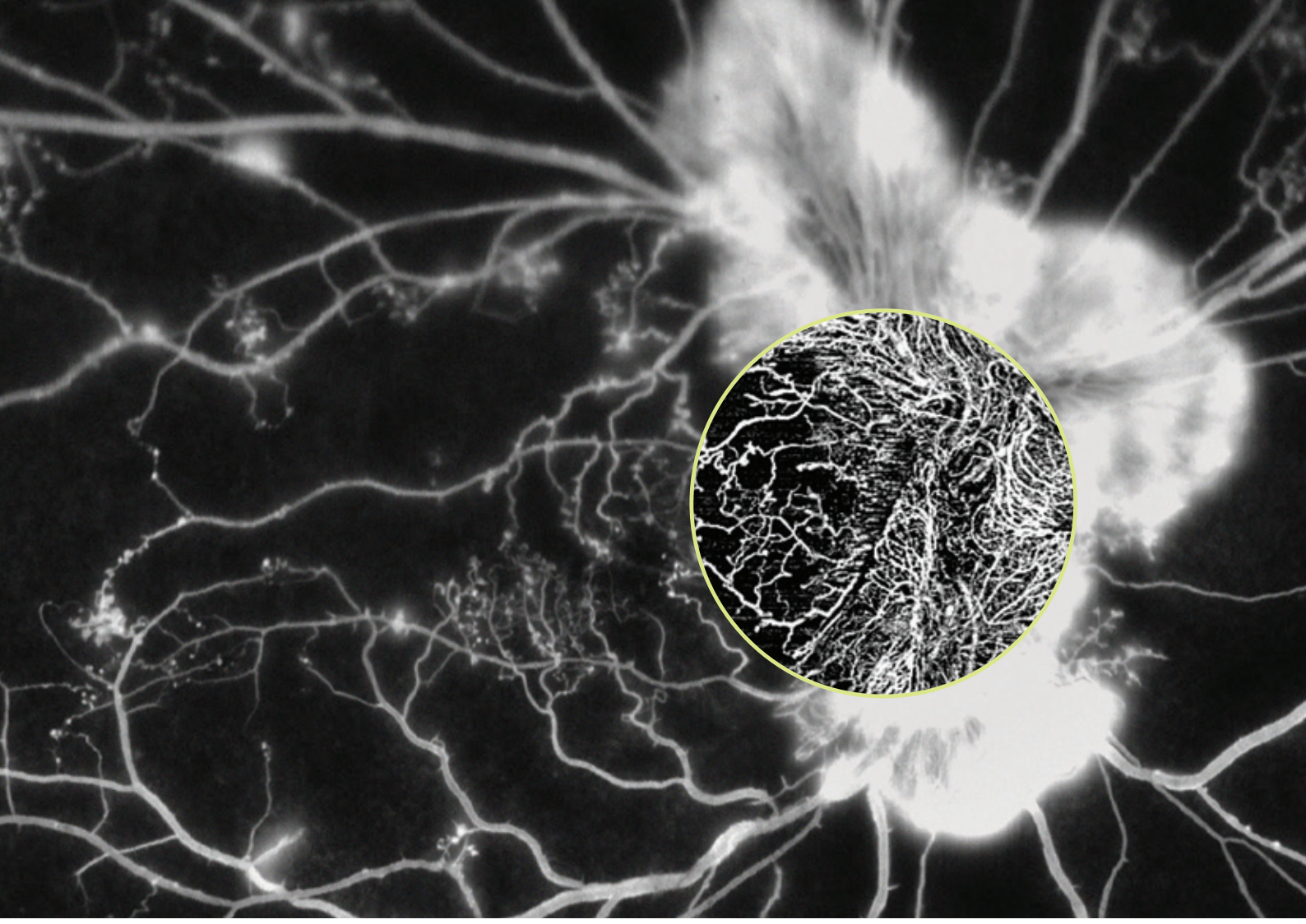
SEPTEMBER 2016 # 01

the Ophthalmologist

The League of Extraordinary Ophthalmologists

The Ophthalmic Premier League educates, excites and amazes – Amar Agarwal explains why

18 – 27



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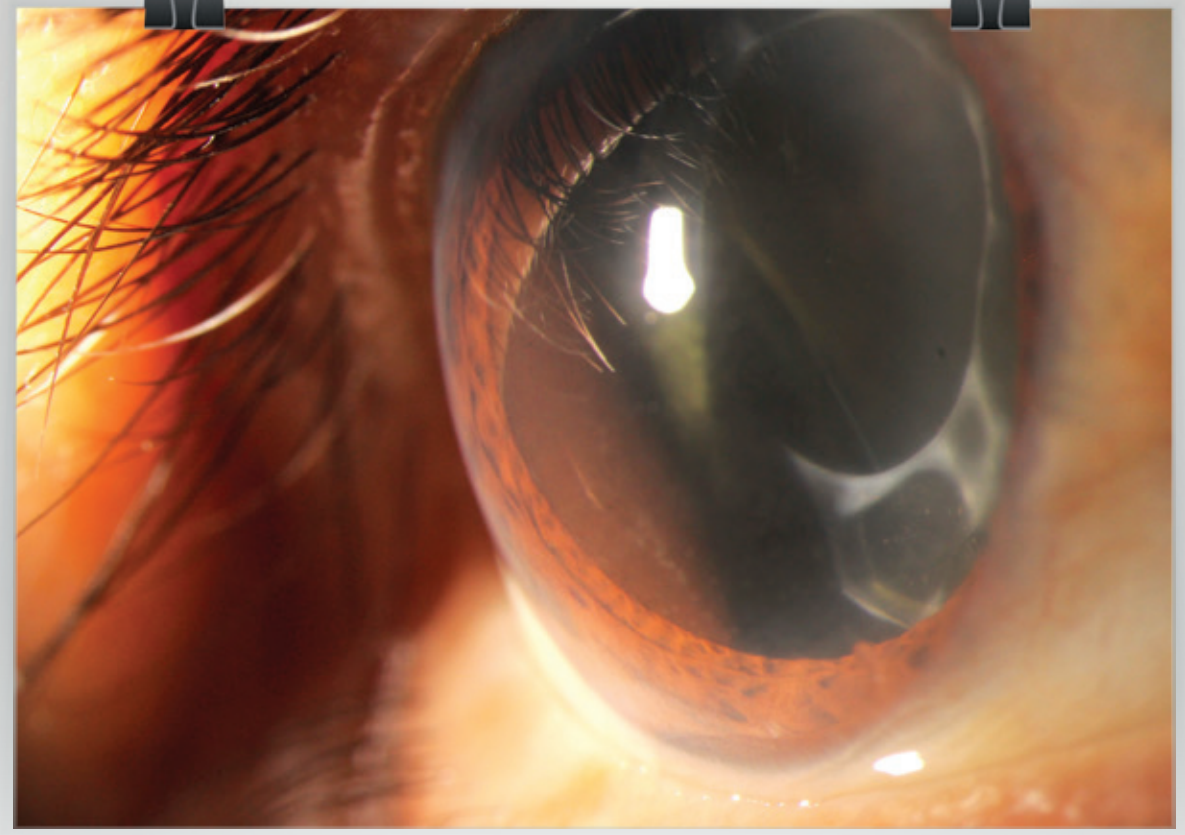

A stromal cyst present in a patient that was originally referred to an ophthalmic oncologist for a possible iris tumor.
Images courtesy of Carrie A. Cooke, an ophthalmic photographer with the University of Texas Health Science Center San Antonio, Medical Arts and Research Center, Department of Ophthalmology.

Do you have an image you'd like to see featured in The Ophthalmologist?
Contact mark.hillen@texerepublishing.com.

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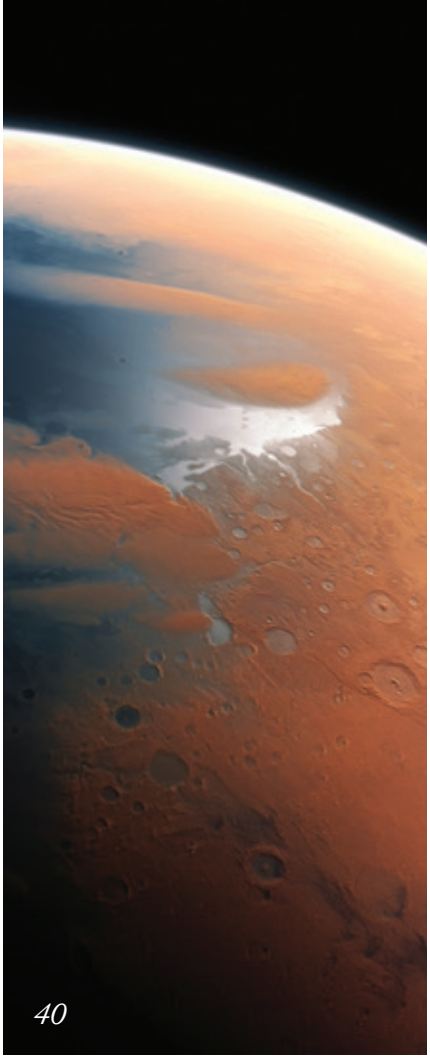

In Practice

NextGen

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Sitting Down With

the Ophthalmologist
ISSUE 01 - SEPTEMBER 2016

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tracey.nicholls@texerepublishing.com
Tracey Nicholls, The Ophthalmologist, Texere Publishing Limited, Haig House, Haig Road, Knutsford, Cheshire, WA16 8DX, UK.
Single copy sales £15 (plus postage, cost available on request tracey.nicholls@texerepublishing.com)
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General enquiries:
www.texerepublishing.com
info@texerepublishing.com
+44 (0) 1565 745 200
sales@texerepublishing.com

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Hello, North America

We're here, and we're clear about what we're bringing to the table.

When The Ophthalmologist launched in Europe more than three years ago, we entered a crowded market. Just like in the US and Canada, there were many print magazines and websites ophthalmologists could read. We wanted – and had – to do something different. We did. And now it's here in North America: a bespoke edition of content that's tailored to your needs and tastes.

Why is The Ophthalmologist different? We view it as an ophthalmologist's magazine, rather than an ophthalmology magazine. We're not offering an impersonal overview of a particular branch of medicine. Rather, we focus on the people who bring it alive – people like you – to present an engaging cover-to-cover read, every month. In short, we're here to tell your stories.

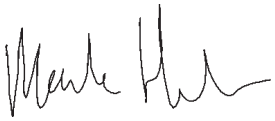
This approach has certainly served us well to date. We've managed to cover some of the biggest stories that speak to the future of eyecare: big data, nanotechnology, the future of ocular imaging, robot eye surgery, stem cells, even what needs to be done to deal with the tidal wave of aging boomers with age-related eye disease (a combination of all of the above, and more, it seems). We've worked with the biggest names in the game to share their motivations, aspirations, fears and successes in the most engaging way possible. We're not afraid of detail, and we're not afraid of being controversial either. We only commission articles that we know will be interesting; your time is precious, and you should be entertained and informed by your magazine, not bored by it.

We are big on engagement. I consider that everything we publish is the start of a conversation. Even if you're reading this in our glorious print edition, you can go online and comment on absolutely anything and everything we publish. We want your feedback, your suggestions and your submissions. This is your publication, after all.

As you'd expect, our content is available in the formats that you use; print, PDF, iPhone and iPad apps, and on the web at www.theophthalmologist.com. Even though the North American edition of The Ophthalmologist is custom-made for you, everything we've ever published is available online; you are denied nothing of what the rest of the world sees – and this won't change going forward.

So hello again, North America. Welcome to The Ophthalmologist.

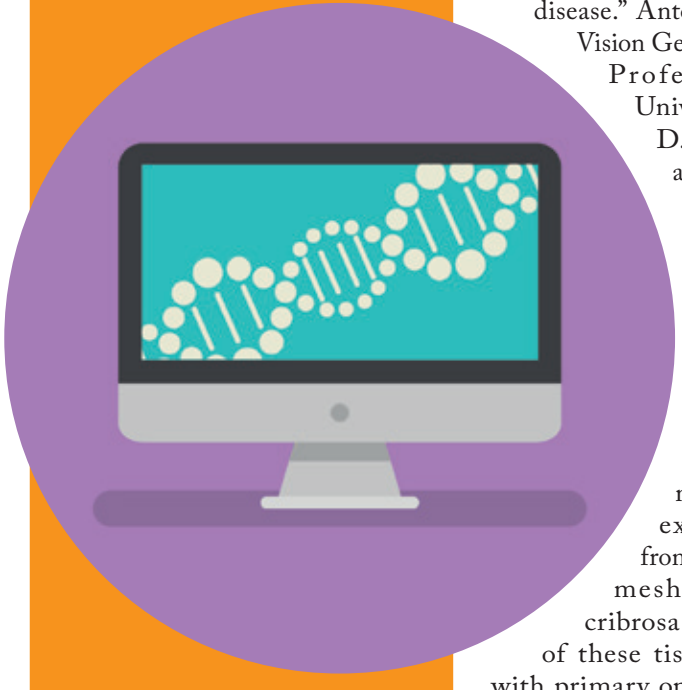
Mark Hillen
Editor



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 mark.hillen@texerepublishing.com



Finding Fibrosis

Pro-fibrotic signatures may play a role in causing glaucoma...

A team of bioinformatics researchers, forged by a collaboration between scientists from several commercial and academic organizations, have recently published in silico findings suggesting that pro-fibrotic signaling pathways may be activated in glaucoma (1). "Like most ophthalmic diseases, glaucoma is age-related. Our team is dedicated to combatting aging and age-related diseases using a computational approach with a broad range of signaling pathway and deep learning tools," says Alex Zhavoronkov, CEO of Baltimore-based InSilico Medicine, and lead author of the paper (1). "We applied these tools to study glaucoma, and identified pro-fibrotic signatures in the trabecular meshwork and lamina cribrosa which we believe are likely to be causing the disease." Antonei Csoka, CEO of Vision Genomics and Assistant Professor at Howard University, Washington D.C., comments "We are very excited about these findings – we believe that inflammation and fibrosis are significant factors in the etiology of glaucoma."

In their research, the team studied microarray gene expression profiles from cultured trabecular meshwork and lamina cribrosa cells, and samples of these tissues from patients with primary open-angle glaucoma (POAG) or healthy controls, obtaining the profiles from publicly available datasets. Using a novel software suite optimized for studying age-related macular degeneration (AMD; 2) and glaucoma, they analyzed the activation of intracellular signaling pathways, and found that elevated levels of TGF-β were associated with the activation of pro-fibrotic pathways (such as AKT) in the trabecular meshwork and lamina cribrosa from patients with POAG. Explaining that their results are "correlations, and future confirmatory studies are warranted to validate these observations" (1), the team propose that the resulting pro-fibrotic processes lead to remodeling of the extracellular matrix, which may impede aqueous humor drainage through the trabecular meshwork and alter the composition of the lamina cribrosa.

Although their findings and hypothesis require validation, the researchers the team are enthusiastic about their next steps, with Zhavoronkov confirming, "We also identified a range of promising anti-fibrotic compounds that are likely to target these signatures, and we will be testing these leads once we secure funding." Looking further ahead, Csoka comments, "Combined with our previous study on AMD (2), and moving forwards to investigate other ophthalmic diseases including cataract and diabetic retinopathy, we believe we will arrive at a comprehensive understanding of the aging of the human eye which will pave the way towards developing therapies." *RS*

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Old Sharks, New Tricks

Why are researchers radiocarbon dating the lenses of Greenland sharks?

The Greenland shark is an iconic species of the Artic seas, but it turns out that very little is known about its biology. Females can grow to a length of 500 cm – making it the largest fish native to arctic waters – but they appear to grow very slowly up to that size, at a rate of around one centimeter per year. So just how old can they get?

The answer to that is usually straightforward in most vertebrates: radiocarbon date their bones. But as Greenland shark are cartilaginous fish, this won't work, which brings us to the eye. The lens nuclei of vertebrate eyes are perfect for carbon dating: they develop embryonically, and consist almost entirely of metabolically inert crystalline proteins which are retained over the shark's lifespan.

This is exactly what researchers performed on the eyes of 28 female sharks collected in Greenland over a three-year period between 2010 and 2013 (1). According to their analyses, the largest sharks (≥ 500 cm, or 16.5") need to have lived for at least 272 years to achieve that length, with the oldest one in the sample of 28 being estimated to be 392 ± 120 years old – making it the oldest-lived vertebrate ever known. And all of this would have remained unknown, if it were not for the unique biology of the lens of the eye. *RM*

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H-Y are These Corneal Grafts Rejecting?

When it comes to donor compatibility, it appears that gender matters

When it comes to vascularized organ transplantation, the donor's gender matters. Gender mismatches increase the risk of immunological rejection, and the culprit in most cases is H-Y: a male-specific minor histocompatibility antigen (mHA). H-Y epitopes (the part of an antigen that antibodies attach to) derived from intracellular proteins, can be detected by CD4+ T-cells and presented on their surface by the major histocompatibility complex to tell B-cells to make antibodies. This is bad news for the transplanted organ: it's where immune rejection really kicks in. The bottom line is that there's potential for male tissue to be rejected when transplanted into females, and this is something that has been observed time and time again in cardiac, pulmonary, hepatic, and (particularly) renal transplantation.

But what about corneal transplantation surgery? A healthy cornea is immune privileged, as it has no blood or lymphatic vessels, sits behind the blood-retina barrier, has few mature antigen presenting cells, and a surfeit of immune-suppressing factors. Patients who undergo keratoplasty receive topical steroid drops during the post-surgical healing period, which penetrate the cornea and act as an immunosuppressant too. Might this mean that the cornea escapes the H-Y mHA-induced misery?

Not necessarily. The first (and until recently, the only) signs were present a decade ago, when Böhringer et al. (1) reported that H-Y mismatched – that is, male-to-female (M→F) – corneal transplants were more likely to be immunologically rejected than H-Y matched grafts (i.e. M→M or F→F). Theirs was a small study (229 patients), with a mean follow-up period of two years, and the results weren't stratified by indication or graft type. But the results were clear: at two years, F→F corneal grafts exhibited an 88 percent rejection-free survival rate; for M→F grafts, the rate was 77 percent.

