DECEMBER 2016 # 04

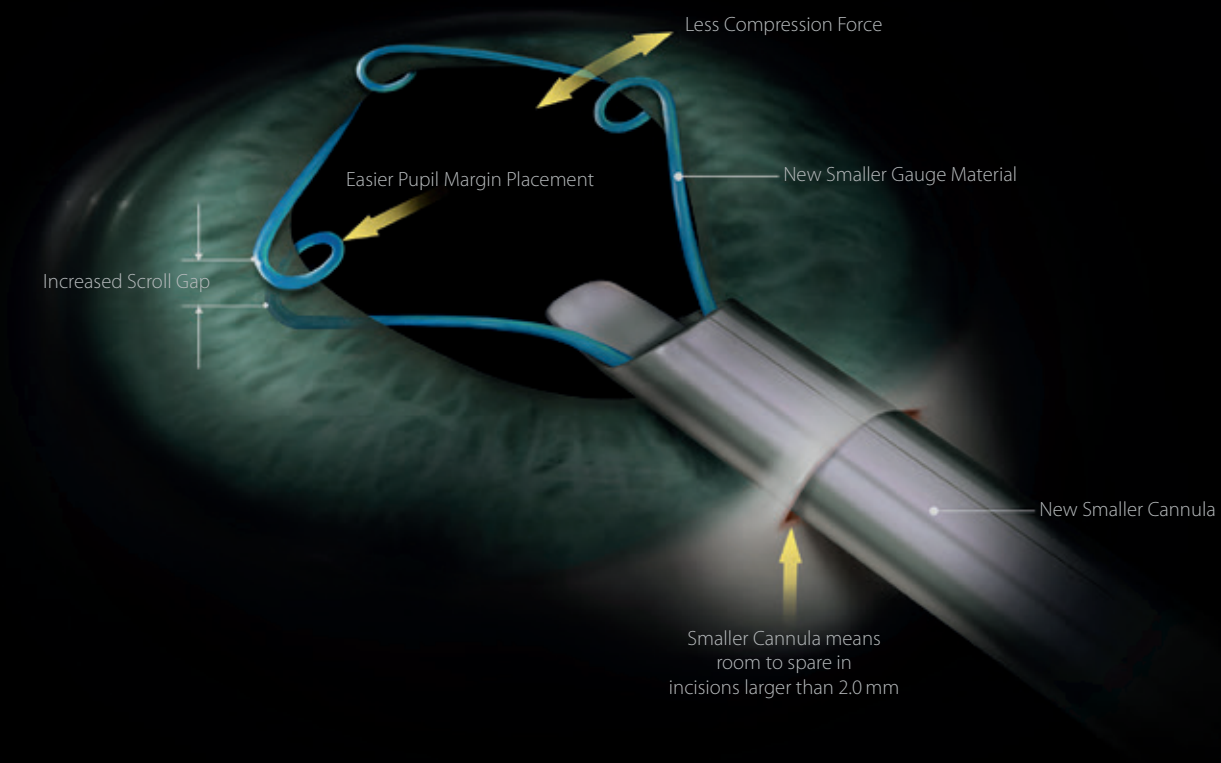
the Ophthalmologist

The Innovators

A showcase of the brightest technology of 2016

Introducing Malyugin Ring 2.0

Nothing's Changed... Except For Everything



When contemplating what the next version of the Malyugin Ring should provide surgeons and their patients, we established three goals:

1. Provide the same or better safety as surgeons have experienced and has made the Malyugin Ring "classic" the standard of care for pupil management.

2. Make it easier to place and remove from the pupil margin.

3. Allow for entry in 2.0mm incisions and more room in wounds larger than that.

After several years of work, we are proud to introduce the Malyugin Ring 2.0. The second generation of the Malyugin Ring that also can be used in 2.0mm incisions.

Malyugin Ring 2.0 requires no surgical technique changes for you, and we believe that you will find it easier to use, that you will appreciate the extra room it affords, and be glad to know that it has softer compression characteristics (in fact Malyugin Ring 2.0 exerts less than half as much pressure on the iris than the "classic" Malyugin Ring).

Malyugin Ring 2.0

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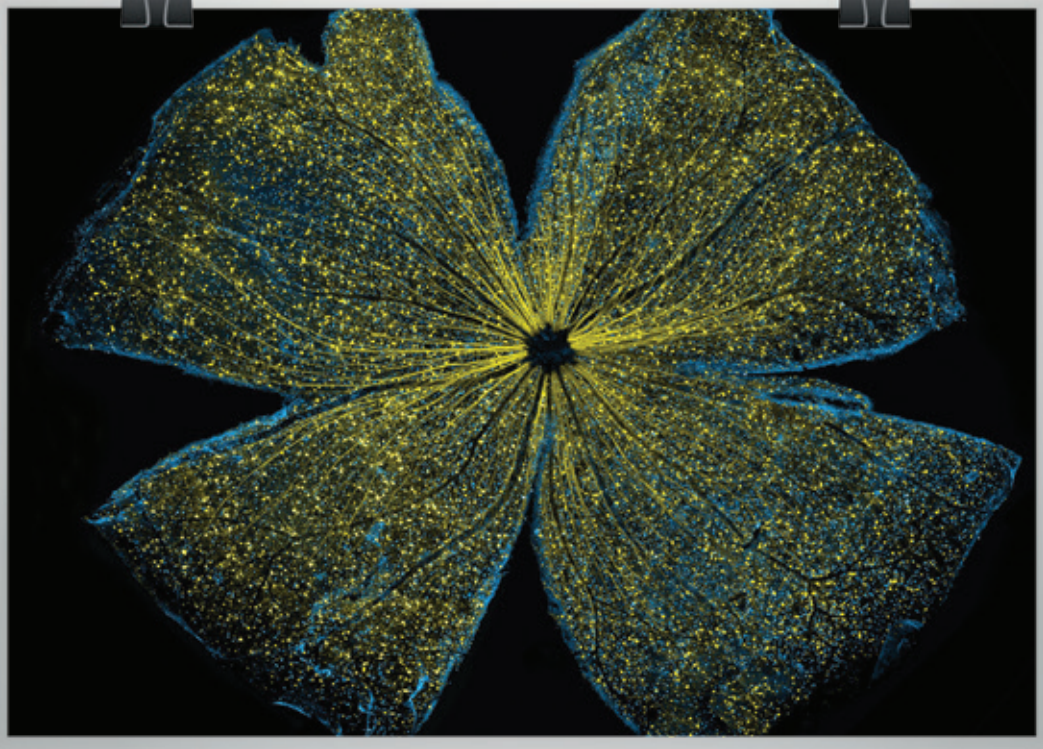

Tie a Yellow Ribbon

This month, we have a large-scale mosaic confocal microscope image of a histological section of the retina of a seven month-old mouse. The image was taken two months after the administration of an *AAV2-GFP* vector; the yellow-green color shows the regions where the GFP gene was integrated and expressed. The image took first prize in the National Institutes of Health's 2016 Combined Federal Campaign "Beauty of Science."

Image courtesy of Keunyoung (Christine) Kim, Wonkyu Ju and Mark Ellisman, the National Center for Microscopy and Imaging Research, University of California, San Diego.

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

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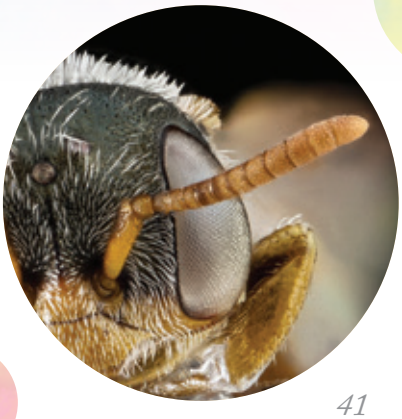

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The Mercy of The Markets

If you're not a billionaire philanthropist like Bill Gates, how are you ever going to raise the money you need to make a difference?

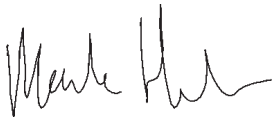
Let me set the scene. It's October 13, 2016. I'm in the Hyatt Regency Chicago's underground ballroom attending OIS@AAO. I'm coming down with the 'flu, the jetlag's kicking in, the fourth coffee of the morning is wearing off and I'm doing my best to live-tweet and follow everything that's being presented on stage. Up walks SightLife's CEO, Monty Montoya. Here's the top executive of a non-profit health organization that I had a vague recollection of being one of the world's big corneal tissue banks. But he was using phrases like "innovating at the speed of need" and seemed to be talking about Bill Link, Flying L Partners, Series A financing, and expanding the corneal innovation space. To my bug-befuddled brain, it seemed incongruous. I wrote a note to myself to follow up with Monty at some point during the AAO congress and find out what exactly he was talking about.

Fast forward a few days later. I managed to meet Monty at SightLife's booth. When he told me what SightLife was up to: I got it. It opened my eyes to how philanthropy has to operate in the 21st century to even have a chance of achieving anything big. SightLife had taken a chunk of its non-profit business and moved it into a for-profit company: SightLife Surgical (SLS). SightLife (the non-profit arm) became a majority equity holder in SLS. SLS went off to the capital market to find investors willing to give capital to accelerate its growth. Eventually SLS will undergo an IPO, and SightLife will (hopefully) be significantly better off – Monty's goal is to make a minimum of $200 million from the whole enterprise.

I wondered: how were they going to achieve that kind of exit? By placing their bets on the roulette wheel of eyecare innovation investment – with an added twist. They have a goal of eliminating corneal blindness by 2040. By their own calculations, at the current cornea therapy innovation rate, it'll take more than 14 years to achieve that – more like another 250. But they will direct all of their investment at promoting corneal research and innovation, with the hope that will be the catalyst that drives the entire field forwards at a far faster rate. Sure, there's risk (some of which will be borne by the market), but they have great advisors (like Dick Lindstrom and Bill Link) on which bets to make. If there's a gambling analogy to be made here, they've stacked the cards in their favor as best they can.

The more I think about it, the more I think it's a genius approach. The world is highly marketized. SLS is playing the game. How can it not?

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

Sugar Rush

Could altering glucose metabolism offer an alternative target for treating retinitis pigmentosa?

Retinitis pigmentosa (RP) comes in many forms. It can be inherited in autosomal dominant, autosomal recessive, X-linked and even maternally (mitochondrial) forms. When it's combined with deafness, it's called Usher syndrome; when the mitochondria are involved, it's Kearns-Sayre syndrome; hypogonadism and developmental delay, it's Bardet-Biedl syndrome. The list goes on, but the point is today, 64 genes have been identified that can cause RP when mutated. This poses a bit of a challenge when trying to take a genetic approach to treating it. But what if you could treat RP at a point downstream of these receptors, bypassing the entire problem?

Photoreceptors are among the most metabolically active cells in the body – they convert between 80–96 percent of glucose into lactic acid via aerobic glycolysis. Under normal conditions, the outer segments of photoreceptors are continuously regenerated in a process that requires NADPH from the pentose phosphate pathway (PPP) to generate phospholipids. Rods shuttle glucose into the PPP to synthesize new membranes and generate new outer segments. Now remember that in darkness, rods are continuously depolarized and have a phenomenal consumption of glucose – and one of the first manifestations of RP in people with the disease is dysgenesis of rod outer segments. All of this suggests that the cell death seen in RP (Figure 1) is a consequence of metabolic dysfunction.

It was this that made a team of researchers from the US and China hypothesize that they might be able to rescue the degenerative phenotype by inhibiting a transcription factor gene called *Sirt6*, which acts as a repressor of glycolytic flux. To find out,

Credit: The Jonas Children's Vision Care, Columbia University Medical Center

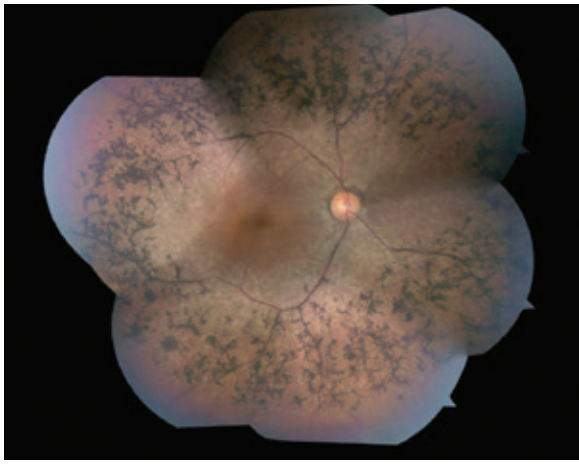


Figure 1. Image of retina from right eye of a patient with retinitis pigmentosa due to phosphodiesterase deficiency. Intraretinal pigments (pink) are seen in areas of photoreceptor loss.

they used a murine mouse model of severe RP: *Pde6*$^{-/-}$ mutant mice, which exhibit near complete photoreceptor loss by two months. Genetically disrupting *Sirt6* resulted in rod cells remaining in a permanent state of glycolysis – and improved rod and cone health, with photoreceptors surviving in these mice far longer than in untreated control mice (although eventually, photoreceptor death still occurred).

"Our study shows that precision metabolic reprogramming can improve the survival and function of affected rods and cones in at least one type of RP. Since many, if not most, forms of the disorder have the same metabolic error, precision reprogramming could conceivably be applied to a wide range of RP patients," says Tsang. "Our next challenge is to figure out how to extend the therapeutic effect of *Sirt6* inhibition," he adds. *RM*

Reference

1. *L Zhang et al., "Reprogramming metabolism by targeting sirtuin 6 attenuates retinal degeneration", J Clin Invest, [Epub ahead of print] (2016). PMID: 27841758.*

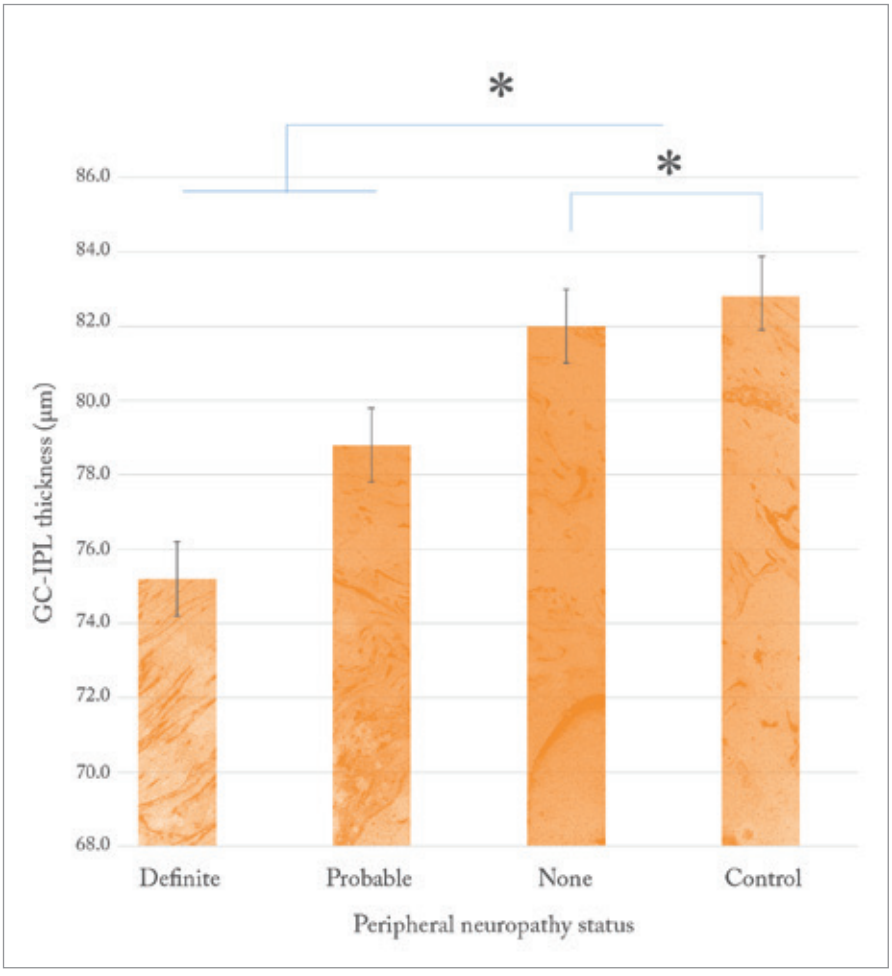
Through Thick and Thin

A thinner retina could predict neurodegeneration in diabetes – and vice versa

Diabetes is a familiar disease to ophthalmologists – they make the first diagnosis in almost half of all cases. And on top of being the leading cause of new blindness in people aged 20 to 74 years in the USA, it's a risk factor for a whole host of other problems, including cardiovascular disease, renal failure, neoplasms and neuropathies. And when it comes to diagnosing diabetic neurodegeneration, ophthalmic examination could once again come in useful: recent research indicates that an OCT examination could predict early signs of neuropathy.

With that in mind, South Korean researchers used OCT to study the connection between retinal thickness, peripheral nerve conduction, and autonomic nerve function in diabetic patients, as retinal neurodegeneration and diabetic peripheral neuropathy are suspected to be initiated by similar hyperglycemia-activated pathways. The group studied consisted of 160 people aged 55 to 75 years, who had a diagnosis of type II diabetes but who did not have diabetic retinopathy or mild proliferative diabetic retinopathy, and 60 age-matched controls. Exclusion criteria included over 10 years' duration of diabetes and a diagnosis of any peripheral neurologic disease except diabetes-related neuropathy. Parafoveal retinal thickness and ganglion cell-inner plexiform layer (GC-IPL) thickness were measured, and peripheral nerve involvement was assessed.

When the study participants were divided into three groups (no neuropathy, probable neuropathy and definite neuropathy), the authors found that parafoveal retinal thickness did not appear to be related to neuropathy. But GC-IPL thickness was significantly lower in the group with neuropathy (75.2 ± 4.2 µm, p=0.002) compared with the probable (78.8 ± 5.0 µm) and no neuropathy (82.0 ± 5.8 µm) groups (Figure 1) – and both peripheral nerve conduction and autonomic nerve function were found to correlate to GC-IPL thickness using regression modeling.



Differences in GC-IPL thickness between control, no neuropathy vs. probable peripheral neuropathy (P=0.009, P=0.011), probable vs. definite peripheral neuropathy (P =0.010), control, no neuropathy vs. definite peripheral neuropathy (both P<.001). Adapted from (1).

