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The powerful magnification in this fundus image montage highlights the Iluvien micro-implant like the bright yellow anther in a stargazer lily. Small enough to fit into a grain of rice 52 times, the intravitreal implant still packs enough power to provide a consistent and continuous therapeutic microdose of fluocinolone acetonide for up to 36 months. While its tiny size can make visualization challenging, this hidden gem is still working hard and providing treatment for the patient.

Credit: Joshua Mali, MD.

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50 John Berdahl, Partner at Vance Thompson Vision, Founder and CEO of Equinox, Sioux Falls, South Dakota, USA.
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ophthalmology is in a constant state of flux. Almost every day, a new technology is introduced, a new technique is perfected, a new voice heard. It is this constant change that makes ophthalmology so exciting – it never sits still. It seems fitting, then, that this issue focuses on innovation and change. Whether a change of thought, a change in practice, or a change in technology, ophthalmology must always move forward. In NextGen (page 42), Sneha Konda and Bala Ambati discuss which MIGS procedures are available today, while casting an eye on those still to come. In Sitting Down With…, John Berdahl talks about the future of healthcare – both here on earth and in outer space – but also reflects on his past. On page 14, Ningli Wang explains how the accessibility and affordability of cataract surgery in China has improved – but why there is still much more to achieve.

Like all our contributors this month, we believe that change is good (often essential) and in that spirit, we are revamping our Power List for 2019. Yes, the list will still celebrate the most influential figures in the field, but instead of selecting the Top 100 ophthalmologists, we are looking for half that number in a more exclusive list; specifically, 50 of the best inventors, mentors, emerging leaders, surgical pioneers and champions of change... With our “Five Top Tens,” we hope to showcase the best, the brightest, and the most forward-thinking that the world of ophthalmology has to offer.

You, The Ophthalmologist community, must decide who will appear on this literal “short list.” If you know a doctor who’s fighting for institutional change, a master surgeon who’s always breaking new ground, or an educator generous enough to focus on shaping the next generation, please put them forward: http://top.txp.to/powerlist2019. Be fair, be kind, but most importantly, be honest. We look forward to seeing your nominations.

Phoebe Harkin
Associate Editor
Restoration Project

Californian researchers have successfully restored sight to blind rats in a landmark study

The saying goes: “When it’s gone, it’s gone” – but what if that wasn’t the case in sight loss caused by severe retinal degeneration? That’s what a team at the University of California, Irvine School of Medicine, set out to prove in a breakthrough study (1). Following fetal retina sheet transplants, the researchers discovered that neurons in the vision centers of blind rats’ brains functioned normally.

“It’s been known that retinal sheet transplants can integrate into the degenerated eyes and allow the animals to detect light. But, beyond rudimentary light detection, it was not known how well the visual system in the brain functioned with the newly integrated retinal transplant,” said David Lyon, Associate Professor of Anatomy and Neurobiology at the University of California, Irvine, in a statement to UCI.

“In this study, we found that neurons in the primary visual processing center perform as well as neurons in animals with normal healthy retinas,” he said. The donor cells were sensitive to various attributes of visual stimuli – including size, orientation, and contrast – as early as three months following surgery. “These results show the great potential of retinal transplants to treat retinal degeneration in people,” said Lyons. “Though more research is needed to determine effectiveness and acuity” (1).

References
Sight Unseen

Are traditional glaucoma tests failing to detect central vision damage?

Glaucoma is a leading cause of irreversible blindness. It has no symptoms and causes no pain, but can lead to complete vision loss if left untreated. Visual field tests are the current standard of care for detecting glaucoma – but they may not be for much longer. According to a study by Columbia University’s Irving Medical Center, the test significantly underestimates the severity of the condition by failing to identify macular damage (1).

“When looking for signs of early glaucoma, clinicians tend to focus on loss of peripheral vision and seldom on the macula,” said Donald C. Hood, Professor of Ophthalmic Science at Columbia University, who co-authored the study. “Our work has shown that damage can and does occur in this area, and the most commonly used field test can fail to detect most of the damage.”

To find out just how much damage is missed, researchers examined 57 eyes from patients diagnosed with early-stage of glaucoma using two different visual field measures – the 24-2 and 10-2 tests. The results were significant. “We found that in using the 10-2 visual field over 75 percent of patients diagnosed with early glaucoma had central vision loss,” said Hood.

As a result, he recommends clinicians test all patients suspected to have glaucoma using the finer grid 10-2 test, supplemented by macular spectral-domain optical coherence tomography, within their first two visits. According to Hood, the alternative method comes at no extra cost and adds just 10 minutes to diagnosis time – yet significantly increases the accuracy of glaucoma diagnosis.

References
Ancient Roots

• Researchers at Johns Hopkins University School of Medicine appear to have uncovered an “ancient” light-sensing mechanism in modern mice (1) – and it is likely found in human retinas too. The team was researching the biochemical pathways of “non-image forming” photoreceptors (intrinsically photosensitive retinal ganglion cells or ipRGCs), when they discovered that one subtype (M4) didn’t use the previously discovered phospholipase C pathway but something novel: HCN-channel-mediated phototransduction. And, perhaps more surprisingly, subtype (M2) appears to use both mechanisms. “Some evolutionary biologists have proposed that […], through evolution, these two mechanisms separated into different cell types. Our research seems to provide evidence that photoreceptors containing both light-sensing mechanisms may still exist in modern mammals,” said King-Wai Yau, a professor of neuroscience, who led the study.

End to AMD injections?
• A Phase II clinical study has trialed an implantable, refillable drug delivery system for wet AMD. The device – no bigger than a grain of rice – contains a refillable reservoir of Lucentis and is implanted under the eyelid. In the study, led by Wills Eye Hospital in Philadelphia, some patients were able to go 15 months between treatments. Researchers hope the device will provide an alternative to the current standard of care for AMD – monthly injections – and result in better visual outcomes. “Fewer injections and office visits is exciting,” said Carl Regillo, Chief of Retina Service and Professor of Ophthalmology. “If you’re a week or two late for a visit from time to time, you may have a decline in vision, and you can’t always recover from that. It’s a relentlessly progressive disease (3).”

References
Accordingly, the schedule for monitoring should therefore be determined by the treating physician based on the individual patient's response. For DMO, initiate treatment with 1 injection/month for the first 12 months of treatment. There is no requirement for monitoring intervals to be shorter than 1 month. Discontinue if visual and/or anatomic outcomes indicate that the patient is not benefiting from the treatment. Treatment should be discontinued if myopic CNV is a secondary indication. Additional doses may be administered if visual and/or anatomic outcomes deteriorate, or if there is a new manifestation of the disease. The schedule for monitoring treatment should be determined by the treating physician. The interval between 2 doses should not be shorter than 1 month. Racemic and/or focal treatment. No specific studies have been conducted. Available data do not support the need for a dose adjustment. Elderly population: No specific considerations are needed. Limited experience in patients over 75 years old. Pandemic population: No data available. Contraindications: Hypersensitivity to active substance or any component, active or suspected ocular or periocular infection, active severe intraocular inflammation. Warnings & precautions: As with other intravitreal therapies endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and idiopathic tractional macular hole have been reported. Aptic injection technique is essential. Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. Patients must report any symptoms of endophthalmitis or any of the above mentioned events without delay. Increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, special precaution is needed in patients with poorly controlled glaucoma (do not inject while the intraocular pressure is >30 mmHg). Immediately after injection, monitor intraocular pressure and perfusion of optic nerve head and manage appropriately. There is a potential for immunogenicity as with other therapeutic proteins; patients should report any signs or symptoms of intraocular inflammation e.g. pain, photophobia or redness, which may be a clinical sign of hypersensitivity. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of vascular endothelial growth factor (VEGF) inhibitors. Safety and efficacy of concurrent use in both eyes have not been systematically studied. No data is available on concurrent use of Eylea with other anti-VEGF medicinal products (systolic or ocular). Caution in patients with risk factors for development of retinal pigment epithelial tears including large and/or high pigment epithelial retinal detachment. Withhold treatment in patients with rhegmatogenous retinal detachment or stage 3 or 4 macular holes, retinal break and do not resume treatment until the break is adequately repaired. Withhold treatment and do not resume before next scheduled treatment if there is decrease in best-corrected visual acuity of >3 letters compared with the last assessment, central foveal subfoveal haemorrhage, or haemorrhage >50% of total lesion area. Do not treat in the 28 days prior to or following performed or planned intravitreal surgery. Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last injection. Not recommended during breastfeeding. Excretion in human milk: unknown. Male and female fertility impairment seen in animal studies with high systemic exposure not expected after oculocutaneous administration. There is evidence of local side effects. Effects on ability to drive and use machines: Possible temporary visual disturbances. Patients should not drive or use machines if vision is impaired. Undesirable effects: Very common: Visual acuity reduced, conjunctival haemorrhage (Eylea phase III studies: increased incidence in patients receiving anti-thrombotic agents), eye pain. Common: Retinal pigment epithelial tear (known to be associated with wAMD, observed in wAMD studies only); detachment of the retinal pigment epithelium, retinal detachment, vitreous haemorrhage, cataract (nuclear or subcapsular), corneal abrasion or erosion, increased intraocular pressure, blurred vision, vitreous flakes, vitreous detachment, injection site pain, foreign body sensation in eyes, increased lacrimation, eyelid oedema, injection site haemorrhage, punctate keratopathy, conjunctival hyperaemia. Serious: COWS & – in addition- blindness, culture positive and culture negative endophthalmitis, cataract traumatic, transient increased intraocular pressure, vitreous detachment, retinal detachment or tear, hypersensitivity (during the post-marketing period, reports of hypersensitivity included rash, pruritus, urticaria, and isolated cases of severe anaphylactic/anaphylactoid reactions), vitreous haemorrhage, cataract, retinopathy, lenticular opacities, corneal epithelial defect/erosion, vitritis, uveitis, iritis, iridocyclitis, anterior chamber flare, arterial thromboembolic events (AETEs) are adverse events potentially related to systemic VEGF inhibition. There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. As with all therapeutic proteins, there is a potential for immunogenicity. Consult the SmPC in relation to the side-effects. Overdosage: Monitor intraocular pressure and treat if required. Incomparabilities: Do not mix with other medicinal products. Special Precautions for Storage: Store in a refrigerator (2°C to 8°C). Do not freeze. Unopened vials may be kept at room temperature (below 25°C) for up to 24 hours before use. Legal Category: POM. Package Quantities & Basic NHS Costs: Single vial pack £83.00, HS Number(s): EU/1/127379/002. Further information available from Bayer plc, 400 South Oak Way, Reading RG2 5AD, United Kingdom. Telephone: 0118 206 3000. Date of preparation: July 2018. Eylea® is a trademark of the Bayer Group.
**Through the Eye of a Needle**

**Could a double-layered eye patch answer common drug delivery problems?**

Ocular drug delivery has its challenges; namely, that it requires high systemic doses, frequent topical doses (poor bioavailability and increased likelihood of side effects) or somewhat invasive intravitreal injections (not exactly welcomed by patients, so a non-compliance burden). Now, researchers at Nanyang Technological University, Singapore, believe they have found the answer... But it does still look like a miniature medieval torture device (1).

What is it?
A flexible eye patch with an array of detachable methacrylated hyaluronic (meHA)-based microneedles that are capable of releasing two different drugs at two different rates.

How does it work?
The microneedles are fabricated with a double layer of meHA and standard HA – which can act as micro-reservoirs for one or two therapeutic compounds, allowing biphasic controlled release. The meHA shell retains its structural integrity as a sharp point, dissolving slowly, while the HA-drug contained within the shell allows more rapid release after the microneedles have penetrated the ocular barrier. In theory, two drugs could work in tandem to offer a potentially more effective treatment for a variety of ocular diseases.

How is it applied?
Much like a contact lens. The patch is placed on the eye, the microneedles detach from the substrate, which can then be peeled away – all within 60 seconds.

And the benefits?
According to Professor Peng Chen, who led the study, "high drug bioavailability compared with conventional topical administration, much better patient compliance and safety compared with conventional intraocular injection, high efficacy due to controlled drug release kinetics and, most importantly, the potential to use a combination of drugs.”

What’s next?
In the paper, Chen and his team assessed quick release of an anti-inflammatory compound (diclofenac) and sustained release of anti-VEGF to counter corneal neovascularization in an alkali burn-injury murine model – but the list of potential applications is long. “There are no apparent limitations to the type of drugs the patch can deliver. Our ultimate goal is to translate the technology to treat other ocular diseases,” says Chen.

**Up in Smoke**

**Small-particle pollution could increase glaucoma risk in older men**

Researchers have found a link between long-term air pollution and intraocular pressure – but only in those susceptible to oxidative stress. In the innovative study, the team collected data from 419 older men, measured each participant’s eye pressure – and collected a host of other health factors – and analyzed the data against a black carbon modeling program. Black carbon – a common air pollutant – is smaller than 2.5 microns in diameter and capable of penetrating deep into the lungs, and the bloodstream. They found that men with certain genetic variations – namely, those vulnerable to oxidative stress – experienced increased eye pressure.

“Oftentimes, when we think about glaucoma we think about risk factors such as age and genetic predisposition – and we don’t think about the environment,” said Jamaji Nwanaji-Enwerem, PhD candidate at Harvard Medical School and lead author of the study. “But one thing we’re starting to appreciate more is how the environment impacts health outcomes (1).”

The findings highlight the potential impact of environmental factors on IOP-related disease, and so Nwanaji-Enwerem and his team hope the study will be useful in future policy or public health initiatives.

