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IMPORTANT SAFETY INFORMATION

Ulcerative keratitis can occur. Patients should be monitored for resolution of epithelial defects.

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These are not all of the side effects of the corneal collagen cross-linking treatment. For more information, go to www.livingwithkeratoconus.com to obtain the FDA-approved product labeling.

You are encouraged to report all side effects to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

*Photrexa® Viscous and Photrexa® are manufactured for Avedro. The KXL® system is manufactured by Avedro. Avedro is a wholly owned subsidiary of Glaukos Corporation.

REFERENCE: 1. Photrexa [package insert]. Waltham, MA: Glaukos, Inc; 2016.

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One Step Back

Recent allegations of image manipulation in a major Alzheimer's disease paper reaffirm the importance of research integrity

The latest scientific development to generate lively conversation in my friend group is the allegations of research fraud in a series of Alzheimer's disease-related research. This development has had us lamenting the falsification of medical research – and talking about the cost of this kind of activity. Coming from a previous life in a dementia research lab, the news has prompted speculation on the impact it will have on Alzheimer's research and beyond… even in ophthalmology.

If you haven't heard, allegations of altering research images were made against Sylvain Lesné at the University of Minnesota. These data manipulations were found in 20 papers, including a Nature paper from 2006 (100 years on from Alois Alzheimer's original description) in which a specific form of amyloid-β (Aβ), Aβ*56, was identified as a toxic oligomer in Alzheimer's disease. Aβ protein deposits are an archetypal hallmark of the disease and have been pursued by many as a target for therapeutic intervention. The falsified data has not only harmed Alzheimer's research since its publication, but could also foster further mistrust in the scientific and medical communities at a time when public trust in science is needed more than ever.

Consider sustainability. This falsification sent many researchers down the wrong path (most couldn't replicate Lesné's findings before the recent revelation came to light), draining researchers' time and money (mainly from public and charity sources) and consuming physical resources such as plastic that will increase the size of scientific investigation's already massive waste footprint.

It's almost certain that there are multiple research papers published with fraudulent data that are still running free. There is even a site dedicated to posting suspected data manipulations (1). Although this paper's claims must now be disregarded, many Alzheimer's researchers have stepped forward to highlight the good work being done on oligomeric Aβ and other Aβ species. Some even question the importance of the 2006 paper and the role of Aβ*56 in the disease. Such is the nature of complex disease – and the reason the mystery of Alzheimer's disease has yet to be resolved.

The net of doubt cast by fraudulent research and medical practice is not exclusive to any one field – but, hopefully, the allegations will not erode trust in ophthalmology. From a financial and humanitarian perspective, we can't afford to waste resources following false leads or undoing the damage done by irresponsible researchers. Although it may seem like common sense, it is vital to emphasize ethical research and clinical practices at every opportunity.

Geoffrey Potjewyd
Associate Editor

Reference

1. *PubPeer (2022). Available at: https://pubpeer.com*

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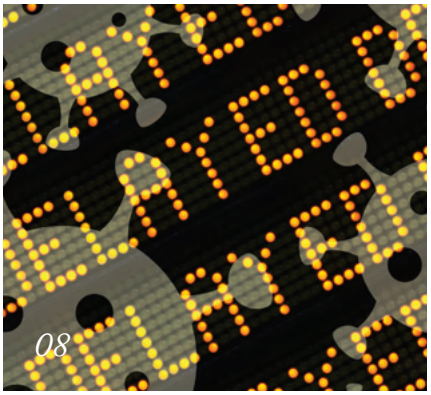
Contents



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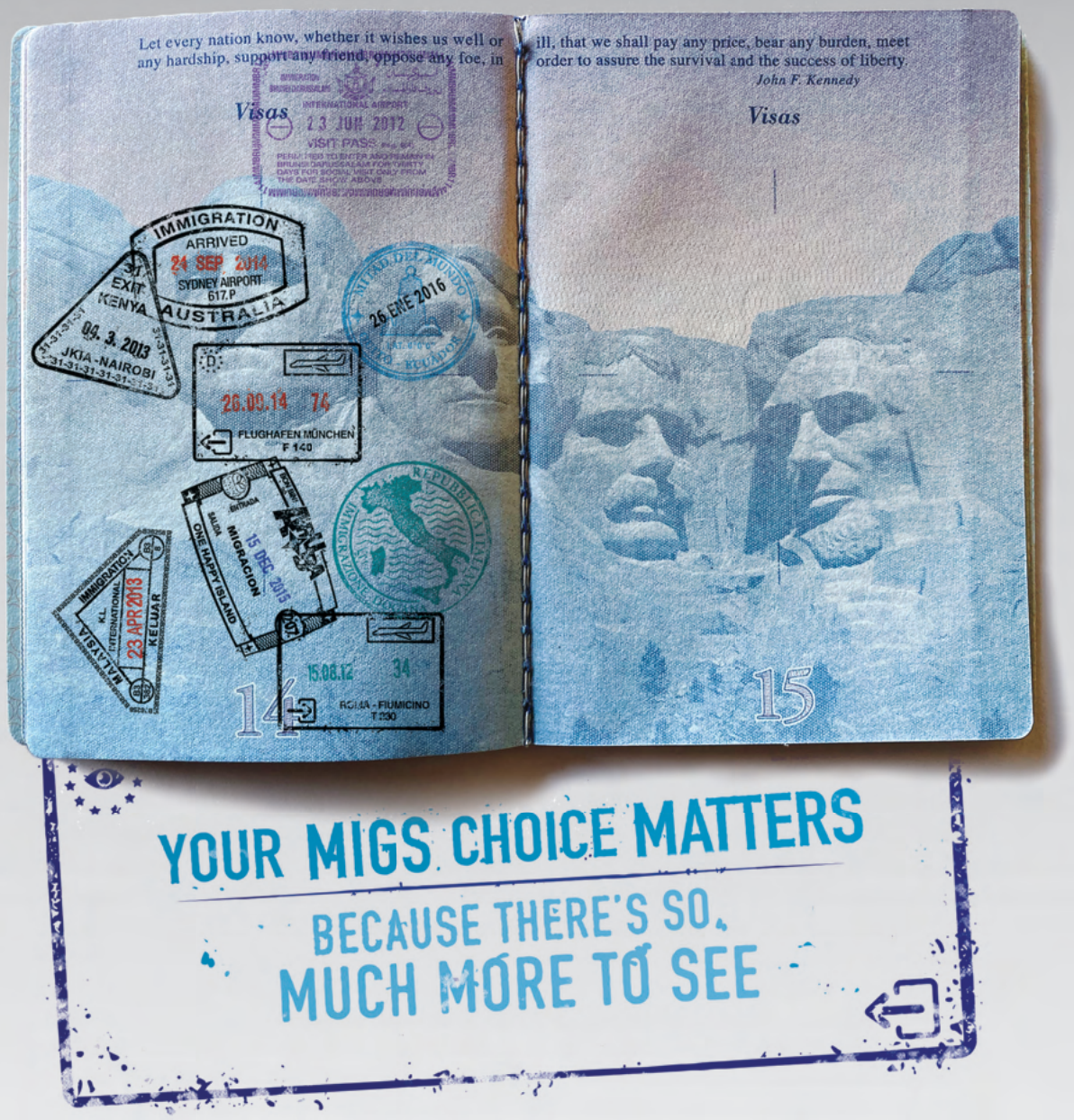

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- Established long-term safety at 60-months with comparable SAE rates reported vs cataract surgery alone[2‡]

*SSI = Secondary Surgical Intervention
† includes trabeculectomy, tube shunt, gel stent, ECP/TSCP, non-penetrating; (9/369 Hydrus and 10/187 CS)
‡ 13/369 (3.5%) in Hydrus eyes vs. 8/187 (4.3%) in the control eyes

Alcon

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IMPORTANT PRODUCT INFORMATION

CAUTION: Federal law restricts this device to sale by or on the order of a physician. INDICATIONS FOR USE: The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG). **CONTRAINDICATIONS:** The Hydrus Microstent is contraindicated under the following circumstances or conditions: (1) In eyes with angle closure glaucoma; and (2) In eyes with traumatic, malignant, uveitic, or neovascular glaucoma or discernible congenital anomalies of the anterior chamber (AC) angle. **WARNINGS:** Clear media for adequate visualization is required. Conditions such as corneal haze, corneal opacity or other conditions may inhibit gonioscopic view of the intended implant location. Gonioscopy should be performed prior to surgery to exclude congenital anomalies of the angle, peripheral anterior synechiae (PAS), angle closure, rubeosis and any other angle abnormalities that could lead to improper placement of the stent and pose a hazard. The surgeon should monitor the patient postoperatively for proper maintenance of intraocular pressure. The surgeon should periodically monitor the status of the microstent with gonioscopy to assess for the development of PAS, obstruction of the inlet, migration, or device-iris or device-cornea touch. The Hydrus Microstent is intended for implantation in conjunction with cataract surgery, which may impact corneal health. Therefore, caution is indicated in eyes with evidence of corneal compromise or with risk factors for corneal compromise following cataract surgery. Prior to implantation, patients with history of allergic reactions to nitinol, nickel or titanium should be counseled on the materials contained in the device, as well as potential for allergy/hypersensitivity to these materials. **PRECAUTIONS:** If excessive resistance is encountered during the insertion of the microstent at any time during the procedure, discontinue use of the device. The safety and effectiveness of use of more than a single Hydrus Microstent has not been established. The safety and effectiveness of the Hydrus Microstent has not been established as an alternative to the primary treatment of glaucoma with medications, in patients 21 years or younger, eyes with significant prior trauma, eyes with abnormal anterior segment, eyes with chronic inflammation, eyes with glaucoma associated with vascular disorders, eyes with preexisting pseudophakia, eyes with pseudoexfoliative or pigmentary glaucoma, and when implantation is without concomitant cataract surgery with IOL implantation. Please see a complete list of Precautions in the Instructions for use. **ADVERSE EVENTS:** The most frequently reported finding in the randomized pivotal trial was peripheral anterior synechiae (PAS), with the cumulative rate at 5 years (14.6% vs 3.7% for cataract surgery alone). Other Hydrus postoperative adverse events reported at 5 years included partial or complete device obstruction (8.4%) and device malposition (1.4%). Additionally, there were no new reports of persistent anterior uveitis (2/369, 0.5% at 2 years) from 2 to 5 years postoperative. There were no reports of explanted Hydrus implants over the 5-year follow-up. For additional adverse event information, please refer to the Instructions for Use. **MRI INFORMATION:** The Hydrus Microstent is MR-Conditional meaning that the device is safe for use in a specified MR environment under specified conditions. **Please see the Instructions for Use for complete product information.**

References: 1. Ahmed I, et al; HORIZON Investigators. Long-term Outcomes from the HORIZON Randomized Trial for a Schlemm's Canal Microstent in Combination Cataract and Glaucoma Surgery. https://www.aaojournal.org/article/S0161-6420(22)00160-9/fulltext 2. Hydrus Microstent Instructions for Use)

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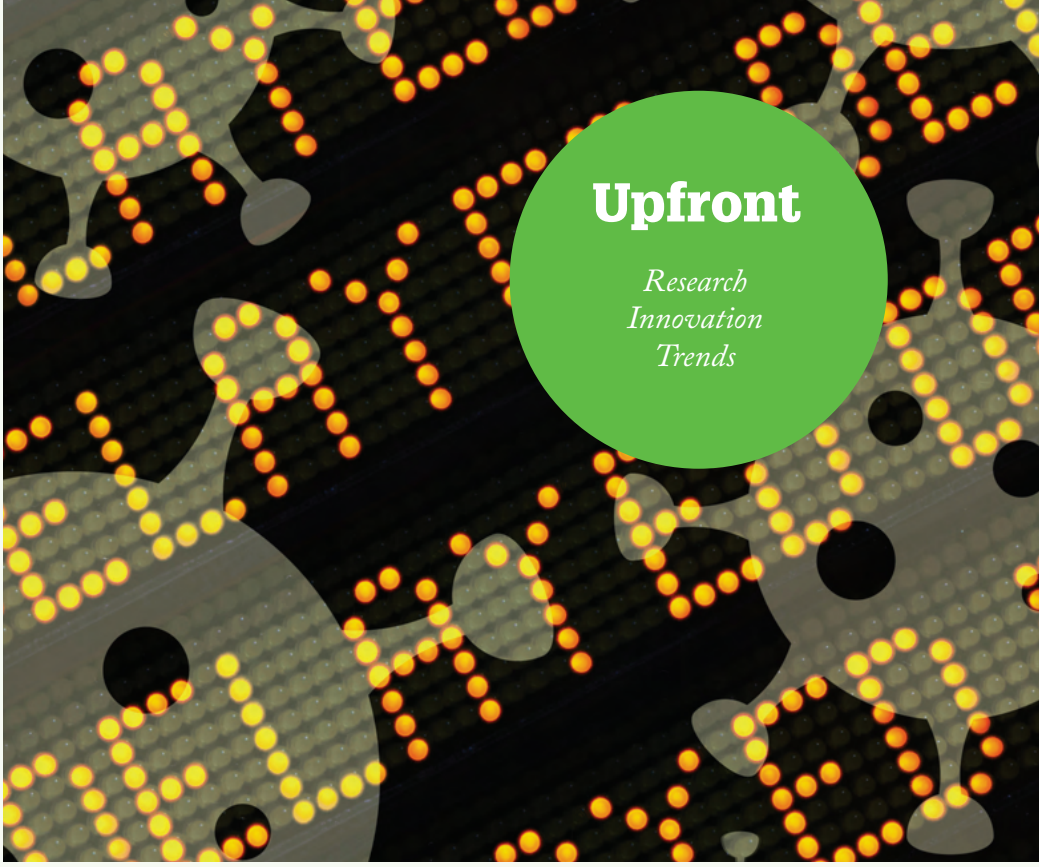

Delay No More

How has AMD progression been affected by pandemic-related anti-VEGF treatment delays?

The COVID-19 pandemic has not been good for ophthalmologists or patients. We have lamented the immediate effects of repeated lockdowns and elective procedure suspensions on our lives – and now the aftereffects of delaying ophthalmic healthcare are rearing their ugly head.

Researchers from Keimyung University Dongsan Hospital and Keimyung University School of Medicine in Daegu, Korea, found that delayed intravitreal anti-VEGF therapies during the pandemic led to a decline in best-corrected visual acuity (BCVA) and residual subretinal fluid height in neovascular AMD patients (1). Although previous studies have warned of BCVA worsening in AMD patients due to delays in anti-VEGF treatment, there has been limited data to show correlations between visual acuity and anatomical changes – a gap this study aims to bridge.

The study retrospectively used data from 57 neovascular AMD patients whose injections were delayed by at least two weeks. Researchers compared BCVA with anatomical changes, measured using OCT, both before and six months after patients received their anti-VEGF treatment. Through this comparison, they can ascertain that the differences in BCVA were caused by physical progression of the disease.

Interestingly, patients' AMD prognosis improved in the two to four months after the delayed treatment, yet faltered to below baseline after the six-month follow-up. This highlights the importance of adhering to scheduled treatments and appointments and emphasizes the need to avoid delaying anti-VEGF therapy in AMD patients. Understandably, given the primarily elderly demographic of people with AMD, a large proportion of these patients may have been avoiding contact and therefore missed appointments for fear of contracting COVID-19.

Given the huge impact of AMD worldwide, it is clear that the data acquired during the COVID-19 pandemic should be applied to future incidents – and that timely anti-VEGF treatments in AMD patients should be prioritized even in emergency situations.

Reference

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INFOGRAPHIC

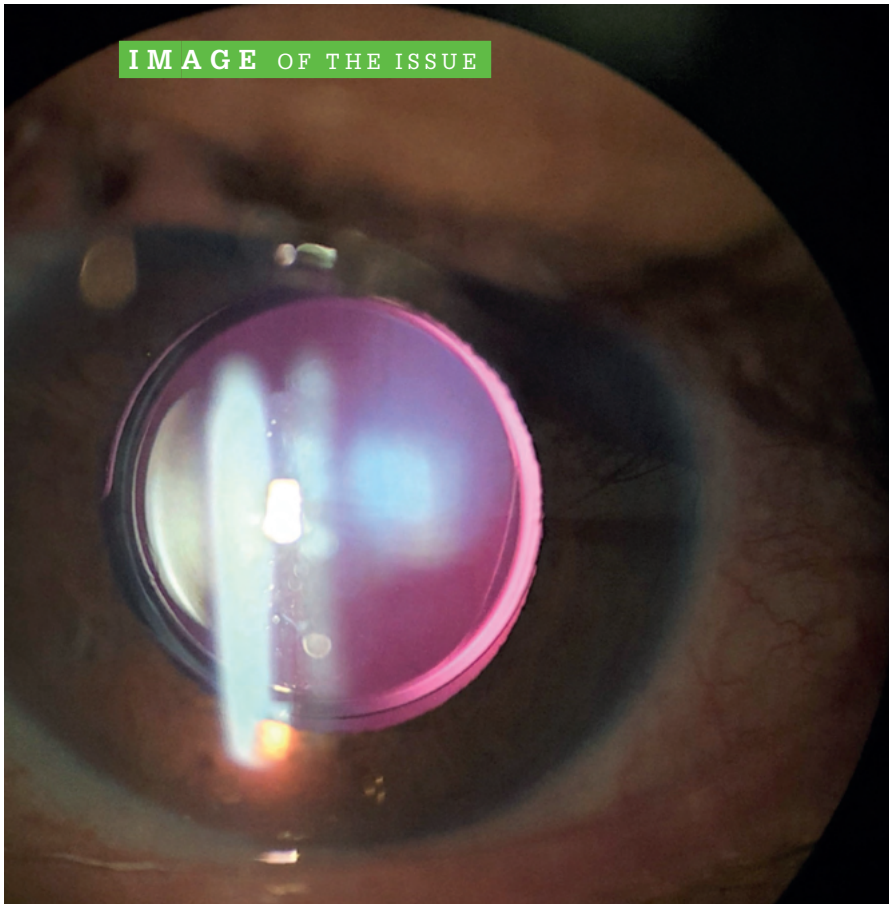
Glaucoma and Ethnicity

Black patients' risk of vision loss from POAG is much higher than for white patients

A Mount Sinai study analyzed close to **210,000** patients over **40**, with no glaucoma at baseline

Their lifestyle, diet, and medical status – including glaucoma diagnosis – was followed at biennial eye exams

IMAGE OF THE ISSUE



Credit: Background image sourced from Shutterstock.com

The Color Purple

This issue's image is a slit lamp photo, titled "(Tryptan) Blue Mixed with Red (Reflex) Equals Purple" by the author.
The image was taken with a Samsung SM-G960x.
Credit: Derek Ho, Department of Ophthalmology, University Hospital of Wales, Cardiff, UK.