Diagnosis of diabetic neuropathy can be a challenge, as symptoms can be widely varied – but further study of the link between neurodegeneration of the retina and nerve degeneration could yield more insights. The authors note, "This study should prompt ophthalmic evaluation in patients with clinical or subclinical peripheral neuropathy or autonomic dysfunction. Also, a thinner retinal nerve fiber layer noted by the ophthalmologist should prompt more detailed questioning of peripheral nerve symptoms." *RM*

Reference

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Edema Enigma

Have reports of NSAIDs preventing post-cataract macular edema been exaggerated?

Macular edema (ME) following cataract surgery isn't fun for anyone. Although it's usually self-limiting, it's particularly bad news for patients' vision if it persists. That's why most surgeons like to take a prophylactic approach to ME and use topical steroids and/or topical non-steroidal anti-inflammatory drugs (NSAIDs) before and after surgery. But a recently-published Cochrane Eyes and Vision systematic review might change that perception.

Their review incorporated results from 34 randomized controlled trials that involved over 5,000 patients who received surgery for age-related cataract that reported ME incidence. Of those, 28 studies compared NSAIDs and steroids versus steroids alone, and the remaining six compared NSAIDs directly with steroids. They found (Figure 1):

- At three months post-op, the risk of poor vision secondary to ME was lower in patients who received NSAIDs and steroids, than steroids alone – but this was classed as "low certainty evidence."
- Also classed as "low certainty" was evidence of a reduced risk of NSAIDs and ME at three months post-op.
- Almost no evidence was found that NSAIDs improve outcomes for patients, with only one study reporting on quality of life – and even then, stated only that there was a "lack of differences between groups."
- Inconsistent data regarding central retinal thickness at three months post-surgery (I^2 = 87%), and little difference in reported BCVA outcomes (inter-group differences were less than 0.1 LogMAR in 31 out of 34 studies).
- The most notable adverse effects associated with NSAIDs were burning or stinging; there was no evidence of serious adverse effects.

So what's the take home message? Blanche Lim, lead author on the paper explains: "Topical NSAIDs may be beneficial as prophylaxis against ME, however there remains a lack of compelling evidence to suggest any visual benefit in the long run. There is also a paucity of data to determine effectivity in certain at-risk subgroups." The authors note that future trials are needed to clear up the uncertainty. In the meantime, Lim comments "The inclusion of NSAIDs as a standard regimen perioperatively still remains surgeon-dependent." *RS*

Reference

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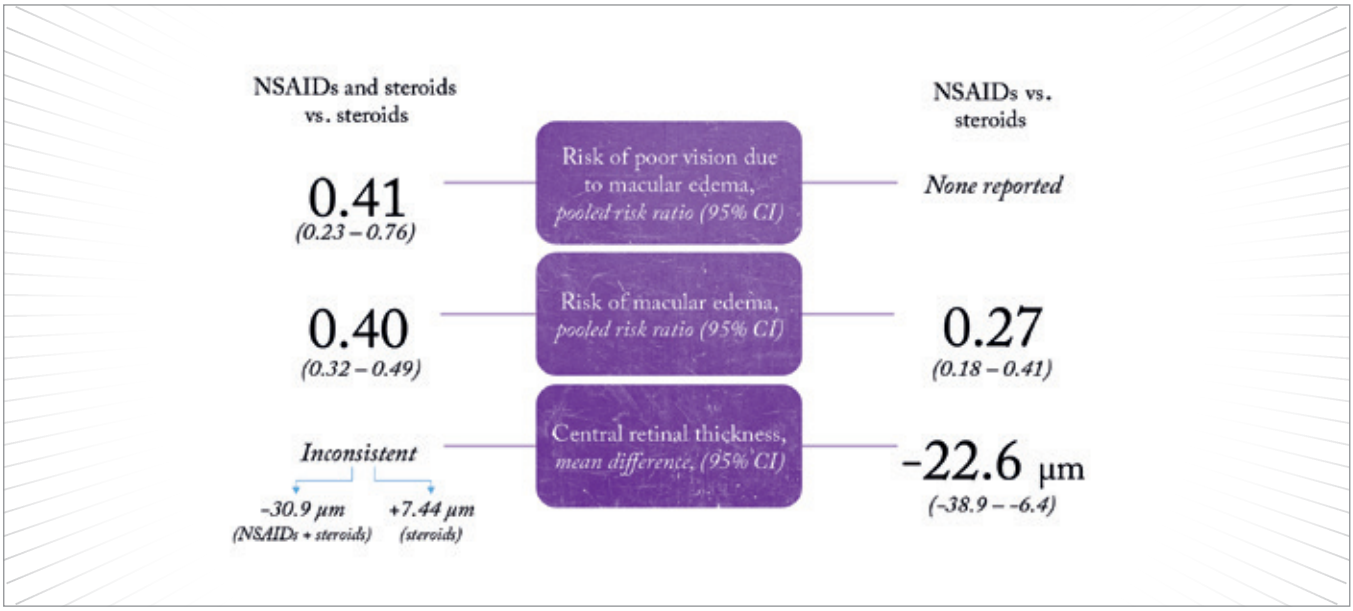


Figure 1. Summary of key results three months post-surgery (1). CI, confidence interval.

Amblyopia: Game On!

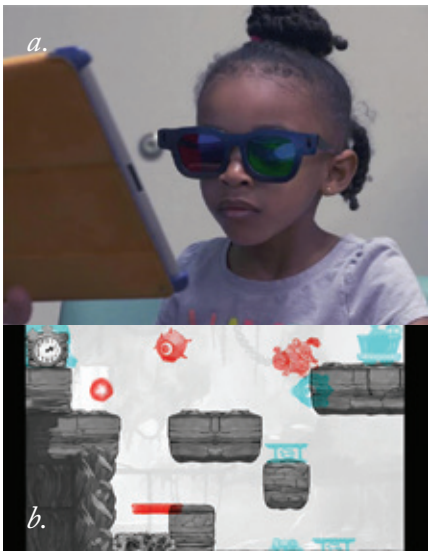
Should children with amblyopia play instead of patch?

Patching might be the mainstay of treating amblyopia, but it isn't perfect. The dominant eye is unused; both eyes aren't taught to work together, and there's no guarantee of a decent outcome at the end of the process – up to half of all patched children never achieve normal visual acuity (VA) at the end of even lengthy courses of treatment, and normal binocularity is rarely achieved. This need for a better approach to amblyopia treatment has spurred on a number of research teams to try and do something a little bit smarter.

But there are alternatives to patching – binocular approaches to treating anisometropic and strabismic amblyopia have shown promise. The basic principle is this: high-contrast images are presented to the amblyopic eye; low-contrast images are presented to the fellow eye. Together, the images form a binocular percept. But keeping young, amblyopic children engaged with these eye training tasks isn't easy – which is why many researchers, including those at the Retina Foundation of the Southwest, Dallas, Texas, have turned to computer games to hold their attention during this dichoptic "contrast-rebalancing" training (1). Their game, "Dig Rush," sees players direct miners to dig for gold, while navigating obstacles and avoiding threats like fire and monsters. Red-green anaglyphic glasses are worn to enable each eye to see different contrast elements of the game (Figure 1).

But does it work as well as patching? The team performed a randomized, controlled trial to find out. Twenty-eight children with amblyopia aged 4–10 years were randomized in a 1:1 ratio to either gameplay or patching. After two weeks, mean BCVA improved by 1.5 lines in those who played the game – more than double the improvement seen in the patching group (0.07 lines, p=0.02). Children who were patched could switch to the game after two weeks, and by week four, their visual gains matched those achieved by the children originally randomized to the gameplay group. "Here, both groups improved by 1.7 lines in just four weeks, and incredibly, 39 percent recovered normal vision for their age," notes Krista Kelly, lead author on the paper (1). "This may be attributed to the excellent compliance with this engaging game – children responded very well and genuinely enjoyed trying to beat all of the levels."

There's still more work to be done. Kelly explains "it's extremely important to determine how contrast changes should occur, how long treatment should last, and how children will respond long-term." As well as investigating how to achieve maximal VA improvements, the group hopes more people will develop games aimed at treating amblyopia. "Most children finished our game's 42 levels within the 4-week study treatment period – providing a variety of games could help with long-term treatment. We also need to explore options such as animations for younger children who cannot play the games." *RS*



Credit: Retina Foundation of the Southwest.

Figure 1. a. A child playing the Dig Rush iPad game; b. A screenshot of gameplay. Each eye sees different elements: the amblyopic eye sees high-contrast red elements, the fellow eye sees low-contrast blue elements and both eyes see grey background elements. For successful play, both eyes must see their respective components. Contrast of the blue elements increased with successful game play, making the amblyopic eye work harder in tandem with the fellow eye.

Reference

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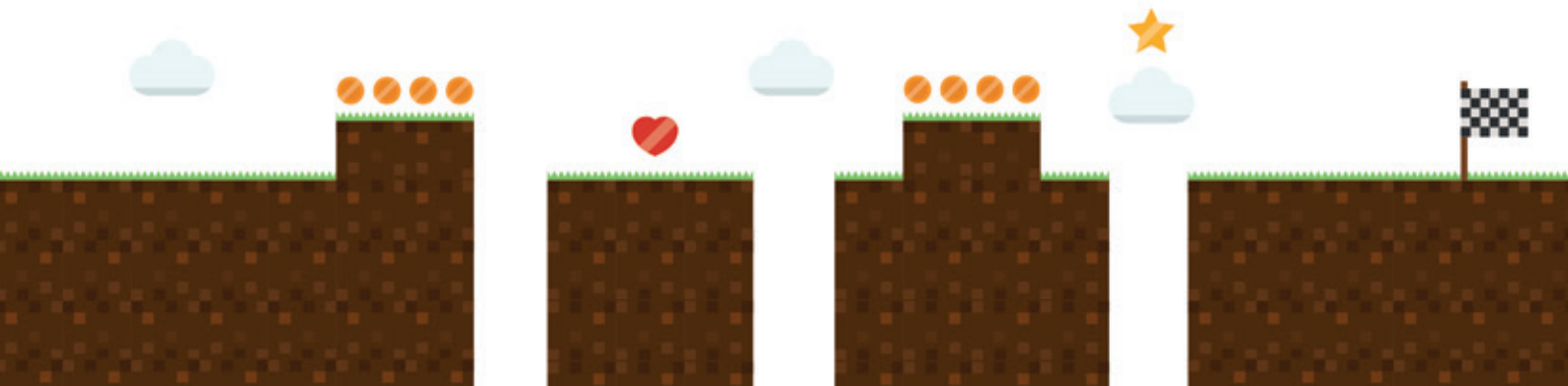


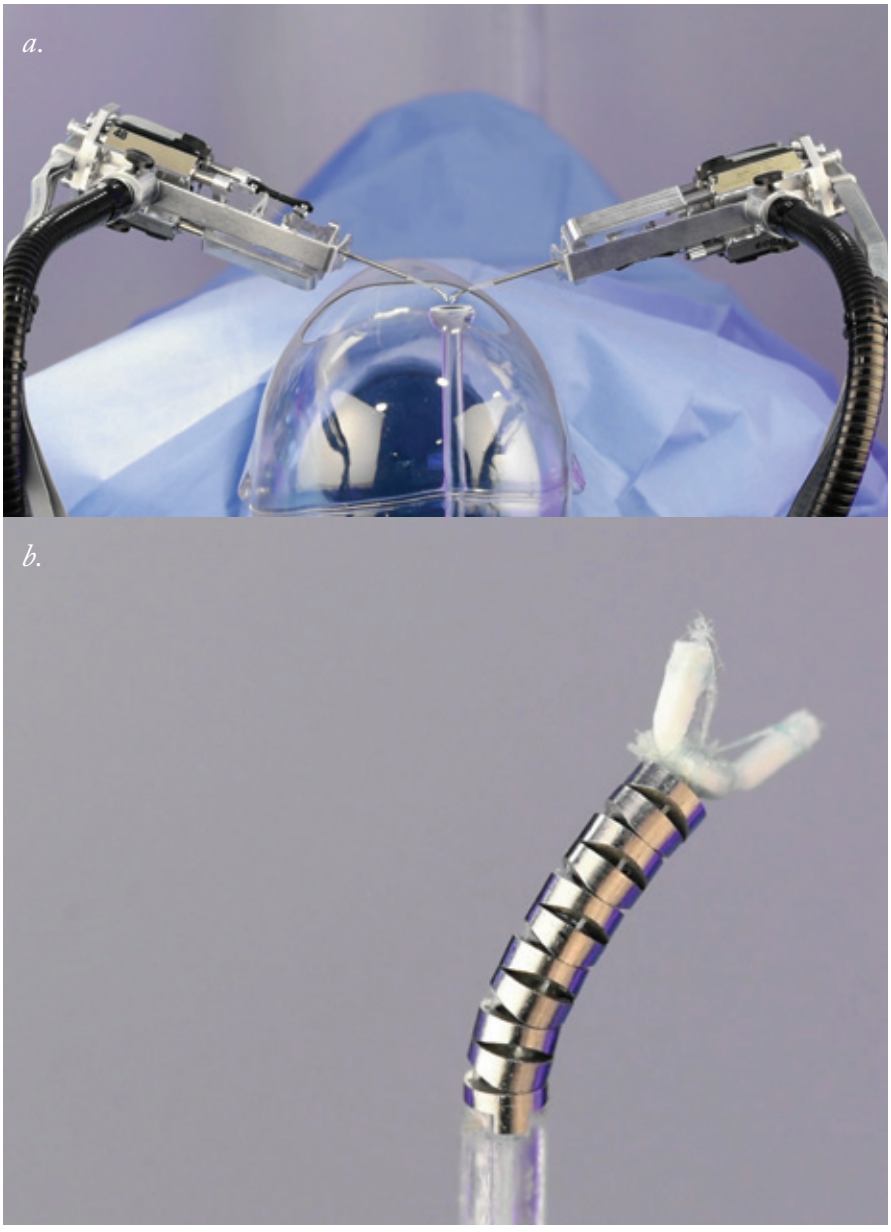
Micro Machines

The future of robotic surgery is getting smaller...

Much like the Borg in Star Trek, resisting the advance of robots into the operating theater is futile. Their superiority is patent. When operated by a surgeon, they have a number of practical advantages: surgeons no longer need to operate at a surgical microscope – or even in the same room as the patient, dramatically improving ergonomics for them. The robots can filter tremor from the surgeon's hands – adding years to their effective lifespan as a surgeon. They hold the promise of automating parts of procedures, too – like suturing – saving time and speeding workflow, and they can do things no human can do, like hold a needle in place without movement for extended periods (as required with subretinal stem cell delivery), or scale movement to achieve more precision than a human hand ever could. In fact, we recently reported on the first use of a robotic assistant in man, when Robert MacLaren used Preceyes' R2D2 robot assistant during retinal surgery to help perform an internal limiting membrane peel (1).

Now there's another robot on the scene: Cambridge Consultants' Axsis robot (Figure 1), built to assist surgeons in performing cataract surgery. Chris Wagner, roboticist at Cambridge Consultants in the UK hopes Axsis will demonstrate what's possible in the next generation of surgical robotics.

Here's what he had to say…



Credit: Cambridge Consultants.

Figure 1. The Axsis robot is operated remotely by the surgeon. The robot's flexible articulating devices (a) are capable of working within the restricted environment inherent with cataract surgery, and the robot's software is programmed to prevent it from puncturing the back of the lens. Panel (b) shows a close-up of the 1.8 mm articulating tool.

What inspired you to develop the Axsis robot for cataract surgery?

Surgical robots are designed to overcome the complications of surgery through features such as motion scaling, tremor reduction, minimally invasive access and critical structure avoidance through image guidance. We noticed that cataract surgery could benefit from all of these. However, building a robot that can work on the size scale of the lens (<10 mm) is difficult. We took on the technical challenge by asking: "Is there anything stopping us from building a robot on this size scale?" So far, the answer is no. We've been able to construct articulating end effectors that are the same size as current cataract surgical tools (1.8 mm) – much smaller than current surgical robot tools.

And does it work?
We've been able to show our high performance articulating tool moves at speeds mimicking that of a surgeon's hands, and we're showing this can be achieved with a small robot, which is critical for easily integrating the technology into the operating room environment.

What have been the challenges so far?
The biggest was finding the correct combination of materials, manufacturing processes, and assembly techniques to let us build mechanisms at this small size scale – for example, finding an actuation cable approximately the same diameter as a human hair, then threading that cable through holes 150 µm wide in has been difficult. We've relied on precision micromachining – along with a healthy dose of steady hands – to assemble this system.

What impact do you think your robot can have?
We're trying to show the potential for reducing the size of these systems, and our goal is to expand the range of procedures that should be considered candidates for robotic technology. In the case of cataract surgery, although we're not intending our current system in itself to be a medical device, we're showing there's nothing in the physics or mechanism design that limits the introduction of a surgical robot into this procedure. So, one day, we might be able to deliver the precision benefits that laser cataract surgery promises, but without the additional workflow steps.

Reference

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The Galactic Eye

In a galaxy, far, far away... an eye-like astronomical structure has formed

Situated far above sea level in the Atacama Desert in Chile, the Atacama Large Millimeter Array (ALMA) telescope is used to study the heavens. Using it, astronomers have discovered two spiral galaxies that have crashed together (IC 2163 and NGC 2207), producing a "tsunami" of stars and gas (1). The result closely resembles a gigantic eye (see Figure 1).

"Although galaxy collisions of this type are not uncommon, only a few galaxies with eye-like structures are known to exist," explains the study's lead author, Michele Kaufman. "Galactic eyelids last only a few tens of millions of years, which is incredibly brief in the lifespan of a galaxy. Finding one in such a newly formed state gives us an exceptional opportunity to study what happens when one galaxy grazes another," she adds.