**References**
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In My View

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

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

Contact the team at edit@theophthalmologist.com

The China Study

Accessibility and affordability of cataract surgery has improved in China – but there is still more to achieve

By Ningli Wang, Director of Beijing Tongren Eye Center, Beijing, China

Access to healthcare has improved dramatically in China over the last two decades. Before 2009, there were only three basic medical insurance systems. But thanks to persistent efforts from the government – and significant financial support – 95 percent of Chinese people are now covered by medical insurance. At present, this insurance covers between 70 and 80 percent of cataract surgical expenses. Not only that, the government initiated the “One Million Cataract Blindness Project” in 2009 to provide free cataract surgeries for poorer patients, with additional financial and medical support from NGOs. To speak from the perspective of ophthalmic resources in China, the number of ophthalmologists reached 37,000 in 2018 – 1.5 ophthalmologists per 50,000 people. 36 percent can perform cataract surgery independently, and of those, 34 percent can perform phacoemulsification. Currently, over 85 percent of hospitals have established ophthalmology departments, with 88 percent providing cataract surgery independently. These developments have all greatly increased access to affordable cataract surgery in China.

After the medical reform in 1998, an increased cataract surgical rate (CSR) saw the number of cataract operations performed per million population rise from 370 in 2000 to 2,205 in 2017. However, the CSR differs greatly in regions, being highest in Shanghai (4,251) and lowest in Hubei (763). Interestingly, in Shanghai, private hospitals completed more cataract surgeries than public hospitals, indicating that private hospitals are becoming an important force in preventing and treating cataract blindness. Furthermore, the cataract surgical coverage (CSC) in China among patients with severe cataract-related visual impairment and blindness has increased from 36 percent in 2006 to 63 percent in 2014, while good visual outcomes have increased from 47 percent to 62 percent in cataract-operated eyes.

But change is not happening as fast as some would like. Despite significant improvement, CSR in China it is still low compared with countries like the US (11,000) and India (6,000). Around 7.58 million patients with cataract-related visual impairment or blindness still await surgery in China. If we want to achieve a CSC of 95 percent, our CSR needs to reach 8,000. Not only that, even though the number of ophthalmologists has exceeded the standard defined by WHO in the “Vision 2020” initiative, most are in economically developed urban areas, with few working in rural zones, where the CSR and CSC are low. Of the 75 percent of county hospitals that can perform cataract surgery, most have only one or two cataract surgeons. Given the lack of experienced surgeons and qualified surgical treatment in county hospitals, some rural patients have to travel a long distance to seek surgical treatment in large cities – which can pose a problem; elderly patients who have difficulty traveling my not receive proper treatment. Though experienced ophthalmologists from provincial or municipal hospitals could come to county hospitals to operate on local patients, it would not substantially improve the surgical ability of local ophthalmologists or the eye care service the hospital provides.
A national training program called “Standardized Training to Elevate Eyecare in Rural China (China STEER)” has been established to improve the capability of county level hospitals to deliver high-quality eye care, including high-quality cataract surgery. Started in 2016, the strategy is set to redress existing CSR disparities between urban and rural areas. Given the expected rise in CSR – paired with a rapidly aging population – the financial burden of medical insurance system is expected to grow as well. Therefore, a multipronged strategy with new fundraising channels is needed to ensure patients receive the highest quality cataract care.

Easing the Pressure

It’s time to change the way we think about premium lenses for glaucoma patients

By I. Paul Singh, President of The Eye Centers of Racine & Kenosha, Wisconsin, USA

The advances in surgical glaucoma technology have got doctors thinking about the possibility of premium lens implantation in a glaucoma patient – but the question is: why and when?

As in many areas of ophthalmology, there has also been an increased emphasis on improving quality of life and patient satisfaction in the glaucoma patient. With the introduction of microinvasive glaucoma surgery (MIGS) technology, we are now better able to reach that goal. Personally, I’m a big advocate of early intervention. If one of my patients has mild or moderate glaucoma, is on topical meds or has IOPs not at target, I will offer some type of MIGS procedure. The new glaucoma surgeries have allowed us to reduce the drop burden for our glaucoma patients, improve compliance, and, due to the high safety profiles, intervene earlier in the disease process.

Another key characteristic of these MIGS procedures is the improved predictability of post-operative refractive outcomes compared with traditional glaucoma surgeries (such as trabeculectomy and tube surgeries). To me, it is no longer acceptable to “just bring the IOP down,” but rather, we should strive to attain target IOP, while maintaining or even improving quality of life. Therefore, why shouldn’t our glaucoma patients deserve premium options during cataract surgery?

Due to the unpredictable post-operative refractive outcomes of traditional glaucoma surgery, and the fact that we would wait to perform surgery until the patient had more advanced glaucoma, many of these patients were not good candidates for premium IOLs. Now that we are intervening earlier in the disease course (healthier fields and ONH), getting more and more patients off drops (decreasing the chance of ocular surface disease and noncompliance), premium IOL technology is often part of the IOL discussion. For me, toric IOLs are a great way to start incorporating premium lenses. There is really no downside to reducing post-op uncorrected astigmatism. On the whole, if a patient has corneal astigmatism – any more than 0.75 diopters – I feel it is worth addressing with a lens; studies have demonstrated improved contrast sensitivity in low light conditions when correcting this level of astigmatism. Even if a patient has advanced glaucoma, I use a monofocal toric lens or accommodating toric lens wherever possible. Sure, the patient may need additional surgery or even a standard trabeculectomy in the future, which could lead to wearing glasses or a change in prescription, but I always explain that to the patient ahead of time.

Historically, one would shy away from multifocal lenses in glaucoma patients because of the potential loss of contrast sensitivity inherent to these lenses, given that, as mentioned earlier, loss of contrast is one of the earliest manifestations of glaucomatous optic neuropathy. The newer lower add multifocal and EDOF lenses claim to offer less loss of contrast sensitivity than the previous higher add multifocal lenses, which has allowed us to re-evaluate the use of multifocal lenses, especially in the mild glaucoma patient. Another choice for me, the Crystalens accommodating IOL, has been a safe lens to implant in glaucoma patients as it is an aspheric monofocal optic that does not negatively affect quality of the image. I’m currently running my own study, looking into the mean deviation of glaucoma patients’ visual field pre and post cataract surgery. By using ray tracing (iTrace, Tracey Technologies), we are also comparing HOA and MTF between Crystalens and various multifocal IOLs. Data should be available by ASCRS 2019.

I’m aware not everyone feels the way I do. As glaucoma surgeons, we are often primarily concerned with getting pressures down, and we sometimes don’t think it is worth using a premium lens, such as toric lens – but I think that paradigm is starting to change.

We have already seen a huge shift here in the US, especially now, when there are so many options available. Don’t dismiss the need for maximizing refractive outcomes in glaucoma patients – they deserve the same uncorrected quality of vision as everybody else.
The Real Power of Low Energy

Highlights from Ziemer Ophthalmic Systems AG’s Satellite Symposium, held on September 22, 2018, at the XXXVI ESCRS Congress, Vienna, Austria.

If we want to crack a hazelnut, we don’t reach for a sledgehammer. Likewise, effective ophthalmic surgery requires precise application of subtle force. Fortunately, Ziemer has hard-wired subtlety and precision into its Z8 system: high-frequency, low-energy femtosecond laser pulses, guided by intra-operative OCT, bring new delicacy and accuracy to the most difficult procedures. How are surgeons applying the new femtolaser system in their daily practice? To find out, Ziemer convened a symposium at the 36th ESCRS in Vienna (September 22, 2018).

Featuring:
Chair: Theo Seiler, MD, PhD, Professor, IROC AG, Zurich, Switzerland
Shady Awwad, MD, Associate Professor of Ophthalmology, Head Cornea and Refractive Surgery Division, American University of Beirut Medical Centre, Beirut, Lebanon
Soon-Phaik Chee, MD, Professor, National University of Singapore and Duke-National University of Singapore Graduate Medical School, Singapore
Jod Mehta, MD, Associate Professor, Head of the Corneal and External Eye Disease Service, Singapore National Eye Center and Duke-National University of Singapore Graduate Medical School, Singapore
Gerald Schmidinger, MD, Surgical Senior Physician at the Department of Ophthalmology, Head of the cornea bank, head of the outpatient clinic for corneal diseases, Medical University of Vienna, Austria

Part I: Low Energy, High Impact

Scarless Femto-Pterygium surgery

Jod Mehta

Femto-Pterygium, a new indication for the femtolaser, is made possible by two critical features of the Z8: the high numerical aperture and the articulating hand piece. The former permits the ability to cut through opaque tissue such as the conjunctiva; the latter allows the surgeon to excise a graft from the superior bulbar surface by rotating the eye down to complete the surgery. In previous work, we showed that Femtosecond Laser-Assisted Pterygium Surgery (FLAPS) worked very well in porcine eyes (1). Subsequently, our first-in-man FLAPS trial (2) reported similarly encouraging results: rapid creation of ultrathin grafts, high case-to-case reproducibility, good cosmesis, and minimal scarring at both bulbar surface and graft site. These results are partly due to the reproducibility of FLAPS: standard deviation and inter-surgeon differences are lower for 60 than for 100-micron grafts. The thickness of FLAPS is also significant: by restricting CAG thickness to 60 microns, we stay within the conjunctiva epithelium, and thereby avoid disrupting Tenon’s capsule. As conjunctiva thickness changes with age, 60 microns will encompass 98–99 percent of individuals (3); shallow grafts help minimize scarring in older patients. Furthermore, the gentle, low energy Z8 causes little inflammation; hence faster and better healing, and what we see clinically (Figure 1) is consistent with OCT angiography data showing rapid revascularization of graft sites (Figure 2). Moreover, scarless healing allows us to re-use the donor site if needed, for example, in glaucoma surgery.

We’ve now compared 30 femto-pterygium cases with 120 standard...
ptyerygium surgeries – and the results are striking (Sidebar 1): i) a mean graft thickness of 74 microns with a graft-lift time of about 5 seconds, ii) time savings of about 5-10 minutes per procedure, and iii) significant reductions in pain score and recurrence rates. The instrument also brings reassuring flexibility to the OR; if the patient moves during conjunctival incision, we simply reprogram the laser, re-dock it on the conjunctiva, and proceed as if it were a virgin cut – with the same outcome. In summary, FLAPS provides faster surgery, less scarring, and less post-operative pain than standard pterygium surgery. Overall, it standardizes procedures, irrespective of surgeon experience.

Sidebar 1
Femto-Pterygium procedures in humans

Femto-Pterygium forms precise, planar cuts, leaves conjunctival blood vessels still patent and functional, and reduces inter-surgeon variability in cut depth.

- 30 prospective patients
- Mean defect size: 5.8 x 9.1 mm
- Pre-set size: 7 x 10 mm
- Actual graft size: 6 x 9.7 mm
- Desired graft thickness: 60 µm
- Actual graft thickness: C 74.2 µm, P 74.8/75.3 µm
- Time to lift graft: 4.9 seconds
- No recurrences after one-year follow up

Figure 2. OCT angiography shows corneal graft revascularization by one month post-surgery and reduces inter-surgeon variability in cut depth.

Low energy versus high density

Soon-Phaik Chee

When faced with a very dense nucleus and a thick, leathery posterior plate, one’s instinct is to use more energy. In fact, it’s possible to manage dense cataracts with low energy levels – by applying high-frequency pulses of nanojoule energy. Such an approach also brings a number of advantages: smoother capsulotomies, lower risk of tag formation or anterior capsule rip, cleaner fragmentation, and lower levels of bubble formation.

Correct technique, however, is essential to getting the most out of the low-energy approach. In particular, we should modulate our procedure according to cataract density. For example, with a moderately dense cataract I would cut eight segments, and keep the offset at 600-700 microns. With denser cataracts, I might cut 16 segments, which makes it simpler to separate the nucleus into smaller pieces to allow the fragments to be easily mobilized from the capsular bag and emulsified. This involves lateral separation of the uncut posterior and peripheral portion of the nucleus.

Similarly, fragmentation of a dense posterior polar cataract is made much easier by pre-cutting it into eight segments without adjusting the posterior offset. This helps the surgeon to remove the fragments in a stepwise manner without rotation. You can apply the same technique even to a dense brown cataract; you simply need to impale the nucleus deeply and then separate the fragments with the second instrument.

In white intumescent cataracts, I find it helpful to use capsular dyes to show up incomplete capsulotomies or areas of capsular tags or sub-capsular fibrosis. Their presence requires one to increase the capsulotomy energy to ensure you cut through any fibrotic strands. Often, dense cataracts are accompanied by weak zonules; if so, I use a capsular bag hook followed by a capsular tension ring, as this approach prevents the vitreous from coming forward.

So the Z8 makes even very dense cataracts relatively simple – the laser does most of the segmentation, and pre-cutting the nucleus helps the surgeon manage complicated cases while preserving both cornea and posterior capsule. The lower energy results in fewer bubbles produced, which both improves visibility and helps surgeons to avoid bubble-induced distension of the posterior capsule.

In summary, a variety of dense cataracts can be more efficiently and safely managed with femtosecond laser-assisted cataract surgery (FLACS) than with manual cataract surgery, but optimal outcomes require adjustment of parameters and technique.
Deep anterior lamellar keratoplasty (DALK) is as difficult, as it is beneficial. Can the femtolaser make it more accessible? In my experience, a femtosecond laser is superior to the manual approach; it achieves better side-cut geometry, more accurate cut-depths (both for side-cut and for lamellar dissection), better trephination centration, less risk of donor cell damage, and OCT feature, which allows intra-operative adjustments of the laser.

