?

Wolf Alexander Lagrèze: There are guidelines on daylight exposure and reading distance. In terms of treatment options, we use atropine 0.01 percent for at least two years for those progressing more than 0.5 D per year. Multi-segment spectacles and contacts are also in use for more refractive solutions. Fast progressors are also offered combined therapy using both atropine and optics. However, there are some problems with atropine that eye care professionals in Germany have to negotiate – the first of which is that its use is off label and only certain pharmacies produce or have it in stock. Additionally, health insurance tends not to reimburse the costs, leaving the burden with the patient (or more likely their parents). From the refractive side of things, there are a few problems with multi-segment spectacles and contact lenses, including the high costs to parents – and the fact that there are no producer-independent clinical trials to give us the reliable data we need!

"One problem is that we still do not have formal screening programs for myopia, meaning that some children commence therapy far too late."

One problem is that we still do not have formal screening programs for myopia (nor a really good one for amblyopia) – and that means that some children commence therapy far too late.

Andrzej Grzybowski: The first and most common therapy adopted for myopia control was atropine 0.01 percent; however, there has recently been a switch to the use of 0.05 percent atropine. Low-dose atropine is used as an off-label therapy prescribed only by physicians. It is reimbursed, meaning that the cost for the patients is relatively low. Contact lenses, including orthokeratology (ortho-k), are relatively uncommon in Poland, although they can be delivered both by ophthalmologists and optometrists. Recently introduced spectacles are becoming increasingly popular, and are delivered both by ophthalmologists and optometrists. One of the problems with optical therapies is that optometrists in Poland are not allowed to use cycloplegic drops, and so cannot measure objective refraction after cycloplegia. In those cases, children are managed either by pediatric ophthalmologists or by joint ophthalmology-optometry clinics.

Dominique Bremond-Gignac: The primary myopia control method in France is defocus glasses because the cost is generally acceptable, being approximately €100 higher than regular glasses, and is clearly easy to adapt. The second method of controlling myopia comes through the use of low dose atropine because it is fully reimbursed. Defocus contact lenses and ortho-k are less common – both because of the cost and the difficulty of adaptation.

To improve the problem, we need to improve screening for the early detection of myopia in children, for those between the ages of three and four, usually by orthoptists, and then again at six-years-old, when they're at school. The environmental risk factors of myopia are not well known or followed by parents, so this must also change. Finally, the fact that myopia control solutions have a cost (except low-dose atropine) may also affect parent perceptions. In young adults, refractive surgery is proposed without comprehension of myopia-related disease.

Paolo Nucci: In Italy, outdoor activity is mainly promoted by pediatric ophthalmologists, pediatricians, and, in some parts of the country, by school teachers. My personal approach is prescribing atropine 0.01 in the treatment of myopia, as soon as it starts. Very recently I have also done so in children younger than six without what I call, "protective" hyperopia in familiar myopia, and do so with or without a glasses prescription, according to the child's needs. Later on, we use a combined optical and pharmacological treatment, while after puberty we switch to defocus lenses until they are age 16–18. At this time, youngsters generally prefer contact lenses, so we try to allow for the possibility of defocus contact lenses.

MEET THE CONTRIBUTORS:

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Andrzej Grzybowski is Head of the Institute for Research in Ophthalmology, Foundation for Ophthalmology Development, Poznan, Poland.

Paolo Nucci is Professor of Ophthalmology at the University of Milan and Chairman of the University Eye Clinic at the San Giuseppe Hospital in Italy.

Kathryn Saunders is Professor of Optometry and Visual Science at Ulster University in Northern Ireland.

Wolf Alexander Lagrèze is the Head of Section for Neuro Ophthalmology and Pediatric Ophthalmology at the University of Freiburg, Germany.

The main problems are related to the fact that atropine is a galenic preparation – and sometimes the preparation is not adequate (19). We can't forget that the cost is also highly relevant, being more than €30 per bottle, and any prescription cannot be used more than once. Additionally, compliance must be checked often. Defocus lenses are expensive and the frequent adjustments hinder adherence.

Carla Lança: Various treatments are used in Portugal, including low-dose atropine, novel myopia control contact lenses and glasses, and ortho-k. However, there are some eye care professionals that still offer single vision glasses. Ortho-k is offered by some optometrists. Some eye care professionals also recommend that children increase their outdoor activities and advocate for changes in lifestyle, such as the reduction of non-educational near work and screen time. Although there are several options available for myopia control, there are still some challenges. An example of this is the fact that parents with children on low-dose atropine, prescribed off-label, need to go to the pharmacy very often. Additionally, novel myopia control treatments may be difficult to implement in low socio-economic settings due to their high costs.

Kathryn Saunders: The optical methods of myopia control available in the UK to optometrists and ophthalmologists include ortho-k, multifocal soft contact lenses, and peripheral defocus spectacle lenses. These are the "treatments" that are licensed for myopia control. Primary care optometrists have good access to all these options and are taking them up and offering them to patients. The major challenge is the cost – they are not covered by the National Health Service's (NHS) voucher, which covers the cost of basic spectacle lens and frame for children under 16 years of age. This obviously limits access for some patients and may be a psychological hurdle for parents not used to paying for their children's spectacles nor understanding the long-term value of myopia control.

Atropine is not licensed for myopia control in the UK – at least, not yet! However, I am aware that it is being used off-label via compounding pharmacies by ophthalmology colleagues. The challenge with that option is the difficulty in knowing what dose is being applied. Low dose atropine comes out of solution readily and therefore the dosage applied is likely variable, making the efficacy pretty much unknowable.

There is also the relatively new option of low level red light therapy. The device from SunRising, which comes from Mingguang He, has MHRA approval – but there is no published data regarding efficacy for myopia control for non-Chinese children (that I'm aware of). However, this home-based intervention, which takes three minutes, twice daily, could be a low-cost option used alone or in combination with other interventions.

Olavi Pärssinen: Children's vision screening in Finland is conducted by nurses regularly throughout a child's life. Generally, screenings will occur around the ages of five, seven, 11, 15 and 17 years old. In addition, if the child has any problems with their vision or if vision in either eye is less than 0.8 on the Snellen scale, they are sent to an ophthalmologist or optician free of charge.

"The environmental risk factors of myopia are not well known or followed by parents, so this must also change."

Atropine drops are not available in Finland, so the primary recommended treatment is the use of full corrected spectacles. Some older school children wear contact lenses. The greatest problem with contact lenses has been corneal infections. During one summer month, more than 50 corneal infections were treated in the Ophthalmic Department of Helsinki University hospital. The infections were predominantly associated with the use of contact lenses. Refractive surgery in young adults is quite common, but the comprehensive data is missing. The opticians market different contact lenses as "correcting peripheral hyperopic defocus," but again comprehensive data is lacking. Generally, Finnish ophthalmologists have a skeptical attitude to these lenses due to somewhat questionable scientific evidence.

Let us take one example about the topic of contact lenses meant to correct peripheral hyperopic defocus: MiSight. The first follow-up results in the prevention of myopia with MiSight lenses were published about five years ago (20). The results were summarized and found that two year treatment with MiSight Contact Lenses produced almost 40 percent lower myopia progression. The difference in myopic progression in that two-year follow-up study was -0.45 D compared with the -0.74 D difference in the single vision group, a difference of 0.145D per year. MiSight children were about one year older, when myopic progression is generally slower. Every practicing ophthalmologist understands the clinical significance of this.

But what if the results could be summarized so the two-year use of MiSight contacts led to 4.82 percent higher myopia?

The authors recently published a reanalysis of the same material (21) and found that, of a total of 41 Caucasian patients treated with MiSight contact lenses, 21 and 16 were considered responders in the first and the second year of follow-up, respectively. They also observed that time spent outdoors was a main factor in controlling axial eye growth in children treated with MiSight contact lenses. Other studies on the efficacy of MiSight are by no means conclusive due to high dropout rates or other flaws in methodologies, and all this for a solution that can cost around 1,000 euros a year!

"Generally, Finnish ophthalmologists have a skeptical attitude to these lenses due to somewhat questionable scientific evidence."

As far as I know, only one optometrist in Finland is fitting ortho-k lenses, and she has around 100 patients, most of them migrants. However, the changes in visual function and corneal shape are reversed after discontinuation of ortho-k lens wear. There is not much data about the changes of axial length and choroidal thickness after discontinuation of the ortho-k treatment. Ortho-k lenses used at night compress and flatten the cornea. Additionally, each contact lens used during the night disturbs corneal metabolism – one symptom of which is night timethickening of the cornea.

If used for years at a time, pathological changes can be seen, including polymegathism and loss of endothelial cells. Physiologically, daily use of contact lenses would be safer. I'm looking forward to seeing randomized controlled clinical trials to show that use of ortho-k lenses would prevent some of the myopia related ophthalmic complications. Without that, it is difficult for me to find a medical justification for this treatment.

Other potential complications of ortho-k include microbial keratitis, pigmented ring formation, and altered corneal nerve pattern through the development of fibrillary lines. The estimated risk of microbial keratitis in children wearing ortho-k lenses is 13.9/10,000 patient-years, as opposed to 7.7/10,000 in all ortho-k wearers. This contrasts with the risk in daily-wear corneal gas-permeable lens wearers, 1.2/10,000, and is fairly similar to the risk in extended-wear soft contact lens wear.

There is insufficient evidence of different contact lens treatments, whether incremental benefits are found over the years and whether the effects are sustained.

What are the limitations in our current knowledge?

Andrzej Grzybowski: One of the major problems is the lack of clear predictors of future progression. We are aware of several risk factors, but it is still hard to decide how early to start the therapy and how aggressive it should be. Another interesting issue is how long to prolong the therapy. We have an increasing number of young adults with myopia progression who inquire about the possible therapy options. All evidence-based data on myopia control is based on populations between six and 18 years old, and, because of this, we unfortunately do not know much about the effectiveness and safety of available methods in this older age group.

There could be a role for new treatment methods, like red-light therapy, that appears to be very effective in clinical trials, but we need more real-life data on both compliance and safety.

Dominique Bremond-Gignac: We have not yet clarified all of the mechanisms involved in eyeball growth and myopia, so treatment is limited to what we know of hyperopic defocus in the retina midperiphery. Low-dose atropine presents a very complex mechanism on sclera and muscarinic receptors. Additionally, prevention and screening are insufficient and the cost of our system may mean that it's actually a self-limiting system.

Paolo Nucci: I believe that, at this time, the main limitations of our knowledge are the result of a number of issues. Firstly, an overly fideistic attitude toward myopia management; the health community that are involved can all too often behave like soccer fans. Ophthalmologists favor pharmacological solutions, while opticians tend toward optical treatment. Myopia therapy works, but inconsistently, and this allows detractors to use this point to discredit both approaches. Secondly, there are problems in the research, with some key debates and controversial literature revolving around questions like atropine concentration or Defocus Incorporated Multiple Segments (DIMS) versus Highly Aspherical Lenslet Target (HALT) technology (22). Finally, the mechanism of action of myopia is not fully understood and there is still more to be done around understanding ortho-k.

Olavi Pärssinen: We need to find the right relationship between near work and avoiding it and, of course, outdoor activities, especially in young children.

Kathryn Saunders: There are lots and lots of limitations to our current knowledge! Myopia researchers are not going to run out of work anytime soon!

I'm particularly interested in finding the best ways to identify pre-myopes so that we can do some pre-myopia onset "mitigation" and hold off the onset for as long as possible. This could be through encouraging lifestyle interventions and applying pre-myopia interventions, such as low dose atropine – there is some emerging evidence for this being effective at slowing onset of myopia. Mitigation is likely to be equally, if not more effective, than intervening with myopia control once myopia is established as the younger the eye the faster axial elongation progresses.

We have developed an evidence-based risk stratification method for grading the risk of a non-myopic child becoming myopic and will be presenting data on the validation of this tool at ARVO 2023 (23). Other practitioners and I have found it useful to start those conversations with parents about lifestyle modifications that they can encourage and also, if the risk indicator shows they are at high or moderately high risk for future myopia, to initiate conversations about future myopia control options for when that child becomes myopic.

I also want to know more about why some children respond to some interventions better than others, and how we can best identify the right treatment for the right child at the right time. More information regarding the efficacy of combined treatments would be very helpful to the clinician, but these trials are expensive.

Carla Lança: There are several limitations to our knowledge on myopia, as the underlying causal mechanisms are still not fully understood. Most importantly, scientific evidence, on the effect of treating myopia progression and the prevention of pathological myopia, is lacking. Prevention of pathological myopia is an important goal that avoids potential conditions that lead to visual impairment.

What will – or should – the future look like?

Wolf Alexander Lagrèze: Public education is extremely important and so are screening programs – not just for children but also for high myopes beyond 40 years of age. We need greater refinement in terms of atropine concentration depending on iris pigmentation and ethnicity. It would also be good to see a switch from refraction to eye length-based myopia control, along with more and better controlled clinical trials. Finally, I think if we are to see advancements in treatment, there must be a sustained and critical look at what might be termed pseudo-innovative technologies, such as light therapy of certain wavelengths.

Dominique Bremond-Gignac: I think the combination of two systems, such as defocus glasses or contact lenses and low-dose atropine, will be useful. Uncovering new physiopathology mechanisms may open a new era for other myopia control systems.