The eyelids are roughly one kiloparsec (3262 light-years) wide, and can be found 114 million light-years away from earth, in the direction of the constellation Canis Major. *RM*

Reference

1. *M Kaufman et al., "Ocular shock front in the colliding galaxy IC 2163", Astrophys J, 831, 161 (2016).*

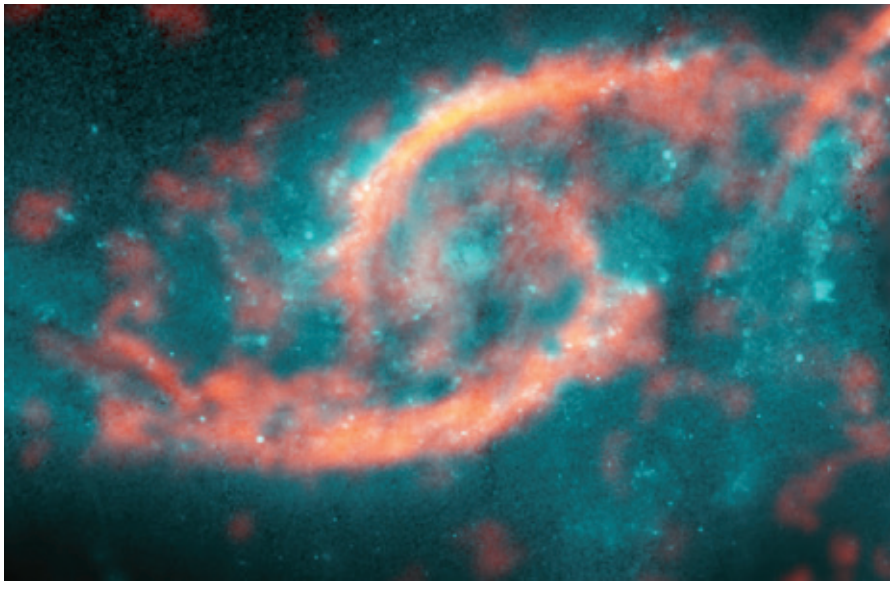

Figure 1. The "eye-like" structure, created when galaxies IC 2163 and NGC 2207 collided.

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

Coming of Age

Why SMILE is my procedure of choice for low-to-moderate myopia

By Dan Reinstein, Medical Director of the London Vision Clinic, London, UK

When it comes to choosing between LASIK and small incision lenticule extraction (SMILE), I think of this as being similar to choosing between a Ferrari and an Aston Martin. LASIK is a great procedure: it is mature, highly developed and highly sophisticated – over 51 million have been performed worldwide, and outcomes today are great. Indeed, my clinic still performs LASIK, but today, we mostly perform SMILE for myopic patients. Let me explain why.

I think that SMILE has come of age – when you look at the SMILE literature, it is clear that SMILE is as effective as LASIK for the correction of low-to-moderate myopia, and has comparable safety outcomes. Some might say that SMILE is not suitable for low myopia because the lenticule is too thin, which people say can make it difficult to handle and there may be a distortion of the second cut caused by an interaction between the two bubble layers. But this can be easily avoided simply by increasing the lenticule thickness by using a larger optical zone (≥7 mm), and using a minimum lenticule thickness of 20–25 µm instead of the normal 10 µm. We've published our results using this approach (1), and 96 percent of our low myopia (-1 to 3.5 D) patients saw 20/20 afterwards – an efficacy that's equivalent to LASIK.

Clearly, the "flapless" nature of SMILE brings a number of advantages. The keyhole aspect appeals to patients because they don't have to wait for a flap to adhere, there are almost no post-operative restrictions and they can resume their normal activities almost straight away. Furthermore, the procedure damages fewer corneal nerves. Although SMILE cuts some nerves at the lenticular interface, there's clear evidence demonstrating that the nerve plexus is for the most part preserved with SMILE, and severed by LASIK, and that corneal sensitivity recovers faster with SMILE (3–6 months versus 6–12 months for LASIK) (2). SMILE also has potential biomechanical advantages because the stronger anterior stroma is left uncut. This means we can use larger optical zones without affecting corneal strength, and as biomechanics are more predictable with SMILE, we induce less spherical aberration than we do with LASIK (3).

But despite these advantages, there are still many myths out there about SMILE, such as: centration is not accurate, it can't treat cylinder, you can't perform custom or wavefront-guided ablation, or that retreatment options are limited and difficult. These are either irrelevant to the technique or simply untrue. Just like the early days of LASIK, there were some issues when SMILE was first introduced, but in my view most of these issues have gone – they're now obsolete. With SMILE, you can center on the visual axis, cylinder is perfectly correctable, custom ablation isn't actually necessary, and you can retreat after SMILE. Indeed, a LASIK enhancement after SMILE is actually better than LASIK after LASIK because the risk of epithelial ingrowth is massively reduced. We've also seen the first SMILE re-treatment (4) – only the lenticule cut was performed and the same cap was used for the enhancement, and the outcome was excellent.

I am not saying there's anything wrong

with LASIK, I've even had PRESBYOND Laser Blended Vision (5) myself – if SMILE were to magically disappear off the face of the earth I'd still be very happy to perform LASIK. But SMILE is my technique of choice, and in my view, it is set to become the "go-to" procedure for low to moderate myopia below -6 D, as well as high myopia in place of phakic IOL.

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Jumping Through Hoops

Increasing regulatory oversight is impacting patient care, and it's a burden we don't need

By Brock Bakewell, Co-Director of Fishkind, Bakewell & Maltzman Eye Care and Surgery Center, Tucson, Arizona, USA, and Chairman of the ASCRS Government Relations Committee

Years ago, physicians had a lot of autonomy. Mostly, we worried about taking care of patients: what were the best treatments and best ways to manage patients' care. But now that the government has thrust so much regulation on us, physicians are forced to be somewhat sidetracked, entering information into electronic medical records (EMRs) – because that is how we get paid. The way that EMRs are designed is not very intuitive, and the whole process of reporting is very cumbersome and laborious – there is just so much more meaningless work than before, and this has led to high levels of frustration among physicians.

All this "quality reporting" started with the 2009 passage of the HITECH act – which first brought us EMRs – and we've just had more and more regulations ever since. We recently got rid of the Sustainable Growth Rate (SGR) formula, and it was replaced with the Medicare Access and CHIP Reauthorization act of 2015 (MACRA). But none of the quality reporting has gone away: the physician quality reporting system (PQRS), meaningful use, and the value-based payment modifier – have all been morphed into the MACRA legislation. And physicians will be subject to possible penalties; in 2019, we could be subject to a 4 percent cut if we don't report things appropriately in 2017, and by 2022, we could face cuts of up to 9 percent. There is a chance for bonus money if one's performance is better than that of peers, but the winners have to be offset by losers since Medicare Part B is a zero-sum game.

So why all this reporting? The government wants to collect data from our practices. They're trying to improve outcomes, and believe that they can achieve this by making physicians report on all sorts of metrics that hopefully will reflect quality. The government wants everything perfectly delineated, but one can't do this with every disease process – one can't quantitate and qualitate every aspect of a patient's health. We are being micromanaged by the government which is using us as data collectors, and physicians are extremely frustrated. Many physicians (who can afford it) are retiring early because of this excessive regulatory environment that is time consuming to comply with and actually takes away from actual patient care and the enjoyment and satisfaction of practicing medicine.

As physicians, we are trying to take care of patients, but now when we go to medical conferences we have to consider taking course offerings on how to avoid penalties, how to protect our practices and so on, rather than concentrating on learning new treatment modalities to help our patients. The government thinks they are going to force us into taking "better" care of patients by making us jump through all these quality hoops, but what is really happening is that we're spending so much time on quality reporting and EMR that we're finding it harder and harder to spend quality time with our patients. There are of course certain doctors who choose to take the penalties, because they have big practices that are able to cope with the cuts. Eventually all physicians who care for Medicare patients are going to have to comply with regulations – or face significant financial penalty. Opting out of Medicare is a possibility, but for most ophthalmologists, including myself, opting out really isn't a viable option. As 65 percent of my patient base is Medicare, my practice would be greatly affected by patient defection to other Medicare physicians if I opted out, and it's likely that I wouldn't do much surgery after that.

Organized Medicine actively communicates these concerns to Congress; physicians have fly-ins in Washington D.C. to talk to the senators, congressmen and their assistants, educating them that the regulatory burdens are significant. But this really only addresses one aspect of the system – the writing of the laws. The laws that Congress creates are interpreted by the

regulatory agencies in the executive branch, and Congress does not really review or oversee these regulations to make sure that they actually reflect the intent of the law. Because of this, Senator Rand Paul of Kentucky has introduced the REINS (Regulations from the Executive branch In Need of Scrutiny) act, and if that could pass, then Congress would have to oversee more of the regulations coming out of the CMS and the FDA. In my opinion this would be a good idea as there would be checks and balances by Congress on the rules created by the regulatory agencies allowing for mitigation of onerous legislation. Right now, there is not enough support for the act, and we will have to see what the mix is now the election has past.

I still love what I do – I love ophthalmic surgery and I love what I do for my patients. But, the government is so pervasive in its attempted control of everything that I and other physicians do, we are feeling smothered. It is a shame that the noble medical profession, consisting of the most highly trained professionals, is being micro-managed by bureaucrats under the guise of quality. We need to reduce this over-regulation for the health of our profession and patients, but until something big happens – like doctors dropping out of Medicare en masse – the government has no real reason to acquiesce to us.

The Laser Liability

My mission: to stop vision loss from handheld lasers

By Fahd Quhill, Consultant Ophthalmologist at Royal Hallamshire Hospital, Sheffield, UK

I am on a mission to stop people losing vision from handheld laser devices.

Why? A few years ago, a patient of mine – a young child – was left with the vision of a 60-year-old because of a handheld laser pointer. At the time, I couldn't believe that a "toy" could cause that much damage, but when the offending device was tested, we found that its power output was actually 40–50 times greater than the recommended level.

This isn't a freak accident. We surveyed 153 ophthalmologists and found that 54 had seen at least one patient with a macular injury secondary to a laser device (1), and shockingly, the vast majority of these were children under the age of 10. Worse, seven of the reported cases involved lasers with an output level exceeding 50 mW – well above the FDA-recommended output of 5 mW. It's easy to understand why. High-power handheld laser pointers are freely available (particularly online), and it transpires that many are mislabeled – they are far more powerful than they state on the label. Clearly, this is a problem that needs to be tackled, so part of my mission is to increase public awareness, improve the safety of available devices and ideally get dangerous and mislabeled pointers banned.

It is a fact of life that some children and adults lose vision to disease. But to lose vision to a device that shouldn't even be available in the first place is unnecessary, and it's a tragedy that children may suffer permanent visual damage because of a momentary lapse in judgement. Indeed, I don't know what the long-term consequences are – I am still observing some of my cases on a longitudinal basis to get a better idea of what is going to happen in the future.

To prevent these types of injuries from occurring, I have a call to action. We need to improve the regulation on these devices worldwide, so that they meet defined safety standards and are labelled appropriately. We have to give out greater penalties for traders who knowingly sell mislabeled devices. Granted, imposing a blanket ban on handheld lasers is not going to solve all of the problems, but action like classifying high-power lasers as offensive weapons would send a strong message about how dangerous these devices can be. Public awareness (particularly in schools) needs to be better, but at the moment funding and support aren't forthcoming as it is viewed as a small problem.

I am continuing my fight here in the UK, and I invite you all to join me. If you are seeing these cases, please raise awareness. Inform your local law enforcement about illegal or mislabeled devices, get local politicians involved, and try to collect as much information as you can. As the physicians who will see the injuries that result from laser pointer misuse, it is incumbent upon us to make sure that we don't remain silent, that we collect cases and data, and make those in power aware of the problem and what needs to be done. We are here to treat, but we also have a responsibility to protect public ocular health.

Reference

1. *F Quhill et al., "Macular Injury due to handheld laser devices: results of a survey among consultant ophthalmologists in the UK". Poster presented at the American Academy of Ophthalmology, Chicago, October 17, 2016. Poster #PO423.*

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THE INNOVATORS 2016

Ophthalmology is one of the most intense incubators of innovation in all of medicine. Competition is driving not just incremental improvements, but some big, game-changing leaps too. Here, some of ophthalmology's lead innovators present their latest creations and pioneering ideas; from IOLs and vitreous cutters, to imagers and the next generation of gene therapies.

PROVIDING INSIGHT INTO CORNEAL BIOMECHANICS

Tonometry and Scheimpflug imaging combined in a single device to deliver more...

Knowing and understanding your patients' corneal biomechanics can be invaluable. It helps with assessing ectasia risk, diagnosing keratoconus, measuring the effects of corneal collagen cross-linking (CXL), and even glaucoma prediction and management. The OCULUS Corvis ST combines a tonometer with an ultra-high-speed Scheimpflug camera, to not only measure IOP, but also provide a detailed assessment of corneal biomechanics. How does it work? By applying an air pulse and simultaneously monitoring the cornea's response, and capturing 140 images of the horizontal sectional plane of the cornea, within just 31 ms.

"This information has helped transform our understanding of the eye's anterior segment. One example is biomechanical-corrected IOP. We know that corneal thickness, age and the biomechanical response of the cornea can affect IOP readings taken by applanation tonometry, and that these factors need to be corrected for," says Sven Reisdorf, Corvis ST product manager. The Corvis ST measures both biomechanical response and corneal thickness with high precision and corrects for both, giving ophthalmologists more accurate IOP readings, and with it, better guidance for making treatment decisions.

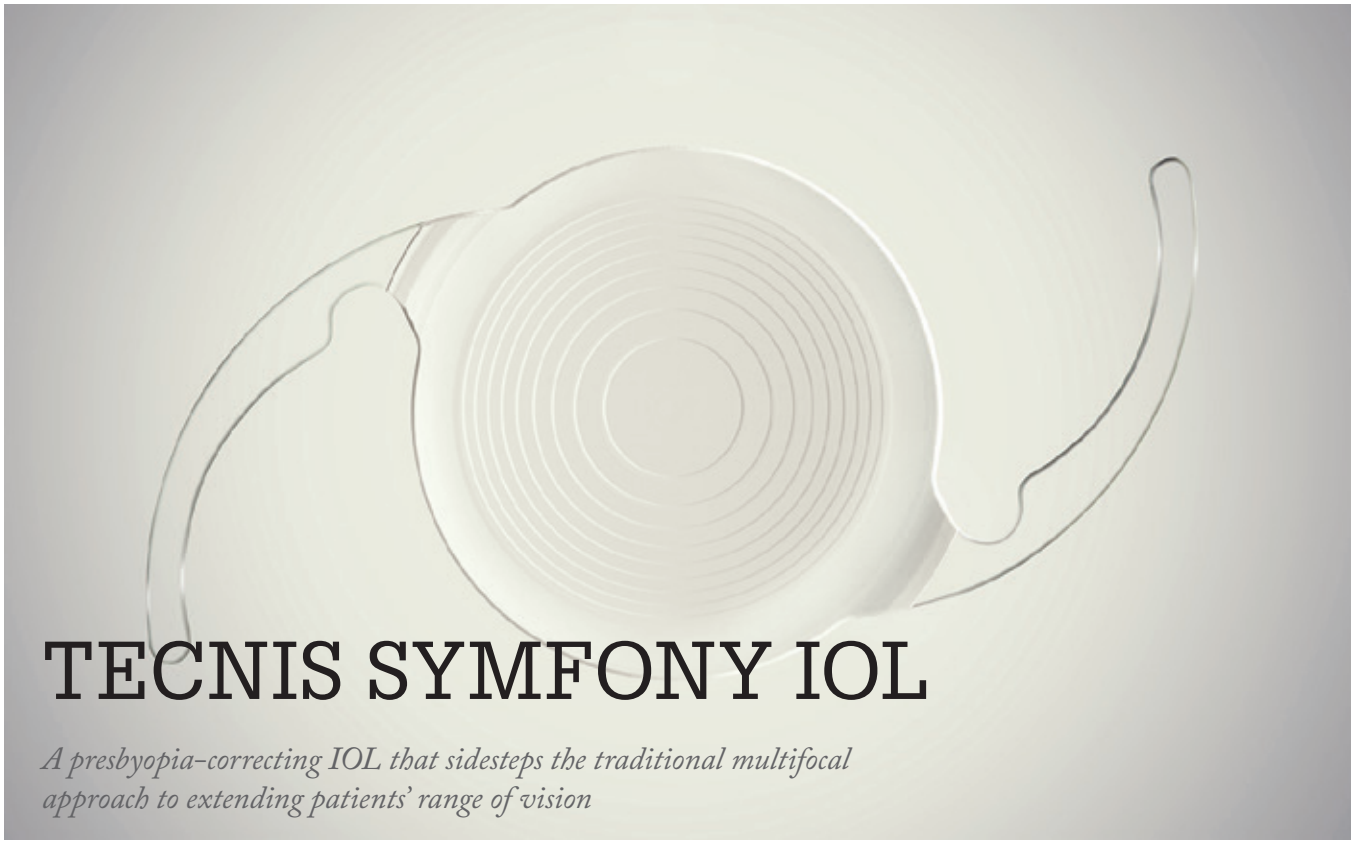
"The Corvis ST is also helping to improve the detection of corneal ectasia – the Vinciguerra Screening Report software combines biomechanical information with pachymetric progression data to generate the Corvis Biomechanical Index (CBI) – and presents these results in comparison with normative values in easy-to-read graphs, making for swift and easy keratoconus detection", adds Reisdorf.

Finally, you can combine topographic and tomographic data from the Pentacam with biomechanical data from the Corvis ST to produce the Tomographic Biomechanical Index (TBI) – an artificial intelligence approach that helps improve the detection of patients with a significant risk for developing ectasia after refractive surgery.

The hardware was developed by OCULUS head of R&D, Andreas Steinmüller, and by engineer Matthias Krug. The analysis software was produced in collaboration with leading researchers, including Renato Ambrósio Jr., Ahmed Elsheikh, Paolo Vinciguerra and Cynthia Roberts.

"Currently, the most important application for the technology is in determining ectasia risk after refractive surgery – we can identify corneas predisposed to the condition by combining the biomechanical information with tomographic data measured by the OCULUS Pentacam, which gives us a truly unique analysis," explains Reisdorf.

Availability of the product and features may vary by country. Currently not for sale in the US.