Clinical outcomes are promising: one group achieved a Type I bubble in each of 14 cases (7), with zero intraoperative laser-related complications (guiding tunnel set at 50 microns from the endothelium, C 74.2mm diameter trephination); my own group achieved Type I bubbles in 92 percent of 36 eyes (8-8.5 mm diameter trephination, guiding tunnel set at 80 microns from endothelium).

Part II: The Inside View

Femto-DALK with guiding tunnel and OCT

Gerald Schmidinger

Deep anterior lamellar keratoplasty (DALK) is as difficult, as it is beneficial. Can the femtolaser make it more accessible? In my experience, a femtosecond laser is superior to the manual approach; it achieves better side-cut geometry, more accurate cut-depths (both for the side-cut and for lamellar dissection) and better trephination centration during applanation (the OCT feature allows intra-operative adjustment of the laser). Furthermore, femto-DALK causes less donor cell damage than manual techniques.

Applying femto-DALK to an eye with advanced keratoconus (www.femtoldv.com/femto-dalk) illustrates how intra-operative OCT enables adjustment of cut depth and maintenance of a safe 150-micron margin. This approach clearly reduces the risk of anterior chamber penetration.

But perhaps the most advantageous aspect of femto-DALK is its ability to form guiding tunnels of precise depth to direct the DALK cannula. This enables deep cuts to be made safely within 50-80 microns of the endothelium, with a high degree of precision (actual distances and intended distances to endothelium are close, with low standard deviations, in both human and porcine eyes (7)).

In conclusion, the Ziemer Femto LDV Z8 is transforming DALK surgery. Intra-operative OCT replaces subjective judgments with unambiguous intraoperative measurements, simplifies and standardizes the procedure, and makes the big bubble step more reproducible. Inexperienced surgeons wishing to participate in DALK will find the Z8 invaluable.

Conclusions

The symposium participants appeared to reach consensus: the enhanced precision and reduced energy of Z8 are transforming established techniques and enabling new procedures. Intra-operative visualization of the entire cornea permits confident positioning of keratoplasty incisions for optimal safety and outcomes. Similarly, OCT-directed positioning of guiding tunnels close to Descemet’s membrane increases confidence, making DALK far more accessible.

Furthermore, the uniquely low energy delivered by Z8 permits delicate procedures, such as ring insertion, without incurring costs related to bubble formation or bridge generation, and also results in rapid vascularization and straightforward healing. Kindness is not the same as weakness, however: the low energy laser can help fragment the densest cataracts, making difficult cases routine.

Thus, with Z8, the surgeon gets not different limitations, but extended capabilities. The instrumentation enables new procedures, such as femto-pterygium, while transforming older procedures, such as DALK and post-phaco LASIK. And that is the real power of low energy.

References

Intra-operative OCT and intracorneal ring segments for keratoconus

Shady Awwad

Corneal rings are essential in keratoconus management; they flatten the central cornea and steepen axis 90 degrees away from the incision. Depth is a key aspect of intrastral ring segments success and safety. Shallow tunnels can lead to anterior stromal melting and neovessels. Deep tunnels can result in Descemet’s perforation due to gas bubbles or due to direct impingement of the ring segments. Cross-linked corneas may also cause problems as they might look deceptively thick on Scheimpflug pachymetry. Finally, advanced keratoconus can raise centration problems, which may be difficult to resolve intraoperatively without real-time pachymetry guidance. Such challenges may cause surgeons to avoid all except the simplest cases of keratoconus.

Now, the Z8 is transforming keratoconus management. Key features include intra-operative OCT and a very low energy laser. The latter enables precise, shallow cuts with minimal collateral damage, and without leaving bridges. The former allows the surgeon to check the depth of the planned tunnel intraoperatively in real time, make necessary adjustments, and then check the actual depth after tunnel creation. Thus, the Z8 empowers surgeons to confidently accept the most challenging corneas. It provides unparalleled safety together with extraordinary precision and reliability; the outcomes speak for themselves. I believe it is the ultimate keratoconus platform.

Free LASIK after Femto-Cataract with Premium IOL

Theo Seiler

Multifocal IOLs have intrinsic limitations; for example, glare and halo become significant where residual astigmatism is 0.5 diopters or less. And that’s why many multifocal IOL recipients are unhappy. Our own data (108 patients) show that 40 percent of patients are dissatisfied with their vision (their mean satisfaction score, on scale of 1-4, was 2.1) for reasons including astigmatism, myopia, hyperopia and higher order aberrations.

Correcting these issues with Z8-mediated LASIK is ideal, as it allows me to select which aberrations to address; for example, so as to modulate only those that interfere with near vision. And the patients appreciate it: one month after surgery, the mean satisfaction score increased from 2.1 to 3.6, and 90 percent of previously dissatisfied patients said they would choose the procedure again.

Therefore, “giving” LASIK to every multifocal IOL recipient patient who requires it should increase overall patient satisfaction. Bundling LASIK with multifocal IOL implantation, however, has economic implications. If we assume that femtoLASIK costs $1300, and that 26 percent of multifocal IOL patients subsequently require corrective LASIK, we can calculate the extra cost per multifocal IOL procedure: $1300 x 0.26 = $338. And that gives us an economic footing from which to offer patients a package that includes LASIK “for free,” if it is required to correct residual refractive errors.
The ophthalmologists we speak with often point out that they chose ophthalmology because it is constantly changing and evolving, which, in turn, gives them great scope to continuously improve patient outcomes.

Few would argue that ophthalmology is one of the fastest moving areas of medicine; relentless improvement and innovation are its beating heart.

The careers of John Marshall and Bert Massie were driven by their ability to constantly seek inspiration for their ophthalmic inventions from other walks of life. Here, we tell their stories, and shed light on a handful of other “out of left field” ideas.
Eye of the Magpie

Researchers have always stolen shiny new techniques from colleagues in other fields – and some ophthalmologists are particularly effective thieves.

By John Marshall

Scientific methods are often applicable in many different areas: hence, developments in one field frequently enable progress in another. Ophthalmology has been one of the biggest beneficiaries of this process. Indeed, without the technologies and instruments we’ve taken from other disciplines and adapted for ocular applications, our specialty would be virtually unrecognizable. I've always been happy to acquire new treatment options for the eye; here are some of my favorite examples.

From silicon circuits to corneal surgery

Back in the 1960s, I did my PhD on laser damage to the retina, sponsored by the Royal Air Force (RAF). They were worried about the potential of laser weapons, so I spent a great deal of time developing safety data to protect air crew. This eventually resulted in me working with the International Committee of the Red Cross, addressing the United Nations, and obtaining a Geneva Convention banning use of antipersonnel laser weapons. From there, it was a natural step for me to advise on laser safety in other environments. In particular, I helped develop good working practices for laser-mediated manufacture of microelectronic circuits. And once, during a factory inspection, it struck me that the laser could be a very special addition to the ophthalmology toolkit. I wrote up a patent, and that was the start of excimer lasers in eye surgery. Fifty million procedures later, I think I can say it was a valuable patent!

When we started laser-mediated refractive surgery, however, I had some concerns, particularly with regard to LASIK. The laser was slicing through millions of collagen fibers in the stroma: would that disturb the eye’s biomechanical properties? To answer that, we borrowed from engineering. In that discipline, investigators frequently have to calculate the strain that each component of a system will suffer under a given stress: for example, to assess how the elements of aircraft wheels will respond to the stress of landing. Engineers do this using an incredibly sensitive technique known as interferometry; and we applied it to the eye. With that resource, we could assess the strain associated with any kind of intervention, be it PRK, LASIK, cross-linking or cataract surgery. It was key to validating the LASIK approach.

From military range-finders to macular degeneration

More recently, I helped develop a new laser therapy concept for age-related macular degeneration (AMD). The advance had its genesis in a thorough understanding of retinal maintenance. Remember, retinal cells don't divide, therefore, they must cope with wear and tear without recourse to cell replacement. Rod photoreceptors get around this through the continual removal of aged pigment material at one end – older material is “bitten off” by pigment epithelium cells – and continual replenishment at the other. When you're young, the light sensitive portion of your photoreceptors is in effect, replaced every two weeks – even though the cells remain the same. Unfortunately, pigment epithelium cells get “indigestion” in later life and pass semi-digested waste products into Bruch’s membrane: the Bruch’s...
membrane gets clogged up, interfering with transport processes and contributing to further waste product accumulation and sequelae, such as accelerated ageing, a risk factor for AMD. My idea was to clean up Bruch’s membrane and thereby rejuvenate the retina. But how? Conventional lasers for treating retinal conditions were all thermal systems and heat flow would destroy the photoreceptors. Short pulsed lasers were designed for posterior capsulotomies, and have their effect by producing cavitation – a kind of micro-explosion. You can’t have that in the retina – it would result in hemorrhage. We had to design a new laser energy delivery system, using concepts derived from military range-finder technology – which I can’t tell you about! Our new laser has a large spot size and an incredibly short (nanoseconds) pulse duration and a pixelated beam. This permits photodisruption of selected regions of the pigment epithelium without the thermal conduction to overlying photoreceptors that you would get with conventional lasers, and without destroying large areas of pigment epithelium (which would starve the overlying photoreceptors). Photodisruption activates pigment epithelium cells to release matrix metalloproteinase, which unblocks Bruch’s membrane and thus modulates associated pathology.

Ellex has recently adopted and developed this concept into the Retinal Rejuvenation Therapy (2RT) product. Data from a three-year, randomized, multicentre clinical trial (1) in intermediate AMD are very promising (Sidebar), and I believe that our hypothesis is proven and this approach will have a significant impact and potentially massive savings on the use of drugs to treat neovascularization.

CRISPR, cleaner cornea

Ophthalmology also commandeers molecular techniques where appropriate: for example, CRISPR-mediated gene therapy. This approach, based on modifications of a naturally occurring antiviral defence system found in bacteria, permits precise excision of specific DNA sequences. With CRISPR, therefore, it is theoretically possible to treat autosomal dominant inherited disorders by cutting out the dominant negative mutation. Indeed, if several related defects are positioned closely enough in the gene, we can excise them all in a single step. Thus, as long as the patient has normal sequences on the complementary chromosome, the approach may modulate or even cure autosomal dominant disorders. CRISPR gene therapy was originally envisaged for simple dominant negative diseases like haemophilia – but now we are applying it to more complex diseases, including ocular conditions, such as inherited retinal dystrophies. My opinion is that the cornea is a more attractive gene therapy target than the retina: rather than dealing with non-dividing neuronal tissue at the back of the eye, you only need to get to the DNA in the easily-accessible dividing cells on the front of the eye. That’s

“With CRISPR it is theoretically possible to treat autosomal dominant inherited disorders by cutting out the dominant negative mutation.”
why we are targeting granular dystrophies, which are all caused by mutations in a small region of chromosome 5. As part of this effort, I'm assisting Avellino Labs, which is developing genetic screening for dystrophy, and also working with Tara Moore, our Head of Research at Ulster, to get our new therapy for corneal dystrophy into clinical trials. CRISPR for cornea really is the low-hanging fruit in ocular gene therapy, so watch this space!

Looking ahead

I expect ophthalmology to continue stealing from diverse fields. In particular, genetics will have a big impact on refractive surgery, and the development of rapid diagnostic systems will revolutionize healthcare in remote locations. For example, people are working on functionalized membranes that a patient could lick and insert into a smartphone to receive a rapid diagnosis anywhere. That could be a very important way of guiding critical therapeutic decisions in difficult environments, such as a space capsule. In the clinic, for example, in cases of red-eye, you really need to know if the condition is of bacterial, fungal or viral origin, so that you can appropriately treat it – get it wrong, and you could lose the eye. I look forward to seeing these kinds of advances appropriated for eye care, as others have been before them. Basically, as long as human ingenuity continues to produce attractive new innovations, the ophthalmology magpie will continue to feather its nest!

References

From Star Wars to a New Hope

With Bert Massie

Bert Massie worked in the aerospace industry for many years, developing his knowledge and expertise in adaptive optics and interferometry. At the height of his career, he followed a calling: advancing the field of ophthalmology by responding to the most pressing needs for retinal imaging. Since then, he has developed the RetCam, used worldwide in screening for retinopathy of prematurity, the Micron for eye research, and, more recently, the ICON – an improved wide-angle imaging system. Here, he shares his passion for entrepreneurship, and describes how innovations in ophthalmology have been driven by the evolution of sensors, microprocessors and lasers.

A curious mind

I'm a scientist and an engineer but I tend to think of myself as an entrepreneur. I don't think that this is something you learn – it is a natural and intense personal drive. It is evident in everything I do; it gets me out of bed early in the morning.

As a young child I was very curious about how things worked. In early grade school I took my toy electric train engine apart because I really wanted to know what all those gears did. I developed an interest in astronomy, and for many nights lay outside on a blanket to watch the stars appear in the evening sky. I knew all the constellations. For an entrepreneur curiosity is foundational, but must be complemented by a creative mind, and a self-confidence and drive to develop the ideas that originate in your mind. For example, as a teenager I built a 12” telescope to explore an idea about how to obtain color images of galaxies.

Aerospace adventures

My first real “creative” step was my PhD thesis, where I tested new ideas to measure the non-linear properties of solids using ultrasound with laser probes. Post graduate school I entered the aerospace field, and for 11 years I was involved in the Strategic Defense Initiative, nicknamed Star Wars, and in my last aerospace role I spent five years working in a senior position at the Lawrence Livermore National Laboratory,
which is a federal research facility in California, US, focusing on finding solutions to security-related challenges. In my aerospace career I was awarded over 25 patents in optics, I published the same number of journal articles, and I edited a reference book on optical technology. I developed techniques for interferometry – classically, interferometers make accurate measurements of optical components – and my most interesting project was a high-performance two-wavelength interferometer. Optical Coherence Tomography uses multiple wavelengths, but at that time the required “low-coherence” sources did not exist, so I had to use two lasers, which required a high level of sophistication. Following this, I developed a novel adaptive mirror for correction of atmospheric aberrations on imaging of space objects.