Would you like your photo featured in Image of the Issue?
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Clearing the Path

Is treating cataracts without surgery a reasonable vision of the future?

Does surgical intervention have to be the only available cataract treatment? Researchers have been exploring the effects of topically administered oxysterol compounds on the optics of the lens. Oxysterol compounds have previously been found to interact with proteins essential for lens transparency, and as a result have been touted as potential anti-cataracts drugs.

As researcher Barbara Pierscionek, Anglia Ruskin University, Chelmsford, UK, explains, "The structural effect of oxysterol compounds on the lens has been examined in the past, but the effect on the functional aspects, the optics, which are critical to vision, has not been considered." In this pioneering study, the researchers observed that treating a murine model of cataracts with the oxysterol compound VP1-001 resulted in an improvement in refractive index profiles in the majority of lenses and a reduction in the lens opacity in nearly half of all cases (1).

See references online.

1,946 participants who developed glaucoma were divided into groups based on visual field loss

Ethnicity was a clear risk factor for early and advanced vision loss due to glaucoma

Black patients' risk of advanced vision loss was **six times** higher than for white participants, while Asian patients had a twofold higher risk of early visual field loss, but not of advanced vision loss

Reference
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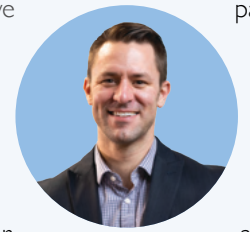
EVO ICL: Long-Lasting Quality of Vision

John Vukich, ophthalmologist specializing in presbyopia correction, refractive cataract surgery, and Implantable Collamer® Lenses (ICLs), and Nick Bruns, optometrist – both based at Summit Eye Care of Wisconsin in Milwaukee, Wisconsin, USA – discuss the increasing role that ICLs play in refractive surgery



How does lens-based refractive surgery compare with other available options?

Vukich: As a refractive surgeon, I want to have all of the available tools in my armamentarium, so the patients' needs are better served. The outstanding global experience with ICLs has established that they are not only an excellent optical solution, but also a very safe option.

Bruns: From my optometrist perspective, modern ICLs provide a great treatment option for our patients. The procedure does not disrupt the corneal tissue and the ICL is totally removable. Because the corneal tissue is left intact, patients may have more options available when it's time for cataract surgery later in life. It is also a great procedure for patients with a history of dry eye syndrome or surface irregularities.

What changes have you been observing in the field of lens-based refractive surgery?

Vukich: These days, all lens-based surgery aims to correct the refractive error. In the case of cataract surgery, it is very rare that the surgeon and the patient would not discuss the desired refractive outcome, and the ability to achieve it using high-technology lenses that either correct astigmatism or provide depth of focus or multifocality. There is also now an understanding that the intraocular space is the ideal location for refractive correction, so ICLs have certainly gained momentum, as more surgeons have also become aware of the selection of lens sizes. ICLs are a perfect example of how a good procedure gains recognition over time through the weight of available data, which continually show excellent outcomes.

I see how the ICL market has grown simply by word of mouth. There was a temporary pause during the early pandemic lockdowns, but the pent-up demand is now really coming to bear. With the recent approval of the EVO ICL in the US, surgeons are taking note of the new technology and the latest upgrade to the Visian Family of ICLs. The EVO ICL is available to be used in a wide variety of patients, with a great margin of safety!

Bruns: We're seeing growing numbers of practices offer ICLs. They help us offer patients a whole spectrum of options, with one or more available to them. Laser vision correction is a good option for many patients, but I anticipate ICL surgery being much more front of mind for a larger percentage of doctors and patients in the coming years, especially with the approval of the EVO ICL in the US.

Which phakic IOLs do you use in your practice and why have you made this choice?

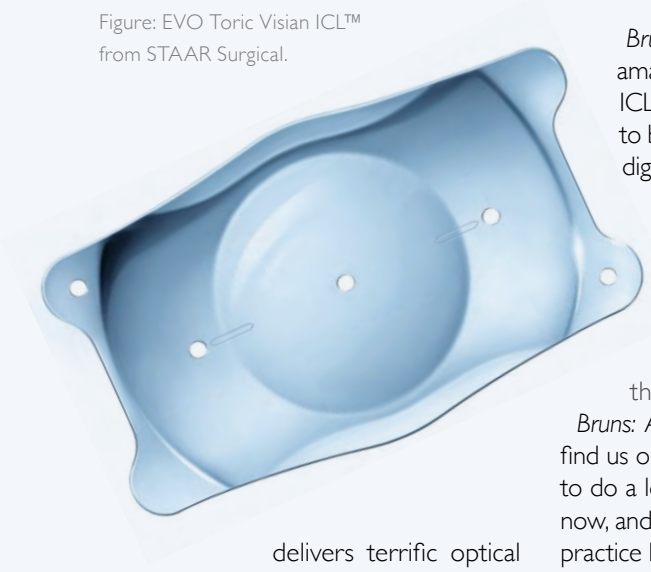
Bruns: Our surgeons exclusively use the EVO Visian ICL from STAAR Surgical. We find that – based on where the lens is placed within the eye – the EVO ICL

"ICLs are a perfect example of how a good procedure gains recognition over time through the weight of available data, which continually show excellent outcomes."
John Vukich

In the US, the EVO Visian ICL™ is

- Made from unique Collamer® material: poly-HEMA based Collagen co-polymer
- Indicated for patients between 21 and 45 years
- Used for the correction
- (-3 to -15 D) or reduction
- (-15 to -20 D) of myopia, with up to 4 D of astigmatism
- Visian ICL is backed by over 20 years of available implantation data, with over 2 million Visian ICLs isold worldwide
- Proven to result in improved visual acuity and excellent night vision (1)
- Removable by the surgeon if needed

Figure: EVO Toric Visian ICL™ from STAAR Surgical.



delivers terrific optical performance and gives excellent visual outcomes, especially for moderate to high myopes. The idea that it's removable is also appealing. It would be very rare for our practice to remove a lens, but simply knowing that this is an option is comforting for patients, especially those who dislike the idea of a laser-based refractive procedure.

Vukich: The EVO Visian Collamer® material has proved itself to be exceptionally biocompatable. The ICL not only achieves excellent quality of vision; our experience demonstrates that the results are sustainable over decades. With STAAR Surgical ICLs, we have in excess of 20 years of data, which makes me very confident that this lens is not only very well tolerated, but it also maintains excellent optical quality in the long run.

What impact has the use of ICLs had on your practice and what results have you seen?

Vukich: In my view, it is challenging to be a comprehensive refractive-based surgeon and not be offering ICLs. The lens has been an important part of my practice since the initial clinical investigations, and it is a great solution for many of my patients. The ICL has provided a dramatic improvement in quality of life for so many patients that I can't imagine not offering that option.

Bruns: The results have been just amazing: the visual quality with the ICL is much better than I expected it to be. Having patients in the double digits in the myopic range who are seeing 20/15 just a few days after surgery is pretty jaw dropping! The results are truly life changing for these patients.

Are you planning to increase the use of ICLs in the practice?

Bruns: Absolutely! Most of our patients find us on their own; we don't even have to do a lot of marketing for the ICL right now, and we're seeing that this part of the practice has grown significantly, especially over the past year or so. Partly due to the pandemic, we're finding a lot more patients seeking out options to get rid of glasses, and ICL has been a huge part of that. To give them the ability to see so well again without glasses or contacts is very rewarding.

For more information about the benefits and risks of the EVO Visian ICL, please refer to the DFU available at https://edfu.staar.com/edfu/.

John Vukich and Nick Bruns are consultants to STAAR and other ophthalmic companies.

References

1. *M Packer, "United States multicenter clinical trial of a posterior chamber phakic implantable lens with a central port for myopia or myopic astigmatism," Presented at ASCRS Annual Meeting; April 24, 2022; Washington, DC, USA.*
2. *E Martínez-Plaza et al., „Effect of the EVO+ Visian phakic Implantable Collamer Lens on visual performance and quality of vision and life," Am J Ophthalmol, 226, 117 (2021). PMID: 33577790.*

Important Safety Information for the Visian ICL Product Family:

The EVO Visian ICL is indicated for phakic patients 21-45 years of age to correct/reduce myopia with up to 4.00 D of astigmatism with a spherical equivalent ranging from -3.00 to -20.0 D and with an anterior chamber depth (ACD) 3.0 mm or greater.

The EVO Visian ICL is contraindicated in patients with a true ACD of <3.00mm; with anterior chambwer angle less than Grade III; who have moderate to severe glaucoma, who are pregnant or nursing; less than 21 years of age; and who do not meet the minimum endothelial cell density (ECD) listed in the Directions For Use (DFU).

A summary of the relevant warnings, precautions and side effects: Endothelial cell loss, corneal edema, cataract, narrowing of the anterior chamber angle, pupillary block, increased intraocular pressure, glaucoma, secondary surgery to reposition, replace or remove the ICL, loss of BSCVA, increase in refractive astigmatism, glare and/or halos, pigment dispersion, iris transillumination defects, endophthalmitis, hypopyon, corneal endothelial damage, ICL dislocation, cystoid macular edema, iritis, retinal detachment, vitritis, and iris prolapse.

Please review the DFU for complete safety and other information before performing the clinical procedure.

Six-Month Results in an FDA Study of EVO/EVO+ (1) Showed:

- Predictability and accuracy: 90.5 percent of patient results within ±0.5 D of attempted correction, 98.9 percent within ±1 D
- Excellent stability at 1, 3 and 6 months
- Post-op UDVA 20/25 or better for 97.2 percent of patients, 20/20 or better for 87.6 percent of patients
- Stable IOP

ALL EYES ON SUSTAINABILITY

Who better to ask about achieving sustainability in ophthalmology than the biggest names in the field? Read on to find out how John Hovanesian is collaborating with the industry on behalf of EyeSustain, how Oliver Findl is working to make the ESCRS Congress environmentally friendly, and how Dan Morris prioritizes sustainability in all his endeavors (and no longer has to chain himself to trees).


AIR

WASTE NOT, WANT NOT

For industry, sustainability and reducing waste has the potential to increase the bottom line

By John Hovanesian, specialist in cataract, refractive and corneal surgery at Harvard Eye Associates, Laguna Hills California and Clinical Faculty at UCLA Stein Eye Institute, California, USA

There is a clear desire for increased sustainability within ophthalmology. The Ophthalmic Instrument Cleaning and Sterilization Task Force, in a collaborative effort of the American Academy of Ophthalmology, the American Society of Cataract and Refractive Surgery, and the Outpatient Ophthalmic Surgery Society, conducted a survey of 1300 cataract surgeons and nurses and found that 93 percent believed operating room waste is excessive and needs to be reduced (1). In the US, a single cataract surgery generates as much waste as a typical person generates in an entire week of their daily activities. Across the country, we perform close to 4 million cataract surgeries per year. If you take the collective waste produced in all of those procedures, it is equivalent to the total waste generated by an individual person across their entire lifetime… if their lifetime lasted 66,000 years. This is already a staggering amount of waste to generate before you remember that that's in the US alone, and just a fraction of the world's cataract surgery waste. Although we are not likely to eliminate all of it, there are several wasteful practices that can be addressed. In the same way that we collaborate with industry to bring care to patients, we must collaborate if we want to reach our goals of reducing waste and increasing sustainability.

It is no secret that industry has disposables to sell, whether that be phaco needles that are discarded after each case – a practice we know to be unnecessary – cassettes or other disposable elements. There are definitely some disposable tools whose temporary nature genuinely benefits us. In the past, we used steel irrigation and aspiration tips, but with extended use they carried an increased risk of sustaining damage and developing irregularities that could cause complications such as capsule tearing. These were replaced by disposable silicone tips, which are soft and very consistent between cases, reducing the number of capsules torn during cataract surgery. Examples like this demonstrate that there are indeed some instances where we can justify throwing away temporary, small, and inexpensive temporary parts. However, we currently discard far more than this with each case, throwing away larger and more valuable equipment in a manner that is not particularly cost- or environmentally effective.

So what role does industry have to play in this?

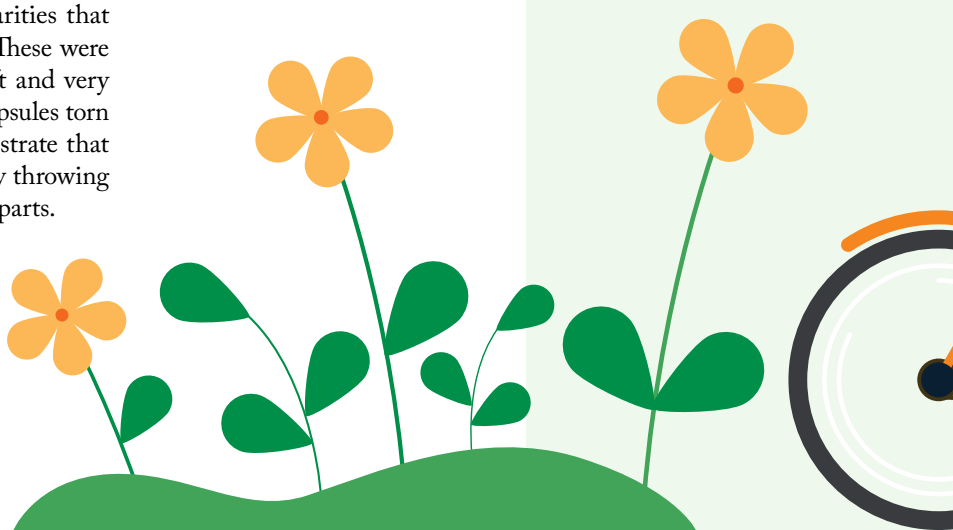
Naturally, companies want to sell products and that, at face value, creates a conflict of interest, as what we're aiming to do is reduce the volume of products discarded, which in turn means fewer products being sold. However, we have started off by approaching the larger companies in the field to begin a dialog, figuring out how we might be able to start reducing waste. I firmly believe that as we progress, industry will find meaningful ways to save the environment without having to sacrifice their bottom line.

One example of this is the "directions for use" that come packaged with IOLs. Previous regulations stated that this documentation had to be in every box. It was a large, folded piece of paper that contained many specifics in multiple languages. The truth is that nobody ever looked at it and automatically threw it away, along with the box, which had to be larger, increasing shipping costs. It had a real ripple effect on the manufacturing process and led to more waste. Everyone in our industry agreed that a QR code printed on the box or packaging, linking to the directions of use, would be a sensible way to mitigate this. Slowly, all IOL manufacturers are moving toward this more streamlined standard, allowing us to use less packaging and, as a result, because they are not charging any less for the IOL, increase their profit margin.

Green manufacturing

Similarly, a number of companies are moving to a green manufacturing process, becoming carbon-neutral globally. The goal is to make a meaningful environmental impact in a way that is "invisible" to the end user – the surgeon, nurses, and operating room staff. This takes some effort and does incur some initial costs but, in the end, it saves these companies money. Additionally, it's highly motivating for the workforce to know that they work for a company which is interested in sustainability.

However, there are many obstacles that industry faces in the move towards sustainability. We have all heard someone tell us that it's in our best interest to throw away material after every case because if we don't, we will face penalization by a regulatory body. We don't always know which regulatory



body that may be or whom to contact to even dispel such myths. This is something that's true for both companies and surgery centers. What we're trying to do, through the combined efforts of volunteers, is demystify the field. A necessary part of this is working with regulatory bodies, although the effectiveness of this can sometimes come down to the specific person within the regulatory body, their views, and their willingness to support what we are doing.

Companies also have to go through similar processes to implement change. As bigger companies tend to operate in more countries, they have to navigate more regulatory environments, are usually under greater scrutiny, and subject to facing greater penalties than smaller companies, meaning that they have to be more careful. On the other hand, they can have a far greater impact as, for a bigger player, a small change can truly add up, which is a great motivator for taking action. Some of the bigger companies have made changes to their evaluation process for prospective products, meaning that alongside factors such as a product's efficacy or sales projections, sustainability will be taken into consideration. This is again a seemingly small change, but the future benefit of this could be immense.