TECNIS SYMFONY IOL

A presbyopia-correcting IOL that sidesteps the traditional multifocal approach to extending patients' range of vision

Everyone wants to offer an IOL that leaves patients spectacle-free after cataract surgery – and that involves making multifocal IOLs. However, multifocality is an optical compromise, and risks glare, halo and loss of distance contrast sensitivity. The name of the game is building a better multifocal lens, with the objective of offering the best-possible range of vision with the fewest visual disturbances.

In 2009, Abbott's R&D team started work on an IOL design that took a completely different approach to other multifocal IOLs. The objective was to offer patients a full range of high-quality vision (enabling less frequent spectacle use), a low incidence of halos and glare, and distance contrast vision comparable to that of monofocal lenses. Eschewing the traditional multifocal IOL approach of splitting light between near and distance focal points, their IOL employs a proprietary echelette design, which creates a novel pattern of light diffraction that elongates the focus of the eye and extends the range of vision. This is combined with achromatic technology to correct chromatic aberration and enhance both image contrast and quality of vision.

What resulted was the Tecnis Symfony and Tecnis Symfony Toric IOLs; the first extended depth of focus (EDOF) presbyopia-correcting lenses for use in patients with and without astigmatism.

The lenses have now been evaluated in multiple studies in over 2,000 eyes across the world, including a US clinical trial. Results show continuous high quality vision at all distances, a low incidence of halo and glare, and a minimization of chromatic aberration. Tecnis was able to deliver 20/20 vision even in the presence of up to 1.5 D of astigmatism, and in one questionnaire, 85 percent of respondents reported being completely or almost completely spectacle-free. Furthermore, as Symfony's EDOF vision is independent of pupil diameter, this allows for good performance under all light conditions.

"These lenses provide a new option for patients that may result in better vision across a broad range of distances. Patient satisfaction has been high, with over 94 percent of patients saying they would recommend them to their friends and family," says Leonard Borrmann, head of R&D at Abbott. "By building on our successes so far, we plan to continue to create innovative IOLs," he adds.

ZEPTO CATARACT SURGERY

Ideal capsulotomies – quick, automated, and inexpensive

The creation of a consistently sized, round and well-centered capsulotomy opening in the lens capsule is perhaps the most challenging step of cataract surgery. Manual capsulotomies using forceps can be tricky, and depend strongly on the surgeon's skill level. Creating your capsulotomy with a femtosecond laser is another option – if you can afford the expensive equipment, and don't mind the extra time or potential complications. What if there was another alternative that offered a convenient automated option without the hefty price tag?

Christopher Keller and David Sretavan were both new to medical device development when they began work on a miniature automated capsulotomy device. Christopher had a background in microelectromechanical systems, and created gizmos such as micro-knives to perform surgery on individual nerve cells grown in petri dishes. David became a customer, and it wasn't long before the pair decided to enter the world of medical device development.

With no money for fancy lasers, they were instead inspired by the elegance of squid suction cups that create a complete force circuit – and leveraged this concept into their own solution to the capsulotomy conundrum: Zepto.

The disposable Zepto device consists of a suction cup that holds the capsule and lens steady while pulling them against the tiny nitinol capsulotomy ring. A four millisecond electrical pulse train runs through the nitinol ring to neatly create the capsulotomy without damaging neighboring tissues. This combination of suction and an optimized pulse train to instantaneously create all 360 degrees of the capsulotomy is unique to Zepto.

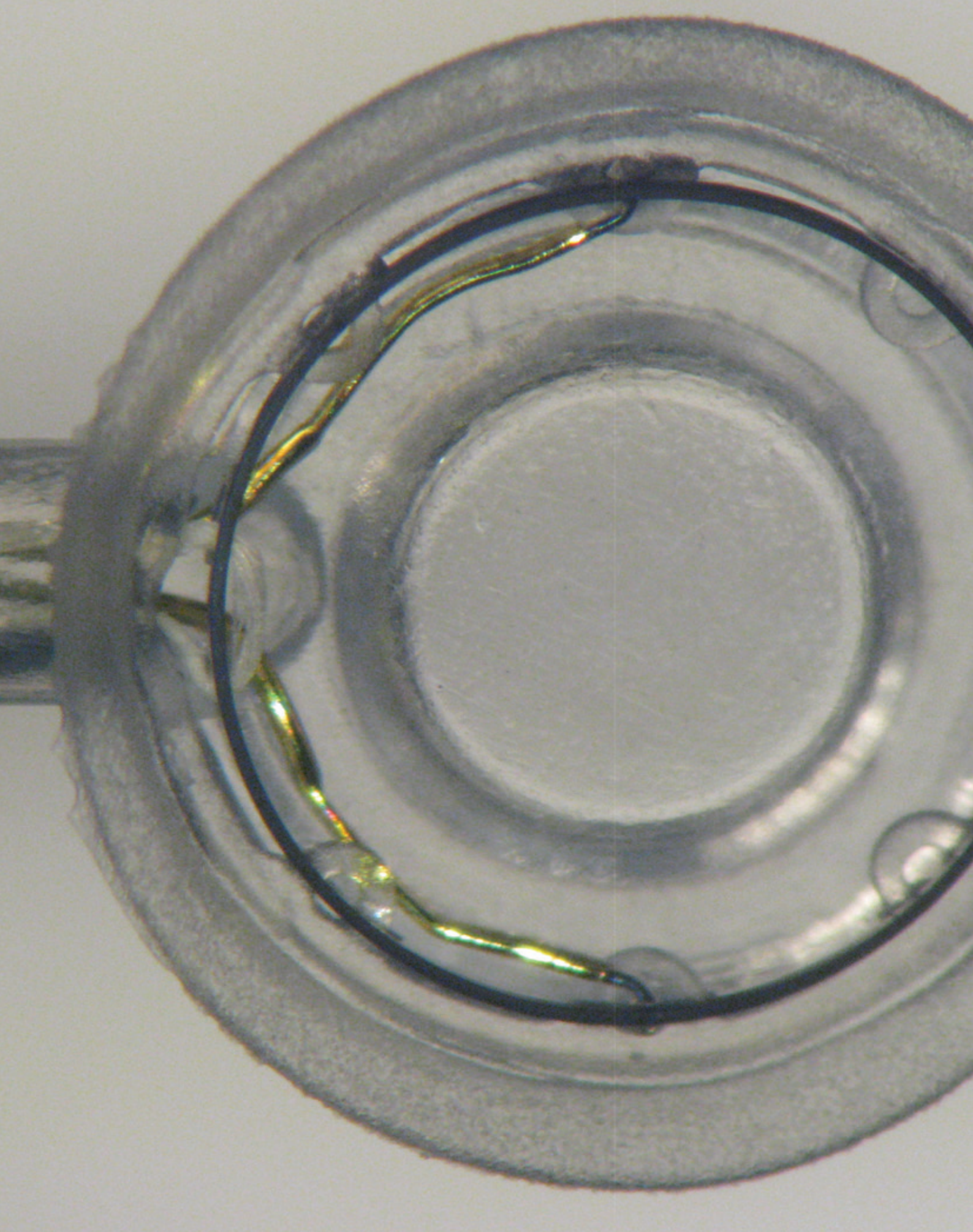
Initial clinical studies were promising. One study involving over 60 patients in El Salvador, where access to cataract surgery is limited, demonstrated Zepto's effectiveness even in challenging cases such as poorly dilated pupils, hard cataracts and zonular pathology. Even without some of the instruments and devices normally used in such cases, all Zepto capsulotomies were successful and delivered good outcomes for the patients. "Zepto can quickly and consistently produce a round capsulotomy with an edge exhibiting excellent tear strength," says John Hendrick, CEO of Mynosys Cellular Devices, "we believe that no matter what kind of cataract you're looking at, or how tricky the case, Zepto can make the procedure safer and easier for the surgeon."

The Zepto silicone suction cup offers another big advantage – it essentially disappears once inside the eye, allowing the surgeon to use patient fixation and Purkinje images for intraoperative centration of the Zepto capsulotomy precisely on the patient's visual axis. This is especially useful for surgeons using premium IOLs. Furthermore, a well-constructed, strong capsulotomy edge that is perfectly centered on the visual axis will be critical for next generation IOLs that are fixed to the capsulotomy edge. The ability for surgeons at all skill levels to automatically and consistently produce round and strong capsulotomies will benefit all patients. This, combined with personalized visual axis centration makes Zepto unique and underlies Zepto-assisted cataract surgery (or ZACS).

The low cost of ZACS makes it an attractive alternative to the more expensive femtosecond laser, which is out of reach for millions of patients around the world. "Zepto puts a great capsulotomy in the hands of all surgeons – the consistent roundness and sizing ensures more effective lens positioning, to benefit visual outcome for patients," explains Hendrick.

As an easy to use and highly effective alternative to the femtosecond laser, Zepto has the potential to be a truly disruptive force in cataract surgery. It is easy to see how Zepto alters the cataract surgery landscape in developed markets, either as a stand-alone technology or integrated into a phaco machine. However, there is also enormous interest from the fast growing international markets where challenging cases are more frequent, and Zepto is beginning to experience tremendous growth in the premium segment. "With ZACs, surgeons can create perfect capsulotomies in both simple and complex cases, whether using monofocals or the latest premium lenses. As Zepto integrates seamlessly into cataract surgery, it doesn't interfere with the surgeon's normal routine, or their patient flow – instead of reaching for capsulorhexis forceps, they simply reach for Zepto," adds Hendrick.

The Zepto device is CE marked, but is not yet available in the US.



THE ALCON NGENUITY® 3D VISUALIZATION SYSTEM

A digitally assisted approach to vitreoretinal surgery

For retinal surgeons, visualization can be a major issue in the operating theater. Opacities and aberrations of the eye, shadows, glare from fiber optic illumination, poor access when navigating around the crystalline lens – there can be a whole host of visual barriers between the surgeon and the tissue they're working on. What does this mean in practice? Hours hunched over a microscope – an instrument that's never been known for having good ergonomics – which can add up to both muscle pain and fatigue.

Alcon, in collaboration with TrueVision 3D Surgical, believes it has designed a product to end those woes in the form of its NGENUITY® 3D Visualization System, a platform designed to digitally assist vitreoretinal surgery, and enhance visualization of the back of the eye with the aim of improving the surgeon's experience. It consists of a 3D stereoscopic high-definition digital video camera and workstation, and acts as an accompaniment to the surgical microscope, displaying real-time or images from recordings. The NGENUITY® 3D Visualization System allows retinal surgeons to operate looking at a high definition 3D screen, instead of bending their necks to look through the eye-piece of a microscope.

The high dynamic range camera provides high resolution, image depth, clarity and color contrast, and the 3D view allows depth perception not previously available on standard television models often used in the OR. Viewing options include increasing magnification but retaining a wide field of view, and using digital filters to customize the view during each procedure (1, 2).

The system can also be used to highlight ocular structures and tissue layers. Engineered with a specific focus on minimizing light exposure to the eye (2), it can be used under lower illumination, and remember, the NGENUITY® display means less time at the microscope – which could help improve posture. Broadcasting the surgery on a larger screen also means that the operating team can see exactly what the surgeon sees, in real-time. "The NGENUITY® 3D Visualization System takes vitreoretinal surgery to a more intuitive operating experience, offering greater depth and detail during surgery," said Mike Ball, CEO of Alcon. "Our goal is to provide surgeons with better visualization, facilitate teaching, and ultimately improve patient outcomes," he adds.

The NGENUITY® is available in the US and most EU countries, with further launches planned over the course of 2017.

References

1. *NGENUITY® 3D Visualization System Operator's Manual (8065830016), 20 July 2016.*
2. *C Eckardt, EB Paulo, "Heads-up surgery for vitreoretinal procedures: an experimental and clinical study", Retina, 36, 137–147 (2016). PMID: 26200516.*

THE A R I NETWORK WITH PLEX ELITE 9000 SWEPT-SOURCE OCT FROM ZEISS

Pushing the boundaries of discovery with OCT diagnostic innovation to advance patient care

One of the defining aspects of research is that it never stops. We might be in the 25th year of OCT, but the advances over that period have been relentless: Time-Domain OCT shifted to Spectral-Domain; we're now entering the era of Swept-Source (SS) OCT, and of course, you're now able to use SD OCT in daily practice as a simple and rapid way of performing OCT angiography too. Yet, as Philip Rosenfeld, Chairman of the Advanced Retina Imaging (A R I) Network explains, researchers at the forefront of retinal disease research always need "better, wider, deeper and faster imaging of the retina and the choroid." These needs are critical – after all, patients' vision is at stake. But they're demanding too. Providing researchers with the best diagnostic instruments requires pushing the boundaries of not just medicine, but also optics, electronics, physics, mathematics and computer science. ZEISS does this in the knowledge that it helps further researchers' discovery and understanding of diseases affecting the retina, and opens new frontiers of discovery in their quest for new clinical applications for different diseases.

ZEISS' approach to this is best described as "innovation through collaboration" and has undertaken a radical new initiative to supporting these top researchers: collaboration networks. Its first is the Advanced Retina Imaging (A R I) Network, a global consortium of the highest caliber of clinicians and scientists – those who are leading retinal research and other disciplines in ophthalmology, such as neurology and pediatrics. They, together with the engineers and scientists at ZEISS, are working to push the entire field of retinal imaging forward, and ultimately advance both clinical practice and patient care.

What drives the A R I Network is the PLEX Elite 9000 from ZEISS. It is a SS-OCT instrument with a tunable laser centered at 1050 nm, a scan speed of 100,000 A-scans/sec at a tissue depth of 3.0 mm, and an axial resolution of 6.3 µm, with a 56˚ field of view… for the moment. Let's revisit Philip Rosenfeld's words, this is: "better, wider, deeper and faster imaging of the retina and the choroid." This wide-field high-resolution visualization provided by the SS-OCT and OCT Angiography imaging modality of the PLEX Elite platform expands clinicians' ability to examine the critical microstructures and microvasculature of the posterior segment at any depth of interest, from vitreous to sclera.

ZEISS' approach with the PLEX Elite system is much like that of a "Formula 1 concept car." It's not just an SS-OCT; ZEISS views it as "an open platform for innovation" that will regularly receive the latest technology – the best that ZEISS' engineers and scientists can provide. Clinicians and researchers will make requests for new features or a different way of doing things – and ZEISS will respond by further developing its technology to meet those requests. The A R I Network members are then able to evaluate those advances and see if they truly make a difference in the clinic. Further, this rapid, iterative development, performed in collaboration with the A R I Network, will result in knowledge of what works, doesn't work, and guide the future development of all OCT instruments – not just the advanced research models – meaning more patients will ultimately benefit. Importantly, the recent US FDA clearance will help US members of the A R I Network to more easily enroll patients and may facilitate faster Institutional Review Board (IRB) review for protocol approval of research further accelerating the pace of research.

The A R I Network with the ZEISS PLEX Elite 9000 at its core supports researchers in the potential to discover and shape future clinical applications for ophthalmology and beyond to other disciplines in medicine – the potential is limitless. This new model of collaboration is the engine that will advance the standard of patient care in the future.

The availability of ZEISS PLEX Elite 9000 in particular markets is dictated by the ARI Network steering committee and available regulatory pathways.


ZEISS
PLEX Elite 9000

AVELLINO LABS

Pioneering personalized medicine

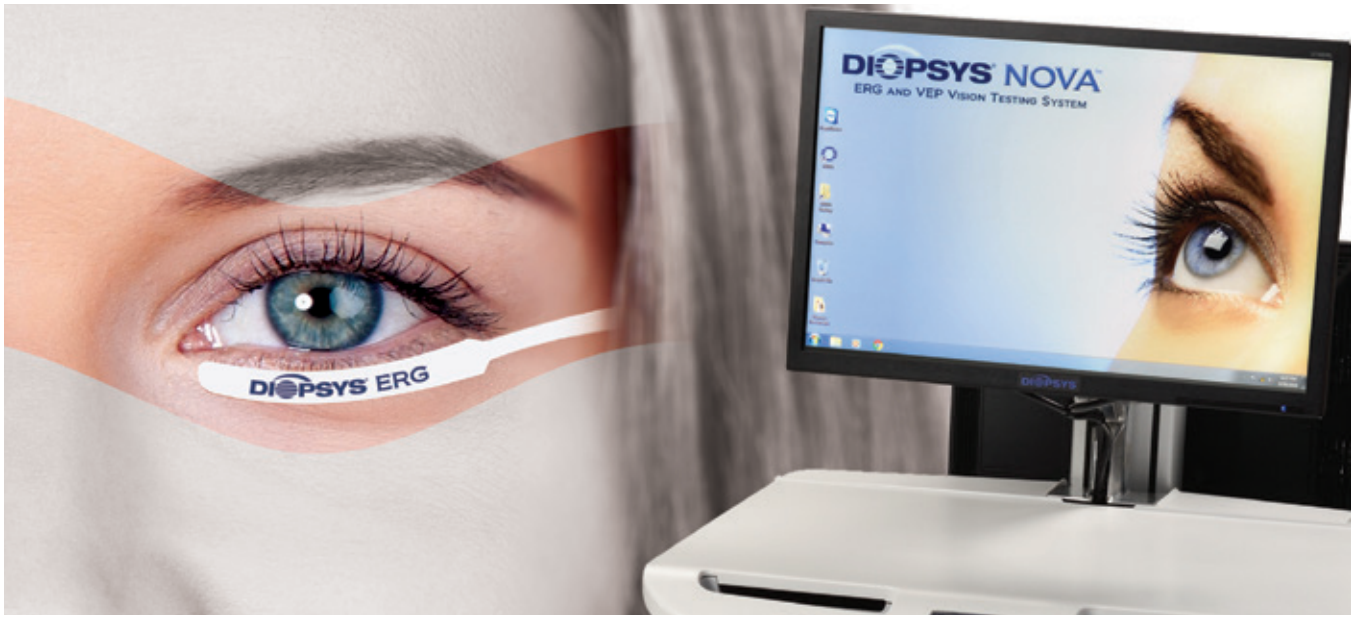
Medicine is becoming increasingly more personalized for the needs of each patient. As our understanding of genetics continues to grow, gene tests and therapies will become an ever-larger part of eyecare. And one company that's bringing the personalized medicine revolution to ophthalmology is Avellino Labs.