In my last position with the national laboratory, together with my colleagues, I developed a technique to image space optics through the turbulent atmosphere without using adaptive optics. This technique was proven in experiments between an object on a mountain top and a lower altitude telescope.

I enjoyed working in the aerospace industry, but from the very beginning of my career – since my undergraduate years, in fact – I sought an opportunity where I could help people with vision impairment regain their sight. I sought a role where I could focus on more meaningful goals.

Problems and solutions

When I decided to make a career in ophthalmology, I found that much of my extensive optics knowledge and experience was applicable. I started working on various ophthalmic solutions, including a non-contact ultrasound-based tonometer, which worked, but was too expensive to merchandise. As it often happens, through a random series of events, I met a very prominent physician - A. Linn Murphree - who introduced me to the challenge of wide-field imaging in children. The device developed by Dr. Murphree and his team did not adequately perform, and I picked where they left off. I redesigned the instrument from the ground up, and this became the RetCam.

RetCam was originally developed to image retinoblastoma but was quickly adapted to image retinopathy of prematurity (ROP). This disorder potentially afflicts infants born before 31 weeks of gestation and weighing less than 1250 g. There is significant ocular morbidity associated with ROP, which usually develops in both eyes. It is among the most common causes of childhood vision loss and often leads to permanent vision impairment.
We were told that we would sell a dozen units, but the RetCam was widely adopted and there are now over 2,000 RetCam units in use around the world. It can be operated by non-ophthalmologists, who can send images to a central facility, where they are professionally evaluated. It greatly reduces the labor costs and the time it takes for the problematic cases to be picked up. A point that is especially vital in developing countries; there are very competent clinicians working there, but they don’t always have the staff to screen every child. If diagnosis and treatment is timely, it is usually very effective and protects patients from lifelong blindness.

Answering the call

When I left the RetCam program, I focused on developing technology for eye and eye-brain research, using laboratory animals such as mice and rats, and introduced a retinal imaging microscope called the Phoenix Micron. Developing the mouse imaging system was quite difficult and there were times where I was certain that failure was just a day away. Nevertheless, the Phoenix Micron retinal imaging microscope became a reality. I was again told that I might be able to sell a dozen units – and we now have over 300 units in use in major institutions around the world.

At the age of 71, when I was about to retire, and with pressure from several sources, including several senior clinical leaders – I decided to return to clinical ophthalmology and develop a successor to the RetCam. The base technology for the RetCam had not changed since inception. Ophthalmologists had been complaining about issues with imaging patients from ethnic minority groups – those with darkly pigmented retinas – such as African Americans and Asians. The RetCam performed poorly with dark retinas and could not image adults. When the retina is dark, the light returned to the image sensor is lower than the scatter in the cornea. As a result, the image is lost in the haze.

In developing what became the Phoenix ICON my team and I accepted an absolute directive to develop high-contrast/high-resolution imaging even in darkly pigmented retinas, and in the process were able to also image adults – something RetCam had not been able to do. The Phoenix ICON design was a complete change from the RetCam and arose from a “blank sheet of white paper.” Getting the light in and to the retina without the scatter is quite difficult – these difficulties were overcome, but only by ignoring a number of classic ophthalmic rules along the way!

The Phoenix ICON lived up to its objectives and is a wide-angle retinal imaging system with high-contrast imaging and ability to image adults as well. I believe Phoenix ICON's capability has the potential to contribute to new areas such as melanoma; all this is the subject of clinical trials for validation. We also have plans to provide the technology to countries requiring humanitarian assistance: we’ve been talking to The Queens Jubilee Trust in the UK, who can help us answer the needs for these systems in India.

Working backwards

I begin my projects by first being certain that the right question is identified. For example, many times RetCam users asked for more resolution, but they really needed improved visibility, meaning higher contrast. Innovations such as the Phoenix ICON and Phoenix Micron need to not only be a technological advancement, but also an advancement that makes a useful difference. Accordingly, as a final and acid test before I launch a project, I imagine myself standing in front of the physician and showing the device; if I do not see excitement from the user, I do not proceed.

Innovations must make a difference, not just be different, and that is one of the most important reasons for the decision on pursuing a project. This means of evaluation has served me well.

N.A.(Bert) Massie, Ph.D., has more than 40 years of experience as a lead entrepreneur of a variety of optical-based technologies. He is currently working for the Phoenix Technology Group.
Vision Restoration in 2D

Can graphene and molybdenum disulphide really find another application in artificial retinas?

After years of speculation about the exact properties and possible uses of graphene, the material was finally properly isolated and characterized in 2004 – an achievement that was recognized in 2010 with a Nobel Prize in Physics for the two University of Manchester physicists, Andre Geim and Konstantin Novoselov. Since then, its applications have included solar cells, dental discs, inks and bioadhesives.

Now, graphene – along with another two-dimensional material, molybdenum disulphide – is being used to fabricate artificial retinas. Nanshu Lu from University of Texas in Austin, who led the first demonstration of the flexible device, acknowledges that research is still at an early stage, but scientists believe the device could one day help restore sight in people affected with retinal diseases, such as macular degeneration or diabetic retinopathy, which affect millions of people around the world, causing vision impairment followed by complete vision loss. Outside of ophthalmologic applications, it is also believed that the device – based on a few thin layers of graphene and molybdenum disulphide, as well as layers of gold, alumina and silicon nitrate – could be used to track brain and heart activity through electronic tattoos on the skin’s surface, possibly with the addition of transistors to amplify the brain or heart signal.

Current implants used to help with restoring vision in affected individuals are silicon based. Unfortunately, the results are often unsatisfactory, with distorted or blurry vision, which in part down to the rigidity and a flat shape of the silicon-based implants; they simply cannot replicate the natural curved shape of the retina. The novel device appears to adapt to the shape of the eye and mimic its structural features. It includes an external circuit board, which is used to store the electronics used to digitally process light, stimulate the retina and receive signals from the visual cortex.

Reference

The Small Print

From semi-conductors to sight-saving therapies: introducing PRINT Technology

The need to produce smaller, more sophisticated drug or drug-delivery particles presents a challenge to pharmaceutical manufacturers. So, how do you guarantee high batch reproducibility and dose uniformity on a commercial scale? Simple – you look to the industries who do it best. Or at least, that’s what Aerie Pharmaceuticals did when they acquired the rights from Envisia Therapeutics, Inc. to use Particle Replication in Non-wetting Templates – also known as PRINT® – technology in October 2017.

Integrating the precision of the semiconductor industry, with the efficiency and scalability of plastic films-based manufacturing, PRINT is capable of producing particles as small as a nanometer. It is compatible with a wide variety of drugs – including many classes of small molecules and biologics – and can be used to make combination products with multiple active ingredients.

Its versatility hasn’t gone unnoticed. Aerie is using the PRINT platform to produce injectable intraocular implants, composed of a bio-erodible polymer that steadily releases drug over 4–6 months, for its two lead clinical development programs in retina – AR-1105 (dexamethasone) and AR-13503 (Rho kinase/Protein kinase C inhibitor) – for conditions such as diabetic macular edema and neovascular AMD. Aerie is also evaluating the use of PRINT-produced sustained-release therapies in glaucoma and ocular hypertension. Watch this space.
The field of ophthalmology is constantly breaking new ground. As one of the most inventive fields in medicine, ophthalmology is often at the forefront of cutting-edge technologies and treatments. Here, some of the leading innovators from the ophthalmic space present their latest offerings: from imagers and diagnostics, to cutting edge refractive surgery and glaucoma care.
R IS FOR RETINA AND REJUVENATION

Meet the only clinically proven laser treatment to delay progression to late-stage AMD

AMD affects 11 million people in the United States alone. As patient populations age, the number will surely grow – and so too will the need for effective treatment. Current therapies are almost entirely focused on tackling late-stage AMD; attempting to manage patient symptoms only after vision loss and/or serious damage have occurred. But what if there was a way to intervene earlier? That was the question Ellex asked itself and then answered with 2RT® Retinal Rejuvenation Therapy – a new laser treatment that offers ophthalmologists the chance to delay the degeneration process in a significant proportion of patients with intermediate AMD – as highlighted in the LEAD trial (1).

So how does it work? 2RT uses Nanopix Technology™ – a nanosecond laser pulse in a unique pixelated beam profile – to exclusively target selected individual cells within compromised retinal pigment epithelium. This patented process stimulates a natural biological healing process in the retina – the rejuvenation – and improves the hydraulic conductivity of Bruch’s Membrane. And because the process is gentle, it does so without collateral damage to the overlying photoreceptor rods and cones of the retina.

In the extensive, multi-center LEAD clinical trial over 36 months, it was shown that 2RT achieves a significant reduction in the rate of progression to late-stage AMD in just over three quarters of intermediate AMD patients. Specifically, post-hoc analysis of the randomized, sham-controlled study of 292 patients showed that 2RT resulted in a clinically meaningful 77 percent reduction in the rate of disease progression in patients without co-existent reticular pseudodrusen (76 percent of patients enrolled).

2RT Retinal Rejuvenation Therapy has already been approved for indications of clinically significant macular edema (CSME) in Europe and the United States – and for early AMD in Europe. And with its revolutionary approach to cell renewal, Ellex’s unique treatment program looks set to change the way ophthalmologists treat AMD the world over.

2RT® is not approved for sale in the USA for the indication of early AMD.

Reference
Glaukos is a name synonymous with innovation. The company focused on revolutionary glaucoma treatments made waves last year with the iStent inject. Building on 2012’s original iStent technology, the iStent inject is even smaller than its predecessor, with an incredible 0.36 mm profile. The device comprises a unique hand-held injector capable of implanting two heparin-coated titanium stents via a single corneal entry point. By creating a permanent micro-bypass into the trabecular meshwork, it allows fluid to flow out of the eye, lowering IOP, which may allow doctors to reduce patient dependence on eye drops. Over 400,000 iStent and iStent inject have already been implanted globally—a number that is set to grow now the device has been approved by the FDA. It’s no surprise: the iStent inject is as versatile as it is effective; surgeons can use the device during cataract surgery or as a stand-alone procedure. Not only is it convenient and cost-effective, it also has an unparalleled safety profile, often requiring no additional follow-up beyond that of a usual cataract procedure.

With such a device in its portfolio, you may think that Glaukos has done all it can in the glaucoma treatment market—but you would be wrong. “Glaucoma remains one of the leading causes of blindness worldwide,” says Tom Burns, CEO of Glaukos. “As a company, we remain focused on bringing the most efficacious technology to users worldwide—and that includes our latest device, the iDose.”

Put simply, iDose is an intraocular implant designed to continuously elute therapeutic levels of medication, with the aim of reducing intraocular pressure. It is filled with a special formulation of Travoprost (a prostaglandin analog used to reduce elevated intraocular pressure) and capped with a membrane designed for continuous controlled drug delivery into the anterior chamber. “We believe it has the potential to overcome many of the drawbacks associated with the chronic use of topical medications that have been shown to cause long-term ocular surface irritation or damage in glaucomatous eyes—not to mention high rates of patient non-compliance,” said Burns.

The iDose is currently in phase III clinical trials, but has already been shown to achieve sustained IOP reduction and a favorable safety profile in 12-month interim cohort; the Phase II trial—a randomized, double-blind study featuring 154 patients—observed a 30 percent reduction in mean IOP. Not only that, the mean number of glaucoma medications ranged from 0.54 to 0.56 in the fast and slow iDose elution implant groups, respectively, compared with 0.72 mean medications in the timolol group (1).

Though the iDose is not yet commercially available, its release is eagerly anticipated. When it does come to market, it will join a portfolio of cutting-edge Glaukos products—from the original iStent to the upcoming iStent infinite™, a refractory glaucoma treatment, scheduled for release in 2021. Watch this space.

Reference
A LENS FOR ALL

Choose from over 3,000 configurations to find the perfect lens for each patient

With a portfolio including the Eden and Lucidis premium IOLs, Swiss Advanced Vision (SAV-IOL) is already known for redrawing innovation boundaries in the IOL landscape. Now, the company is launching a system that brings customizable medicine to the world of cataract surgery.

SAV-IOL’s unique offering comprises a novel IOL – the Harmonis lens – and a web-based configurator. Helping mediate the customization process, the configurator offers patients and ophthalmologists a preview in the form of a range of lens parameters from which the most appropriate can be chosen according to the desired outcome of each individual patient. These parameters include: near, intermediate, and distance vision ratios; reading distance; and extended depth of focus (EDOF). In total, over 3,000 optical configurations are available through the Harmonis-configurator system – an impressive number, and one which offers patients bespoke IOLs manufactured according their specific and individual needs.

The innovative approach was developed in response to a market need expressed by surgeons: namely, IOLs that can provide accommodation characteristics very close to those exhibited by the patient’s natural lens prior to cataract surgery. The Harmonis system is an effective and convenient answer to this need: rather than leaving the surgeon to predict optimal parameters, this novel product enables patients to directly choose a preferred outcome via SAV-IOL’s one-of-a-kind configurator, thereby providing the surgeon with critical information on the product parameters most likely to keep the patient happy.