Paolo Nucci: Perhaps my biggest wish is for myopia to actually be recognized as a problem. If this happens, it should lead to a better understanding of the mechanisms behind the available therapies and, I would hope, avoiding litigious fights around atropine treatment dosage or defocus technologies. We also need a clear and reliable protocol for follow up. Ultimately, we need an increase in the number of pediatric ophthalmologists, and we should offer orthoptists a greater role in refraction.

"Prevention and screening are insufficient and the cost of our system may mean it's actually self-limiting."

Carla Lança: Several therapeutics are in development, such as light-based therapies. Nevertheless, it would be relevant to start early interventions before school age and probably before the pre-myopia state to either avoid myopia altogether or delay its onset. This may involve continued research on lifestyle interventions and a better control of environmental risk factors. Additionally, it may also involve collaboration between eye care professionals, public health professionals, and educational institutions.

Kathryn Saunders: I am not involved in the development of any new therapies myself, but combinations of the currently available therapies are likely to be useful and more application of early interventions, ideally before onset, on top of the lifestyle changes have promise. Over the next 10 years, I'd like to see if there is potential for NHS funding for myopia management in primary care settings so that access is more equitable and care is provided in the community by the largest eye care workforce who are best

placed to identify and manage the vast majority of myopia.

Obviously, the small subset of children who are not "regular" myopes (some clinicians use the rule of thumb that if the number of diopters meets or exceeds the number of candles on the child's birthday cake then they aren't regular) may require ophthalmological input in a secondary care setting.

"It is an urgent task to find the most appropriate concentration and dosage of atropine."

Olavi Pärssinen: It is an urgent task to find the most appropriate concentration and dosage of atropine, as well as clear and reliable guidance on when and to whom it should be recommended.

Andrzej Grzybowski: I believe that artificial intelligence (AI) algorithms can help develop non-invasive diagnostics of myopia; for example, based on fundus pictures, that would not need cycloplegia and enable us to conduct massive screening projects. Cycloplegic refraction is presently a major limitation for both high-volume screening projects and including optometrists in children's myopia diagnosis in some countries. Moreover, AI can help prepare risk prediction models for both myopia onset and progression. The European Network for Myopia Prevention and Control that I coordinate works on both projects and we welcome experts who are interested in joining us.

I look forward to future therapies that can be more effective than what is currently available. In the meantime, however, I await clinical studies that show how combination of new modes of control can increase therapeutic efficacy.

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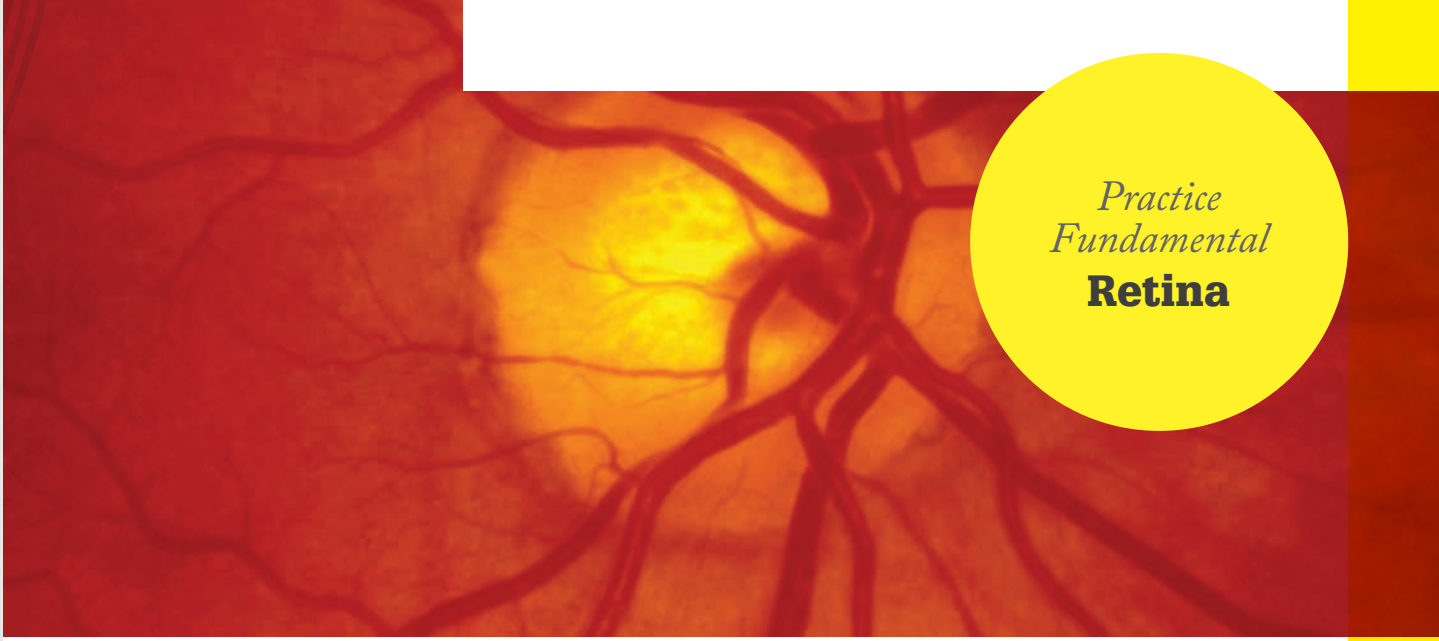

Can't hide from the artificial eye. After conducting a diagnostic study from 4095 retinal fundus images, researchers found that AI was still able to learn patterns associated with self-reported race, indicating that AI models don't necessarily remove the potential of racial bias (1).

At risk of ROP. A database cohort study used the Healthcare Cost and Utilization Project Kids' Inpatient Databases and collated the data of 125,000 ROP discharges from over 23 million births. The researchers discovered an 86 percent increase in ROP incidence found in at-risk populations (2).

Silicone oil tamponade removal. To compare the efficacy of two surgical techniques used for removing silicone oil tamponade post-vitrectomy– triple air-fluid exchange and balanced salt solution lavage - researchers used X-ray photoemission spectroscopy to measure silicone content of fluid samples taken during both procedure, concluding neither technique worked as a well-mixed box dilution (3).

Imitating the eye. Scientists from Penn state have developed a sensor array that mimics the light-sensitive photoreceptor cells. The device connects to a neuromorphic algorithm that produces high-fidelity images once the imputed information is processed. The work could spur developments in artificial retina biotechnology, as well as offer a step towards battery-free camera technology (4).

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IN OTHER NEWS

New drug for ROP. *Scientists have discovered that K-604, a potential drug candidate for Alzheimer's and cancer, might also limit pathological retinal neovascularization during retinopathy of prematurity (5).*

New cell and gene therapies. *Researchers at Cedars-Sinai Medical Center are using engineered stem cells to treat retinitis pigmentosa, marking an important milestone in providing personalized therapy treatments (6).*

Spider sense. *New research has determined that bold jumping spiders lose photoreceptors in the high-density region of their retina when they are underfed or starving; the findings potentially offer more insight into understanding the pathophysiology and mechanism of AMD in humans (7).*

Second sight. *Scientists from Singapore and Sweden have successfully produced progenitor photoreceptor cells and transplanted them into experimental models of damaged retinas (8).*

Off-Label, On Point

Why I support the off-label use of semaglutide for many indications – including weight loss

In a recent newsletter, we discussed the increased off-label use of semaglutide for weight loss and asked whether ophthalmologists should be wary of this, given studies that demonstrated an increase in diabetic retinopathy associated with semaglutide use, we hear from Blake Cooper – co-author on one of those studies, but also someone who has intimately witnessed the benefits of off-label Ozempic use.

As a retina physician who has been practicing for the past two decades – and the father of a child who has had diabetes for the past decade, I wanted to share my perspective and strong support of the off-label use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) for many indications, including weight loss. Moreover, I view the recent concerns regarding the worsening of retinopathy as an opportunity for eye care professionals to educate themselves on – and improve – the ocular, systemic, and mental health of their patients.

A little perspective

Approximately one in five of all prescriptions written in the US are for an off-label indication (1). For example, in ophthalmology this flexibility in prescribing FDA-approved medications has allowed the use of bevacizumab in patients with several ocular diseases, including the treatment of advanced stages of diabetes-related retinopathy (DR). The decision to prescribe off-label medications is done in the patient's best interest. It is grounded on sound clinically-based evidence and based on experience of treating conditions where medications have not yet been formally tested.

GLP-1 RA is a modified form of the potent incretin hormone GLP-1, which is secreted by intestinal L-cells of the distal ileum during a meal. This naturally occurring hormone acts to enhance insulin and decrease glucagon production, slow gastric emptying, and act within the brain to increase satiety. GLP-1 RAs have not only emerged as powerful medications for type II diabetes mellitus (T2D) management and weight reduction, but have also been shown to provide strong cardiovascular and renal risk reduction.

When considering the recent use for weight loss of this class of medications, I believe it is important to remember that, despite medical professionals' best efforts, rates of obesity and obesity-related chronic diseases continue to rise. Roughly one in three adults in the US is obese (2), a condition which increases early mortality and other comorbidities. The estimated annual medical cost of obesity in the US was nearly $173 billion in 2019 – and the medical costs for adults with obesity were $1,861 higher than medical costs for people of a healthy weight (3).

Weight and mental health

The practice of medicine is not only shaped by clinical trials, but also by our clinical experiences – both good and bad. Shortly after my daughter was diagnosed with type I diabetes mellitus (T1D) at 12, one of my dearest patients passed away from complications of heart failure. She was only 34 and had struggled with T1D since she was 14. Her battle had been with diabulimia. Eating disorders are more common in individuals with T1D than in the general population – likely related to the complex and constant requirements of diabetes management and the impact of living with a chronic medical condition on psychosocial functioning (4). In many ways, I failed my patient by focusing on her recurrent vitreous hemorrhages and traction retinal detachments that required multiple surgeries and periodic intravitreal injections to maintain reading and driving vision. I never once questioned why she was barely

100 pounds and always had double-digit A1Cs. Awareness of potential eating disorders and a lower threshold for referral to mental health professionals could be life-saving in a condition such as diabetes, where outcomes are so dependent on behavioral adherence.

Currently, the primary treatment for those with T1D combats insulin deficiency but neglects disease progression, alpha cell dysfunction, and cardiovascular and renal health. GLP-1 RAs have a unique mechanism of action in T1D, addressing alpha cell dysfunction and thereby suppressing inappropriate glucagon secretion. To this end, adding GLP-1 RAs to the treatment of diabetes, when indicated, can improve adherence with glycemic management by providing a reduction in the need for insulin, a strong cardiovascular and renal risk reduction, and help maintaining a healthy weight.

Ophthalmic opportunity and unmet needs

Despite clear evidence that near-normalization of blood glucose levels reduces the long-term risk of diabetic retinopathy, early worsening of DR is a well-described phenomenon evident in patients with T1D and T2D, in those who have undergone bariatric surgery, and in pregnant women (5). Worsening of retinopathy does not appear to be agent-specific as it has been described in patients receiving diverse treatments, including intensive insulin therapy, sulfonylureas, thiazolidinediones, and now GLP-1 RAs. Though the mechanism leading to early worsening remains unclear, most evidence suggests an association with rapid improvement of hyperglycemia and the severity of pre-existing diabetes-related retinopathy at baseline. Even with the potential for initial progression of retinopathy, intensive glycemic treatment reduces the risk for the onset and progression of DR over time, compared with conventional treatment.

Given that nearly one-third of patients with diabetes are unaware of their diabetes, and 10 percent have already developed DR (6), the eye care community is failing those with diabetes and needs to stress the importance of annual eye screenings. Early detection of diabetes and DR allows for the treatment of retinopathy when indicated. Anti-VEGF pharmacotherapy has become a first-line treatment for center-involved diabetic macular edema and proliferative diabetic retinopathy. What is potentially overlooked is that anti-VEGF medications can be used proactively to prevent vision-threatening complications of DR and can lead to a two-step disease regression on the Diabetic Retinopathy Severity Scale. Treatment of severe nonproliferative DR (NPDR) with intravitreal aflibercept injections in the PANORAMA clinical trial reduced the severity of retinopathy and showed an impressive 70–80 percent reduction in the rates of vision-threatening complications.

According to the American Diabetes Association guidelines, patients who have been newly diagnosed with T2D should have a comprehensive eye exam at the time of diagnosis (7). After the initial exam, subsequent eye exams should be conducted annually. As with any potent glucose-lowering agent, clinicians should consider retinopathy status at the time of treatment initiation and follow guidelines for monitoring patients with established retinopathy. In patients who have recently been initiated on a GLP-1 RA, especially those with a prior history of retinopathy, close monitoring for signs of new or worsening retinopathy should occur. Though DR has been identified as a potential adverse effect of GLP-1 RAs, there remains a positive benefit–risk profile when used accordingly with the FDA-approved prescribing information. Moreover, DR, when detected early, is treatable with anti-VEGF agents.

"The decision to prescribe off-label medications is done in the patient's best interest. It is grounded on sound clinically-based evidence."