"Our Universal Test is the world's first DNA test used to check LASIK candidates for genetic mutations that are associated with poor outcomes," says Tara Moore, Avellino Labs Research & Development Director. Moore is also the Director of the Biomedical Research Institute at Ulster University in Northern Ireland, and there, she has amassed over twenty years of experience in progressing novel diagnoses and treatments for blinding eye diseases towards the market. "At Avellino Labs we have diagnosed over 700 cases worldwide of confirmed corneal dystrophy related to the *TGFBI* gene mutations. This contraindication for refractive surgery is easily detected using the non-invasive Avellino genetic test and I cannot emphasize strongly enough how important it is to eliminate any potential of such corneal dystrophies as part of the pre-screening process for refractive surgery," adds Moore.

Headquartered in California, with operations in Korea, Japan, China and the UK, Avellino Labs is currently expanding its repertoire to include a diagnostic test for keratoconus. In a recent study involving more than 200 keratoconus patients, Avellino Labs used state of the art next generation sequencing (NGS) to identify genetic risk factors in nine to 21 percent of patients tested in Korea. Based on these findings, the company intends to launch a test to screen for mutations in Korean, Japanese and Chinese populations in 2017.

To pursue its goal of developing gene therapies and delivering personalized medicine, the company has also entered into a collaborative research agreement with Ulster University. Moore explains: "We hope to develop new technologies, and create a therapeutic platform that's applicable to a wide range of inherited ophthalmic conditions. We're investigating CRISPR gene editing as a means of managing and potentially curing corneal dystrophies and other inherited eye diseases"

Named a 2015 Technology Pioneer by the World Economic Forum, based on its potential to impact global health, the company continues to expand its offerings in molecular diagnostics, including further NGS studies of inherited keratoconus.



THE DIOPSYS ERG VISION TEST

Can office-based electroretinography help diagnose disease earlier and track treatment efficacy? Yes

Electroretinography (ERG) provides an objective measurement of retinal function and is especially useful in detecting glaucoma. How? By identifying "stressed" retinal ganglion cells at a subclinical stage, when the cells have become dysfunctional, but are still alive. To put its value into context, a reduction in pattern ERG signal in glaucoma suspects has been shown to precede structural changes to the retinal nerve fiber layer by eight years – so this represents a huge window for intervention before permanent damage occurs.

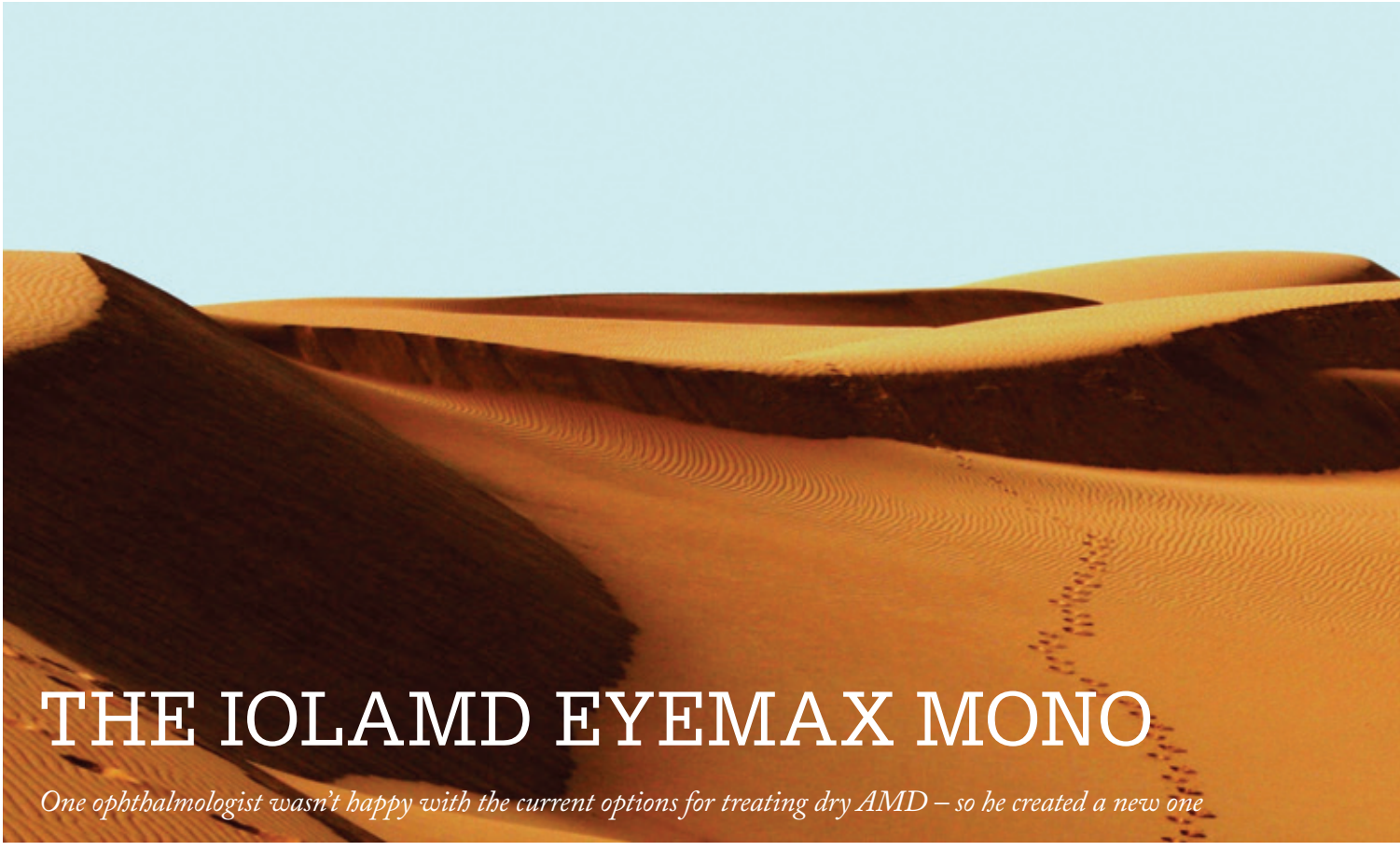
But can you efficiently use this technology? ERG instruments have historically been expensive and cumbersome, and the test difficult to perform and interpret. In response to these challenges, Diopsys created an accessible, in-office visual electrophysiology suite, including ERG, VEP, and ffERG vision tests.

To overcome the device and result interpretation issues, "We developed two different practice-friendly testing platforms, the Diopsys NOVA cart system, and the Diopsys ARGOS tabletop system. And through our extensive clinical research, we can now provide ophthalmologists with clear test results that are color-coded based on documented reference ranges", explains Joseph Fontanetta, Diopsys CEO.

Another hurdle that the developers had to overcome was that traditional ERG requires sensors that make contact with the cornea – typically a contact lens or an electrode placed directly on the eye. This both risks damage to the cornea and causes patients discomfort, jeopardizing patient compliance and quality test results. Some ophthalmologists have turned to generic skin electrodes, but these sensors cover a large surface area, and come into contact with the facial muscles, often contaminating test results by picking up excess electrical energy. By developing a small external sensor that is placed under the eye, the Diopsys development team avoided these problems.

"We wanted to make this important vision test a practical, everyday diagnostic tool for ophthalmologists and their patients to help diagnose disease earlier and enhance patient management," says Fontanetta, "so we took the same beneficial ERG vision testing found in large research institutions, and made it accessible to eye care practices all over the world."

Availability varies globally.



THE IOLAMD EYEMAX MONO

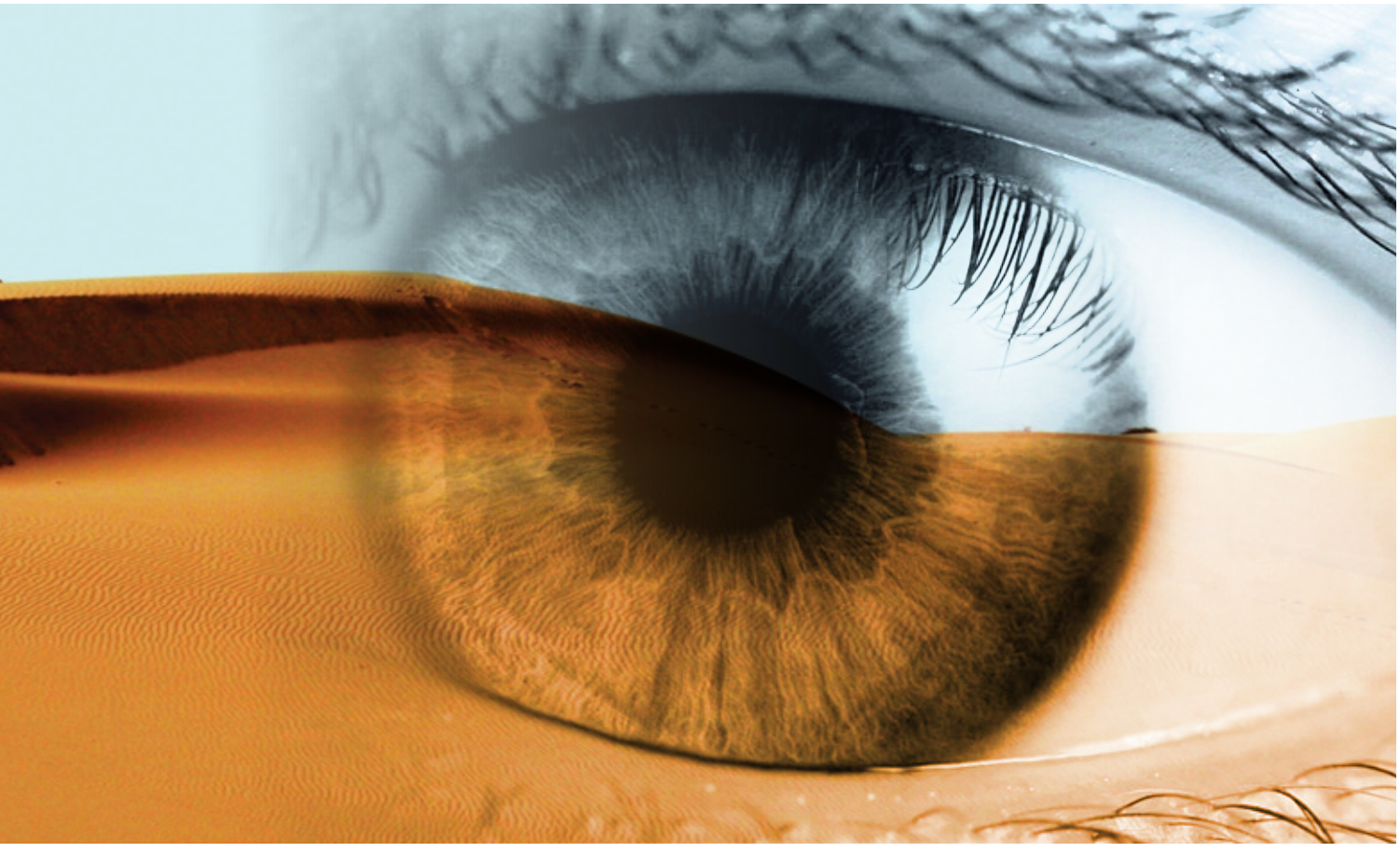
One ophthalmologist wasn't happy with the current options for treating dry AMD – so he created a new one

Treating AMD is always a challenge. But although wet AMD can be managed (albeit with frequent appointments and costly injections), for dry AMD the situation is even bleaker. Currently, the only options are vitamin supplements and telescopic optics. But the lenses are large (requiring a 7 or 8 mm incision), and the surgery is time-consuming and associated with extracapsular type complications. One ophthalmologist felt they simply weren't good enough – so he decided the only solution was to make his own.

"The biggest unmet ophthalmic need in the world right now is dry AMD, and we have no suitable treatments. I've implanted many telescopic lenses for AMD, and you have to put several things into the eye, then fix them together like Lego. It's a nightmare. Developing a new IOL for AMD was the greatest opportunity I could see. The first iteration of my design, iolAMD, was encouraging – it's foldable and can be inserted through a small incision. The total procedure, including cataract extraction, takes less than 10 minutes," says Bobby Qureshi, founder and CEO of LEH Pharma.

The EyeMax Mono is the successor to iolAMD. A single lens system with patented optics never used before in any IOL – it's the world's first (and currently only) extended macular lens. Like its predecessor, it's much less bulky than other offerings, and was designed to be as simple to implant as a typical monofocal, with a recovery period much shorter than for a normal telescopic IOL – a matter of weeks, rather than months.

So how does it work? "The EyeMax is completely unique, and represents a whole new method of improving vision in AMD patients. It creates a high quality image across 15 degrees of the macula, and magnifies this image by 20 to 30 percent," explains Qureshi. The theory behind the lens is that using innovative new optics, the patient should be able to achieve the visual potential of any residual part of the macula, and can change their preferred retinal locus as the AMD progresses – and if implanted binocularly, it will help the visual cortex to fill in the central visual field using the healthy areas of the



macula from both eyes, creating a compound image – further work is being done to evaluate this effect.

The EyeMax has now been implanted in over 1,000 eyes, with studies showing a mean gain of at least two, and in some studies as many as five, ETDRS lines for distance and reading; some studies soon to be published also show significant improvement in reading speed. More studies are now underway to better understand which patients will benefit – although Qureshi envisions the technology being a possible choice for any patient with macular disease as an alternative to a monofocal. There are also plans to submit the lens for FDA approval in 2017.

"For the first time, surgeons can offer something for this very large population of patients that may be able to restore some vision, without the downsides of complicated, risky surgery, or compromises such as one eye needing to adapt after surgery, or a reduction in visual field," says Qureshi. "This lens is suitable for patients with early and intermediate AMD, and continues to work even as the disease progresses – something no other option can offer," he adds.

As for the future of the lens, a sulcus variant for pseudophakic patients is expected to launch in 2017. Qureshi also aims to further refine and improve upon the EyeMax to expand the current patient selection criteria – and it's already being used by some surgeons in patients with diabetic maculopathy, epiretinal membranes, and other macular disorders. There are other plans in the pipeline too, including bespoke spectacle optics, and laser treatments for AMD.

"This IOL is the culmination of almost a decade of work, that was originally inspired by my own experience in implanting thousands of telescopic implants of every kind, and an optical error in the Hubble telescope. I feel it could be one of the greatest innovations of recent times – and now, it's finally going to market," says Qureshi.

The EyeMax Mono will be available in the EU in 2017, and is currently unavailable in the US or Japan.

MADE IN GERMANY

HAAG-STREIT SURGICAL: applying the lessons of the past to improve the future

When you're working out where a company is going, it helps to look at where it has been. HAAG-STREIT SURGICAL can trace its roots back over 150 years, to when Johann Diedrich Möller began producing high-precision optical components in Wedel, Germany. New technology was always embraced, such as products which included combinations of binoculars and cameras, and also anamorphotic lenses used in film projectors.

In 1963, Möller Wedel produced the world's first ceiling-mounted microscope for use in either micro surgery or ophthalmology, and entered the microsurgical field. In the 1990s it became part of HAAG-STREIT Group, and continued to focus on innovation in ophthalmology. The next major milestone was the launch of the world's first intraoperative OCT (iOCT®) device, to provide noninvasive imaging of structures and layers within the tissue of the eye during surgery – a technology HAAG-STREIT SURGICAL is now continuously working to improve and refine.

According to the HAAG-STREIT SURGICAL team, "understanding the needs of physicians is our main source of inspiration. By thinking beyond today's standards and looking at what the next unmet need will be, we work on solving surgical challenges and improving medical workflows."

THE KAHOOK DUAL BLADE

A versatile tool for trabecular meshwork removal in glaucoma

The Kahook Dual Blade (KDB) wasn't originally created for treating glaucoma. The aim of its creator, Malik Kahook, was to remove a section of trabecular meshwork (TM), intact, for imaging studies – but he quickly realized that he had created a device that solved an unmet need in surgical glaucoma: the ability to remove TM without damaging adjacent tissue.

So, what makes the device different? The tip provides controlled entry into Schlemm's canal; a ramp lifts the TM as the device is advanced, stretching the tissue before it's cut by the dual blades. These precise, parallel incisions leave behind wide open canal space for aqueous to flow into the collector channels.

"In the past, attempts to open up flow channels at the level of the TM centered on single incisions, or on ablating tissue – causing collateral damage and only partially removing the TM. More complete removal with a simple but elegant surgical device is a practical and cost-effective solution," explains Yasir Iqbal, New World Medical's Marketing Director. "The KDB is versatile; it can be combined with cataract surgery, or used in a standalone procedure, and it gives surgeons a single tool they can use to bypass the TM with confidence," he adds.

MACH4 Vitreous Cutter

How do you make vitrectomy faster, safer and easier? Doubling the cut rate

Traditional vitrectors do the job – but they can always be made better: to cut and aspirate more effectively, cause less traction on the retina and make the action more discrete, i.e. closer to the aspiration port. To do that, you have to cut faster.

In 2014, Geuder introduced the MACH2 double-blade vitreous cutter. It could perform up to 12,000 cuts per minute (cpm), made two cuts per work step, and the aspiration window was permanently open – making for faster core vitrectomy, with fine control and a delicate action. How could that be improved?

A doubling. The MACH4 vitrector features four blades and cuts up to 24,000 cpm. Above and beyond MACH2, it's designed to reduce traction, increase safety, and makes for precisely controlled shaving. It's faster and more efficient at vitreous aspiration, causes even less mechanical stress on the retina (leaving it virtually immobile). Like MACH2, the port remains permanently open, rendering duty cycle management obsolete and giving a constant aspiration flow and controlled shaving.

"We believe surgical procedures need to be constantly improved and updated in order to minimize risks and complications", says Hamadi El-Ayari, Geuder Sales and Marketing Vice President.

Currently in clinical testing. Not available in the US.