Harmonis now sits alongside the Eden and Lucidis premium IOLs, and, like its sister products, is based on SAV-IOL’s Instant Focus technology. This patented system extends IOL depth of focus by means of the pseudo non-diffracting beam principle (PNDB). Harmonis is, however, unique in providing ophthalmic surgeons with a convenient, truly customizable EDOF lens for cataract patients. And SAV-IOL is continuing to innovate; planned products include R-TASC, a next-generation active IOL with real-time autofocus, enabling app-controlled adjustment of optical parameters. These exciting developments are all part of SAV-IOL’s overall mission: to invent and launch products that fully restore missing accommodation in all IOL patients.
THINK IN SYSTEM

A start-up ophthalmic instrumentation company from Switzerland is redefining “state-of-the-art” when it comes to phacoemulsification systems – and kicking off a new era in phaco surgery

Founded in 2014, THIS AG brings together experts with proven and practical experience in medical device R&D and commercialization. Such backgrounds imply an appreciation of the importance of market research – and indeed, THIS AG’s product development program is informed by three broad requirements in the field of phacoemulsification instruments: mobility, simplicity and safety. Together, improvements in these areas can enhance efficiency before, during and after the phaco procedure, and benefit both the patient and the surgical team.

Accordingly, THIS AG has developed the SWISS OPHTHALMOLOGY INNOVATION (SOPHI) brand. The advance is based on three pillars of innovation which, in sum, address the above market requirements. Firstly, the exceptional mobility and flexibility of SOPHI enable the surgical team to adapt the new system to their needs on a day-to-day basis. Secondly, SOPHI’s highly effective sinus phaco function, combined with multiple energy saving modes, reduces the amount of energy delivered to the eye. And thirdly, the unique triple-pump fluidics system integral to SOPHI enhances overall efficiency and safety throughout the entire phaco procedure.

The three advantages arise from a suite of technical innovations built into the SOPHI system. Novel features include: a communication system, incorporating a simple touchscreen graphical user interface with text-to-speech functionality and color-changing LEDs, as well as wireless data communication and WiFi-enabled video inlay. In terms of advanced fluidics management, SOPHI incorporates three coordinated pumps: two peristaltic devices (for improved aspiration and for unique active infusion control (IOP control)) and a clean Venturi pump, which provides a mechanical barrier between the patient fluids and the device, thereby preventing contamination. The pumps are supported by an infusion level guard, an automatic cassette slot, and individual sensors within the cassette monitor surge detection, flow measurement within the Venturi, water/air detection – and monitoring of the waste bag (a warning is triggered when full).

Finally, SOPHI offers various electromechanical enhancements to make the surgeon’s life easier, including battery-supplied operation; an internal compressor; an easy-move foot pedal with inductive charge; a rotatable screen and tray allowing unparalleled flexibility of placement; and an easy-brake system for comfortable positioning.

The overall result? A high-end device that sets new standards in the field of phacoemulsification instruments – as CEO Thomas Köppel puts it: “The SOPHI brand itself is a commitment to innovation.” SOPHI has already reached the final stage prior to CE marking, and launch is anticipated for 2019, reflecting THIS AG’s ability to rapidly and efficiently re-think the future of phaco instrumentation. THIS AG’s philosophy of innovative device development in areas that can be improved is a mode of thinking that retains a focus on individuals, including employees, partners, customers and, not least, patients.

And this is just the beginning. Köppel asserts that SOPHI is only the first milestone in THIS AG’s journey, and states that the ophthalmology community should expect further advances from the company. So if you need gentler, safer treatments for your patients, and more ergonomic, better-optimized systems for your surgery, think seriously about THIS.
A TOTAL IOL SOLUTION

Rayner has been at the forefront of intraocular lens technology since manufacturing the world’s first IOL in 1949. Now, the company has set its sights on “total solutions” in the premium IOL market: innovations include not only a presbyopia-correcting IOL, but also a state-of-the-art digital platform to collect IOL outcomes data.

Sulcoflex Trifocal
For presbyopia correction, Rayner’s solution is to combine the technologies of two advanced IOL systems – Sulcoflex and RayOne Trifocal. Sulcoflex IOLs are designed to be implanted in the ciliary sulcus as a pseudophakic supplementary IOL, and are validated by over 10 years of clinical success; the RayOne Trifocal reduces light loss to 11 percent, and – by virtue of having fewer rings and a patented optic surface – reduces potential visual disturbances and improves night vision compared with other trifocal IOLs. Amalgamating these two unique technologies into a single lens – the Sulcoflex Trifocal supplementary IOL – enables surgeons to correct presbyopia (DUET procedure) and fine-tune the postsurgical outcome, which, in turn, relaxes patient selection criteria. It can be removed with ease, and therefore offers an adjustable solution for patients who desire a spectacle-free lifestyle. Sulcoflex Trifocal is not limited to new aphakic patients; it is also the first supplementary IOL that can provide state-of-the-art trifocal technology to pseudophakic patients.

RayPRO
All Rayner IOLs, including those with the latest trifocal technology, will be supported by the RayPRO digital platform. This free resource for Rayner users – informed by best practices taken from successful fitness apps like Strava and Garmin Connect – proactively collects Patient Reported Outcomes (PROs) over three years. During this period, patients receive five simple email questionnaires covering: i) satisfaction, ii) spectacle independence, iii) refractive achievement, iv) visual disturbances, and v) requirement for additional procedures, for example Nd:YAG or laser top-up. Each questionnaire takes less than five minutes to complete and can be done from home.

Anonymized PRO data are compiled into clear reports that surgeons can access from anywhere, via a web browser or the RayPRO smartphone app. Results can be filtered by date, hospital and IOL model to identify trends by time, location or product. RayPRO’s intelligent algorithm also calculates a personal score from a combination of metrics allowing surgeons to rank themselves against peers. Thus, RayPRO allows surgeons to monitor longer-term outcomes and patient satisfaction – information that postoperative visual acuity and refractive attainment data alone cannot reveal. Furthermore, it removes the burden of PRO collection from the surgeon.

One key driver behind RayPRO is Rayner’s vision to give surgeons on-demand access to surgical outcome measures in the same way that other information can be instantly accessed at any time via smartphones. But it won’t end there; as Rayner CEO, Tim Clover says: “RayPRO will generate data-driven insights into product performance and trends, and will help ophthalmology join other healthcare fields in exploiting ‘big data’ to advance patient care.” In this way, RayPRO – together with the level of control over presbyopia correction provided by the Sulcoflex Trifocal IOL – truly positions Rayner as a provider of total solutions in the IOL space.

Sulcoflex Trifocal (launched 2018) is CE-marked, but not FDA-cleared. RayPRO will be launched globally in early 2019, with patient questionnaires initially available in English, French, German, Italian, Spanish and Portuguese.
A PERSONAL SOLUTION TO A GLOBAL PROBLEM

From outer space to the inner eye, iDESIGN Refractive Studio is revolutionizing laser vision correction

Johnson & Johnson Vision has been at the cutting-edge of laser vision correction for 30 years. It developed the first femtosecond laser for LASIK flaps and corneal transplants, pioneered the use of 3D active tracking in LASIK procedures, and played an instrumental role in the approval of LASIK for NASA and US military personnel – and the company is about to make history again with the iDESIGN Refractive Studio: the first and only system to use topography-integrated, wavefront-guided technology for laser vision correction.

The platform, which received FDA approval in June 2018, is currently available worldwide. It is the only available LASIK platform approved by the FDA for monovision LASIK in presbyopic myopic patients; a procedure that corrects vision in patients over 40 years old who are nearsighted, but who also have trouble seeing up close. The development of the sensor within the iDESIGN System was the result of an earlier discovery by Johnson & Johnson Surgical Vision Scientists, which NASA also used to accurately measure and shape the mirrors in the James Webb Space Telescope and transmit the high resolution images of deep space back to earth. The same sensor technology in the iDESIGN Refractive Studio now allows surgeons to take a number of precise measurements prior to LASIK treatments. Using an “inside-out” approach, the system performs a wavefront analysis of the inside of the eye, detailing any imperfections in the patient’s vision. The system then turns to corneal topography, scanning the outside surface of the eye to measure and analyze tiny variations in curvature and elevation – all in just three seconds. The resulting combination of measurements allows the iDESIGN Refractive Studio to deliver a one-of-a-kind personalized treatment plan for patients – and a number of benefits for surgeons:

- Improved planning to optimize outcomes
- Improved diagnostic capabilities to ensure an informed view of the patient’s refractive error
- Improved workflow for better practice and patient efficiency

“Personalized treatments rely on accurate measurements – and that’s exactly what you get with the iDESIGN Refractive Studio,” says Griffith Altmann, Head of R&D for Surgical Instrumentation at Johnson & Johnson Vision. “Our technology helps surgeons deliver outstanding patient outcomes and grow their practice. It’s simple – when you measure better, you treat better.”

The iDESIGN Refractive Studio is just one example of Johnson & Johnson Vision’s commitment to the eye care community. It will join a suite of innovations working to restore sight to the 250 million people worldwide struggling with visual impairment – but it won’t be the last. With the company’s global footprint and strong relationships with key thought leaders in ophthalmology and optometry, Johnson & Johnson Vision will no doubt continue adding to its legacy of innovation for years to come.
SEEING DOUBLE (IN A GOOD WAY)

A double-needle stabilizing guide and globe fixation ring – developed by Dr Shin Yamane of Yokohama University and Geuder – is about to enter commercial scale production.

The double-needle technique for intrascleral IOL fixation in the aphakic eye can be tricky – and calls for a clear eye and a steady hand. The standard method requires the surgeon to identify sclerotomy sites by means of axis markers, calipers and ink; however, it is difficult for the surgeon to precisely control the needles when piercing the conjunctiva and advancing through sclera – and hence very hard to form predictable insertion angles when creating the tunnels. As a consequence, the double-needle technique appears conceptually simple, yet is not easy to master and can be challenging in terms of standardization and reproducibility.

Dr Shin Yamane, Assistant Professor in the Department of Ophthalmology and Microtechnology, Yokohama City University Medical School, Japan, has now refined the double-needle technique with the invention of a device that both stabilizes the eye and guides needles into the sclera at appropriate angles. This helpful handheld innovation comprises a toothed ring for fixing the globe during needle insertion, and two integral “landmarks” for orientation and identification of the sclerotomy sites. The landmarks are located 2 mm from the limbus and 180 degrees apart, eliminating the need for axis markers, calipers or ink. Furthermore – and perhaps most crucially – the device features two grooved platforms to help guide needles through the fixation ring. The needle guides are set at angles of 20 degrees with respect to the corneal limbus, and 10 degrees with respect to the iris surface – an arrangement that enables creation of reproducible scleral tunnels and avoids putting stress on the IOL haptics.

The result? Very precise (up to 0.25 D) IOL placement in aphakic eyes by scleral fixation alone, with no requirement for conjunctival incisions, suturing or glue. Furthermore, the technique simplifies the procedure and shortens the surgical time, leaving haptics strongly fixated onto sclera in a minimally invasive way.

THE INTELLIGENT IOL

How Precisight® IOL technology allows for lifelong adjustment

Premium lens patients have high expectations. But how can surgeons guarantee optimal outcomes with soon-to-be outdated technology? Enter the Precisight® IOL by InfiniteVision Optics. Unlike conventional IOLs, the Precisight® anticipates the potential for future enhancement to the patient’s vision or the replacement of optical technology in the eye. The platform is composed of two optics, a base, which also functions as a docking station, and a front lens. In cases where a patient’s vision needs to be enhanced, only the easily accessible front lens is exchanged, minimizing the dangers associated with full lens explantation. “Surgeons can be very cautious about which patients they recommend a multifocal lens to – and for a good reason: nobody wants dissatisfied patients,” says Carsten Laue, President of InfiniteVision Optic. “But with the adjustable Precisight® platform, there is no need to worry. Both the surgeon and the patient know that there is a way to fix potential issues, and achieve the best possible vision – now and in the years to come.”

The concept of an intelligent IOL can be traced back to Theodore Werblin, a surgeon from Princeton, who had the idea to separate spherical power from toricity and multifocality to reduce the inventory of lenses at a clinic. InfiniteVision took that concept to the next level by creating the adjustable Precisight® platform. “With the potential to make lifelong adjustments, patients no longer have to settle for sub-optimal visual outcome after cataract removal. Our personalized solutions have been designed to suit each patient’s personal preferences and anatomical precondition, accommodating for the inevitable vision changes that happen over time,” says Laue.

The Precisight® IOL is currently only available in Europe with a monofocal aspheric optic. Toric and multifocal optics are in development.

www.theophthalmologist.com
“Think Dry Eye—Before Your Patient Does”

Do we always appreciate the full impact of dry eye—in all of our patients? Or are we only “scratching the surface” when it comes to managing this pernicious disease? To find out, we convened a panel of experts at the Ocular Surface Disease Forum (October 5, 2018, London; hosted by The Ophthalmologist, and sponsored by Allergan), namely:

- Sheraz Daya, Medical Director of Centre for Sight, East Grinstead, UK
- Ingeborg Stalmans, Head of the Glaucoma Clinic, University Hospitals UZ Leuven, Belgium
- Maurizio Rolando, Professor of Ophthalmology, University of Genoa, Italy
- Dawn Sim, Consultant Ophthalmic Surgeon, Moorfields Eye Hospital NHS Foundation Trust, London, UK

It’s easy for us to get wrapped up in our specialties—that’s how we’ve been trained. If we are to do the best for our patients, however, we sometimes need to think (and act) outside those boxes. Consider ocular surface disease (OSD): this condition is not only troublesome in its own right, but also has a major impact on outcomes in LASIK, glaucoma and retinal surgery. Conversely, interventions associated with these and other specialties may actually trigger serious OSD—sometimes with unfortunate consequences for the doctor-patient relationship (1).