Real-world experiences and ongoing trials

GLP-1 RA cardiovascular outcome trials (CVOTs) provide long-term follow-up, allowing examination of retinopathy outcomes. It is also important to remember that none of the included CVOTs were designed or powered to assess retinopathy outcomes – nor were definitions of retinopathy in most of these trials standardized for these analyses. The ongoing FOCUS trial seeks to further investigate the long-term effects of semaglutide on DR in patients with T2D (8). This clinical trial will use validated and standard ophthalmic assessments to measure the presence of early treatment diabetic retinopathy level progression in 1500 patients with an A1C of 7–10 percent. The time frame of the trial will be five years and it is estimated to be completed in early 2027.

Until then, we can continue to use real-world data and experiences to guide our practice patterns.

See full version and references online: top.txp.to/off/label/on/point

Weighing the Cost

When we compare Ozempic's rates of diabetic retinopathy and adverse ocular events with other GLP-1 agonists, should we be concerned?

In this second article exploring Ozempic and its ocular effects, we speak to Albert Li, medical and surgical retina specialist and Clinical Assistant Professor of Ophthalmology at Zucker School of Medicine at Hofstra/Northwell. Li co-authored an abstract that was presented at the 2020 ARVO Annual Meeting that presented data from an analysis of events recorded in the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). The data showed that the use of Ozempic is associated with higher rates of diabetic retinopathy and adverse ocular events compared with other glucagon-like peptide 1 (GLP-1) receptor agonists, such as Tanzeum, Trulicity, and Victoza.

With the recent increase in the use of Ozempic, especially its off-label use for weight loss, should ophthalmologists be wary – or is there more to take into account?

What makes Ozempic a more threatening GLP-1 receptor agonist in terms of diabetic retinopathy and ocular effects?

Semaglutide received this reputation from the "Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes" (SUSTAIN-6) trial (1). In the trial, a secondary analysis by the investigators showed a statistically significant association of semaglutide use with worsening of diabetic retinopathy. Keep in mind that this apparent worsening of diabetic retinopathy is in the setting of rapid reduction in HbA1c achieved

Albert Li

with semaglutide use. This echoes a similar finding from an earlier trial, the "Diabetes Control and Complications Trial (DCCT)," which showed that strict glycemic control – with the use of insulin – and subsequent lowering of A1c in patients with type I diabetes mellitus resulted in early worsening of diabetic retinopathy.

Those studies showed that this effect was transient, with few patients having progression of retinopathy to the point that it required ophthalmic intervention. The lessons that we learned from DCCT are applicable to what we are seeing with semaglutide; we need to observe patients closely for worsening retinopathy as they achieve tighter glycemic control in the rare chance they develop complications requiring treatment, such as diabetic macular edema or progression to proliferative diabetic retinopathy. That being said, the multitude of benefits from achieving tighter glycemic control and lower A1c, such as decreased risks for heart disease and stroke, among others, should not deter physicians from prescribing semaglutide or other GLP-1 agonists. Judging by the number of my patients with uncontrolled diabetes who have been prescribed GLP-1 agonists, this appears to be the case.

What are the ocular effects that off-label use of Ozempic can have on individuals using the drug as a weight loss solution?

Semaglutide and GLP-1 agonists have been studied primarily in the context of diabetes. As obesity and diabetes are both found in metabolic syndrome, I would imagine that patients with both diabetes and obesity would be at risk for the early worsening of diabetic retinopathy that was noted in the clinical trials. As for patients without diabetes? Well, the ocular effects of Ozempic use remain unclear.

Do you think this is an issue to which ophthalmologists should be paying more attention?

Ophthalmologists certainly should be aware of this finding of worsening diabetic retinopathy with semaglutide in the diabetes literature. I have had a number of patients who were aware of this adverse effect and asked me about it. Given the findings from the clinical trials on semaglutide, I observe patients more closely to monitor for this early worsening of diabetic retinopathy. At the same time, I advise patients that we have excellent treatments for the ocular complications of diabetes, including anti-VEGF intravitreal injections and laser. Additionally, I feel it's important to state that the benefits of improved glycemic control in the long term outweigh the potential for worsening of diabetic retinopathy in the short term. Based on my experience and the findings from the DCCT, I have seen and anticipate very few patients who experience this "early worsening of retinopathy" progress to the point where they need treatments for the worsening disease.

What can ophthalmologists do to tackle the ophthalmic consequences of Ozempic use – and other medications – whether on or off label?

It's simple really: Close monitoring.

We have had a history of on-label use of medical treatments with unforeseen ocular side effects, let alone off-label use. Hydroxychloroquine, tamoxifen, vigabatrin, and more recently, pentosan polysulfate sodium, immediately come to mind as systemic medications with ocular effects. Many of these are late effects and were difficult to ascertain at the time of the initial clinical trials. At the level of the patient, it underscores our responsibility as physicians to elicit a comprehensive medical history and medication history. More broadly, perhaps ophthalmic examinations should be included as part of baseline testing in clinical trials, in addition to an assessment of the typical systems in a comprehensive physical alongside the heart, lungs, and so on.

"The lessons that we learned from DCCT are applicable to what we are seeing with semaglutide; we need to observe patients closely for worsening retinopathy as they achieve tighter glycemic control in the rare chance they develop complications requiring treatment."

As an aside, I wonder if the lack of including a comprehensive dilated eye examination in a "comprehensive" physical is related to minimal exposure to ophthalmology in the medical school curriculum of future doctors who design these trials for various therapeutics. Just like any other organ, the eyes are easy to ignore until they do not function properly.

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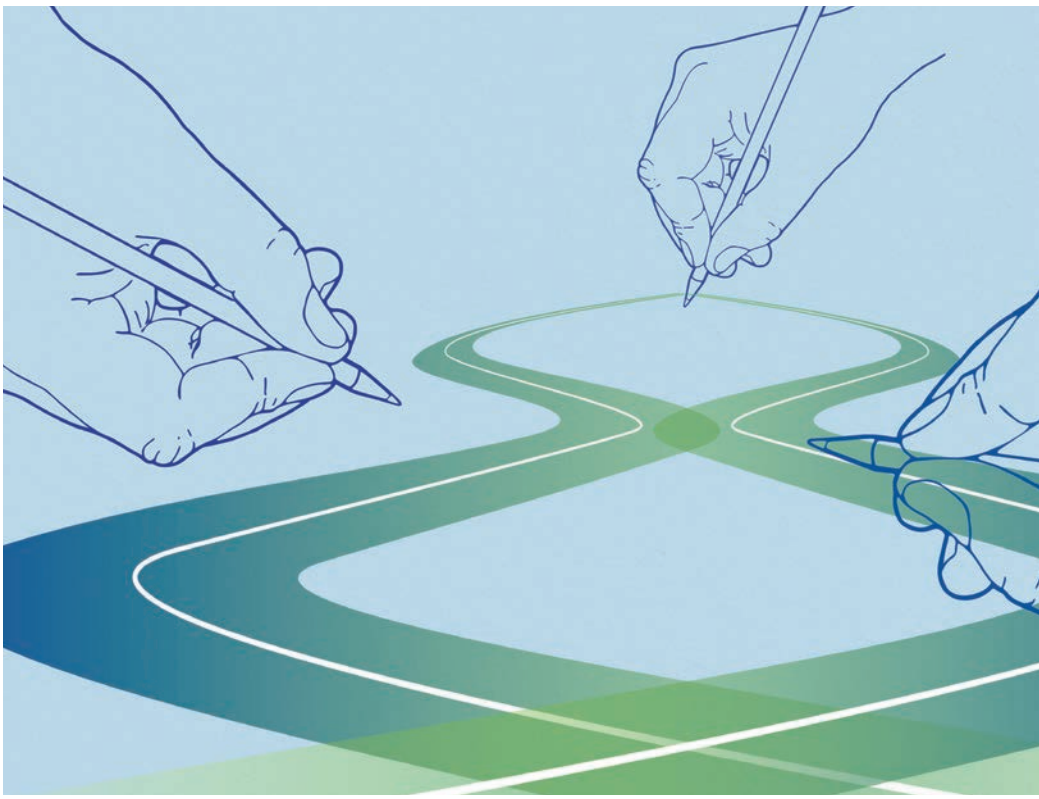
When One Becomes Two

A second hallmark lesion of AMD may spark future treatment options



Age-related macular degeneration (AMD) has long been studied and delineated on a straight-forward path of development; when soft drusen appear in the later decades of life and are not curbed by preventative measure, the macula deteriorates to intermediate and advanced disease. Because AMD is studied as a singular disease, correlations between AMD and other systemic diseases commonly associated with the aging population have been tenuous at best. Our new research suggests that perhaps this is where we are going wrong with AMD research – rather than studying it as one disease, we should be studying it as two.

Theodore Smith – Director of Biomolecular Retinal Imaging at the New York Eye and Ear Infirmary of Mount Sinai and a professor of ophthalmology and neuroscience at the Icahn School of Medicine at Mount Sinai – has been interested in the pathophysiology of AMD for over a decade. As a research associate in Smith's team, I am proud to report on our findings and ongoing research.

Our recently published paper underlines a fork in the path of AMD development, describing two distinct pathways that lead to the progression of geographic atrophy (GA) (1). These two suggested routes of pathogenesis revolve around the differentiation of hallmark lesions: classical drusen and the less understood, subretinal drusenoid deposits (SDDs).

Evidence for the development of the two disease pathways in the formation and progression of intermediate AMD (iAMD) extends beyond our recent publication; we have previously reported a strong connection of SDDs, and not drusen, to varying serum and genetic risk factors, supporting the two-disease hypothesis (2). Histological evidence also links soft drusen spatially with the cone photoreceptors and SDDs with the rod photoreceptors peripherally, while further differences in laser treatment response corroborates this as well (3, 4).

Canaries in the coal mine

Perhaps the most unique aspect of differentiation is not within the retina at all, but instead its vasculature. We have previously revealed a strong connection of SDDs, and not drusen, to cardiovascular disease and stroke, consistent with a vascular component of the unique mechanism of pathogenesis (2). Backtracking the arterial blood supply associated with drusen and SDDs leads to the unique correlation of SDDs, choroidal thinning, and choriocapillaris insufficiency (5, 6). Therefore, we can see that a local or systemic cause that reduces the supply of nutrients to the area of drusen and SDD formation leads primarily to SDD formation and not drusen.

Smith has hypothesized a straightforward vascular mechanism for the association. He says, "We have strong evidence for what actually happens: the blood supply to the eye is directly diminished by these diseases, either by heart damage that diminishes blood supply throughout the body or from a blocked carotid artery that directly impedes blood flow to the eye [...] A poor blood supply can cause damage to any part of the body, and with these specific diseases, the destroyed retina and leftover SDDs are that damage." SDDs may simply be the consequence for when an already under-supported choroidal perfusion cannot compensate for a reduction in arterial blood supply.

Connecting the dots

Our primary focus in Smith's lab is to identify the missing link between the

leading causes of blindness and death in the developed world: namely, AMD, cardiovascular disease (CVD), and stroke, respectively. New approaches to proper multi-disciplinary screening of these insidious chronic diseases in at-risk populations may serve to greatly reduce morbidity and mortality.

Our research in BMJO was the first to identify which types of systemic diseases are the key culprits (7). Out of the 200 subjects studied with intermediate stage AMD – 85 percent of whom had a history of myocardial infarction, heart failure, major valve disease, and ischemic stroke – we found that all had SDDs on multi-modal imaging. We were able to conclude that AMD patients with severe cardiovascular disease and stroke were nine times more likely to have SDDs than those without them. With this research we have reinforced existing evidence that suggest SDDs are markers for a retinal disease distinct from soft drusen, and may even be a retinal disease driven by systemic vascular disease. Smith says, "We know that the highest level of patient care occurs when we use every available form of systemic and ophthalmic imaging."

As indicated in the findings above, patients with SDDs found at the eye clinic warrant more than standard vitamin supplementation – they need a trip to the heart or brain clinic for the evaluation of underlying disease. Standard work-up of heart function includes transthoracic echocardiogram (TTE), and standard work-up of the arterial blood supply in the neck includes computed tomography angiography (CTA). After their participation in our study, we provided many of the patients referrals for these tests and often found previously undiagnosed diseases in the neck vessels and heart. Several of these patients now have regular follow-ups and care in newly established cardiologist and neurologist relationships. Many patients were grateful for the discovery of a brewing but undetected heart disease or stroke risk – the very precursors for a life-threatening event.

A curative treatment

The long-established treatment options for AMD have either been preventative (multivitamins) or reactive (laser treatments and intravitreal injections). Without a localized region to address, curative treatment has long eluded ophthalmologists. Perhaps now, with an increased correlation of the SDD phenotype of AMD to vascular compromisation, a surgical operation could feasibly be developed and employed to tackle the root cause of AMD.

Although the discussion in this article has already addressed arterial blood supply to the retina at the level of the heart and the neck vessels, there is a final artery that connects systemic (the internal carotid artery) and ophthalmic vasculature (the choriocapillaris) – the ophthalmic artery (OA).

A recent, first-of-its-kind study describes the use of OA angioplasty for the treatment of AMD (8). Five subjects with advanced AMD were found eligible for "Compassionate Use" eligibility (which is to say, patients in an environment where conventional, recognized therapy is ineffective or non-existent) and volunteered for the operation. The feasibility and safety of the OA angioplasty was demonstrated, and a subjective benefit was immediately perceived in all five patients. At regularly spaced follow-ups, four out of the five patients experienced increased visual acuity, with one achieving six-month postoperative 10-line gain in the Snellen eye chart.