"WHILE IT MAY SEEM INITIALLY THAT SUSTAINABILITY INCURS COSTS, REDUCING WASTE WILL BE GOOD FOR ALL OF US – PATIENTS, MEDICAL PRACTITIONERS, AND INDUSTRY PROFESSIONALS."

Sustaining eye care

As part of EyeSustain, a new, multi-society sponsored sustainability group, we want to celebrate and recognize various achievements and efforts. At the ASCRS meeting in Washington, DC, when EyeSustain was launched under the leadership of David Chang, we held a session where we heard from a number of large and smaller companies about sustainability initiatives and efforts that each is making. The larger companies are not necessarily far ahead of their smaller counterparts in this area. Both groups are making dramatic changes, such as decreasing their packaging, saving energy, recycling in the manufacturing process or allowing products to be reused. It was encouraging to hear of the many initiatives that are being undertaken in the field, and it was truly an opportunity for those who attended to celebrate the successes of their compatriots. There is no competition when it comes to sustainability; we're all in it together. Companies can and should learn from each other, and EyeSustain is definitely seeking to help with such efforts. In the future, we hope to have standards in place so that companies can periodically be assessed on the effectiveness of their sustainability efforts to earn accreditation as a sign that their efforts are sincere and effective.

There is good evidence that when it comes to sustainability, profits do not have to suffer. While it may seem initially that sustainability incurs costs, reducing waste will be good for all of us – patients, medical practitioners, and industry professionals – and our individual goals in the long run. Nobody wants to benefit or make money by damaging the environment. While it could be easy for companies to look away and decide that the only their bottom line matters, they have already demonstrated more altruistic motives. Companies are recognizing the importance of sustainability and its scope and are rising to meet that challenge. We really are just at the beginning. We have reached a point where the consumer is acutely aware of the problems of climate change and global waste and recognizes the need for true change. People have already shown that they will be willing to spend money on sustainability in the same way that they do for other factors of importance, such as safety and efficacy, making sustainability worthwhile for everyone touched by the procedures we perform.

See references online.

CLEANING UP CONGRESS

ESCRS President Oliver Findl shares how the organization is moving towards a more sustainable future in both the operating rooms and the conference halls

What led you to the idea of making the ESCRS Congress more sustainable?

I first became aware of the climate emergency and the need for pursuing sustainability quite a few years ago through my daughter who, like a lot of the younger generation, is enthusiastic and highly motivated about being more sustainable. Then, a couple of years before the COVID-19 pandemic, together with other ESCRS decision makers, I looked into the idea of making the Congress sustainable, and one of the things we considered was how much carbon we would need to offset for delegates' flights. When the COVID-19 pandemic came, our focus naturally shifted, but now that things are quieting down again on that front, ESCRS is bringing sustainability back into focus with two goals in mind: the first is making the Congress more sustainable, and the second is incorporating sustainability into surgeons' operating theaters.

Ahead of the upcoming 2022 Congress in Milan, Italy, we have sought the guidance of The Global Destination Sustainability Movement (GDS) to track, report on, and generally help with the project. We have a number of initiatives that we are looking to implement. All delegates will have the option of donating a few extra euros to offset their travel. We will have a relaxation lounge for people to engage in self-care. We're encouraging our members to bring a reusable bottle and use the water fountains that will be located throughout the congress center to avoid the use of thousands of single-use plastic bottles that we would usually go through. We're also looking to serve less meat. Any leftover food will be donated instead of thrown away. One of the most important factors will be our green partners, non-governmental organizations who will be able to offset the Congress' carbon emissions, supporting projects that benefit the less fortunate. Milan is just the first step as we will be analyzing data throughout the conference and afterwards to see what we can do better for the 2023 Congress in Vienna, Austria, for which I have the goal of being carbon-neutral.

How far are you from a carbon-neutral Congress meeting?

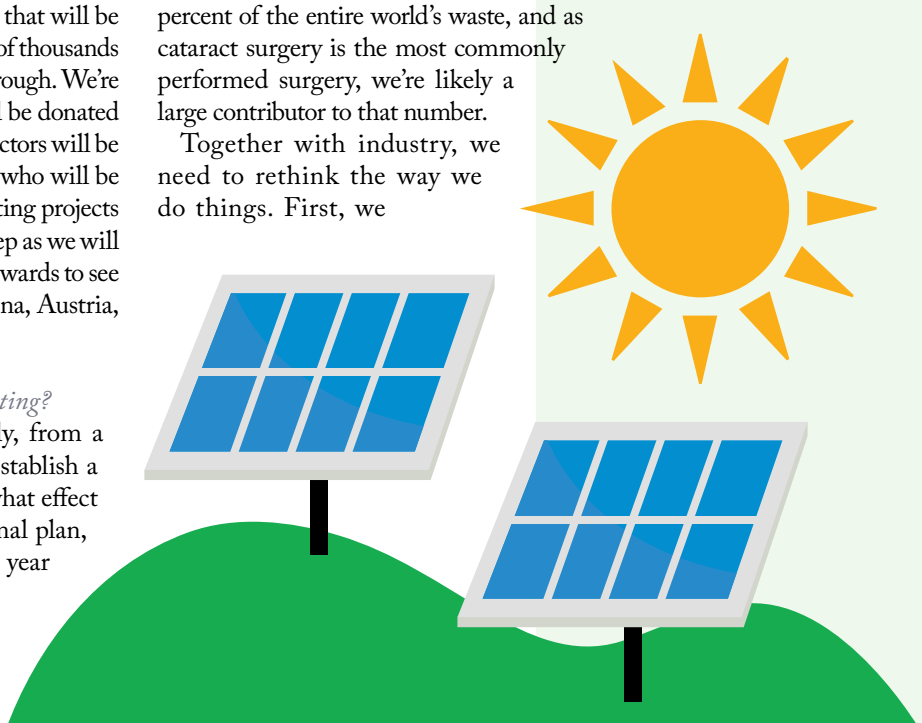
Honestly, we will only know after Milan. Ideally, from a research perspective, we would analyze Milan to establish a baseline before we make any changes, to truly see what effect each of the initiatives has – and that was our original plan, but I feel like we don't have the time to let another year pass before we take action; we have to act now. We also don't have the scope to retroactively compare previous congresses as we weren't monitoring all of the required data points. We did a review of the Paris Congress in 2019, looking at where all of the 9,500 delegates came from, but I am not sure how applicable the data will be to this year as some things will likely be different as a result of the COVID-19 pandemic. We are expecting fewer people coming from outside of Europe.

This analysis will still give us a good place to work and improve from, and GDS will be taking note of a lot of data points. They will be looking at the amount of electricity we use, the carpets used for soundproofing, which currently have to be thrown out afterwards, the industry partners and their booth setups, the amount of paper and the number of plastic bottles used. We will also be looking at the hotels, flights, and other elements, so we can get a holistic view to make plans for the next few years. After the conference, GDS will produce a report, and that's when we'll truly know how close we are to the goal of being carbon-neutral.

What is your approach to working with the industry to achieve sustainability?

The truth is that we won't be able to reach the goal of being carbon-neutral as a Congress alone, it's a combined effort. I know that industry is very aware of the topic of sustainability, and we're really starting to see them get on board with it. Touching on our other goal of instigating sustainable changes in the OR, we have a lot of projects aimed at this. Currently, we use a lot of disposable instruments that end up as infectious waste, which is incinerated according to European guidelines. We're looking at ways to make the production chain more sustainable and finding ways to measure and assess that. Medical waste makes up around 5 percent of the entire world's waste, and as cataract surgery is the most commonly performed surgery, we're likely a large contributor to that number.

Together with industry, we need to rethink the way we do things. First, we



need to challenge the regulations put into place over the last 30–40 years that are restricting our ability to reduce waste, without reducing quality and hygiene or increasing the risk of infection. This will be a long process as we will need studies to prove safety and convince politicians and lawmakers. We also have shorter-term goals. One project that ESCRS will be leading together with EyeSustain is the development of a Sustainability Index for cataract packs. These packs are one of the major contributors to our waste, so we need to check how sustainable they are and how different packs compare. An index like this could be incorporated into tender processes, allowing clinicians and hospitals to factor sustainability into their decision-making process; something that would likely motivate companies into further investments into sustainability. It needs to become a part of doing business.

Are there any steps for working with the industry to increase sustainability that have already been implemented in Europe?

There's a difference between the US and Europe when it comes to the regulatory systems. In the US, regulation stopped surgeons from reusing eye drops between patients. In Europe, that was never really an issue because we have always reused bottles. David Chang from ASCRS has been instrumental in getting sustainability projects and partnerships going with EyeSustain. He's had a close connection to India and has really analyzed the way cataract surgery is performed at Aravind Hospital – with very low endophthalmitis rates, but using a lot of reusables. I think there are important questions we need to ask: how can we change the regulatory environment to allow us to work in a similar way to Aravind? The answers will differ between the US, Europe, and other continents, and between countries. It's a big undertaking, but EyeSustain will help with that. It is a network where we can exchange ideas so that if somebody has already achieved one goal, we don't have to reinvent the wheel.

I'm really looking forward to Milan, because we have planned internal meetings with industry at the Congress. We've planned an Innovation Day, a new symposium-style event where KOLs and industry representatives will meet to talk about new trends, and view presentations from startup companies. I'm really hopeful that we'll have a very useful discussion on how we can move forward.

What steps have you already implemented in your practice or will do soon?

Austria is a small country, with nine million inhabitants and around 33 hospitals that do cataract surgery. This means that we all know each other, which makes it easier to analyze data. One thing we looked at was packaging of tools and consumables needed for cataract surgery. We sent samples to a company for analysis of the materials used and we found that there was a lot of variation between packages in terms of their size and components. We also noted that for each pack of four knives, only one or two were needed per surgery. Surgeons have different knife preferences, but this means that from every pack, at least two knives are thrown away without being used. As a result of this, we set a benchmark for the minimum accepted package needed for cataract surgery, which led to a reduction in carbon emissions of 25 percent.

Another thing we noticed was that we rarely recycled because we had no way to easily determine which plastics were okay to recycle and which were not, making the process a hassle. We do have a lot of ideas for improvement; one is to recycle the titanium within phaco tips by sending them to the supplier to melt and reform new tips, reducing the need to mine titanium. We need to look into the details of this, but some industry partners are very enthusiastic.

As ESCRS President, how do you avoid greenwashing?

We are aware of greenwashing and have definitely tried to avoid it. I can't say that we are "green," because we aren't yet. We've set up a Green Group of 12 young ophthalmologists who will be coming up with many new ideas and making sure our steps are constructive and they make a real difference. The Sustainability Index will show us the true positive impact of our Congress changes.

I think when it comes to sustainability, everybody has to give something away, compromise. For us, it's likely going to be convenience. Right now, I can just open a package and everything I need for cataract surgery, and more, is there – but this may need to change. For companies, it may mean selling fewer products. Individually, we also have a responsibility. We're going to have to use less heating in the winter and less air conditioning in summer. Maybe we need to reduce our meat intake. We all need to sacrifice something for the greater good and I think the same will hold true for the cataract surgeon, for any eye care professional, for the industry, and for the patient.

LOOK UP

How we can turn the tide of sustainability to our favor in ophthalmology

By Dan Morris, specialist in cataract and oculoplastic surgery based in Cardiff, UK

Gone are the days when people engaged in sustainability were labeled tree-huggers, or just plain weird. Finally, it has become the mainstream, and that is really gratifying. These days, I am a specialist in cataract and oculoplastic surgery based in Cardiff, UK, but back when I was a student, I was chaining myself to nuclear power stations and getting dragged off by the police – I am a bit more sedate these days, but the passion to preserve our environment still burns inside. I've been interested in this topic throughout my life, and now that I am at last seeing colleagues and younger doctors taking up the mantle of sustainability, and I am very happy to support them. Given the current rate of climate change, this was just a matter of time, and there is now a sense of urgency and a state of emergency.

The big issues in ophthalmology

I picked cataract surgery for our 2013 sustainability-focused paper (1), because it's the most common procedure that we as ophthalmologists perform. It's also an operation that's producing a lot of waste. The study was intended to raise awareness, and at the time it was unique in looking at the carbon footprint of a surgical procedure. The idea was that benchmarking this and raising awareness might make surgeons stop to think about how much waste they are producing. Thankfully, other papers have come out since then, and we've developed an app called Eyefficiency that allows surgeons to look at surgical throughput and efficiency as well as the carbon costs involved. According to our calculations, one cataract operation is equivalent to about 180 kilograms of CO_2 equivalent greenhouse gases, which is about the same as a flight from London to Geneva. When you consider the hundreds of thousands of cataract operations performed, every surgeon should be thinking of ways to reduce this carbon burden, and there's a lot of low-hanging fruit. One simple way is by dropping the post-op visit to the office, with the patient visiting an optometrist instead. This has worked well in the UK, but may not be appropriate in other countries. Another example is the intraocular lens that we put in during every cataract surgery, which comes in a plastic box that weighs 200 grams, with a 68-page booklet in many different languages, all of which just goes straight in the waste, often to be incinerated and not even recycled. When you consider the number of operations that we're doing, it starts to add up. Little things like this should be easy to change and can make a big difference.

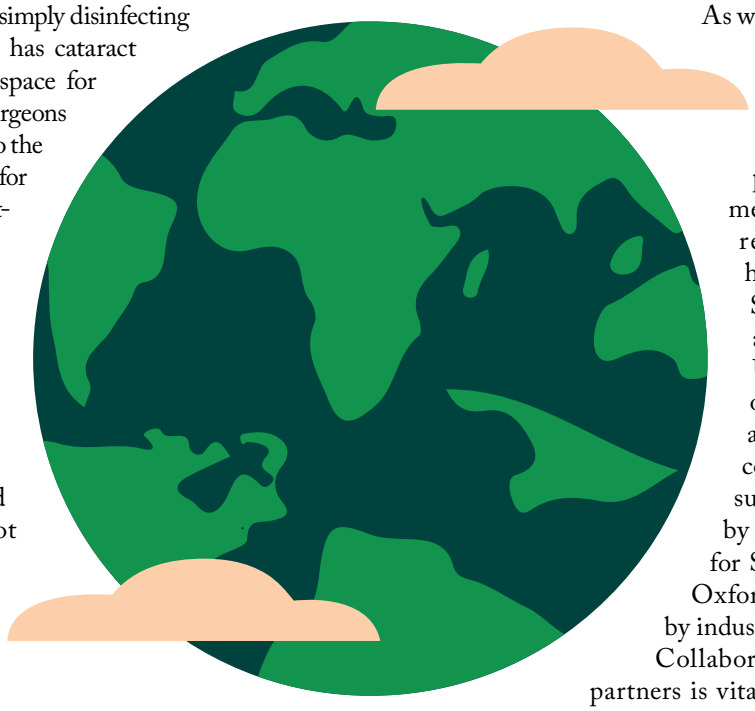
Part of the bigger conversation in sustainable surgery circles is about disposable versus reusable instruments. Reusables are better for the environment, but if the disposables that we do have to use were made in an ethical and environmentally friendly way, so you could recycle rather than incinerate them, they could become a more reasonable, sustainable option. Even the reusable instruments can have a high footprint, especially if the cleaning and sterilizing is performed off site in an inefficient way. This discussion needs to happen in all surgical facilities across the world.

The argument for immediate sequential bilateral cataract surgery is gaining traction and will eventually become the norm during routine surgeries and this will be much better for the patient and the environment. There is a very small risk of bilateral complications, but it is outweighed by the improved patient experience, increased efficiency, and decreased carbon footprint. However, it needs to be introduced in a safe manner so that the whole team is comfortable – and patient selection is of course vital. There are still

political and financial obstacles to overcome and it will take time, but the clock is ticking.

Learn by example

The carbon footprint of cataract surgery differs widely across the world. One of our American colleagues compared our findings in the UK with Aravind Hospital in India (2), and found that only 6 kg of CO2 equivalent greenhouse gases were produced for each cataract surgery, as opposed to 180 kg in the UK, with similar visual results and fewer complications. This is almost embarrassing; the sheer efficiency of Aravind is clear. There are many small and simple things that make a difference overall, like using the same pair of gloves all day and simply disinfecting between operations. Aravind has cataract ORs known as barns, with space for four patients in a row where surgeons move rapidly from one patient to the next. This may be hard to palate for many surgeons, especially post-pandemic, but it works in India, so we should learn from it.



Sustainability is not just about saving the planet, or indeed saving money, although the two usually go hand in hand. The third aspect of the triple bottom line of people, planet, and profit are the people – not just our patients, but also our colleagues and the healthcare workforce in general. We cannot hope to achieve any of our goals without a sustainable workforce who are well looked after. Right now, in the UK, we are facing the biggest workforce crisis ever across the board, and our political leaders need to urgently address the issues that make doctors and nurses leave the profession in droves.