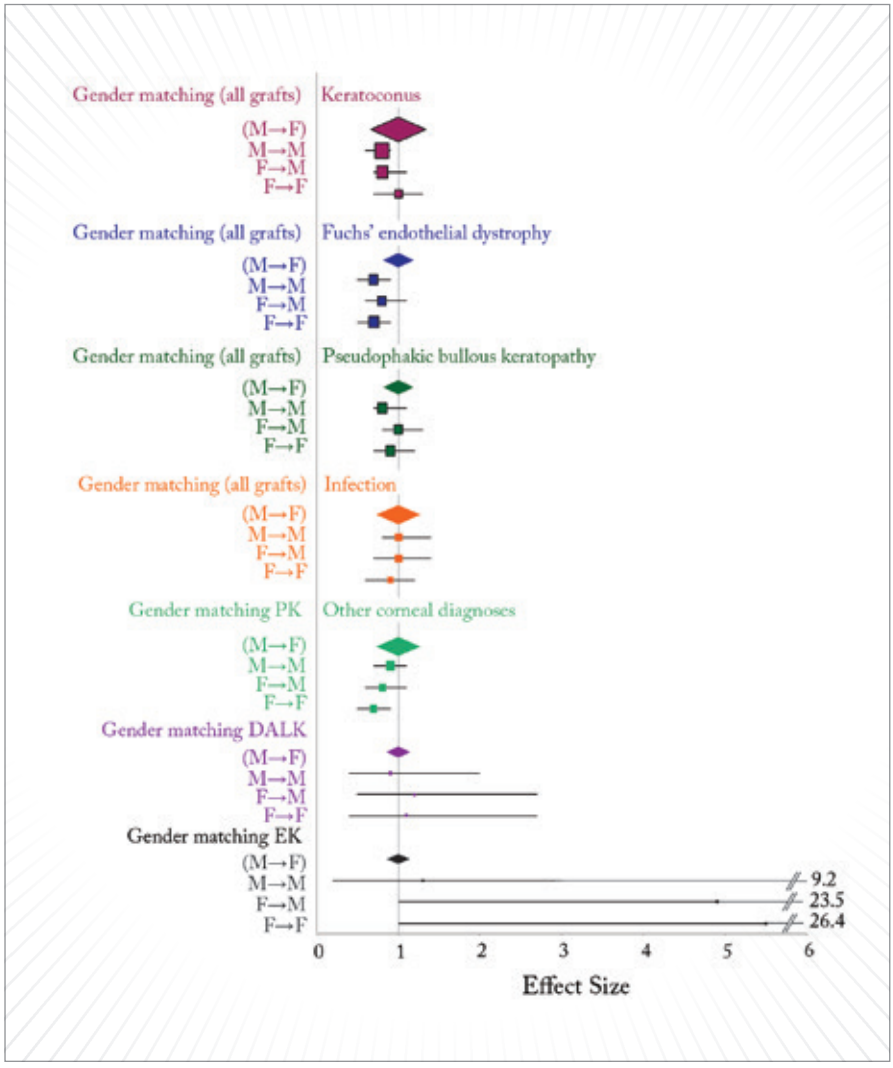

Figure 1. Forest plot of the relative risk of graft rejection over five years, after risk-adjusted gender matching.

Recently, Hopkinson et al (2) have published the results of a study that examined the influence of gender incompatibility, including H-Y incompatibility, on corneal transplant graft rejection and failure in patients (n=18,171) who had undergone a first corneal transplant (for indications such as keratoconus, Fuchs' endothelial dystrophy, pseudophakic bullous keratopathy or infection). They fitted a Cox regression model for each indication in order to determine the factors affecting graft failure and rejection at five years, and – after accounting for the effect of other known risk factors – analyzed the

impact of gender (including H-Y epitope status) on these outcomes.

What they found was that H-Y mismatched (M→F) corneas were at greater risk of graft failure or rejection (Figure 1). For patients with Fuchs' endothelial dystrophy, compared with M→F transplants, F→F grafts were 40 percent less likely to fail ($p<0.0001$) and 30 percent less likely to reject ($p=0.01$), M→M were 20 percent less likely to fail ($p=0.04$) and 30 percent less likely to reject ($p=0.01$). In patients with keratoconus, M→M matched corneas were 30 percent less likely to fail ($p=0.05$) and 20 percent less likely to reject ($p=0.01$) compared with H-Y mismatches. H-Y antigen mismatched (M→F) patients had a greater risk of rejection or graft failure.

Stephen Kaye, the study's corresponding author, called for more research to be performed on this topic: "It is important that other centers in the world investigate these results and undertake similar work. Although it would appear that the effect of gender incompatibility is based on H-Y incompatibility, there may be other gender related factors, which are of importance. We would therefore like to undertake a prospective study, examining in more detail these and other potential factors." *MH*

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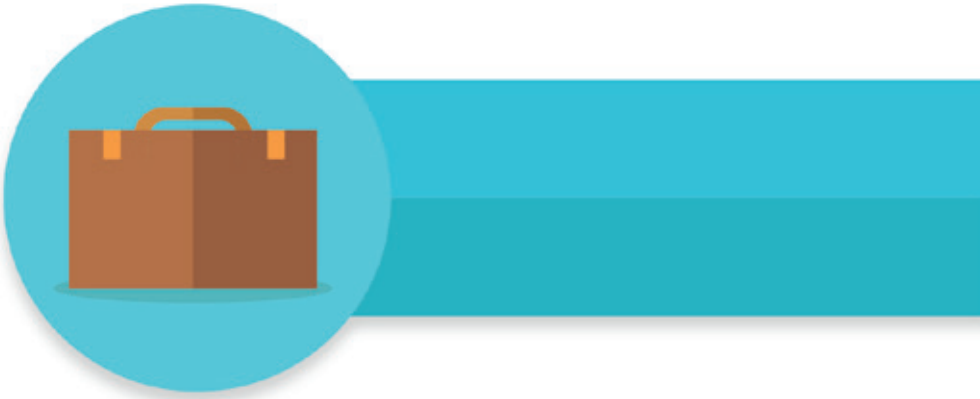


This Month in Business

TrueVision and Alcon team-up on "heads-up" technology, Pfizer returns rights to ranibizumab biosimilar, and more...

- TrueVision Systems has entered a partnership agreement with Alcon for their "heads-up" 3D Digital Microscope Platform, a real-time vision system that allows surgeons (and the surgical team) to view the ophthalmic surgical field on a monitor or projector screen.
- Allergan has entered into an agreement to acquire ForSight Vision5. The deal includes an upfront payment of $95 million and a launch milestone payment for ForSight Vision5's lead development program - a bimatoprost-eluting periocular ring for extended drug delivery in patients with glaucoma.
- Pfizer has returned its rights to PFEnex's ranibizumab biosimilar candidate, PF582, despite Phase I/II results showing the candidate exhibits comparable safety and tolerability to ranibizumab in patients with neovascular AMD who were naïve to anti-VEGF therapy.
- Presbia Ireland (a wholly owned subsidiary of Presbia PLC) have purchased the assets of Neoptics AG, including the Swiss-based company's comprehensive patent portfolio containing intellectual property for Microlens technology.
- In a letter to the US Department of Justice, health insurer Aetna have threatened to cut their participation in Affordable Care Act (ACA) public exchanges if they are blocked from acquiring Kentucky-based health insurer Humana.
- Several companies have released their financial figures for the second quarter of 2016: compared with the same quarter in 2015, Alimera Sciences and STAAR Surgical reported increases in revenue (66 and 12 percent, respectively); Second Sight's revenue was $1 million, down from last year's $2.7 million; and Ocular Therapeutix reported another net loss of $11.4 million ($1.4 million more than the same quarter in 2015).
- We interviewed James V. Mazzo about his new role at CZM and his ongoing role as Executive Chairman at Neurotech Pharmaceuticals. To find out what he had to say, head on over to: top.txp.to/issues/0816/207

Featherweight Optics

High-resolution retinal imaging… with an SLO/OCT device weighing a mere 94 g

In a bid to overcome the challenges associated with acquiring retinal images from young children, and to increase image resolution, a team at Duke University have been developing an ultracompact handheld SLO/OCT probe (Figure 1). Having demonstrated their device obtains high-resolution retinal images in children as young as 14 months of age (1), Cynthia Toth, Joseph Izatt, and Francesco LaRocca tell us more…

Why did you decide to develop a handheld SLO/OCT probe?

Measuring the impact of injury or diseases (genetic or otherwise) on the photoreceptors of infants has not been possible, because diagnostic tools that examine and image the retina – although well-designed for adults – are exceedingly difficult to use in infants and young children.

Some weigh several pounds, making holding them still over a child's eye tiresome and difficult, and none provide a high enough resolution to see individual photoreceptors. Without the ability to image children's eyes at high resolution, studying how our retinas grow and change during the crucial early stages of development is difficult. This limits our knowledge of how diseases affect a child's vision early in life and makes diagnosis of blinding diseases that affect children more difficult.

What are the key findings so far?

The probe's novel optical design and ability to image via both SLO (for high lateral resolution) and OCT (for high axial resolution) makes it uniquely optimized for imaging critical cell layers of the developing retina – like photoreceptors. For the first time, we have been able to evaluate the density of cone photoreceptors in infants during an eye examination under anesthesia (1).

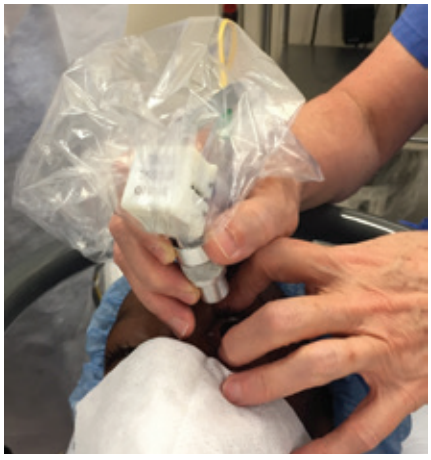
We found that photoreceptor densities far away from the fovea for very young children were greater than those at the corresponding location for adults, supporting the hypothesis that there is a central ward migration of cones with age. Tests also showed different microscopic pathological structures in diseased children that are not normally visible with current lower-resolution clinical-grade handheld systems.

Can you summarize how the probe is used?

Imaging sessions take approximately 10 minutes, including SLO imaging at two different fields of view (field of view [FOV]; 6.4° × 8.8° and 3° × 3°) and OCT volumetric imaging (6.4° × 6.4° FOV) for multiple regions of the retina near the fovea and optic disc. SLO and OCT can be switched by simply changing the fiber connections to the appropriate detection hardware.

Any challenges?

The traditional 4F correlator-based telescope design limited how small we could make a handheld probe, so we created a new design using converging rather than collimated light which reduced the telescoping length of the device by a third. However, this design inherently introduces significant optical aberrations (mainly field curvature) into the system, which we could not correct for with the few off-the-shelf lenses with high focusing power and small form factor that are available today. To enable high-resolution imaging at a minimal device size, we designed and specially fabricated custom lenses. Creating a custom mechanical design to hold these tiny optical components stably (whilst allowing room for focus correction adjustment) without adding much bulk or weight to the probe was another challenge.



Credit: Joseph Izatt, Duke University.

Figure 1. A clinician using the handheld probe to collect high-resolution SLO and OCT images of the retina from an anesthetized child.

What has been the main feedback so far?

Very positive – clinicians really appreciate imaging performance, and how light and compact the handheld probe is. Some enhancement requests include increasing FOV and incorporating motorized focus adjustment over a longer correction range to facilitate imaging of subjects with significant refractive error.

Next steps?

We will finish testing and developing the next generation probe, and prepare the process to make our device more widely available, which is anticipated within 3–5 years.

Achieving precise photoreceptor measurements in the retina opens doors to new research and tools that will be key in the future diagnosis and care of hereditary diseases.

Reference

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The Thinner, the Poorer

A reduction in retinal thickness may be associated with a decrease in cognitive function

One of the many challenges associated with Alzheimer's disease (AD) is timely identification and diagnosis – the earlier the disease can be caught, the higher the potential to prevent, or slow down, its progression with interventions like brain training or nootropic drugs. Retinal exams might be the answer, and already multiple research groups are investigating their diagnostic potential: a team from the University of Minnesota are evaluating retinal non-invasive hyperspectral endoscopy to look for signs of amyloidopathy in a mouse model of AD (1), and another group at the University of Waterloo in Ontario have shown that ß-amyloid deposits in neural retina can be detected non-invasively using their polarized light microscopes (2). But this isn't the whole story: results from a large cohort study (3) have shown that retinal nerve fiber layer (RNFL) thinning is significantly associated with poor cognitive function, which immediately suggests that regular retinal thickness measurements could represent an important method of catching early signs of the disease.

An international team of researchers are behind these findings. Using data from the UK Biobank study (a major ongoing health resource project which features over 500,000 volunteers) they identified over 30,000 participants with spectral domain (SD) OCT scans, and performed multivariable regression modeling to compare RNFL thickness data with results from cognitive measures (including tests for prospective memory, numerical and verbal reasoning, and reaction time). What they found was the RNFL was significantly thinner in participants who had "abnormal" cognitive test results (see Figure 1) – and thinner RNFLs were linked with poorer outcomes in prospective memory, pairs matching, numeric and verbal reasoning, and reaction time tests ($p<0.001$). They also found that, for each cognitive test failed, RNFL was significantly thinner by 1 µm. The researchers analyzed all macular subfields, and found that outer nasal RNFL thickness "appeared [to be] the most sensitive to changes to cognitive function" (1). So could we one day see ophthalmologists and optometrists play a leading role in identifying this debilitating disease in its early stages? We will be following this development very closely. *RS*

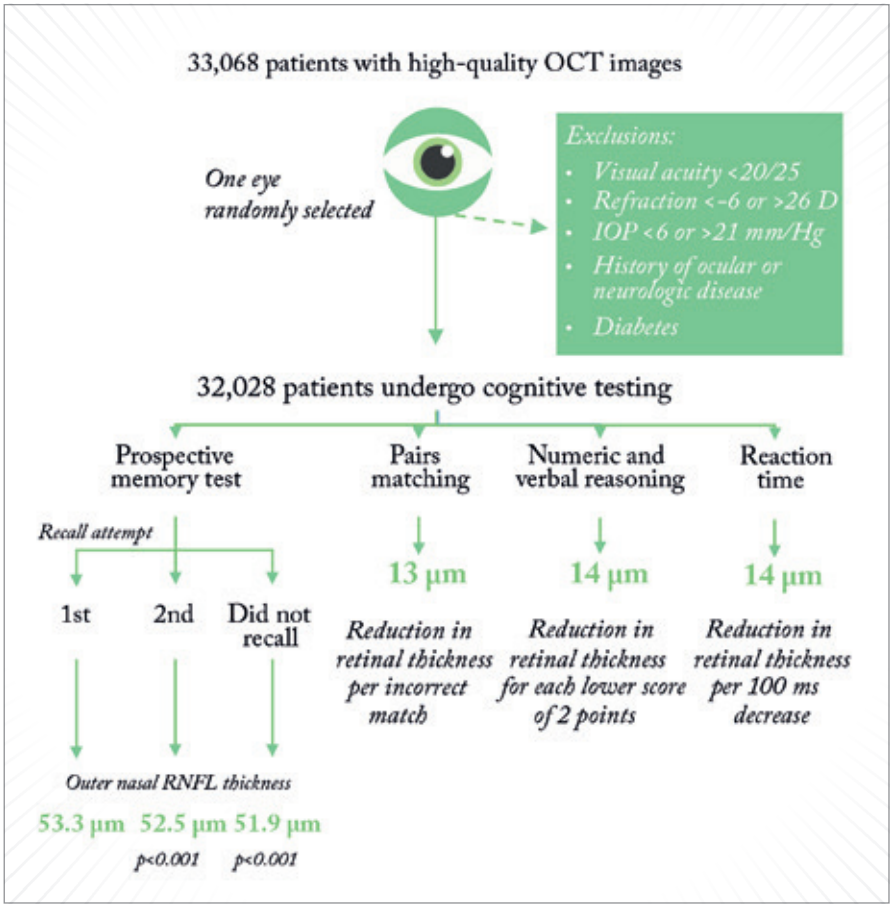

Figure 1. Outcome of multivariable regression modeling of UK Biobank study data comparing RNFL thickness with cognitive measures. Adapted from data reported in (3).

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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 editor at mark.hillen@texerepublishing.com

Communicating With Local Politicians

How ophthalmologists can get involved in local politics to overcome key issues and influence legislation

By Paul Sternberg, Jr, Retina Specialist and G.W. Hale Professor and Chairman, Vanderbilt Eye Institute, and Janice C. Law, Associate Director for Residency Education, Department of Ophthalmology and Visual Sciences, Vanderbilt University, Tennessee, USA

Why would a small group of ophthalmologists and ophthalmology residents quietly celebrate the results of a Democratic primary election for a seat in the Tennessee General Assembly in August, 2014? It turns out that the defeated incumbent, Gary Odom, had held this seat since 1986. When the Democrats were in control of the state legislature, he was House Majority Leader; with the Republicans now in control, he was the House Minority Leader. What was critical to the ophthalmic community was that Representative Odom was also the Executive Director of the Tennessee Optometric Association. For almost three decades, he had been ideally positioned to use his political power to leverage optometric issues. So when organized ophthalmology continued to face "scope of practice" challenges in Tennessee, we decided that one tactic would be to try to unseat Representative Odom. And while the ophthalmic community can't take full responsibility for this success, we were actively involved in and supported Odom's opponent, John Ray Clemmons: contributing and raising funds, volunteering, going door-to-door, and most importantly, making certain the medical community got out to vote.

In the end, fewer than 4,500 voted, and the margin of victory was only a few hundred votes: but at this local level, it doesn't take a lot to make a huge difference. And with Clemmons not facing any Republican opposition in the November general election, his primary victory ensured he replaced Odom in the legislature. The newly elected Clemmons is now a lifelong friend of ophthalmology, annually visiting our institution to meet with our residency and talk with them about the importance of advocacy.

Success in advocacy requires effective communication with politicians. Effective communication requires access, which in turn requires relationships. And relationships start and end with elections and re-elections.

To start, it is important to know the key issues that affect ophthalmology and medicine in general. The best way to learn about this is to join your state ophthalmology society and, in turn, join your state medical association. The leaders of these organizations will help you identify issues that put your patients or your practice at risk. They will let you know which politicians are friendly and which less so. And they will help you become involved.

The best place to begin is by supporting candidates in their election campaigns. It certainly is best to get in early – the Clemmons election is a good example. Your involvement can take many forms. Candidates need money, so you should start building a relationship with your own contribution. But the only thing better than your personal contribution is getting others to donate through hosting a fundraiser, or bringing colleagues to a fundraiser. You also can help by putting a sign in your yard or even volunteering to make phone calls, pass out flyers, or knock on doors in your neighborhood. And remember that the first priority of an elected official is re-election! The Gary Odoms of the world may take their defeat seriously and immediately start their preparations to take back their lost seat – keep this in mind and at least be equally supportive when your candidate is up for re-election.

"Encourage the legislator to phone you with any questions about healthcare related issues, whether ophthalmic-related or not."

After your candidate is elected, you need to maintain contact with your new ally. Make an effort to get together periodically outside the legislature. This could be meeting for breakfast or lunch, or even inviting the legislator to visit your office or ambulatory surgery center (ASC). Be sure that the legislator has your business card and your cell phone number. Encourage the legislator to phone you with any questions about healthcare related issues, whether ophthalmic-related or not. It also would be valuable to develop a social relationship. This is not essential; however, if you truly enjoy the legislator's company, consider a golf outing or fishing expedition.

It is even more impactful for you to take a morning away from your practice and travel to the statehouse during the legislative session and visit your legislator there. You visit not just when your issue is on the docket: you don't want to be viewed as a "one trick pony." You must definitely visit when there is an ophthalmology-critical issue under consideration and bring colleagues (and your trainees) with you. Make sure that your local politicians are aware of your key issues of concern. It is important they know to notify you if they hear about legislation being considered that could be relevant to you. And if you (or your society) want to propose proactive legislation, do not hesitate to ask them to help you by sponsoring the bill.