This situation suggests that we should pay more attention to proactive management of the eye’s exterior, both before and after treatment of the patient’s primary condition. Indeed, some experts assert that maintenance of a healthy ocular surface—particularly in the high proportion of ophthalmology patients who are predisposed to ocular surface problems—is key to surgical success. Unfortunately, the optimum methods of avoiding, identifying, and managing OSD are not always obvious or broadly appreciated. Hence this supplement: we hope that the advice and tips outlined herein will support those ophthalmologists keen to optimise post-surgical results, and patient satisfaction, regardless of specialty.

Reference

Staining the ocular surface

“Conjunctival examination is critical for detection of very early dry eyes.” — Maurizio Rolando

“Use fluorescein unless there’s an indication to use lissamine green or rose bengal; for example, in Sjögren’s disease.” — Sheraz Daya

“Lissamine green is good for conjunctival staining, but fluorescein is very quick and is all you need in most cases. With fluorescein, use a yellow filter to increase contrast and reveal conjunctival fluorescein staining, which is a very good indicator of dry eye. If fluorescein is retained in the meniscus after about six minutes post-application, it demonstrates tear production is low, indicating a high-risk patient.” — Maurizio Rolando
Today’s definition of ocular surface disease (OSD) recognizes that it is a multifactorial condition characterized by symptoms including tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities. For reasons which remain unclear, OSD is increasing in prevalence. Dietary and environmental factors may play a part – but what about iatrogenesis? It seems that a substantial proportion of patients without overt disease are significantly predisposed to OSD: in these patients, ocular interventions may trigger full-blown OSD – and the finger of blame can point squarely at the ophthalmologist.

Reference

Growing incidence – environmental factors

“Eye-drop toxicity is partly due to preservatives. Glaucoma patients need chronic long-term treatment, and the toxic effect of preservatives is cumulative.” – Ingeborg Stalmans

“Growing incidence – iatrogenic factors

“Intravitreal injections cause ocular surface dysfunction, not least because of the associated eye drops: anaesthetic and povidone iodine.” – Dawn Sim

Growing incidence – environmental factors

“My experience – 30 years in the field of ocular surface disease – indicates that the problem is significant and growing.” – Maurizio Rolando

“We live in a highly oxidative, pro-inflammatory environment: lipids quickly become oxidized, resulting in slower spreading and less effective hindering of evaporation from the tear-film. Lipid peroxidation is a chronic part of industrial life.” – Maurizio Rolando

“Pre-operative evaluation of patients for dry eye is fast, simple, and inexpensive: observe eyelids and blink rate; ask about symptoms; and – most critically – stain the ocular surface.” – Maurizio Rolando

“Just watch the patient: how often do they blink? Frequent blinkers have a low tear break-up time – you know that even before you put the fluorescein in.” – Sheraz Daya

“You should give Schirmer’s to a patient at least once – you have to understand if they can react.” – Maurizio Rolando

Top tip: Check for contacts

“Use of contact lenses is a red flag – always evaluate the ocular surface in more detail for those patients.” – Sheraz Daya

“Tear production is a reflex reaction to evaporation-induced temperature falls detected by the temperature sensor in the cornea. Contact lens wearers tend to be less temperature-sensitive, and hence produce progressively less tear flow.” – Maurizio Rolando

“Contact lens wearers blink less often, and then only partially; fluorescein stain follows a line – everything above it is clear; everything below is stained.” – Sheraz Daya
Effective dry eye management, both pre-surgery and post-surgery, significantly improves the chances of a successful outcome. This reality applies to the entire spectrum of patients likely to consult an ophthalmic surgeon – not least LASIK candidates, glaucoma patients and retinal surgery candidates. What key points should inform our patient management strategy?

Steroids – the right choice?

“All my serious dry eye cases get steroids as a first-line approach, to manage the inflammation. That’s very important, because inflammation depresses tear production.” – Maurizio Rolando

“In less serious cases, managing ocular inflammation is like steering a ship – if you turn too quickly, you’ll tip over! Better to drift carefully in the right direction: start on artificial tears, and only move to steroids if necessary.” – Sheraz Daya

“Consider preservative-free pre-operative steroids to enhance post-surgical healing.” – Ingeborg Stalmans

“Avoid preserved NSAID formulations – they can lead to extreme reactions, including corneal melt. Better to use higher doses of preservative-free steroids.” – Dawn Sim

“The ocular surface naturally produces endogenous cortisone to down-regulate reactions to environmental irritants – why not support this with topical hydrocortisone? It is relatively mild and is rapidly metabolized into non-active form.” – Maurizio Rolando

Stop it before it starts

Effective dry eye management, both pre-surgery and post-surgery, significantly improves the chances of a successful outcome. This reality applies to the entire spectrum of patients likely to consult an ophthalmic surgeon – not least LASIK candidates, glaucoma patients and retinal surgery candidates. What key points should inform our patient management strategy?

Checks and choices

“There are five things to assess in any patient with ocular surface problems: inflammation, tear film instability, epithelial damage, lid problems, and nerve problems.” – Maurizio Rolando

“I advise pre-surgical identification of patients at risk of OSD, and administration of ocular lubricants to every patient post-injection.” – Dawn Sim

“Less is more... multi-therapy can lead to inflammation-induced IOP elevation and can impact surgical outcomes. Switching (and even reducing) the number of eye drops to eliminate pro-inflammatory agents such as preservatives and to improve compliance can result in a better IOP control, sometimes avoiding the need for surgery. Safer surgical options nowadays facilitate the choice for earlier surgery.” – Ingeborg Stalmans

Premium tears, not pretend tears

“It’s not true that a more severe dry eye should have more viscous artificial tears.” – Maurizio Rolando

“Cellulose-containing artificial tears adhere to the ocular surface and thereby protect the epithelium – but use lower concentrations to avoid blurred vision.” – Maurizio Rolando

“Hyaluronic acid-containing artificial tears are also protective, but are less viscoelastic, so they give the patient a better blink; furthermore, they can be sufficient in themselves to stabilize the ocular surface. Multiple action tear substitutes (MATS) combine the viscosity of hyaluronic acid with the protection of cellulose – and protect the ocular surface against the different conditions experienced in a broad range of lifestyles.” – Maurizio Rolando
What should we ‘take home’?

The result of our expert forum provides the ophthalmology community with key guidance, as follows:

Firstly, note that OSD is a significant and growing problem, and that although not all OSD cases are the same, they all share key aspects of a multifactorial etiology – not least, inflammation. As Sheraz Daya says: “Both under-productive dry eye and evaporative dry eye are driven by an inflammatory component. Assessing its magnitude and cause is essential for long-term management of OSD.”

Secondly, be aware of the very significant pool of patients with sub-clinical dry eye; any given clinical intervention could be enough to push these patients over the edge into more serious OSD. “Remember,” says Maurizio Rolando, “dry eye may be just around the corner – and it will influence patient perceptions, because they will blame their OSD on your surgery.” But forewarned is forearmed: at-risk patients can be identified by careful application of standard diagnostic procedures. These include blink-rate assessment, Schirmer’s with anesthetic to measure tear-flow, and vital stains – notably, the fluorescein stain as modulated by a yellow filter.

Thirdly, as a consequence of careful diagnostic triage, pre-disposed patients may be managed so as to protect and stabilize the ocular surface. Broad strategies include: avoiding eye-drop formulations that contain preservatives or particularly problematic active ingredients (such as NSAIDs); reducing the number of eye drops; and applying lubricant after interventions, such as intravitreal injections. As Ingeborg Stalmans puts it: “If you want surgical success, take care of the ocular surface.”

Finally, be aware that the issues outlined in this supplement apply to a very broad spectrum of patients – the advice given here is therefore pertinent to a correspondingly broad range of ophthalmologists. Not everybody appreciates this: “The problem with retinal specialists is that they tend to see the cornea only as a window to our area of interest,” says Dawn Sim. “We don’t always pay attention to the ocular surface, but it makes such a difference for patients.” Ingeborg Stalmans agrees: “Glaucoma specialists are no different. We know preservatives are bad, but we don’t always act like we know it in the clinic.” And Sheraz Daya, in the LASIK field, is well aware of the benefits of careful pre- and post-surgical management of the ocular surface. The last word goes to Maurizio Rolando: “Think dry eye – before the patient does.”

Dry eye respects no specialty...

LASIK:
“‘In high-performance surgery – multifocals, trifocals, and similar – you must ensure the ocular surface is optimal.’ – Sheraz Daya

“Sometimes, with standard OSD management, your post-LASIK patient will come back with worse dry eye than before the surgery, and with a wound that’s melting down.” – Sheraz Daya

Retina:
“Intravitreal injections require regular administration to be effective, but eyedrop-associated ocular surface discomfort contributes to increased non-compliance rates in patients with diabetic retinopathy.” – Dawn Sim

“We assess the cornea pre-injection, to identify at-risk patients, and protect the ocular surface by administering lubricants post-injection. This actually gives the patient a better overall injection experience.” – Dawn Sim

Glaucoma:
“Everyone knows that preservative-containing eye drops are bad for the ocular surface, but rather than thinking ahead, we often start treating a chronic condition with preserved eyedrops, even though the toxic effect is cumulative.” – Ingeborg Stalmans

“The number of eye drops and the duration of treatment correlates with conjunctival infiltration of inflammatory cells and fibroblasts, which promote post-operative inflammation and scarring – if you want surgical success, you must take better care of the ocular surface.” – Ingeborg Stalmans

“Eye-drop preservatives may cause anterior chamber inflammation, which could impair trabecular meshwork function – a possible mechanism for inflammation-induced increases in IOP.” – Ingeborg Stalmans
Watch The Ophthalmologist's panel of globally recognised leaders in cataract surgery as they come together to discuss the many questions, concerns and barriers in the adoption of new procedures in the field.

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Our expert panel

Boris Malyugin (Chair)  Arthur Cummings  Damien Gatinel  Florian Kretz  Ozana Moraru

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Mighty MIGS
As MIGS becomes an increasingly popular way of maintaining IOP, the question remains: what procedures are available, and when, and on whom, should they be used?

It’s All in the Small Print
Eyenovia is changing the eye-drop delivery process by using piezo-printing technology, capable of delivering small, precise doses.
Mighty MIGS

Minimally invasive glaucoma surgery looks set to transform IOP management – but which interventions are currently available, and when, how and on whom should they be used?

By Sneha Konda and Bala Ambati

MIGS is a growing area of interest for glaucoma specialists and general ophthalmologists alike – and there are four reasons why. The first is the growing population and longevity of glaucoma patients; second, the financial burden, cost-ineffectiveness, and subsequent noncompliance to routinely prescribed/first line standard of care: pressure lowering eye drops; third, the reported toxicity and exposure to preservatives that these daily drops impose on the ocular surface; and fourth, the complications of filtering surgery, such as a trabeculectomy or tube shunts. But which MIGS procedure is right for your patient? To help you decide, here’s a concise overview of approved and emerging surgical interventions to decrease patient dependence on glaucomatous drops.

Surgical technique

Angle surgery frequently involves intraoperative use of the gonioprism. Manipulation of this device has a steep learning curve, involving coordination and maneuvering of the position of the patient, lens and microscope, while visualizing the tissues and structures of the angle. The Volk gonio lens (Volk, Tuscon, AZ) combines the prism with a fine-ring type stabilization system, which facilitates visualization without compression of the cornea. Prior to using the prism in conjunction with glaucoma surgery, surgeons should familiarize themselves with the lens intraoperatively alongside routine cataract

### At a Glance

- MIGS represents a world of possibility in interventional glaucoma management because of their excellent safety and efficacy profile, as well as patient convenience
- To optimize surgical success, surgeons should assess several factors prior to attempting MIGS by conducting a thorough, pre-operative clinical examination
- While there are many approved and pending options available, a lack of data makes it difficult to come to definitive conclusions
- Glaucoma specialists and general ophthalmologists alike should collaborate to develop a framework that details when MIGS approaches are suitable – and for whom.

<table>
<thead>
<tr>
<th>Confounding factors</th>
<th>Examples</th>
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| Conditions that may obscure the angle | (a) corneal opacities  
(b) conjunctival disease/scarring  
(c) ocular surface disease  
(d) significant anterior synechiae  
(e) certain facial anatomy – small palpebral fissures |
| Conditions that impair proper positioning/maneuvering | (a) cervical spine instability  
(b) inability to follow commands, necessitating increased anesthesia |
| Presence of conditions that carry a higher failure rate | (a) aphakia  
(b) neovascular glaucoma  
(c) diabetes |

Table 1. Surgeons should assess several factors prior to attempting MIGS.
cases, as adequate visualization seems to be the rate-limiting step in angle surgery.

Anatomic underpinnings
While visualizing the tissues and structures of the angle, it is important to orient with certain anatomical landmarks and know the normal/abnormal variants of each – and it is especially critical for eyes with preexisting pathologies, such as diabetic eyes, where the anatomy can be extremely delicate. If the first attempt at manipulating the tissues and placing the device or performing the procedure is unsuccessful, a second attempt in the same location is often impossible. A thorough, pre-operative clinical examination is vital to optimize surgical success (Table 1).

Getting on top of IOP
There are several different mechanisms by which each device/procedure exerts its desired effect on reduction of intraocular pressure (Table 2).

With respect to risks, the physician and the patient should be aware of the following:

i. Schlemm’s Canal: this reservoir is similar to the physiological pathway of aqueous humor, and literature touts a higher safety profile. Reflux from collector channels can lead to hyphema. As with any glaucoma procedure, hypotony can occur. Devices like iStent and Hydrus can dislocate.

ii. Suprachoroidal space: this reservoir is dissimilar to physiological pathway, allowing for risks, such as cyclodialysis cleft with hypotony, late closure of the cleft with rapid rise in pressure due to atrophy of natural outflow structures, hemorrhage, inflammation, and hyphema.

iii. Sub-conjunctival space: similar to (2), this reservoir is not physiologic, and carries similar risks as above. Devices like the Xen or InnFocus can dislocate. In addition, though potentially as efficacious as trabeculectomies – a similar mechanism to filtration – it carries similar risks due to bleb-related complications, such as infection and fibrosis.