Setting an example

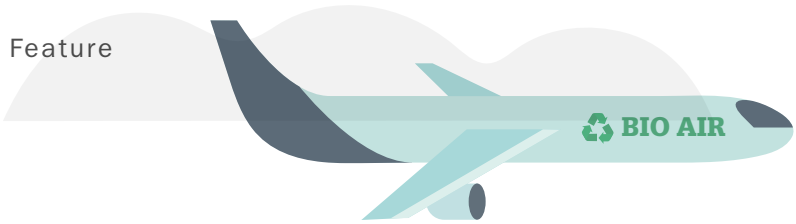
One of the questions I always get asked by colleagues is "What can I do and will it make a difference?" My answer is twofold, firstly: if everyone does a small amount, this will make a big difference, and secondly: as healthcare leaders, we have a massively important contribution to make by influencing others who look up to us to set an example. With that in mind, look at everything you do, and try to make it more sustainable by working out how you can make a positive impact on that triple bottom line of people, planet, and profit, which is not just saving money, but saving the environment, and making sure the workforce is happy. That starts at home from when you get up in the morning until you get back into bed at night. Consider the type of coffee you're drinking, the water you're using up, the transport you're relying on, whether you're leaving the lights on. At work, appraise everything you are doing both in and out of the OR and do your best to influence others in a positive way.

Evidence driven collaboration

As with any changes in clinical practice, they must be evidence-based, so we need to collect data, run audit cycles, use patient-related outcome measures, and publish our results. Therefore, we have set up a network of Sustainability Fellows and Scholars across the UK, relying on junior ophthalmologists, but also allied professionals, to help collect this data. They are supervised and supported by colleagues at the Centre for Sustainable Healthcare in Oxford, and often sponsored by industry.

Collaboration with our industry partners is vital to make our profession more sustainable, as the procurement aspect of our carbon footprint is by far the biggest component. These companies already have sustainability policies and are looking hard at their end product consumers as we start to question the environmental and ethical credentials of their products. Bausch + Lomb has been hugely supportive of our initiatives in the UK, sponsoring our clinician network, funding a sustainability prize at our Royal College of Ophthalmologists (RCOphth) Annual Congress, and designing a lean phaco pack. Thea Pharmaceuticals has also been very forward thinking in this area, helping interested junior ophthalmologists achieve their goals with sustainability scholarships and online learning.

Through these initiatives, we have been able to embed ourselves



"TECHNOLOGY IS KEY TO ACHIEVING GOALS IN SUSTAINABLE HEALTHCARE, BUT ONLY IF USED WISELY."

into the RCOphth in the UK with a sustainability working group and therefore influence other policy decisions on how to make ophthalmology more sustainable, and I would encourage other countries to do the same if they have not done so already.

The times are changing

There are some places in the world where the effects of climate change are more obvious; when I started studying medicine 25 years ago, I enjoyed ice climbing in Scotland and venturing further afield to the Alps and the Himalayas for more challenging climbing. Now that ice has gone, and the glaciers I used to trek up have receded. When I was an ophthalmology trainee, I started an eye clinic in Northern Kenya, and now the weather patterns there are so disrupted that survival is a struggle, with the region blighted by drought one year, and extreme flooding the next.

With the climate changing so rapidly, it is encouraging to see medical schools trying to embed sustainable healthcare and quality improvement into the curriculum. The students are far more aware of the issues and how it will affect them in their lifetime so we encourage them to question and challenge the practices they see in our hospitals, especially if they can see a way to improve it. It is also very positive to see some senior colleagues respond to this and finally think about sustainability.

Embracing tech

Technology is key to achieving goals in sustainable healthcare, but only if used wisely and with the same rigorous evidence-based approach that we use for other changes in clinical practice. The pandemic proved that many tasks, meetings and consultations can be done virtually and should continue in this way. There are exciting developments in the world of AI, especially in the world of screening as well as robotic surgery and 3D printing for customized prosthetics, which has revolutionized other specialties.

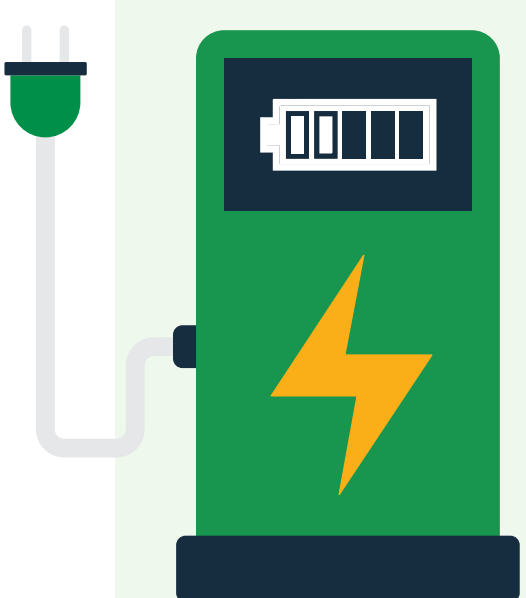
The bigger meetings and conferences that we all love have had to adapt fast, both to the pandemic and concerns over their carbon footprint. Gone are the hefty printed programs, the piles of conference bags, and plastic freebies, and I think hybrid events are the best way forward, giving people the choice as to whether they want to travel; they also allow delegates from overseas to take part at a greatly reduced rate, which helps minimize global inequalities.

Every little helps

We need a bold vision for sustainability in ophthalmology, and the core of that vision should be carbon negative cataract surgery. We have to make ORs as efficient as possible, with solar panels on the roof, and more efficient ventilation systems, perhaps radically re-designed. We designed a carbon neutral cataract theater suite, which we're hoping someone will build, and we were shortlisted for a national BMJ Award as a result. It may also be possible to offset the carbon footprint of surgery, for example by planting trees locally, but these strategies need to be approached cautiously to avoid greenwashing.

The UK government has ambitious decarbonization targets for healthcare as well as the rest of the economy, and we are well behind on that at the moment. In the end, legislation might have to be introduced to improve sustainability in healthcare, but doing it ourselves rather than being forced to do it will be far less painful.

Getting people thinking about sustainability is so important, but actions speak louder. A lot of people just think, "There's no point in me cycling to work, because no one else is," but if enough people started cycling to work, then the workplace would have to build a secure bike pound and provide better cycle lanes. The same principles apply to introducing changes to our surgical practice. We have to act now, and every little bit done by each of us counts.



See references online.

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With the Light Adjustable Lens™ from RxSight®, your patients can test drive their vision after cataract surgery. Show them the vision that's possible—with their own eyes.

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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 brochure. 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 Brochure for a complete list of contraindications, warnings, precautions, and adverse events.**

RxSIGHT

Thomas Bernhard
CEO
Haag-Streit Group

What is your vision for achieving sustainability in eye care?

There are two distinct aspects – the present and the future. Firstly, I see our current organization, which is totally committed to sustainability and has already optimized its processes in many areas – group-wide. However, I also see great potential in the future, with new and innovative projects that embrace solar power, waste reduction, and recycling in our Haag-Streit sites around the world. In addition, I foresee exciting future sustainable solutions for our eye care customers, such as developments in teleophthalmology, AI, and VR. My vision encompasses increased longevity of diagnostic medical devices in the market. Notably, Haag-Streit's "gold-standard" slit lamps are renowned for having an extremely long life-cycle – many are still fully operational despite being more than 50 years old!

During the design and development of our solutions, our engineers pay very close attention to sustainability and reliability, as well as robustness. Haag-Streit is famous for these features, which are highly-appreciated by our customers, worldwide.

I would like to see less plastic in manufacturing, not only to increase longevity but also because it has a major impact on the environment. Plastic does not break down naturally, and pollutes natural systems, including rivers and oceans. The production, use, and disposal of plastics also creates significant greenhouse gas emissions throughout the various stages of the plastic value chain.

Another goal would be to see a reduction in single-use medical supplies and an increase in reusable supplies, such as micro-surgical instruments. Our own John Weiss brand of "gold-standard" stainless steel and titanium reusable instruments has been established for over 230 years and continues to be distributed worldwide – as a group, we were very early sustainability adopters!

How has Haag-Streit worked towards achieving its sustainability goals?

Sustainability is a global challenge and Haag-Streit recognizes that it has a responsibility to help society meet its current human, social economic, and environmental needs without compromising future generations. This commitment has been baked into our DNA for many years. We use four pillars of sustainability to drive our goals: employee development and motivation, climate and energy, sustainable use of resources, and social responsibility.

Our primary contribution to society is to develop high-quality, premium solutions addressing our customers' needs in terms of effectiveness, while saving natural resources and complying with environmental laws and regulations. We integrate environmental considerations throughout our business when developing new products or planning new manufacturing plants. We constantly improve the performance of our solutions, and our own production facilities.

As a member of the Metall Zug Group, we closely observe its "Code of Conduct," and we follow such rules both in letter and in spirit. The entire Metall Zug Group consistently pursues a mid-term net-zero-emissions-goal.

HAAG-STREIT GROUP

Look closer See further

www.haag-streit.com

Jeannette Bankes
President and General Manager, Global Surgical Franchise
Alcon

What is your vision for sustainability in eye care?

Sustainability is a key pillar of Alcon's Environment, Social and Governance commitment, alongside championing access to eye care for all. We regard sustainability as an opportunity to improve lives and strengthen communities through eye care and caring for our planet at the same time. As we manufacture around 90 percent of our products internally, we have the ability to reduce their environmental impact (1). With our customers and industry partners, we can make a positive impact on the environment.

What steps has Alcon taken towards achieving your sustainability goals?

We are focused on three key areas: incorporating sustainability into product development, reducing product-related environmental impact, and reducing operational environmental impact.

We've implemented a Sustainability Scorecard into our R&D processes to ensure we are integrating sustainability measures immediately from the inception of each new product. We're also finding solutions to reduce our packaging and shipping waste through internal projects such as our Green Innovations Surgical Team (GreenIST) and surgical equipment refurbishment program.

Which innovations have affected your sustainability goals?

Since the establishment of GreenIST last year, we have created a version of our Centurion® Fluid Management System (FMS) within a Custom Pak® without its tray or lid, reducing FMS waste by 90 percent (2). The impact is three-fold – minimizing waste, plastic usage, and our carbon dioxide footprint.

GreenIST also identified other opportunities, including replacing packaging Styrofoam with Green Cell foam in the US for shipments of our Ophthalmic Viscosurgical Devices. Green Cell foam is sustainable, functional, biodegradable, and dissolvable in water (3). This has eliminated more than 12,000 lbs of waste and more than 100,000 lbs of Styrofoam annually (4). GreenIST has also helped implement the removal of printed Directions for Use booklets in some markets, decreasing the total weight of certain intraocular lens packages by 53 percent (5).

We are proud to share that this year, three Alcon facilities received the GreenCircle Zero Waste to Landfill Certification for diverting 100 percent of total waste from landfills, making Alcon the first healthcare company to be GreenCircle certified for Zero Waste to Landfill operations.

One other key advancement involves Alcon becoming the first eye care device company to allow customers to perform carbon neutral cataract surgery. Alcon UK & Ireland partnered with Sandro Di Simplicio, consultant ophthalmologist from the Newcastle Eye Centre, and the Newcastle upon Tyne Hospitals NHS Foundation Trust, on the pilot program. The carbon management plan was audited by the National Quality Assurance, granting PAS 2060 verification, an internationally recognized standard in achieving carbon neutrality.

See references online.

Alcon

www.alcon.com

The ART of EYES

Eyesight, arguably the most precious of our senses, is naturally associated with perceiving beauty, and many artists are preoccupied with capturing the intriguing organs we use to view the world. We present this year's best ophthalmic images, through the eyes of photographers, cartoonists, and painters, as well as those using artificial intelligence in their artistic pursuits – a true feast for the eyes.

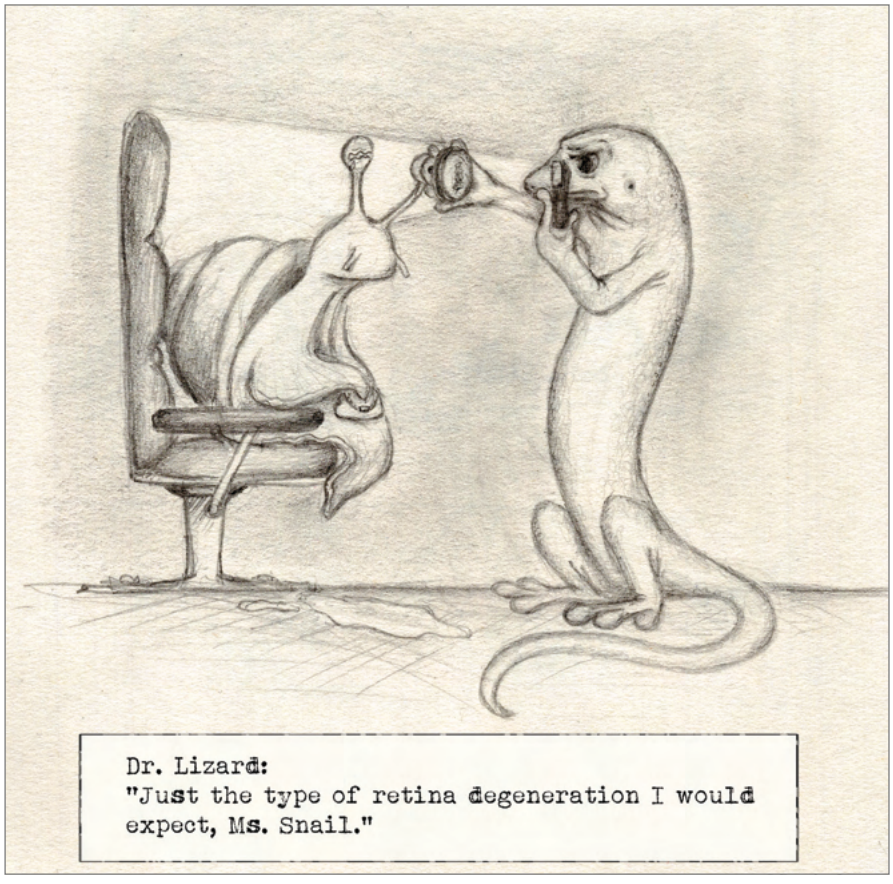
Credit: Karl Taylor, "The Valley of Litter"

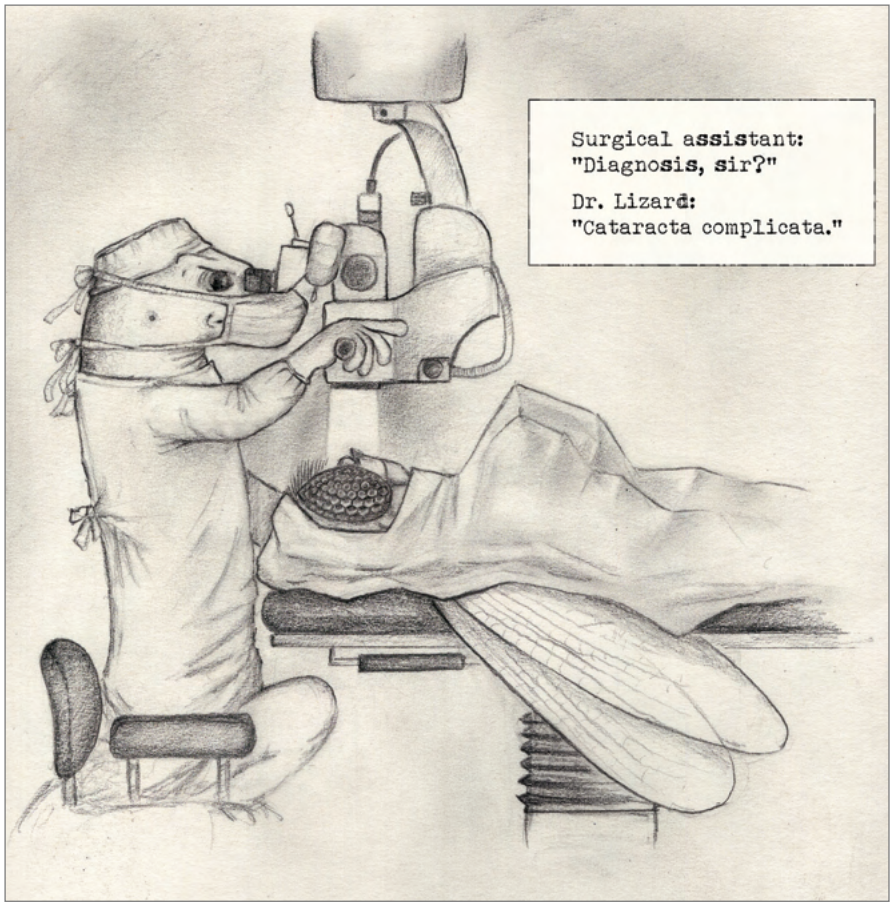
INTELLIGENT DESIGN

Nima Ghadiri is a Medical Ophthalmology Consultant and Honorary Senior Lecturer, Liverpool University Hospitals NHS Foundation Trust.

"All of the images are created by the same process: I've used my own brush strokes, paintings, sketches, or drawings on either canvas or paper. These are then scanned and inserted within a deep learning algorithm that interprets the style (using a "tokenizing system"). Then I use an image of the eye, either one of my own or a stock, as the input image, and apply the algorithm to get these outputs."

See more images on our website.





DR LIZARD AND HIS PATIENTS

Dorothea Laurence has just completed her first year of ophthalmology residency at Dr Hoffmann's Eye Clinic in Braunschweig, Germany. She graduated from the University of Göttingen medical school, where she also completed her doctoral thesis and received the German title of "Dr. med."