Success in local politics is all about relationships: you must develop them and nurture them. Effective communication with your local politicians is not possible without a relationship. You will be more successful in convincing your legislator to support your position if he or she knows you and knows that you have been supportive of them. Dropping in at the eleventh hour is rarely successful. And remember that "all politics is local" – it doesn't take a big gift to get on the radar of your local legislator. However, playing a key role in getting a candidate elected the first time may lead to a lifetime relationship of friendship, good will, and support.

We Can't See Everything

Intraoperative OCT should be considered for macular surgery

By Justis P. Ehlers, The Norman C. and Donna L. Harbert Endowed Chair for Ophthalmic Research, Cole Eye Institute of the Cleveland Clinic, Ohio, USA

Evidence is building that intraoperative OCT is useful for macular surgery. Before evaluating the role for OCT in the operating room, consider the perspectives on its clinical use when it first became available 20 years ago. Back then, some experts doubted the potential role for OCT in the management of ophthalmic diseases. In fact, many clinicians believed their own exam was superior, and asked questions like, "Is there any real use for this?" and "Is it just a cool new toy?"

Fast-forward to ophthalmic practice today: OCT drives diagnosis, therapeutic decision-making and disease surveillance more than any other imaging modality available. It's superior to our own exams in many situations, including for the diagnosis of various pathologies, such as vitreomacular traction, epiretinal membranes, and myopic schisis. The opportunities for understanding anatomic relationships (such as the vitreoretinal interface) with OCT are outstanding.

This technology that has already transformed the clinic is now beginning to make its mark in our operating rooms. Intraoperative OCT gives immediate feedback on the completion of surgical objectives, it allows visualization of translucent tissues and membranes, and it has the potential to improve clinical judgment, personalize care, and improve outcomes. The evidence is mounting – there are a growing number of published peer-reviewed papers which demonstrate the impact of intraoperative OCT on surgical decision-making (1–4).

The PIONEER study, for example, looked at over 500 eyes, and in 15 percent of cases, intraoperative OCT actually altered surgical decision-making (2). How does this translate to outcomes? If we look at imaging-assisted epiretinal membrane (ERM) surgery without mandated internal limiting membrane (ILM) peeling, we see the recurrence rate is less than 1 percent. That's comparable to rates achieved solely with ILM peeling in addition to ERM peeling.

"Although we would like to believe we can see everything, we can't."

Similar themes have been described with the DISCOVER study and others (1,3,4). In the DISCOVER study, in 16 percent of cases where surgeons felt they had completely peeled the membranes, occult residual membranes remained that required peeling. Conversely, in 20 percent of cases where surgeons believed there were residual membranes to peel, intraoperative OCT revealed that all membranes has been successfully removed. In these cases, intraoperative OCT prevented unnecessary additional surgical manipulations and improved efficiency. Overall, surgeons reported that intraoperative OCT impacted their surgical decision-making in over one-third of cases – for example, affecting their gas tamponade choice or reducing adjuvant dye use.

The early evidence suggests that – similar to the use of OCT in our clinics – although we would like to believe we can see everything, we can't. When it comes to the question of intraoperative OCT in macular surgery, one of the real challenges is that it is impossible to know which cases will be impacted by the technology and which ones will not. Randomized clinical trials that assess long-term outcomes are still needed to further validate the specific role for intraoperative OCT in vitreoretinal surgery, and the planning for these studies is underway. Intraoperative OCT is an emerging and exciting technology that may provide a paradigm shift for surgical visualization and image-assisted vitreoretinal surgery.

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Heads Up!

Vitreoretinal surgeons – is it time to lose the microscope?

By Claus Eckardt, Chief of Ophthalmology, Klinikum Frankfurt Höchst, Frankfurt, Germany

In heads-up surgery, the surgeon performs microsurgical procedures, not by bending over and looking through the eyepieces of a surgical microscope, but by viewing images sent from a three-dimensional (3-D) camera on a large flat panel display. My department has adopted this technology, and our five "heads-up" surgeons have now performed over 3,500 cases. However, there are only a few studies available on this technique, and most of these concentrate on the anterior segment. So when I discuss the use of heads-up surgery, I receive some common questions.

The first: is "Isn't it difficult?" The short answer is no, not at all. We have young and old surgeons doing it, and anyone can learn within a couple of days. Another is "How good is the 3D image compared to a direct microscope view?" Well, we performed a study (1) in which we measured the depth of field, and found little difference between the heads-up view and the view through the microscope. We also measured the resolution and found it to be around 30 percent lower than traditional microscopy. This isn't surprising, since the retina has incredible resolution. For example, for a visual field of 120 degrees, theoretically more than 500 megapixels have to be filled in order to make the display image indistinguishable from the surgical microscope image for our eyes. But this is only valid with eye movement. If the eyes are not moved to scan the whole image with the fovea, the brain only receives an image with a resolution of seven megapixels, in the area of foveal fixation, and one megapixel elsewhere. My camera system delivers a resolution of four megapixels, and in the future the pixel density will increase, until the pixels are no longer detectable.

Another important feature is dynamic range. My two-year-old camera which I used before I switched to heads-up surgery, had a small dynamic range. In contrast, my TrueVision camera today has a dynamic range of 14 f-stops. What huge progress in only two years! We can expect further improvement if – instead of a camera placed on top of a traditional microscope, where it receives only a virtual image – we use a fully digital microscope, where the camera sensor receives the true image directly.

The large image is another major advantage of heads-up surgery. In our department, we feel that the large image improves depth perception, allowing for more precise surgery. Illumination has always been an issue for the vitreoretinal surgeon, but digital image processing that brightens the image can also help us during surgery. Then there's ergonomics – which would you prefer, a hunched posture, or one that allows you to move your neck, head, and back? And when it comes to teaching, for the first time surgeons in training can see exactly the same image as the surgeon is seeing. The large projected image makes this effective and comfortable for both of them.

"For the first time, surgeons in training can see exactly the same image as the surgeon is seeing. The large projected image makes this effective and comfortable for both of them."

Looking forward, overlay guidance systems may also be of some use for vitreoretinal surgery, and another useful tool which could be integrated is intraoperative OCT – you could simply split the screen and view both. In my view, the benefits of heads-up surgery are undeniable – and provide a strong argument for a future in which we stop looking through eyepieces to perform surgery.

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THE STAGE IS SET...
THE PRIZES ARE READY...
THE COSTUMES ARE ON...
LET THE FUN BEGIN!

The League of Extraordinary OPHTHALMOLOGISTS

The Ophthalmic Premier League educates, excites and amazes. Here's what we learned in Las Vegas!

By Amar Agarwal

Complicated case presentations are worth attending. They're supremely informative, and the knowledge gained can make an impact at any point during a surgeon's career. But they can be a little dry. That's why I took a different approach:

- Sixteen of the world's best eye surgeons
- Four-minute video presentations
- Trash-talking – and costumes, and crucially...
- A total PowerPoint ban.

This is the Ophthalmic Premier League (OPL). Something that's as educational as the driest of presentations, but with as much fun as anything that would happen in the bars at the end of a long day. Where else can you see Boris Malyugin dancing in a pirate costume? Abhay Vasavada firing a ping pong gun at delegates? Richard Lindstrom in a wig? OPL.

Origins

Here in India, we have the Indian Premier League professional Twenty20 (T20) cricket league. For those who aren't aware, first-class cricket (i.e. the big international and domestic matches) feature some of the best players in the world, and you'll often see some of the best cricketing ever. But these matches consist of four innings, can take three or more days to complete, and it certainly isn't all constant action. Instead of lasting three days, T20 matches last three hours. The cricketing is some of the best you'll see – it's considered to be a more "explosive" and athletic form of the sport, and everything is considerably less formal – players have been known to wear costume elements, moustaches, and poke fun at their opponents, thereby entertaining the crowd. It's a serious competition, but also fun.

Now, I always hold the annual conference of the Indian Intraocular Implant & Refractive Society (IIIRS) in Chennai in July. One day I thought, why don't we hold an Ophthalmic Premier League during it? I thought about the format, and decided on four teams with four players each. You have 16 of the top surgeons in the world, showcasing their craziest cases, how they handled them, each with four minutes to present their story – it's a great learning opportunity. I ask each team to "attack" the other teams – with banter, a bit of "trash talking". It's great fun, and we involve the audience too – they get to vote for their favorite teams and presenters with keypads at the end. It's a real competition.

In addition to running it at the IIIRS meeting, we've held it once during ESCRS, once at the World Ophthalmology Congress, and each time was a great success. The alternative, yet hugely entertaining event has now been held twice at the annual meeting of the American Academy of Ophthalmology (AAO), and we'll be running it again in Chicago this October. Here are some of the highlights last year's OPL@AAO – depicted in a unique format that captures the spirit of the event.

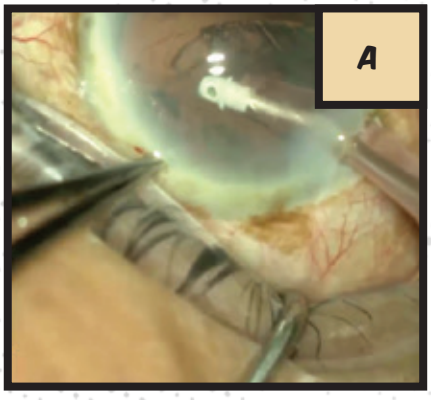
Ophthalmology on Ice

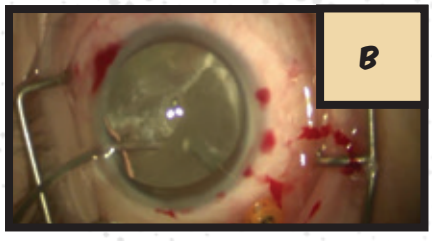
A. I'm going to show some amazing innovative examples of how to save IOLs. What we can see here is an example of stripping zonules. I'm not sure what the process is called yet – we won't mention any surgeon's name here. The zonules are stripped away by the surgeon, who isn't paying attention, and the crowd is just absolutely horrified! So we're going to try and fix these zonular problems.

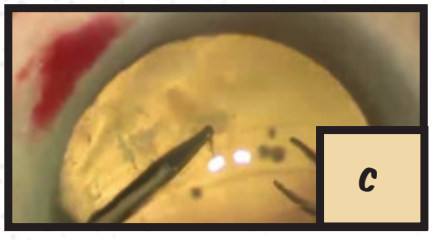
B. Here's an example from one of the other teams. This was an attempted small incision ECCE gone wrong. It's so important to manage the vitreous in these cases, because the vitreous will get in the way of us scoring goals.

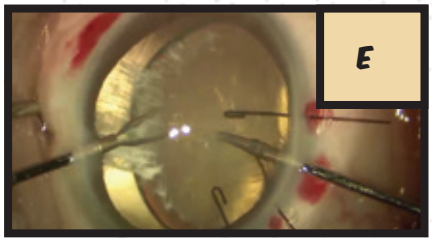
C. So, we've got to manage the vitreous through a pars plana approach, and using the right hockey sticks for our game is so important. Here we can see micrograspers grabbing the lens, levitating it forward, and simultaneously passing the capsulorhexis from one hand to the next.

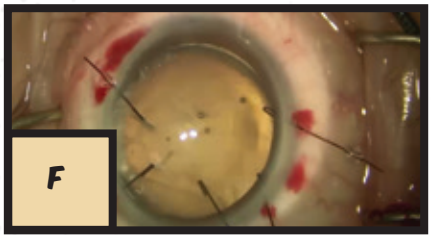
D. It's important, whether you're a right- or left- handed stick, to be able to use those sticks, working together hand to hand. This is basically passing to each other; the best hockey players know where the puck is going – an Ike Ahmed-modified Wayne Gretzky quote there – and the best surgeons know where the capsulorhexis is going, right?

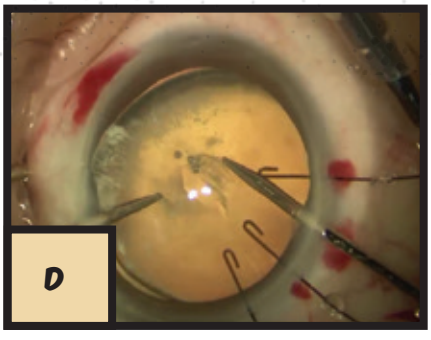


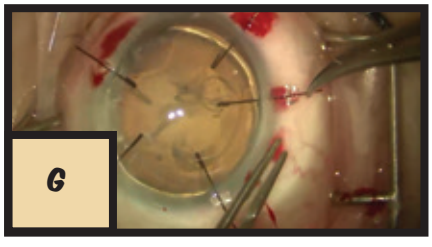


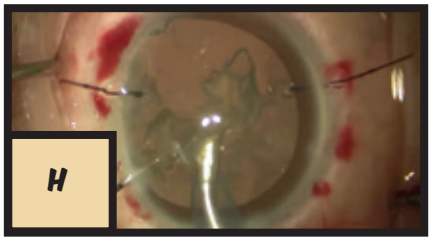


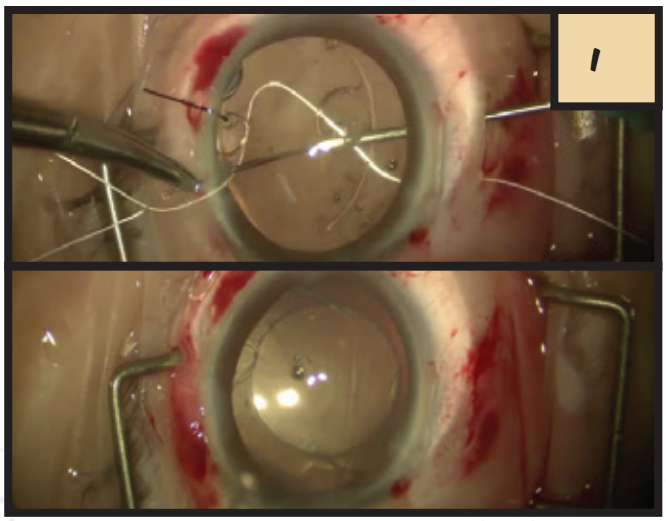


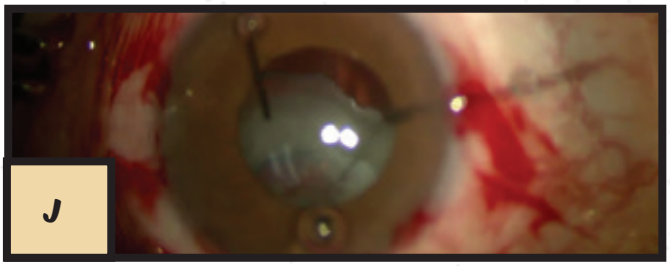


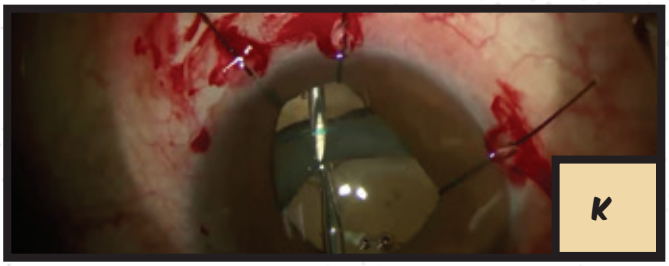


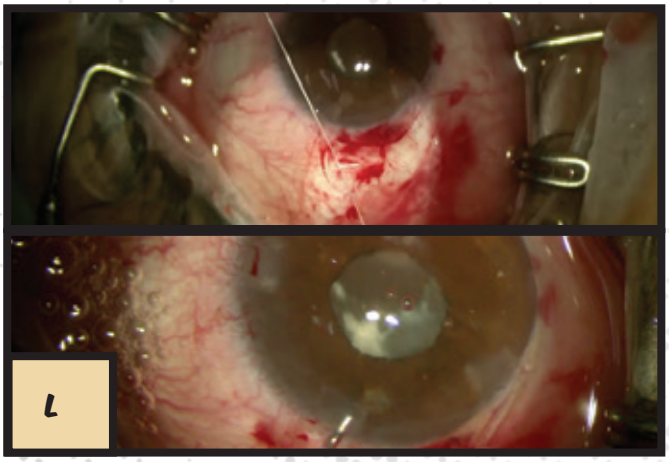












E. You see how we're also using iris hooks for support – it's a team game here, and in a team game, we use other players, including other instruments. We need to have some of these zonules left to help out – thank goodness for the three zonules that were left!

F. So the zonules are some of the grunt players on the team. You can see how well they've held up here, but we've got to help them out. This is one of the benefits of using some of the latest capsular tension devices.

G. This is some of the latest technology in eye hockey, allowing us to really center these lenses, making sure these pucks score us a goal and are shot in to the net. A capsular tension ring (CTR) helps circumferential support, to make sure we have a well centered lens, again making sure that we have optimal fixation.

H. At this point, the game is in hand. We have the capsule on lockdown, we'll approach the cataract as we routinely do through a small incision phacoemulsification. We'll then need to rely on extra suture support and we're using the latest technology: Gore-Tex suture. It has excellent durability – we use it in some of our hockey gear too!

I. This is our preferred suture using an ab externo technique to fixate both segments. These segments are versatile and that's important; you need players that work in the corners. I think the crowd will like the story here – we fixated the IOL in position, and this is definitely a goal in overtime.

J. Here's another shot on goal. The IOL was nowhere to be seen, and we used a posterior levitation technique. Using a 30 G needle entering through pars plana, bringing the lens up, we like to refixate these lenses when we can – notice we have a couple of strategic iris hooks present. You've got to know where to pass the puck, and make sure that the players are working together.

K. Again, using an ab externo technique, and a 25 G needle, going through the peripheral capsule to basically surround the haptic here with a loop of suture, and we'll refixate the lens back in position. Some of these players are old and have played hockey for the past 15 years. With this technique, they can still last another 15 years.

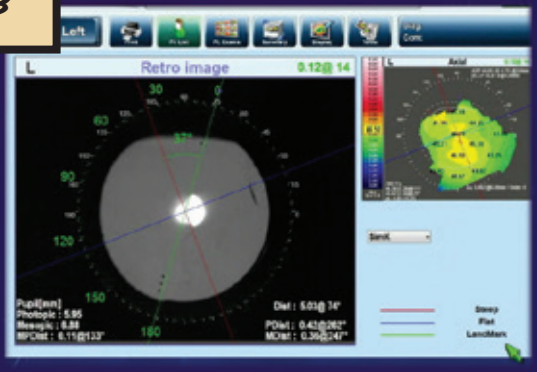
L. Here we refixated the haptics with that suture again. We've got a well-centered IOL here, and a well-positioned small incision technique. So we're ending with a good score!

A

WE ARE THE BURSTING BUCCANEERS, AND WE HAVE... INTRAOPERATIVE ABERROMETRY!

OUR PATIENT: 59-YEAR OLD HYPEROPE
POST OP DAY - 20/25 UCVA
1 WEEK LATER - 20/70 UCVA, TORIC ROTATED 43 DEGREES

B



WHAT DO I DO?

C

RE-ROTATION AND HOPE IT WILL STAY?

