JANUARY 2019 # 29

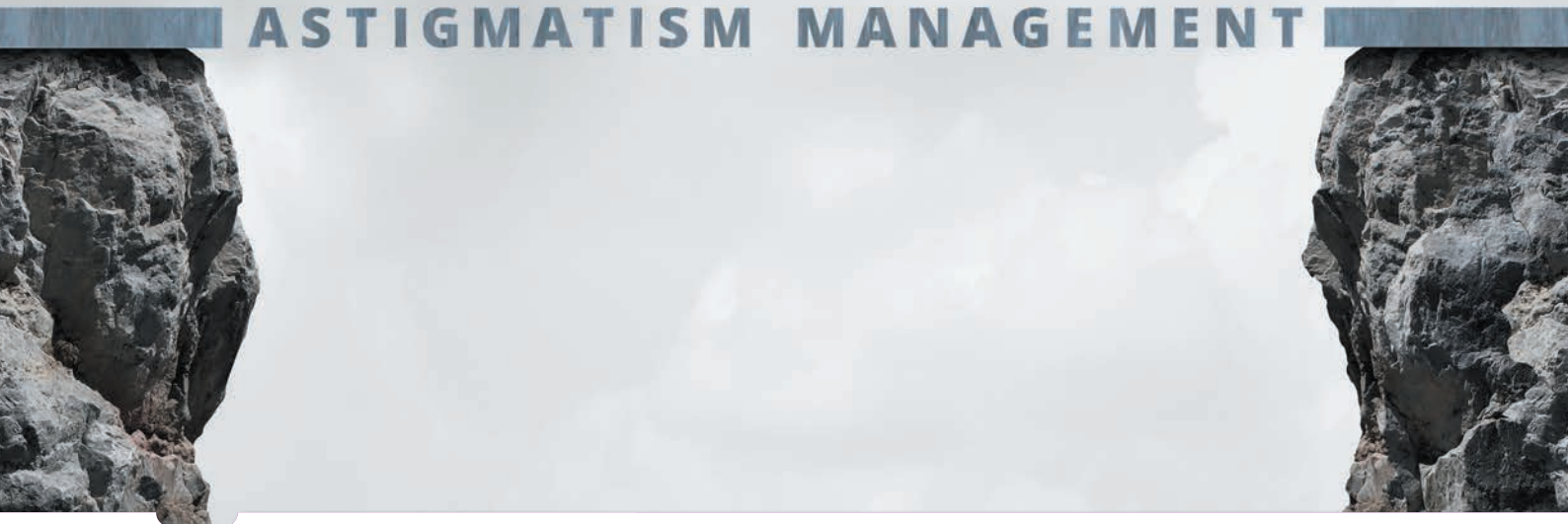
the Ophthalmologist™

A Year in Ophthalmology Research: 2018

Our experts select the most high impact developments and groundbreaking literature of the past year.

1,386,254.5 Diopters

of astigmatism went unmanaged in U.S. cataract ORs in 2017.*,[1]



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* Based on data from Dr. Warren Hill. Assumes mid-range distribution of pre-op astigmatism. Excludes irregular or other conditions that impact Toric selection.

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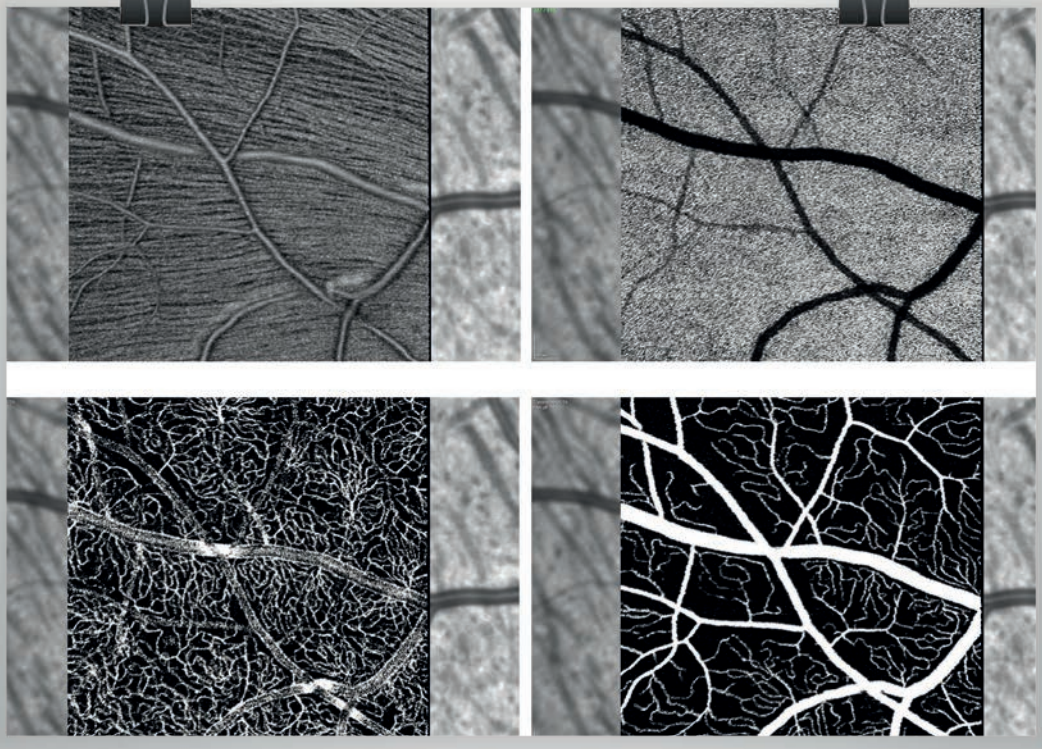
Image of the Month



In Full Flow

Taken at differing anatomic depths, these monochromatic volume scans offer a detailed visualization of the superior arcade of a non-human primate. The ability to image at this resolution allows for careful monitoring of disease progression, granting accurate diagnosis of patients with inner and outer retinal pathology.

Credit: Nimesh Patel, Houston School of Optometry

Do you have an image you'd like to see featured in The Ophthalmologist? Contact edit@theophthalmologist.com

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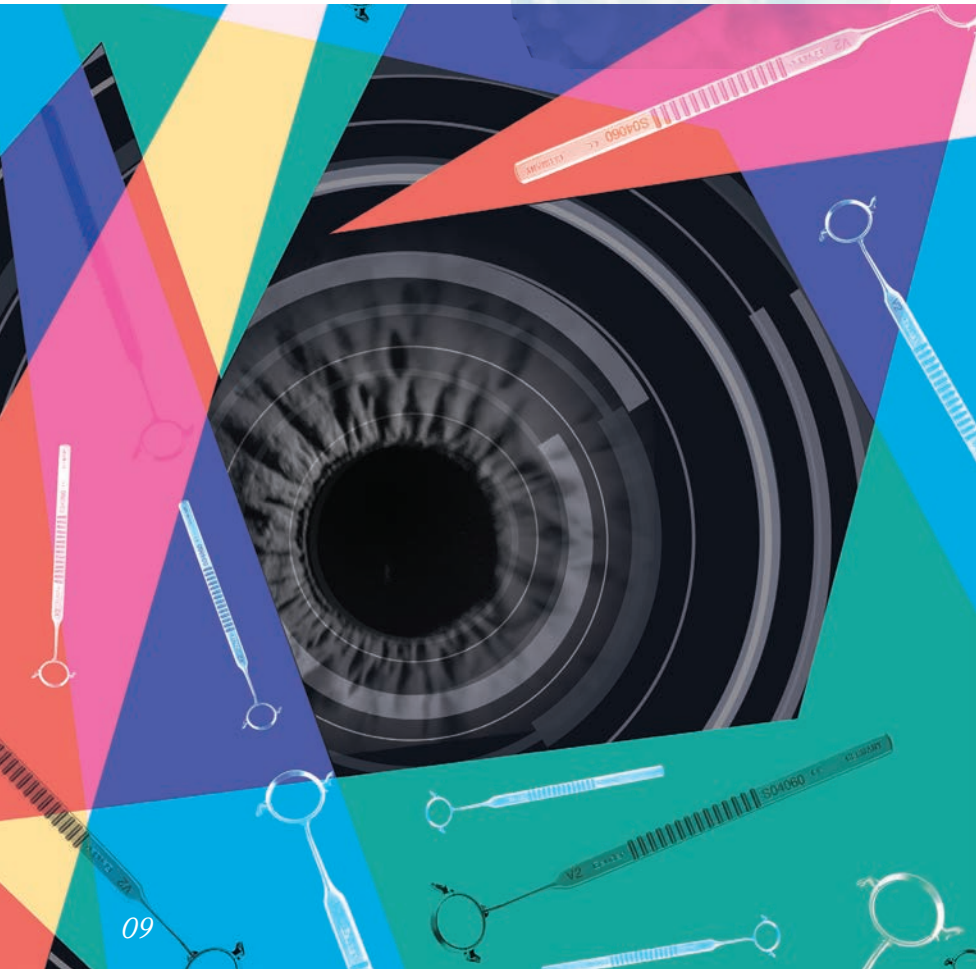

On The Cover

We have asked some of the biggest names in ophthalmology about the most eye-catching research they came across in 2018.

Feature

In Practice

NextGen

Profession

Sitting Down With

the Ophthalmologist

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The Power To Do Good

As you nominate your colleagues for the 2019 Power List, consider the wider impact of your choice.

Just before the end of the year, The Ophthalmologist editorial team was busy promoting the opening of our 2019 Power List nomination process. With a closing date fixed earlier than usual – the end of January, we were slightly apprehensive that we would not receive the usual impressive response. We should not have been concerned! I kept an eye on my inbox over the holiday period, and the number of nominations cast every single day of the winter break was overwhelming. If you haven't nominated your peers yet, please do so here: *http://top.txp.to/powerlist2019*

While you are considering the most worthy candidates for each of the list's five categories, I have a favor to ask: though you must, of course, take merit into account, please don't forget to consider diversity. There has been a slow increase in the number of women entering ophthalmology in the last decade or so, but the number of professionals from underrepresented minorities (URMs) in the USA has not risen, and there has actually been a decrease in the number of URM residents (1). As our societies become increasingly diverse – a process that is unlikely to slow down or stop – it is important that professionals in all walks of life come from equally varied backgrounds. In ophthalmology, increased diversity can help confront ethnic and racial disparities in eye care; for example, women and ethnic minorities are more likely to work in disadvantaged areas (2).

The concept of meritocracy, a term coined by Michael Young (a British egalitarian who became entirely disillusioned with the idea), has been increasingly exposed as a myth, with conversations around implicit or hidden social biases becoming more prevalent over the past few years. Cultural, social and educational opportunities, as well as overall attitudes must be taken into account, if we are to talk about individual achievements.

Initiatives do exist to level the ophthalmic playing field: the Minority Ophthalmology Mentoring (MOM) program, summer internships with Diversity in Vision Research and Ophthalmology (DIVRO), and those organizations and societies working on increasing the female profile in the field, such as Women in Ophthalmology or Women in Vision UK.

To see positive effects of a more diverse ophthalmic workforce, an immeasurable number of small steps must be made. One of those steps might just be taking diversity into account when nominating an esteemed colleague to our 2019 Power List. I, for one, cannot wait to see the results.

Aleksandra Jones
Editor

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1. *IM Xierali et al., "Current and Future Status of Diversity in Ophthalmologist Workforce", JAMA Ophthalmol, 134, 1016–1023 (2016). DOI: 20162257.*
2. *KO Walker et al., "The Association among Specialty, Race, Ethnicity, and Practice Location among California Physicians in Diverse Specialties", J Nat Med Assoc, 104, 46-52 (2012). PMID: 22708247*

Upfront

Reporting on the innovations in medicine and surgery, the research policies and personalities that shape the practice of ophthalmology.

We welcome suggestions on anything that's impactful on ophthalmology; please email edit@theophthalmologist.com

From Darkness

Introducing a personalized antisense gene therapy for inherited retinal diseases

After decades of study into inherited retinal diseases (IRD), researchers at the Scheie Eye Institute at the University of Pennsylvania have tested an antisense gene-therapy approach for the treatment of Leber congenital amaurosis (LCA) caused by a specific mutation to the ciliopathy gene centrosomal protein 290 – CEP290 (1). The intravitreal injection was developed by ProQR Therapeutics.

"LCA is the most severe form of IRD and thus has the greatest treatment potential," says Artur Cideciyan, who led the clinical trial. "We were cautiously optimistic that successful pre-clinical experiments performed in the lab would translate into positive results in patients."

And the cautious optimism was justified: the majority of the patients who took part in the multi-center study experienced an improvement in visual acuity within the first three months – with no serious adverse events. And one responder improved from barely being able to perceive light to 20/400.

Patients received intravitreal injections of a short RNA molecule (an antisense oligonucleotide) designed to counter the mutation. Cideciyan explains in more detail: "The most common mutation in the CEP290 gene is a single nucleotide change in intron 26, which results in the introduction of aberrant exon and reduces the amount of CEP290 protein." The oligonucleotide essentially blocks recognition of the aberrant exon, boosting the amount of non-mutant CEP290 protein in photoreceptors.

"We are in an era of personalized medicines and this is especially true for monogenic conditions, such as IRD. Many of the treatment avenues currently considered are specific to the gene involved – such as gene augmentation for recessive loss of function, or gene knockdown and replacement for dominant gain of function conditions," explains Cideciyan.

"Our current work takes this gene-specific personalized medicine for IRDs one step further by making the intervention mutation specific."

Naturally, patients with different molecular mechanisms of the disease cannot benefit from such specific treatment, but does the research hold wider promise? According to Cideciyan: yes. "Our study showed for the first time that intravitreally injected oligonucleotides can modulate splicing in human photoreceptor cells and result in positive changes in vision. This work opens the door to evaluating similar approaches in other inherited retinal diseases."

Reference

1. *AV Cideciyan et al., "Effect of an intravitreal antisense oligonucleotide on vision in Leber congenital amaurosis due to a photoreceptor cilium defect", Nat Med [Epub ahead of print] (2019). PMID: 30559420*

Yamane: Revisited

The pioneer behind double-needle intrascleral IOL fixation, Shin Yamane, Assistant Professor at the Yokohama City University Medical School, Japan, introduces the Yamane-Geuder needle guide – a stabilizing device for globe fixation.

What inspired your original double-needle technique?

Gabor Scharioth was my main influence. I took his method and tried to make it as minimally invasive as possible by creating small wounds using 27 gauge needles. I focused on preserving the conjunctiva through cutting and suturing – something I've altered slightly in my new technique, whereby a square knot secures the suture to the haptic.

What is different about the flange IOL fixation technique?

I now recommend grabbing the trailing haptic from outside the eye first, then pushing it into the eye via the main incision. It is less invasive than the previous technique, yet the fixation of the haptics is strengthened.