Although the study did not differentiate by SDD presence, the connection between SDD phenotype AMD and GA, opposed to drusen phenotype AMD and GA has already been established by Smith's team. And this surgery represents the first step in addressing the OA as a viable target to increase blood flow to the eye, restore retinal perfusion, and perhaps disrupt AMD disease progression.

Though the screening of SDDs in several at-risk patient populations has been discussed above, the relationship between AMD and vascular disease, particularly relating to standard-of-care imaging, has never been fully evaluated. The exact parameters and cutoff needed for adequate, non-invasive, and cost-effective screening are currently being evaluated by our team. OA angioplasty is a now explored potential curative procedure to address the root cause of vascularly-derived AMD that is highly associated with the presence of SDDs.

To summarize, we believe that SDDs are strongly associated with vascular disorders. These lesions may one day be widely recognized as biomarkers of cardiovascular and neurovascular compromise, giving ophthalmologists the license to refer patients to specialists who can prevent not only blindness, but also death.

Yang "Ryan" Fei is a Retinal Research Associate with Theodore Smith's Team at New York Eye and Ear Infirmary.

See references online at: top.txp.to/one/becomes/two

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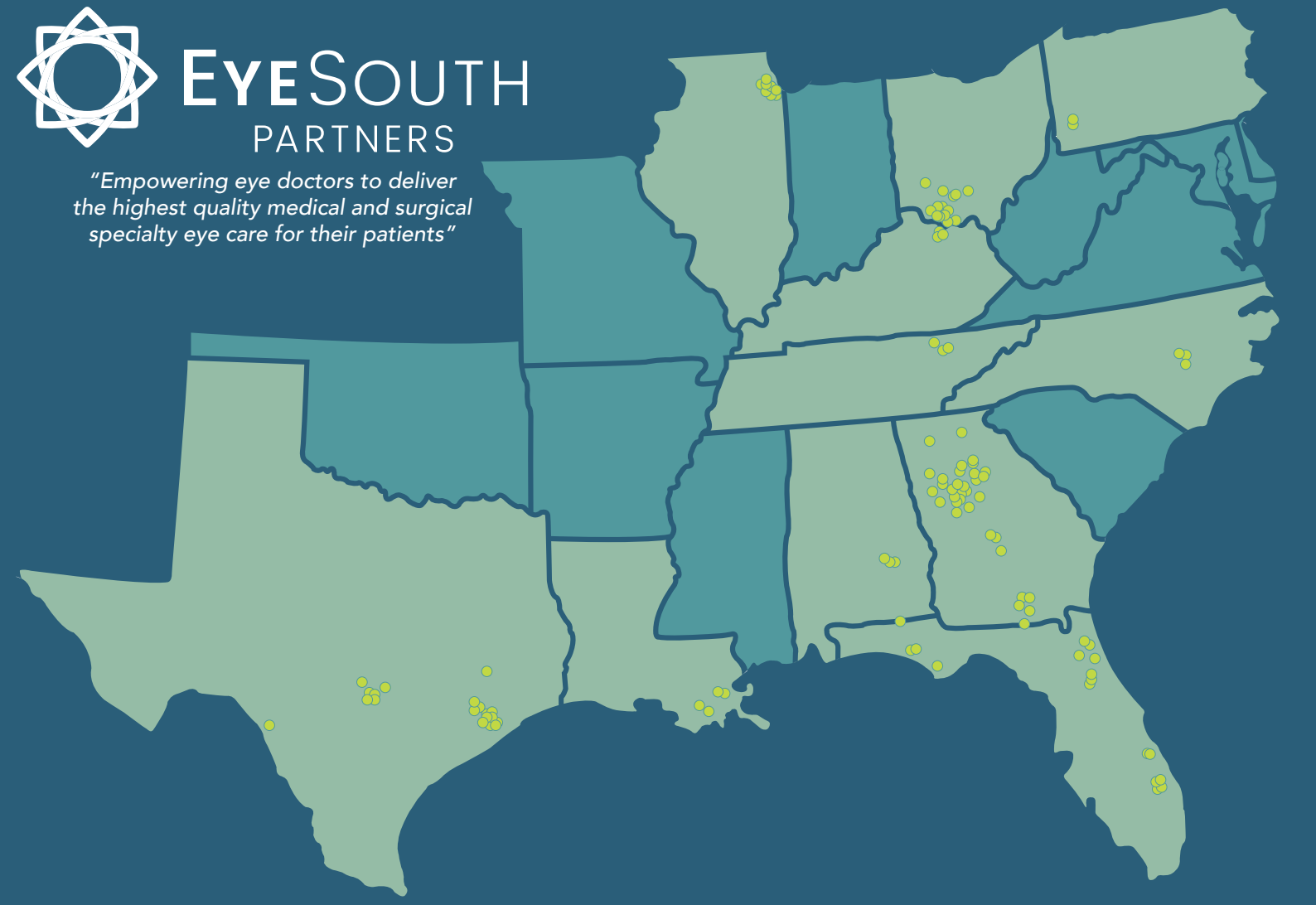

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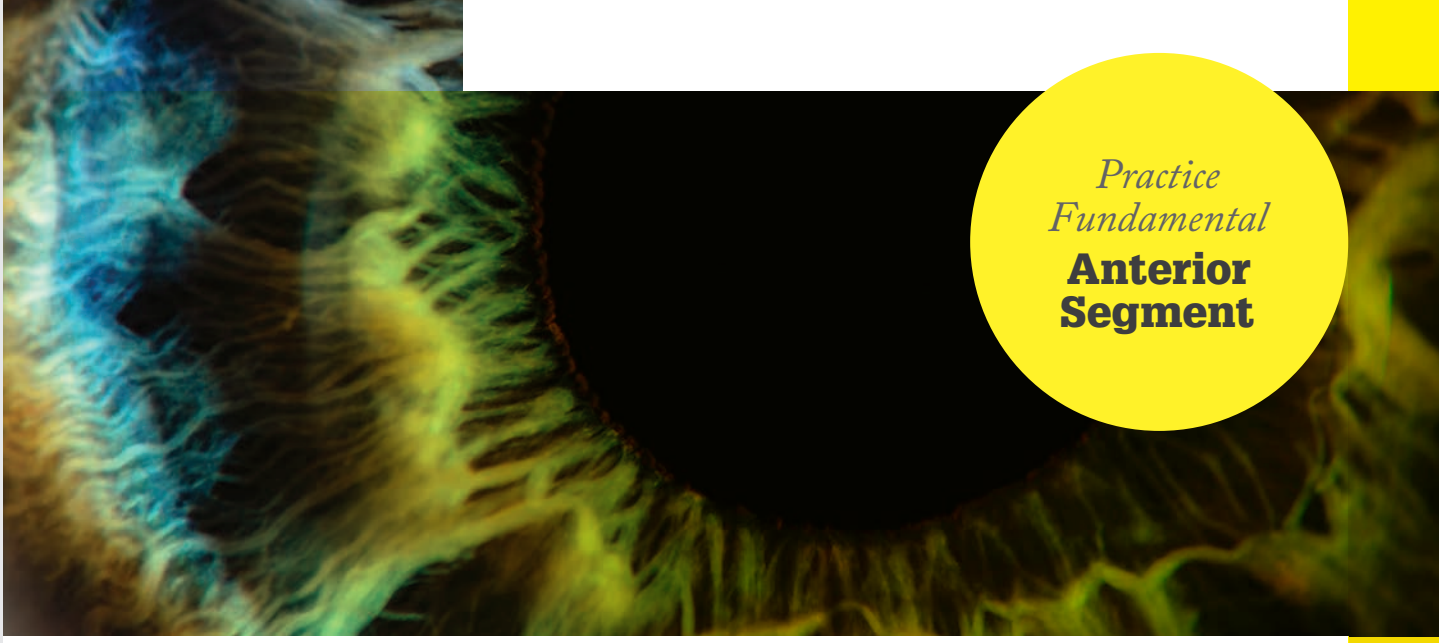

One drop is all it takes. A randomized clinical trial of 312 participants (1) aimed to identify whether perfluorohexyloctane eye drops are effective for patients with dry eye disease (DED) associated with meibomian gland dysfunction (MGD). The study found that the drops significantly and safely improved the symptoms of MGD-associated DED.

Sussing out subpopulations. What is the mechanism responsible for the clinical efficacy of cell injection therapy with fully differentiated cultured cells? To find out, researchers analyzed the polarized expression of ion transporters on cultured human corneal endothelial cells subpopulations (SPs) (2). They identified that the differences in intracellular pH between two SPs results in variations in the expression profile of specific ion transporters and mitochondria functions.

Counting the cost. An economic analysis (3) that used time-driven activity-based costing aimed to determine whether the incremental Medicare reimbursement for complex cataract surgery compared with simple cataract surgery is enough to offset the increased costs. The results suggest that the reimbursement undervalues complex cataract surgery.

Cyclosporine conclusions. To determine whether a water-free cyclosporine (0.1%) eye drop was effective in treating dry eye disease (DED), researchers conducted a randomized trial of 834 patients with moderate to severe DED (4). They found the solution was effective for treating dry eye-related keratitis and was well tolerated.

Another dimension. Scientists from the Centre for Ocular Research & Education have created "one of the most sophisticated 3D printing environments for ocular research in the world" – an innovation that is said to have widespread applications, potentially accelerating the future development of drug delivery systems.

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IN OTHER NEWS

Eat your greens. *Prospective cohort study from the UK Biobank finds that more fruit and vegetable intake – especially legumes, tomatoes, and pears – is associated with a lower risk of ccataract (5).*

Quick off the mark. *Randomized clinical trials show that a three-week course of weekly oral azithromycin is equivalent to a six-week course of oral doxycycline for treating moderate to severe meibomian gland dysfunction (6).*

Predicting with pterygiums. *A study finds pterygium-associated changes in optical parameters, including a significant induction of corneal astigmatism, irregularity, and some higher-order aberrations (HOAs), can be predicted by the area of the pterygium (7).*

Eyes wide shut. *Researchers have looked at plant-derived heteropolysaccharide pectin as having potential bioadhesive advantages for corneal injuries, finding pectin strongly adheres to the corneal glycocalyx (8).*

Amniotic Membrane How-To: Techniques for In-Office and Surgical Use

From severe dry eye disease to delayed healing, here's how this procedure benefits patients


Credit: Collage images sourced from Unsplash.com

For challenging cases with corneal surface damage, we have traditionally performed punctal occlusion, patched the eye, and then ordered some antibiotics. Now, we can add amniotic membranes into our armamentarium as a therapeutic intervention to help the eye heal faster.

Amniotic membranes control inflammation, promote healing, reduce scarring, and can improve visual acuity as the corneal surface heals (1, 2, 3, 4). And they are not just for anterior segment surgeons – far from it; they can be used by both ophthalmologists and optometrists for defects (various corneal ulcers and severe dry eye disease), delayed healing (keratoconjunctivitis or keratitis), dystrophy (epithelial or recurrent corneal erosion), degeneration (band keratopathy, nodular corneal degeneration), and damage (chemical, thermal, and acid burns, Stevens-Johnson syndrome).

We can insert an amniotic membrane in a simple in-office procedure or apply it in the surgical suite to promote postoperative healing. Either way, the procedure is reimbursable for multiple diagnostic codes with a documented ocular surface defect (CPT code 65778, average Medicare $1,400, private insurance $900-$1,300) and so it is a welcome addition to any practice.

Back to basics: What is an amniotic membrane?

The amniotic membrane is a layer of tissue derived from placentas donated by mothers undergoing planned C-section deliveries. The placenta's amniotic membrane layer is selected for use in the eye because it is acellular and immune privileged, avoiding an immune response that can hinder healing (5). The amniotic membrane is made up of extracellular substrates, including collagen, elastin, glycosaminoglycans, and fibronectin. This reservoir of bioactive components encourages healing and epithelial cell migration while inhibiting scarring, angiogenesis, inflammation, and microbial growth (1, 2, 3, 4).

When the amniotic membrane is prepared for clinical use, it can be processed naturally, without any harsh chemicals. One option, AcellFX, is air dried and ready to use right out of the package – either alone or under a contact lens. Another amniotic product in the market is Prokera (BioTissue), which is maintained in moisture and stretched across a malleable ring.

How to implant amniotic membrane

Among the categories of pathology that we treat with amniotic membranes, defects and delayed healing are most commonly treated in-office, while we often also treat postoperatively for dystrophy, degeneration, and damage. In my experience, the membrane lasts 3-5 days on the eye in most cases and works over 6-10 days.

We follow two basic techniques: place or place then cover. The first simply entails placing the membrane in the fornices, where it adheres and goes to work. It's an appropriate technique in many cases, including cases involving an active infection. In place and cover, we cover the membrane with a bandage contact lens, which allows longer healing time and makes it more comfortable to apply topical medication. Cases of active infection usually rule out a bandage contact lens. I can use AcellFX with both techniques, whereas Prokera has an integrated ring that helps keep the membrane in place for a place-and-cover effect.