D

E

POSSIBLE SOLUTIONS
– PART ONE

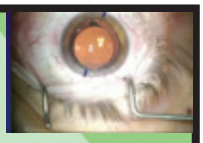
INSERTION OF CAPSULAR TENSION RING (CTR).

- BUT THE IOL MIGHT STILL ROTATE!

WHAT ABOUT...?

- A SECOND CTR TO STABILIZE THE TORIC IOL?

POSSIBLE SOLUTIONS
– PART TWO



WHAT ABOUT...?

– A MODIFIED CTR? IT MIGHT CENTER THE IOL, ADD RESISTANCE, AND TAKE UP ADDITIONAL SPACE

F

Aye aye captain, ARRR!

So this is about cataract complications, and you know, those videos that the Canadian Choppers showed, c'mon, anyone could do that. That's easy stuff – baby talk! I wanted to present something that we see all the time. This might not be sexy, but it's very relevant.

A. The case I'm presenting is one of a 59-year-old hyperope who had phacoemulsification with a toric lens. Postop day one she's great, a week later she comes back and her vision has decreased – the toric has rotated 43 degrees!

B. I brought her back to the OR two weeks later and repositioned the toric lens with intraoperative aberrometry once again. The day after surgery, her vision was wonderful! A week later, she comes back and it has rotated again – 37 degrees.

C. Now remember she's a hyperope. We've seen these cases before but usually the patients are axial myopes – they keep rotating, you keep repositioning, and your patient keeps coming back again and again... so what should I do?

D. If you believe in some higher power, are you going to re-rotate and pray? Or what about a reverse optic capture?

E. How about placing a CTR? Lots of authors have published on this, but the problem is that even after the insertion, the IOL can still rotate. How about inserting two CTRs? Sagiv and Sachs reported that implanting two can stabilize the toric IOL.

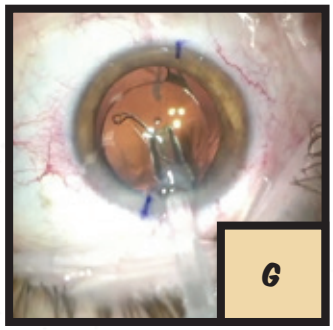
F. Another option is to place a modified CTR. The idea being that the CTR centers the lens, and takes up additional space, while the indentations in the modification will hopefully hinder the rotation even more by adding resistance.

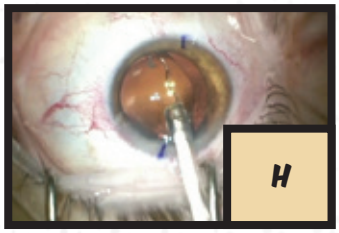
G. One tip is to inject the modified CTR counter-clockwise, because if injecting clockwise, you can inadvertently capture the CTR in the haptic-optic junction.

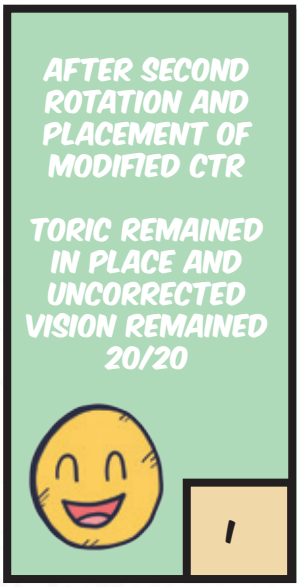
H. If you insert it counter-clockwise, the CTR will be inserted in the same direction as the haptic, and therefore it is harder to become trapped in the haptic-optic junction which can move the IOL out of position.

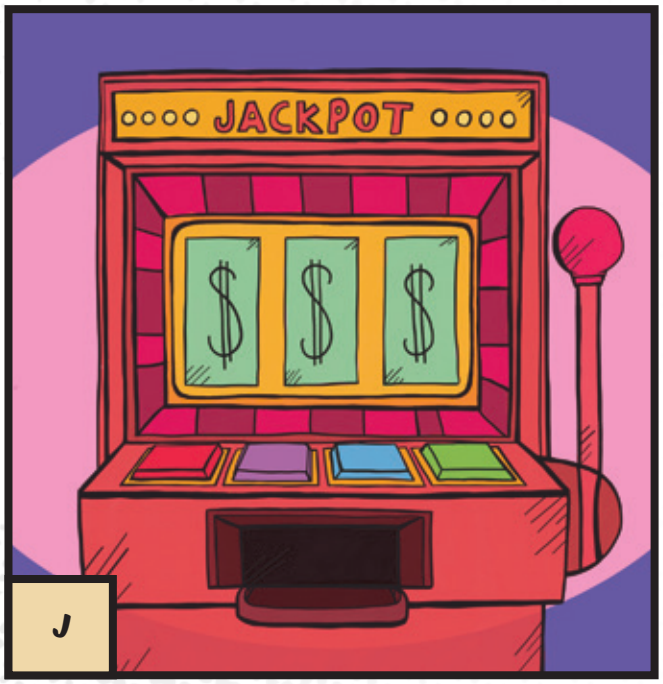
I. After the second rotation and placement of modified CTR, the toric IOL stayed in position and the patient did well.

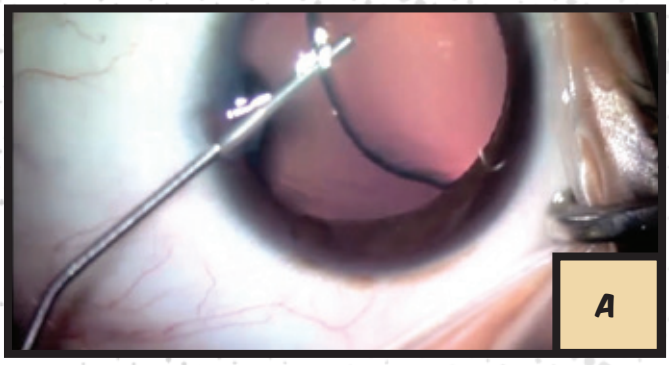
J. In conclusion, when a toric IOL rotates, placing a CTR can help stabilize the position. And remember, toric IOLs can rotate off-axis even in hyperopes. It is common to associate myopes with long anterior chamber depths and rotating IOLs. And in fact, this patient did have a pretty long anterior chamber depth, but a short axial length, which threw us off. So fixing a roulette wheel toric with a modified CTR can really lead to hitting the jackpot!

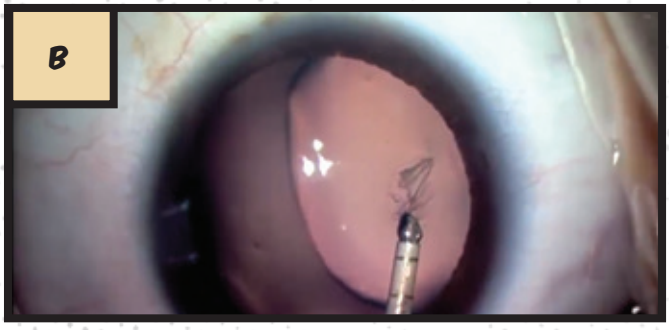


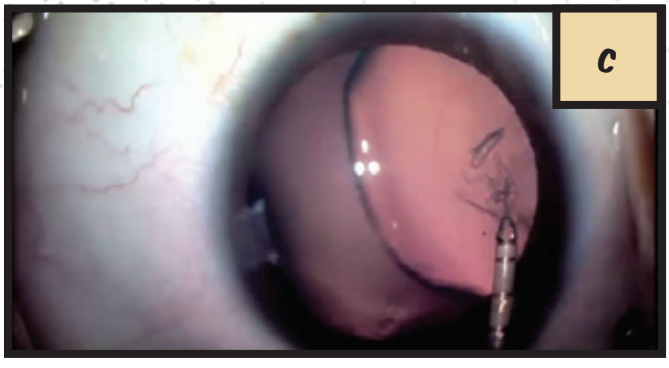












Captain Ectopia (Lentis)

Well ladies and gentlemen, it's hard out there for an avenger. Take this first case – this is actually the unfortunate child of one of my arch enemies. The last time we fought, I hit him so hard, his kid developed ectopia lentis.

A. As you can see here we've got a very dislocated lens, about 50 percent visible through the pupillary aperture, so we put in viscoelastic to block any vitreous from coming through those weakened zonules.

B. Now we start our rhexis here with a cystotome, and then we're going to use some forceps – a pediatric capsule is very elastic, so I like a micro capsulorhexis forceps.

C. We're going through the main incision here as I'm able to do most of the work through this, but I can also go through a paracentesis if I need to. I'm pulling against the direction of the tear, so that the 'rhexis doesn't go out, and I can get a good size.

D. Remember, you don't need a very big 'rhexis in a kid's eye; a small one will suffice. We'll do a thorough hydrodissection, and I replace my viscoelastic to make sure I've got good vitreous tamponade, and I just use I&A to take these lenses out, as they're very soft.

E. In a non-dislocated lens, I'll use a coaxial I&A, because I've got the big port, but with this case I use bimanual, so I can come from either side. Now I wasn't able to get it all easily, so I fill with viscoelastic and try to put my CTR in. I also do a little viscodissection to get any cortex off the anterior capsule.

F. Now we like to dial our ring in from the strong area into the weak area, but that would be difficult in this direction. And even in the other direction I can't make it happen, so I'm going to take my ring out and not force it.

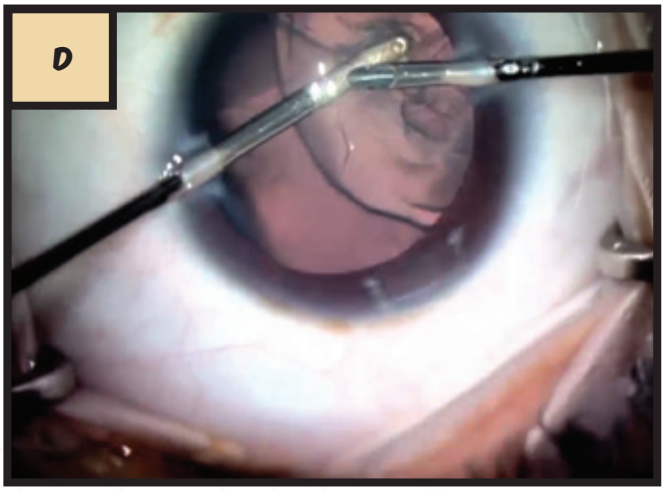
G. And getting a little bit more of that ring going in actually loosened my cortex, so I can get most of it. I make a little peritomy, and I just like to do two side port incisions here, about 2 mm from the limbus.

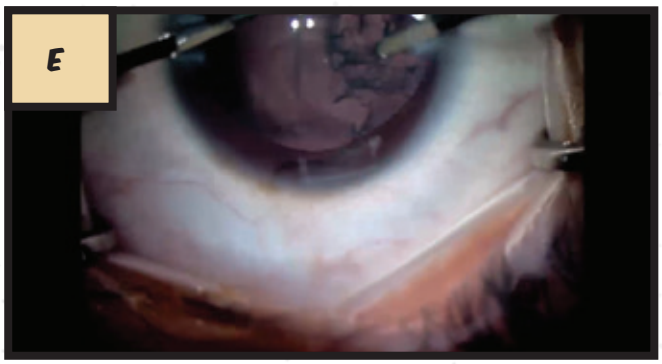
H. When you have an intact vitreous they don't leak, so they work very easily. I'm going to put in an Ahmed segment here, and I like to use a Gore-Tex suture. This is a kid, so this is going to be in their eye for a very long time. If I use a Prolene suture, I know it's going to degrade eventually, and I'm going to have to replace that, or fix a dislocated lens.

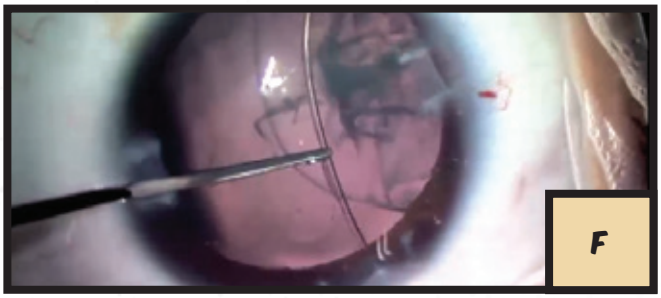
I. I put a little groove in between those incisions so that suture sits down really nicely, and then I can pull my capsule over.

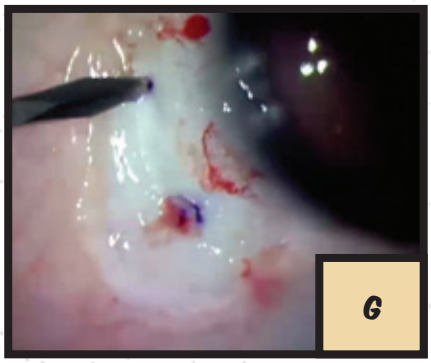
J. Now I can finish my viscoelastic removal, and dial the ring in. I like doing this with instruments rather than an injector, I think I can feel it a little bit better. I drop that ring in with a Sinskey, then I can suture that and finally place my capsule. When you do the capsular tension segment in without the ring, it can tilt, so you don't want to pull it too tight, or you can actually pull it out of the capsule.

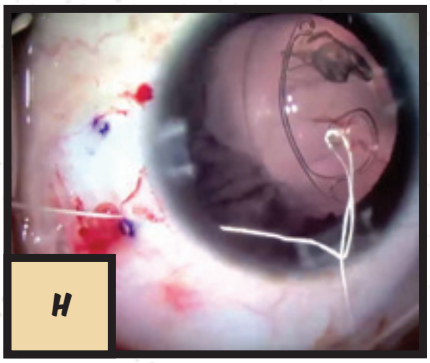
K. Now I can inject my lens very easily, and I've got a case with a lens in the bag, in a kid who has a good future ahead of him.

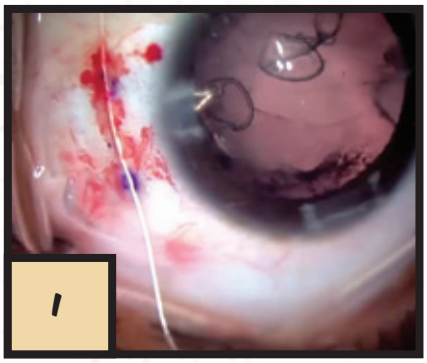


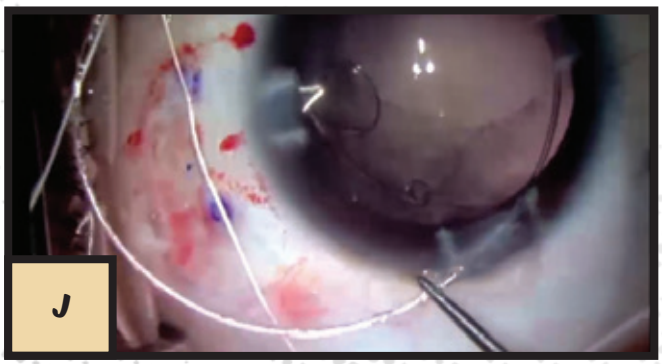


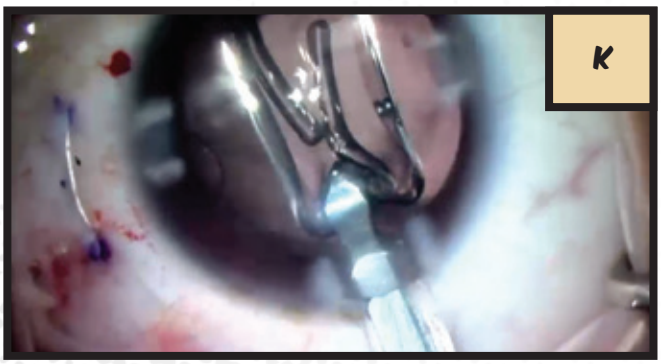












Ninja-ing In and Out of a Tight Spot

Abhay Vasavada: Ninja George, do you remember last year we had some problems – we taught somebody how to remove an IOL… and what happened?

George Beiko: I do, Sensei. We taught David Chang, but he doesn't remember!

Abhay Vasavada: And that's why we kicked him out of the dojo!

George Beiko: This year I will show him how to take the lens out of a 3 mm incision rather than a 6 mm incision. I think that man can learn.

A. Typically, we put IOLs in through a 6 mm incision, but this means you risk inducing astigmatism and vitreous prolapse. Here's the idea – first performed by Lawrence Brierley back in the nineties: a 3 mm incision at the limbus, going back 3 mm, and then tunneling through the sclera and the cornea in order to place the lens.

B. So, the technique can be used for putting in IOLs, or for taking out dislocated IOLs.

C. And I'll show you first of all putting in an IOL, so the idea is 3 mm at the limbus, going back 3 mm, and then tunneling in order to get the other 6 mm.

D. We mark it (the pupil is miotic because for IOLs you want that).

E. We make our groove, go back 3 mm, and at this point you can either use a blunt keratome or a diamond.

F. I felt comfortable enough with the procedure to continue on with the diamond. So we tunnel in, being careful not to penetrate the anterior chamber until we create the whole incision.

G. George Beiko: I wonder where David is, because we could show this to him again, seriously.

Abhay Vasavada: David, are you listening?

H. Put the viscoelastic in, so now you have your incision and the lens can fit through. You hydrate that wound, and I don't use sutures. I like to use MST forceps in order to enclavate, so you can use this to put lenses in…

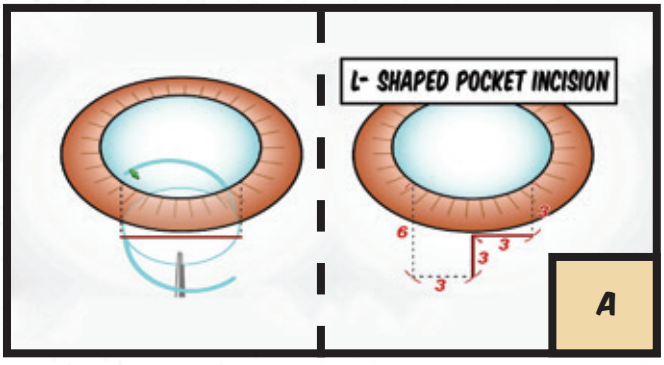
I. … and you can also use it to take lenses out. In this case, the plan is to remove this PMMA lens and replace it with a lens that's a more appropriate power for the eye. So I'm using a blunt dissection.

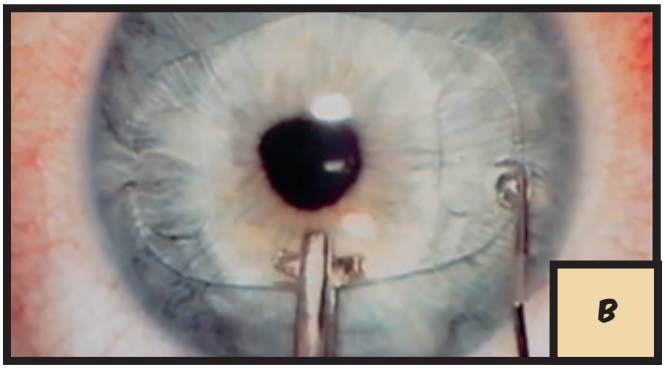
J. Again, 3 by 3, by 6, enter. The IOL easily comes out of the eye.