Why have you decided to change your technique?

Doctors said my original insertion technique was too difficult to master – requiring the surgeon to stabilize the needle using only their hands. I found it easy, but only because I had performed more than 200 surgeries using this technique – not everyone has that level of experience.

How have you made it easier?

I worked with Geuder to create a stabilizer. The device has a toothed ring for fixating the globe during needle insertion, and two integral "landmarks" for orientation and identification of the sclerotomy sites. Geuder is known for its excellent instrumentation, and this piece is no different – it is even better than I imagined.

Why?

Control is essential to this surgery, but it is difficult to make a controlled incision using only the microscope – particularly for beginners. The stabilizer makes the whole process easier by giving surgeons standardized insertion angles for every scleral tunnel. I also hope it will make the learning curve less daunting for trainees, and improve the consistency of surgical outcomes. For anyone wary about using the stabilizer, I would recommend practicing on a model eye first.

When do you use the stabilizer?

Now, I always use the stabiliser for IOL fixation, but I'd say it is especially important in difficult cases where the patient has small or deep-set eyes. Although I can technically do it without, I have much more control with the stabilizer than if I were to just use my hands.

What's next?

There is nothing planned for now, but there may be more improvements coming. I simply want to continue making surgery easier for all.

The Power List 2019

Nominations are now open for our most exclusive list yet. Have your say online today.

Last year we celebrated the 100 most influential figures in ophthalmology. This year, there will only be 50 – five 'Top Tens' chosen from five distinct categories.

1. Champions of Change
Philanthropists, humanitarians and lobbyists pushing for a better tomorrow – for everyone

2. Emerging Leaders
Movers and shakers influencing the world of ophthalmology – and beyond

3. Inventors
Intelligent and inquisitive minds opening the door to the future of ophthalmology

4. Mentors
Seasoned clinicians, professors and educators guiding and inspiring the next generation of ophthalmologists

5. Surgical Pioneers
Trailblazing surgeons presenting alternative approaches to the ophthalmology community

If you know a doctor who's fighting for institutional change, a master surgeon who's always breaking new ground, or an educator generous enough to focus on shaping the next generation, put them forward, so that their efforts are properly recognized.

Voting will close on January 29th. Nominations will then be passed on to our judging panel, who will select the Top 50 to be featured in print and online. Submit your nomination at: http://top.txp.to/powerlist2019

Business in Brief

Approvals, announcements, acquisitions and an all-new training program for refractive surgeons

- Ocular Therapeutix has announced FDA approval of DEXTENZA for ocular pain following ophthalmic surgery. It is the first FDA-approved intracanalicular insert delivering dexamethasone to treat post-surgical ocular pain, offering up to 30 days' relief with a single administration.

- Alcon launched its annual Retina Fellows Institute training program in Fort Worth, Texas. Participants took part in a weekend of hands-on surgical training exercises, as part of the company's commitment to developing the next generation of retinal surgeons. Alcon also announced the acquisition of Tear Film Innovations Inc – the manufacturer of iLux® – signifying its move into the dry eye treatment space.

- Novartis has announced landmark European approval for one-time gene-therapy Luxturna. It is the first treatment of its kind to improve or restore sight to patients with inherited retinal degenerative diseases caused by mutations in both copies of the RPE65 gene.

- Notal Vision has been granted breakthrough device designation by the FDA for its home-based OCT platform – a patient-friendly device intended for use between regularly scheduled clinic assessments. The company also announced the appointment of a new CEO – Susan Orr – after the retirement of Quinton Oswald.

- Results of Glaukos' recent iStent inject® study have now been released. The prospective, non-randomized trial found a 20 percent IOP reduction in 78 percent of eyes and a mean medication decrease from 68 percent to 0.8 percent. Glaukos is also pursuing FDA approval for additional MIGS surgical and sustained pharmaceutical therapy products.

In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of ophthalmology. They can be up to 600 words in length and written in the first person.

Contact the team at edit@theophthalmologist.com

(Not) Seeing Eye to Eye

George Beiko's controversial take on refractive lens exchange, published in our November issue, elicited a strong response from readers. Here, 12 respected surgeons provide a counterpoint.

By Arthur B. Cummings, Daniel S. Durrie, Guy M. Kezirian, Lance J. Kugler, Jennifer Loh, Greg Parkhurst, R. Luke Rebenitsch, Ik Hee Ryu, Evan D. Schoenberg, Jason E. Stahl, Blake Williamson and Roger Zaldivar

In this piece, we hope to provide a different perspective to the article, A Clear-Eyed Look at RLE written by our friend and colleague, George Beiko. Beiko notes that "refractive lens exchange (RLE) is becoming an increasingly common procedure" and then explains his rationale for discouraging his own patients from having an RLE. His reasons mainly point to limitations of the optics of multifocal IOLs, the potential for surgical and postoperative complications, and problems encountered with earlier lens materials. Though his argument appears to be compelling on the surface, it fails to adequately consider three main points:

1. Not all RLE patients are alike. Risks for complications vary based on age, refraction, ocular history, co-morbidities, and other factors. To conflate the risk for retinal detachment (RD) in a high myope with that of a hyperope is not valid. Beiko's own reference points this out (1). Careful pre-screening, with a detailed peripheral exam, and treating high myopes and others who have increased risk for retinal detachment (for example, via retinal barrier laser to at-risk peripheral areas) prior to RLE may actually lower the incidence

"Though Beiko's argument appears to be compelling on the surface, it fails to adequately consider three main points."

of retinal detachment in these eyes. Beiko notes the increased risk of RD in "younger, more myopic patients" and states that these patients are "most likely to elect for RLE procedures," but in the hands of a surgeon well-versed in vision correction options, these highly myopic patients are commonly directed toward phakic IOLs such as the STAAR Visian ICL, unless they have substantially dysfunctional lenses. If they do have dysfunctional lenses, they are simply embracing likely inevitable lens replacement a few years early. It is true that high myopes who undergo lens replacement are accepting an increased risk of retinal detachment compared with those who do not, but if they are no longer an acceptable candidate for phakic IOL, it is generally a question of when, not if, they take that risk.

Lens centration is vital to the visual outcome of RLE with multifocal IOL technology. Beiko suggests that late decentration is surprisingly common, writing that "at 10 years there is a one percent risk of IOL dislocation requiring surgery, a 0.7 percent risk of pronounced pseudophakodonesis and a 1.4 percent risk of moderate pseudophakodonesis" based on a 2009 study by Mönestam (2). He does not share, however, that in this study approximately 40 percent of patients had pseudoexfoliation syndrome. In fact, a more recent review of the literature states that "a predisposition to zonular insufficiency and capsular contraction is identified in 90 percent of reviewed cases" of late IOL dislocation, with pseudoexfoliation representing the most common risk factor (3). We agree with Beiko that the risk of dislocation is an important consideration in the implantation of a multifocal IOL; however, the true risk of this complication must be considered for an individual patient, and the risks of an at-risk population should not be the measure against which the general population is considered. Not every patient is a great candidate for every procedure, and it is incumbent upon the surgeon to be willing to say "no."

"To impose an expectation of perfection on presbyopia treatments is to discount the morbidity, inconvenience, and frustration of presbyopia."

2. No one promised perfection.

Beiko argues that current IOLs require compromise and do not satisfy 100 percent of the patients 100 percent of the time, and cites an impressive list of references to bolster his claim. No one disputes that current IOLs have optical limitations, and even blended vision with monofocal IOLs is a compromise. However, the optical compromise of presbyopia is 100 percent, and it is present in every eye. Where are Beiko's references about the morbidity of presbyopia? The alternatives to RLE, including bifocals, contact lenses, or monovision LASIK do not provide complete satisfaction 100 percent of the time, either; nor are they without their own risks (particularly contact lenses, which have been shown to carry higher risk of infection than LASIK (4) and, by logical extension given relative rates of endophthalmitis, RLE). Choosing the right optical solution is one of the key skills in vision correction surgery. We would all prefer to have the vision of a 20-year-old emmetrope. To impose an expectation of perfection on presbyopia treatments is to discount the morbidity, inconvenience, and frustration of presbyopia. RLE provides a solution that is convenient and it is effective every waking minute, not just when you can find your readers.

"The fact that about half of MFIOL recipients have some photic phenomena does not invalidate RLE; on the contrary, it speaks to the significance of presbyopia."

Photic phenomena are indeed a concern with all multifocal IOLs (MFIOLs), and every patient receiving such a lens should first be screened carefully for candidacy and then be counseled regarding these phenomena, via thorough informed consent. RLE surgeons should be comfortable with performing lens exchange if needed, though fortunately this is rarely

"Neither concerns about one lens, nor comparative statements about an author's opinion of the superiority of another, should be used as evidence to question the efficacy of an entire surgical procedure."

required, as satisfaction rates with MFIOLs are high. The fact that about half of MFIOL recipients have some photic phenomena does not invalidate RLE; on the contrary, it speaks to the significance of presbyopia. The vast majority of patients who receive MFIOLs are pleased to "look past" these phenomena in exchange for the benefits of unfettered sight. Beiko's complaints about specific IOLs are grounded in old studies that most likely don't apply to currently-implanted lenses. For example, eight of the nine studies he cites regarding glistenings and associated aberrations in Alcon's Acrysof lenses are from prior to 2012, and the ninth study from 2015 is a five-case series describing IOLs implanted between 2000 and 2010. This is important: in 2012, Alcon changed its manufacturing process leading to an 87 percent reduction in glistening formation in Acrysof lenses (5). Regardless of specific IOL critiques, there are many IOLs on the market, and neither concerns about one lens, nor comparative statements about an author's opinion of the superiority of one IOL over another, should be used as evidence to question the efficacy of an entire surgical procedure.

3. Surgical skills vary. Not every ophthalmologist is qualified to be a vision correction surgeon.

Vision correction surgery is demanding. Complications carry high morbidity and the refractive outcomes must be excellent. Not all ophthalmologists have the skills, the interest, or access to state-of-the-art technology needed to succeed as vision correction surgeons. Nor are all ophthalmologists willing to embrace the range of surgical options needed to ensure that the right approach is used for the right patient. Many of the complications that Beiko cited would be unacceptable to most modern vision correction surgeons. Surgeons who break capsule, decenter IOLs, or who cannot deliver on a final refractive outcome in every eye probably should not perform vision correction surgery.

No one argues that surgery does not bring risks. It is the job of all vision correction surgeons to employ their skills to balance the risks of complications against the benefits sought by their patients. Not all patients will qualify, yet many will – and many will benefit. Generalized arguments that RLE is either good or bad without consideration of the context are misguided and potentially misleading. Conflating all patients into one group undermines reasonable discussion!

We agree with Beiko's premise that vision correction should be performed safely, and that surgeons should exercise a very high level of skill in screening, pre-treating, counseling, and operating on every patient who undergoes vision correction surgery. We also agree that we need prospective studies using current technologies and methods. But we disagree with an article that argues against a valuable and important procedure, especially when it conflates arguments and ignores current methods. Let us not forget that vision – not physiology – is the primary purpose of eyes. Our ability to correct nearly all refractive errors at all stages of adulthood represents a turning point in the human condition. RLE holds an important place in that story and, in the right hands, provides great benefit to a great many people.

Arthur B. Cummings, MD, FRCS, PCEO is a Consultant Ophthalmologist and Medical Director of Wellington Eye Clinic in Dublin, Ireland, and a

"No one argues that surgery does not bring risks. It is the job of all vision correction surgeons to employ their skills to balance the risk of complications against the benefits sought by their patients."

member of the executive committee of the Refractive Surgery Alliance Society. Daniel S. Durrie, MD is the founder of Durrie Vision in Kansas City, Kansas, and a Senior Advisor in the Refractive Surgery Alliance Society.

Guy M. Kezirian, MD, MBA, FACS is the founder of the Refractive Surgery Alliance Society, and underwent a successful refractive lens exchange for presbyopia in 2016.

Lance J. Kugler, MD, PCEO is a founding member of the RSA, Physician CEO at Kugler Vision, and Director of Refractive Surgery at the University of Nebraska Medical Center, Omaha, Nebraska, and past-president of the Refractive Surgery Alliance Society.

Jennifer Loh, MD, is the founder of Loh Ophthalmology Associates in Coral Gables, Florida, and a member of the executive committee of the Refractive Surgery Alliance Society.

Greg Parkhurst, MD, PCEO, is the Physician CEO of Parkhurst NuVision, San Antonio, Texas, and past-president of the Refractive Surgery Alliance Society.

R. Luke Rebenitsch, MD, PCEO, is a Vision Correction Surgeon, the Medical Director for ClearSight Center in Oklahoma City, Oklahoma, and a member of the executive committee of the Refractive Surgery Alliance Society.

Ik Hee Ryu, MD, MS, is the CEO of B&Viit Vision, Seoul, South Korea, and a member of the Refractive Surgery Alliance Society.

Evan D. Schoenberg, MD, is a Vision Correction Surgeon at Georgia Eye Partners in Atlanta, Georgia, and a member of the executive committee of the Refractive Surgery Alliance Society.

Jason E. Stahl, MD, PCEO, is a Vision Correction Surgeon, the Director of Refractive Surgery at Durrie Vision in Overland Park, Kansas, an Assistant Clinical Professor of Ophthalmology at the Kansas University Medical Center, and a member of the Refractive Surgery Alliance Society.

Blake K. Williamson, MD, MPH, is a Vision Correction Surgeon at Williamson Eye Center in Baton Rouge, Louisiana, and a member of the executive committee of the Refractive Surgery Alliance Society.

Roger Zaldivar, MD, MBA is the Scientific Director of Instituto Zaldivar in Mendoza, Argentina, and the current president of the Refractive Surgery Alliance Society.

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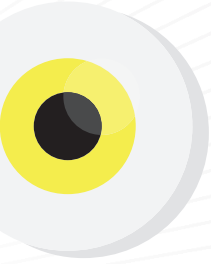
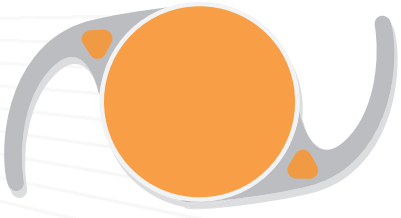
A YEAR IN OPHTHALMOLOGY RESEARCH 2018





At the end of the year, we asked our Editorial Advisory Board members and contributors to share the most interesting, engaging and thought provoking research that they came across in 2018. This is what they chose.

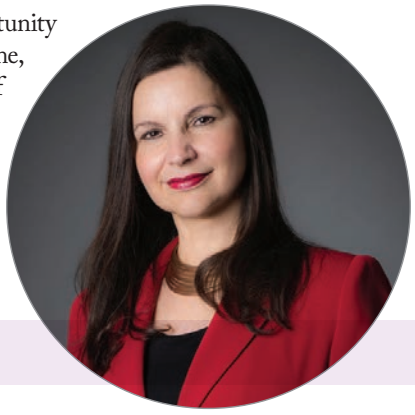
It Was a Very Good Year (for IOLs)

Getting a green light for intraocular lens power adjustment.