She comments: "In my spare time, I love to illustrate and do calligraphy; my favorite media are dip-pen, ink and watercolors. I have a special love for children's book illustrations, inspired by my two young daughters, and animal characters. Dr Lizard is illustrated using pencil on paper. So much of the terminology in ophthalmology lends itself to puns, so Dr Lizard and his animal patients were a natural outgrowth of the many hours I spent in the eye clinic over the past year."

www.dorothealaurence.com
Instagram: @dorotheaslaurence

**Illustrations may not be reused without permission.*

BEHIND THE LENS

Ophthalmology and photography are two disciplines that benefit from a deep understanding of the eye. Although both require skilled practitioners to optimize the underlying mechanics of vision to achieve intended outcomes, the manner in which they are achieved is very different. Where an ophthalmologist focuses inwards on the mechanisms allowing vision to occur, correcting the patient's visual maladies, a photographer instead uses those mechanisms to frame, compose, and capture a subject in a singular moment of time. At its core, this distinction is one between science and art, but both disciplines require years of dedication, training, and practice, to master.

What does it take for one to excel in both of these complementary but seemingly contrasting specialties? Meet Marc Safran, a general and strabismus surgeon with over 30 years of experience and an award-winning studio photographer.

See the Sitting Down With... section to find out more.

THROUGH THE EYE OF AI

Fares Antaki is a senior resident in the Department of Ophthalmology at the University of Montreal, Canada, where he held the position of chief resident in 2022. He received his MD from McGill University in 2018. He is interested in digital innovations in medicine and, in particular, the applications of emerging technologies such as AI, VR, and telemedicine in ophthalmology. At the end of his residency in 2023, he will complete a fellowship in Artificial Medical Intelligence in the UK and then plans to pursue a clinical fellowship in retinal diseases and surgery.

Antaki says: "Growing up in Aleppo, Syria, my father – also an ophthalmologist – was extremely passionate about visual arts. His collection includes more than 300 paintings, mostly by Syrian, Lebanese, and Armenian artists. Over the years, my appreciation for art refined my observational and interpretive skills and, since starting ophthalmology residency, I have continuously found myself inspired by the forms I found on fundoscopy and even on OCT images.

I started doing research in AI in 2020, so I followed a few relevant Twitter accounts. I came across DALL-E on my feed a few months ago, quickly signed up and was granted access a few days ago. The first prompt I wanted to write naturally had to do with ophthalmology. I thought of cataract surgery and after many trials and errors I found the perfect prompt and applied the styles of different artists to it: Picasso, Klimt, Basquiat, and Munch. Is it creative? Possibly… but honestly to me it just felt like I was connecting things."

AI paintings generated by Fares Antaki using DALL-E 2 (OpenAI). View more of his art on our website.

MANDALA EYES

The artist, Katherine McVeigh who is an ophthalmologist practicing in Berlin, Germany, comments: "The eyes are unique. Not only are they a window to the mind and the soul, but also they allow us to look inside: revealing signs of disease within the eye, as well as further away in the body. As an ophthalmologist with a long-standing fascination for the eyes and vision, as well as a passion for crafting and design, I recently found myself wondering how art has been used in the past to document and present the structure of the eye. How would those representations fit in the modern world, with our OCT scans and high-definition cameras?"

IPIΣ

This is an abstract interpretation of how the iris can be compared to an ocular version of a fingerprint.

MANDALA #3 SOUL

This collage mixes coronal plane anatomical and histological images of the eye. The anterior structures are shown peripherally and the posterior structures centrally.

The image is part of a series that you can see in full on our website.

Sustained Innovation

Dompé unites science with need

With Georgea Pasedis , Senior Vice President, Global Head of Medical Affairs, Dompé

What is your model for drug discovery and R&D?

As an international biotech company, Dompé focuses its research and development strategy on sustainable growth, with our greatest attention devoted to patients. Our ophthalmic research discoveries are rooted in innovation with the aim of meeting the highest unmet needs of patients. We target development of new therapies and pull-through to commercialization through rigorous science with ambitious goals, seeking therapeutic answers to the unmet medical needs in ophthalmics. By combining new biotechnological knowledge with our proprietary Exscalate intelligent platform leveraging supercomputing and AI to streamline drug discovery, Dompé is accelerating the pace towards new and effective treatments.

How does Dompe ensure continued innovation in your drug discovery pipeline?

Dompé exemplifies a sustainable model with research and medical affairs activities conducted as part of a network of institutions and universities worldwide. High levels of diversity characterize our preclinical pipeline, and our research and development pipeline targets some of the hardest to treat diseases. We focus on medical conditions that are often untreated or have unmet therapeutic needs, such as neurotrophic keratitis, type I diabetes, and acute respiratory distress syndrome.

We have several ongoing clinical trials, and continue to build on this growth by investing a significant portion of our revenue into research and development to continue the sustainability needed to produce data for scientific advancement.

How is your approach advancing therapeutic options in eyecare?

Dompé's commitment to eye care is entrenched in collaboration with ophthalmologists, optometrists, patient societies, hospitals, universities, and research centers across the world.

Our researchers produced the first topical biologic treatment for neurotrophic keratitis. Additionally, Dompé specifically created the only GMP facility producing a topical growth factor for ophthalmic use. Cenegermin-bkbj (rhNGF) received "Fast-Track", "Orphan Drug" and "Breakthrough Therapy" designations from the FDA, conferring upon it the "Priority Review" granted during the registration process.

With one-market authorization utilizing rhNGF for neurotrophic keratitis, Dompé will use the neurotrophins platform to sustain the development of new applications. Our expertise of the science behind neurotrophins is driving the evolution of our programs to evaluate potential applications of rhNGF to various ocular and systemic conditions, with the goal of further advancing potential treatments in eye care and beyond. Just recently, Dompé has started two ongoing parallel investigational studies in Sjögren's Dry Eye Disease. Recent literature continues to evolve that there is a key neurosensory component to the ocular surface manifestations in Sjögren's Dry Eye, with alterations in corneal nerve structures and function associated with reduced tear function, inflammation, and epithelial damage. A therapeutic agent targeting the etiology of neurosensory abnormalities could be beneficial, as improved nerve health and tear production may restore ocular homeostasis.

rhNGF is under investigation in patients with Sjogren's Dry Eye Disease, rhNGF is only FDA approved for neurotrophic keratitis.

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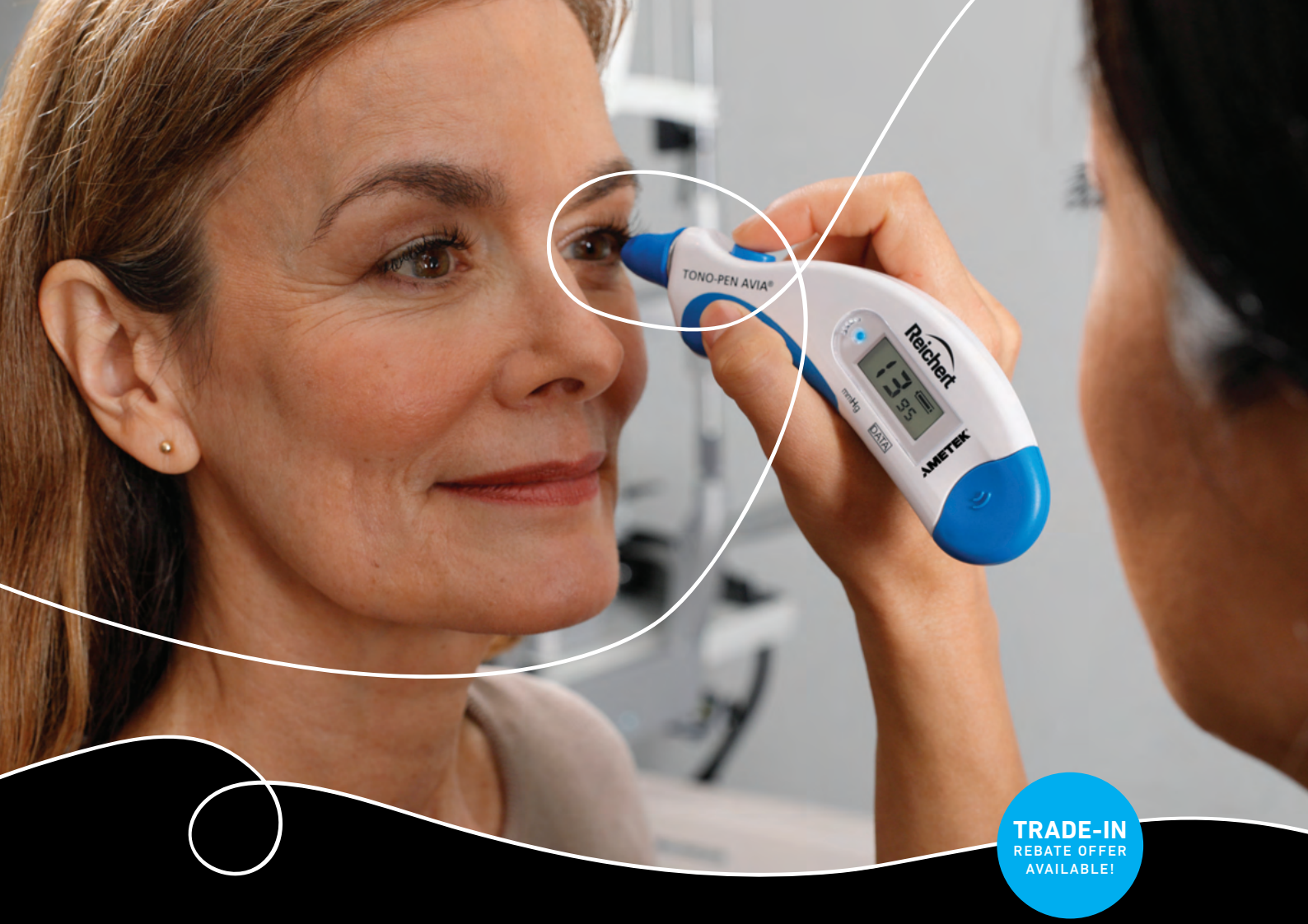
3. *K Tsubota et al., Int J Mol Sci, 21, 9271 (2020).*

The FDA-approved product labeling can be found here:



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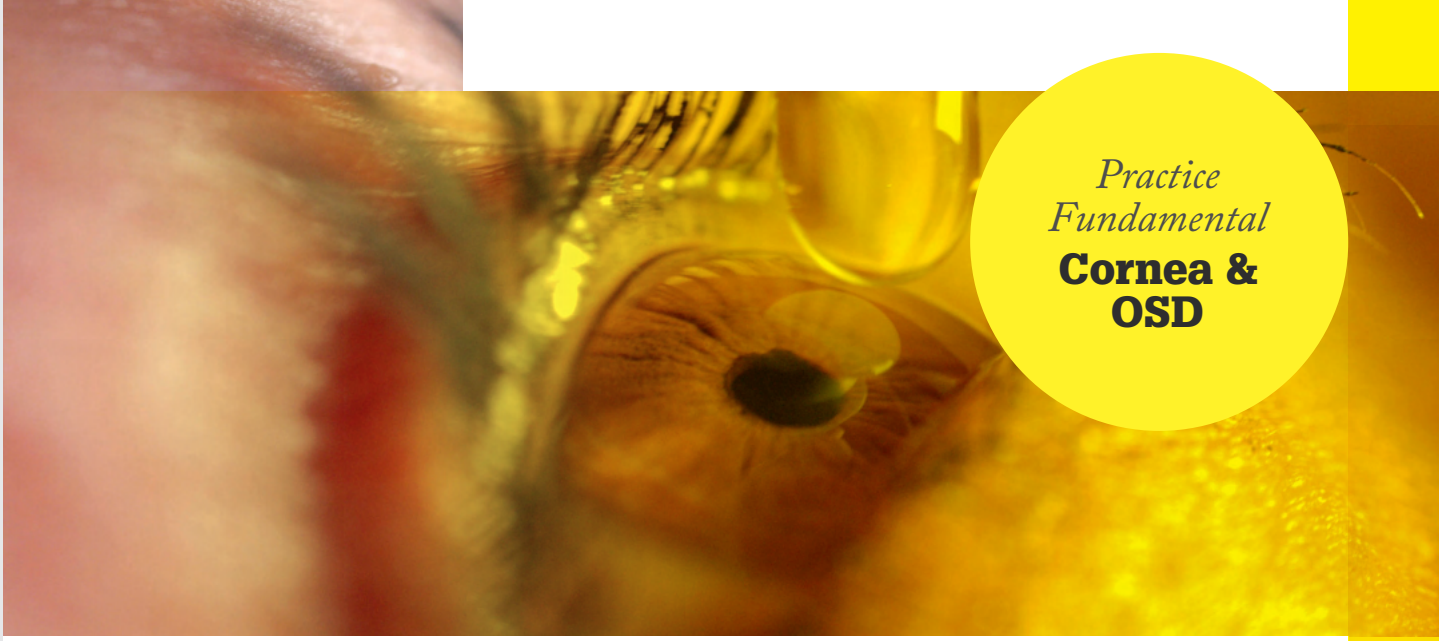

Monkey see? Researchers have developed a new non-human primate model of desiccating stress-induced dry eye disease using Rhesus macaque monkeys. The monkeys demonstrated similar clinical symptoms to those shown by humans. Additionally, they showed increased corneal fluorescein staining and decreased tear-film break up time after corticosteroid treatment.

Never forget. Tissue-resident memory T cells have been imaged patrolling the surface of healthy human corneas for the first time, indicating that they form in response to ocular infection and remain once the infection has been fought in order to provide local protective immunity and prevent secondary attacks by the same antigen.

Pain management. Severe neuropathic dry eye-like pain reversed in three patients by treating occult surface disease. Patients either responded after 48-hours of significantly relieving the symptoms, or one-week after treating superior conjunctivochalasis. Rigorous testing of surface disease may avoid systemic treatments that could cause serious side-effects.

Tear jerker. A Researchers develop a method to identify biomarkers of health and disease from the proteome of tear fluid. The non-invasive technique uses mass spec to analyze the tear film of the eye, which may one day be used for diagnosing ocular diseases, or even neurodegenerative diseases such as Alzheimer's disease. Link

Diagnosing discomfort. Contact lens-induced discomfort is often a cause for people ditching their lenses. There is an increase in ocular surface immune cells following this discomfort, which exemplifies the importance of immune system awareness during lens development and when treating ocular surface pain.

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IN OTHER NEWS

Pollution problems. *Air pollution causes ocular discomfort and damage, as well as tear film instability. Particulate matter and other air based pollutants influenced dry eye disease through separate mechanisms and at differing rates.*

The thick of it. *Corneal parameters heritable in families with keratoconus – genes associated with corneal thickness – warrant further investigation. Pachymetry indices could potentially be used as predictors of keratoconus occurrence.*

Dry eye relief. *A mucomimetic and antioxidant based eye drop is effective at treating diabetic dry eye, and implies a usefulness for treating ocular surface defects with antioxidants.*

Stopping scarring. *The combination of losartan and prednisolone acetate reduces corneal scarring following alkali burns in rabbits. Further study is needed to determine effectiveness as a clinical therapy in humans.*

Costing Up Cross-Linking

According to modeling, corneal collagen cross-linking is a cost-effective method of treating keratoconus

By Richard L. Lindstrom

If you ask a cornea specialist, we would tell you that we want to see patients the moment they develop signs of progressive keratoconus (KC) and then intervene with corneal collagen cross-linking while the patient still has relatively normal corneas and good vision. We'd all be happy to never perform another keratoplasty (PK) procedure for KC.

But today's reality is far from that ideal. We are still seeing KC patients identified for the first time in their 30s with high astigmatism, thin corneas – with keratometry values of 55-60 or more – and significant reductions in best-corrected vision (1). When I see a patient like this, there is always a sense of regret that they couldn't have been diagnosed and treated earlier, before losing vision.

Put simply, stopping progression of KC in Patient A is beneficial at any stage. Frankly, that is good enough for Patient A and for me, as their doctor, to say that treatment is worthwhile. But my colleagues and I wanted to answer some harder questions: over the course of a lifetime, does the outcome of cross-linking justify its cost, when compared with conventional management with glasses and contact lenses? Is it worthwhile to society and healthcare systems? Though these may sound like cold-hearted questions, they play into the economic decisions that third-party payers and large national or private health systems have to make on a regular basis.

To find answers to these questions, we used a type of discrete-event microsimulation model that has been widely used to evaluate cost-effectiveness of medical interventions (2).It compares clinical and health outcomes and quality of life between intervention and control groups – so, in the case of our study, between eyes undergoing the FDA-approved iLink cross-linking with Photrexa Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution), Photrexa (riboflavin 5'-phosphate ophthalmic solution) and the KXL system (Glaukos) versus not undergoing cross-linking treatment. Patient-level microsimulation is complex, but it allowed us to model the impact of individual patient and eye histories on keratoconus progression and adjust future risks (such as the probability of PK or of graft failure) accordingly.

We simulated outcomes for both eyes of 2,000 individual patients over a lifetime horizon, using data from the US multicenter phase III pivotal trials that led to FDA approval of iLink to define the characteristics of the preoperative population (3).Data from that study and elsewhere in the published literature on the natural history of keratoconus was used to account for a variety of factors affecting disease progression, such as the impact of age on the rate of progression. Rates of anticipated adverse events associated with penetrating keratoplasty (graft rejection/failure, cataract, glaucoma) were also derived from the literature.