To apply the amniotic membrane,

first I place an anesthetic drop in both eyes and clean the eyelid with lid scrub solution. With the eye held open by an assistant or a speculum, I dry the cornea with a sterile spear sponge and debride if needed. For a place technique, I grasp the membrane with sterile forceps and place it deep in the lower fornix, smoothing with a dry surgical spear to establish contact. Using the place and cover technique, once the eye is prepared, I remove excess water from a bandage contact lens, place the membrane on the lens, and place the lens on the eye, pressing it gently in contact. I patch the eye and see the patient back the next day. An amniotic membrane is applied the same way in the surgical suite – and postoperative care and follow-up follow the normal routine, along with the following home care instructions that I give to all amniotic membrane patients:

- Patients use an artificial tear with hyaluronan every two hours while awake for two days, followed by every four hours on days 3–6.
- Patients apply moist heat therapy at least 2–3 times a week starting at week four, and then drop to once per week after two months.
- Patients use a mild facial cleanser or eyelid hygiene solution daily for ongoing maintenance.

Three cases

Severe dry eye disease: A 65-year-old woman was unresponsive to standard therapy for dry eye disease, including cyclosporine and thermal pulsation. She presented with an OSDI score of 63 and lissamine green staining across the board (4-4-4). I inserted AcellFX at the slit lamp, placed in the lower fornices with no contact lens cover. She followed my home care instructions (above) and returned at one week showing improved appearance and quieting of inflammation. At one month, her OSDI score was 23 and her staining was clear.

Poor corneal healing after cataract surgery: A 75-year-old woman experienced poor healing in the left eye after cataract surgery, followed by corneal failure after cataract surgery in her right eye. Immediately after the second surgery, I placed one AcellFX membrane in the right eye with a bandage contact lens and another in the inferior fornix of her left eye. Where it took several weeks to attain her final vision in the left eye, the prophylactic approach for the right eye reduced her rehabilitation time to just two days beyond normal healing.

"Amniotic membranes control inflammation, promote healing, reduce scarring, and can improve visual acuity as the corneal surface heals."

Acute intervention after trauma: A 23-year-old male working for a cleaning service suffered severe exposure to an ammonia cleaning agent. In the emergency room, he had corneal irrigation with a Morgan lens using a 0.9% sodium chloride injection USP until the pH was neutral. He was referred to my office and taken immediately to our minor operation suite. I inserted a Prokera ring 6.0 mm, placing gatifloxacin 0.5% before and after insertion. I prefer the Prokera ring in such cases because it maintains the fornices in an anatomical position that is best for accelerated healing. Without the ring in this type of case, I've found that patients can have excess scarring of the fornices. The patient healed completely and was able to quickly return to work.

A breadth of benefits

Given the breadth of clinical applications for amniotic membranes, this is just a glimpse of the patients who can benefit. If you want to start using them in your office or surgical suite, the learning curve is short and the manufacturers offer quality resources and support.

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Disclosures: Dr. Stonecipher is a consultant for BioTissue, Thea, and Verséa Biologics.

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Three Tips to Find the Best Artificial Tears for Dry Eye Disease

A dry eye specialist's guide to recommending artificial tears that actually help rather than harm your patients

When I asked a new dry eye patient which treatments she'd tried recently, she told me she was using store-brand redness relief eye drops several times a day. The drops contained saline, a vasoconstrictor, preservatives, and other additives. I explained, "Inflammation is making your eyes red. Although these drops make them temporarily less red, they don't offer adequate lubrication – and their ingredients can actually increase inflammation."

Instead of helping her condition, my patient was actually making it worse. Unfortunately, this is rather common. When it comes to eye drops, consumers have lots of options, many of which don't offer the benefits they need and contain preservatives that can cause toxicity with frequent use. As a dry eye specialist, my approach to recommending specific types of quality artificial tears is based around the following points.

1. Know what to look for

The TFOS DEWS II report lays out the components of artificial tears and their importance (1). In addition to water, artificial tears include a range of other ingredients that we can easily find in current products.

DEWS II explains that, as a viscosity-enhancing agent and lubricant, naturally occurring hyaluronic acid (HA) has been shown to "bind to ocular surface cells," offer healing properties, and "improve dry eye symptoms." The study also specifically calls out the natural osmoprotectant trehalose for its water retention, bioprotective properties, protection of corneal cells from desiccation, acceleration of corneal healing, and contribution to restoring osmotic balance and homeostasis.

On the negative side, DEWS II notes that "chronic exposure of the ocular surface to preservatives is now well recognized to induce toxicity and adverse changes to the ocular surface." This is important to me; after diagnosis, I start patients on frequent, proactive use of tears for immediate relief, while simultaneously pursuing treatments that address the underlying cause of their dry eye. Patients with mild dry eye might use tears once or twice a day and at bedtime, while patients with moderate to severe disease can use drops up to every hour to replenish their tear film. Even after we bring their dry

"When it comes to eye drops, consumers have lots of options, many of which don't offer the benefits they need and contain preservatives that can cause toxicity with frequent use."

eye under control, they will continue to routinely use artificial tears, and I prefer they avoid preservatives.

2. Choose the most beneficial product

In our referral practice, most patients have moderate to severe dry eye disease. Many have seen multiple doctors, searching for a therapeutic approach that works, and they need the right combination of therapies.

I have all patients use a heat mask (Bruder) and eyelid cleanser at home. Depending on the nature of their condition (aqueous deficient dry eye or evaporative disease caused by meibomian gland dysfunction), I might recommend an in-office therapy, such as thermal pulsation (LipiFlow, Johnson & Johnson Vision; TearCare, Sight Sciences) to clear the glands of inspissated meibum, a short course of topical corticosteroids (Eysuvis, Kala Pharmaceuticals) to reduce surface inflammation, and/or topical immunomodulators, such as cyclosporine (Cequa, Sun Pharmaceuticals; Restasis, Allergan), and lifitegrast (Xiidra, Novartis) to help reduce inflammation and stimulate tear production.

In addition, I always recommend starting with high-frequency, preservative-free lubricant eye drops, as well as a gel or ointment for nighttime lubrication. I explain to patients that there are a handful of artificial tears that are most beneficial for their condition, emphasizing for frequent use patients that they should only use tears that are clearly labeled preservative-free. By avoiding preservative-related toxicity, patients can be sure that the tears are safe to use with high frequency.

I've recently been recommending iVizia (Thea), a newer artificial tear that contains both HA and trehalose as described in DEWS II, which has received great feedback from my patients. I'll also point to Refresh (Allergan) and Systane (Alcon), which contain HA, TheraTears (Alcon), which has trehalose, and several other preservative-free tears. I advise patients to avoid any generic artificial tears, as they may contain preservatives.

Patients should also know that preservative-free eye drops come in either individual vials or multi-dose bottles. Individual vials require a bit more dexterity, which can be challenging for older patients or patients with arthritis in their hands; patients with decreased visual acuity can also struggle to see the tip of the small bottle. Multi-dose bottles are easier for many people to use, and they create less plastic waste. Patients should, of course, choose the right container for them. Finally, I tell them they are free to shop for sales or buy multi-packs online, as long as they stick to one of the recommended preservative-free tears.

3. Reinforce your recommendations

All of my dry eye patients go home with our Dry Eye & Meibomian Gland Dysfunction/Blepharitis Treatment Plan – a single sheet that outlines our specific recommendations. During my discussion with a patient, I go through the sheet and check off all the therapies that apply. Each category includes instructions (use up to every hour, use 4-6 times per day, use at bedtime, and so on) and a list of specific brands for patients to buy.

With recommendations clearly written on this take-home sheet, patients don't get overwhelmed when they're shopping for products – and I know they're getting the right ones to improve their condition.

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The author discloses financial relationships with Alcon, Allergan, Johnson & Johnson, Scope, Sight Sciences, and Thea.

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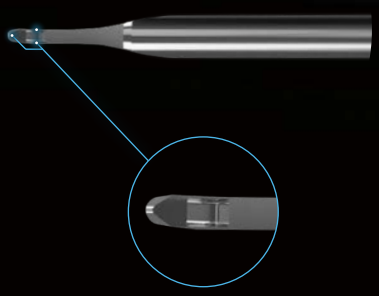

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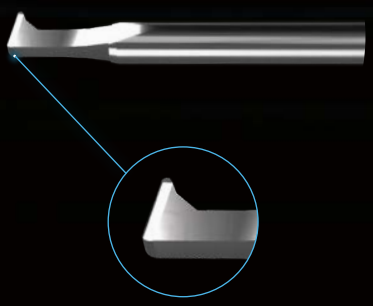

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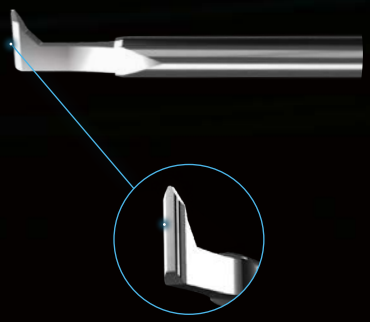

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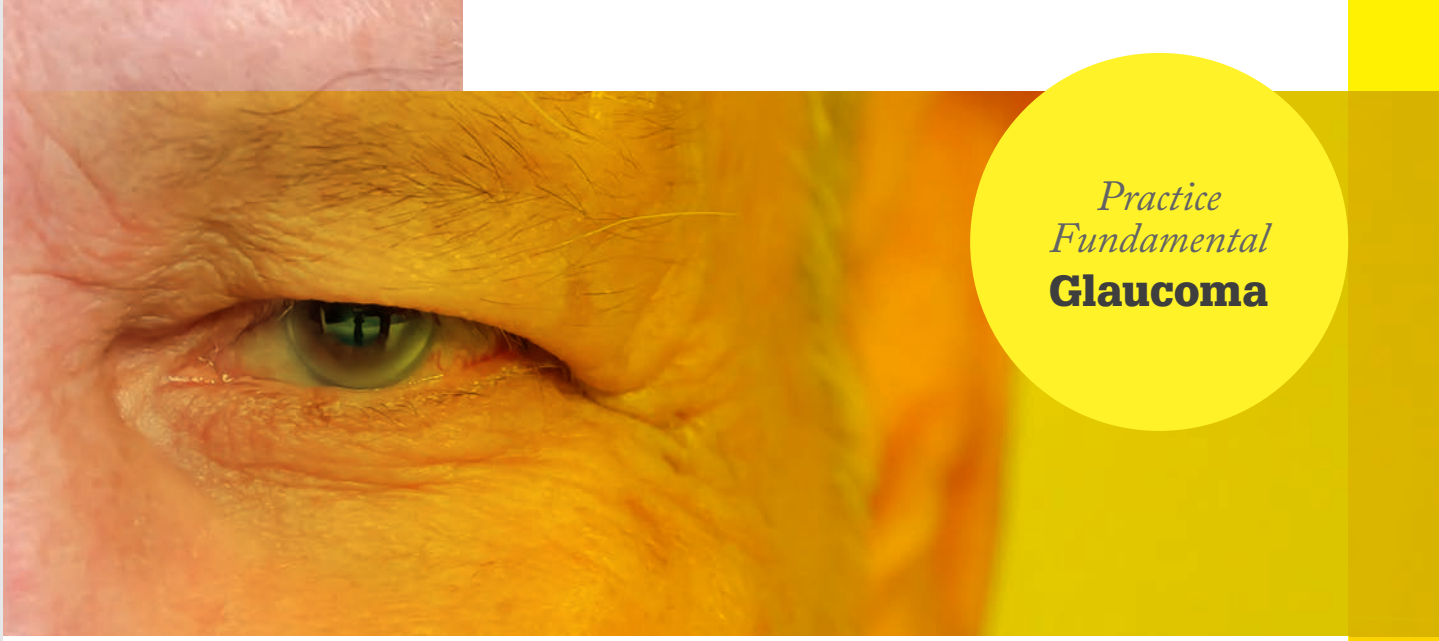


Picking parameters. A research group conducted a cross-sectional study to assess the accuracy of the performance of various optical coherence tomography (OCT) parameters in detecting glaucoma in highly myopic eyes (1). From this study, which included 132 patients, the researchers found that inferotemporal macular ganglion cell-inner plexiform layer thickness was the parameter that gave the highest diagnostic utility. They also noted that combining the temporal raphe sign with single OCT parameters, as was done in the University of North Carolina OCT index, may further enhance diagnostic performance in patients with high myopia.

Results translated. After developing a Moroccan Arabic dialect version of the Glaucoma Quality of Life-15 questionnaire, researchers examined the psychometric properties – including internal consistency, test-retest reliability and construct validity – of the translated tool (2). They found that the questionnaire, which was administered to 148 patients, took an average of just over three minutes and demonstrated adequate reliability and validity, positioning the tool as a valid and reliable tool for quality-of-life assessment within patients with glaucoma in Morocco.

Cannabis characterizations. What are the epidemiology and factors associated with cannabis use among open-angle glaucoma (OAG) patients? To answer this question, a University of California research group conducted a cross-sectional study of participants in the All of Us Research Program with OAG, finding that nearly half of this cohort were cannabis ever-users, with there being diversity within both ethnicity and socioeconomic characteristics including marital status, housing security and income and education levels (3). The findings may help identify patients who need additional outreach on unsupervised marijuana use.