By Liliana Werner

The year of 2018 was, without any doubt, a fruitful one in terms of ophthalmology research. Regarding the specific area of intraocular lenses (IOL) – my area of expertise – I believe one of the most interesting and potentially ground-breaking advancements can be found in research on adjustable IOLs. Perfect Lens LLC (Irvine, CA, USA) has developed a femtosecond laser system for IOL power adjustment based on the concept of refractive index shaping (RIS) (1,2). It uses green light (520 nm), and operates with energy levels that are below the threshold for ablation or cuts. IOL power changes are obtained through laser-induced chemical reactions in targeted areas of the optic substance, with increase in hydrophilicity and decrease in refractive index, while the laser builds a RIS lens within the treated area. The technology can be applied to any commercially available hydrophobic or hydrophilic acrylic IOL, as a special IOL material is not necessary. Power adjustment is noninvasive, fast, and can be done under topical anesthesia. Multiple adjustments can be performed, as they change a very thin layer within the IOL optic substance, and they are potentially reversible.

We had the opportunity to evaluate this technology in our laboratory, at the John A. Moran Eye Center, University of Utah. In an in vitro study, IOL power, modulation transfer function (MTF), light transmission, and light scattering of a commercially available blue-light filtering IOL were assessed before and after power adjustment (3). After laser treatment, a mean power change of -2.037 D was associated with an MTF change of -0.064, and a light transmittance change of -1.4 percent. Back light scattering increased within the lens optic in the zone corresponding to the laser treatment, at levels that are not expected to be clinically significant. Treated areas within the optic could be well appreciated under light microscopy, without any damage to the IOLs. We concluded that the power adjustment by femtosecond laser produced an accurate change in dioptric power, without significantly affecting the quality of the IOL.



We also had the opportunity to evaluate, for the first time, the biocompatibility of this technology in vivo in a rabbit model (4). The study showed that postoperative outcomes in terms of uveal and capsular biocompatibility were similar between treated and non-treated commercially available lenses. The laser power adjustment procedure did not induce inflammatory reactions in the eye, or do any damage to the IOL optic. The change in power obtained was consistent among the treated rabbit eyes.

In vitro and ex vivo studies by other researchers had already demonstrated the accuracy and repeatability of this process, without affecting the IOL optic quality (5,6). They also showed that this technology can be used to create multifocality in a monofocal lens, and to cancel the diffractive multifocal add of a traditional multifocal IOL, all without significant changes to the IOL optic quality (7,8). Furthermore, the hydrophilicity based refractive index change could be used to create a toric diopter change of up to 7.6 D in a monofocal hydrophobic acrylic lens (9).

Pre-clinical studies generated a lot of interest by the ophthalmology community on this promising technology, and we are now looking forward to learn more about it through clinical studies, which are set to start soon.

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High Fliers

HAWK and HARRIER results show promise for a longer-acting anti-VEGF treatment for neovascular AMD.

By Elad Moisseiev and Anat Loewenstein

The treatment of retinal diseases has gone through a dramatic revolution over the past 15 years, since the introduction of anti-vascular endothelial growth factor (VEGF) agents delivered by intravitreal injection. This therapy achieved far better results than those of prior treatment modalities, such as laser or photodynamic therapy (PDT), and also transformed several retinal diseases from uncurable to manageable. Due to their simplicity and excellent efficacy and safety profiles, intravitreal injections of anti-VEGF therapy rapidly gained popularity, and became the most commonly performed procedure in ophthalmology. Today they are considered the first-line of therapy in most retinal diseases, and specifically in the most common ones: age-related macular degeneration (AMD), diabetic macular edema (DME) and macular edema secondary to retinal vein occlusions (RVO). There are three available anti-VEGF agents – ranibizumab, bevacizumab and aflibercept – all of which are delivered in the same manner of intravitreal injection and require close monitoring with frequent repeated injections.

Significant research attention has been devoted to developing a longer-acting anti-VEGF agent to reduce the treatment burden; however, no new drugs have become available in the past few years, and the number of intravitreal injections continues to rise steadily. The promising results with brolucizumab, a new anti-VEGF agent, reported in 2018, suggest it will become a prominent component of treating retinal diseases in the very near future.

Brolucizumab is a humanized single-chain antibody fragment. It is the smallest active unit of an antibody, with a low molecular weight of only 26 kDa (compared to 48 kDa, ~100 kDa and 148 kDa of ranibizumab, aflibercept and bevacizumab, respectively). The low molecular weight allows for a significantly higher molar concentration of anti-VEGF active molecules (approximately 10 times higher than that achieved with other agents), which may enable it to act for a longer period of time following intravitreal injection. Phase I/II studies (SEE and OSPERY) have shown that brolucizumab achieved significant resolution of intra- and sub-retinal fluids in AMD patients with a longer duration of action (delivered every eight weeks). A larger phase II study has shown that a significant proportion of eyes with neovascular AMD could be treated every 12 weeks with brolucizumab, with comparable results to those achieved with aflibercept.

These results led to larger phase III clinical trials (HAWK and HARRIER), designed to compare two dosages of brolucizumab (3 mg and 6 mg) with aflibercept over two years of treatment for neovascular AMD. Following three-monthly injections, aflibercept is administered every eight weeks and brolucizumab every 12 weeks, with earlier intervention if disease activity is detected in monthly monitoring visits.

The two-year results of these trials were reported in 2018 (by Jaffe at ARVO and Dugel at AAO), highlighting comparable visual improvements and safety profiles in all three treatment groups. However, a significantly greater proportion of patients treated with brolucizumab achieved complete resolution of intra-retinal, sub-retinal and sub-RPE fluids at months 4, 12 and 24. There was also a greater reduction on central macular thickness on OCT in all timepoints in patients treated with brolucizumab. Over half (55 percent) of the patients treated with brolucizumab did not need earlier repeated injections and maintained the 12 week schedule throughout the study period. Moreover, it was shown that over 80 percent of patients who successfully reached the first 12-week interval without needing earlier treatment maintained this success over the first year; 75 percent maintained it over two years, indicating that early observation has a predictive value for individual patients.

These results have demonstrated non-inferiority of brolucizumab therapy for neovascular AMD compared with aflibercept, and have also shown that, in most cases, the desired results can be achieved and maintained with 12-week intervals. The findings represent an important step forward in the direction of longer-term treatment, which could reduce the burden of injections and patient visits. Future studies will be required to evaluate its long-term effects, efficacy in other retinal diseases and possibly even its use with larger treatment intervals. Looking forward, it appears that brolucizumab will soon join the other commonly used anti-VEGF agents in clinical practice, and will hopefully benefit patients, physicians and healthcare systems in the management of retinal diseases.

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AI Versus ROP

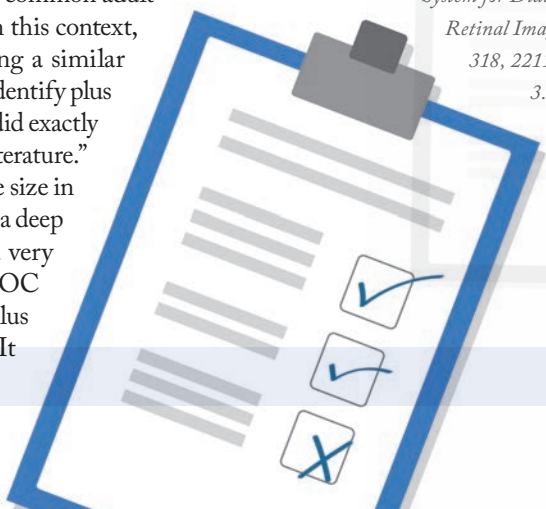
A promising application of artificial intelligence and deep learning in the search for plus (and pre-plus) disease in retinopathy of prematurity.

By Kang Zhang

Landmark paper: JM Brown et al., "Automated Diagnosis of Plus Disease in Retinopathy of Prematurity Using Deep Convolutional Neural Networks", JAMA Ophthalmol, 136, 803–810 (2018). PMID: 29801159.

Retinopathy of prematurity (ROP), a retinal vasoproliferative disease affecting premature infants, is a leading cause of childhood blindness worldwide. Standard clinical criteria have been established for diagnosis and treatment, and severe ROP can be successfully treated – if it is diagnosed early. The Early Treatment for Retinopathy of Prematurity multicenter clinical trial showed that "plus disease" is the most important parameter for identifying severe treatment-requiring ROP. Plus disease is defined as arterial tortuosity and venous dilation in the posterior pole, and accurate and consistent diagnosis of plus disease is critical to ensure that infants at risk of blindness receive the appropriate treatment. An intermediate stage – the pre-plus category – is defined as retinal vascular abnormalities that are insufficient for plus disease, but have more arterial tortuosity and venous dilation than normal.

Traditionally, ROP screening has been carried out in neonatal intensive care units (NICUs) using indirect ophthalmoscopy, or by obtaining retinal images using a contact fundus camera, with grading by a pediatric ophthalmologist or retinal specialist. The process is very time consuming, and the quality is variable. Recently, artificial intelligence (AI) including deep learning technology has been applied to fundus photographs and OCT images for accurate diagnosis of common adult retinal diseases (1, 2, 3). Within this context, it is natural to consider applying a similar approach to ROP screening to identify plus disease – Brown and colleagues did exactly that in my choice of "landmark literature." Despite a relatively small sample size in training and testing, outcome of a deep classification model performed very well, as demonstrated by the ROC curves generated for detecting plus disease and pre-plus disease. It is apparent that deep learning is well suited to this task. A common problem that plagues most deep learning studies is the lack of an accurate and pristinely-labeled dataset; however, this study did not suffer from such a problem, as the diagnosis and image quality were independently reviewed by three trained graders, and, more importantly, determined by an experienced ophthalmologist after a full evaluation in the NICU. As the study involved a sequential pass through a fully-convolutional U-Net model before the classification model, the diagnosis was not made upon the original image itself, but rather a black-and-white "mask" where the blood vessels were colored white, and the rest of the image was colored black, ignoring all information other than the shape of the blood vessels. It is very exciting to see that all the information the deep learning model in this paper used to make an accurate diagnosis was found in the width, orientation, and tortuosity of the vessels. However, as the dataset was rather small (approximately 5500 eye exams), it is difficult to determine if this method can reliably mimic physician performance in a variety of real-world scenarios. On the other hand, given that there is a wide variation in quality and consistency when grading the same ROP photographs among very experienced physicians, the method is expected to outperform physicians when given a large dataset (and trained and validated in a variety of clinical settings). I believe this method has the potential to be a great tool in aiding ROP clinical care.



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Begone Floaters!

The tide is turning for patients with vision-degrading vitreopathy.

By David R.P. Almeida

Landmark paper: J Sebag et al., "Long-Term Safety and Efficacy of Limited Vitrectomy for Vision Degrading Vitreopathy Resulting from Vitreous Floaters", Ophthalmology Retina, 9, 881–887 (2018). DOI: e201803011.

This study, published in September 2018, looked at outcomes of patients undergoing vitrectomy for vitreous opacities, also known as vitreous floaters (1). Vitreous opacities contribute to the disease entity of vision-degrading vitreopathy, which can lower visual acuity (VA) and degrade contrast sensitivity function (CSF). Vitrectomy for floaters has remained controversial, and much debate has occurred about the appropriateness of vitreoretinal surgery for patients with good VA but bothersome floaters; however, with the widespread adoption of micro incisional vitrectomy surgery (MIVS), efficient and safe surgical approaches are available that should be considered. Prior to this study, long-term results in a large series with objective quantitative outcome measures were lacking.

This case series enrolled 145 patients reporting bothersome vitreous floaters, which were compared to 70 age-matched controls. Posterior vitreous detachment (PVD) alone was the documented reduced vitreous density, improved visual acuity, and normalized contrast sensitivity function.

But above all in importance has been the exceptional degree of patient happiness (confirmed with VFQ-39 testing), making the journey greatly satisfying.

Inside perspective

First author Jerry Sebag shares the background and impact of his "landmark literature"…

Myodesopsia (Greek for floaters) is experienced by young people with myopic vitreopathy and older people with posterior vitreous detachment. When vitreous opacities also cause degradation in contrast sensitivity function, the condition is known as vision degrading myodesopsia. Patients with this ailment have long been dismissed by doctors as not having a disease because, until recently, there were no tests that could quantify severity and identify individuals deserving intervention. Once we developed quantitative ultrasound to evaluate vitreous structure (1) and began measuring contrast sensitivity function to quantify vision beyond visual acuity (2, 3), we realized that there are patients who suffer greatly with this problem. Case selection was thus enabled, and a cure could legitimately be offered. Vitrectomy was modified to minimize risks of infection, retinal detachment, and cataract. The safety profile has been very high in the short term (4) and long term (5). Quantitative outcome measures

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"By having long-term follow-up in the case series, we can better counsel patients on the efficacy and safety profiles of this intervention during the informed consent process."

cause in 96/195 (49.2 percent), myopic vitreopathy alone was the cause in 30/195 (15.4 percent), PVD with myopic vitreopathy was the cause in 56/195 (28.7 percent) and asteroid hyalosis was the cause in 13/195 eyes (6.7 percent).

Limited vitrectomy with 25-gauge instruments was performed without surgical PVD induction, preserving 3 to 4 mm of retrolental vitreous in phakic eyes. The study had excellent follow-up of mean 32.6 months (range 3–115 months) and defined main outcomes measures of VA, 39-item National Eye Institute Visual Function Questionnaire (VFQ) results, CSF (Weber index), and quantitative ultrasonography results.

The study found that with the surgical technique employed, vitreous echodensity decreased by 94.1 percent ($P < 0.0001$), VFQ results improved by 19.3 percent ($P < 0.0001$) and VA improved ($P < 0.0001$). Of particular importance, preoperative CSF was degraded by 91.3 percent compared with controls ($P < 0.0001$) and this normalized at 1, 3, 6, 12, 24, 36, and 48 months after surgery ($P < 0.00005$ for each time point).

During the study period, there were no cases of endophthalmitis. There were three retinal tears and three retinal detachments that underwent successful repair. Clinically significant vitreous hemorrhage developed in two patients, clearing spontaneously. Two epimacular membranes and four recurrent floaters from new PVD were treated by re-operation. Cataract surgery occurred in 21 of 124 patients (16.9 percent) at a mean age of 64 years (no patients younger than 53 years required cataract extraction); cataract surgery occured at an average of 13.1 months after vitrectomy.