All of this led to a baseline age of 31 years for the modeling and a mixed population with a ratio of slow to fast progressors of 4:1.

Simulation results

We found that treatment with cross-linking results in a 26 percent reduction in the rate of PK and 28 fewer years spent in the advanced stages (Amsler-Krumeich stage 3-4) of the disease (4).

Imagine the consequences for daily function, independence and productivity of avoiding nearly three decades of meaningful visual disability! We found that treatment conveyed, on average, 1.88 more quality-adjusted life years (QALYs). QALY, a cost-utility measure commonly used in health economics studies, is a combined measure of how long the treatment will extend life and the expected quality of life during those years. Estimates of the value of 1 QALY in the US vary from $50,000 to $150,000. When the cost of the intervention is well below the value gain (and cross-linking costs far less than 1.88 x $50,000, let alone $150,000) we can consider it to be highly cost effective.

According to our modeling research,

MODELING RESULTS ON THE COST EFFICIENCY OF CROSS-LINKING FOR KERATOCONUS

- 26 percent reduction in the rate of penetrating keratoplasty
- 28 fewer years spent in the advanced stages of keratoconus
- Gain of 1.88 quality adjusted life years (QALYs)
- Average patient savings of $8,677 in direct costs
- Average patient lifetime savings of $44,000
- National savings of between $150 million and $736 million
- Cost savings for insurers within 4.5 years

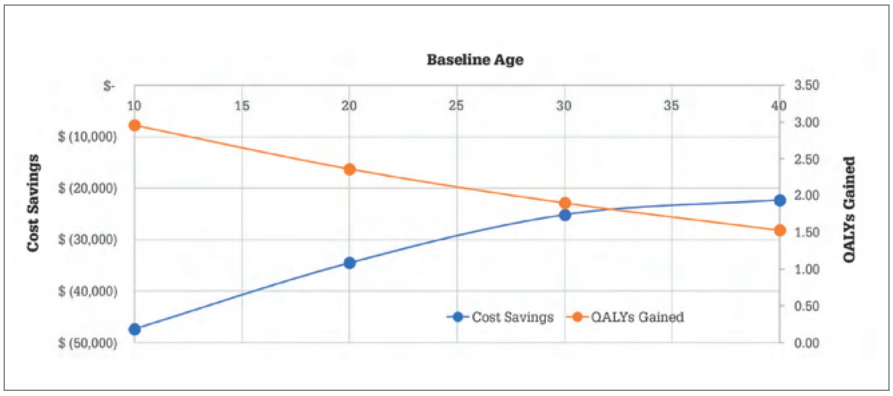

Figure 1. Plotting the impact of age of intervention on cost savings and quality-adjusted life years (QALY) demonstrates that cross-linking treatment at a younger age is more cost-effective (4).

cross-linking saves everyone money! Patients experience lower direct medical costs, with average savings of $8,677. Including the cost of lost productivity, which is known to be affected in KC (5), the lifetime saving is nearly $44,000. Nationally, this translates into a savings of between $150 million and $736 million, depending on one's estimate of prevalence. From the payer perspective, cost savings are achieved within 4.5 years.

Scenario analyses in the modeling, in which the baseline age was varied, demonstrated that iLink intervention at a younger age maximized both cost savings and QALYs gained for each individual patient (see Figure 1). In fact, earlier intervention is so impactful that not only do patient productivity and quality of life improve, but the associated economic burden of progressive keratoconus on the country's healthcare system can also be significantly reduced.

Our study has some limitations. Primarily, we relied on existing literature data to build our microsimulation model; because we based the clinical effectiveness of the iLink procedure on the 12-month results of the phase III clinical trials, the long-term benefits were also extrapolated from this short-term outcome.

However, the cold, hard numbers show that cross-linking is a win, not just for patients and their advocates, but also for third-party payers and society at large. And that's not surprising – treatment of other progressive conditions, such as glaucoma, hypertension, and diabetes, is also cost-effective when we weigh the modest costs of treatment against higher-cost late-stage surgical interventions and many years of potential disability. Unfortunately, when it comes to keratoconus, the message isn't getting through as loudly as my co-authors and I would like.

I am optimistic that we will see earlier diagnosis and referrals for treatment in the future, driven in part by changing approaches to the epidemic of childhood myopia. With new options to slow the progression of myopia, I think primary eye care providers will soon be capturing many more younger myopes at age five or six and treating them with behavior modification, specialized glasses and contact lenses, and topical pharmaceuticals, such as low-dose atropine. Out of all those mildly progressing myopic children, some will begin to develop asymmetrical and non orthogonal astigmatism as they reach their teen years. But because they are being regularly followed for myopia, we'll be able to diagnose KC and cross-link them earlier, preventing advanced KC. I look forward to that day.

STRATEGIES TO GENERATE EARLIER REFERRALS

- Provide rapid access to tomography/topography when KC is suspected
- Educate referring doctors about the benefits of cross-linking for patients with progressive keratoconus
- Be sure to send cross-linked patients back to their referring doctor for ongoing care and monitoring
- Refer specialty contact lens fits to local optometrists
- Remind patients and referring doctors that immediate family members of KC patients should also be screened.
- Develop relationships with doctors providing myopia control care, as they will be seeing the at-risk population (young progressing myopes) consistently from an early age.

Richard L. Lindstrom is Founder and Attending Surgeon Emeritus, Minnesota Eye Consultants in Minnesota, USA. He is Senior Lecturer and Foundation Trustee Emeritus, University of Minnesota, and Visiting Professor, UC Gavin Herbert Eye Institute in California, USA.

He has served as a consultant for Avellino, CLXO, Glaukos, iVeena, and KeraFlow. The modeling study discussed in this article was supported by Glaukos.

See references online.

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Sniffin' Sticks. A cross-sectional study using the Sniffin' Sticks smell test on 20 primary open-angle glaucoma patients, 20 exfoliative glaucoma patients, and 20 exfoliation syndrome patients to determine the threshold value, and assess the patient's ability to identify and differentiate between smells showed that the exfoliative glaucoma and exfoliation syndrome groups had reduced smell sensitivity and identification when compared with the primary open angle glaucoma patients and a control group, without glaucoma. These results provide new insights into neural degeneration and pseudoexfoliation.

Raised risk. Through a retrospective review of the medical records of 122 eyes of 122 patients who met the Hodapp-Parrish-Anderson criteria for POAG, researchers found long-term fluctuations in IOP and disc hemorrhage to be independent and additive risk factors of visual field progression in advanced glaucoma, even at low IOPs. For patients in whom these risk factors are identified, close monitoring and vigorous treatment is necessary.

Calculating glaucoma. Aiming to clinically validate the performance of two OCT-based glaucoma diagnostic calculators (GDCs), scientists conducted a retrospective, consecutive sampling of POAG patients, glaucoma suspects, and controls. Using the OCT-based GDCs, they were able to identify 30 percent more cases than conventional pRNFL inferior OCT classification in both groups, indicating that GDCs could be used in clinical practice to improve diagnoses.

Virtual viewpoints. A cross-sectional, anonymized online questionnaire was distributed to all European Glaucoma Society-registered specialists with the aim of analyzing and characterizing their current use, characteristics and perspectives on virtual glaucoma clinics (VGCs). The researchers found that a significant proportion of European glaucoma units are currently using VGCs while others are considering implementing them. Of those who use them, the majority reported higher patient acceptance compared with traditional care. Financial reimbursement and consensus guidelines are likely crucial steps needed for VGC uptake.

See references online.

IN OTHER NEWS

Studying sodium. *Frequent dietary salt intake was potentially associated with increased POAG risk in antihypertensive salt users of the Thessaloniki Eye Study looking at incidence.*

Comparing characteristics. *OCT-defined parapapillary beta and gamma zones exhibit different characteristics for primary open angle glaucoma and primary angle closure glaucoma.*

Bias busting. *Properly designed prospective trials are needed to identify mechanisms driving disparities in treatment and address bias in glaucoma management for populations of African descent.*

Simultaneous supervision. *Remote monitoring of visual field testing allowed technicians to supervise testing of two patients at the same time with the same performance and reliability.*

Grading Ghanaians. The incidence and rate of visual field progression are high in a study of urban Ghanaians with glaucoma.

My MIGS of Choice, with Robert A. Van der Vaart

The benefits of incorporating MIGS into your comprehensive practice, and my go-to MIGS device: XEN

Robert A. Van der Vaart.

Comprehensive ophthalmologists have helped shape a new glaucoma treatment model by incorporating MIGS. The threshold for shifting from management to surgical referral for MIGS is far lower and more individualized than it was in the past, when trabeculectomy and drainage procedures were the only surgical options. MIGS devices have also broadened the scope of personnel able to provide glaucoma treatment, expanding beyond subspecialists to include cataract surgeons and also those of us who provide comprehensive care.

A strong demand for MIGS procedures in my region has resulted in me flipping my case mix to 75 and 25 percent surgical and medical, respectively. Although the exact proportion for each practitioner will vary, MIGS technologies present an opportunity to control that mix while offering patients with glaucoma a broad range of options beyond medications.

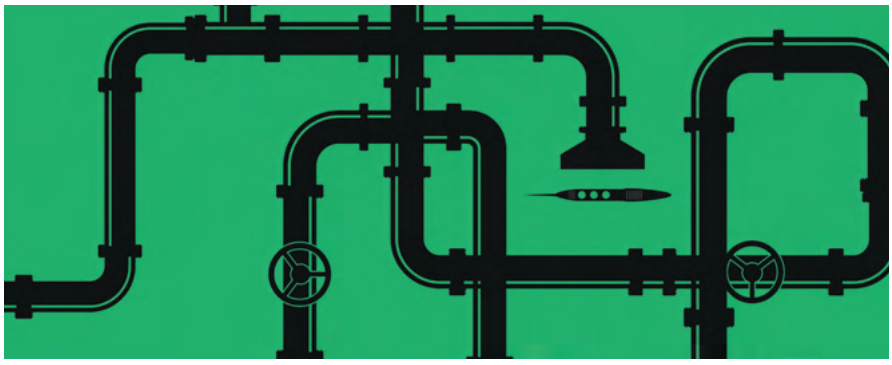
One of the strongest arguments for comprehensive surgeons to use MIGS devices is that it leads to new referrals, which can be great in number. In my small- to mid-sized community of about 200,000 people, two fellowship-trained glaucoma surgeons are booked all the time. As word got out that I offered MIGS and some filtration procedures, my surgical practice grew exponentially. I even have more general cataract referrals because of the rapport I've built with doctors referring to their glaucoma patients.

In my experience, MIGS are not difficult to learn or fit into the schedule of a comprehensive practice. As a result, I think we'll see more comprehensive ophthalmologists implement MIGS within their own practices.

Choosing which MIGS device to offer

At this point, MIGS technologies are so well established that virtually every surgeon offers at least one procedure performed concurrently with cataract surgery. These MIGS offer the opportunity to improve chronic disease while we're already in the eye, without additional risk, and rely on the same basic skills.

For me, it's important that I also offer other MIGS options, including standalone procedures that allow me to treat pseudophakic patients and those who don't need cataract surgery yet. The XEN Gel Stent, the only subconjunctival option, can be used alone or during cataract surgery for patients with refractory open-angle glaucoma. XEN has revolutionized how I care for more advanced cases where patients are refractory to medications and may have already had other glaucoma surgery. Instead of moving to trabeculectomy, I can do this 15-minute procedure with similar recovery to cataract and no negative effect on vision (1). Additionally, both viscodilation and goniotomy procedures are also approved for standalone use.



The learning curve for standalone MIGS is about the same as that for MIGS we use concurrently with cataract surgery. I also do several standalone in-office glaucoma procedures, including selective laser trabeculoplasty (SLT), YAG peripheral iridotomy for narrow angles, and placement of the bimatoprost intracameral implant.

How I schedule MIGS and follow-up care

MIGS procedures are not lengthy, so their incorporation into a schedule is relatively straightforward. In the surgery center, I schedule three time slots:standard cataract surgery, cataract with MIGS, and standalone MIGS, for which I allocate 20, 25 and 15 minutes respectively.

All MIGS have similar scrub tech setups, with small variations. We use the same techniques and materials, and the differences are small enough to make for an easy flow. As a result, I'm very comfortable performing different procedures successively rather than blocking time. In-office scheduling involves both surgical follow-up and office-based procedures. My follow-up schedule is the same for all MIGS, with the first two visits occurring at one day and one week, and a third visit based on the one-week status, ranging from three weeks to two months. We keep some slots open as a contingency, in case someone needs an extra follow-up visit, revision or bleb needling for XEN, or an urgent in-office laser procedure.

To handle in-office glaucoma procedures efficiently, we block out two mornings per month. Both our techs and patients are happy with this approach because there's no waiting. Everything moves along very quickly and smoothly when techs are doing the same thing, rather than interrupting regular clinic days with prep and consent forms. They get patients checked in, consented, and prepared with drops or Betadine, and then patients receive treatment.

Case studies: moderate and advanced glaucoma

My MIGS recommendation comes from my 85 percent success rate of getting patients to their pressure goal. This goal depends on the history and stage of the disease. Sometimes the goal is to reach the target pressure with no medications, while in advanced cases the goal may be to lower pressure enough to control it with just one drop. One of our advanced glaucoma patients, an 85-year-old woman, had visual field loss and fixation in both eyes. She had undergone bilateral trabeculectomy and revision in one eye, but neither bleb was functioning. With four medications through three drops (one was a combination), her pressure was 16-18 mm Hg in both eyes.

I implanted XEN bilaterally in 2020, approximately one month apart, with the aim of getting the patient down to one medication. Two years later, her pressures have remained 9-11 mm Hg on no drops. This overwhelmingly positive result is rare in advanced cases, but even controlling the patient on one drop would have been a success. Without XEN, she would have needed a tube shunt, which requires significant postoperative healing. However, with her MIGS procedure, she returned to baseline vision and activities within a week, and was incredibly happy with the results.

In another case, a 68-year-old man with mild glaucoma showed early thinning in both eyes on OCT. He'd been at target on drops for five years and had pressures of 15 mm Hg. Despite trying three different classes of drugs, he continued to have severe red eyes. The patient was retired and enjoyed socializing, but hated the way his eyes looked. Previous SLT had not worked, so he was referred to me to eliminate drops.

I used XEN on the first eye, and he was off drops at day one. At one month, the redness had disappeared and he was beating down the door asking me to operate on his other eye! He was ecstatic about controlling his disease without feeling anxious about his looks. Four years later, his pressures are in the 13-16 mm Hg range on no medications.

By reducing or eliminating topical medications, MIGS devices also diminish the impact of shaky compliance on glaucoma management. Additionally, with no drops, patients don't have to deal with detrimental effects on the ocular surface. In these two cases, the patients were thrilled that a MIGS device could get them off drops. As always, I was pleased to help them get the results they need to preserve their vision and quality of life.

Robert A. Van der Vaart is a Comprehensive ophthalmologist and cataract and glaucoma surgeon at Wilmington Eye in Wilmington, North Carolina, USA.

Reference

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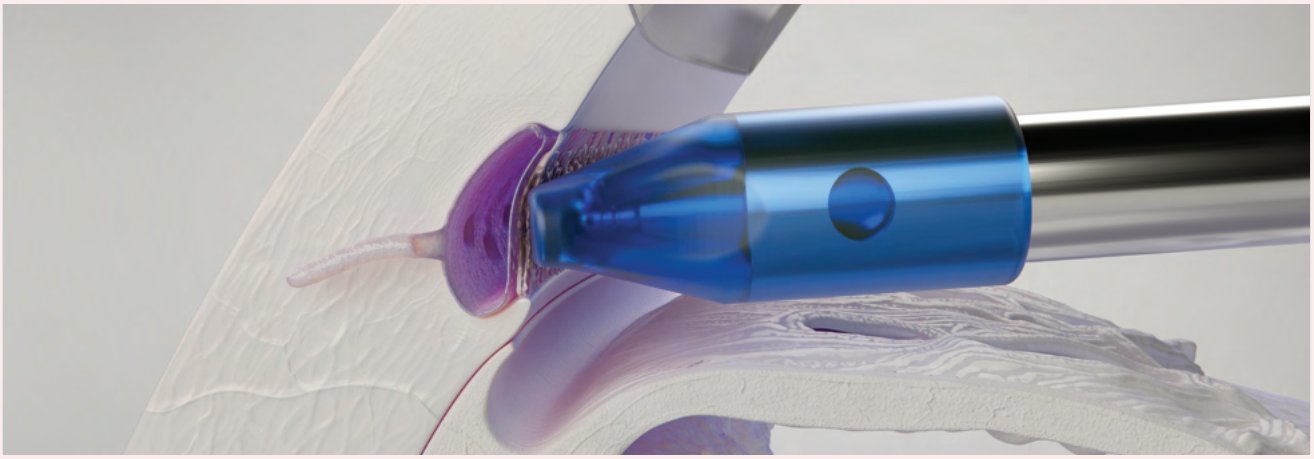
PRECISION MULTIPLIED

The STREAMLINE™ Surgical System is a first-line, implant-free solution that provides an unparalleled combination of precision and flexibility for angle surgery

NEW WORLD MEDICAL



Surgeons and patients benefit from an intuitive and implant-free approach to angle surgery. Ideally, the best approach would allow for either a standalone procedure or one combined with cataract surgery while preserving the opportunity for future surgical interventions. The STREAMLINE Surgical System from New World Medical is uniquely positioned to address these attributes using innovative ClickPulse® technology.