Ratifying reports. Looking to provide direct clinical evidence to support the implication of heat shock protein (HSP)-specific T-cell responses in glaucoma pathogenesis by previous laboratory reports, a research team conducted a cross-sectional case-control study aiming to correlate SHP-specific T-cell levels with glaucoma severity in patients with primary open angle glaucoma (POAG) (4). They found that higher levels of HSP-specific Th1 cells are associated with thinner retinal nerve fiber layer thickness (RNFLT) in POAG patients and control subjects. This significant inverse relationship between RNFLT and the cell count of HSP-specific Th1 cells supports these T cells in glaucomatous neurodegeneration.

See references online.

IN OTHER NEWS

Differing damage. *Differences in optic nerve head structure between OAG and acute angle-closure glaucoma (AACG) suggest alternate optic nerve damage mechanisms in the two diseases (5).*

Non-causal code. *DNA testing showed no non-synonymous mutations of EFEMP1 in juvenile open-glaucoma suggesting they are not a common cause of glaucoma (6).*

No Added Ocular Surface Disease. *Changing from preserved to preservative-free cyclosporine 0.1% improves ocular surface health and IOP control (7).*

Counting the cost. *At six years post surgery, prophylactic laser peripheral iridotomy (IPL) is cost-effective in primary angle closure suspects with more accrued quality-adjusted life years (8).*

Prayer pressure. *Performing traditional Muslim prayer positions significantly increases IOP in both healthy and POAG patients, not immediately resolving in over a quarter of individuals (9).*

A Non-Invasive ICP Solution

Two depth transcranial Doppler technology provides a non-invasive alternative for monitoring intracranial pressure with implications for glaucoma

In a recent article, we covered new research from the Kaunas University of Technology that has identified translaminar pressure difference and lowered intracranial pressure as possible risk factors for normal tension glaucoma. In this follow-up article, we speak to Arminas Ragauskas – the developer of the two depth Transcranial Doppler technology that enabled researchers to non-invasively measure the intracranial pressures of patients.

How did the development of the two depth transcranial Doppler come about?

The only technologies that are clinically available for intracranial pressure (ICP) monitoring are invasive. There is a growing demand for non-invasive ICP measurement and monitoring technologies in wider fields of medicine outside of neurosurgical intensive care units. Unfortunately, other proposed non-invasive technologies are still unable to measure ICP value in pressure units without the calibration of a system – something that is needed to eliminate systematic errors of proposed non-invasive methods. Such calibration is impossible because a "gold standard" non-invasive ICP meter needed for calibration does not exist.

How does this new technology differentiate itself?

Our two depth transcranial Doppler (TCD) technology works by applying external pressure to a closed eyelid and taking simultaneous measurements of blood flow velocities in intracranial and extracranial (orbital) segments of the ophthalmic artery (OA). The value of extracranial pressure is almost equal to ICP value in a pressure balance case when blood flow velocities in both OA segments are the same. Our patented pressure balance method is the only method that does not require calibration but still produces accurate and precise ICP measurements outside of neurosurgical ICU.

Our software solution is able to identify – for the first time – very small intracranial pressure and intracranial compliance changes using automatic analysis of recorded pulse wave morphology. To accurately diagnose glaucoma, it is important to capture extremely high resolution small changes in the brain's physical parameters – our technology demonstrates this, providing high resolution results for traumatic brain injuries, stroke patients, and brain tumor neurosurgery patients included in our comparative study.

What does this technology mean for the future of measuring intracranial pressure?

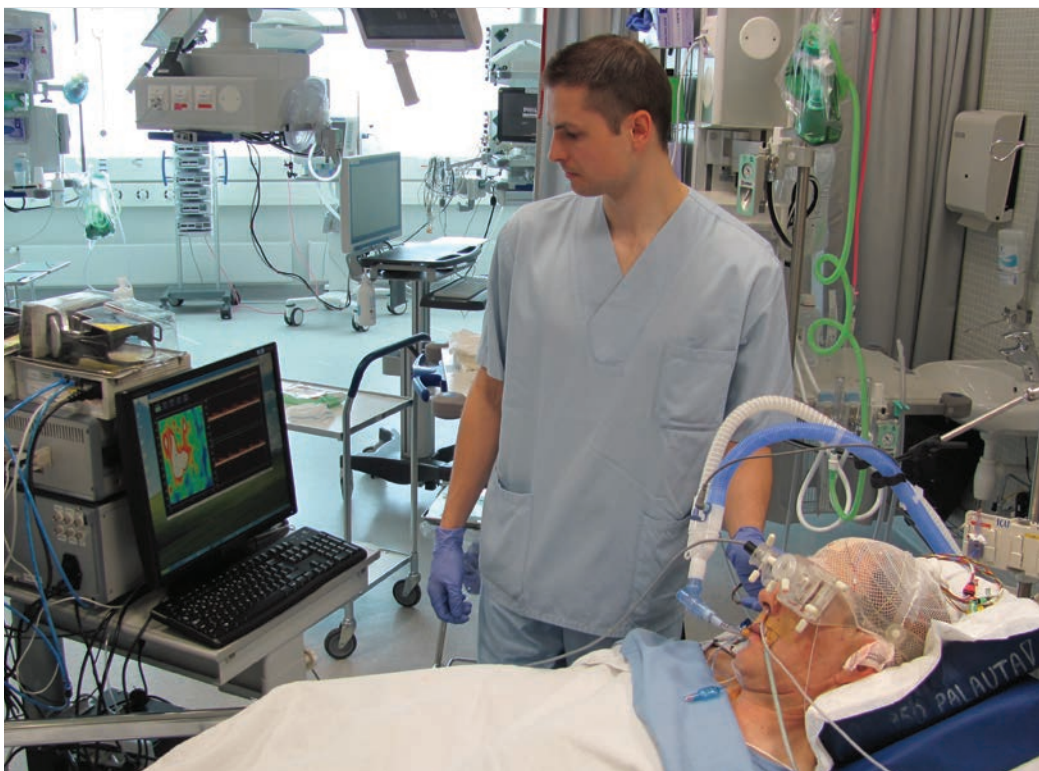
I believe that our patented, non-invasive ICP technologies will be used as widely as non-invasive blood pressure measurement in the near future. We also believe that our technologies will help create much more effective methods to treat glaucoma than currently available methods.

Are there any ways the technology could be improved?

Yes, of course. This product will continue to be developed as a radical innovation in the global market. That said, the preliminary results of a prospective comparative invasive and non-invasive clinical study of our passive, disposable, and non-invasive sensor already showed that the correlation between invasive and non-invasive recorded intracranial pressure pulse waves is between 0.97 and 0.99. Such high correlation means that a very strong association exists between physiological and pathological ICP pulse waves and our non-invasively recorded electrical signal in an output of a pressure sensor.

Can this technology realistically be implemented in clinical settings?

The latest version of our technology is already in clinical practice! We are using it to examine different brain pathologies, including those of glaucoma patients.



John Berdahl

Time to Take FLigHT?

Why we must strive for more precise visualization systems and treatment approaches when it comes to primary open-angle glaucoma

Ophthalmologists have always had a significant visualization advantage relative to our colleagues in other medical specialties. Even as the advent of various imaging modalities – including x-ray, magnetic resonance imaging, and computed tomography – allowed other specialties to gain advantages similar to those we enjoy in eye care, ophthalmologists also benefited from technological advances, including OCT, endoscopic cameras, epithelial mapping, and ultrasound. Despite this, proper visualization of some ocular regions – including the angle – remain challenging.

Gonioscopy innovations have offered improved characterization of many glaucoma cases and have enabled SLT and MIGS to flourish. Continued advances in imaging and treatment modalities are vital to our growth, and ensuring that the glaucoma surgery of tomorrow is more efficient, effective, and less invasive than the glaucoma surgery of today.

Imaging and therapy-based innovation thrive in some ophthalmic subspecialties, however, doctors treating glaucoma have historically had limited access to intraoperative imaging technology able to improve precision or present opportunities for new surgical strategies. Today, there is a surgical approach that looks set to change the game: femtosecond laser image-guided high-precision trabeculotomy (FLigHT) for the treatment of primary open-angle glaucoma (POAG). This new platform represents a significant advancement in trabeculotomy creation.

See better, treat better

Notably, ViaLase, the company that pioneered FLigHT, is helmed by Tibor Juhasz, who previously co-founded the company that brought LASIK to market. (The discovery that femtosecond lasers created micron-specific incisions, without compromising the surrounding ocular tissue, led to improved safety and visualization, forever changing the landscape of refractive surgery.)

Combining a femtosecond laser and micron-accurate OCT imaging into a single platform, doctors using FLigHT can non-invasively image the angle using a specialized gonio camera to determine the surgical location, before precisely guiding the femtosecond laser for a pristine trabeculotomy without a clear corneal incision. FLigHT treatments offer a new level of imaging and precision for glaucoma therapy that may deliver outcomes similar to OR-based treatments, such as goniotomy, without the risks or burdens of surgery.

Moreover, it presents another option for glaucoma treatment outside the setting of cataract surgery, a common – and limiting – requirement for MIGS procedures. FLigHT illustrates how strategic, creative thinking can lead to more precise interventions as well as improved experiences and outcomes in glaucoma treatment – all while maximizing safety and efficacy, and minimizing the burden of care of patients, providers, and health care systems.

Other pipeline developments relying on live imaging will also likely improve our ability to deliver safe, effective care to glaucoma patients. Research on the safety, efficacy, and utility of intraoperative endoscopy may push the possibilities of glaucoma surgery even further. Other imaging-based diagnostic platforms should also enhance our ability to diagnose POAG and characterize the condition's response to therapy.

It is difficult to treat what we cannot see, so improved visualization is key. With glaucoma intervention, microns matter; our patients' potential outcomes improve with increased in precision. Ophthalmologists have helped lead medicine in the sphere of visualization since the inception of the field. We must continue to blaze this trail which means not settling for historical success but instead pushing ourselves forward.

John Berdahl is a Partner at Vance Thompson Vision, CEO of Equinox and Founder of ExperOpinion.md; all in Sioux Falls, South Dakota, USA. He is a consultant for ViaLase, Sight Sciences, Glaukos, Alcon, and New World Medical.

Two depth TCD technology in the US

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Tackling Burnout with Hard-Won Wisdom

We may not always love our work, but here are some tips for avoiding the perils of burnout and disillusionment

By David Lockington

Modern life is complex. Unfortunately, it has also become difficult, with increasing levels of disillusionment both towards and within healthcare. The recent RCOphth survey shows serious staff shortages and we know we have an increasingly aging population – a combination that places higher demand on ophthalmologists than ever (1). Worryingly, rates of burnout are on the rise in ophthalmology post-COVID – and, as with so many things, prevention is better than cure (2).

Hard-won wisdom

There's so much to love about being an ophthalmologist, but we shouldn't be naive. No matter where in the world you work – and no matter the healthcare system, huge stresses and pressures are placed on ophthalmologists.

Whatever the source of your stress, I've gathered some hard-won pearls of wisdom to steer you away from burnout.

Protect your time and autonomy

One of the important triggers for burnout

"If you develop a range of different interests, you are less likely to get bored, and more capable of compartmentalizing issues when they arise. So, get involved!"

is a lack of autonomy. We doctors are generally high achieving; we value the freedom to make choices on our own terms. However, systems can often take our autonomy away, and so my first tip is to effectively time manage your schedule – on your own terms where possible. The solution to a lack of autonomy is not greater effort, but better protection of our time and energy. A pet hate of mine is the ideal of giving 110 percent to something; even if you give 100 percent of yourself to work, that leaves 0 percent for anything else. And let's face it, there is much more to life than work – we only need to think of Maslow's hierarchy of needs to know this. At the very top are self-actualization and esteem – when those concepts are absent, you'll get resentment and, ultimately, burnout.

Diversify and engage

There is a great deal of talk in healthcare about the importance of resilience – an ability to respond and grow despite adversity and stress. Remember life as a junior medic? The stresses of learning decision making as a junior doctor promoted greater confidence as a senior, through previous exposure to complex clinical scenarios. A great way of building resilience is through teamwork and mentoring – including reverse mentoring, where all members of the team are valued, and seniors can gain unexpected insights from their juniors. Ask yourself these questions: Who are you mentoring? And who is mentoring you? Engaging in these relationships will reduce isolation attitudes, allowing us to thrive rather then simply survive.

Diversification can help you thrive too – if you only do the same thing day in, day out you can get ground down by workplace dramas. If you develop a range of different interests, you are less likely to get bored, and more capable of compartmentalizing issues when they arise. So, get involved! This can be through engaging with professional societies, giving tutorials or writing talks – developing these interests and relationships will also make you a much better doctor. Whatever enables you to develop new skills is liable to help you love your job for longer.

Don't forget the ice cream

One of my greatest joys is protected time with my family. We shouldn't just schedule our work time day to day, but also our leisure (including exercise!). Planning time and space away from the stresses of work will make you much better able to deal with it on your return, and it can help us work more effectively. Look out for symptoms of work encroachment causing anxiety – and be proactive in addressing them as soon as possible. And if some of it appears to be self-inflicted? Perhaps high achievers like ophthalmologists need to learn to say one of the hardest words – enough!

Ancient wisdom still applies

Most of these concepts are not new. There is great deal of evidence that having a higher calling and purpose in life promotes resilience (consider those who endure despite persecution). Timeless principles, such as ensuring a day of rest, and not being jealous of others' achievements can help us reach a greater level of contentment.