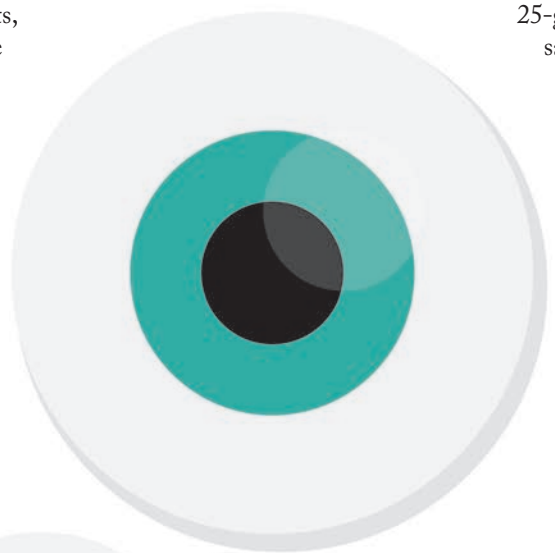
Vitrectomy for vitreous floaters remains a controversial topic. But as any ophthalmologist or vitreoretinal surgeon knows, this is a common problem and patients who present for treatment options are significantly bothered by symptoms.

This case series has two major takeaways:

First, patients with vision degrading vitreopathy have clinically relevant effects on visual function, contrast sensitivity, vitreous echodensity and visual acuity compared to controls. This study helps give credence to these patients and gone are the days where the symptoms of "floaters" were trivialized. The diagnosis of vision degrading vitreopathy helps give credibility to a pathologic state with significant objective markers.

Second, the authors show that limited 25-gauge MIVS provides an effective and safe treatment approach that decreases vitreous echodensity, improves patient well-being, improves VA, and normalizes CSF.

Specifically, by having long-term follow-up in the case series, we can better counsel patients on the efficacy and safety profiles of this intervention during the informed consent process. As the authors correctly point out, these findings warrant a prospective randomized trial and highlight the evolving surgical spectrum of MIVS.



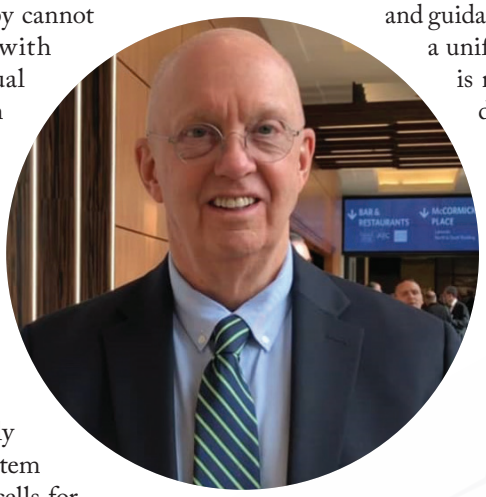
See the Light

New advances in regenerative medicine bring hope to patients suffering from blinding disorders of the outer retina.

By Steve Charles

Landmark paper: YH Jung et al., "3D Microstructured Scaffolds to Support Photoreceptor Polarization and Maturation", Advanced Materials, 30 (2018). DOI: 201803550.

Regenerative medicine is a promising and relatively new area of research inclusive of both gene therapy and cell-based approaches. There are many misconceptions regarding regenerative medicine approaches for retinal disorders; gene therapy should be thought of principally as a prevention scheme dependent on early intervention before significant cell loss. Gene therapy cannot produce visual improvement with the exception of the modest visual improvement observed with Luxturna (voretigene neparvovec-rzyl) for RPE 65 type of Leber Congenital Amarosis and RPE 65 subtype retinitis pigmentosa. On the other hand, cell-based therapies do have the potential to restore function. But intravitreal, subretinal stem cell or retinal progenitor cell injection cannot produce highly organized retinal architecture. Stem cells must be converted to RPE cells for geographic atrophy associated with AMD or to photoreceptors for inherited retinal disorders or possibly chronic retinal detachment treatment. The conversion process is complex, takes over 100 days, and has many potential pitfalls.



Blinding disorders of the outer retina involve dysfunction and degeneration of photoreceptors. One potential approach to treat these forms of blindness is to repopulate the outer retina via a simple bolus injection of donor photoreceptors. This approach may not be ideal due to the highly polarized organization of photoreceptors that include apical light sensing photopigments and basal axon terminals. In addition, bolus injections create uncertainty with regard to the area, density, and retention of donor cells. Jung, Phillips and colleagues recently published a highly cited paper on a revolutionary approach to photoreceptor replacement – my choice of landmark literature. The paper describes a novel and robust microfabrication process developed to create 3D, micron-sized complex structures in ultrathin and biocompatible elastomer films, such as non-biodegradable polydimethylsiloxane and biodegradable polyglycerol-sebacate that can serve as polarizable photoreceptor delivery scaffolds. The scaffolds consist of an array of cup-shaped photoreceptor capture wells that funnel into microchannels. This "wine glass" scaffold design promotes efficient capture of human pluripotent stem-cell-derived photoreceptor cell bodies and guidance of basal axon extensions, ultimately achieving a uniform level of organization and polarization that is not possible with bolus injections or previously described scaffolds.

In addition to future therapeutic applications, their scaffold design and materials provide a platform to generate reproducible and scalable in vitro models of photoreceptor-based diseases.

"Gene therapy should be thought of principally as a prevention scheme dependent on early intervention before significant cell loss."

Seeing Is Remembering

The link between cataract surgery and age-related cognitive decline.

By Paul Ursell

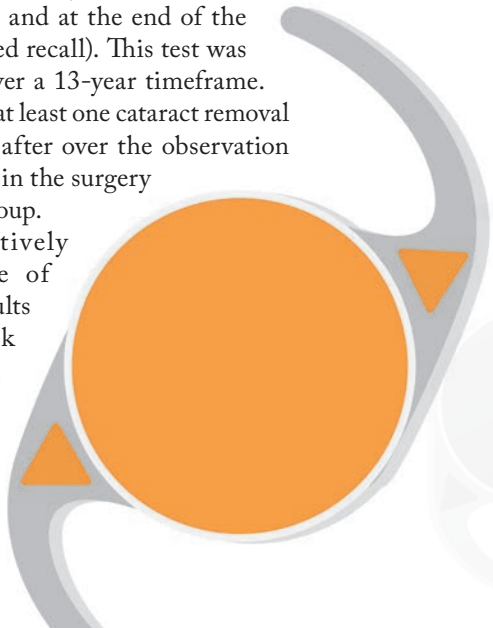
Landmark paper: A Maharani et al., "Cataract surgery and age-related cognitive decline: A 13-year follow-up of the English Longitudinal Study of Ageing", PLOS ONE, 13 (2018). DOI: e0208045.

Most cataract surgeons would agree that the improved vision patients experience after cataract surgery has a positive impact on those patients' lives. This is felt to be particularly so in patients who have concurrent cognitive impairment, such as dementia. Unfortunately, most of the studies to date looking at the depth of dementia after cataract surgery have failed to show an improvement, probably because of the structure of the dementia assessments used before and after surgery. A paper in PLOS ONE has shown, however, that the cognitive decline associated with normal ageing was slowed by cataract surgery.

The English Longitudinal Study of Ageing (ELSA) forms part of the SENSE-Cog multi-phase research program, which is funded by the European Union Horizon 2020 program. The researchers looked at cognitive function before and after cataract surgery in the respondents and compared it with a control group. Cognitive function was measured using episodic memory scores as part of a wider panel of questions looking at ageing in general. In the memory test, the interviewers read a list of 10 simple nouns once. The respondents were asked to repeat those nouns twice: immediately after the words were read out (immediate recall) and at the end of the cognitive function module (delayed recall). This test was performed at least three times over a 13-year timeframe. Cataract surgery respondents had at least one cataract removal after the first test and then two after over the observation period. There were 2,068 patients in the surgery group and 3,636 in the control group.

Cataract surgery was positively associated with a lower rate of cognitive decline among older adults in England, independent of risk factors for cognitive impairment, including those related to age, gender, education, wealth, chronic diseases, depressive symptoms, and physical inactivity.

Vision loss and cognitive decline, particularly in dementia, is an increasing part of the workload in our clinics. My choice of landmark paper shows us the benefit of visual rehabilitation on cognition and by extension the potential deficit caused by visual loss on patients ageing. The topic will be discussed further at the RCOphth Congress in Glasgow, May 20-23 2019.



"Cataract surgery was positively associated with a lower rate of cognitive decline among older adults in England, independent of risk factors for cognitive impairment."

Singing the Blues

Not a single research paper: the Blue Journal of Ophthalmology deserves an honorable mention for launching Ophthalmology Glaucoma in 2018 (and Ophthalmology Retina in 2017).

By Kevin L Waltz

For this feature I decided not to follow the brief exactly. This year, we should not just be recognizing and celebrating a single article in a single year; rather, we should be celebrating the amazing increase in quality eye research over time and the exceptional response that has supported it. And we should be celebrating the American Academy of Ophthalmology and the Blue Journal of Ophthalmology for launching Ophthalmology Retina and Ophthalmology Glaucoma, which provide new opportunities for eye researchers to share their work under the imprimatur of ophthalmology.

The American Academy of Ophthalmology and its predecessors have published the original Blue Journal of Ophthalmology and its predecessors for a long time. In 2018, it published volume 125 – the first issue of the Blue Journal of Ophthalmology was published in the 1890s. In the subsequent 125 years, the journal became one of the premier options for publishing top-quality eye research; for instance, most of the landmark publications from the ETDRS study were published in Ophthalmology (1).

It sounds like the Blue Journal of Ophthalmology is on a multigenerational roll. In that case, why would it need to change? The volume of eye research is exploding. That research needs a quality venue and a quality audience to make an impact. Ophthalmology Retina and Ophthalmology Glaucoma provide both that venue and that audience. The venue of Ophthalmology is known for very high-quality peer review and publishing important research papers with a high citation rate.

Ophthalmology Retina was launched in January 2017 and published an issue every other month the first year and every month in 2018, its second year. Ophthalmology Glaucoma was launched in 2018 and published an issue every other month for the first year. These two new ophthalmic journals provide high-quality venues for publishing ophthalmic research, concentrating it into an easily accessible format. That, in my opinion, is worth celebrating.

"Research needs a quality venue and a quality audience to make an impact. Ophthalmology Retina and Ophthalmology Glaucoma provide both that venue and that audience."

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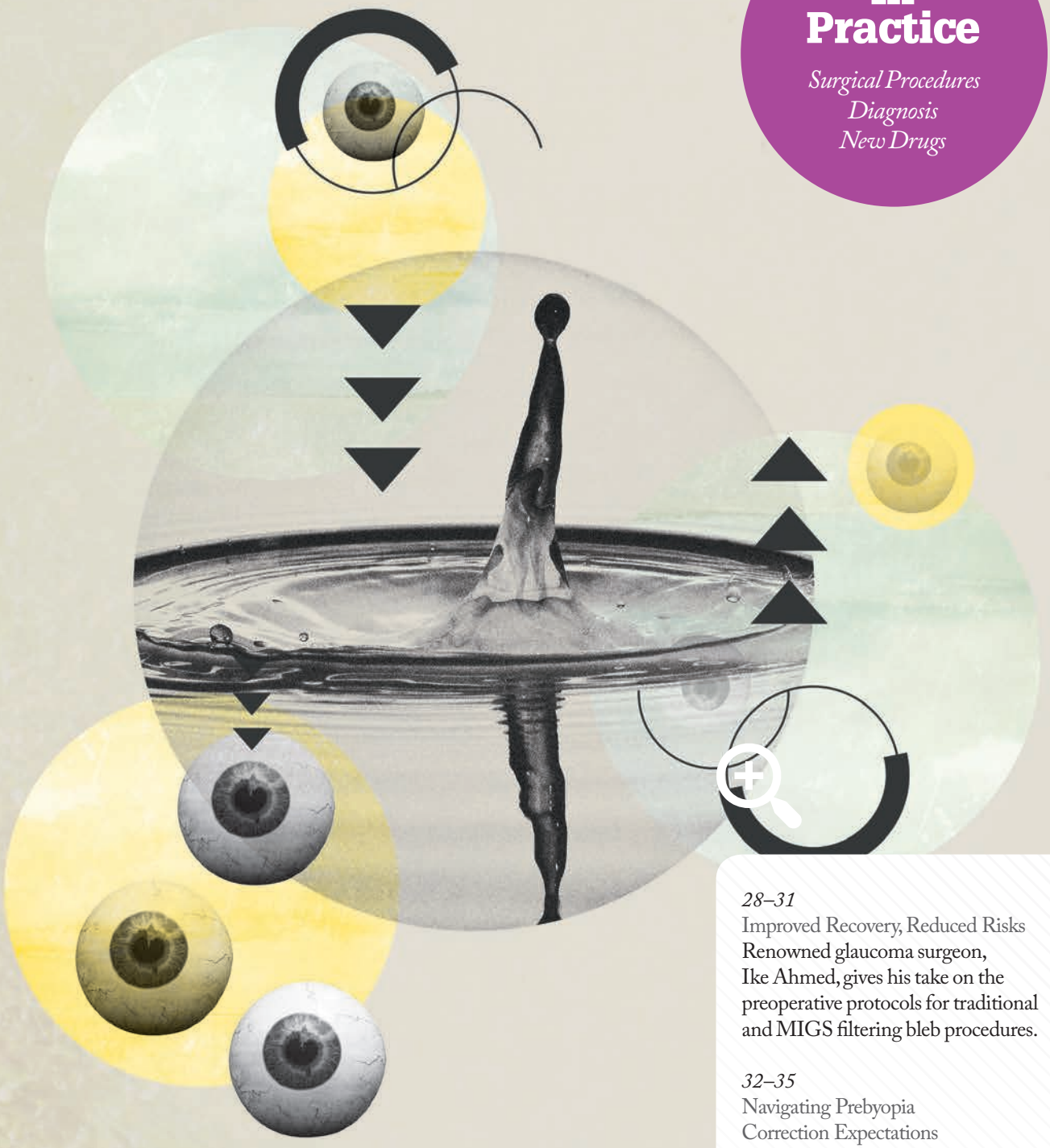


Improved Recovery, Reduced Risks

A doctor's take on the preoperative protocols for traditional and MIGS filtering bleb procedures.

By Ike K. Ahmed

Regardless of the operation, preoperative protocols have an essential role in helping us prevent infection, reduce pain and bleeding, and lower the risk of inflammation after surgery. Sometimes the steps are developed in the course of the procedure's investigational process, other times we learn as we go and publish our results – and, often, we do both. For nearly every surgery, we continually adjust protocols based on new data or new drugs, working to incrementally improve our outcomes. Over time, the well-honed, evidence-based protocols become more effective and reliable. One example is the protocol for glaucoma procedures that involve a filtering bleb. Bleb procedures include traditional trabeculectomy and tube shunt surgeries, both of which are ab externo procedures that permit the aqueous to drain from the anterior chamber to the subconjunctival space. Another newer bleb procedure is the XEN Gel Stent (Allergan), a MIGS device that also creates drainage to the subconjunctival space with a stent implanted through an ab interno approach. XEN has a similar pressure-lowering effect with fewer risks than trabeculectomy and tube shunt (1), which can cause loss of best-corrected visual acuity, hypotony, choroidal effusion, cataract, and flattening of the anterior chamber (2-5).