The STREAMLINE Surgical System is a first-line, implant-free solution that is specifically designed to facilitate the creation of a series of precise incisions in the trabecular meshwork with the use of ClickPulse technology. The surgeon can simultaneously incise the trabecular meshwork and deliver precise volumes of viscoelastic fluid (up to eight applications) into several clock hours of the canal of Schlemm in one unified step. Additionally, at the surgeon's discretion, ClickPulse incisions can be extended into titratable incisional goniotomies over several clock hours of the trabecular meshwork independent of viscoelastic delivery.

ClickPulse technology with STREAMLINE has been developed to integrate seamlessly into surgical routines and standard workflows. This offers surgeons freedom and flexibility for current and future procedures. What's more, the procedure is intuitive to learn, so it can be adopted efficiently. A key advantage of using the STREAMLINE Surgical System is that it leverages an established reimbursement code (category I CPT® Code 65820) whether used as a standalone procedure or in combination with cataract extraction.

In summary, the unique features of the STREAMLINE Surgical System optimize the surgeon's experience and increase control during angle surgery. Surgeons now have a flexible method for creating incisions in the trabecular meshwork with injection of viscoelastic into the canal of Schlemm combined with tailored therapy to titrate incisional goniotomies over several clock hours. Add in the ability to leverage the 65820 CPT code and it is clear to see why the STREAMLINE Surgical System should be the first option surgeons reach for when caring for patients across a range of needs.

The STREAMLINE™ Surgical System is only available in the USA at present.

"The STREAMLINE Surgical System provides me with the ability to confidently combine an angle-based procedure with my premium IOL patients. In my early experience, I see quiet eyes post-operatively, with no impact on my premium IOL results. This makes STREAMLINE my first-choice recommendation for my patients."

Nicole Fram, MD Advanced Vision Care, Los Angeles, California, USA

TRAINING THE WORLD

Eradicating blindness and visual impairment due to cataract requires thousands of new cataract specialists to be trained and sent out into the world – and this in turn requires a concerted, global-scale effort. Saro Jahani, President and CEO, describes how HelpMeSee is contributing to this ambitious endeavour.

How did you get to your position at HelpMeSee?

I was raised in Sweden, where I studied electrophysics. After graduating, I entered the technology and finance industry, which eventually took me to the USA. There, I made a career leading Technology and Innovation departments in financial institutions, including Sanguard Trading, Lehman Brothers, and the National Stock Exchange.

By 2019, however, I had come to recognize that the needs of the blind were greater than those of Wall Street, so I walked away from my financial career to join HelpMeSee; I'd fallen in love with the organization's mission. I've been with it ever since, first as the Head of Global Innovation and Technology, and now as the President and CEO. I truly believe it's the right place for me.

What is the HelpMeSee mission?

Cataract-associated blindness is a humanitarian crisis of global scale: it affects 100 million people, impacts the quality of life for entire families, accelerates poverty, and causes annual economic productivity losses estimated at $410 billion, according to the Lancet Global Health Commission on Global Eye Health. All this could be avoided – if only we had enough cataract surgeons. Our mission is to help eliminate the crisis by training large numbers of MSICS cataract specialists in developing regions.

What kind of skills do these specialists need?

We can't rely on expensive, sophisticated technology such as phacoemulsification – it is just not feasible for developing countries. We train our cataract specialists in manual small incision cataract surgery (MSICS) procedure. This permits low-cost, effective, rapid interventions, estimated at $100 per surgery. A single clinic can perform hundreds of MSICS procedures per day – which means that 30,000 new surgeons could help eradicate blindness due to cataract and visual impairment! That's the aim. But, this endeavor requires the creation of a cataract treatment ecosystem that is sustained over time – because new cataract patients appear continually, and always will.

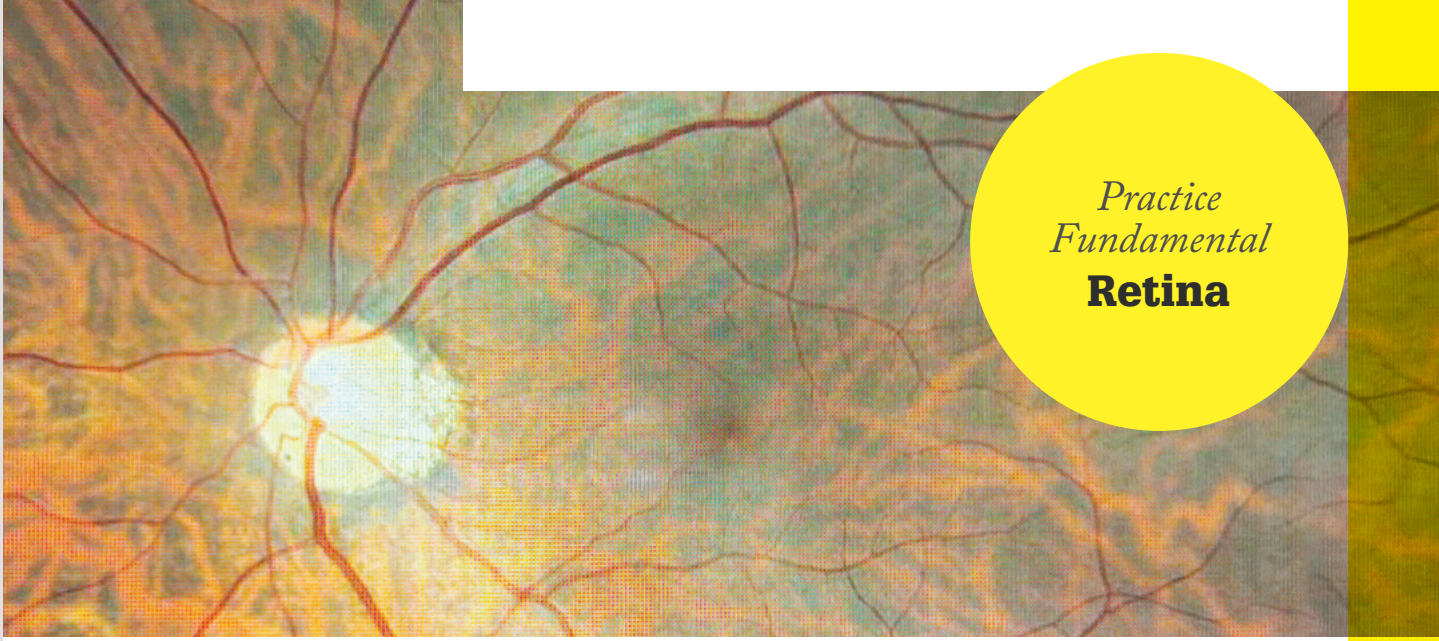
How do you train novice surgeons?

By employing transformational innovation! We developed a purpose-made, virtual reality surgical simulator which allows us to provide MSICS training and instructor led-curriculum without ever putting a real patient at risk. The virtual reality microscope displays the entire anatomy of the eye, using extraordinary visuals and graphics, so trainees see exactly what cataract surgeons see in real life surgery. Furthermore, the simulator's advanced haptic feedback system allows them to literally get a feel for the MSICS technique!

The MSICS simulator training is preceded with our eBook, which contains thousands of pages of learning material including videos, animations, and text. This is a key resource. We have made the eBook available for purchase in the USA, EU and the UK, and will soon offer it in other regions. The idea is for people to link their eBook purchase to a donation, thereby allowing an eBook to be given to a cataract specialist in the developing world. By rolling out the eBook in this way, we hope to give everyone the opportunity to participate in the struggle against cataract-associated blindness. This is about inclusion!

Any final thoughts?

Eradicating cataract–associated blindness will be extremely difficult; it requires a global effort backed by government-level support. This won't happen unless people understand that there is not only a problem but also a solution – namely, an extra 30,000 cataract surgeons. But at present, HelpMeSee trains less than a thousand cataract specialists per year; we need to scale up dramatically, and that requires broad support and sponsorship. HelpMeSee will always provide the best, most innovative training technology, but to succeed in our mission we need commitment from other organizations and governments. Vision is a human right, and we must all work together to ensure that this right is not taken from the world's poorest people.



Baby blue. A multinational study led by researchers at the University of Leicester, UK, has deciphered how genetics influence visual development in developing babies' eyes – more specifically looking at genes associated with arrested development of the fovea. They investigated a cohort of almost one thousand people with confirmed genetic disorders associated with foveal hypoplasia - classifying how foveal development correlates to genotype and the visual outcome.

Extending family. NEI researchers have identified a novel early-onset macular dystrophy that occurs as a result of new mutations in the gene TIMP3, already known to be associated with the disease. These new mutations were not in the mature protein, but in the signal peptide preventing the immature protein from being cleaved.

Marked targets. Fibroblasts from primary open angle glaucoma patients were reprogrammed into stem cells and differentiated to form a model of the retina and optic nerve to identify unknown genetic markers of glaucoma. 312 genetic variants were associated with the target retinal cells and 97 genetic clusters were linked to glaucoma caused damage.

Pixel by pixel. A machine learning model uses a pixel stratification approach to comprehensively reconstruct and examine the vitreous anatomy in 3D. The technique produces high quality 3D movies, similar to triamcinolone-assisted vitrectomy or postmortem dye injection. By examining the vitreous structure beyond the vitreoretinal interface there are applications for many macular diseases and diabetic retinopathy. The approach uses swept source OCT (SS-OCT) scans that are analyzed through Fiji (is just image J) to stack into cubic voxels. After processing the signals from the vitreous gel, spaces within, and interfaces between them, two classes of "Septa" and "Other" were defined - these pixels were assigned to either of the classes, which in turn trained the classifier system.

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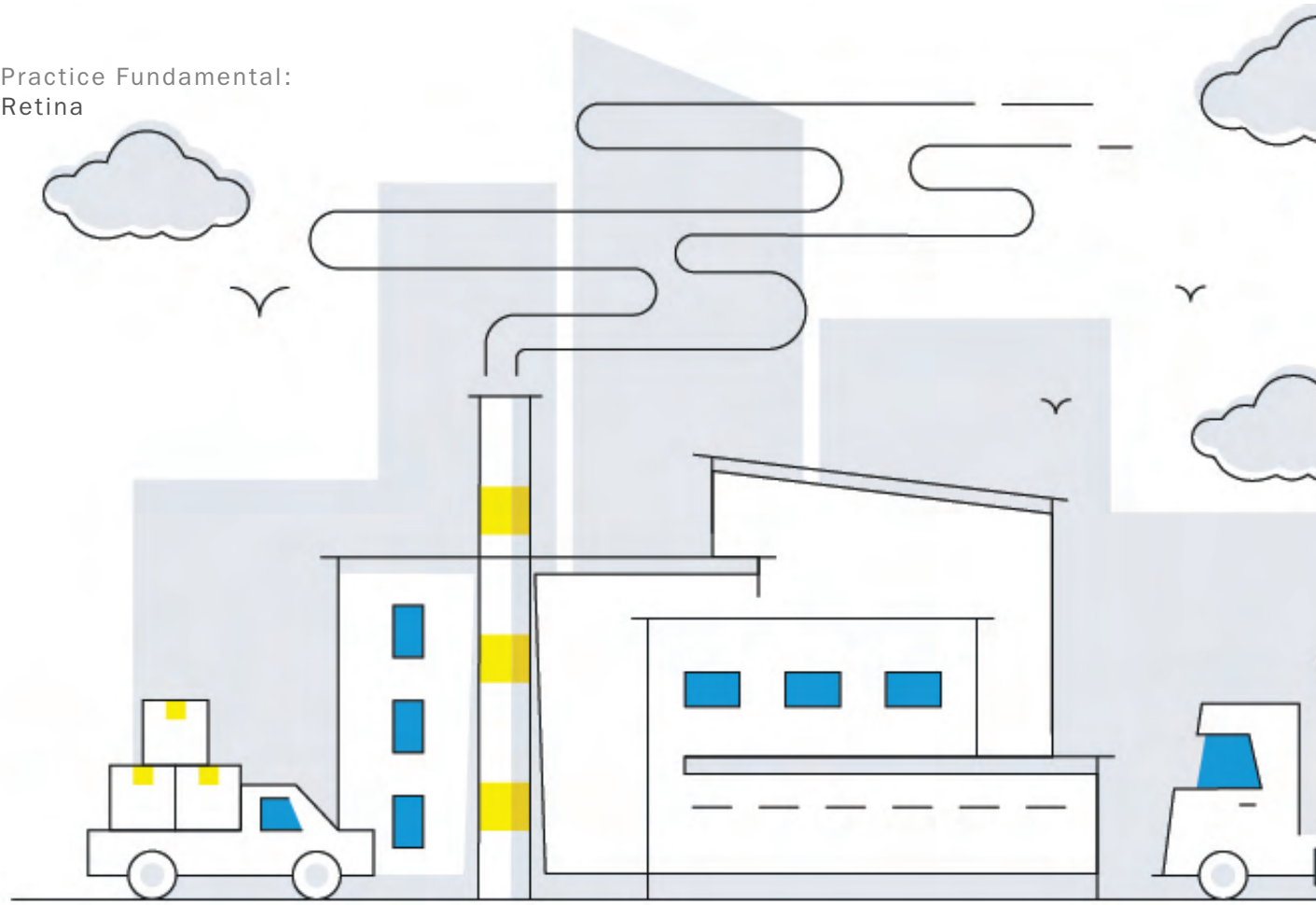
IN OTHER NEWS

Intelligent reclassification. *A new proposed framework for classifying diabetic retinopathy uses OCT and OCT-A with AI to provide specialized classification, all under one imaging modality.*

Safe but inefficient. *An early LHON clinical trial shows that gene therapy treatment trial is safe but not effective at improving or slowing vision loss.*

Plateau in progress. *Although visual impairment in adults with diabetes was in decline since 2000, this may have plateaued from 2012. The study performed by the CDC provides insights into vision impairment in adults with diabetes.*

Through thick and thin. *Retinal nerve fiber layer thickness is associated with cognitive function and subsequent cognitive decline. This information could be applied to OCT eye tests as a predictive biomarker for cognitive function in older patients.*



A Tiny Factory

Scaffolding a solution to macular telangiectasia with encapsulated cell therapy

By Thomas Aaberg, Jr.

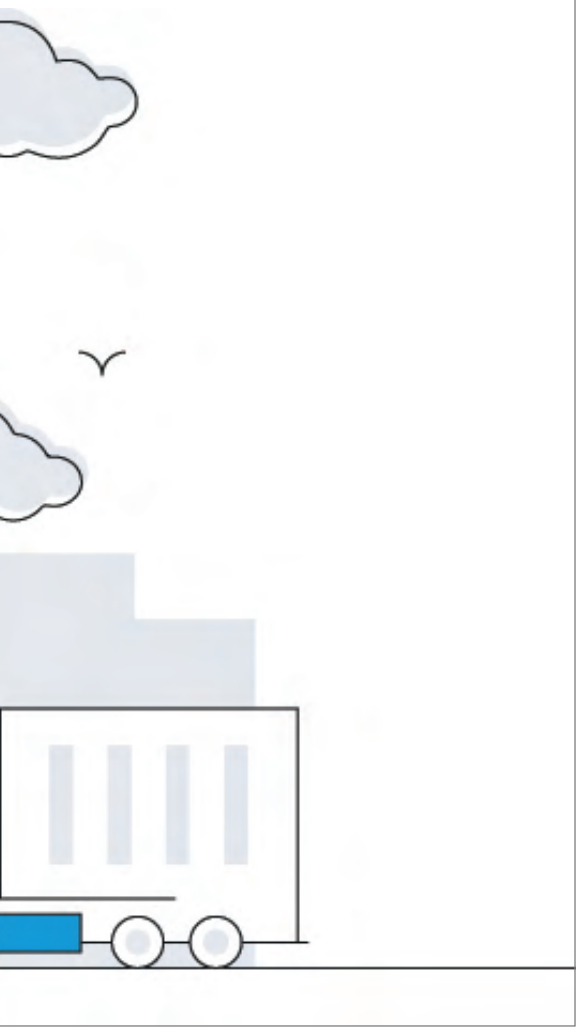
Macular telangiectasia type 2 (MacTel) is an uncommon, progressive, degenerative eye disease that can leave older patients with devastating reductions in their quality of sight and quality of life. Given that there was no medical, surgical, or lifestyle intervention to alter disease progression, Neurotech Pharmaceuticals stepped up to the plate with an encapsulated cell therapy (ECT) device. For MacTel patients, it could represent the first real chance to slow the disease's destructive effects and pace of ongoing vision loss.

Understanding how ECT can improve MacTel patient outcomes relies on understanding the general mechanism of action and the specific design choices made during development. These factors also highlight the potential for new encapsulated cell therapies to treat a variety of under- and untreated eye diseases. In short, ECT is a promising realm for clinical research and technical innovation.

ECT and NT-501

The concept of encapsulating cells to treat disease has been around since the 1930s, but only recently has the technology matured to the point where reliable therapeutic effects can be offered to patients. In essence, ECT introduces a miniature medicine factory into the body to continuously deliver a therapeutic agent directly where needed. To treat MacTel, and possibly other eye diseases, the drug-producing device – the NT-501 – is placed into the vitreous cavity, where it manufactures and delivers drug to the retina or other targetable intraocular structures. The NT-501 comprises four key elements: i) specially engineered human retinal pigment epithelium (RPE) cells (the drug-making machinery), ii) the scaffold to which the cells attach (the factory's bricks and mortar), iii) a porous membrane that houses the cells and scaffold, iv) the caps where a titanium loop is affixed to facilitate manipulation during implantation (see box for more details).