SalutarisMD®

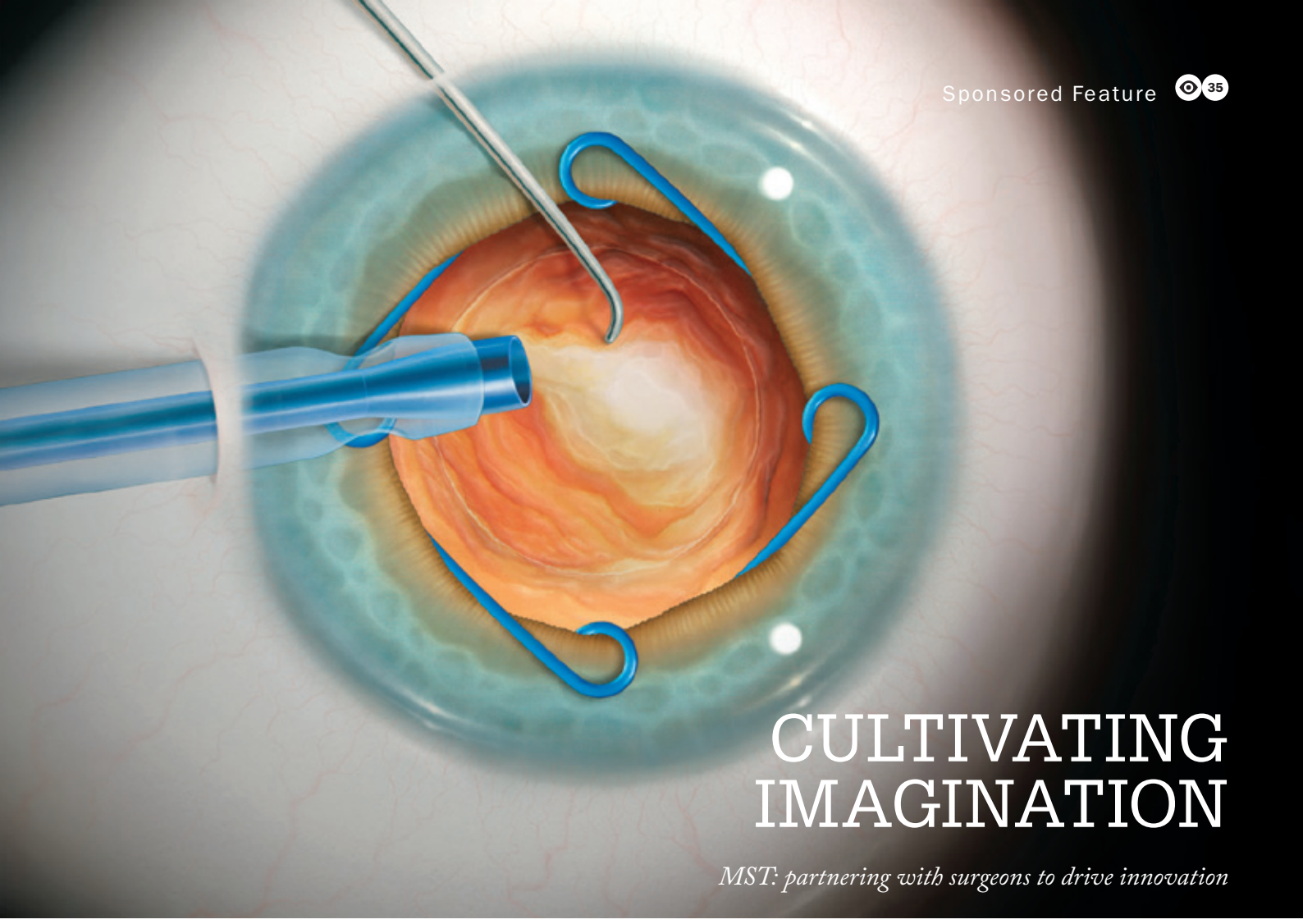
Developing a revolutionary treatment for wet AMD

A leading cause of blindness, wet AMD, can be managed – but doing so is a hefty burden. The time and cost of the monthly anti-VEGF injections is considerable to patients and healthcare systems alike – and worse, only 34 percent of patients respond with improved vision. SalutarisMD aims to reduce that treatment regimen and address the unmet need.

What do they propose? Minimally invasive brachytherapy – an outpatient procedure that can be performed in 15 minutes. A single-use, sterile applicator is used to place the therapeutic radioisotope behind the eye, adjacent to the area requiring treatment. Nothing is left behind and the intraocular space isn't violated.

"A small clinical study has produced encouraging patient outcomes, including visual improvements and absence of the pathologic lesion, with no additional interventions for two years," says Laurence Marsteller, CEO of SalutarisMD, "and new clinical trials are currently planned at the University of Arizona and Moorfields Eye Hospital." He hopes that "in the future, SalutarisMD technology can offer a new treatment option for wet AMD patients."

Caution: Currently limited to investigational use only.



CULTIVATING IMAGINATION

MST: partnering with surgeons to drive innovation

Partnering with surgeons to make their ideas a reality is the fastest way to foster innovation. Here's one example. Small pupils and intraoperative floppy iris syndrome limit visibility – and access – during cataract procedures. If there's no safe way to expand the pupil, the potential for complications skyrockets. Boris Malyugin's idea: the Malyugin ring, a pupil expander that's gentler and easier to use than iris retractor hooks. MicroSurgical Technology (MST) partnered with Boris to develop and commercialize his eponymous ring, and has helped to make challenging small pupil cataract cases safer and more routine. Since it was launched onto the market over nine years ago, the Malyugin Ring has been continually modified and improved – for example, the Osher modification to the injector enabled easier release and re-engagement of the ring. The Malyugin Ring 2.0 was released in May 2016 – an updated version that is even gentler on the iris and even easier to use. Today, over one million Malyugin Rings have been used in cataract surgeries around the world.

MST is dedicated to solving clinical problems in partnership with some of the most prominent ophthalmologists in the world: Ike Ahmed, Bobby Osher, David Chang, and (of course) Boris Malyugin. For challenging procedures such as IOL exchange, scleral fixation of an IOL, and iris repair, MST developed their anterior segment micro-instrumentation for safer management of complicated surgery. "These instruments could be described as the fire extinguishers on the wall: good to have in the event of complications," says Jeff Castillo, Company President.

One newer innovation is the Allegro silicone I/A system. "Its complete silicone coverage and unique geometry help provide a safer, more precise way to remove cortical material, while also providing excellent sub-incisional access," says Castillo. "Our Allegro system is a revolutionary change to the I/A stage of cataract removal", he adds. The first generation of Allegro was released in 2015, with the next generation to hit the market in 2017.

"MST is always looking to partner with surgeons with ground-breaking ideas," says Castillo, "and we will continue to develop products inspired by ophthalmologists, in order to solve clinical problems and help to provide the best patient outcomes possible."

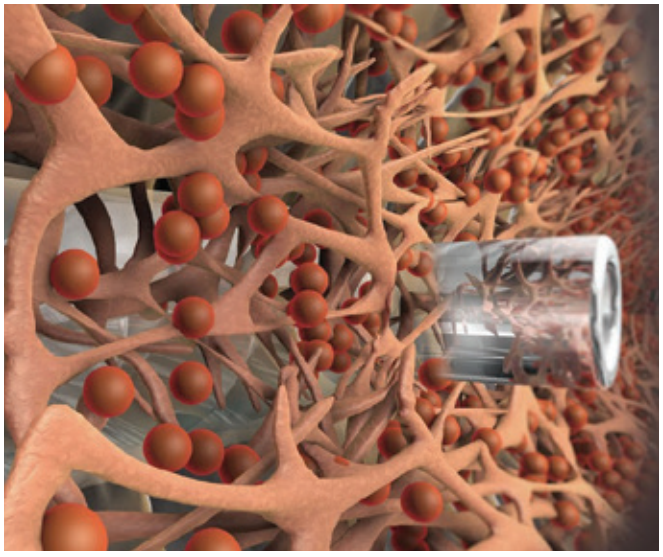
GLAUKOS: MIGS AND BEYOND

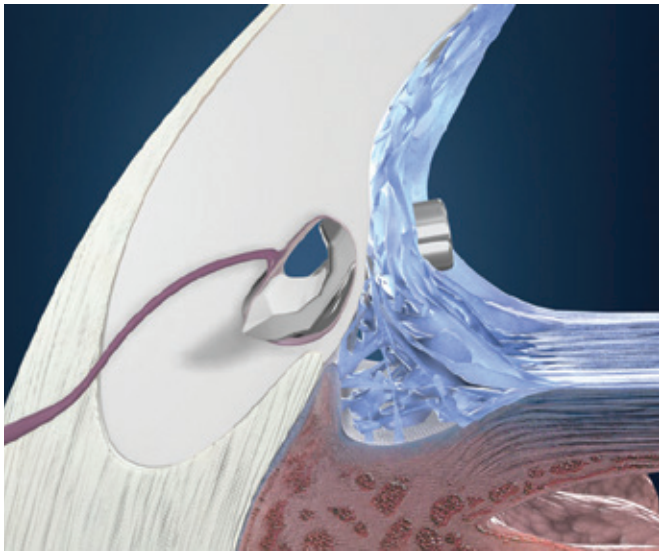
Pioneering ideas in glaucoma – from microinvasive surgery to new drug delivery platforms

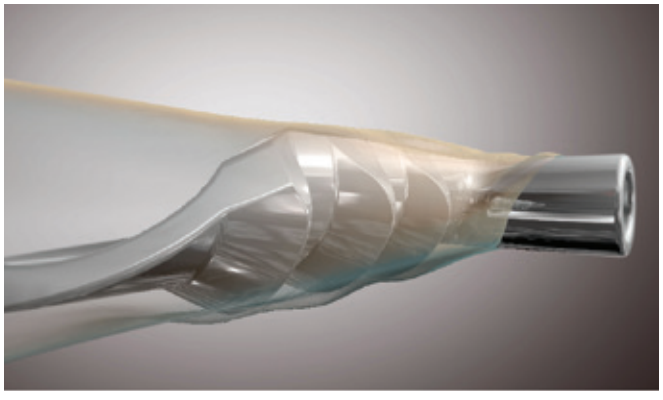
Glaucoma is an area of ophthalmology that has become a hotbed of innovation in recent years. As a leading cause of blindness worldwide with limited treatment options, it isn't hard to see why. The disease is often treated by administering eyedrops to control IOP, although many patients struggle to adhere to their sometimes oppressive regimens. For patients whose IOP cannot be controlled with medication, surgery is often the next step. But traditional surgeries, such as trabeculectomy, are invasive and come with a significant risk of adverse events, or failure. This was the challenge that glaucoma surgeons faced – until the advent of microinvasive glaucoma surgery (MIGS).

Today, MIGS is changing the way that glaucoma is treated. But not so long ago, the term didn't even exist. Enter Glaukos: it took the company over 10 years of research, testing and commercialization to bring its idea to market, and it all began when life sciences investor Olav Bergheim brought a family member with glaucoma to meet ophthalmologist Rick Hill for an assessment. Rick told Olav's relative that he had advanced glaucoma, and that he required bilateral trabeculectomies. But Olav thought there had to be a better way – and Rick put forward his idea of a trabecular bypass with an internal approach, using a stent small enough to maintain the bypass and restore outflow. However, Rick had been advised that the technology simply didn't exist to manufacture the tiny stent with enough precision. Olav wasn't so sure, and he brought in a fluid dynamics expert to work on the idea. Together, the three men created the concept for the first iStent® prototype. But commercializing a medical device that established an entirely new category of glaucoma surgery was never going to be easy.

"Our first major challenge was the development of the microstent implant and procedure. At that time, producing devices of this size challenged the limits of micromachining. Our next big challenge was establishing a regulatory path for our company, and the emerging category of MIGS – a daunting task, which involved working with the FDA to figure out how







the iStent could be evaluated for safety and efficacy," explains Thomas Burns, CEO. Establishing a new class of treatment meant the company was subject to a high level of scrutiny from regulatory bodies, and had to work to present the benefits of its product to glaucoma surgeons.

Now that the device is on the market, the company is working to bring the iStent to a wider audience, and to provide support and education for surgeons who wish to introduce it to their own practices. Its mission, explains Burns, is "to lead the global glaucoma market, and advance the existing standard of care."

"We pioneered MIGS in order to revolutionize the traditional glaucoma treatment and management paradigms. The first prototype of the iStent was made in 1999, and launched in the United States in 2012 – and to our knowledge, it was the smallest medical device ever approved by the FDA. The treatment of glaucoma is our sole focus, and we now have 55 peer-reviewed articles published on iStent, long-term clinical results and over 200,000 implanted globally," says Burns.

Looking further ahead, Glaukos plans to use its existing platform technology to build a portfolio of injectable, microscale therapies for the treatment of the complete range of glaucoma disease states. With its next generation product, the iStent inject®, it envisions transitioning to an injectable therapy. iStent inject is designed to further reduce intraocular pressure by potentially delivering multiple stents into the trabecular meshwork through a straightforward click-and-release motion. An extended drug delivery and implantable platform, named iDose®, is in clinical trials and is designed to deliver months of prostaglandin therapy for glaucoma management – tackling the ubiquitous issue of non-adherence to medication.

"There are now more options available for glaucoma patients than in the past," says Burns, "and defining them helps both ophthalmologists and the wider ophthalmic community to administer treatment. Early detection and treatment of glaucoma is key to the long-term well-being of patients, and we aim to remain one of the leaders in this area."

Welcome to The Ophthalmologist North America

Building on the success of The Ophthalmologist, our new edition will offer professional, technical and groundbreaking ophthalmic content which caters to practicing ophthalmologists residing in the US and Canada.

Editor of The Ophthalmologist, Mark Hillen, believes the time is right for a dedicated publication.

"Right from the launch of The Ophthalmologist in Europe some three years ago, we've had calls to bring the magazine to North America. I'm absolutely delighted that we can now give our friends across the Atlantic their own edition."

Publisher, Neil Hanley, says

"It was always our aim to take The Ophthalmologist to the US and Canada. We have taken our cues and influences from some of the most recognizable magazines in the world to create a modern media brand for ophthalmologists, and the whole team are thrilled to properly serve what is perhaps the fastest-paced ophthalmology market in the world."

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NextGen

Research advances
Experimental treatments
Drug/device pipelines

It's All About Perspective

Consign your surgical microscope to the scrapheap. Digital light field imaging promises the elimination reflections, aberrations, blur and more

By Christos Bergeles

"You want to make a portrait of your wife. You fit her head in a fixed iron collar to give the required immobility, thus holding the world still for the time being. You point the camera lens at her face; but alas, you make a mistake of a fraction of an inch, and when you take out the portrait it doesn't represent your wife – it's her parrot, her watering pot – or worse." – Le Charivari magazine, 1839.

When it comes to improving ocular imaging, we can learn a lot from the first days of photography. Back then, focusing was the challenge – early lenses had small apertures, a shallow depth of field… and exposure times that were so long, fixed iron collars were deemed necessary to get people to remain still for long enough to take an unblurred photograph. Even now, a blurred photograph (either through motion or a focusing error) evokes a sense of loss – you can't refocus the photograph after it's taken; the image is lost forever.

Let's look at vitreoretinal surgery. Whether the surgeon's using a surgical microscope or a 3D (stereo) camera with a head-up display, there's still a shallow depth of field. There will inevitably be times where tissues you'd like to see in focus… aren't. Then there's illumination. When a professional photographer lights a scene or a set, they can adjust where the lights are placed and the camera is positioned to get the best possible image. Although light sources have improved greatly over the last 20 years, that's not really a luxury surgeons have.

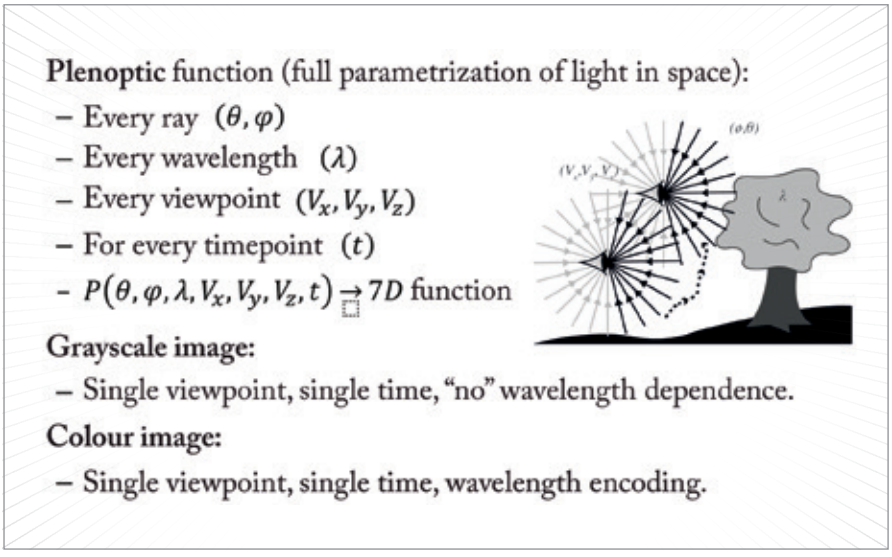

Figure 1. What do we mean by "plenoptic"? It captures the direction, wavelength and intensity of every ray of light captured by the digital image sensor, for each and every timepoint captured.

What's limiting imaging

Digital cameras have made a huge difference to what can be achieved in photography. Manufacturers are able to produce incredibly light-sensitive sensors that measure in the hundreds of megapixels, and the fact that the information is digital means that algorithms can be applied to the image data – both in the camera at the time of acquisition and afterwards (1). The flash, tripod and studio lights haven't been eliminated from photography, but it's now possible to take reasonable photographs in near-dark conditions with just a digital camera with a great sensor and a good processing unit. It's important to realize that today's digital images are not just directly recorded – they are computed too. Clever algorithms make them sharper, brighter, and help the colors stand out. But they don't solve the issue that stalks all lenses: aberration. It's unavoidable – a natural consequence of refraction. Not all light converges on a single point on the sensor, and the bigger the lens, the bigger the problem they become. If only there was a way of correcting for them…

Tailor the hardware, not the algorithm

You might refer to a photograph as a "snapshot." That's a great term – it evokes what a photograph is in terms of light: the total sum of light rays striking each point at an image in a single point of time.