I choose traditional filtering surgery for patients with open-angle glaucoma who are looking for a very low single-digit target pressure. XEN is used with mild to severe glaucoma patients who are uncontrolled or noncompliant with medications and/or are progressing but ideally need pressures in the low teens – with or without combined cataract surgery. Though different, all three procedures share preoperative considerations and protocols related to the filtering bleb.

The "basic" protocol

Although the goal of a preoperative protocol is to standardize the steps before surgery, it does not exist in a vacuum.

At a Glance

- *Almost every type of surgery requires preoperative protocols, which should be regularly adjusted to be effective; one such protocol for glaucoma procedures is a filtering bleb*
- *Steroids are regularly used before bleb surgery, and topical glaucoma medications are usually withheld or replaced with preservative-free glaucoma drops*
- *Ocular surface disease and lid margin issues should be resolved well ahead of surgery; procedures should be delayed if the patient is still suffering from red eye or other symptoms.*

Following Footsteps

Arsham Sheybani, MD, trained with Ike Ahmed and continues to adhere to strict preoperative protocols for filtering bleb surgeries. We asked him to share his experiences.

Is your preoperative protocol similar for trabeculectomy, tube shunt and XEN patients?

Yes. The most important thing for all three procedures is to minimize the amount of preoperative inflammation. I have patients use a corticosteroid (difluprednate) four times per day the week before surgery.

How important is it to resolve ocular surface problems before surgery?

We have to do everything we can to reduce inflammation – and ocular surface disease can be a major source, if we do not treat it properly. If a patient has significant conjunctival inflammation, then I consider stopping some pressure-lowering drops and instead move to oral acetazolamide, if the patient can tolerate it. I also determine if the patient has dry eye or lagophthalmos, in which case a period of treatment with lubricants and ointments is necessary before surgery.

Has patient compliance been an issue with your preoperative protocol?

Our surgical scheduler sends out prescriptions according to the schedule. For example, XEN, trab and tube patients all get steroids the week before. The process is streamlined, so it's easier for our patients as well as our surgeons. We know that our patients received their medication on schedule; our job is to make sure that we educate them as to the utmost importance of following the medication to ensure successful surgery.

How have MIGS procedures changed the field?

Medications cause conjunctival toxicity, and trabeculectomy is less likely to succeed for patients taking multiple medications. It's possible that this is the case for all conjuctival filtration surgeries, including XEN. If we can treat patients earlier with a MIGS option, we may be able to avoid reaching the point where a patient must take multiple medications, receive filtering bleb surgery, and still not achieve the desired outcome.

"For nearly every surgery, we continually adjust protocols based on new data or new drugs, working to incrementally improve our outcomes."

Patients with glaucoma can have other ocular diseases, systemic comorbidities and medications that may affect surgery. Any preoperative approach must be customized to fit the individual's needs and limitations. That customization does, however, begin with the same basic foundation.

Our standard protocol before bleb surgery is topical steroid drops (typically dexamethasone 0.1 percent or prednisolone acetate 1 percent) four times per day for seven days (6). If the eye is infected or inflamed, we start topical steroids two to four weeks prior to surgery and watch for a potential steroid IOP response. To reduce this risk, when using steroids for more than two weeks, I advise using loteprednol 0.5 percent four times a day. We readily withhold offending topical glaucoma medications (ideally for one month prior to surgery), if we feel they are causing conjunctival infection or inflammation. To replace these medications, or if the IOP is uncontrolled, we add oral carbonic anhydrase inhibitors as needed. Changing to preservative-free glaucoma drops is another option, if preservative is thought to be the culprit. Topical antibiotics are only used two days before surgery. If a patient is taking anti-coagulants or anti-platelet medications or supplements, we discontinue these preoperatively to help reduce the risk of intraoperative bleeding (if cleared to do so by the patient's internist) – the duration depends on the medication's half-life.

"In treating ocular surface disease and/or blepharitis before glaucoma surgery, we sometimes need to tolerate moderate elevation of IOP for a few weeks."

Resolving ocular surface pathology

Ocular surface disease and blepharitis can also contribute to postoperative inflammation and scarring. When a patient has a healthy ocular surface and lid margins, we can schedule surgery and proceed with standard preoperative medications. However, if any problems are present on the ocular surface or lid margins, we need to resolve them before scheduling surgery and initiating standard steroids.

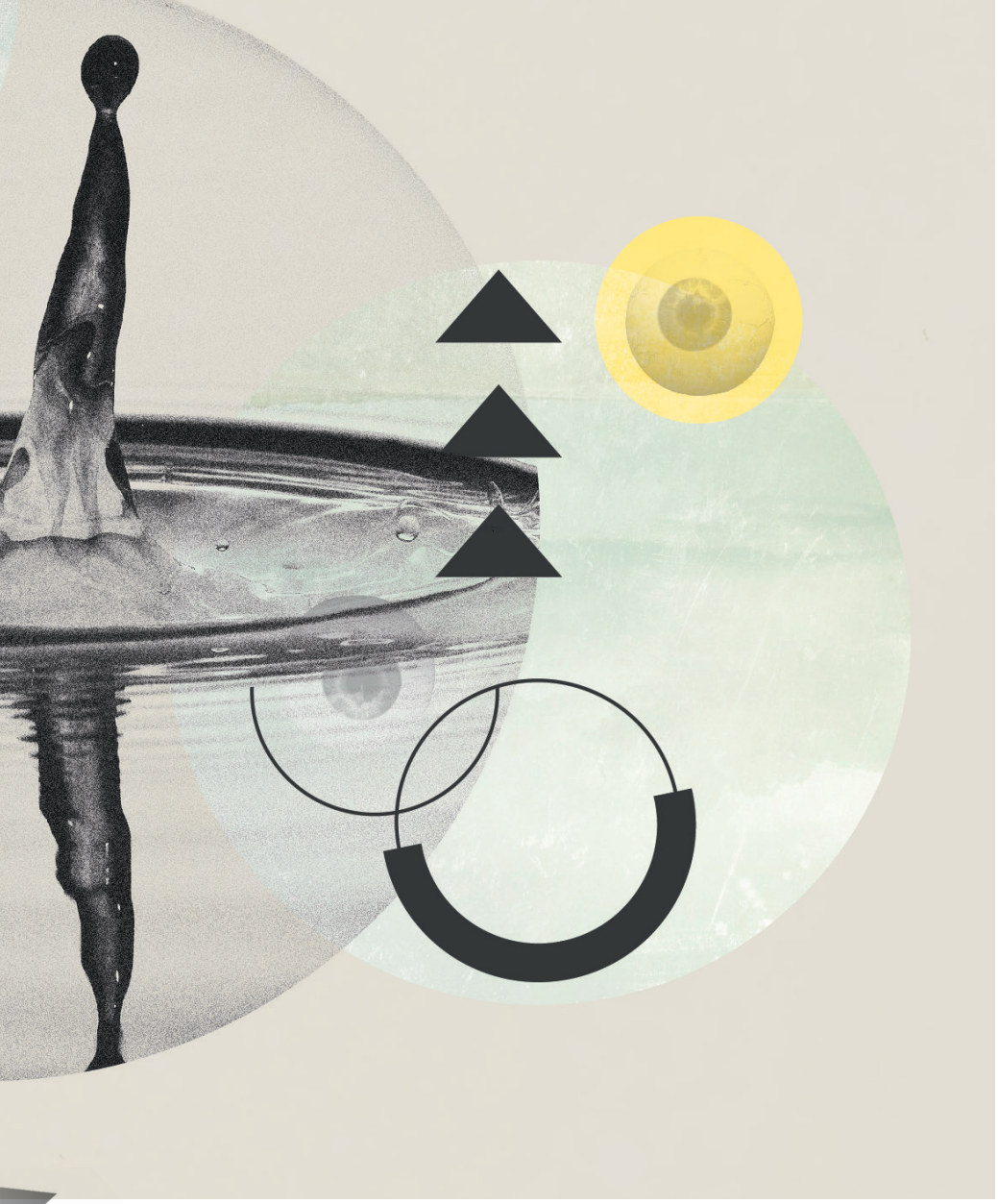
Patients with dry eye should use non-preserved tears or gel lubricants, oral Omega 3 supplements and, if needed, cyclosporin A. If blepharitis is present, I have patients perform lid hygiene, take oral doxycycline, and use erythromycin ointment and topical steroids. For patients with a combination of any of these ocular surface and lid margin problems, treatment is customized to ensure that all issues are addressed before surgery. These therapies may need to be continued postoperatively and indefinitely to preserve conjunctival health for good bleb function.

All of these therapies are initiated at least one month before surgery. If the ocular surface is clear and quiet at this point, we can proceed with the standard week of steroid drops before surgery. If the patient still has red eye or other symptoms, my advice is to delay surgery and adjust treatment before continuing therapy.

In treating ocular surface disease and/or blepharitis before glaucoma surgery, we sometimes need to tolerate moderate elevation of IOP for a few weeks. Certain therapy choices may also require additional IOP monitoring. For instance, if we add steroids for more than two weeks, I would check the IOP again.

Completing the protocol in the surgery center

Once ocular surface and lid margin problems are resolved, the patient has come off any medications as instructed, and the standard course of preoperative medications is complete, the remaining steps of the preoperative protocol can take place in the surgery center. Here, patients are prepared with topical steroids, NSAIDs and antibiotics. We use topical tetracaine 0.5 percent for anesthesia and instill a drop of phenylephrine 2.5 percent on the superior conjunctiva for



"Preoperative protocols go a long way to reducing surgeon stress and building confidence in the procedures."

vasoconstriction to minimize bleeding risk.

For my trabeculectomies and XEN procedures, I administer 0.1 cc of mitomycin-C (0.4mg/cc) subconjunctivally posterior to the limbus (>6 mm from limbus) for most eyes to provide wound-healing modulation. I inject this intra-Tenons to prevent it from dispersing everywhere, and keep it posterior, avoiding limbal pooling. I do not typically use mitomycin-C for the Baerveldt Glaucoma Implant (Advanced Medical Optics), but do use it occasionally when implanting the Ahmed Glaucoma Valve (New World Medical).

The outcome we anticipated

Preoperative protocols are designed to optimize outcomes and improve predictability. When we adhere to them routinely, we know what results we can comfortably expect from surgery. For filtering bleb surgeries, that can mean less fibrosis, bleeding and inflammation. Particularly for traditional surgeries like trabeculectomy and tube shunt, preoperative protocols go a long way to reducing surgeon stress and building confidence in the procedures.

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Navigating Presbyopia Correction Expectations

First, understand what the patient actually needs. Next, ensure they understand what level of presbyopia correction is possible – and what compromises it will entail.

By Francesco Carones

In a perfect world, every patient who wants and needs a presbyopia-correcting IOL would receive one. But in the real world, this aspiration is tempered by considerations of IOL safety and performance. Such issues mandate a degree of patient selection: we must ensure a safe implantation procedure above all else, but we must also consider which patients are likely to be satisfied with the inherent compromises regarding spectacle independence and quality of vision. How can we distinguish between different presbyopia candidates and manage them accordingly? I advise paying attention to three key areas:

- Pre-existing anatomy and pathology
- Likely long-term sequelae of existing disease
- Personality and needs of the patient

Pre-existing anatomy and pathology

All candidates for presbyopia correction should be screened for pre-existing diseases. Among systemic conditions, be particularly alert for diabetes, rheumatoid arthritis and Sjögren's syndrome. Regarding ocular conditions, be sure to thoroughly check all patients for ocular surface disease; if present, make every effort to resolve it prior to any lens implantation procedure. Screen for glaucoma, and don't forget to look for corneal irregularities, including keratoconus and pellucid marginal degeneration. Also, assess the ocular endothelium, and note the consequences of any prior refractive surgery. Finally, observe the status of the vitreous, and use OCT or angio-OCT to identify any pre-existing macular disease.

Screening patients in this methodical way should allow you to identify conditions that may compromise the safety of presbyopia correction. But do exercise judgment when acting on your findings – not every pre-existing issue rules out a presbyopia-correcting IOL (Table 1: "Stop or Go").

Long-term sequelae

In making the final decision regarding presbyopia correction in patients with pre-existing conditions, I am guided by the types of long-term sequelae that might reasonably be expected given the condition in question. In brief, we should be very cautious where expected sequelae include macular dysfunction, decreased contrast sensitivity, or tear film deterioration. Conditions which may contra-indicate presbyopia correction therefore include glaucoma, macular degeneration, pucker, and severe systemic disease, such as diabetes, rheumatoid arthritis,

At a Glance

- *All presbyopia-correction candidates should be screened for pre-existing systemic conditions, such as diabetes, Sjögren's syndrome or rheumatoid arthritis, but not every disease means that a patient can't receive a presbyopia-correcting IOL*
- *Patients' lifestyles and individual requirements are critical for choosing the right IOL for a particular patient*
- *Various available presbyopia-correcting lenses have different properties and will be right for different patients.*

"It is very important to understand the specific motivations and needs of the patient with regard to presbyopia correction."

Stop	*Go*
Type 1 diabetes with any retinal involvement	Type 2 diabetes with no retinal involvement
Sjögren's syndrome	Meibomian gland dysfunction responding to therapy
Pellucid marginal degeneration	Stable, early form fruste keratoconus
Asteroid hyalosis	Posterior vitreous detachment, few floaters
Confluent macular drusen	Posterior pole drusen, no macula

Table 1. Stop or Go? Pre-existing disease and presbyopia-correcting IOLs

and Sjögren's syndrome. In short, if the pre-existing condition may progress to significant vision impairment, I prefer not to implant a presbyopia-correcting IOL.

Patient factors

Lastly, it is very important to understand the specific motivations and needs of the patient with regard to presbyopia correction. How old is the patient? What kind of job and leisure activities are they likely to do – now and in the future? What level of spectacle independence do they seek, and for what activities? In brief, the surgeon should take time to assess key aspects of the patient's lifestyle, and very much take these into account when advising the patient about presbyopia-correcting IOLs.

In this context, relevant evaluation techniques include chair-time conversations, discussions with relatives and friends, and self-assessment questionnaires. Always remember that the most important thing is to grasp what patients really want: hence, chair time is necessary not so much for explaining things to patients, but for truly understanding them. To give a simple example, a typical Nordic computer worker, very tall, will probably want to read from a computer screen at a significant distance because his arms are relatively long. By contrast, an elderly woman who wants to read small print is more likely to benefit from optimization of near vision. Thus, different patients have rather different needs, which in turn will dictate different IOL parameters. And that's why it is important to first understand and then match each person's specific requirements to the most appropriate surgical option.