Which drug to make? Ciliary neurotrophic factor (CNTF) is a well-studied neurotrophic factor produced endogenously by neurons and Müller glial cells. It has been demonstrated to be effective in retarding photoreceptor neuron loss in animal models of retinal degeneration. However, CTNF has an extremely short half-life, requiring it to be produced and delivered continuously. Unlike other retinal therapies that



may only require one injection per month, CTNF would require multiple injections each day. That's what makes ECT such an elegant solution for MacTel; the effective drug is made constantly, right where it's needed. Put simply, we obtained, verified, and transfected the CNTF gene into our master stock cells to form a new cell line: NTC-201-6A.

After implantation of NT-501, the NTC-201-6A cells continually produce and release CNTF into the vitreous cavity. Importantly, the cells within the implant are protected from the host's immune system.

Beyond MacTel

Neurotech Pharmaceuticals has almost 20 years of experience with the versatile and hardy cells that power NT-501, so we are well poised to create devices that "manufacture" other therapies within the vitreous cavity, producing different drugs, proteins, peptides, or other therapeutic agents. Our cell biologists and engineers are working diligently to exploit this opportunity, and I have confidence that we'll be able to modify our encapsulated cell technology to treat a variety of intraocular diseases.

I am excited about the future of ECT in ophthalmology – and even more excited to help introduce the resulting real-world therapeutics!

Thomas Aaberg, Jr., Retinal surgeon at the Retina Specialists of Michigan, and the Chief Medical Officer of Neurotech Pharmaceuticals. He is based in Michigan, USA.

NT-501 DEEP DIVE

The NT-501 device is sterile, non-pyrogenic, and retrievable. The current implant is approximately 6.5 mm long and is placed, via a pars plana incision, well outside the visual axis. The device's housing consists of a sealed, semipermeable, hollow fiber membrane (HFM) capsule surrounding a scaffold of six strands of polyethylene terephthalate (PET) yarn. Produced by wet-spinning technology using similar methods to those used to manufacture kidney dialysis or plasma filtration membranes, the HFM is fabricated from polyethersulfone (PES) and provides the functional body of the NT-501. The membrane portion of the implant houses the encapsulated NTC-201-6A cells, allowing the outward diffusion of therapeutic agents while supporting cells with the inward diffusion of environmental nutrients, and preventing the host immune system from "seeing" the NTC-201-6A cells.

The hydrophilic polymer polyvinyl pyrrolidone (PVP), which improves the overall hydrophilic characteristic of the membrane, is incorporated into the chemical synthesis of the membrane. This hydrophilic membrane modification results in very low levels of protein binding to the inner and outer structure of the membrane during in vitro and in vivo exposure to encapsulated cell-produced proteins, to culture media proteins, and to host implant proteins and cells. The co-formulation of PES and PVP structure enhances the stabilization of the device membrane pore structure compared to membrane formulations of PES alone. This ensures that the functionality of the medicinal product is not impacted by the medical device for the duration of treatment.

The NTC-201-6A cells come from our NTC-200 cell master stock, which traces its ancestry back to ARPE-19 cells, a spontaneously arising RPE cell line derived from a human donor in 1986. This particular cell culture had marked potential for growth, extensive pigmentation, and large areas of polygonal cells when compared with other RPE cultures. The ARPE-19 cell line was purified to remove weakly adherent and fibroblastic cells – a process that was repeated until a uniform, highly epithelial culture of RPE cells was obtained. Cells from the original explant culture were ultimately expanded to create a bank of cells, which were heavily tested for contaminants and thoroughly studied.

PET yarn was chosen as the scaffolding material to provide surface area for cell attachment and growth within the capsule. The scaffolding is distributed within the membrane interior, with voids residing between individual monofilaments, maximizing the permeability between cells, and cell access to diffused nutrients from outside the device. Additionally, the PET monofilaments impart strength to the assembled PAC. Each implantable NT-501 is loaded with human CNTF-secreting NTC-201-6A cells before the capsule is sealed with methacrylate adhesive. A titanium loop is attached to one end to aid placement and retrieval of the implant. The cell number expands and growth stops due to cell contact inhibition.

The Swiss Watch of Ophthalmic Equipment

The role of Haag-Streit in our practice

Warren E. Hill, MD, and Yuri McKee, MD, ophthalmic specialists at East Valley Ophthalmology in Mesa, Arizona, USA, discuss the benefits of partnering with a Swiss company deeply committed to innovation and customer centricity

About your practice

Warren Hill: Our practice is a little different from the average, although we are far from unique: frequently, we are sent complex cases that require challenging IOL power calculations, referred from around the US and sometimes internationally. When other surgeons depend on our results, it demands the best diagnostic and surgical equipment. For this reason, we've invested much time and resources into researching and choosing the technology we use.

Yuri McKee: While my fellowship training is in corneal and refractive surgery, I also specialize in glaucoma surgery and advanced anterior segment reconstruction, which includes pars plana vitrectomy for vitreous prolapse and, of course, retrieving dislocated IOLs.

On the outside of our building, East Valley Ophthalmology appears to be a standard medical practice, but on the inside, there is a wealth of specialized testing equipment, a surgery center, and a lot of exciting diagnostic and surgical equipment typically found only in large university centers. Working with Warren Hill, an ophthalmology household name, carries many responsibilities. Patients with unique conditions are referred to us from a wide geographical area and arrive expecting cutting-edge technology that provides predictable and consistent, improved outcomes.

What equipment and devices do you use?

Hill: The Lenstar optical biometer is the workhorse of our practice. It provides highly accurate measurements for every aspect of the eye important to an anterior segment surgeon. The Lenstar appeared at a time when biometry needed to change. The Lenstar pushed keratometry to a different level – something we needed to see in our practice. We found that dual-zone autokeratometry provided a new level of accuracy, especially for our toric IOL patients. For each keratometry measurement, the Lenstar shows the reflected images, allowing us to include or exclude any one of six sets to increase the final accuracy. The ability to selectively edit measurements is beneficial for challenging cases. I believe the Lenstar is also ideally suited to routine work, and not just challenging cases. It's easy to use, doesn't require a change in thinking, and consistently delivers correct information.

McKee: When we recently expanded our office, we installed a considerable amount of Haag-Streit equipment. We know the company's slit lamps will last a career. We have the Lenstar biometer and the Octopus perimeter, which are in constant use. Haag-Streit instruments are all intuitive to use and easy to switch between, and we have total faith in their effectiveness, consistency, and durability. On top of this, ergonomics is critical in our clinical spaces. A great deal of time is spent at these stations, and the wrong posture, over many years, can be debilitating. We are using Haag-Streit and Reliance (USA) chairs and stands, which provide an excellent, non-fatiguing platform for our daily practice. We have found a partner in Haag-Streit, not just a supplier: one that sees the whole picture, from cutting-edge innovation in instruments to the wellbeing of the operator.

> *"We have found a partner in Haag-Streit, not just a supplier: one that sees the whole picture, from cutting-edge innovation in instruments to the wellbeing of the operator."*
> *Yuri McKee*

What's your experience with Haag-Streit as a partner?

McKee: I find Haag-Streit to be a wonderfully stable, reliable company. I have made several personal connections that have made all the difference in

procurement and service. Just one or two contacts at the company can always answer any question or solve any issue. The company's nature also fosters good employee retention, so I know investing in these relationships also brings a long-term advantage. These personal connections allow me access to the right people when I need to solve issues, but equally, it also gives me a sounding board when I have ideas for improvement or new products. My Haag-Streit connections are always willing to talk enthusiastically about the field. They are wonderfully patient-focused, so I feel that together we can bring significant benefits to the clinic and ophthalmology.

Hill: What sets Haag-Streit apart for me is the company culture. This Swiss company has been in business for a long time and has exceptionally loyal employees. It is also a personable company, not a cold, distant multinational, and this philosophy permeates its products.

We all know that ophthalmology is the "poster child" for innovation, as we see many new technologies successfully introduced and then swiftly become a standard of care. As such, reliability and consistency help us to navigate these constantly changing waters. Haag-Streit excels in both areas, stemming from its long-term involvement with the practitioners and the scientists supporting this field, coupled with care and pride. We greatly value the quality of the devices that begets a long shelf life. We can depend on them day after day, year upon year.

Haag-Streit is also a company of forward thinkers. They consider the needs of the industry as far out as they can. To achieve this, they actively engage with us as practitioners and scientists. The company is inclusive and responsive but, importantly, prepared to commit to what others may see as simply expensive "blue-sky" opportunities. For example, Haag-Streit worked with me in a collaborative effort to design a method of performing IOL power calculations that involved an entirely different approach from traditional formulas, instead using the mathematics of artificial intelligence (AI). The study used to create the Hill-RBF IOL power selection method based on AI evolved from this initial conversation. A decade later, the rest is history.

Several years into this study, we began exploring the commonly held but yet-to-be-explored belief that the Han Chinese eye often has anatomic differences compared to the European Caucasian eye. And these differences may influence the accuracy of IOL power selection. It is also felt that these differences may account for disparities in cataract surgery refractive accuracy when comparing these two population groups. Haag-Streit responded to this possibility and committed to finding a solution, even though this had no immediate downstream effect on new equipment sales. Through these experiences, I feel I am working with people who understand what I do, and the many challenges eye care professionals encounter worldwide.

Hill: When you work with Haag-Streit equipment, you can be sure your measurements are good, and you have a good company to back you up, with people you make real connections with. It's important, as in healthcare, we are all about people.

"Haag-Streit is a company of forward thinkers."
Warren Hill

Yuri McKee on the Haag-Streit Surgical Microscope

When thinking of Haag-Streit, ophthalmologists immediately think of slit lamps; understandably, it's hard to argue against Haag-Streit having the best quality slit lamp optics. For me, this is also true of the company's surgical microscopes: their quality, reliability, durability, depth of focus and depth perception, clarity, color reproduction and light transmission provides an "optical experience" that is simply on another level from any other product I have used. Better outcomes are a direct result of having fewer complications, and the superior clarity offered by these microscopes improves our precision, accuracy, confidence and, thus, improves outcomes. Often, we need to focus from the very back of the eye to the front. In surgery, we use the EIBOS 2 non-contact wide-angle retinal viewing system. With a simple flip of the EIBOS 2, we have crystal clear images of the back of the eye. The integrated inverter body is exceptionally slim, allowing simultaneous visualization of the fundus and the incision area, upright in the same orientation. At medium or high magnification, you have the impression of being in the eye instead of just looking at the fundus.

Double Exposure

Sitting Down With… Marc Safran, Former Medical Director, Syracuse Specialty Surgery Center – and an award-winning photographer, based in Syracuse, New York, USA

Which passion came first: photography or ophthalmology?

I was first introduced to photography by my father – an amateur hobbyist. I constructed a small darkroom in the basement of our house in New York City and spent hours developing black and white film, as a teenager. This was all put on hold once I started college and later entered medical school. Then, about 20 years ago, a patient told me about an adult education photography program offered by Syracuse University (not far from my practice), which focused on learning to use strobes, light meters, and digital cameras for portraiture. I became hooked and soon found myself spending my weekends renting out studio space at the university. I would read anything I could find on photography and Photoshop. From there, I began subletting space with professional photographers. I now have my own studio, where I currently spend as much time as my ophthalmology career and family life allows.

Do you think ophthalmology gave you an advantage with photography?

All ophthalmologists have an intrinsic understanding of how the laws of optics and biology allow us to see clearly focused images; after all, we repair the human camera! One might think that our knowledge about the eye maps to photography in a fairly linear way. However, these two domains often diverge – and that's where it becomes interesting! Attractive photographs often use depth-of-field blur to create drama. Shadows and light can be used to create strong contrasts. Color balance, black and white renderings, and grain textures can also be used. All of these factors are completely different from how our brain and retina actually display visual signals. In a way, our eye functions like a very basic point-and-shoot style camera. The differences in how large-sensor DSLR and film cameras record an image and how our eyes perceive it are vast. I look to exploit those differences.

"All ophthalmologists have an intrinsic understanding of how the laws of optics and biology allow us to see clearly focused images; after all, we repair the human camera!"

OK – so has your passion for photography changed the way you approach ophthalmology?

Interestingly, yes. I am a general ophthalmologist but specialize in strabismus. The emphasis in training as a strabismus surgeon was that ocular misalignment was a disease first and foremost in causing amblyopia and loss of fusion. But that's really just a half-truth. As a photographer, I came to realize that the first thing someone looks at in a portrait is the subject's eyes. We read – consciously and subconsciously – the emotion of a subject by where their gaze is fixed, how relaxed the eyelids are, and how vibrant, bright, and alive (moist) the cornea is. If a subject is uncomfortable with the camera, the eyes show it immediately. I came to understand that with strabismus, the greatest harm is that it alters the natural gaze of a person and, in so doing, doesn't allow the person to communicate normally with their eyes. In essence, a person with strabismus can no longer "speak" normally with their gaze – nor can they be accurately "read" by others. I never fully appreciated this until I really got into portraiture.

How do you compose a visually striking image?

Someone once said that to take interesting and beautiful photographs, it's best to start with interesting and beautiful subjects. After opening my studio, I tried to invite subjects talented in arts, performance, modeling, and fashion. I share my work with them in return for working with terrific subject matter. I have now worked with scores of actors, dancers, models, and colorful subjects whom I recruit and meet through Instagram or via recommendation. These individuals include members of Cirque du Soleil, burlesque troupe members, boxers, figure models, professional ballet dancers, rock climbers, rock and rollers, and more. The shoots are always dynamic, exciting, and highly personal. People are made to feel comfortable, and there's a great vibe with an inviting space and good music. I always come away supercharged – and most subjects are so excited by how they can see themselves in creative and artistic ways.

Tell me about your photography mentor… and his connection to ophthalmology.

Howard Schatz is one of the foremost studio photographers in the US. I was introduced to his work by someone who mentioned that he was formerly a highly regarded retina specialist. I bought some

"In a way, our eye functions like a very basic point-and-shoot style camera."

of his art books and ultimately contacted him. Howard invited me to see his high-end, celebrity-frequented studio in New York City. And I was in awe. Eventually, I attended one of his five-day courses and we became friends. He is still actively working – winning awards, and shooting big name subjects – even though he is in his 80s. I am lucky to have this influence; without our shared connection to ophthalmology, I wouldn't have had the opportunity…

Any other instances where your two careers have crossed paths?

I like to take my camera when I travel. Over the past 15 years, I have participated in 10 international eye care trips, mostly to Ecuador, with a group called Healing the Children. A team of four surgeons and 15 support personnel take over a wing of a small hospital and perform around 100 pediatric strabismus cases. It's an exhilarating and uplifting experience. On my most recent trips, I wanted to take portraits of our patients – to capture their humanity more than the pathology. I set up a makeshift studio just outside the operating room and photographed the children with their parents just before their strabismus surgery. I called the project Estrabismo.

Do you have any free time?

I run a solo private practice in upstate New York, which keeps me fairly busy. The one thing I love about ophthalmology is that I can enjoy free time when the work day is done. In addition to my photography, I spend a lot of time playing the piano. I grew up playing the keyboard and really enjoy improvising, and playing jazz and contemporary music. Music is challenging to me, but is still so relaxing and liberating. Plus, it keeps my hands limber and controlled. Additionally, I'm lucky to be married to a pathologist who has her own hobbies; we allow one another to indulge our creative sides.

Any final thoughts?

I would encourage any ophthalmologist who has a serious interest in photography to display some of their better images in their office; patients truly enjoy seeing them. In fact, it can become a form of transference: they will perceive you as having a good eye!

EYLEA® (aflibercept) Injection
For Intravitreal Injection

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

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

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

4 CONTRAINDICATIONS

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

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

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

5 WARNINGS AND PRECAUTIONS

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

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

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

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity [*see Contraindications (4.3)*]
- Endophthalmitis and retinal detachments [*see Warnings and Precautions (5.1)*]
- Increase in intraocular pressure [*see Warnings and Precautions (5.2)*]
- Thromboembolic events [*see Warnings and Precautions (5.3)*]

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 USE IN SPECIFIC POPULATIONS

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

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

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

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

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

8.4 Pediatric Use
The safety and effectiveness of EYLEA in pediatric patients have not been established.

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

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

REGENERON

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

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

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

EYL.20.09.0052

WHAT COULD THEY SEE THIS YEAR?

EYLEA® (aflibercept) Injection
For Intravitreal Injection

10 years & COUNTING
FDA approved 2011

Inspired by real patients with Wet AMD, MEfRVO, and DME.

- **First-line efficacy and safety data from 8 clinical trials[1]**
- **Dosing flexibility across several FDA-approved indications[1]**
- **>20 million doses administered to >1.6 million eyes since launch[2]**
- **Broad first-line coverage and dedicated support with EYLEA4U®[2]**

EXPLORE THE DATA
at hcp.eylea.us

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

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

ADVERSE REACTIONS

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

INDICATIONS

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

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

References: 1. EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. June 2021. **2.** Data on file. Regeneron Pharmaceuticals, Inc.

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