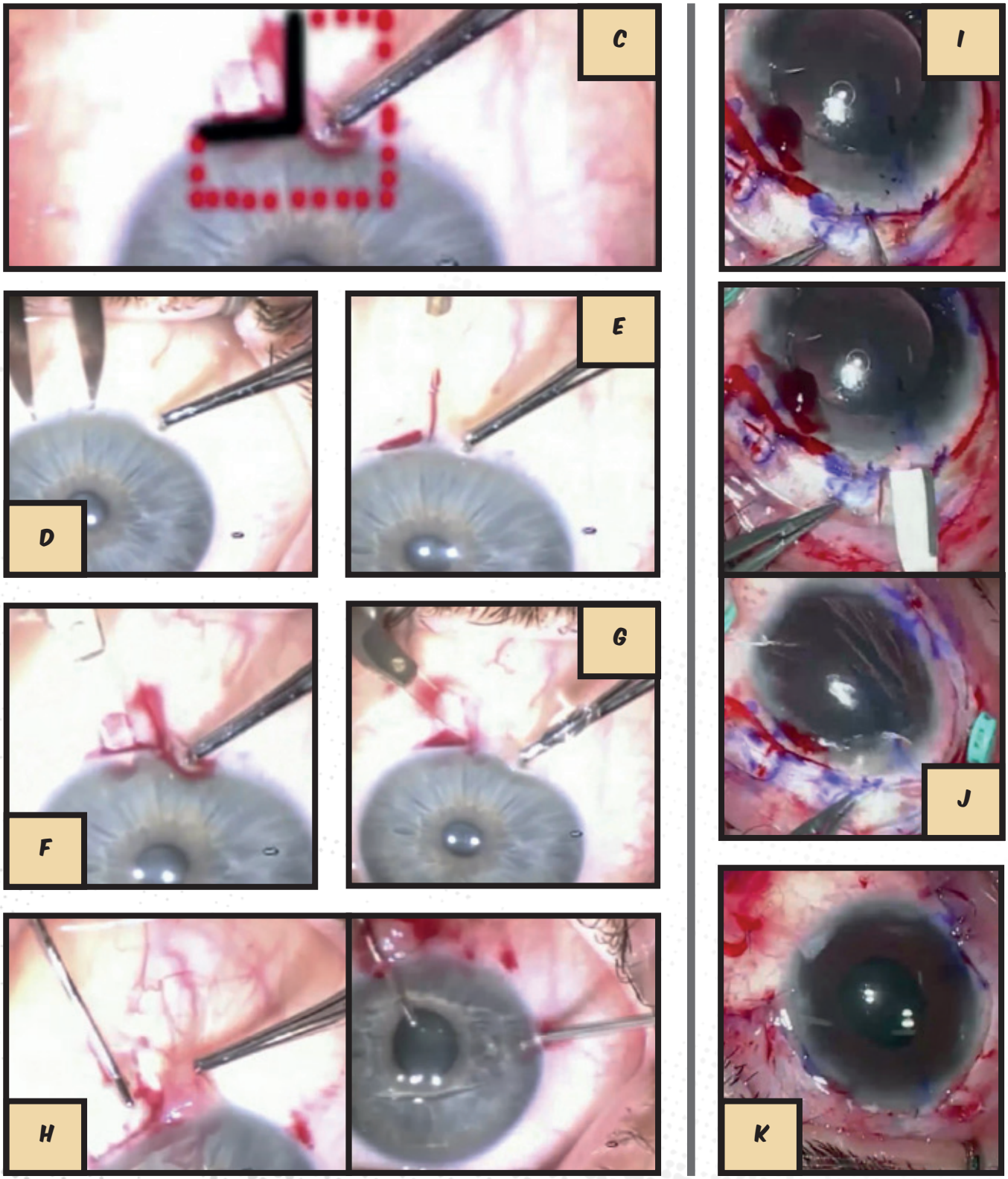
K. We place a 3 piece lens back into the eye, and externalize the haptics, and then you can either glue them or fixate them with the suture.

We performed keratoscopy immediately afterwards and 3 months later – and not one case showed a change in topography.

Abhay Vasavada: Thank you Ninja George!



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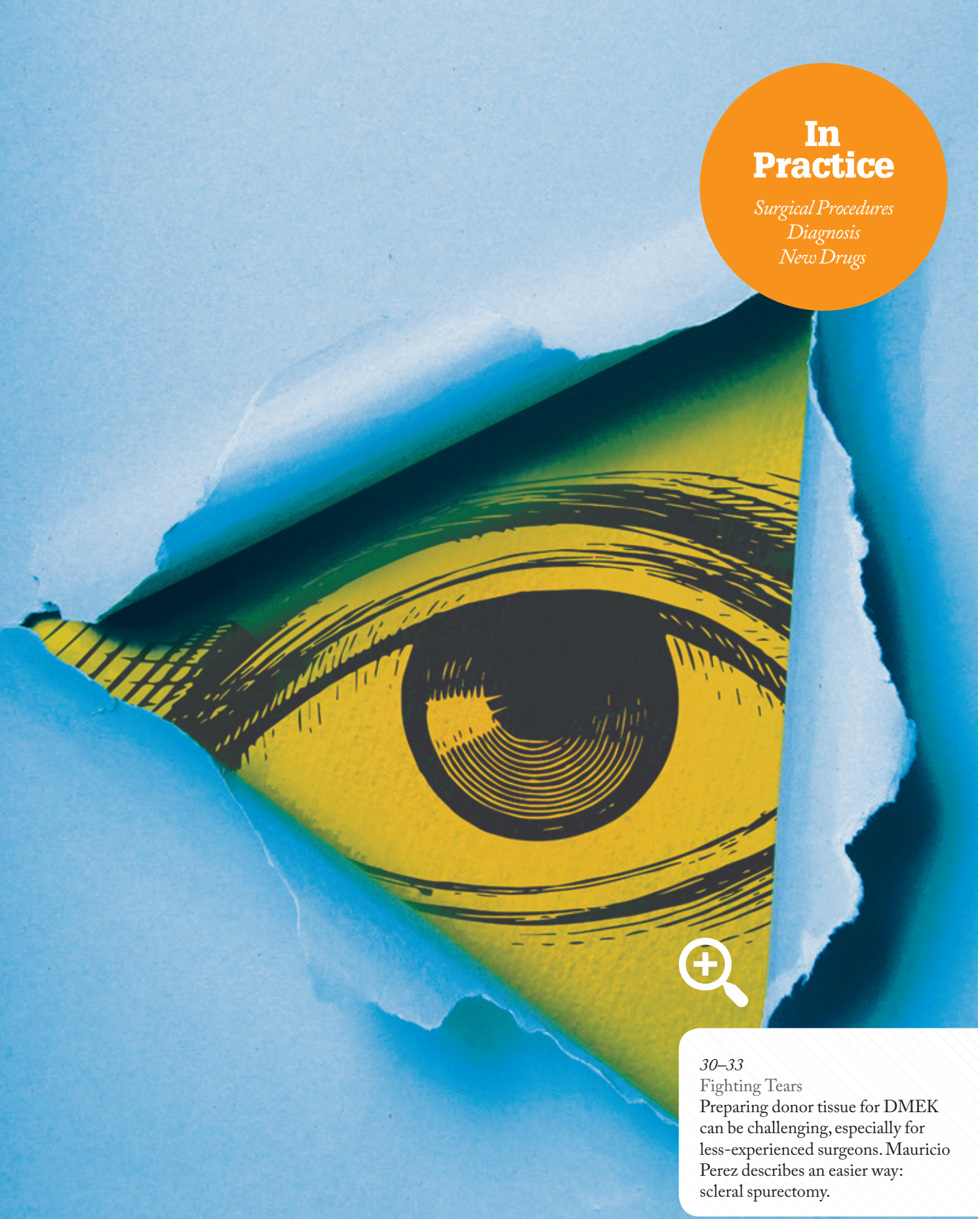

In Practice

Surgical Procedures
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Fighting Tears

Scleral spurectomy can simplify DMEK tissue preparation and reduce damage to donor endothelial tissue

By Mauricio Perez, Randall Ulate and Neera Singal

Since it was first described 17 years ago (1), Descemet Membrane Endothelial Keratoplasty (DMEK) has become a popular and widely-accepted technique in the cornea community. But despite its clear advantages in terms of visual results and rejection rates (2), its adoption has not been widespread in some areas worldwide. Why? The technique has a steep learning curve, mostly due to donor tissue preparation. Donor cornea tissue is a precious resource; in countries with limited availability, many surgeons might opt to persist with full-thickness grafts rather than risk donor corneas during the DMEK learning curve.

Is there a better way? Multiple different techniques have been described for donor tissue preparation (3–5), all with the aim of standardizing the steps that are needed to achieve a suitable endothelium-Descemet's membrane (E-DM) complex to restore endothelial function. We describe another here.

At a Glance

- *DMEK can deliver great outcomes in corneal endothelial transplantation, but the learning curve can be steep*
- *David Rootman from the University of Toronto cleverly modified Gerrit Melles' original technique for donor tissue preparation, and his method has seen success in many cases – but going through the learning curve remains a challenge for some*
- *This new modification, known as scleral spurectomy, involves scleral spur disinsertion to facilitate peripheral blunt dissection of the trabecular-endothelium-Descemet's membrane complex, decreasing the risk of tears which can compromise donor endothelial tissue viability*
- *Scleral spurectomy is easy to learn, can reduce the number of possible complications during the dissection process, and is likely to be useful for surgeons who don't have access to pre-stripped DMEK donor grafts*

Getting ahead of the learning curve

We were all trained to perform DMEK under David Rootman's supervision at the University of Toronto. Everything we know about this technique, we owe to his generous teaching. His standard technique for donor tissue preparation (6) brilliantly modifies the original Melles technique (3), and starts with a blunt dissection of the trabecular meshwork on a corneoscleral rim using a Rootman-Goldich modified Sloane's LASEK micro hoe (Katena Products). It involves careful dissection of the peripheral trabecular insertion from the scleral spur, and continues anteriorly, freeing the trabeculo-Descemetic junction from its insertion at Schwalbe's line, and then the E-DM complex from its stromal attachment.

This technique has been used successfully in more than 300 cases – but it's not without challenges. It still involves a learning curve, and can still present problems with some donors. These include: difficulty finding the correct plane of dissection by dissecting either behind or in front of the scleral spur (sometimes including the dissected spur into the membrane complex), the creation of one or multiple adhesive tags between the scleral spur and the E-DM complex (Figure 1a), and the creation of radial or circumferential tears (that generally tend to extend centrally) during the initial dissection of the internal aspect of the trabecular meshwork from the scleral spur (Figure 1b). These tears can be explained by the radial or para-radial vector force that results from the centripetal force that's applied by the surgeon to free the membrane from its insertion, and the force applied from the scleral spur insertion itself at the spot right next to the dissected area (Figure 1c).

Although these challenges can usually be overcome by an experienced surgeon, it can be difficult to survive the learning curve and become confident using this technique, especially when every donor tissue counts.

Two main attachments of the donor endothelium need to be broken for a successful peripheral dissection before starting the standard stripping motion. One is the external, strong and thick attachment at the level of the scleral spur, and the second one is a relatively loose and anterior attachment at the level of Schwalbe's line. We call this new technique of scleral spur disinsertion to facilitate peripheral blunt dissection of the trabecular-E-DM complex "Scleral spurectomy" (see Sidebar, "Taking a Technique From the Lab to the OR").

"Donor cornea is a precious resource... many surgeons might opt to persist with full-thickness grafts rather than risk donor corneas during the DMEK learning curve."

This method was initially applied to 30 consecutive donor corneoscleral rims at the lab at the University of Toronto, before moving to the operating room. Since then, we (and several other surgeons) have fully converted to it for the past year and a half. It has already been presented in our DMEK Course at the ASCRS and ESCRS meetings, and is currently part of the surgical toolkit that we teach to cornea surgeons in training.

Do it yourself

The main advantages we've found with this technique include less difficulty in finding the correct dissection plane, as removing the scleral spur essentially eliminates the anterior versus posterior to the scleral spur dissection dilemma. Since the scleral spur is not there anymore, it eliminates the adhesive tags between the scleral spur and our dissected membrane, which in the standard technique, needed to be commonly cut with Vannas scissors for a successful dissection. Furthermore, it eliminates the radial or para-radial force vector created by the scleral spur insertion during centripetal dissection with the micro hoe, which results in a reduced likelihood of creating radial or circumferential tears that might compromise the viability of our donor endothelial tissue button. We have yet to see a peripheral tear during dissection using this technique.

Scleral spurectomy can be especially useful for the newer DMEK surgeon, since it reduces the amount of possible complications during the dissection process, which a more experienced surgeon could most likely manage. In our experience, we believe it is a very quick, easy to learn, reproducible and effective technique which has the potential to decrease the rate of donor tissue tears if you are experiencing them, and helps in the management

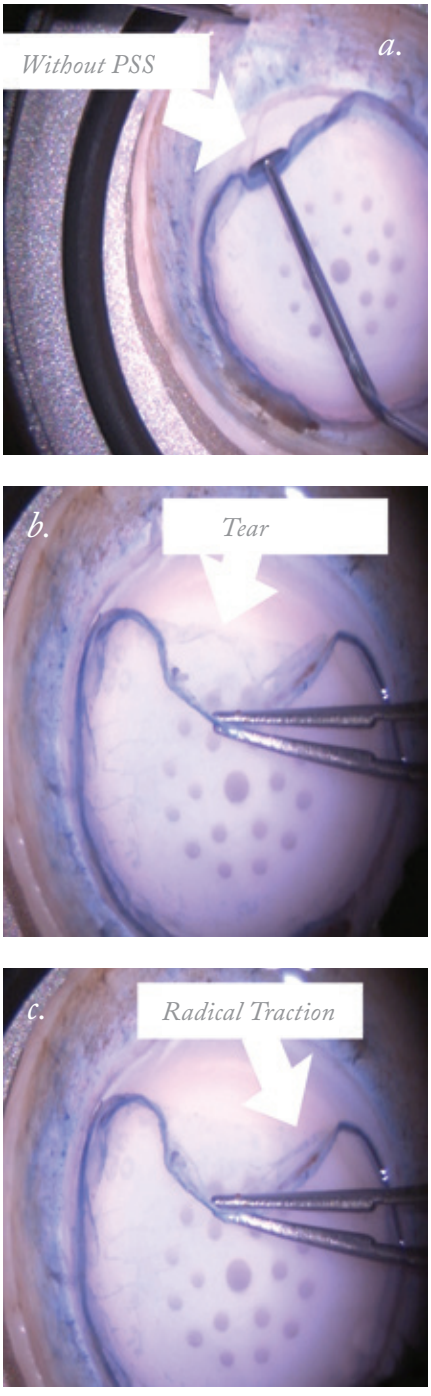

Figure 1. a Adhesive tags between scleral spur and E-DM complex during dissection without physiologic salt solution (PSS). b. Horseshoe tear on donor. c. Radial traction line connecting the grabbing point by the forceps and the attachment at the scleral spur level.

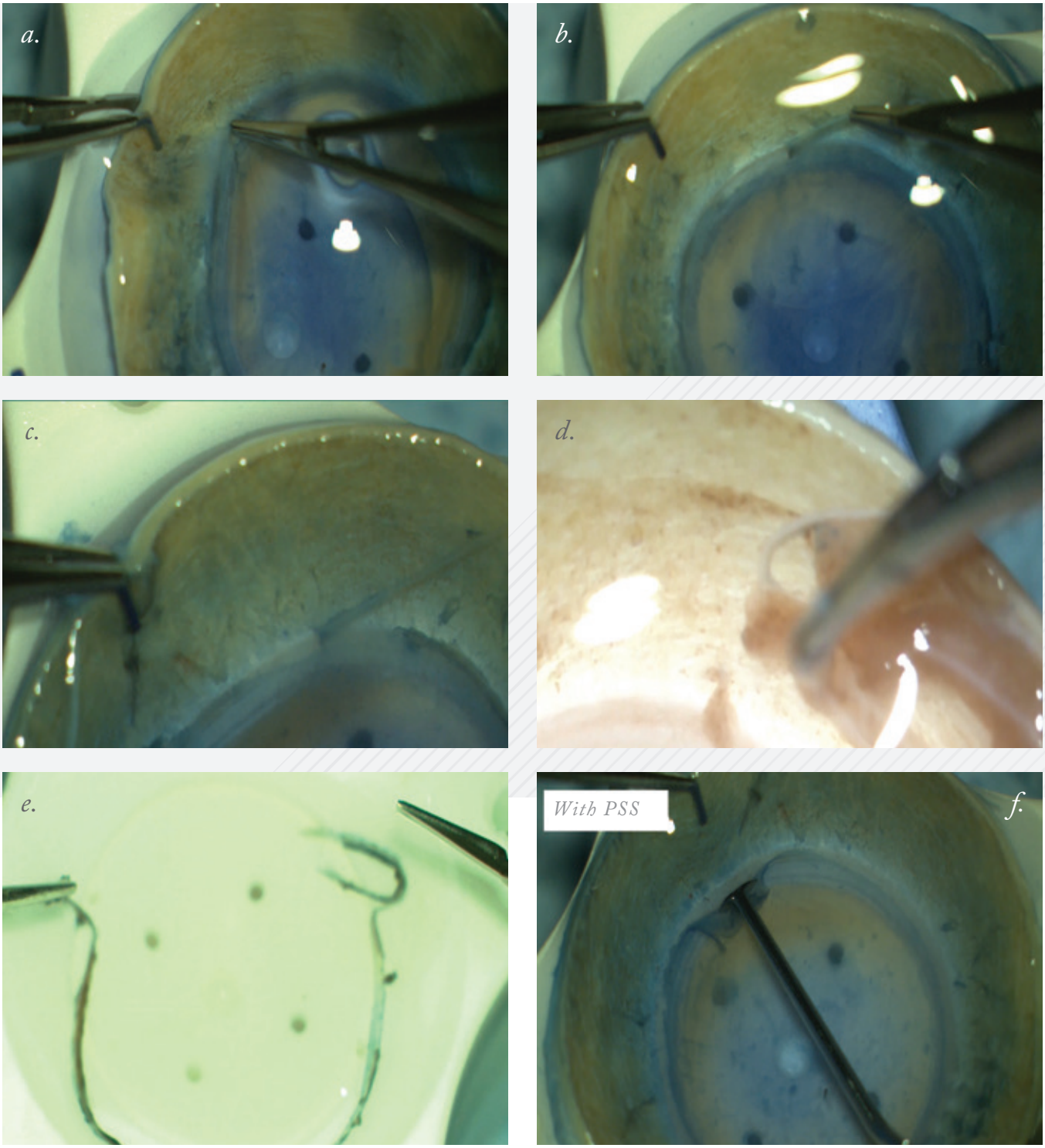

Figure 2: Steps for PSS: a. Deep scleral grab at the scleral spur level with toothed forceps. b. Focal disinsertion of the scleral spur by applying traction on the Z-axis. c. 360 degrees scleral spurectomey. d–e. Scleral spur fully dissected, with its characteristic "snake-like" white stripe configuration. f. Plane of dissection revealed after PSS. The edge of the E-DM is now free, similar to the free edge of a curtain hanging from the wall.