The art of compromise

To appropriately advise your patients you must also understand the respective performance attributes of available presbyopia-correcting IOLs: some are better for one purpose, others are more suitable elsewhere (Sidebar). In particular, some provide more presbyopia correction than others – an important point because the more presbyopia correction provided by an IOL, the greater the chance of associated visual disturbances.

Communicate the compromise, set the expectation, accept the outcome

- Disclose the compromise involved with presbyopia-correcting IOLs, and help the patient fully understand it
- Ensure the patient has a clear and realistic expectation of the level of spectacle independence attainable by the IOL
- Ensure the patient is willing to accept the compromise necessary to meet the expectation

Take care to inform your patients of this inverse correlation between spectacle independence and quality of vision; it is vital that they understand the compromises inherent in each of the three categories of presbyopia-correcting IOLs.

Once the patient has a realistic expectation of the level of presbyopia correction that can be attained, and a clear understanding of the visual compromises required for this, we can confidently undertake surgery to deliver both expectation and compromise. In my experience, patients usually understand and accept the trade-offs without any problem. Thus, communication of the level of spectacle-independence that an IOL will provide, and the associated effects on quality of vision, are key to keeping patients happy.

Nevertheless, I always try to under-promise and over-deliver. Above all, I am careful to manage expectations regarding haloes. I do not say that the haloes they see on day one will completely disappear, because this almost never happens and then the patients then get worried or frustrated. It's not fair to set patients waiting for something that probably won't happen; rather, I prefer to tell them that they're likely to experience small haloes, but they won't be bothersome and won't affect their ability to do what they want to do, like driving. And then, when the haloes decrease, or even disappear, the patients are even happier. So my philosophy is to relieve them of the expectation of vision that is completely free of haloes or glare, and then they are not concerned if they have a very mild vision impairment at night.

"To appropriately advise your patients you must understand the respective performance attributes of available presbyopia-correcting IOLs."

Finding the balance

In conclusion, having fully appraised the patient of the compromises associated with presbyopia-correcting IOLs, and of the degree of spectacle independence they can realistically expect, I make sure that the patient is willing to accept the compromise required to attain the expected outcome (Sidebar 2). Only then do I perform the surgery required to meet those patient expectations, which involves careful choice of IOL category and power. Always under-promise and over-deliver: this avoids the patient having unrealistic expectations – and developing unjustified concerns – regarding visual disturbances. Using my approach, I believe you will find that many patients experience a better outcome than they had expected, and are correspondingly happier with the surgery.

The right IOL for the right patient

EDOF-ERV IOLs

Nearly half (47.5 percent) of patients are suited to EDOF-ERV IOLs, where the compromise in terms of quality of vision is low. Typical patients include those who want spectacle independence but are concerned about quality of vision (for example, because of active lifestyles with high demands for distance vision and significant demands for intermediate vision). Taller patients, and patients unsuited for trifocals, also tend to benefit from EDOF-ERV IOLs. For this category of patient, I set post-operative expectations as follows:

- You will be independent of spectacles in a manner fitting your lifestyle, but you may need glasses for near vision (but good illumination may allow spectacle-free reading)
- Your vision quality will be almost uncompromised and you will experience almost no glare or haloes at night

Trifocal IOLS

Patients most suitable for trifocal IOLs (again, 47.5 percent) tend to be active patients seeking complete spectacle independence, who are willing to accept small compromises in quality of vision. Patients who have received laser vision correction are also suitable for these lenses. For these patients, I set post-operative expectations as follows:

- You will attain almost complete spectacle independence but may need good lighting to read (or require glasses when reading in poor light)
- A consequence of almost complete spectacle independence is that you may experience some glare and haloes at night – this is normal

Bifocal IOLs

Only about 5 percent of my patients are good bifocal IOL candidates. Mostly, these are previously myopic patients in the range -2.5 to -4D, who used to read without spectacles and who now seek spectacle independence for near vision; they have few activities based on intermediate vision. For these patients, I set post-operative expectations as follows:

- You will be independent of spectacles over a wide range of distances, with very good reading vision
- However, you may require spectacles for intermediate vision, and you may need good light to read small print, or glasses when reading under very dim light conditions
- You may experience some glare and haloes at night; these are likely to decrease with time but in some cases may never fully disappear

EDOF-ERV IOLs	*Trifocal IOLs*	*Bifocal IOLs*
Any age	Any age	Older patients
Best for quality of vision	Best for spectacle independence	Best for reading and similar tasks
Good for intermediate vision	Good over the entire range of vision	Good for near vision
Good for active lifestyles	Good for active lifestyles	Good for sedentary lifestyles
Good for heavy driving	Good for normal driving	Good for occasional driving
Suits PC, laptop, tablet, smartphone	Suits PC, tablet, smartphone	Suits smartphone
Not best for book reading	Okay for book reading	Best for book reading

Table 2: Best fit between patient type and IOL category.

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NextGen

Research advances
Experimental treatments
Drug/device pipelines

38–39
An Eye on AI
Daniel Ting discusses deep learning for medical imaging, with advances being made in the detection of glaucoma, AMD and diabetic retinopathy.

An Eye on AI

Algorithms that can help screen for eye diseases can make overworked diagnosticians' lives easier

Many instances of ocular diseases go undiagnosed because of a lack of trained professionals to handle the vast amount of necessary screening. Algorithms capable of distinguishing referable images from those that don't require extensive human scrutiny can help lighten the load – and could potentially be the answer to the challenge of overworked, under-resourced diagnostic specialists. Here, we gain the perspective of Daniel Ting, Assistant Professor at the Singapore National Eye Center, SingHealth Duke-NUS Medical School, National University of Singapore.

What developments have led to the rise of artificial intelligence in medicine?

AI has been around over the last few decades. Over the past few years, deep learning using graphic processing unit (GPU) servers has revolutionized the field of computer science, sparking tremendous interest in image recognition, speech recognition, and natural language processing. In medical imaging, deep learning has shown to be comparable, if not superior, to human graders in detection of many medical conditions, including diabetic retinopathy, skin melanoma, breast metastases and tuberculosis.

Tell us about the deep learning system you developed for retinal disease screening...

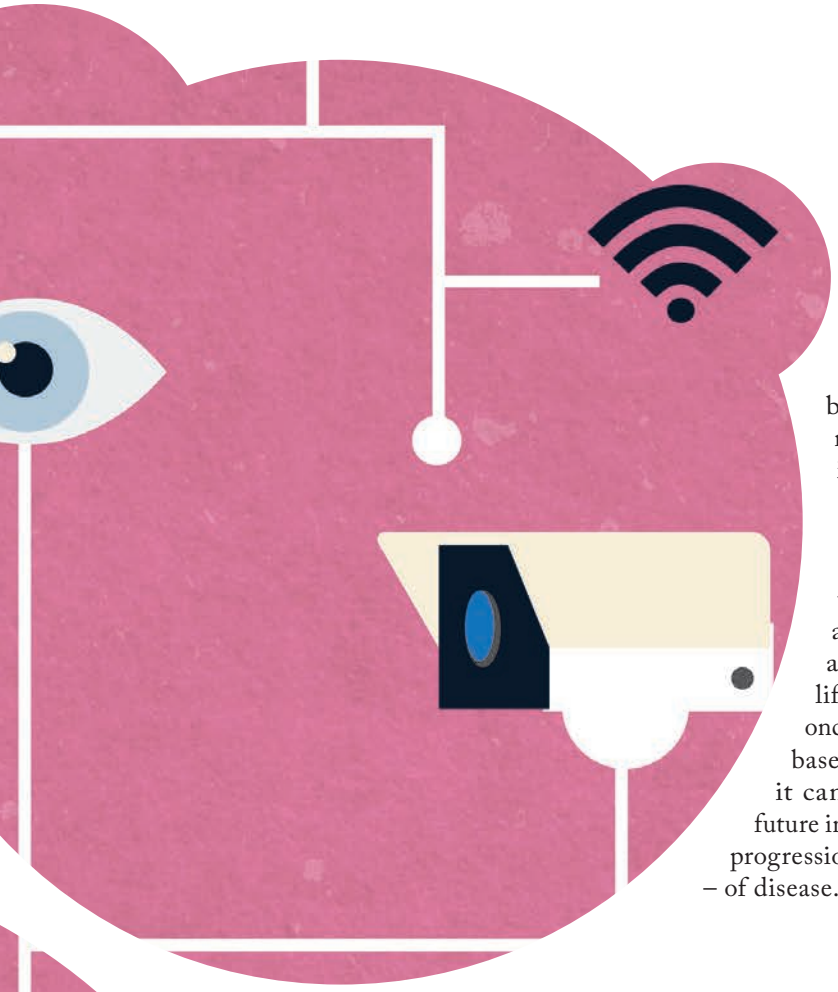
Our system is effective in using retinal images to automatically detect three conditions: referable diabetic retinopathy, glaucoma, and age-related macular degeneration. We are currently in the midst of developing algorithms for other retinal conditions, including retinal vein occlusions and retinal detachment.

The designs and concepts of AI algorithms are fairly similar across different medical disciplines. Most importantly, we need to know the right research questions to ask so that we can design the algorithm accordingly. Training datasets with labeled "ground truth" – that is, known results the computer can learn from – is equally (if not more) critical than the technical architecture of a deep learning system both within and outside ophthalmology. For instance,

"Algorithms capable of distinguishing referable images from those that don't require extensive human scrutiny can help lighten the load."

At a Glance

- *Daniel Ting explains how AI is changing the medical imaging field, assisting in detection of medical conditions*
- *The deep learning system for retinal disease screening is currently being used to detect three conditions: glaucoma, referable diabetic retinopathy and AMD*
- *AI can be used for lifelong monitoring of a patient's health and could track the progress of specific diseases*
- *In the future, AI could help predict the incidence and progression of various retinal conditions and even systemic diseases.*



total diagnostic workload by at least 50 to 70 percent, simply by removing the non-referable images so that the human graders can focus on the retinal images that need extra attention. AI is also useful for lifelong monitoring; once the machine has baseline patient data, it can easily compare future images to signal the progression – or resolution – of disease.

I am involved in several AI grants in radiology at Johns Hopkins University, looking at developing a chest radiograph algorithm to differentiate normal from abnormal X-rays and identify different lung diseases. Eventually, I hope to also apply AI to dermatology and tissue pathology.

What are the pros and cons of using AI as a diagnostic tool?

AI as a diagnostic tool has several obvious advantages, including cost and time savings, a sustainable workforce that will get smarter over time, and zero intra-rater variability. Our system in particular can reduce the

"The designs and concepts of AI algorithms are fairly similar across different medical disciplines."

That's not to say that there are no disadvantages to AI in the clinic. It requires a large dataset to train, for instance, which is not only time-consuming, but also creates a need for technical expertise and supporting infrastructure. The challenges are easing every day, as cloud-based services become cheaper and more readily available, but effort and expense will remain. In my opinion, the benefits of AI are certainly worth the process of establishing, training and maintaining it!

What lies ahead for your work – and for medical AI in general?

Our team has come a long way. My four co-inventors (Tien Wong, Wynne Hsu, Mong Li Lee and Gilbert Lim) and I began developing and testing this AI system over five years ago using retinal images we collected over a decade ago. We've poured enormous financial and manpower resources into this project, and I'm thrilled that the system has overcome all of the initial obstacles and now shows promise in assisting diagnostic professionals (1).

AI is the fourth industrial revolution in human history. As far as I can see, it's definitely set to revolutionize medicine over the next few decades. In ophthalmology, we hope that AI will help with the repetitive diagnostic workloads for diseases like diabetic retinopathy, glaucoma, and age-related macular degeneration. Using different retinal imaging modalities, AI can potentially help us see the changes to retinal neurovascular structures that have thus far been invisible to the human eye, and help us predict the incidence and progression of various retinal conditions and even systemic diseases. By having a robust algorithm, we also hope to deliver personalized medicine to the global population of patients with diabetes. There are similar trends in other medical specialties – not just ophthalmology and pathology, but also radiology, dermatology, oncology and others.

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Profession

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Are You Cybersecure?

From backing up your security software to encrypting mobile devices, here's a physician's guide to keeping your practice safe from virtual or physical threats.

Ravi D. Goel

Every industry has its "good old days." In sports, it was the 1920s, when games became the cornerstone of American life. In film, that golden era lasted five decades – from 1929 until the '60s. But in medicine? That's a little more subjective. If you ask me, the "good old days" were during residency and my first years in practice in the early 2000s. Why? Because that was when a physician could find out everything they needed to know about a patient – from their visual acuity to the date of their last visit – on a single piece of paper. Now things are a lot more complicated. The same patient's electronic health record (EHR) is seven or eight pages long, complete with forms, drop-down boxes and click buttons. There are sections dedicated to everything from dry eye to LASIK – with diagnoses taking even longer to input. A recent study by the American Medical Association (AMA) found that for every hour a doctor spends in clinic with a patient, they spend two hours at home on the EHR (colleagues across medicine refer to this as "pyjama time"). But time – or lack thereof – may not, in fact, be the biggest challenge tied to online record keeping. The under-appreciated and often hidden title belongs to cybersecurity.

Famed investor, T. Boone Pickens, once said his secret to cyber security was a yellow notepad (and thus a pen over a stylus!). In a society dealing with increasing challenges with data and privacy breaches, many believe that the only way to stay safe online is to not be online at all. But that's not feasible for those of us in healthcare. Electronic health records are an essential part of modern ophthalmology. EHRs have often simplified access to patient information through remote access. With these benefits, EHRs have also made practices vulnerable to cyberattacks, with 83 percent of physicians having experienced some form of online threat (1). Of those, 55 percent were targeted by phishing, 48 percent by viruses or malware and 9 percent by ransomware. As physicians, we know we have to protect our practice and patient information from virtual thieves, too. But where do we start? The first step is knowing what measures you already have in place. You can do that with a security risk analysis.

Identify, assess, document

The purpose of a security risk analysis is simple – to identify potential threats, determine the likelihood of a threat occurrence, and assess and document existing security measures. It is important that the main leader in the practice performs the analysis – not a vendor, website provider or EHR provider. Because there are a significant peripheral

At a Glance

- *Ophthalmologists are increasingly dependent on electronic health records, which makes practices vulnerable to cyber threats*
- *A security risk analysis should be performed by the practice's key leaders. Practices should assess their relationship with vendors, subcontractors and electronic health record (EHR) companies*
- *Establishing a secure culture, aimed at protecting both the virtual and physical ways of accessing patient data, is paramount*
- *Online cyber security modules are helpful in ensuring best practices to protect the practice's network and hardware infrastructure.*

health information that could be vulnerable to attack, the safer, smarter, and efficient method is to perform the analysis yourself. You can find a free analysis tool online at healthit.gov, along with a list of practical cybersecurity tips (Table 1), but we will get to that later. You will also be required to assess your practice's relationship with vendors, subcontractors and EHR companies, or – more generally – anyone who deals with patient information. The analysis is an essential step in protecting you against online threats – not least of which is ransomware. Remember, 9 percent of practices in the United States have been held to ransom – and you don't want to be one of them.