In short, be yourself – that's all you can be! Make every effort to protect your time and energy. Diversify where you can to keep your passions engaged. Remember your purpose and that work should be just one aspect of your life. Learn to be content. And, most importantly, don't forget the ice cream!

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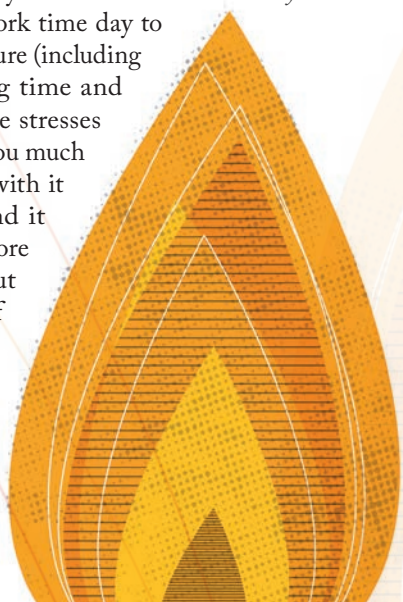
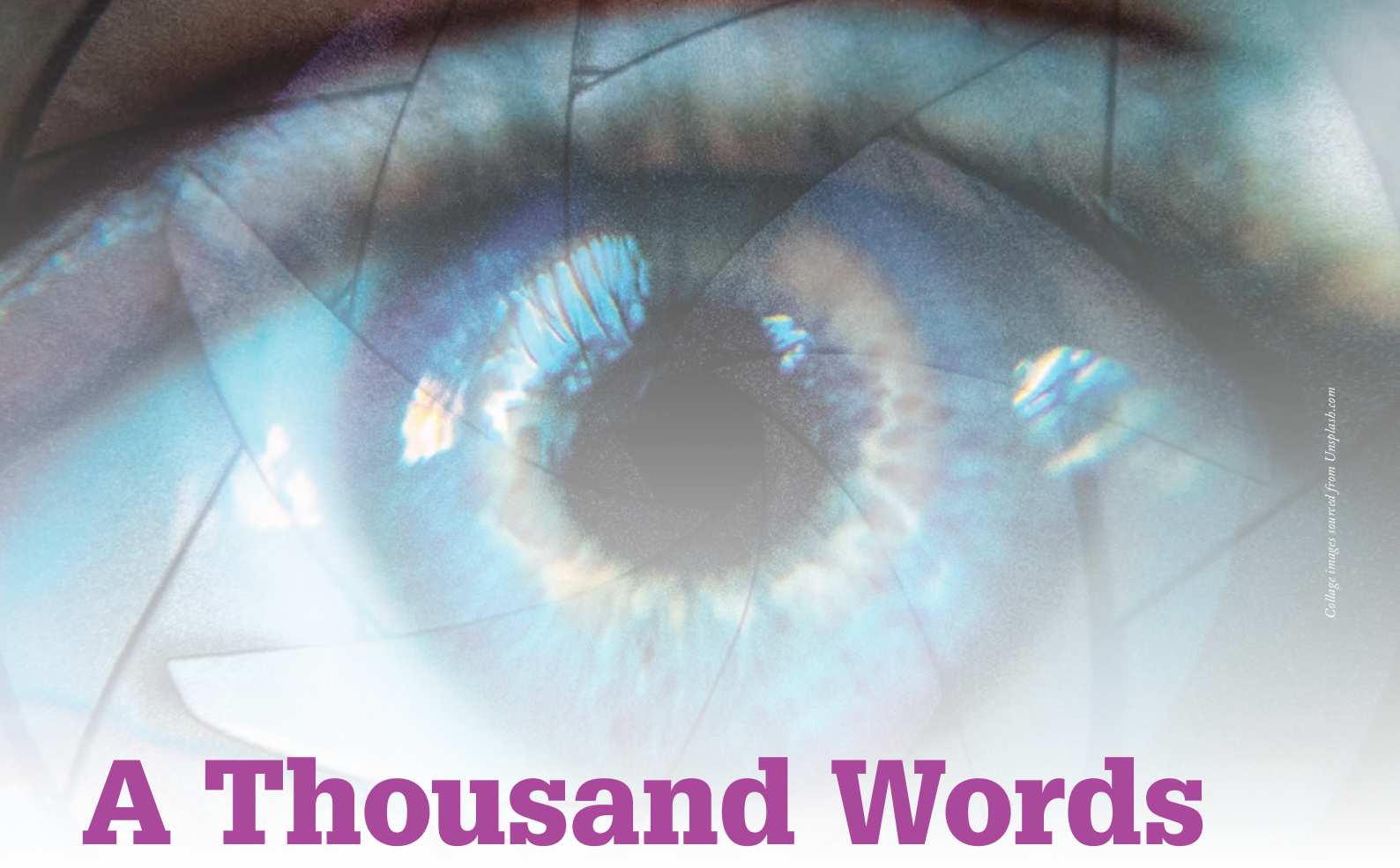




Collage images sourced from Unsplash.com

A Thousand Words

Why digitally photographing patients' eyes is essential

By Tommy S. Korn

"How does my eye look? Is it getting worse?" Those were the questions asked by a patient during my cornea fellowship many years ago. I reviewed the scanned hand-written notes and, unable to tell if she was getting better or worse, I typed out as many descriptive words I could think of into the EMR computer. I swallowed, took a deep breath, and asked the patient to wait for my attending surgeon to deliver the news.

What's surprising is that this scenario of hand-written notes in paper or electronic medical records still happens in the 21st century. "There's absolutely no way you can remember. You have to take eye pictures and compare," my fellowship mentor at the University of California, Los Angeles, Dr. Bart Mondino, told me as he pulled out some Kodachrome slide photos of the patient's eye from past visits. Thinking back, he was absolutely correct and taught me an extremely important lesson.

Taking photos of your patients' eyes as an ophthalmologist should be an important part of any clinical practice. Creating detailed drawings, recording copious notes, or grading various eye conditions cannot compare with the information one receives from viewing a crisp, tack-sharp photo of an eye. In my career, I've conducted at least 150,000 patient eye exams, and there is no way I can remember every single eye and how it appeared in the past – no doctor can! Taking these photos has many benefits for both ophthalmologists and patients. The obvious reason is to track progress. As I see the same patient over time, I can compare their eye photos and monitor their condition if it gets better or worse (this goes for myriad conditions but includes cataract progression, conjunctival pigmented lesions, healing corneal abrasions/ulcers). This helps me be a better ophthalmologist and it allows for quicker follow-up visits and better patient satisfaction – because the patient is an active participant in their care. They can see what's going on instead of just processing their diagnosis. The words I often hear from patients after I show them their eye photo are – "Wow!" or "I get it now!"

A digital boon?

Back in the beginning of the 21st century – just before the dawn of the digital photography revolution – it was easier for my mentor, working at an academic institution, to take a photo of every patient because of the available resources: a dedicated ophthalmic photographer, a photo processing lab, and plenty of space to store hard-copy Kodachrome slides of patient eye photographs. Joining a private clinical

practice (with no residents/fellows to help) and taking a photo of every patient's eye was just not practical from an economic and workflow standpoint. Slit-lamp mounted cameras were expensive and there was no way to justify the ROI when reimbursement for eye photos was so low. Thus, with the surge in popularity and the steadily declining costs of digital SLR cameras in the 2000s, I began to take digital photos of my patients' eyes using a heavy DSLR camera with a large macro lens.

When used in front of a patient's eye, it was intimidating – like looking down the barrel of a gun. There were other friction points too; I had to take pictures of the patient's eye using the camera, then take the SD digital card out and upload it to the slow hospital EMR computer. This took a lot of time and wasn't feasible for every patient. As the years passed, I migrated to a point-and-shoot digital camera that I mounted to a slit lamp with an expensive adapter. This was less intimidating for the patient, but the photo quality wasn't very good – and I still had to manually take the SD digital card out of the camera and upload it to the slow, clunky hospital EMR computer.

The smarter revolution: large screen phones with better cameras

The key moment for me as an ophthalmic photographer was the introduction of the iPhone 6 Plus in 2014. The combination of the iPhone's large screen, improved camera sensors, fast Wi-Fi connectivity, and a growing ecosystem of mobile electronic medical record (EMR) apps started to redefine what a smartphone could do for an ophthalmologist. Our team began to tinker and develop a custom mount for the iPhone 6 Plus to connect it with the slit lamp I normally used.

The larger iPhone screen size meant that I no longer had to upload photos via an SD card to a nearby hospital or office PC; I could take the photo and show it to the patient instantly. The birth of EMR imaging apps shortly after the debut of the iPhone 6 Plus also meant that I could upload the patient's eye photo into their record within seconds – another time-saving point for a busy ophthalmologist. Certainly, these photos are important for the me as a clinician – but they could also help other clinicians, who may treat the same patient in the future, by allowing continuity of care. For me, the iPhone essentially became a portable camera with a fast computer attached to it.

Patients often face difficulty accessing eye photos when they travel, move, or have to engage with another healthcare system. I developed the idea of using Apple's AirDrop feature to wirelessly send these photos straight to the patient's iPhone, allowing them to access it whenever it was needed. For Android users, I send the photos via Doximity Dialer using a HIPAA secure text with attachments, while safeguarding my phone number. This ensures the patient's eye photo stays with the patient – not with a potentially hackable or misused cloud EMR server.

Smartphone macro eye photography and telehealth

The introduction of the iPhone 13 Pro was also another key moment for ophthalmic photography. A pro-level camera was now available on a smartphone that was connected to an ultra-fast 5G connected miniature computer in your pocket. For the first time ever, it was possible (with proper lighting) to take a high-definition macro image of the eye without the need for an expensive slit-lamp.

I posted this feature on LinkedIn and immediately faced criticism from macro-photographers all over the world. They were missing the point. It wasn't about me as an ophthalmologist taking great smartphone eye photos. It was about everyone else in the world now having the ability to do so.

Imagine the potential for improved access to expert eye care for patients in remote areas of the world – all thanks to the ability to take a photo of their own eye and send it digitally to an ophthalmologist via telehealth. This truly revolutionary step forward in healthcare could empower patients to get the care they need without having to travel. And it could have an immensely positive impact on the lives of people who would otherwise be unable to get access to expert ophthalmic care.

"Taking photos of your patients' eyes as an ophthalmologist should be an important part of any clinical practice."

Embrace the eye photo

The future of visible light eye photography is incredibly exciting. With the rapid advances in smartphone camera and telehealth technologies, we are able to provide previously unseen levels of in-person and remote ophthalmic healthcare. It has never been easier to take digital eye photos, and, with the right knowledge and guidance, it can empower your patients.

As a practicing clinician, you have the power to collaborate and innovate in ophthalmology. With a digital eye picture you can say so much more than a thousand words – so, go take some photos and see what you can discover!

Tommy S. Korn, M.D is a cornea surgeon with Sharp Rees-Stealy Medical Group in San Diego, California USA.

Choose Your Words Carefully

How standardized terminology helps patients understand their conditions and treatment options to make better informed decisions

By Tanya Trinh, and Balamurali K. Ambati

When we as doctors seek medical care, we have the unique privilege of having some innate understanding of the terminology presented to us in the general field of medicine. Outside of our respective fields however, we are still at the mercy of the expertise of the physician whose help we have sought. We can therefore only imagine the difficulties for our patients – especially those who come with little to no health background. Like them, there are two virtues we value most during consultations: firstly, that the doctor is clear at explaining our conditions, and secondly, that the doctor is concise when explaining our treatment options. In the end, no matter our knowledge level, we all want enough information to make informed decisions about what might be best for our health.

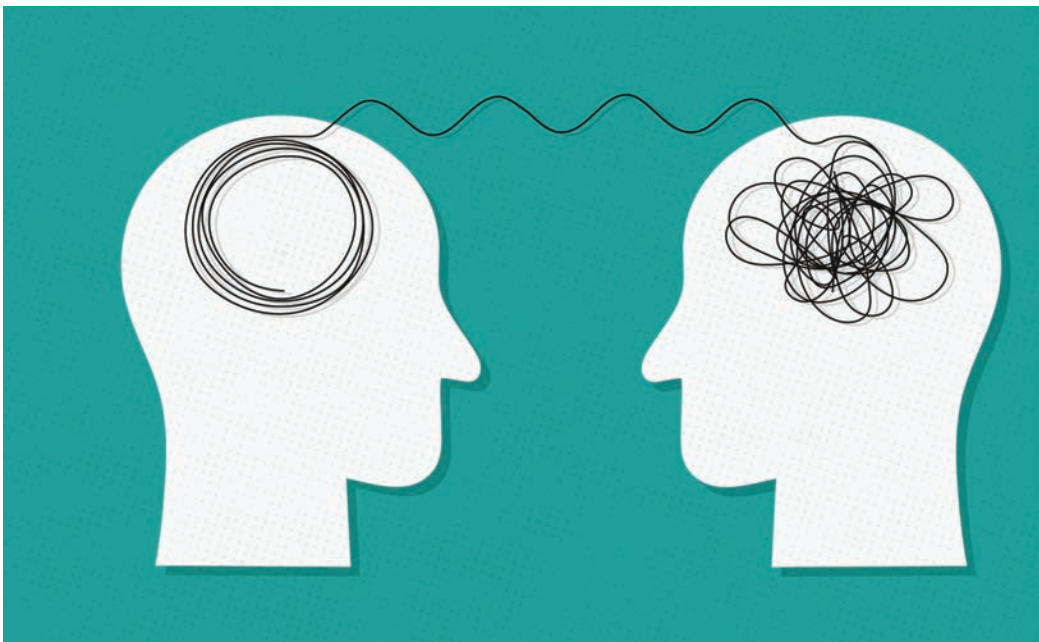
The plethora of acronyms springing up in every subspecialty of medicine has increasingly obscured the clarity sought after by patients, making the decision-making process confusing and complex to the layperson – and even surgeons beginning their subspecialty learning journey. If this is a source of confusion to the average resident or fellow embarking upon the field, how can we expect our patients to partake in their own health decision-making?