At a Glance

- *To take a great image, you need your camera to be in the right place under perfect lighting conditions*
- *These conditions are virtually non-existent with surgical microscopes – and there's little that can be done about it*
- *Digital light field imaging takes a completely different approach to light sensing and rendering, and allows refocusing, changes of point of view and the removal of reflections*
- *This approach promises great benefits in terms of enhanced periprocedural tissue visualization for surgeons, but ultimately, surgical robots too*

What a photograph doesn't do is record the amount of light travelling along the individual rays that make up the image, which as we'll see soon, can be very useful. An apt analogy is that of an audio recording studio (1): a photograph is a recording of all instruments being played together on a single track; but what works better is the recording of each individual instrument on a separate audio track – it means producers can improve and fix things in the mix.

"The secret to unlocking the potential of DLFP (and rendering the final image) lies in raytracing."

In terms of digital photography, there is a way of achieving "multitrack" imaging: digital light field photography (DLFP). It works by exploiting the fact that you can produce digital camera photosensors with hundreds of megapixels – yet you don't really need more than two megapixels for a standard 4" × 6" photograph. You use that spare capacity to sample each individual ray of light that contributes to the final image – the full parametrization of light in space, or the plenoptic function (Figure 1). What's sampled, therefore, is termed the "light field" – a term borrowed from computer graphics, and just like in a virtual model, you can start to process that information, and generate different outputs – like points of focus.

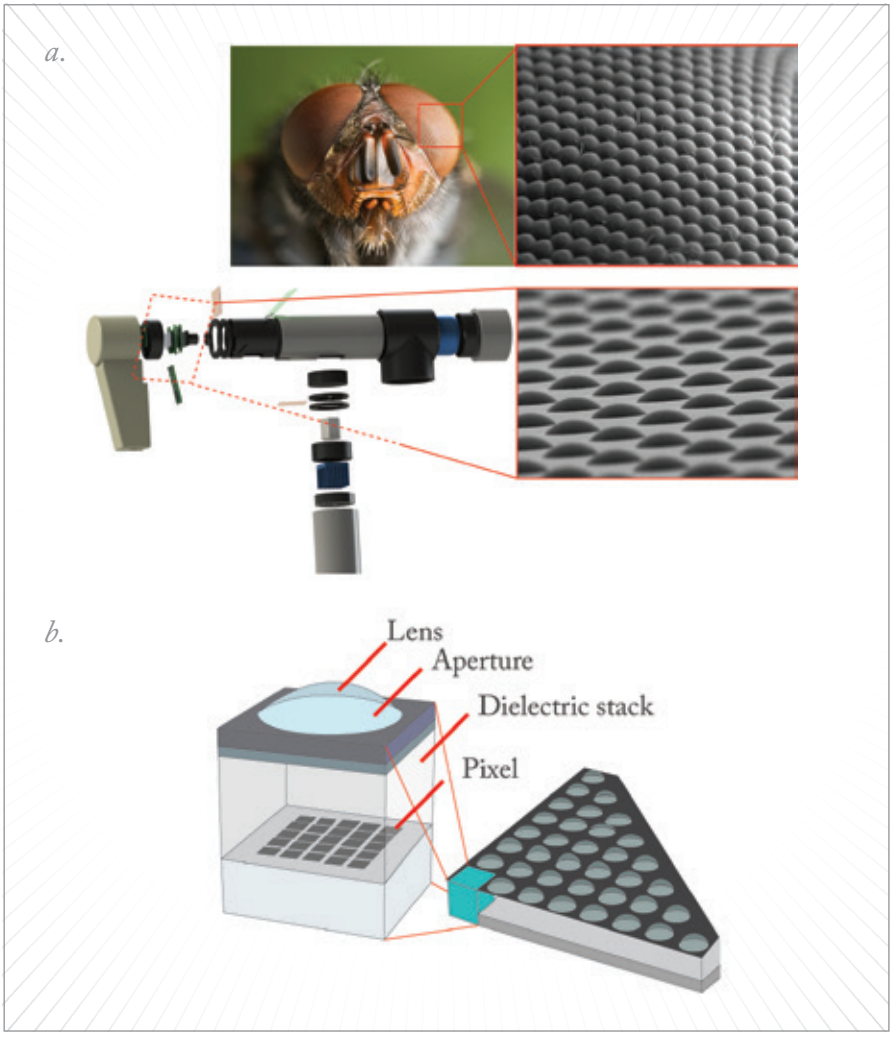

Figure 2. What is light-field imaging? a. The compound lens of an insect, compared with the microlens array present in a light field camera; b. A specialization of the plenoptic function that preserves the encoding of viewpoints, ray angles and $L(\phi, \theta, V_x, V_y, V_z) \rightrightarrows 5D$ function unlocks the technique; it requires both 2D orientation and a 3D position to work.

To capture all of this information, DLFP requires a microlens array – somewhat like the compound eyes of insects (Figure 2) – to be placed in front of the photosensor, with each microlens covering a small array of photosensor pixels. What the microlens does is separate the incoming light into a tiny image on this array, forming a miniature picture of the incident lighting – sampling the light field inside the camera in a single photographic exposure (1; Figure 3). In other words, the microlens can be thought of as an output image pixel, and a photosensor pixel value can be thought of as one of the many light rays that contribute to that output image pixel. Finally, each microlens has a slightly different and slightly overlapping view to the next one – each has a different perspective, and that can be exploited too. But the secret to unlocking the potential of DLFP (and rendering the final image) lies in raytracing.

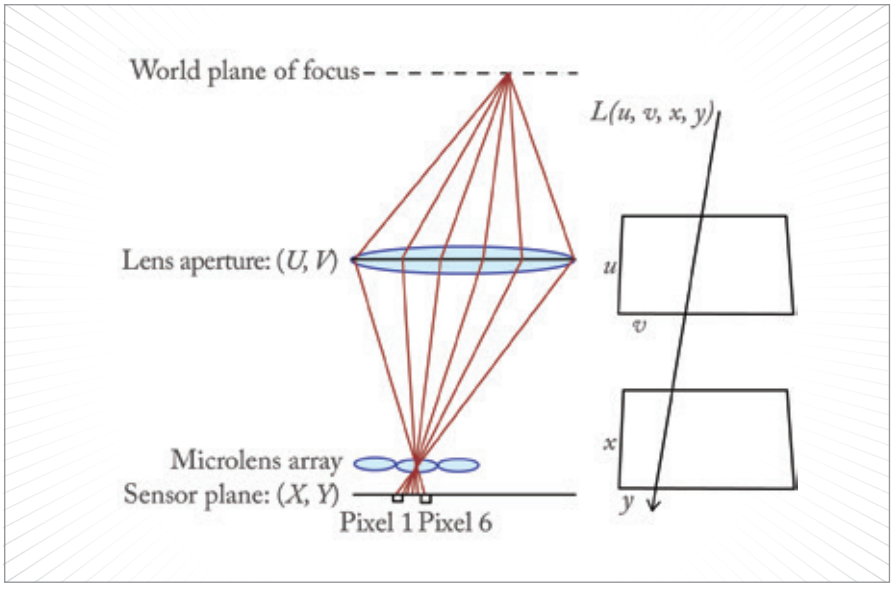

Figure 3. The basic principles that underpin the light-field camera. By placing a microlens array in the focal length, the pixel underneath each microlens, samples position, intensity and the direction of each ray – which means you can get multiple views by selecting different rays under each microlens.

Refocusing after the event – and more

Imagine a camera configured in exactly the way you want – and that you could (re)trace the recorded light through that camera's optics to the imaging plane. Summing those light rays then produces the photograph. Raytracing also gives you the tools to start correcting for the aberration that's always present with physical lenses – you can start to handle the unwanted non-convergence of rays and get a crisper, more focused image in the final computation, as you're focusing not through a flawed real lens, but a perfect, imaginary lens instead.

But really, what's most impressive is the fact that this approach lets you refocus the image over a range of distances after the fact – you can adjust the image sensor plane, post hoc, so the image is focused as desired – or all of the image can be rendered in focus (and if it's video footage, this can be performed in real-time too). You might be aware of this technology already: it's what underpins the commercially available Lytro and Raytrix cameras.

But what can be performed with light field imaging doesn't stop there: it also offers reflection removal. If a reflection affects some, but not all of the image perspectives – it can be computed away. And finally, this approach of taking multiple images from many different angles even offers you high resolution, three-dimensional information.

What this means for ophthalmologists

The applications in ophthalmology are obvious (Figure 4) – let's work through each feature in turn.

Aberration removal

It's always nice to have a better quality image, and the removal of aberration is clearly something that's nice to have for everyone. Where it might have the greatest impact is in screening – something at the periphery of an image that has started to get distorted, now isn't. It not only lets those screening images for potential pathologies see them more clearly, but as computer algorithms start screening fundus photographs – like the Google DeepMind/Moorfields Eye Hospital collaboration – they're more able to reliably and reproducibly flag pathologies too.

Reflection removal

This is a truth across all surgical procedures, but is particularly apparent with eye surgery, and particularly retina surgery: illumination causes problems (Figure 4). Unlike professional photographers in a studio who have the luxury of placing studio lamps in optimal locations, and can block out off-camera reflections with black drapes, surgeons have no such comfort: they have to illuminate as best they can, and try their best to work around the reflections and shadows that occur. Eliminating these issues should result in safer and easier surgery, but it also adds the potential for using lower levels of illumination, which might reduce any potential heat or phototoxicity issues too.

Everything in focus

Nothing in the eye is on a flat plane. Resolution and depth of field are reciprocals of one another, and surgical microscopes are designed to strike a compromise between both – with an excess of image sensor pixels, light field imaging should eliminate the need for that compromise. If you want it to be like that, everything could be sharp and in focus. Motion blur (Figure 4) can also be caught and eliminated and corrected for too; it's just a matter of computation to direct the directions in motion, and to correct for it.

The third dimension

Bear in mind that light field imaging essentially gives you many views of the tissue that you want to manipulate – and these can be combined into a much richer representation of the tissue. Surgeons can choose to see what's behind the surgical instruments – or even the tissue that you're directly manipulating. But in addition to that, these multiple views give you information about the third dimension. This can be useful in many ways.

There's a clear trend towards using head-up displays in retinal surgery –

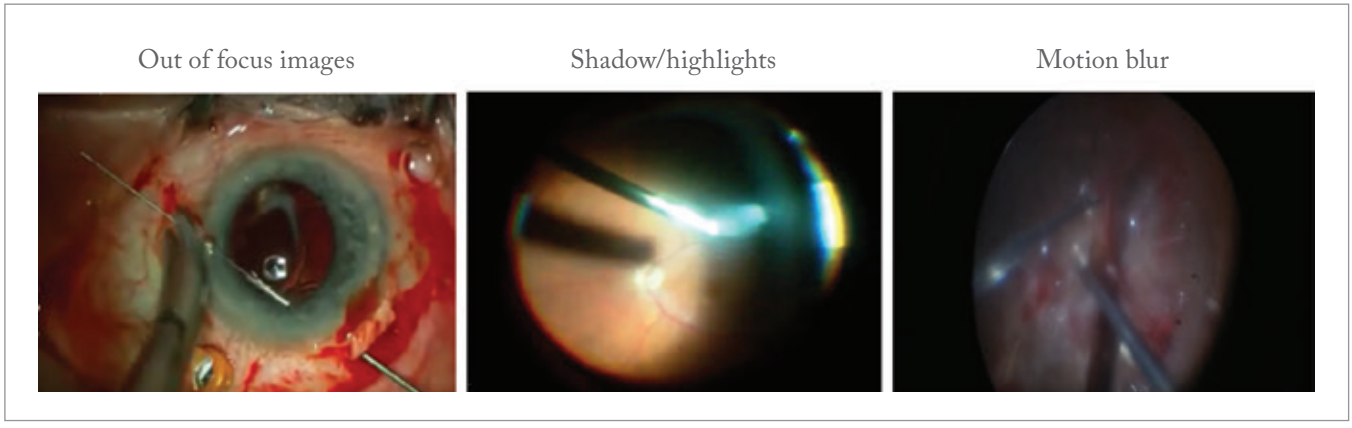

Figure 4. Some examples of everyday issues with surgical microscopes that light field imaging promises to help eliminate.

operating at a surgical microscope soon becomes uncomfortable. Today's head-up displays do a great job of approximating the stereopsis that you experience using surgical microscopes, but light field imaging might be able to let instrument manufacturers synthesize an enhanced 3D view, and this automatically lends itself to augmented reality – the overlay of pertinent images onto the 3D display the surgeon looks at. Feeding such input into virtual reality headsets like the Oculus Rift, however, is feasible – but initial attempts have proven unpopular; it takes surgeons away from reality, and they lose situational awareness. Of course, there are more avenues where light field imaging might come in useful: Three-dimensional measuring of the optic nerve from normal fundus camera setups, corneal topography, or even forms of tomography if the approach also works with absorbing wavelengths…

Robotic eyes

There's an obvious extrapolation of the use of light-field imaging: guiding robots to perform minimally invasive interventions. The robots get an extremely detailed (in theory, down to 10 µm precision), rich 3D environment in which to operate; more data to help it determine where to ablate, augment, cut, debride or suture.

Light field imaging for medical applications is still in its infancy, though (2–4) – which makes us among the first to explore this topic, especially in ophthalmology, where we build upon our digital autofocusing ophthalmoscopes (5). There is still much to be done to optimize and customize both the hardware and software for medical use in general, and ophthalmic applications in particular. Light field imaging was first conceived in the 1980s, but now we're well past the point where digital photosensor technology and computer graphics processing power has made this a feasible digital imaging approach: things are progressing rapidly now. I am lucky to have the support of Fight for Sight and the Academy of Medical Sciences, the two foundations that have bootstrapped the project. My clinical collaborator Pearse Keane from Moorfields Eye Hospital, and the PhD student we are co-supervising, Sotiris Nousias, complement the team, and are fundamental assets in bringing these new imaging technologies and algorithms to the clinic.

So if you're a surgeon, imagine a reflection-free surgical microscope approach that has, in effect, adaptive optics (without the expensive, deformable mirror), where nothing is out of focus, and surgical instruments can be removed from your field of view. Add to that a spectacular three dimensionality and the added feature of a head-up display – without a single iron collar being required. Just imagine…

Christos Bergeles is a Lecturer and Assistant Professor in the Translational Imaging Group in the Centre for Medical Image Computing at University College London's Department of Medical Physics and Biomedical Engineering.

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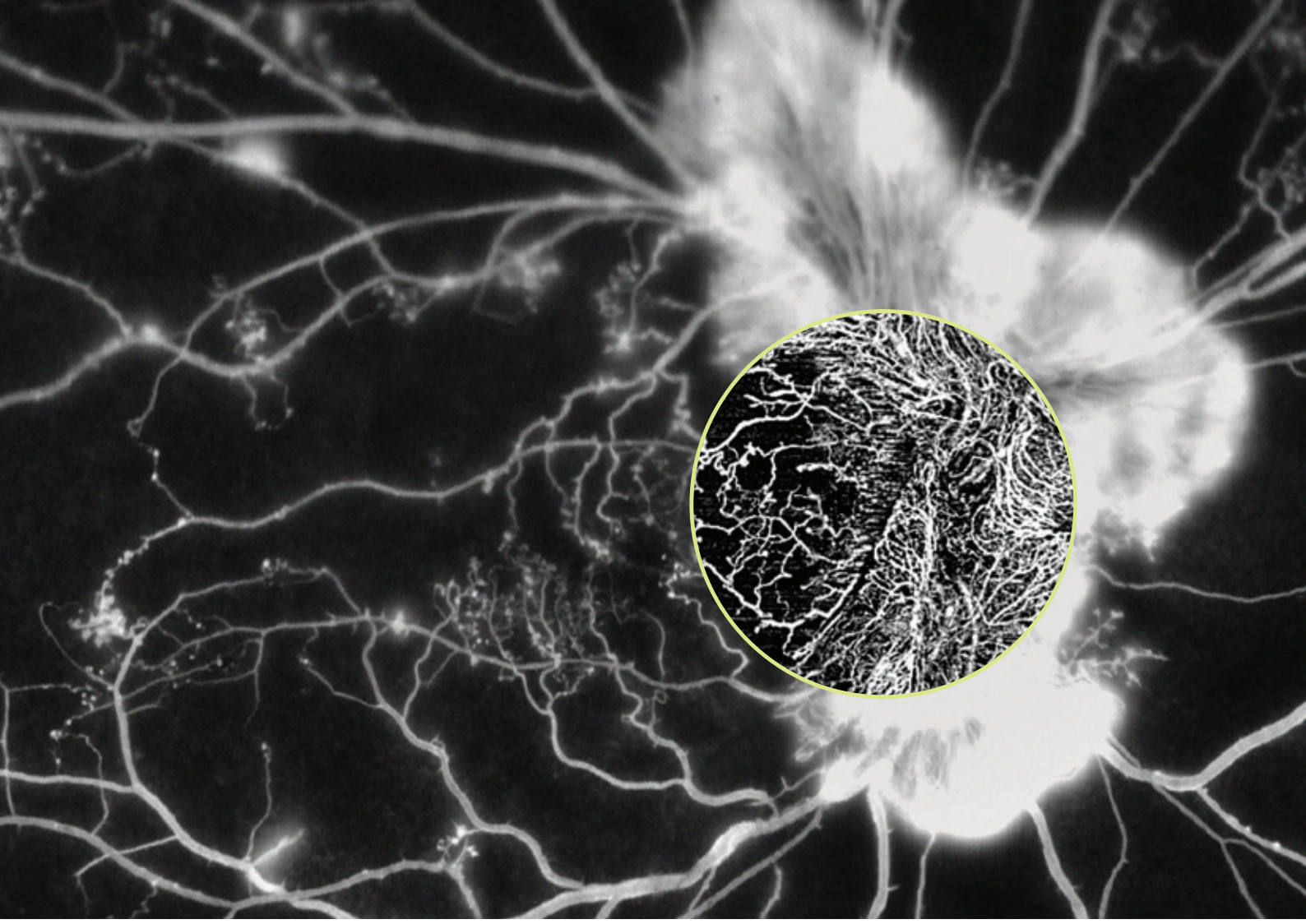

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On Innovation…

Advice from one who's been there and done that

Mark Hillen interviews John Marshall

If you work in eyecare, it's almost certain that you already know of John Marshall – his reputation precedes him. John is many things: educator, mentor, academic, entrepreneur and most definitely, a serial innovator. He's accumulated a great deal of knowledge and experience of innovation over his career – so that's precisely what we asked him about.

How important is experience to successful innovation?