Taking a Technique From the Lab to the OR

- We start by locating the scleral spur's base, which in most cases will be evident, or will become visible behind or right next to the trabecular meshwork, after an initial minimal blunt dissection of its base (video available at: http://top.txp.to/mp-ss).
- We continue by using a toothed forceps to apply countertraction to the edge of the corneoscleral rim and a second toothed forceps (preferably 0.12 mm) to tightly grab the scleral spur deep into the sclera (Figure 2a), and gently apply perpendicular traction on the Z-axis.
- This traction creates a focal disinsertion of the scleral spur from the sclera (Figure 2b)
- This is then further extended circumferentially (Figure 2c) using both toothed forceps, one for traction, the other for countertraction.
- In most cases, the entirety of the circumferential scleral spur ring will dissect out as a single "snake-like" strip, 360 degrees around (Figure 2d–e).
- If the scleral spur strip happens to break, the dissection can be continued by regrasping the scleral spur where the break occurred, until the full circumference is disinserted. It is very important that you see a white stripe of tissue disinserting from the corneoscleral rim, since one can mistakenly disinsert the iris root, which would not accomplish the goals of our technique.
- Once the scleral spur is removed, the plane of dissection of our DMEK donor tissue is revealed (Figure 2f), as we have removed its main adhesion to the scleral rim, and this can be found anteriorly adjacent to our initial dissecting plane, in a configuration that resembles the inferior free edge of a curtain hanging from a wall.
- This edge can be lifted and gently pulled anteriorly, in order to continue with our standard approach, using the Rootman-Goldich modified Sloane's LASEK micro hoe to further anteriorly dissect the trabecular-E-DM junction.
- This breaks the only remaining main hurdle for our donor dissection, Descemet's insertion at the level of Schwalbe's line, and allows us to continue the disinsertion of the E-DM complex from the stromal bed.
- Luckily, this second attachment at Schwalbe's line is not as strong, creating less resistance to dissection and generating far less radial tension.
- At this point, you can gently push the membrane centrally, instead of actively scraping the insertion to break it (as was done for the scleral spur attachment using the original technique).

of friable corneal tissue, especially for surgeons that do not have access to an eye bank that can pre-strip DMEK donor grafts and require self-prepared tissue, as is the case in most parts of the world.

We hope that this scleral spur dissection/stripping technique will help to popularize DMEK among cornea surgeons, and make tissue preparation a less daunting process.

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NextGen

Research advances
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The Dark Side of the Moon

How does humankind make it to Mars? By redefining glaucoma, for starters…

By John Berdahl

I like to use the phrase "The dark side of the moon" when referring to glaucoma. Why? Because we have real problems with it: we don't fully know what glaucoma is or what causes it. Just as we on Earth only see one side of the moon, we ophthalmologists have only really looked at one side of glaucoma – the eye side. The common belief is that glaucoma is a "one pressure" disease – intraocular pressure (IOP). And although IOP certainly matters in glaucoma, the reason why is not that clear.

At a Glance

- *We still don't really know what glaucoma is, but dogma states that it is caused by elevated IOP*
- *What's more likely is that glaucoma results from an imbalance of two pressures that act on the optic nerve: IOP and ICP – as does pseudotumor cerebri and VIIP, something that many astronauts on the international space station experience as a consequence of microgravity*
- *Pressurized goggles, which decouple IOP from ICP, may help to rectify this imbalance*
- *Trials are underway to investigate the pressurized goggles for the control of eye pressure in patients with glaucoma, and future studies may help astronauts hoping to make it to Mars someday*

Re-hypothesizing

My belief is that the balance between IOP and intracranial pressure (ICP), i.e. the pressure differential, is what really matters in glaucoma, not just the absolute pressure inside the eye. And reaching this hypothesis began when I was 30 feet underwater wondering why scuba divers don't get glaucoma.

At this time, I was an ophthalmology resident at Duke University Eye Center, and excited by the idea, so I presented it to one of my Professors. Their response of "You're probably not right but you should study it," resulted in a collaboration between Duke and the Mayo Clinic, and along with R. Rand Allingham and the late Doug Johnson, we published our first paper in 2008 (1). We performed a large retrospective analysis on over 50,000 patients who had undergone lumbar puncture over the past 20 years at the Mayo Clinic, and we compared ICP in patients who had glaucoma with those who didn't. What we found was clear: patients with glaucoma have low ICP. Our second publication (2) showed that relative to non-glaucomatous controls, ICP was lower in patients with primary open-angle glaucoma (POAG) and patients with normal tension glaucoma (NTG), but higher in patients with ocular hypertension (OHT).

So with human clinical data supporting the concept that ICP matters in glaucoma, our next step was to consider how we could use this information to actually help people. And what makes it meaningful? At this point, whilst doing my fellowship with Dick Lindstrom, I shared this information with him and he said "I think you are right. What are you going to do?" To my response of "I don't know!" he then advised "Opportunity favors the prepared mind." And his advice stuck with me. I kept thinking, and then one day I realized that the reason astronauts in the NASA International Space Station (ISS) were developing papilledema was probably because their ICP is higher than their eye pressure.

The minus alpha

It was at this time that I and my business partner, Vance Thompson, started thinking about how to help these astronauts. Ping-ponging ideas back and forth we thought about the use of a pressurized helmet, but we realized that this would change both the eye pressure and the ICP, so the differential wouldn't change. But what about goggles, which would relieve some pressure just on the eyes but wouldn't affect ICP? And that's where our idea was born.

Excited by this, I set about making a prototype by ordering some goggles and a small pump, putting together tubes, and playing with them to see if I could get a seal and get the pressure to change – this was really whatever is before an alpha product! The idea was that the goggles can be used to control eye pressure, by drawing a small vacuum or applying pressure above the eye, thereby decoupling IOP from ICP. Since then, we've been refining the goggles; not only do they have to work but they need to be comfortable too. Our challenge at the moment is to demonstrate that we can control IOP, and we have a number of small clinical trials examining this.

The clinic… and beyond

Although we are thrilled with what we see so far, we feel that there are four constituencies we need to convince. To make it to market, we need to convince regulatory bodies like the FDA and the EMA, but we aren't yet sure what their expectations for a trial are going to be. What we really want to do is find a way to first understand if we can actually control eye pressure. And because this theory and treatment is so novel, it's a double-edged sword: we have this really different approach to treating glaucoma, but the hard part is designing trials that are going to have to be very different from what has been done in the past. And we don't totally know how to do this yet. We are going

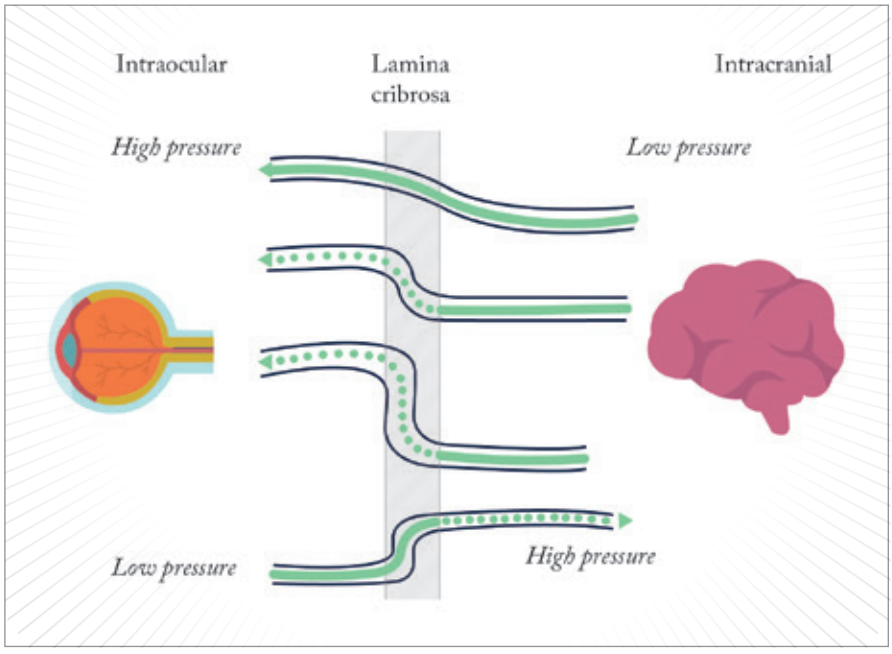


Figure 1. Schematic showing axonal transport across the lamina cribrosa in cases of a pressure differential (IOP high/low and ICP low/high).

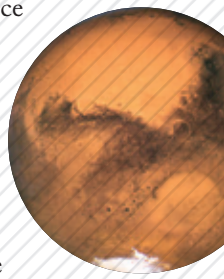
to need to convince doctors that this is a real treatment, and convince payers that this treatment provides a good adjunct or an alternative to current therapies. And finally, we have to convince patients that this is meaningful, and we hope to do this by letting the data lead us in the right direction.

We also hope that, for the first time ever, we will be able to dial in patients' IOPs to exactly where we need them to be. And although it would be ideal to know patients' ICP, it isn't totally necessary, as we could argue that it would be ideal to know patients' ICP for any glaucoma therapy that we use right now. Currently, when we set a target IOP for a patient, we aren't basing this on ICP, we are basing it on clinical intuition. The goggles should work the same way: we know we want to lower IOP, and we are hopeful that the goggles can do that.

In 2015, we were invited to be part of the vision for Mars team on the vision impairment and ICP (VIIP) project (3). VIIP, a syndrome of globe flattening, hyperopic shift, choroidal folds, and optic disk edema, has affected almost half of the astronauts who have stayed for an extended period on the ISS. Why? In space, ICP increases at the level of the eye as there is no gravity to draw the cerebrospinal fluid (CSF) down the caudal spinal column.

To put the problem in context, it's hypothesized, given optimal orbital alignments of Earth and Mars, to take a minimum of seven months for astronauts to reach Mars. A long-term mission on the ISS is six months, and a significant proportion of ISS crew who have spent that amount of time on the space station experience (what's thought to be VIIP-related) vision problems, such as hyperopic shifts, scotoma, cotton wool spots, choroidal folds, optic nerve sheath distension, globe flattening and optic nerve edema (3). Unless something is done, many of the astronauts heading to Mars are going to have eye disorders. To this end, we have been further developing our goggles with NASA and the National Space Biomedical Research Institute

The IOP-ICP hypothesis



It's likely that glaucoma arises from an imbalance between IOP and ICP. When IOP is increased – or ICP is decreased – a pressure differential across the optic nerve is created. We know that ICP affects the optic nerve, as we see it in pseudotumor cerebri (idiopathic intracranial hypertension); the raised ICP forces the optic nerve to bow forwards. In glaucoma, we see optic nerve cupping, likely because a high IOP and a low ICP force the optic nerve backwards.

I also believe that glaucoma may be a metabolic disease. In a normal situation, axonal transport through the optic nerve delivers metabolic needs and removes metabolic waste across the lamina cribrosa. But when the IOP gets raised (or ICP is reduced), this axonal transport may get stopped at the level of the lamina cribrosa (Figure 1). In this situation, the metabolic needs of the optic nerve aren't met, the nerve slowly withers, ganglion cell death occurs, and glaucoma ensues.

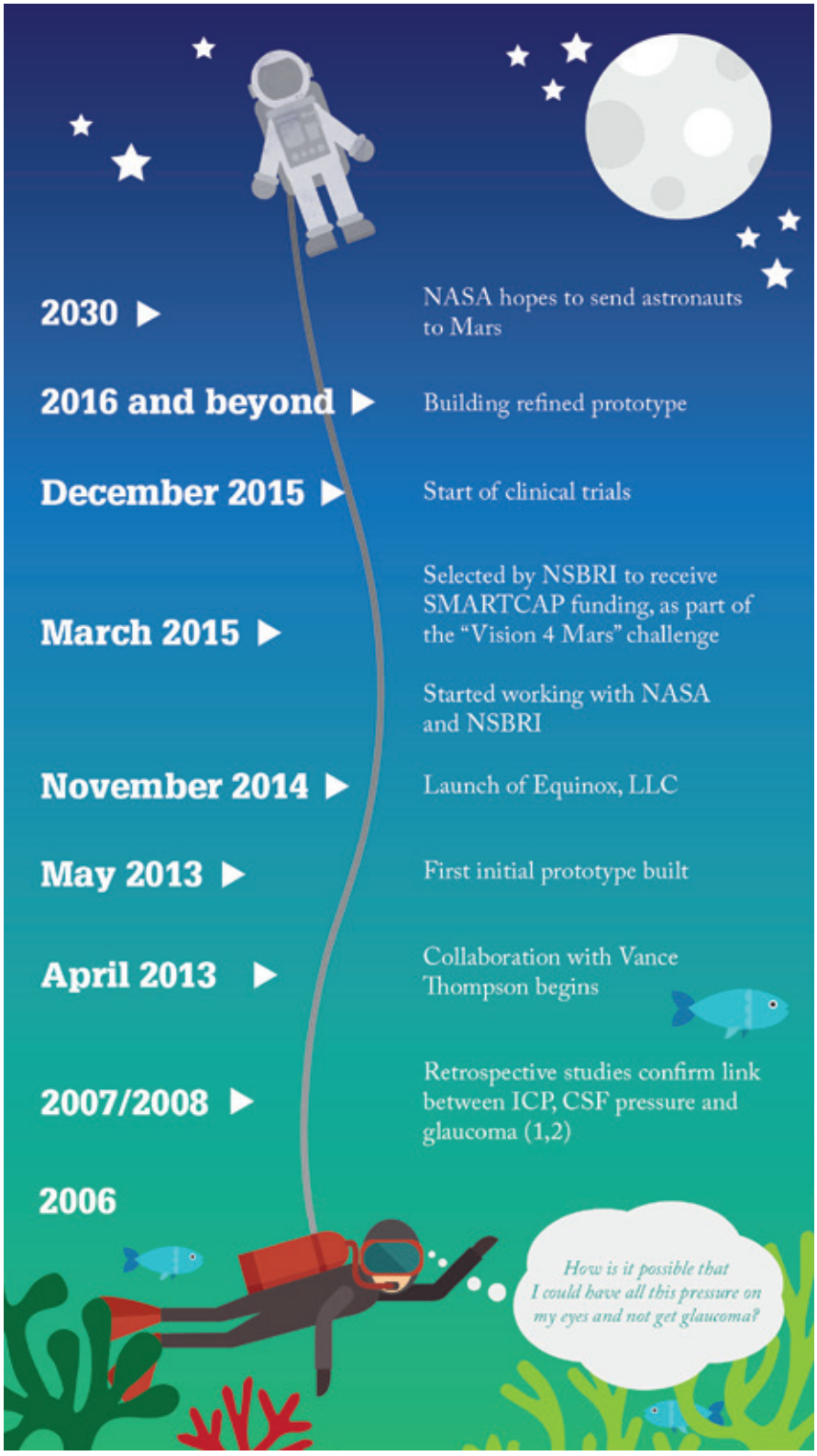
The hope is that these goggles will provide adjustable control over a patient's IOP, allowing us to balance it with ICP. For patients (on Earth) with glaucoma, we hope to remove some of the eye pressure by drawing a small vacuum (10–15 mmHg) above the eye. For astronauts, the idea is that the goggles would elevate IOP to balance the effects of elevated ICP in space.

(NSBRI) to balance the microgravity-induced increases in ICP by elevating IOP, by applying a small positive pressure within the goggles, as opposed to a small negative pressure when the goggles are in use by patients with glaucoma.

Next steps

As well as the necessary clinical and safety trials, we also have to demonstrate that people will actually wear the goggles. We have some advantages, as the goggles are non-invasive, can be worn during sleep, and are complimentary to existing therapies. For patients taking eye drops (or who have had any type of glaucoma surgery in the past), we expect that the goggles could be a nice adjuvant to those in addition to standalone therapy – it means we have an additional tool in the toolbox to treat glaucoma. As we are probably years away from having something that is clinically available, we are excited about what the future holds.

John Berdahl is an ophthalmologist at Vance Thompson Vision in Sioux Falls, specializing in cataract, corneal, glaucoma and refractive surgery. He is also Medical Director of South Dakota Lions Eye Bank, and the CEO and founder of Equinox LLC.



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Tasting Vision

The story of the BrainPort V100 – from vibrating plates, to balance aids, to a visual aid that helps users "see" with their tongue

By Roisin McGuigan

Neuroplasticity – the brain's ability to reorganize, adapt, and form new neural connections throughout adulthood – is an area of neurology with a checkered past. For many years it was thought that the adult brain was "hard-wired" with fixed neuronal circuits – a notion that's now disproven. Today, there's solid evidence of adult neuronal plasticity and an active, experience-dependent reorganization of the synaptic networks of the brain involving multiple interrelated structures – and this includes the cerebral cortex, the region of the brain where most visual input is processed. The BrainPort V100 is a device that was developed to exploit exactly these plastic processes, in order to help users "see" objects with their tongues…

At a Glance

- *Visual information can be sent, via the tongue, in a manner that allows visually impaired people to receive and interpret it in a meaningful way*
- *BrainPort works by sending information from a camera to an array of sensors on the tongue, which form patterns by electrostimulation which, after training, are interpreted by the user*
- *In test subjects without visual impairment, tongue electrostimulation results in activation of the somatosensory cortex (as expected). But in those who are blind, it's the visual cortex that becomes activated*
- *The technology could offer a less expensive and nonsurgical alternative to retinal implants, and might even be able to be used alongside other technologies to help improve independence for the profoundly blind*

Brain barriers

American neuroscientist Paul Bach-y-Rita had a great interest in neuronal plasticity (1). In 1958, his father suffered an ischemic stroke that affected his mobility and ability to speak. His family was told he was unlikely to ever fully recover. The treatment options were fairly limited back in the 1950s, but Paul's brother George, a psychiatrist, worked hard to provide rehabilitation treatment for their father. Happily (and against all expectations) their father went on to live a normal life for the rest of his years. When he died decades later, an autopsy revealed an unrepaired, severely stroke-damaged brainstem.

To Bach-y-Rita, this presented strong evidence of the existence of neuroplasticity: he believed his father's recovery could only be explained by reorganization of the brain. Indeed, he's recognized as one of the first to propose the concept of sensory substitution to induce neuroplasticity as a therapeutic modality. In the late 1960s, Bach-y-Rita and his colleagues at the Smith-Kettlewell Institute of Visual Sciences in San Francisco used some spare equipment to design and build a chair with a bank of 400 vibrating plates that rested against the user's back. The plates were connected to a video camera placed above the chair, and the pattern in which the vibrating plates was stimulated enabled blindfolded users to "see" the objects that the camera recorded – they had produced one of the earliest examples of a haptic feedback device (2). Bach-y-Rita suggested what was occurring was an example of neuroplasticity, as he believed the signals sent to the brain from the skin were being processed in the visual cortex. As he famously said, "You don't 'see' with your eyes, you 'see' with your brain."