The standardization of terminology is crucial in ensuring accurate and consistent communication between healthcare providers and patients. Surgeons play a vital role in leading this change, being at the forefront of healthcare and able to influence and shape medical practice. By adopting standardized terminology and promoting its use among our colleagues and during our industry interactions, we can reduce misperception among patients and professionals alike.

Standardized terminology also allows for proper classification and discernment between procedures. It sets foundations for more stringent comparisons between various procedures of the same type, and, concurrently, enables improved and nuanced understanding of procedures, differing in principle, that treat the same issue. The adoption of such standard terms should filter into the realms of the medical literature and set solid foundations for meaningful comparison.

It is also imperative that the standardized terminology adopted is industry independent.

Industry manipulation of language promotes profound confusion for patients, particularly where direct-to-consumer marketing is concerned. They may be swayed by companies with more effective or larger advertising budgets or become fixated on a particularly named procedure, giving the surgeon the difficult task of realigning the patient's understanding and expectations, with time, mental energy, and resources being wasted in the process. Industry manipulation also monopolizes the playing field, hindering the speed of adoption and



exploration of new technologies aiming to address the same issue. Using brand names for procedures is neither appropriate nor professional, especially where longevity in a particular field may create unfair advantages for a single manufacturer over newcomers that may have developed superior technology, but has had less time "on the playing field".

We, as surgeons, must lead the conversation in the consultation room, as well as in our industry interactions. We have a unique opportunity to define the terminology and set the appropriate standards accordingly.

To this end, the Refractive Surgical Terminology Committee (a subcommittee of the Refractive Surgical Alliance) was formed in 2022 to define standardized terminology for the following procedures. The committee consisted of experienced refractive and cornea surgeons from Europe, the Americas and Asia-Pacific region to ensure that the terminology was not only accurate and reflective, but sensitive to language translation in various geographical regions. The terminology was then presented to the RSA membership at large for input and commentary before formal endorsement.

Lens replacement

In considering standardized terminology for lens replacement procedures, the term "lens replacement" stood out as the most appropriate choice. It is simple, yet elegantly encompasses the essence of the procedure – the replacement of a dysfunctional lens with a custom-fit replacement. The term "lens replacement" allows for improved flexibility in the language used by clinicians in different contexts, and factors in various language considerations and subtle differences in counseling techniques. In addition using the term "dysfunctional lens" in consultation with patients effectively communicates the need for the procedure, while "customized lens replacement" accurately describes the solution.

Furthermore, the term lens replacement is already widely adopted by patients, indicating a level of stickiness and ease of understanding. The use of "replacement" instead of "exchange" also aligns with the terminology used in other medical specialties, better conveying the idea of switching an old lens with a new one. Alternative terms were considered but ultimately discarded as they did not convey the same level of simplicity and understanding for patients.

Overall, the use of the term lens replacement in the refractive surgery industry promotes clarity and understanding for both patients and colleagues in the fields of ophthalmology and optometry, and supports the goal of standardization in terminology.

LALEX

The term LALEX – laser assisted lenticule extraction – elegantly encompasses all lenticule extraction procedures and does not demonize one laser vision correction procedure over another. Another key advantage of using LALEX is its minimization of technical jargon that may not be easily understood by patients such as, "femtosecond" or "intrastromal."

It should also be noted that LALEX has already been adopted by our German colleagues, and we recognize their contribution in arriving at this term.

Other terms were considered but ultimately rejected as they did not effectively encompass all lenticule extraction procedures or have the desired level of simplicity and ease of understanding for patients.

STODS

STODS – surgical temporary ocular discomfort syndrome – is the endorsed term to describe the temporary discomfort experienced by patients after vision correction procedures. The priority when naming this syndrome was conveying the understanding that the discomfort is temporary and will heal over time. This is important to validate patient experiences and to avoid any unintended media manipulation. STODS encompasses the neurological deviation that can occur after all types of vision correction procedures – this is not solely a "dry eye condition" but a distinct clinical entity as evidenced by research evaluating the differences in inflammatory markers between dry eye disease and STODS.

It is important to note that STODS is not a unique complication, but rather a normal and temporary part of the healing process after vision correction procedures. Alternative terms were considered, but they did not convey the temporary and healing nature of the discomfort experienced.

Words Matter.

Technical jargon used carelessly can create barriers to understanding and lead to needless confusion and stress. It is important for doctors to present information in a clear and concise manner, using terms and language that are easy for the patient to understand. Avoiding brand names and eliminating industry manipulation is not only the ethical and transparent thing to do, but also keeps things simple and engenders trust. Clarity and consistency also ensure that patients fully comprehend their health status, treatment options, and any potential risks and benefits. For the surgeon and for the advancement of refractive surgery, the adoption of standardized terminology and classification also clears the path for newer technologies to find their rightful place and allows for clearer and more robust comparison between different technologies.

Ultimately, the adoption of the RSA endorsed terms – "lens replacement", "LALEX", and "STODS" will improve patient engagement and understanding, leading to improved patient experiences and, in the end, better health outcomes.

The authors wish to thank the other members of the RSA Terminology Committee: Drs. Dagny Zhu, Lance Kugler, Luke Rebenitsch, Guy Kezirian, Arthur Cummings, and Brett Mueller, as well as the RSA membership.

Balamurali K. Ambati, MD, PhD, MBA, FWCRS and Tanya Trinh MBBS, FRANZCO, FWCRS, PCEO.

Taking the Wider View

Sitting Down With… Jugnoo Rahi, Professor of Ophthalmic Epidemiology at UCL Great Ormond Street Institute of Child Health and the UCL Institute of Ophthalmology

When did you decide to pursue ophthalmology?

It's funny – both of my parents, as doctors, were involved in ophthalmology and I was determined I would not be following in their footsteps. So, I did my pediatric training before my ophthalmology training. But with both of those specialties I was struck by the fact that, as a doctor, you get to be involved not just with a patient's medical needs but their whole life course. And working with children, you get to care for your patients in the context of their family life too. So I settled on pediatric ophthalmology.

Which mentors have most influenced your career?

How many professors does it take to make an ophthalmologist? In my context, the answer is quite a few! I've benefited enormously from some exceptionally supportive colleagues and mentors. At the Institute of Ophthalmology, I have to mention Andrew Dick, current Director of the Institute, and Tony Moore. From my background and training in epidemiology, there is Catherine Peckham – the first professor of pediatric epidemiology in the UK – Carol Dezateux who co-supervised my PhD and my first supervisor, Claire Gilbert, an ophthalmologist who very much helped spark my interest in epidemiology and population studies in the context of childhood eye diseases. Of course, I have to also mention David Taylor, the leading pediatric ophthalmologist of his generation and Sir Peng Tee Khaw – both giants of ophthalmology who have been a consistent source of help and support. At my own inaugural professorial lecture, I got to look at the audience and see all of these people who had helped to shape my career.

You also specialize in epidemiology – how did this arise?

Ophthalmic epidemiology wasn't a well established discipline when I started my training. One of the reasons I chose it as my academic discipline is the variety of science this offers. The Vision and Eyes Group I lead at the Institute of Ophthalmology is widely multidisciplinary – currently we have members whose expertise spans epidemiology, statistics, health psychology, health economics and genetics; and a mix of scientists and clinicians from different disciplines. There is now quite wide recognition of the power and value of 'Team Science' to address complex problems and I have always been aware how this improves our ability to translate the science into innovations in practice or policy or to inform future research. It's also great fun to work with people who bring lots of different perspectives to a problem!

What do you think of the growing interest in global ophthalmology?

I think it's a great thing. What I'm particularly pleased about is that we're moving towards the idea of building capacity within lower income countries and away from the older model of flying in a surgeon to do a cataract surgery camp but not leaving any legacy. Although on the individual level, it's obviously good that people receive the surgery they need, however, without building the systems to generate capacity, all those structural needs remain when you fly off home again. That's not the way people approach things now. There are many of us – particularly when we are a little more senior in our careers – with the scope to help through partnerships, training programs, and other methods for building capacity. It can be a bit of a leap – there is a certain tendency for ophthalmologists just to talk among themselves – but I'm really interested in seeing if we can help encourage the eye and vision world to look outwards a little more.

"There are many of us – particularly when we are a little more senior in our careers – with the scope to help through partnerships, training programs, and other methods for building capacity."

Given your work with the World Health Organization, how important is macro-level policy making?

It's vital! I'm increasingly directing my energy in that direction. Collectively, the eye and vision community has maybe not done the best job of explaining to policymakers why sight impairment matters. It's still a niche. In the world of pediatric ophthalmology, that's largely because most people have never met a child with a vision impairment. Blindness in adult life is more common, and yet we still don't seem to be in the mix whenever people talk about chronic disorders that have a major impact on life.

Take the example of the COVID-19 pandemic. It was very difficult to manage if you had a vision impairment – how do you know if you are socially distancing

appropriately? Schools moved online, but for children with visual impairment that was very hard and often they didn't get the right provision. Where does the fault lie with stories like this? Well, to be honest some of it lies with the eye and vision professional community. We have to take this information to policy makers, which in the UK means Members of Parliament and government organizations. This requires time and a change in our communication style. From my point of view in relation to children in the UK, I would like to see initiatives for childhood visual impairment coming from – for example – the Royal College of Pediatrics in partnership with the Royal College of Ophthalmology rather than just from the eye world.

I'd like vision to be something that everyone involved with child healthcare thinks about. This goes across educational needs, environmental needs, social needs, as well as health care needs. Clinicians are already involved in policy decisions – the patients you see in your clinics determine those you don't see. That's a policy choice on a micro level. Our work has these wider implications and maybe we need to widen our perspective.

You are also involved with RCOphth; in light of the RCOphth staff survey, what do you think of the state of UK ophthalmology?

The survey puts numbers to the worries we've had in UK ophthalmology for a long time. With an aging population and the innovations, for example in treating AMD, there is more we can do about the causes of visual impairment than ever before. We have more patients than ever before, but just not enough resources. Quietly – a little behind the scenes – we've been particularly worried about pediatric ophthalmology and we have unfilled posts across the country. I think the numbers probably reflect what we see in the NHS generally, which is that there has been little by way of proper workforce planning. Any of the clinical specialties would have said that, with an aging population, demand is simply outstripping supply in terms of staff levels. Things are perhaps not as bad as other specialties – you need only look at mental health care provision to see some very stark numbers on waiting times and staffing levels. The UK Government is about to publish an NHS workforce plan, so let's hope that offers some solutions to the workforce crisis.

"Collectively, the eye and vision community has maybe not done the best job of explaining to policymakers why sight impairment matters."

It's common to hear people say that these problems in ophthalmology can be solved with better partnerships with other health care professionals allied to ophthalmologists, but there is a limit to what they can achieve. Ophthalmologists are, after all, doctors. And yes, our colleagues in optometry, for example, can certainly do a great deal of clinical care, but that won't entirely solve the problem. It takes five years of medical school and then a further nine years of training to produce an ophthalmology consultant – and that's the quickest you can do it.

One of the issues that new President of RCOphth, Ben Burton, wants to address is the effect of large numbers of ophthalmic procedures, in particular cataract surgery being done by Independent Service Providers (ISP) – the private sector contracted to provide NHS care. This has destabilized many NHS ophthalmology units and has to be addressed urgently.

I chair the British Ophthalmic Surveillance Unit (BOSU) and a few years ago we did a study looking at harms from delays to treatment in adults. We're repeating that study right now, doing so for children and hopefully this will help

What changes in pediatric ophthalmology do you want to see in the next 10 years?

I would like us to be successful in really getting the message out that pediatric ophthalmology is a fantastic subspecialty to go into. Your impact really shapes a patient's whole life. As an individual clinician, the impact you have when you first see a patient as a baby is immense. Improving childhood vision means improving health and life chances across a life course – and that's something unique. Academically, it has huge potential – you aren't confined to just one set of diseases. We tackle eye conditions in the context of broad health systems. We interface with pediatrics, education, and with social care, so, in a way, the pediatric ophthalmologist is the last of the generalists. You do everything – you are defined by your patient population. Even that's not static, as children grow and develop too. There's a breadth you just can't get from other specialties.

I think we see trainees far too late during their early training in ophthalmology – if there was one thing I'd change it would be to ensure ophthalmic trainees rotate to pediatric ophthalmology a little earlier and have more of a chance of experiencing this incredible subspecialty in its best light!

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

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

PATIENT COUNSELING INFORMATION

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

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

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

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

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

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

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

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

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

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

INDICATION

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

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

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

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

SYFOVRE™ (pegcetacoplan injection) 15 mg / 0.1 mL

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