Ransomware takes many forms, and can make its way into your computer in the most innocuous of ways. All it takes is for someone to go online and click on an unsafe link– and it can truly be anything, from an email to a pop-out box – for the website to begin infecting every file on your computer. If you want to access those files, you will have to pay a ransom to receive an unlock key. This happened to major health care system, the Hollywood Presbyterian Medical Centre in California, a few years ago. One morning, they walked into the office and found their entire healthcare system had been shut down. The hackers said they could have access to their computer systems back if they gave them 20 bitcoins, which were worth about $70,000 at the time. Had they asked when bitcoins hit their peak valuation, that number would have been closer to $4 million. Of course, not all ransomware cases are this extreme. Often, the ransomware asks for an amount a practice can afford to lose and less than the cost of a new system. The problem is that the ransomware will continue baiting, unlocking and re-locking your system to force you to pay more.

But malicious links aren't the only form of cyberattack you should be aware of. Job listings can also open your practice to outside threats. Say a potential employee emailed their CV to your practice. If you, or one of your colleagues, were to download that file, not knowing it contained malware, you could very well infect your entire computer system. Data breaches can also occur from within. Here's an example: a former US President had surgery at a major medical center. An employee at the health system who was not involved in his care inappropriately

"The purpose of a security risk analysis is to identify potential threats, determine the likelihood of a threat occurrence, and assess and document existing security measures."

accessed the VIP's laboratory information. Though the practice was able to identify the perpetrator, the damage had already been done.

Establishing a secure culture

Of course, knowing which threats exist is not enough to stop them from happening. According to healthit.gov, to truly protect patient information, you need to establish a secure culture – and that means using a firewall, installing and maintaining anti-virus software, using strong passwords and, most of all, planning for the unexpected (you can find a full checklist in Table: Healthcare Tips). Though all of the tips concern your cyber health, number 7 – control access to protected health information – is a good reminder that physical access to patient information should be controlled as tightly as online access. Say someone walked into your practice today – would they be able to physically steal your server? What about the mobile devices your team use to access patient information on the go – are they secure? These are the kind of questions you need to ask your practice.

If you need more information, take the Cyber Security Module on healthit.gov. It gives you possible answers to common scenarios like this one:

Imagine you attend a conference and learn about the importance of securing your office network and hardware infrastructure. How do you proceed?

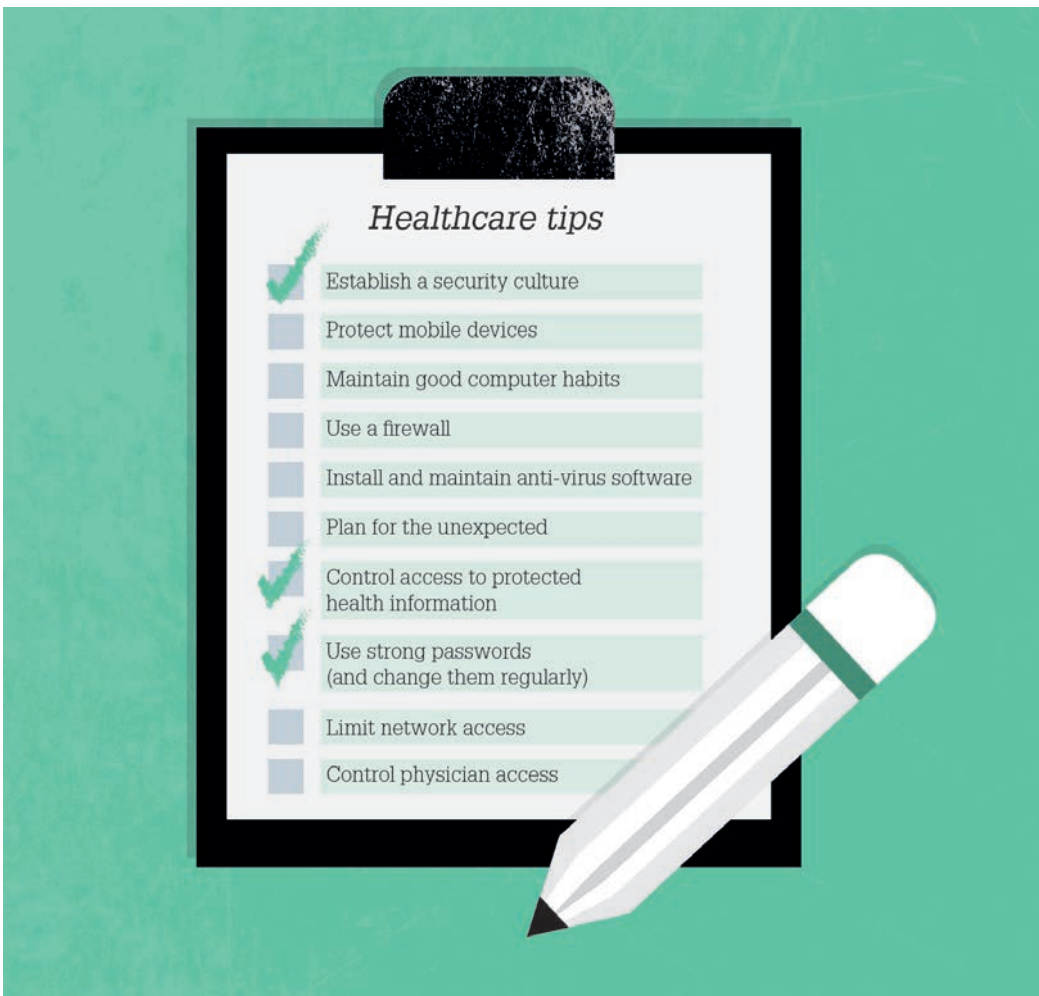
i. do you research network security to select the best configurations for the needs of your office?
ii. buy the hardware and software to secure the network and ask around for someone to do the installation?
iii. ask technical support to access your current network configuration, recommend and explain operations and improvements to secure your network before getting the cyber office manager to secure it?

The correct answer is number three. If you didn't get that right, try some of the other questions online.

From one physician to another

So with all this in mind, here are my six practical pearls for a safer practice, based on my own experiences as an ophthalmologist.

1. *Who is your IT guy/gal?*
   Could you text that person if there was a problem with your system on a Saturday morning? That's the kind of relationship you would ideally like to have with your IT and cyber-security provider.
2. *Who backs up the data and how often is*
   In my personal practice, we have a server-based system. We make a point of knowing who backs it up and how often. In case of a fire, what would happen to those servers? How is the data secured? If it is backed up in the cloud, how secure is that?
3. *Does your team use Internet from desktop or servers?*
   In my personal practice, we use dummy terminals which means there is no patient information on the desktop. Instead, data is kept in a server, which we access remotely. That way if someone were to steal the computer or the hard drive, they wouldn't be able to access any patient information. Another benefit is that any potential malware should only affect individual computers, not the remotely accessed server.
4. *Are all mobile devices encrypted and Wi-Fi secure?*



Patients want free Internet when they come to the office. If you're able to offer Wi-Fi, make sure patients access it through a separate login to protect your data. Why not also treat it as an opportunity to get new patient reviews? Direct patients to a feedback form on your practice homepage via the login. It's a win-win.

5. *How often is your security software backed up?*
   The ideal answer is: often. And don't ignore software security notifications. Updates are critical to protecting your practice.
6. *Don't outsource your cyber security.*
   This is the most important pearl, especially in terms of MIPS (Merit-Based Incentive Payment Systems). If you practice in the United States and would like to participate in MIPS, you must do the security analysis properly. If you don't, you may not pass your EHR audit.

But cybersecurity goes beyond the four walls of your practice. To make sure your practice is protected against any eventuality, you need to protect your website, too. Take a look at these bonus pearls for tips on improving your website security:

1. *Is the PHI collected on your website cryptic?*
2. *Are your forms HIPAA compliant – including comment boxes?*
3. *Do you have BAAs (Business Associate Agreements) with your vendors?*
   Don't underestimate the importance of this – it is where 62 percent of violations occur surrounding healthcare information.
4. *Do you have consent for patient videos and testimonials?*
   Some states prohibit testimonials altogether. Check if you're allowed to promote patient testimonials before obtaining consent.
5. *Is the site SSL (Secure Sockets Layer) secure?*
6. *Are you ADA compliant?*

Follow these six pearls and know you have done all you can to protect your practice. If you have your doubts, take the advice of a college classmate who became a computer science professor, "If there is no downside, there is an inherent upside." This is one of those situations. You have nothing to lose by following these pearls, but everything to gain. So perform that risk analysis, install that firewall, speak to those vendors, do what you can to keep your practice secure – you may just thank me later. A perfect New Year's resolution.

Ravi D. Goel, M.D. is an ophthalmologist and cataract surgeon working in Cherry Hill, New Jersey, USA.

Cybersecurity resources

- The American Medical Association has excellent security resources for physicians. The best part is you don't have to be an AMA member to access them.
- Jessica Barker is a cybersecurity specialist. She offers consulting services at cygenta.co.uk and tips for healthcare business on Twitter: *@drjessicabarker.*
- Healthit.gov offers free modules for physicians and practice leaders, with information on remaining compliant.

How to Prevent Patients from Missing Out on Laser Vision Correction

The number of laser vision correction surgeries being performed in Europe has been steadily declining, despite the procedure being safer than ever and soaring patient satisfaction.

What needs to be done to improve laser vision correction rates, and get potential refractive surgery candidates to commit to the procedure? Here, Allon Barsam discusses the future of laser eye surgery, explores potential challenges and points out differences between the world's regions.

The global story

According to predictions, global demand for refractive surgery will grow at the compound annual growth rate of 5.5 percent between 2016 and 2021, with patient fees increasing from $5.9 billion to $7.6 billion and annual procedure volume increasing from 3.8 million to 4.9 million. A number of emerging economies are expected to contribute significantly to the global figures, but what does the situation look like in established markets? Myopia and presbyopia are prevalent in societies with high levels of education and literacy, but as surgical abilities and technologies are improving, so are the technologies responsible for producing glasses and contact lenses.

In the USA, the number of patients with myopia undergoing laser vision correction is almost twice as large as the European average. It is common knowledge that there is a large number of patients who could potentially benefit from laser vision correction, and it is often assumed that financing of vision correction is the biggest barrier for those people. I don't think this is necessarily the case, especially in Europe, although it might play a bigger part in the decision-making process of potential refractive surgery candidates in the USA.

Technology adoption cycle and the fear factor

Oft-asked questions in the refractive surgery space are: is LASIK following the adoption cycle model (Figure 1)? What point of the model are we currently at? Have the innovators and early adopters not been vocal enough in encouraging the potential majority of adopters? Have the efforts to market LASIK to new generations of adopters – people with different habits, values and attitudes – been in vain?

In the early days of LASIK surgery, which also happened to be when the economy was booming, many early adopters – who were presumably not as fearful or worried about potential adverse outcomes – simply "went for it." And the numbers grew steadily, until a couple of negative stories appeared in the media, discouraging whole communities from undergoing LASIK. Japan is a good example of the downward spiral of bad press: its refractive vision market plummeted overnight because of one bad story in the press. Some of the negative stories come from the very early days of laser surgery, when there were fewer safety mechanisms and procedures that have to be followed. Today, the technology has moved on considerably – but the legacy of those negative stories remains.

Industry insiders have a good understanding of potential outcomes, but members of the public without an in-depth knowledge are not usually particularly good at evaluating risk. The result? The fear factor often wins over high probability of improved quality of life. And that's why I think the refractive surgery industry has a responsibility to communicate the message responsibly – and in a way that the public can understand.

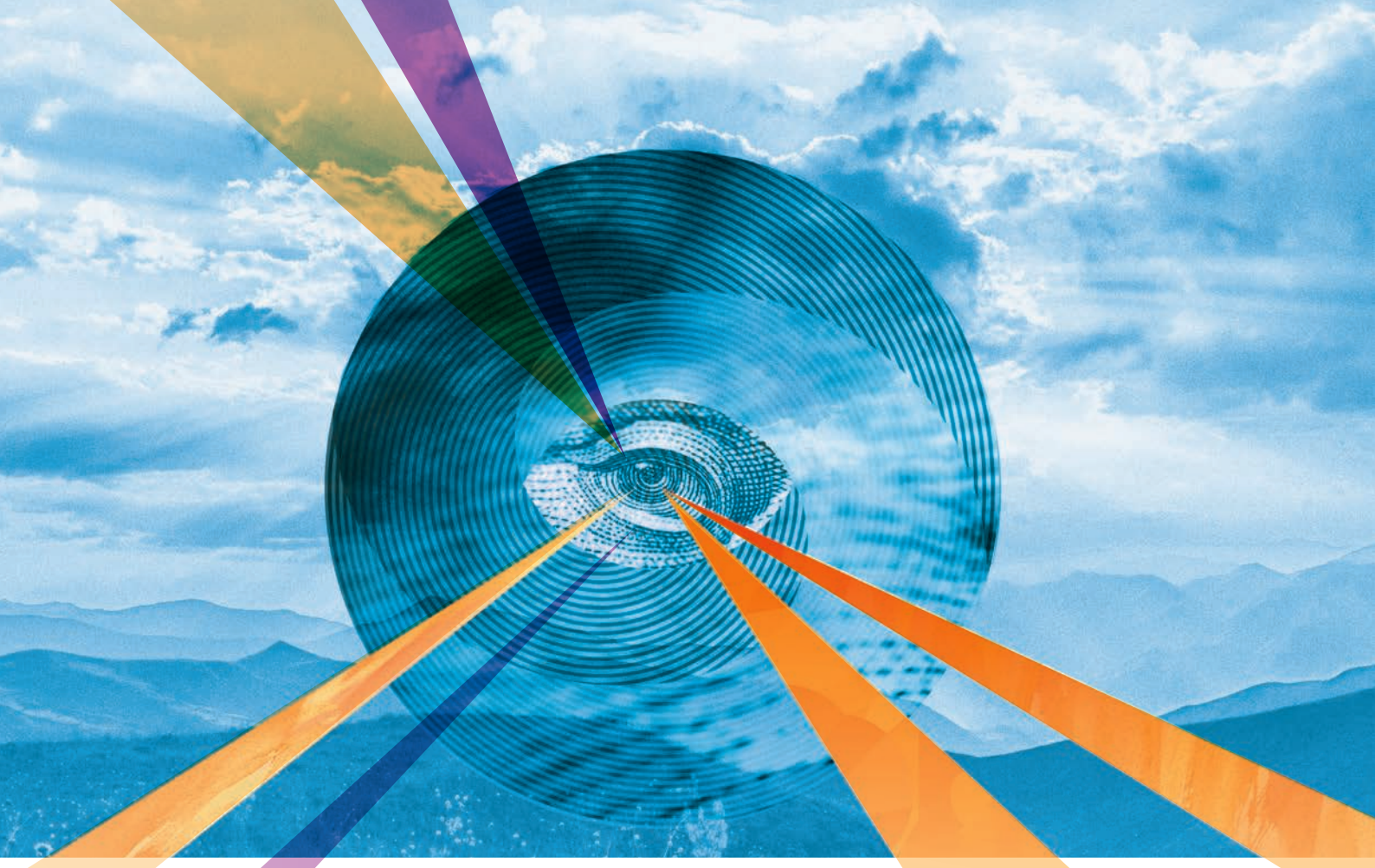
What can refractive surgeons do?