On balance

Originally, Bach-y-Rita designed a device to help patients with balance disorders. It detected the position of patients' heads with an accelerometer, and relayed that information to the patient, by way of electrostimulation of the tongue. Stimuli on the right side of the tongue meant the body was leaning to the right, stimuli on the left side meant that the body was leaning to the left (3). This information was then used in conjunction with a series of exercises to treat balance disorders. But could it be used for anything more demanding? His next step was to evaluate this technology as a vision aid. Sadly, Bach-y-Rita died in 2006, aged 72, but his research continued.

"Just give the brain information and it will figure it out"

Vision substitution technology isn't new: Louis Braille developed his code back in 1824 and the white cane rose to prominence in the 1930s. Exploiting the tongue is the place where the device meets the body – as BrainPort does – is a newer phenomenon. It consists of three interconnected units: a pair of sunglasses with an integrated video camera, a 20 × 20 array of stainless steel electrodes that are placed on the tongue, and a handheld computer that processes the video camera's input, contains contrast and stimulation intensity controls, and activates the electrode array with patterns based on the camera input (Figure 1). In terms of the camera feed, a black pixel results in no tongue stimulation, and as a pixel gets brighter, so does the intensity of tongue electrostimulation. Through training, users learn to understand these levels of stimulation and form "pictures" in their mind of what the camera is

Figure 1. BrainPort consists of a pair of sunglasses (with an integrated video camera), a 20 × 20 array of stainless steel electrodes that is placed on the tongue, and a handheld computer that processes the video camera's input, contains contrast and stimulation intensity controls, and activates the electrode array.

viewing (see Figure 2).

Neuroimaging studies have shown that blind users activate the visual cortex to transfer information from the tongue to the brain after even a short period of training, whereas, sighted control subjects activated the somatosensory cortex (as you would expect with tongue stimulation) (4–6). Over time, and with training, blind users start to learn how to interpret what they feel on their tongue as real world objects and scenarios. Bach-y-Rita said, "Just give the brain information and it will figure it out" – and certainly with training, it does.

Unlike the original balance-correcting device (which involved a chair), BrainPort needed to be small, portable, and the tongue stimulation component was required to sit on the tongue comfortably, and (understandably) be moisture resistant. Fortunately, advances in technology over the years have helped achieve these goals.

A different angle

There are a number of similarities between BrainPort and some of the retinal prostheses that are available today: principally, the camera-embedded sunglasses and the small portable computer, although the main difference is the interface to the body – BrainPort sits on the tongue, rather than requiring surgical implantation on or under the retina. But does it work?

There are signs that it does. A number of relatively small studies (n=11–42) have been performed that have examined BrainPort's visuo-tactile performance, including assessments of direction of motion, shape recognition and orientation and motility performance in blind subjects and non-blind controls (see Figure 3; reviewed in 7). While on the whole these studies have not demonstrated that blind subjects perform significantly better than blindfolded, sighted controls, they have shown a trend towards improved performances on these tests with training and repeated experience. However, early anecdotal reports from BrainPort users suggest that the device has been able to help profoundly blind patients regain some level of mobility, independence and confidence, and BrainPort's manufacturer, Wicab, state that "some users with congenital blindness have even found that BrainPort has changed their understanding of how sighted people see – such as objects appearing closer when nearer, and that objects look different when viewed from different angles."

Echolocation and apps

There's no reason why, in principle, devices like BrainPort cannot work synergistically with other products like retinal prostheses or assistive aids like ultrasound or echolocation devices – and according to Wicab, some of

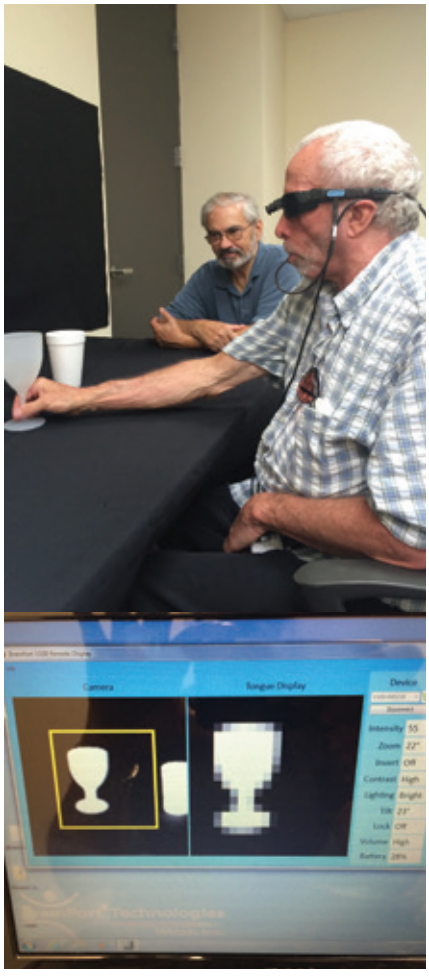

Figure 2. Supervised training is central to people deriving benefit from the BrainPort device. Typically, most individuals can start to recognize shapes after a few hours of training, and after more training, users can identify familiar objects and avoid obstacles.

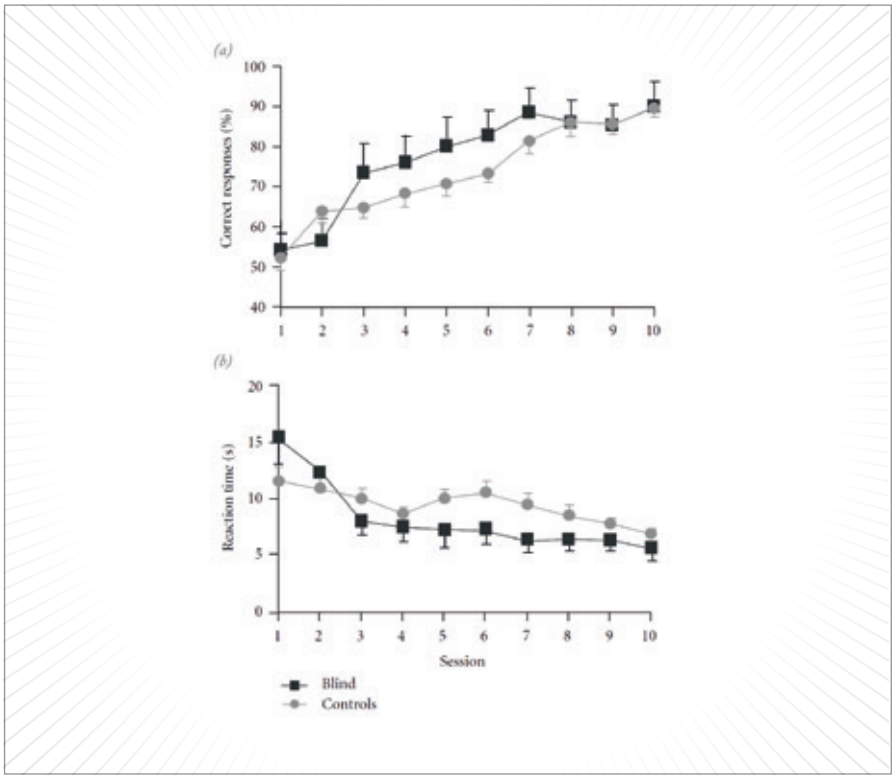

Figure 3. Learning curves for a four alternative forced choice shape recognition test in congenitally blind (n=8) and blindfolded control (n=10) subjects. (a) Mean percentage changes ± standard error of the mean (SEM) of correct responses and (b) mean reaction times ±SEM. No significant differences in performance were observed between the groups. Reproduced from (5).

these combinations are currently under evaluation.

The combination of digital video input and computer processing also raises possibilities of building upon the feature set of these devices. It's reported that one of the top requests from BrainPort users was "the identification of exit and bathroom signs, without needing to ask for assistance," and its manufacturers are looking into developing an app for the device that will allow the user to select the type of sign they wish to "see," and the device will vibrate or make a noise whenever it identifies it. This is something that could be expanded to specific structures too, like pedestrian crossings and traffic lights. Finally, outside of its primary purpose, there's also been interest from the military and the gaming market. Who knows what it might be used for in five or 10 years' time?

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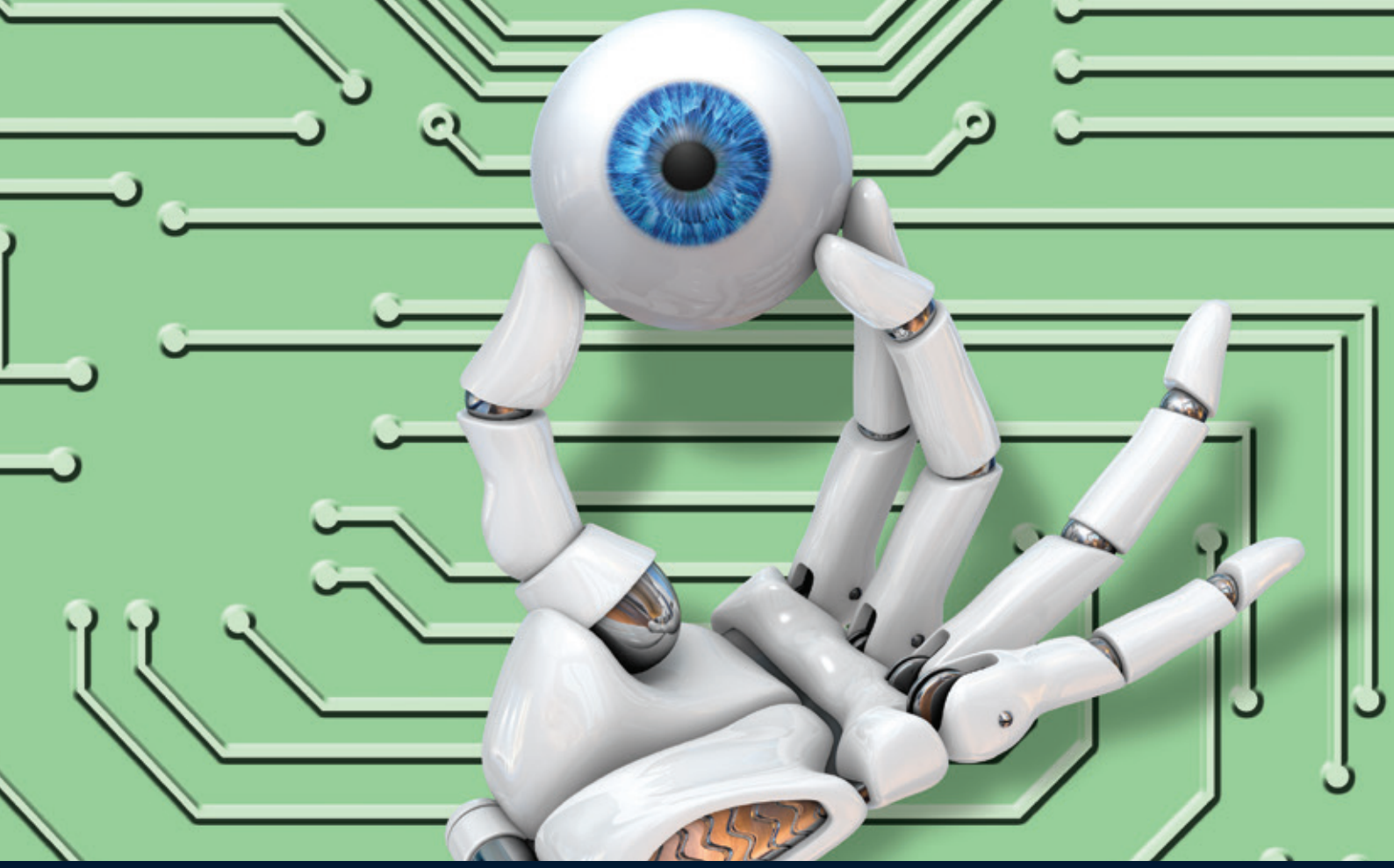

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So You Think You're an Expert?

When it comes to providing ethical expert witness testimony, there are easy obstacles to avoid

By Ron Pelton

Being an expert witness in a medical malpractice case can be daunting, especially when you realize how important your role is. For me, it's the point when the judge instructs the jury with words like, "When you are deciding whether the physician was negligent, you must base your decision only on the testimony of the expert witnesses who have testified in this case." A jury relies on expert witnesses' explanations to reach their conclusion, and in medical malpractice cases, they're going to need your help to understand the complicated medical information that's presented by both sides.

The American Academy of Ophthalmology (AAO) have some advice in their Code of Ethics, and Rule 16 (see Sidebar) pertains solely to expert witness testimony. In short, it specifies that testimony must be: based upon sound medical knowledge, objective, non-biased, and not contingent on compensation. If either side feels that you, as an expert witness, have presented false or deceptive information in court, they may submit a complaint against you for review by an ethics committee. Sometimes these cases are very straightforward, sometimes a formal hearing is needed to hear the physician's side of the story. In extremely complex cases, an ethics committee may call in an outside expert for review. These rulings can go one of two ways: either no problems are found with the expert witness testimony or sanctions are brought against the expert witness.

At a Glance

- *In medical malpractice cases, the role of the expert witness is paramount in helping the jury to understand who may be liable for any injury*
- *But being an expert witness can be a challenging experience*
- *There are existing rules and guidelines for providing ethical expert witness testimony, for instance, Rule 16 of the AAO's Code of Ethics*
- *I share ten things to avoid when being an expert witness*

Approach with caution

I want to share 10 easy ways about how you can get into "hot water" as an expert witness, and how to avoid doing so.

10 – Misrepresenting your training or experience

Misleading the jury with inaccurate claims of expertise is an easy way to get into trouble. For example, if a comprehensive ophthalmologist expert witness sells themselves as an expert in the field of pediatric ophthalmology and is called to provide guidance in a case against a pediatric ophthalmologist, this could be problematic. Don't misrepresent yourself.

9 – Allowing personal or competitive issues to bias testimony

As an expert witness, you may come up against people in your local area who you consider to be competitors or who you don't agree with. Avoid allowing personal relationships or competitive issues to bias your testimony.

8 – Viewing a case with tunnel vision

Your own views on how a specific procedure or case should be handled can cause tunnel vision, meaning the larger clinical picture can be missed. Don't forget your way isn't the only ethical or reasonable way of handling a specific situation.

7 – Allowing yourself to be solicited by the attorney

Sometimes you may feel a lot of pressure from attorneys to mold your testimony into their theory of what happened. Don't let attorneys encourage you to stretch your beliefs and alter your testimony. Sometimes you have to walk away.

6 – Resisting answering truthfully or objectively if the answer is damaging to your side

When you are up on the stand being grilled by the opposing attorney, you can feel bullied. Although a natural response may be to "push back" you can't let the truth be influenced, no matter how damaging it may be to your side.

5 – Confusing personal opinions with legal standard of care

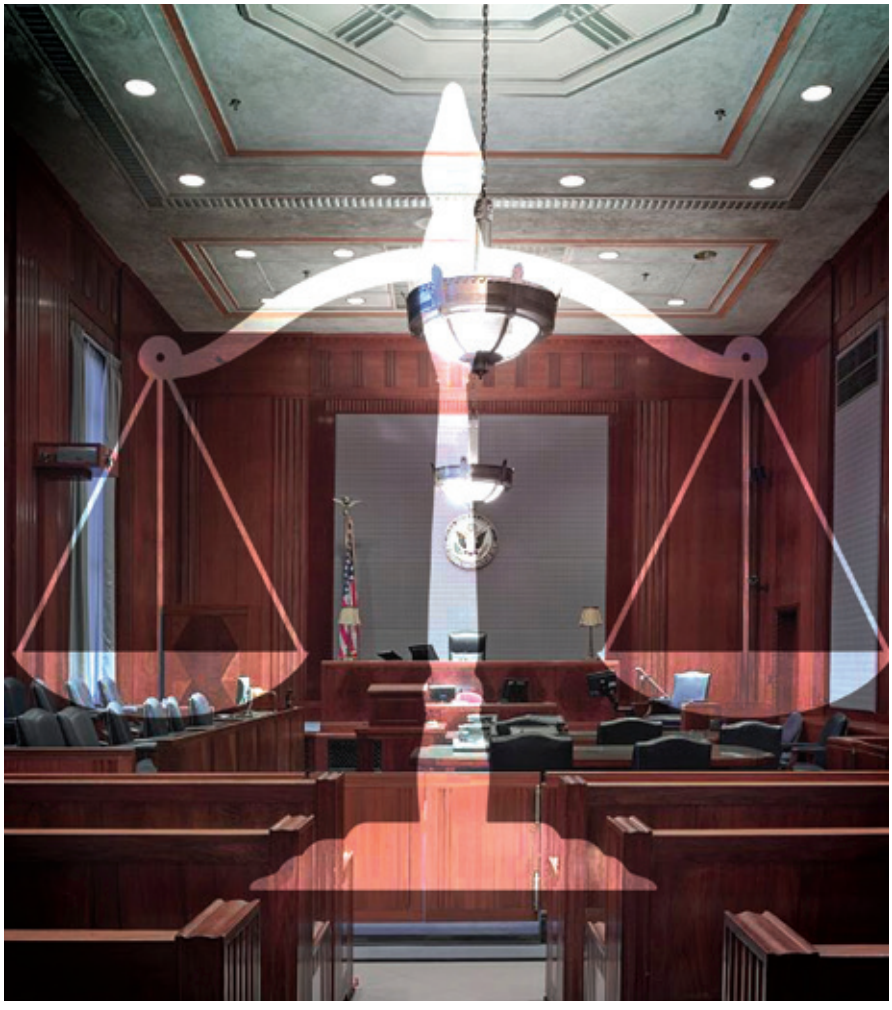
The definition of legal standard of care differs in every community. I know we all have our own personal opinions or preferences when it comes to handling a case, but remember, your way is not the only way!

4 – Unwillingness to acknowledge possible maloccurrence

Maloccurrence does not constitute malpractice and therefore does not warrant legal action. We have all had patient cases which haven't gone the way we wanted, or expected, them to. There are times when testifying where you have to be willing to say "Your Honor, this was just maloccurrence."

3 – Being unfamiliar with the intricacies of the specialty of concern

Some people are happy to give an expert opinion despite not knowing the subject. But these "expert witnesses" are unable to recognize the nuances of care, and



Rule 16 of the AAO's Code of Ethics

Expert testimony should be provided in an objective manner using medical knowledge to form expert medical opinions. Nonmedical factors (such as solicitation of business from attorneys, competition with other physicians, and personal bias unrelated to professional expertise) should not bias testimony. It is unethical for a physician to accept compensation that is contingent upon the outcome of litigation. False, deceptive or misleading expert testimony is unethical. For purposes of this Rule, expert testimony shall include oral testimony provided under oath, affidavits and declarations used in court proceedings and certificates of merit signed, ratified or otherwise adopted by the physician (1).

this matters when it comes to defining probabilities versus certainties. You must be willing to acknowledge that there may be specific nuances of a case you aren't really familiar with.

2 – Underestimating comprehension levels in the courtroom

As a physician, you probably know more about the subject at hand than anyone in the courtroom, meaning you may underestimate the comprehension level of the judge, jury or other side. Make sure that your explanations are clearly and concisely explained and tailored for an audience of non-experts, but don't belittle the idea that they can come to a reasonable understanding of what is going on.