Approved MIGS
Xen (Allergan, Dublin, Ireland)
Placed through a clear corneal incision, the Xen device opens up a subconjunctival filtration pathway creating a fistula and resultant bleb. The bleb may cause conjunctival scarring, so an antimetabolite is often used. Formation of posterior blebs is preferable to anterior blebs, because of the decreased likelihood of bleb dysesthesia. This conjunctival procedure is relatively contraindicated in patients with aphakia, intraocular silicone oil or prior failed filtering/conjunctival surgery. Patients on multiple drops pre-operatively are typically told to substitute with oral acetazolamide at least one month prior, to optimize ocular surface. This device is only approved by the FDA in cases of refractory glaucoma unresponsive to drops and failure of initial surgery.

Limited studies exist that speak to the safety and efficacy of this device. In a clinical study of 30 eyes, mean IOP reduction was 6.2 mmHg at 12 month follow-up. Literature speculates that filtration bleb formation, as occurs in trabeculectomy, may result in complications such as encapsulation and subsequent scarring (1-3). In the study cited above, encapsulation of the filtration bleb was reported in one case (3.3 percent), which typically requires close postoperative follow-up with needling, revision procedures or prolonged course of topical steroids to reduce inflammation.

iStent (Glaukos, San Clemente, CA)
The iStent is a trabecular bypass device that is placed with a 25-gauge MST micro-canal, bypassing the trabecular meshwork. This device is ideally placed in the area of

<table>
<thead>
<tr>
<th>IOP Reduction Mechanism</th>
<th>Specifics</th>
<th>Example</th>
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<tbody>
<tr>
<td>Increase in outflow of aqueous humor…</td>
<td>i) through trabecular meshwork to Schlemm’s canal via penetration/perforations ii) through suprachoroidal space via shunts and drainage devices</td>
<td>i) iStent, Hydrus, Goniotomy, Canaloplasty ii) CyPass, Solx</td>
</tr>
<tr>
<td>Decrease in production of aqueous humor…</td>
<td>through ablation of ciliary body epithelium</td>
<td>Endoscopic Cyclophotocoagulation</td>
</tr>
<tr>
<td>Increase in subconjunctival filtration…</td>
<td>through creation of a new opening/formation of a bleb through which aqueous humor can flow</td>
<td>XEN-gel stent, InnFocus</td>
</tr>
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Table 1. Mechanisms of IOP reduction and surgery/technology on offer
Schlemm’s canal with the highest density of collector channels, targeting drainage into large aqueous veins. Some investigators speculate the future use of imaging, such as optical coherence tomography (OCT), to accurately localize high-concentration areas of collector channels/aqueous veins pre- and perioperatively. The possible additive effect of inserting two or three stents instead of one is currently being investigated. The iStent inject, consisting of two stents placed at two different areas of Schlemm’s canal, is still in the process of FDA approval.

In one retrospective study of 134 eyes in 100 patients undergoing combined cataract extraction and implantation of iStent, mean IOP reduction was 3.6 mmHg at one year follow-up, with 94 percent of patients achieving their preoperative IOP goals (1,4). Several head-to-head comparisons of iStent and phacoemulsification versus phacoemulsification alone have been shared in the literature. In a systematic review of 37 studies, iStent implantation was reported to have a 9 percent IOP reduction rate at 12 months follow-up, compared with 4 percent with phacoemulsification alone (5). The safety profile of iStent and cataract surgery was reported to be similar to phacoemulsification alone.

The most common complication reported with iStent implantation is transient hyphema (up to 19 percent). Other reported complications include stent obstruction/malposition (up to 10 percent), but reported cases typically did not require additional corrective intervention (4).

**Goniotomy**

A surgical procedure typically performed with a trabeculotome (NeoMedix, Tustin, CA), goniotome (Neomedix) or a Kahook Dual Blade (KDB; New World Medical), goniotomy removes a portion of the trabecular meshwork, increasing aqueous humor outflow. It does not penetrate the sclera, and is not associated with blebs. The most common reported complication is blood reflux; occasionally, cyclodialysis clefts with associated hypotony can occur.

Historically, this procedure was used mainly in the context of congenital glaucoma, where the procedure was incisional. There is a wealth of scientific studies that evaluate the efficacy of this procedure in the pediatric population, but more literature is needed to address its increasing use in the adult population. In the adult version, dual blade systems are used to excise a portion of trabecular meshwork. In a recent retrospective study of 71 adult eyes, there was a mean decrease of 4.6 mmHg IOP 6 months post-operatively (6).

**ABiC**

Ab interno canaloplasty (ABiC) uses a flexible microcatheter inserted through a clear corneal incision viscodilating and catheterizing Schlemm’s canal, the trabecular meshwork and the distal collector channels circumferentially. It is a modified version of the traditional canaloplasty, but does not require a suture to create tension and maintain aqueous outflow. An attractive feature of this procedure is that it restores the natural anatomical outflow system of the eye with no implantation of artificial devices. In a case series of 228 eyes reported by Ellex iScience, an IOP reduction of 8.1 mmHg was reported at 12 months follow-up. However, this procedure is technically complex and relatively long to perform. It can rupture Schlemm’s canal or travel into false channels with potential complications.

**Cypass** (Alcon, Fort Worth, TX)

Approved in the US in July 2016, Cypass has been used in Europe for over a decade. It creates a passage of flow from the anterior chamber to the suprachoroidal space. Supraciliary devices, such as Cypass, are associated with a higher degree of complications – such as hypotony and IOP elevation – than trabecular bypass devices, limiting their use to milder forms of glaucoma. In a study involving 167 eyes of 142 patients, mean IOP decreased by 4.3 mmHg at 12 months follow-up, with the most common complication being early hypotony (up to 23 percent) (4,7). Reports of late closure of the cleft with rapid spikes in IOP are emerging.

**Endoscopic Cyclophotocoagulation**

Endoscopic cyclophotocoagulation uses laser technology to ablate the ciliary body epithelium to decrease aqueous body production. Its precise delivery of laser beams allows direct visualization of the ciliary processes without damage to the surrounding structures. In a randomized control trial of 636 patients, ECP and phacoemulsification was compared with phacoemulsification only; combined treatment resulted in an IOP reduction of 3.3 mmHg, with no significant reduction in IOP (8). As its efficacy has not been clearly demonstrated, it has not become popular.

**MIGS pending approval**

**Soli (Soli Inc, Waltham, MA)**

This gold microshunt, similar to CyPass, increases outflow from the anterior chamber into suprachoroidal collector channels. However, it does so ab externo, via trans-scleral dissection versus corneal incision. It is under FDA investigation undergoing phase III clinical trials, with preliminary clinical data showing about 9.3 mmHg mean IOP reduction at 12 months follow-up. Complications reported include anterior chamber inflammation and hypotony.
numerous potential benefits over conservative treatments (eye drops) and more aggressive surgical options, such as trabeculectomy or tube shunts. MIGS procedures, along with advances in laser technology—for example, SLT, micropulse cyclophotocoagulation—could conceivably move to the forefront in glaucoma management because of their excellent safety and efficacy profile, as well as patient convenience. They provide a viable venue for earlier, long-term intervention for glaucoma with less need for strict patient adherence, and can be done concurrently with cataract surgery, reducing patient costs and operative/anesthesia risks.

There is no shortage of options in this growing sector of glaucoma treatment. Although comparisons between several MIGS devices and trabeculectomy do appear in the literature, more comparative head-to-head clinical studies between different MIGS devices need to be performed. Such comparison will better address the pros and cons of each option to better guide surgical management and patient selection. Though clinical trials are underway, the data points and investigation methods are not uniform, making definitive conclusions about the utility of each difficult. Standardized, universal evaluation of each of these devices and procedures needs to be devised and implemented, including the following criteria:

- Safety endpoint
  - frequency of complications
  - types of adverse events
- Efficacy end points
  - complexity of surgical technique
  - scope of tissue manipulation
  - reduction in IOP
  - reduction in medications
- Guidelines for patient eligibility and contraindications
  - preoperative clinical examination
  - severity and type of glaucoma
  - number of preoperative glaucomatous drops
  - prior failure of surgical/medical treatment

Glaucoma specialists and general ophthalmologists alike should collaborate to develop a framework that details when MIGS approaches are suitable—and for whom. Nevertheless, the growing myriad of options is promising; together, they represent a whole new world of possibility in interventional glaucoma.

References
It's All in the Small Print

Eye drops rely on “Grandma technology,” says Sean Ianchulev, and patients deserve better. His solution? Use inkjet instrumentation to print drugs onto the cornea: smaller doses, smarter delivery, safer therapy.

With Sean Ianchulev and Louis Pascale

Patients dislike glaucoma eye drops; the delivery mode is inconvenient and imprecise – in fact, unlike no other medical field, in ophthalmology we deliver the wrong dose more often than we do the prescribed one – with many studies now demonstrating that only one third to a half of all patients are able to successfully deliver the indicated topical dose to their eye (1). Most of the time they miss the eye altogether or deliver 200–500 percent overdose causing side effects, waste and missed compliance. Ophthalmic formulations cause a range of unwanted side effects from discoloration to periorbital dermatitis. Hence the famously high non-adherence levels associated with topically-applied glaucoma medication. But given that the standard eye-dropper method dates from before the 20th century, should we really be surprised that it’s problematic? Ianchulev certainly takes this view, and is indignant that the subject isn’t more broadly discussed. “Physicians are using a 150-year-old device to deliver 50 microlitres of drug into a seven microlitre tear film volume – no wonder eye drops are poorly tolerated!” But now Ianchulev’s company, Eyenovia, is bringing 21st century engineering to ocular drug delivery. “By marrying piezo-printing technology with smart drug delivery, we’re completely disrupting the eye-drop technology,” he says. In fact, the implications of the Eyenovia technology go far beyond issues of drug tolerability: some of the off-target effects associated with eye drops are life-threatening, and include cardiotoxicity symptoms, such as arrhythmia and bradycardia. So, by reducing off-target tissue exposure, Ianchulev’s microdosing approach may improve not just patient comfort, but patient safety – good news for patients, physicians and healthcare systems alike.

What’s new about the Eyenovia approach? Discarding the ancient eyedropper, Ianchulev’s team has turned to piezo-electric ink delivery systems – well known for precise delivery of suitable amounts of ink onto paper – by modifying such technology to administer 6–8 µL drug doses that are more compatible with natural physiology; in other words, the volume delivered does not overload the eye with fluid in the same way as an eyedropper. Louis Pasquale, Ianchulev’s clinical collaborator, makes another important point: “Keeping the administration volume to 8 µL or less is important; larger quantities cause a lachrymal reflex that washes much of the dose out of the eye,” he says. “When you think about it, it’s amazing that glaucoma eye drops work at all – much of the administrated dose is washed out by the lachrymal reflex.” Avoiding this washout is not only more efficient in terms of drug use, but also more pleasant for the patient.

When and where

But it’s not just about how much drug is delivered. Piezo-electric technology is also precise (imagine if your inkjet printer was not!). Eyenovia’s device aims to accurately and uniformly coat the small volume of drug onto the corneal surface (where intraocular drug penetration occurs) (2). Could such efficient drug delivery also lead to less frequent administration? Time will tell.

In any case, microdosing intuitively indicates less drug-associated toxicity. And if the side effects are reduced, patients should hopefully be less reluctant to adhere to treatment regimens; hence, one of the first indications being explored by Eyenovia is glaucoma medication (Box 1), where satisfactory regime compliance is a long way off. In this context, it’s interesting that Eyenovia has taken compliance one step further by coupling an app that reminds patients when their dose should be taken with Bluetooth-enabled monitoring of device...
Small doses, big target: microdosed latanoprost for chronic angle closure glaucoma.

We spoke to Louis Pasquale, a glaucoma specialist at Mount Sinai who is working with Eyenovia on the chronic angle closure glaucoma (CACG) trial.

Until recently, I was at the Massachusetts Eye and Ear Infirmary; now that I’ve moved to Mount Sinai, it’s easier to be actively involved in the Eyenovia CACG-latanoprost microdose trial. The Eyenovia collaboration has grown from work that Sean and I did on telemedicine and microdosing a few years ago. At that time, we were investigating the efficacy of microdosed phenylephrine for mydriasis. As an eye drop, phenylephrine can cause problematic side effects, not least elevated blood pressure. However, we showed that the microdose formulation has no such effect (1).

Now, we are following up the phenylephrine work with an investigation of microdosed latanoprost for CACG; current efforts are aimed at extending our recent proof-of-principle study on latanoprost microdosing. In the present trial, we have tested the product in 30 healthy volunteers, and demonstrated that latanoprost microdosing mediates IOP reduction equivalent to latanoprost eye drops at 80 percent lower total dose exposure, at least in the short term. And now that we have shown short-term efficacy, I’m helping to design a bigger trial, hopefully a six-month study. This will, inter alia, answer questions about topical and ocular side effects, which of course we would expect to be much lower for the microdose product than for eye drop latanoprost. The plan is for a large multicenter trial in 2019; New York might be one of the centers, because it has a huge volume of CACG patients and a wonderful clinical research centre. Overall, the aim is to have an FDA-approved device in patients’ hands within two years.