It's incredibly important. In my first "innovation exercise" with the excimer laser, I didn't fully understand the value of what I had. I didn't understand business practice, I didn't understand financial input – and I certainly didn't understand stock dilution! These are all things that you learn about as you innovate.

When I first had the idea of the excimer laser, despite having the original patents of the technique, I found it virtually impossible to raise money from conventional sources in the UK – people there didn't believe in the idea of cutting away parts of the center of the cornea. But in the US, we managed to raise plenty of money by approaching their money markets, but this came at a cost: a big equity involvement from the investors…

Here's the thing: most research workers are naïve and might not understand the value of what they have. They soon learn (like I did) that if you take company money, they will want a big share of it and may want to "gobble up" the intellectual property (IP).

But if you have a novel idea and good IP, it is relatively easy to raise money, and, importantly, if you can move forward quickly with the idea, then you shouldn't encounter too many problems. Then there's the "flash-to-bang" time.

"How quickly will your idea become essential to the community at large? This is 'flash-to-bang'."

What do you mean by "flash-to-bang"?

How quickly will your idea become essential to the community at large? This is "flash-to-bang", and it matters in successful innovation. An example of this is vitreous fluorophotometry. The technique involved giving patients an intravenous bolus of fluorescein, then measuring the diffusion of the dye from the retinal architecture through the vitreous, into the anterior chamber – more dye would diffuse through in diseased eyes than in healthy eyes. Although it was a simple and elegant concept, a brilliant device, and was designed by two very bright people, it didn't get anywhere. On the other hand, there's the example of OCT – also a brilliant device designed by very bright people – which was introduced and was instantly successful. So in one case a brilliant idea didn't really get anywhere, and in the other case a brilliant idea led to huge commercialization. It all relates back to this "flash-to-bang" time – the community embraced OCT as they immediately saw how useful it would be to their daily practice.

Are diagnostic devices easier to develop than therapeutics?

Both are hard. Treatment innovations are generally faster, as diagnostics can be very difficult. Not only is it difficult to secure funding to develop diagnostic innovations (because of concerns about obtaining reimbursement later), there's also the problem of patients in the diagnostic process. If you need them to respond with an answer, you're likely to have issues. Patients can be the biggest variable: they are trying to please you rather than doing the test, and frankly, if you can remove them from the process, diagnostic innovations may have more potential!

Here's an example of a diagnostic technique with great potential that avoids the patients trying to please you with their answer: genetic screening. In the old days, you'd take a buccal swab, send it to a lab to perform PCR, and six weeks later you'd have your answer. Today, that's still the same process, but it still takes 48 hours. Imagine something like red eye, where a simple test could discriminate if the cause is bacterial, viral or fungal, potentially even by

At a Glance

- *Taking an idea and turning it into reality can be an incredibly long and arduous journey*
- *There are a number of pitfalls you need to avoid – IP, finance and competitors*
- *John Marshall has invented and pioneered many technologies in eyecare and beyond – he's far more than the inventor of the excimer laser*
- *Here, he shares his insights and his stories of innovation*

using a coated strip that you push into a smartphone. That's a wholly objective answer right there.

That doesn't mean that we can stop treatment innovation – and we certainly need more of that. But even treatment innovation can be hard – and I think part of this is down to the procedures involved with innovation. Why don't we have any new antibiotics? It isn't because there aren't any good laboratories capable of doing the work, but rather that the regulatory hurdles are so huge and expensive that a lot of companies don't see the process of developing antibiotics viable, or in some cases, possible. And this is just one of the many ethical issues with innovation.

So what are the ethical issues attached to the innovation process?

When is a treatment really an experiment, and when does an experiment become a treatment? This is very difficult as an ethical problem, but it is also a scientific issue – and the problems only increase when commerce becomes involved. Let's say a hypothetical new device has gone through fundraising and a number of limited trials, and receives endorsement from a regulatory authority. The inventor can then start charging money – charging patients for something that may only give them limited help yet is going to cost them a lot of money.

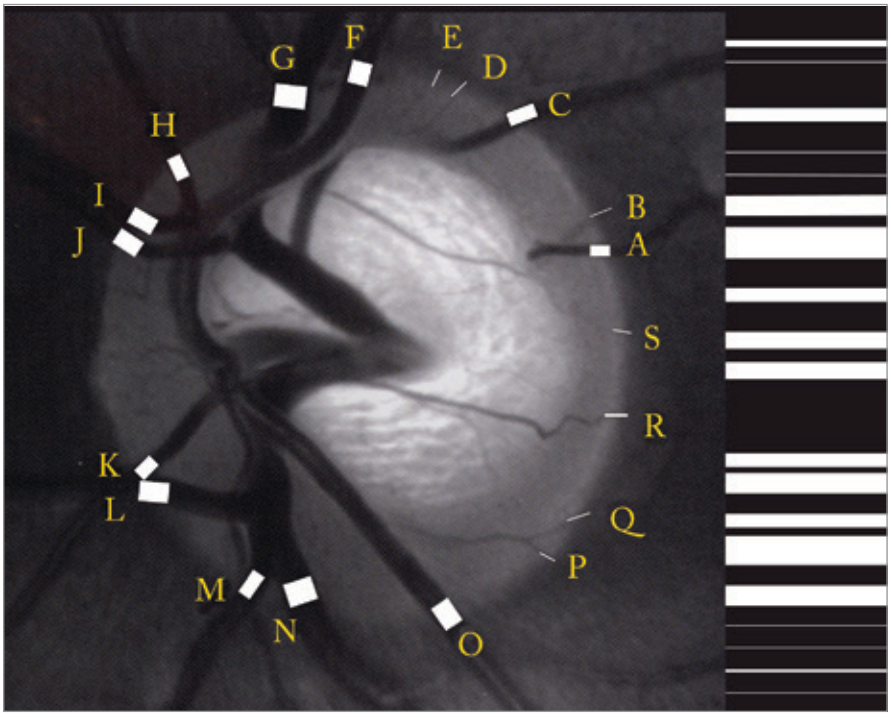
We need to define success, and we must set the end-points at a level where true benefit to the patient is taken into account. It seems to me that there is a situation where any limited improvement in a patient's vision is deemed to be successful, and the media adds to this hype through describing treatments as "sight restoring." But is being able to see a bit of light coming through a window worth $100,000?

Another issue is at what point do you release Mark I devices knowing that you have also developed a Mark II version? Commercially, you need to release the Mark I device onto the market to demonstrate that your innovation works, but your research and development team know that there is something better coming along. So what do you do? Do you let people know that there are these further developed technologies in the pipeline? Or do you let people know that this is where we are now, but there will be an improvement?

The ethics of innovation can be complex, and I think it is why we have seen a number of so-called treatments which are really experiments coming out.

Does regulation help?

Regulatory frameworks exist to look at efficacy and safety, but the elements of these frameworks are not necessarily policed well. For instance, there is a huge regulatory framework for breast implants, but a company in France chose to ignore it and it led to a significant number of problems. It's no good having tables of performance and efficacy if at the end of the day you're not going to



Credit: John Marshall.

Figure 1. The blood vessels coming in and out of the optic nerve (A–S) can be measured in terms of their proportions and analyzed as per a barcode would be to give a unique read-out for each individual.

enforce them – enforcing them after the problems have arose is just too late.

In my opinion, all these factors have led to the situation we have now, where companies with a pre-production product will have key opinion leaders speak at meetings. By doing this, companies are getting information out there without going through the necessary peer review process – other than standing in front of an audience.

How can you avoid innovation pitfalls?

If you are an innovator today, there are a lot of pitfalls. One lesson I have learned is that surgeons and scientists make the world's worst CEOs – you shouldn't try to do everything yourself outside your area of confidence. If you have an idea, there is research technology available to help you determine if others have similar ones. There are then pitfalls with IP. Filing for a provisional patent gives you a year's grace but also makes others aware of what you are doing. A good pre-patent tip is to get your lab books notarized by a lawyer – whilst it isn't a patent, it is a legal document confirming that you had the idea at that time. After filing a patent, there are several routes to take. You can keep the product to yourself and start paying for IP protection, or you can look for a commercial partner in the field to license the technology.

There are also commercial aspects to this. The real issues start when you get to a trial stage – clinical trials these days just cost a fortune. We have seen them migrate from the US to Europe, and now to China, simply because they progress faster and at a lower cost than the "creeping death" we now see in countries with more regulatory restrictions. With trials, you want to look at safety and efficacy, but instead of trying to look at progressing your device, you end up focusing on getting through all the steps in the process.

But it can be fun too, right?

Yes. This was a brilliant idea that went to the military – retinal biometrics as barcodes. An infrared camera that hunts for the highest infrared reflection in your eye – which is your optic disc. The camera goes into scan mode, and it scans the transition of blood vessels as they go from myelinated fibers of the nervous background to the tissue. Barcodes these days are 13 digits in length. Everyone has between roughly 14 and 17 vessels coming out of their optic nerve. If you measure the relative proportions of vessel to non-vessel – essentially a black bar then a white bar – around the circumference, you got a perfect barcode, which was unique to each eye. So this is a very, very high security biometric.

One cracking invention was an idea that came to me in a pub. I walked in and said to the barman: "I'm gasping for a cup of tea, any chance?" The answer I got was "Nope." I asked "Why?" He said "It's no, unless you want to come out to the kitchen." I went "Fine, I don't mind going to the kitchen… but why?" He said, "You have no idea! People come in at the end of lunch time, ask for a cup of tea, I come back, and they've nicked all the money out of the fruit machine!" And then I thought, well, it's so simple to design a device to give you a lot of warning. So I put a little device together that had a light trap, so if anyone handled the system in an improper way, a huge klaxon went off. The barman said "It's fantastic!" – and and it actually made money – it was adopted by several elements of the gambling industry!

John Marshall is the Frost Professor of Ophthalmology at the Institute of Ophthalmology in association with Moorfield's Eye Hospital, University College London, UK. He invented and patented the excimer laser – an innovation which has been used in over 50 million procedures world-wide.

Hitting the Clinic with the KDB

The Kahook Dual Blade is being successfully used in glaucoma surgery procedures – but what are the important considerations when deciding to adopt it?

Glaucoma and cataract specialists Leonard Seibold (Assistant Professor and Co-Director, Glaucoma Fellowship, University of Colorado School of Medicine, USA) and Nathan Radcliffe (Director of Glaucoma Service, New York University, USA) share their techniques and tips for effective application and achieving optimal outcomes with the Kahook Dual Blade.

When to use the dual blade

Nathan Radcliffe: "If you have experience with trabecular bypass, or other types of incisional trabecular meshwork (TM) surgeries, you want to approach the Kahook Dual Blade (KDB) with an open mind. In my experience, the dual blade has delivered unsurpassed efficacy in terms of lowering IOP, which I couldn't have predicted based on my experiences with other types of trabecular bypass."

Leonard Seibold: "The KDB has allowed me to perform a more complete goniotomy than other methods available, and a more complete TM removal, in a simple yet elegant manner. But you should have a good foundation in intraoperative gonioscopy in order to perform this surgery to the best of its capabilities."

Selecting the right patient

NR: "The KDB procedure is versatile – it can be performed in patients combined with cataract surgery, and also in phakic patients with 20/20 vision. It can also be used in patients who are already pseudophakic, and alongside other procedures, such as other types of trabecular bypass (if one wants to expand the number of accessed collector channels), glaucoma drainage devices, endocyclophotocoagulation, and more."

LS: "Any patient with open angle glaucoma, whether primary or in some cases secondary, can be a candidate. The most profound pressure reductions I've found are in patients who have pigmentary or pseudoexfoliative glaucoma – where we know the site of obstruction is at the level of the TM, so by removing that tissue you can dramatically increase aqueous outflow and lower IOP. Additionally, any patient with uncontrolled IOP despite medications, or who is intolerant, allergic, or not adhering to their medications, could potentially benefit."

Getting the preparation right

NR: "Using gonioscopic visualization, you want to make sure that you have adequately inflated the anterior chamber, as this is going to be important during the TM treatment. You want the eye to be slightly pressurized, certainly higher than episcleral venous pressure, but not so high that you'll collapse the TM. A pressure of around 20 mmHg is ideal."

LS: "Like in any angle surgery, a good view of your target tissue is key – in this case that's the TM. Examine these patients closely in your preop evaluation, because when you're deciding who's a candidate you want to be able to visualize good angle anatomy and landmarks, so you know you'll be able to see the target tissue well in surgery."

Top technique tips

NR: "You have several choices for how to make the parallel incisions in the TM, but these days I start straight nasally, so either the 3 o'clock or 9 o'clock position, and I do two passes. The first is a forehand pass, so if I'm operating on the right eye, I make a temporal incision, and I'll treat from the 3 o'clock position up to about 1 o'clock, as far superiorly as I can. I make sure that I'm seeing the bare posterior wall of the canal of Schlemm. Then, I don't bring the KDB out of the eye, but simply reverse its direction and treat from the 3 o'clock position down to 5 o'clock or lower.

When the dual blade procedure is performed with cataract surgery and TriMoxi is given intravitreally, excellent outcomes can be achieved, without the need for any postoperative pressure lowering or anti-inflammatory drops – which patients really appreciate."

LS: "You want to avoid pushing outward too much on the eye – if you see the eye rotate as you move the blade, you're pushing too far, and could potentially damage the back wall of the canal of Schlemm. If you're not pushing enough or you're not well seated within the canal, you'll only be superficially scraping the TM, and you won't get the full benefit of what the blade can do. You should ensure the blade is seated well within the canal so that it glides smoothly as you advance it."

IOP lowering and medication reduction: what to expect

NR: "Trabecular bypass has a reputation for being relatively safe, but lacking efficacy. With the KDB, we are seeing postoperative IOPs in the low teens, and getting 5–6 mmHg of pressure reduction, depending on whether cataract surgery was also performed."

LS: "Reviewing our KDB cases combined with cataract surgery, we are achieving IOP reductions of around 30 to 35 percent, in addition to eliminating one topical medication. In some cases, I've been able to take patients on three medications and uncontrolled IOP down to a controlled pressure without medication. Decreasing the number of eyedrops a patient has to take reduces the worry, hassle and cost associated with chronic topical therapy. It can truly have a profound effect on their quality of life."

On a Mission

Sitting Down With... Hugh Taylor, President, the International Council of Ophthalmology, Melbourne Laureate Professor and Harold Mitchell Chair of Indigenous Eye Health, Melbourne School of Population and Global Health, University of Melbourne, Australia

Why ophthalmology?

For a time I had my sights set on neurosurgery, but I realized that I'd be spending a lot of time in a dark room, and afterwards many of my patients wouldn't talk to me much. Ophthalmology presented itself as a terrific combination of both medicine and surgery, and the eye itself is a beautiful organ when you look closely, it's like a little jewel box.

How did you get involved in public health?

I worked with a program addressing Aboriginal eye health issues here in Australia, and that showed me how much one could do if one looked at the community. Then in 1980 I spent some time in Pakistan, examining children in the Afghan refugee camps, and examined a couple of thousand children in around four days. Based on those findings, and sitting down with the WHO, UNICEF, and the UN High Commissioner for Refugees, we ordered treatment for one and a half million people. This allowed me to help many more people than I could by just treating my patients one at a time. It showed me the power of a public health approach and of dealing with much larger groups.

One of your goals is to eliminate trachoma – how close are you to achieving it?

Australia has the dubious distinction of being the only developed country that still has trachoma, and it really has been a national disgrace. That said, I think we're making some very good progress – in the last eight years, we've reduced the rates from 21 percent on average, to less than 5 percent. So I think we're well on target for eliminating trachoma as a public health problem by 2020.

I've also been very involved in global efforts, and the work going on is truly breathtaking. A huge effort has been made over the last two years in mapping all of the remaining communities that have trachoma, and something like 150 million people are receiving antibiotic treatment this year. Trachoma may not be fully eliminated in every country by 2020, but a lot of work has been done, and I'm confident that we're going to come very close.

How do you get people in positions of power to make meaningful changes to public health?

Firstly, it has to be evidence-based. You need to have firm data to show what the problem is, and firm data and recommendations for the solutions. Politicians and policymakers want solutions, they don't want to hear problems, they've already got more than enough of those. Next, make sure you have broad sector or stakeholder support. Because if one group approaches the minister or secretary one day and says "We should do X," and then somebody else comes the next day saying "We should do Y." It's all too easy for the minister to say "These guys don't know what they're talking about. Forget it!"

If you can get everybody singing from the same hymn sheet, you're much more likely to have a powerful presence. You've also got to be persistent – keep at it, and don't walk away if you're rebuffed. And make sure your proposal has community support and endorsement.

What would you consider your career highlights?

There are a number of things I'm proud to have worked on – such as the link between UV exposure and cataracts, ivermectin use for the terrible blinding scourge that is river blindness, and being involved in some ground-breaking work on excimer laser treatment of astigmatism and higher degrees of myopia. Another highlight and lasting legacy was the establishment of the Centre for Eye Research Australia which has become one of the leading eye research institutes.

Something else that sticks out to me is a photograph on my notice board. It shows the former Minister of Health, who later became the Attorney General of Australia, holding a plain labelled packet of cigarettes that has a big photograph of an eye on it. My colleagues and I did a lot of work on the link between cigarette smoking and cataract, and macular degeneration. Later, I realized that this data had sat around in dusty journals for years, and nothing had happened. So I went to the Australian cancer council and told them we needed to start publicizing the harmful effects of smoking on the eye. Eventually, we had TV commercials and warnings on packets, and this was later picked up in the UK, Thailand, and many other countries. To have the former Minister of Health announce the plain packaging of tobacco products, and again to emphasize that it was eye-related, was really gratifying.

What tips would you give to young researchers hoping to make their own mark on the field?

Good research takes a lot of sustained energy. You need to have a discrete and achievable target that you're working towards, and you shouldn't try to do too much all at once – target a particular area. And make sure that that area, if you can unlock it, is important and relevant. Research that sits in a lofty journal is fine, but you want research that goes to the next step, and helps improve lives.

Looking back at your career so far, is there anything you would change?

I've had such a great time. It's been a real privilege to be an ophthalmologist, to do the research I've done, and work with the people I have. One only gets to do all these things with a lot of teamwork and collaboration.

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