1 – Accepting compensation contingent on the outcome of a trial

An expert witness who receives a fee for testifying that is contingent on the outcome of the trial is not ethical. This is never acceptable.

Two key principles

Being an expert witness is a challenging experience. If you volunteer for this duty, make sure you are ready to know the case in great detail: that means going through the charts and through every page line-by-line. Above I offer ten things to avoid. Now, I offer two principles that an expert witness must follow throughout the whole process to maintain integrity and protect their reputation: remain truthful and ethical.

Ron Pelton is Chair of the AAO Ethics Committee. He specializes in oculoplastics and facial reconstructive surgery, and runs a solo practice in Colorado Springs, USA.

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Lessons I've Learned

With Patricia Bath

Born in Harlem, Manhattan in 1942, Patricia Bath is a dedicated ophthalmologist, inventor, and a lifelong campaigner for equality, breaking new ground for women and African-Americans in her field. Her long and successful career to date has seen her pioneer laser treatment of cataract, file multiple patents, and serve as Associate Professor of Ophthalmology at UCLA Department of Ophthalmology where she currently holds an Emeritus appointment on the medical staff. Here, she tells us how she did it and what she learned along the way.

Education and poverty

I was interested in a career in medicine since childhood. Growing up in Harlem, many people would have considered my family poor – but we didn't apply that label to ourselves. My family taught me that I could achieve anything through a combination of hard work and education, and my brother and I were raised to believe we were unstoppable, unconquerable winners. We had such an intense work ethic that when I was awarded a scholarship at Hunter College in 1960 to study chemistry, we decided as a family that I didn't need it. Admission to Hunter College was based on academic merit and test scores, and tuition was a mere few hundred dollars. Because of my father's intense sense of pride, he looked upon the scholarship as charity and preferred to pay for my books and tuition. I recall the look of surprise when I met with the committee and advised them that I did not need the money. In today's society there are those who would argue that I should have accepted it and spent it on luxury items, but my family had a simplistic, easy notion that if your clothes were clean and honestly obtained that you were okay. So from my perspective, I was rich, not poor. I carried this drive and motivation throughout my life.

Ophthalmology inspiration

As a student, I was inspired to enter ophthalmology by an ophthalmologist I admired greatly, Lois A. Young. She was one of my medical school professors, and I admired her medical brilliance, swag, and character. She was so dedicated to her patients, students, and family – her love for humanity and joie de vivre was palpable. When I began my residency training at New York University, I had no idea that I was the first and only African-Americans ophthalmology resident. I did not know, or even care! But I did know that my superior grades, scores and credentials had earned me a coveted spot in a highly competitive residency, and that was awesome. I was happy and excited that I was about to capture my dream and become a great ophthalmologist by training in one of the most prestigious programs in the USA. We five first year residents functioned effectively as a team without any bias or acrimony, and there was more of a camaraderie fueled by our lowly status as first year residents at the bottom of the totem pole, than any discord from ethnic and cultural differences.

"When I began my residency training, I had no idea that I was the first and only African-American ophthalmology resident."

Debating, designing and dancing

The biggest challenge I overcame in my career was wanting to do research, but not having the funding or a lab to do it in. When I encountered discrimination, I stayed focused on my goal and worked to outsmart the racism I faced – with ingenuity, rather than wasting my time and energy complaining about it. Taking the high road may be arduous and long, but it will lead to justice and triumph. When I failed to get grants for various research projects, I used my research talents to identify labs and like-minded scientists with a passion for discovery and invention.

When I couldn't get any grants to do my laser research in the USA, I looked for the best labs for laser research in the world, identified the principal investigators and nagged them until they agreed to provide access to their labs. First, I presented a hypothesis and well organized experimental plan,

At a Glance

- *Patricia Bath was the first African-American to become an ophthalmology resident, in 1973*
- *Later, in 1975, she became the first woman ophthalmologist at UCLA's Jules Stein Institute*
- *Patricia is one of the pioneers of laser technology in cataract surgery, inventing the Laserphaco probe in 1986*
- *In this interview, Patricia talks about her life, career and future aspirations*

Timeline

1942	Born in Harlem
1964	Graduated with a Bachelor of Arts in Chemistry from New York's Hunter College
1968	Graduated from Howard University College of Medicine
1973	Became first African American to complete a residency in ophthalmology at New York University
1975	First woman ophthalmologist in the Department of Ophthalmology at UCLA's Jules Stein Institute
1978	Co-founded the American Institute for the Prevention of Blindness
1978	Founded UCLA Ophthalmic Assistant Training Program at UCLA
1979	Proposed Community Ophthalmology as new discipline for blindness prevention
1983	Became the Chair of an Ophthalmology residency program at King/Drew, UCLA, becoming the first woman ophthalmology chair in USA history
1986	Invented the Laserphaco probe
1988	Patented the Laserphaco probe
1989	Inducted into Hunter College Hall of Fame
2001	Inducted into the American Medical Women's Association International Hall of Fame
2003	Awarded 5th US patent for combination laser and ultrasound cataract device

and I was willing to argue my case and debate the pros and cons. But I think I really succeeded because of a shared zeal to discover and invent, be a part of something new and adventurous, and shared adrenaline for chasing the high of that climatic eureka moment of discovery.

So, like the explorer Columbus I sailed across the Atlantic and found a welcoming collegial atmosphere at the Loughborough Institute of Technology in England, the Rothschild Eye Institute in Paris and the Berlin Laser Medical Institute. I didn't waste time with phone calls or petitions about the unfair and discriminatory practices of the National Institutes of Health or the National Eye Institute. Instead of worrying, I spent my time enjoying myself – thinking, designing and dancing.

Patenting firsts

Historians have credited me as the first African American physician to receive a medical patent, but I prefer

"I didn't waste time with phone calls or petitions about the unfair and discriminatory practices of the National Institutes of Health or the National Eye Institute."

to be recognized simply as the first to develop and demonstrate Laserphaco, a laser cataract surgery technique. In the nomenclature of modern cataract surgery, we have evolved from the ultrasound era to the laser era. No one called ultrasound phaco "millisecond cataract surgery" or laser phaco "nanosecond cataract surgery." YAG laser capsulotomy triggered the launch of the laser cataract surgery era. But in YAG laser capsulotomy the laser was deployed after removal of the cataract, and never during cataract surgery. When I introduced Laserphaco, the era of laser cataract surgery began – and has continued to advance and evolve with the introduction of new technology and equipment. The fact that cataract surgery is accomplished with femtosecond lasers changes the time metric, but the device is still a laser device, therefore it's still Laserphaco, in my humble opinion. There were others before me and certainly there will be many others after me, but I am very grateful to be included among the pioneers of laser cataract surgery (1,2).

Standing up for STEM

I've achieved so much in my career, and it's important to me that I pass on the torch and help to inspire others to get involved in science, technology, engineering and medicine (STEM) – whatever their backgrounds or circumstances. I realize some of the slights, oversights and omissions I have experienced in my career are the result of systemic societal, gender and racial bias, and are not aimed at me personally. And realizing that you are not alone is empowering. A common denominator for discrimination against women and minorities has been the denial of voting rights. Accordingly, I have begun a campaign I call Suffragettes for Science. I want to champion the cause for all women in science like Rosalind Franklin, Ada Lovelace, Chien-Shiung Wu, and Lise Meitner, who did not receive their deserved level of recognition, respect and rank during their lifetimes.

Being poor shouldn't hold you back either – when I talk to disadvantaged school kids about poverty, I tell them that the label of "poor" is a tactical assault of naming and shaming. I tell children to "shake it off" à la Taylor Swift and believe in themselves. Repeat after me: I am a winner!

I hope that through my past legacy and future advocacy, that the current and future generations of young scientists will not experience the hurtful wounds of discrimination of any kind.

Vision for all

My other lifelong passion is, of course, the prevention and cure of blindness, especially for underserved populations. On a personal level, each time I have restored or improved someone's vision through surgery, it's a very special moment. As an inventor and surgeon, I'm happy to look back on my contributions to the field, as I feel I have played a part in the continuing advancement of the specialty I love. Finally, I have always worked to increase the availability of eye care for those who can't afford or access treatment, using community outreach programs and telemedicine. I have also been involved in efforts to educate visually impaired people on the technologies and programs available to assist them – such as working with an organization that provides computers configured with assistive technology to blind children in Kenya and Tanzania. I've always worked to further my belief that sight is a basic right, and the ability to access treatment shouldn't depend on where, or who, you are.

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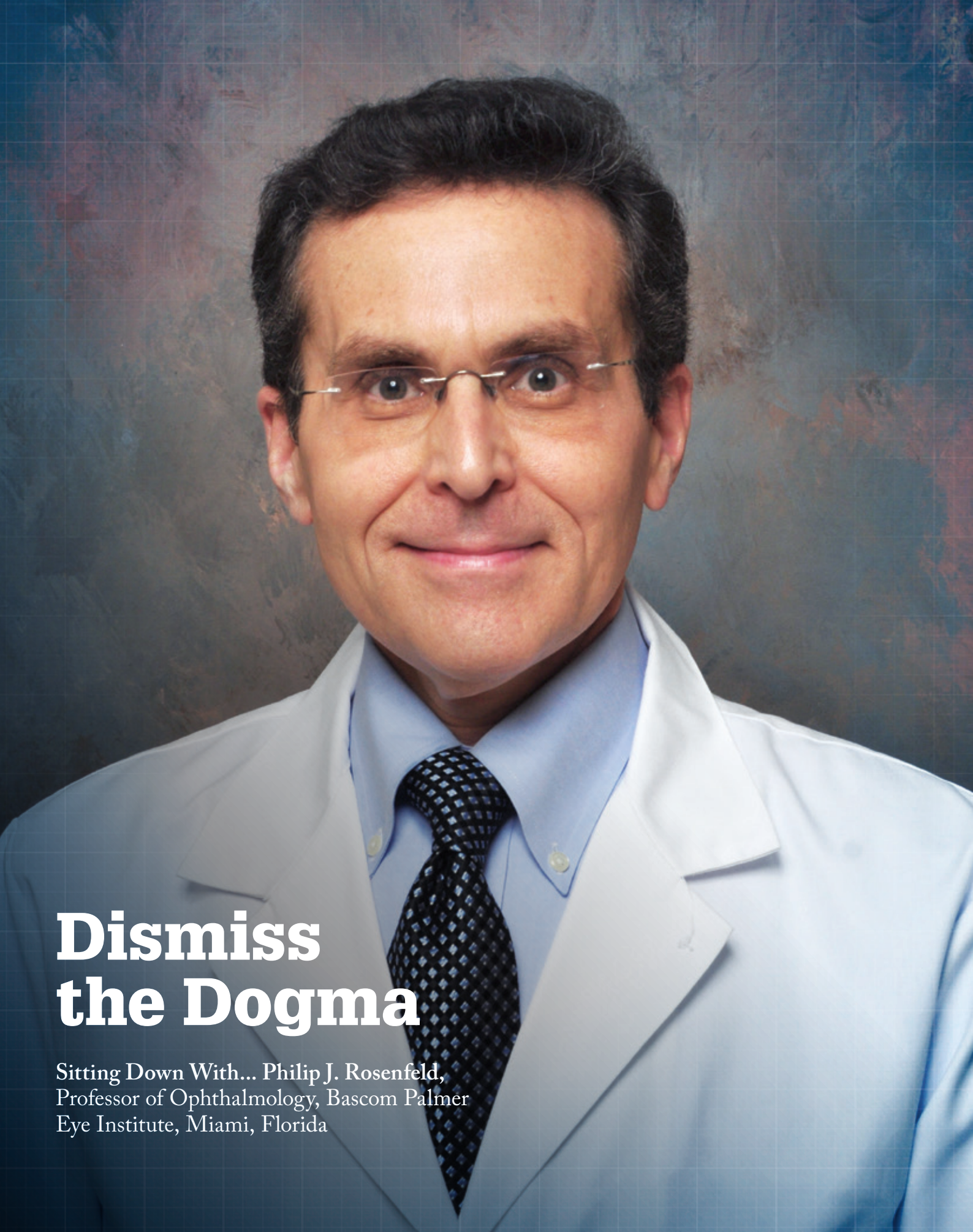

Dismiss the Dogma

Sitting Down With... Philip J. Rosenfeld, Professor of Ophthalmology, Bascom Palmer Eye Institute, Miami, Florida

What drew you to age-related macular degeneration (AMD)?

It was my background interest in molecular biology and genetics. At Johns Hopkins, I got both my MD and PhD degrees at the same time – my research focused on genetics and I had a particular interest in the evolution of disease in the back of the eye, and specifically, retinal degenerations. I started with a post-doctoral research fellowship at the Massachusetts Eye and Ear Infirmary (MEEI) working with Ted Dryja – who was the first to clone the retinoblastoma gene – and Eliot Berson. I fully intended to pursue a career in retinal degeneration and other vitreoretinal diseases, but I was drawn to AMD, as Johanna Seddon clued me in that it was a genetic disease. I became fascinated with both her clinic and her studies that looked at twins with AMD, and this started me on the path of AMD; the genetic and the clinical aspects, and the realization that there was a huge unmet need for treatments.

What do you find the most rewarding aspect of working on clinical trials?

To this day, what I enjoy doing the most is designing clinical trials with appropriate endpoints and necessary controls, so that at the end of the trial we will get a definitive answer. I like asking questions that no-one else is asking, and I had always seen myself running a laboratory and being involved with both medical and surgical retinal diseases. Starting at the Bascom Palmer Institute, I quickly learned there was nothing better than running your laboratory in the clinic – it is an excellent way to blend my research and clinical interests and compliments both aspects of my career.

Any challenges throughout your career?

With every study that I have participated in, or designed, I have come away with a better appreciation of what needs to get done. In the photodynamic therapy trials in the 1990s, I learned a tremendous amount, and that set the groundwork for my ability to design clinical trials with anti-VEGF therapy. At the time, coming up with a treatment for wet AMD seemed like a herculean effort. Now, focusing on dry AMD makes focusing on wet AMD "low-hanging fruit." We have a huge unmet need in dry AMD, but I think that everything is positioning so that hopefully in the next few years we are going to be able to demonstrate unequivocally that there is a treatment that can slow down disease progression. It is a big area. If we can stop dry AMD at an earlier stage, then all the downstream vision loss that occurs from both advanced late dry macular degeneration and wet AMD can be avoided.

What is exciting you at the moment?

Right now, I am currently working with collaborators to develop the next generation of OCT, swept source OCT, and we really hope to move the field forwards with this cutting edge technology. As for treatments, I still believe in the "holy grail" of genetics research, that is, if you identify the genetic locus involved in the disease and manipulate the gene product from that locus, then you should alter disease progression and improve outcomes. But when we talk about complex genetic diseases, like AMD, the question is how we can manipulate pathways to improve patient outcomes? AMD clearly looks like a complement-mediated disease, and I feel that complement inhibition, or some form of complement regulation, is going to be very, very important in controlling macular degeneration at some stage.

You were the first to inject off-label Avastin into someone's eye. How did you feel?

It was nerve-wracking! That is why I had to choose the right patient, where there was really no other option as all the approved therapies had failed. She was a nurse, she understood the risks – she was going blind. So we gave it a shot, and to this day I see her, and she is just so grateful because we were able to preserve her vision.

What anti-VEGF dosing strategy do you prefer – treat and extend, or as needed (PRN)?

I consider myself to be the father of PRN dosing, and that all came about from the PrONTO study, which was designed when we began to appreciate the power of OCT as a technology for following disease progression and the need for re-treatment. But I have evolved. What I have learned over the years is that patients don't really mind injections, and they much prefer a treatment regimen where they can avoid coming in as frequently. So most of the time I use the treat and extend strategy, but I do still use PRN in some patients who really don't want the injection.

If you could go back to the beginning of your career, what would you tell yourself?

The best advice I would give myself is to focus on the unmet needs of your patients and be willing to pivot with your research objectives and follow where the data points. And this pivoting strategy pertains to one of my favorite sayings of "sacred cows make the best hamburger" – always question what someone thinks as dogma, and never be satisfied unless the answers make sense. After all, everyone knew antibodies against VEGF wouldn't be effective if injected into the eye. Not!

An extended version of this interview is available online at: top.txp.to/issues/0816/701/

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INDICATIONS FOR USE The TECNIS Symfony Extended Range of Vision IOL, Model ZXR00, is indicated for primary implantation for the visual correction of aphakia, in adult patients with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model ZXR00 IOL is intended for capsular bag placement only.The TECNIS Symfony Toric Extended Range of Vision IOLs, Models ZXT150, ZXT225, ZXT300, and ZXT375, are indicated for primary implantation for the visual correction of aphakia and for reduction of residual refractive astigmatism in adult patients with greater than or equal to 1 diopter of preoperative corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model Series ZXT IOLs are intended for capsular bag placement only. **WARNINGS** Patients with any of the conditions described in the Directions for Use may not be suitable candidates for an intraocular lens because the lens may exacerbate an existing condition, may interfere with diagnosis or treatment of a condition, or may pose an unreasonable risk to the patient's eyesight. Lenses should not be placed in the ciliary sulcus. May cause a reduction in contrast sensitivity under certain conditions, compared to an aspheric monofocal IOL; fully inform the patient of this risk before implanting the lens. Special consideration should be made in patients with macular disease, amblyopia, corneal irregularities, or other ocular disease. Inform patients to exercise special caution when driving at night or in poor visibility conditions. Some visual effects may be expected due to the lens design, including: a perception of halos, glare, or starbursts around lights under nighttime conditions. These will be bothersome or very bothersome in some people, particularly in low-illumination conditions, and on rare occasions, may be significant enough that the patient may request removal of the IOL. Rotation of the Tecnis Symfony Toric IOLs away from their intended axis can reduce their astigmatic correction, and misalignment >30° may increase postoperative refractive cylinder. If necessary, lens repositioning should occur as early as possible prior to lens encapsulation. **PRECAUTIONS** Interpret results with caution when refracting using autorefractors or wavefront aberrometers that utilize infrared light, or when performing a duochrome test. Confirmation of refraction with maximum plus manifest refraction technique is recommended. The ability to perform some eye treatments (e.g. retinal photocoagulation) may be affected by the optical design. Target emmetropia for optimum visual performance. Care should be taken to achieve IOL centration, as lens decentration may result in a patient experiencing visual disturbances under certain lighting conditions. For the Tecnis Symfony Toric IOL, variability in any preoperative surgical parameters (e.g. keratometric cylinder, incision location, surgeon's estimated surgically induced astigmatism and biometry) can influence patient outcomes. Carefully remove all viscoelastic and do not over-inflate the capsular bag at the end of the case to prevent lens rotation. **SERIOUS ADVERSE EVENTS** The most frequently reported serious adverse events that occurred during the clinical trial of the Tecnis Symfony lens were cystoid macular edema (2 eyes, 0.7%) and surgical reintervention (treatment injections for cystoid macular edema and endophthalmitis, 2 eyes, 0.7%). No lens-related adverse events occurred during the trial. **ATTENTION** Reference the Directions for Use for a complete listing of Indications and Important Safety Information.

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