Communication to potential recipients should be transparent when it comes to your profile – your surgical experience and background – and avoid focusing on low pricing and upselling. After all, patients do realize that the surgeon's experience and expertise is important. It might also be a good idea to feature the equipment used by your practice on its website, so that you can direct patients to it; in my experience, many people like to have this information available.

I believe the terminology being used in the laser vision surgery market could be another factor that dissuades patients from accessing intervention. Think about it: if you have too much choice, you often don't end up making a choice at all. PRK, Trans PRK, LASIK, Epilasek, Keyhole LASIK, SMILE, Relex SMILE are all labels being used in the industry.

At a Glance

- *The refractive surgery market is set to grow in the next few years, but the situation in established markets could be improved*
- *Negative press about isolated cases in the early days of LASIK surgery has had a big impact on the uptake of laser vision correction procedures*
- *Educating patients about success and satisfaction rates and good communication, using terms patients understand, are vital for ensuring growth in the market.*



But, in my opinion, all of those should and could be marketed as "laser vision correction," with an explanation of each possible procedure in the small print. I do not think that practices should use the labels to encourage patients to spend their money on a particular type of surgery, but nowadays there are instances of LASIK being presented in a negative way to promote SMILE, as one example. Such behavior does not help the industry as a whole. There are advantages to each procedure, and they should be individually discussed with each patient, not brought up to upsell a particular type of procedure.

My practice's website lists the different options on a single page called: laser eye surgery. Categories based on different types of surgery give more detail on what exactly happens in each of the procedures. I truly believe that the industry should be working collaboratively to grow the market share, rather than fight for a particular piece of slowly growing market.

Our focus should be on long-term patient education, not short-term confusion over which type of laser vision correction to choose.

Promoting satisfaction, educating patients

The published reality of modern laser vision correction allows for an almost evangelical approach to patient satisfaction. Some excellent and very large studies put the satisfaction level at 99 percent for laser vision correction as a whole. And let's face it:

99 percent satisfaction for a surgical procedure is unbelievably high, when considering that it covers the whole psychological spectrum of people, including those who will never normally be entirely happy with any outcome. Such figures show just how much of an impact this type of correction has on people's quality of life. Additionally, the risk of complications is very low, compared with using contact lenses, but that is not the message that surgery candidates are receiving.

Patient education is extremely important. In the past I had occasionally received negative comments from my colleagues about the way my practice used to market, for example on social media. But what they perhaps failed to realize is that I was never talking to them nor trying to convince other surgeons (that's what conferences and other events are for!) – instead, whether on my website or during consultations, I was communicating with people who might not be medically or scientifically educated. It makes sense to find and use language that speaks to our patients – a way of communicating that works for them rather than bemusing them.

My take home message? Our field is one to be proud of, and I truly believe that we must unite in our efforts to boost the number of patients benefiting from laser vision correction.

Allon Barsam is Consultant Ophthalmic Surgeon and Director at Ophthalmic Consultants of London.

Region	Country	2016			2021		
		Population (in millions)	Presbyopes (in millions)	Percent	Population (in millions)	Presbyopes (in millions)	Percent
US	United States	325.2	111.6	36.2%	337.1	126.1	37.4%
Western Europe	Germany	80.7	37.9	46.9%	80.0	38.0	47.5%
	France	66.6	26.4	39.7%	68.1	28.0	41.1%
	United Kingdom	64.4	25.4	39.3%	66.1	26.3	39.8%
	Italy	62.0	27.7	44.7%	62.5	29.4	47.0%
	Spain	48.6	19.6	40.4%	50.3	21.8	43.3%
	Other WE	84.0	34.7	41.3%	89.6	37.0	41.3%
Japan	Japan	126.7	59.5	47.0%	125.1	62.4	49.8%
Other Wealthy	Korea, South	49.2	19.2	39.1%	49.4	21.2	42.9%
	Canada	35.4	14.6	41.2%	36.6	15.4	42.1%
	Saudi Arabia	28.2	4.3	15.3%	30.2	5.3	17.5%
	Taiwan	23.3	8.8	37.9%	23.6	9.8	41.3%
	Australia	23.0	8.4	36.4%	24.2	9.1	37.6%
	Other Wealthy	61.0	20.2	33.1%	66.6	23.4	35.1%
Wealthy Nations Total		1,078.2	424.2	39.3%	1,109.4	453.1	40.8%

Table 1. Global presbyopia figures.

Myopia prevalence in different countries/regions:

Asia:
- *Singapore:* up to 80 percent
- *China*: 77.3 percent in high school, more than 80 percent in college
- *India and Malaysia*: up to 80 percent
- *Jordania:* 53.7 percent (ages 17 to 40)

Europe:
- *UK:* 50 percent of British whites, 53.4 percent of British Asians

United States: 25 percent (ages 12 to 54)
Australia: up to 17 percent
Brazil: 6.4 percent (ages 12 to 59)

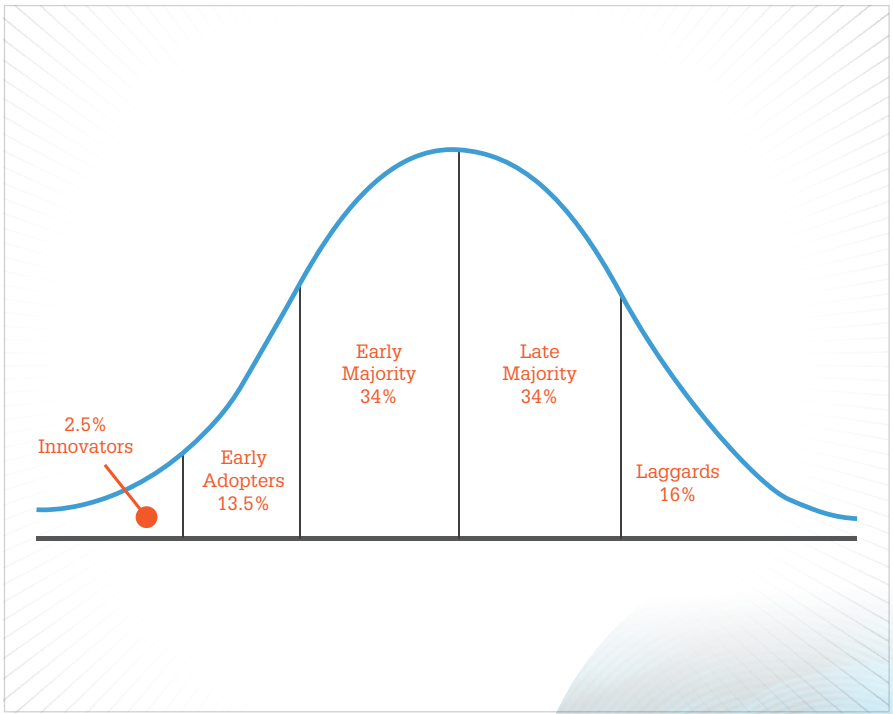


Figure 1. Technology adoption cycle model.

Country	*Population (millions)*	*Refractive Surgeons*	*Laser Centers*	*2016 LVC Procedures*	*LVC Per 100,000 Population*
Germany	80.7	426	209	144,949	179.6
France	66.6	340	158	74,324	111.7
United Kingdom	64.4	318	98	73,000	113.3
Italy	62.0	741	195	85,000	137.1
Spain	48.6	470	176	94,778	195.2
Netherlands	17.0	85	39	22,664	133.2
Portugal	10.8	26	15	7,007	64.7
Belgium	10.5	18	13	11,000	105.2
Sweden	9.2	17	20	10,301	112.3
Austria	8.2	15	7	11,000	133.7
Switzerland	7.7	14	5	4,284	55.6
Denmark	5.6	16	7	6,589	117.8
Finland	5.3	35	18	14,789	280.5
Norway	4.8	18	14	12,545	263.0
Ireland	5.0	13	8	5,099	103.0
Total	406.3	2,552.0	982.0	577,329	142.1

Table 2. Refractive surgeons in Western Europe (2016).

Country	*Region*	*2016 Population (millions)*	*Percent of Global Population*	*Estimated 2016 LVC Procedures*	*LVC Per 100,000 Population*	*Percent of Global LVC Procedures*
United States	United States	325.2	4.4%	635,000	1.95	17.7%
Japan	Japan	126.7	1.7%	75,750	0.60	2.1%
Germany	Western Europe	80.7	1.1%	144,949	1.80	4.0%
France	Western Europe	66.6	0.9%	74,324	1.12	2.1%
United Kingdom	Western Europe	64.4	0.9%	73,000	1.13	2.0%
Italy	Western Europe	62.0	0.8%	85,000	1.37	2.4%
Korea, South	Other Wealthy	49.2	0.7%	156,237	3.18	4.3%
Spain	Other Wealthy	48.6	0.7%	94,778	1.95	2.6%
Canada	Western Europe	35.4	0.5%	103,000	2.91	2.9%
Saudi Arabia	Other Wealthy	28.2	0.4%	17,685	0.63	0.5%
Taiwan	Other Wealthy	23.2	0.3%	51,500	2.22	1.4%
Australia	Other Wealthy	23.0	0.3%	37,563	1.63	1.0%
Netherlands	Western Europe	17.0	0.2%	22,664	1.33	0.6%
Greece	Western Europe	10.8	0.1%	10,887	1.01	0.3%
Portugal	Western Europe	10.8	0.1%	7,007	0.65	0.2%
Belgium	Western Europe	10.5	0.1%	11,000	1.05	0.3%
Czech Republic	Other Wealthy	10.1	0.1%	7,417	0.73	0.2%
Other Wealthy Nations		106.8	1.5%	114,558	1.07	3.2%
Wealthy Nations Total		1,099.2	15.0%	1,722,319	1.57	47.9%

Table 3. Laser vision correction rates by country.

Star Eyes

Sitting Down With… Dan Reinstein,
Medical Director, London Vision Clinic,
London, UK.

Why medicine?
Being a doctor puts you in the extremely unique and privileged position to attend important moments in people's lives – delivering a baby, being present when someone is told they have a fatal diagnosis, witnessing severe psychotic behavior, or performing surgery on the human body. My career choice came down to choosing a specialty where I'd be using my academic strengths in math and physics, alongside my human strength of engaging with patients of all ages. I also wanted to become a surgeon, but needed a surgical specialty that would not impinge too heavily on evenings and weekends; I didn't want to give up being a musician – something I started at the age of four.

How do these two skills, music and medicine, complement each other?
Refractive surgery and jazz, to me, are analogous. Both require you to be able to make instantaneous decisions based on huge amounts of experience and expertise, as well as creativity and collaborative work – and of course, they both give extraordinary emotional satisfaction.

What's exciting you in the refractive surgery space right now?
There are three things. I feel like I'm surfing on the crest of a 50-foot wave in refractive surgery between SMILE and PRESBYOND. And, at the same time, I feel that I have reached a place in corneal refractive surgery safety where virtually every complication that may be generated can be returned to a good visual state. The other thing that is really exciting me is my increasing involvement in teaching – for example, publishing our textbook The Surgeon's Guide to SMILE and running training courses. I get really excited when surgeons change their perspective on presbyopia, moving from clear lens exchange to PRESBYOND, particularly when opting for this on their own eyes.

You've had PRESBYOND LASIK surgery yourself – how did you feel?
It was an amazing experience on the one hand and an anti-climax on the other. Having treated thousands of patients myself with this technique, which I developed 15 years ago, I didn't expect many things to be a surprise – and they weren't. I am 100 percent spectacle independent at the age of 56, having been a -0.75 D myope – or some might say plano-presbyope. But there was a moment that I wasn't expecting. On the day of my procedure, I had been operating that morning. I was the last patient on the list. So I finished my last case and came back to the operating room – this time as a patient. When I lay on the bed waiting for the procedure to start, it suddenly dawned on me that there was a finite probability of something going horribly wrong with my vision. I then thought about the fact that my surgeon, Glenn Carp, had been my fellow for a year and a half and then worked with me for the next nine years, so I knew that there couldn't be an intraoperative complication that he would not know how to handle perfectly. And then my mind went to postoperative complications. But again, I realized that both he and I would be there to decide how to repair things. All of those thought processes took place in the 15 seconds it took for the bed to move into position under the cone of the VisuMax. I took a deep breath, felt very relaxed and enjoyed the show for the next 10 minutes!

You have had countless successes – including being the first person to map and measure the corneal epithelium – what has been your career low?
LASIK Vision going bankrupt in 2001. I had set up really effective training accreditation, quality assessment and quality control systems for what was the very first chain of laser eye surgery centers in the world. Disappointingly, the business side outstripped its "blood supply." But success is built on failure; as devastating as it was at the time, the experience that I gained not only as a surgeon, but as a clinician scientist working through the systematization of a surgical technique, was invaluable. I couldn't have got it any other way.

The London Vision Clinic works closely with Carl Zeiss Meditec – what's that like?
It's like Christmas – you write a letter to Santa and you actually get some of those presents! I have really appreciated being able to contribute ideas for improving existing or new products, and features that I would like to use on my own patients. It's a very privileged position to be in, at the interface between the surgical profession and the engineering profession.

What do you hope to achieve over the next 10 years?
I hope to develop software based on layered anatomical imaging of the cornea that will enable any surgeon to correct any complication; to continue the quest to develop refractive surgery as a primary means of helping the poorest in the world suffering from refractive errors; and to play a lot more saxophone, hopefully kick-starting it with the release of my first record in 2019. In a wider sense, I also hope that refractive surgeons will learn to work as colleagues, not as competitors – look after each other, our patient base, and the market so that refractive surgery becomes the standard for anyone suffering from refractive error disabilities.

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*Compared against AcrySof® IQ (SN60WF), HOYA AF-1™ FY-60AD and enVista® IOLs (MX60).

Reference: 1. Data on file. Chromatic aberration of the TECNIS® Symfony IOL. Johnson & Johnson Surgical Vision, Inc. Santa Ana, CA.