We also intend to look at the feasibility of self-administration by patients. That’s what the device is designed for: glaucoma is a chronic 24/7 disease, and ultimately we need a device that patients can operate themselves, so that they can manage their glaucoma independently. We’ll have to teach patients how to work the device, but we don’t anticipate many problems – it’s very straightforward. The device has an LED light; the patient looks at the light, and actuates the device; one spray, and eight microlitres of drug get printed onto the cornea. It couldn’t be simpler. And since the spray speed is faster than the patient’s blink speed, it will be very difficult to get that step wrong.

Looking ahead, this trial will hopefully kill two birds with one stone: it will give US physicians an effective product for CACG, and at the same time it will get the microdose device into the mainstream of glaucoma treatment. This is important – there is a real need for a product that significantly helps CACG management, and my view is that the time has come for us to consider alternative methods of drug delivery in this field. Eyenovia technology should also be a game-changer in the pediatric setting: dilating children’s eyes can be a little traumatic, and our system should be a better way of doing it. And there are many other opportunities for our system: for example, future products might include newly approved drugs and fixed combinations of older drugs. Microdosed atropine for slowing myopic progression in children is also very promising.

I have worked with Sean for some years now, and I’m very fortunate that he keeps involving me in his innovative ideas. The Eyenovia approach is a particularly exciting step forward, and I believe it represents a fundamental paradigm shift in terms of treating glaucoma patients. It is a long-overdue advance: even when I was a resident, back in 1987, I knew that the eyedropper approach was problematic. When used correctly, they work, but we can do better. So that’s what the Eyenovia approach is about, and it’s great to be involved.
Font of wisdom: piezo-printing drugs

- Piezo-print technology in a handheld device allows ocular drug delivery in precise 6-8 microlitre volumes
- Exposure to formulation-related irritants is decreased by 80 percent – while retaining a biological effect equivalent to that mediated by eye-dropper delivery
- The technology is applicable to monotherapy products and to drug combinations, and is anticipated to reduce side effects and improve compliance
- Indications include large markets: adult glaucoma, office-based dilation, and pediatric patients, such as premature infants and children with myopia (prevalence: 5 million)
- The device is in Phase III trials in three indications: microdosed latanoprost for chronic angle-closure glaucoma, microdosed atropine for prevention of myopia progression in children, and microdosed phenylephrine/tropicamide for eye dilation.

Lost on Eyenovia. Potential markets for the technology are large, and include not only adult glaucoma and pediatric myopia patients, but also the 80 million patients in the US alone per year who undergo dilation in the doctor’s office – and suffer stinging or burning eyes from the preservative and the dual overdose, since doctors often use two agents simultaneously to dilate the pupil (tropicamide and phenylephrine) (4). “Eyenovia microdosing delivers the same therapeutic benefit as eye drops, but much more mildly – in a high-precision single microdose of a fixed co-formulation of the two drugs,” says Ianchulev. He adds that the improved safety associated with controlled microdoses suggests that GPs could start administering drugs that previously were only provided by specialist ophthalmologists, making patient management more straightforward and cost-effective. Ultimately, however, Ianchulev sees the technology as far more than just a means of enabling delivery of third-party drugs; the company is building a pipeline of proprietary formulations, including three products in Phase III – for mydriasis, myopia and chronic angle closure glaucoma – and one in Phase I for dry eye.

And the longer-term aim? Ianchulev has set his sights high: nothing short of resolving the world’s myopia problem… In the meantime, he’ll settle for lower side effects and a transformation in adherence monitoring. If Eyenovia’s tech does end up being disruptive, what of the loser? Well, when compared with piezo-electric Bluetooth-enabled microdose delivery, the humble eyedropper starts to look like something not just from a previous century, but from the dark ages!

References
The Ocular Surface Disease Forum is a joint initiative between Allergan and The Ophthalmologist highlighting the importance of a healthy ocular surface in every ophthalmic procedure. We have drawn together globally recognised experts in Cataract & Refractive, Cornea, Glaucoma and Retina to share their experiences and to provide access and expertise to our live and online audience via a live and online discussion forum.

Expert Panel

Sheraz Daya (Chair)  Maurizio Rolando  Dawn Sim  Ingeborg Stalmans

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This event is organised and funded by Allergan, and hosted by the Ophthalmologist. This meeting will contain educational and promotional content.

October 2018 INT/0399/2018q
Time Well Spent

Sitting Down With... John Berdahl, Partner at Vance Thompson Vision, Founder and CEO of Equinox, Sioux Falls, South Dakota, USA.
How did you come to work at Vance Thompson Vision?
My grandma is my hero. So when Vance was recruiting me from fellowship, he took a selfie with her and said: “Your grandma wants you to do her cataract surgery and she’s not willing to travel more than 75 miles for it. Looks like you’re joining me.” That sealed the deal.

What’s the best thing about being an ophthalmologist?
Delivering on the trust that my patients put in me in their moments of vulnerability. In a professional capacity, I try to inspire students, fellows and colleagues the same way my heroes inspired me. We’ve only got one swing at life, so we need to go for it!

You’re a member of the Vision for Mars team – what’s it like working with NASA?
I feel like a kid in a candy store… To grow up in a town of 500 people and be able to assist the professionals who are dedicated to getting the first humans to Mars – it’s not the typical story. I think it will be the single, most unifying moment in human history. If I can play even a tiny role in that monumental feat, my kids will think I’m cool. It’s especially gratifying that the principle of intraocular with intracranial pressure to treat glaucoma could help long term space flight. So terrestrially Equinox is using negative pressure goggles to treat glaucoma, while in space perhaps positive pressure goggles could treat papilledema.

You also co-created the MKO Melt – what was the idea behind it?
The most painful part of cataract surgery is starting the IV, and we weren’t convinced we needed it. We tried sublingual administration in liquid form and thought it worked well, but it didn’t have everything that we needed – the same with IV ketamine and midazolam. So I approached Imprimis and said, “I’ve come up with something a little different. I think we have a real opportunity to help patients.” Historically, there has been very little innovation in anaesthesia for eye surgery, but the MKO Melt is getting adopted quite rapidly.

You seem to have an innovative streak… If I have an idea and it won’t go away, I’ve got to act on it. I don’t feel like I have some special ability — my mind just doesn’t rest until I come to a conclusion.

Can you tell us more about your current project – Expert Opinion?
It’s an online second opinion service that basically gives people access to world class care from anywhere. For example, if someone was diagnosed with Fuchs dystrophy and their ophthalmologist wasn’t great at explaining the procedure, they could go to ExpertOpinion.md. There is a list of ophthalmologists with prices by their names: the doctors choose the price they charge and patients choose their doctor. World experts may command a higher price, where other fantastic doctors may choose a lower price. The patient can see a video of us, along with our online ratings, how many surgeries we perform, and our publications. The doctor you pick reviews your records, writes a report and sends you an audio file telling you what your treatment options are and recommendations.

What are the benefits?
Patients can choose a doctor without having to take a day off work, and doctors don’t have to be in the clinic. It’s good for everyone. Ten years ago it would have been crazy to say: “I’m going to pick somebody up and take them to the airport for $20.” Now Uber is a $52 billion company. Airbnb is the same story. All they do is connect people who have a service with someone who needs a service, and make that as frictionless as possible. In my mind, there is no more precious and valuable service than what doctors provide to patients, but it is one of the hardest to access. We’re trying to make that as easy as possible.

What’s the future of ophthalmology?
Of course, I think noninvasively dialing in IOP will be important for normal tension and severe glaucoma patients. I believe changeability/upgradability versus adjustability is going to be the story of IOLs 10 years from now. I also think drug delivery is going to be a big deal and, as a burgeoning presbyope, I really hope we get a consistent solution in the next three to four years – whether that means better IOLs or an eye drop we can use on demand.

What drew you to ophthalmology?
I originally wanted to be an optometrist; it was actually my family optometrist who suggested I should become an ophthalmologist instead. He gave me the single most actionable piece of advice I have ever received: “A few years of work on the front end of your life to do what you’re meant to do for the rest of your life is always time well spent.” He said: “Humor me and do the MCAT,” so I did, and it’s been like a hand in a glove from the moment I started my residency.

Any final comments?
If I had been given a blank piece of paper 25 years ago, I would not have had the courage to write my story as well as it has turned out. I’m just really grateful for our profession.

“I try to inspire my students, fellows and colleagues the same way my heroes inspired me.”
NEW iMULTI POWER

PRESERVATIVE-FREE CONTROL NIGHT & DAY

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Abbreviated Prescribing Information

**Product Name:** COSOPT® Preservative-Free 20 mg/ml + 5 mg/ml, eye drops, solution, single-dose container. COSOPT® iMulti 20 mg/ml + 5 mg/ml eye drops, solution.

**Composition:** Each milliliter contains 20 mg dorzolamide (22.26 mg dorzolamide hydrochloride) and 5 mg timolol (6.83 mg timolol maleate). Please refer to the Summary of Product Characteristics (SmPC) for a full list of excipients.

**Indication:** Treatment of elevated intra-ocular pressure (IOP) in patients with open-angle glaucoma, or pseudophakic glaucoma when topical beta-blocker monotherapy is not sufficient.

**Posology and Method of Administration:** One drop of COSOPT in the conjunctival sac of the affected eye(s), two times daily. If another topical ophthalmic agent is being used, administer COSOPT and the other agent at least ten minutes apart. COSOPT is a sterile solution that does not contain preservative. Safety in paediatric patients less than 2 years of age has not been established. Please see the SmPC for use in children of more than 2 years.

**Contraindications:** Hypersensitivity to any component of this medicine, reactive airway disease, including bronchial asthma, or a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, sick sinus syndrome, sino-atrial block, second- or third-degree atrioventricular block not controlled with pacemaker, overt cardiac failure, cardiogenic shock, severe renal impairment (GFR <30 ml/min) or hyperchloremic acidosis.

**Warnings and Precautions:** The same types of adverse reactions found with systemic administration of beta-blockers or sulphonamides may occur, these include severe reactions seen with sulphonamides such as Stevens-Johnson syndrome and toxic epidermal necrolysis. In patients with cardiorespiratory diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypertension, therapy with beta-blockers should be critically assessed and therapy with other active substances should be considered. Patients should be watched for signs of deterioration and adverse reactions. Beta-blockers should only be given with caution to patients with first degree heart block. Patients with severe peripheral circulatory disturbance (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution. Respiratory reactions, including death due to bronchospasm in patients with asthma, have been reported following administration of some ophthalmic beta-blockers. Use with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk. Use with caution in patients with hepatic impairment. Concomitant use of dorzolamide with oral carbonic anhydrase inhibitors is not recommended. Use of two topical beta-adrenergic blocking agents is not recommended. Caution in patients subject to spontaneous hypoglycaemia or with labile diabetes. These signs and symptoms of acute hypoglycaemia and hypothyroidism may be masked. Caution in patients with corneal diseases. The anaesthetist should be informed when a patient is receiving timolol as beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g. of adrenaline. Though no acute-base disturbances have been observed with COSOPT (preserved formulation), patients with a prior history of renal calculi may be at increased risk of urticaria. Patients with acute angle-closure glaucoma require therapeutic interventions in addition to ocular hypotensive agents. This medicinal product has not been studied at clinical acute angle-closure glaucoma. Corneal oedema and irreversible corneal decompensation have been reported in patients with pre-existing chronic corneal defects and/or a history of intraocular surgery while using dorzolamide. Precautions should be used when prescribing in these groups of patients. Patients with a history of contact hypersensitivity to silver should not use COSOPT iMulti as dispersed drops may contain traces of silver from the container. This medicinal product has not been studied in patients wearing contact lenses. There is limited experience with COSOPT in infants and children. Please refer to the SmPC.

**Interactions with Other Medicinal Products:** There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, cetrabatolamine-depleting drugs or beta adrenergic blocking agents, antiarrythmics (including amiodarone), digitalis glycosides, parasympathomimetics, quinidine, narcotics and monoamine-oxidase (MAO) inhibitors. Potentiated systemic beta-blockade (e.g. decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol. Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

**Pregnancy and Breast Feeding:** Do not use in pregnancy or during breast-feeding.

**Driving and using machines:** Possible side effects such as blurred vision may affect some patients’ ability to drive and/or operate machinery.

**Undesirable Effects:** (Refer to SmPC for complete information on side effects). The side effects observed with COSOPT or one of its components include: headache, depression, burning and stinging, conjunctival injection, blurred vision, corneal erosion, ocular itching, tearing, eyelid inflammation, eye irritation, iridocyclitis, signs and symptoms of ocular irritation including blepharitis, keratitis, decreased corneal sensitivity and dry eyes and visual disturbances including refractive changes (due to withdrawal of miotic therapy in some cases), phorias, bradycardia, syncope, syncopal episode, dyspnoea, dysgeusia, nausia and dyspepsia, urolithiasis, signs and symptoms of systemic allergic reactions, including angioedema, urticaria, pruritus, rash, anaphylaxis, asthenia/fatigue, hypoglycaemia, cardiac arrest, heart block, AV block, cardiac failure, chest pain, palpitation, oedema.

**Overdose:** Treatment should be symptomatic and supportive. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored. Special Precautions for storage: Do not store above 25°C. Price: COSOPT Preservative-Free 50 x 0.2ml, single-dose containers £28.59; COSOPT Multi 1 x 10ml bottle (60 days treatment) £38.00.

**MA Holder:** Santen Oy, Niittyhaankatu 20, 33720 Tampere, Finland.

**MA Numbers:** COSOPT Preservative-Free P. 16058/0015 COSOPT iMulti PL 16058/0025

**Legal Category:** POM

**Date of Prescribing Information:** September 2018.

**Job Code:** NP-CSPTPF-UK-0005

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