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Whilst in Barcelona for the XXXIII Congress of the ESCRS 2015, Mark Hillen, editor of The Ophthalmologist, invited seven key participants of the conference to take part in a series of informal interviews – go to www.theophthalmologist.com to watch the videos online now…
The Ophthalmologist Innovation Awards

The 2015 Innovation Awards celebrate this year’s diagnosis, therapy and surgery stars – as nominated by you.
In Practice

30 Small Incision Femtosecond Refractive Lenticule Assisted CXL in Corneal Ectasia

CXL is the only intervention that can slow or halt the progression of corneal ectatic disorders like keratoconus. These disorders thin the cornea – but if the cornea is too thin, CXL can’t be performed. Hemlata Gupta and colleagues propose a smart work around that should make you SMILE.

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The Light for Sight foundation provides ophthalmologists around the world with CXL training and ensures that no young patient must go without treatment, writes Nikki Hafezi.

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50 Christoph and Thomas Bosshard, Oertli Instrumente AG, Berneck, Switzerland.
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NEW! AcrySof® IQ PanOptix™
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Last month’s cover feature – the stories of two teams of eye care professionals (from Germany and the UK) going to Uganda and restoring sight to hundreds of people – got me thinking. They only knew of each other’s projects months after their return to Europe. It seemed to me that there were some efficiencies that (perhaps) could have been achieved by pooling their efforts and resources – if only they had known of each other’s mission in advance, they could have done more with what they had.

I wondered how that could be achieved. My idea: a website. Mapping, multi-device messaging, resource pooling and transport planning tools, educational materials, robust security – and even SMS messaging that could work in the most rural parts of Africa. Yes, I’d come up with Slack for philanthropic ophthalmologists, plus Google Maps. It was all very clever (or so I thought), and with some funding and the advocacy of one or more of the large ophthalmology professional societies, it might actually work. It actually formed the basis of the first draft of this editorial. But then I was introduced to Michael Brennan, ex-President of the AAO. Michael is a fantastic gentleman, an “ophthopolitics” veteran – and someone who has been there, and done that around the world… many times over.

The main message I took from meeting him was this: a gung-ho attitude can get you into a lot of trouble – and spoils it for the rest of us. If a mission goes into a country without having gone through the appropriate channels (as some appear to have done), much is risked. Local ministries of health and professional associations have to be consulted. Local protocols (and laws) need to be followed. They might be restrictive, tedious, unhelpful – but following them keeps you out of a lot of trouble, resentment and possibly jail. Like the groups we featured last month, the right approach is to follow the rules, educate the local professionals, and be generous with equipment you bring, and leave. A website can’t really help with that.

To implement a joined-up electronic method of coordinating and streamlining philanthropic efforts in ophthalmology therefore requires a whole lot of high-level international negotiation beforehand. There’s a place for that: Geneva, at the World Health Organization, where national ophthalmology representatives meet every year or two. If consensus is achieved, legislative cogs may turn, guidelines are made, doors open, and maybe, years later... we might be where we need to be.

So it comes down to this: would such a website be useful in any event? Would the ophthopolitical effort be worth it to make all philanthropic work safer and easier? Or are there more worthy battles to fight?

Mark Hillen
Editor
Contributors

Hemlata Gupta
Hemlata Gupta is a surgeon specializing in cataract and refractive surgery with 12 years of experience in the field. A rising star in Indian ophthalmology, she practices at the Centre for Sight, Delhi, India. Hemlata has a special interest in refractive surgery, and has presented papers and given instructional courses at both national and international conferences. Hemlata and her colleagues discuss refractive lenticules as a safer, more effective way of administering collagen cross-linking to thin corneas on page 30.

Florian Kretz
One of The Ophthalmologist’s Top 40 under 40 cadre, Florian is a lead surgeon at the Eyeclinic Ahaus-Raesfeld-Rheine, Ahaus Germany, as well as a consultant ophthalmologist and research fellow at the International Vision Correction Research Centre Network and David J. Apple International Laboratory for Ocular Pathology at the Department of Ophthalmology, University Hospital Heidelberg. When not in the clinic, lab, office, or on the autobahn, Florian enjoys spending time with his wife and young family. Kretz shares his experience using toric IOLs to correct corneal astigmatisms during cataract surgery on page 34.

Nikki Hafezi
Nikki Hafezi is the Managing Director and CEO of GroupAdvance Consulting and EMAGine SA, which provide business development and fundraising advice to companies in the medical technology field, and develop, manufacture and market medical products to address unmet ophthalmic needs. She is also in charge of business strategy and development at the ELZA institute, a new eye hospital and research center in Zurich. Her current focus is translating CXL technology to treat infectious keratitis into clinical applications. In this issue, she discusses the work being done by the Light for Sight Foundation to reduce preventable blindness among children and adolescents with keratoconus, on page 46.

Keith Barton and Kuldev Singh
Keith Barton runs a joint glaucoma/uveitis clinic at Moorfield Eye Hospital. His research interests include secondary glaucomas, particularly the etiology & management of uveitic glaucoma. He is Editor-in-Chief of the British Journal of Ophthalmology and Chairman of the International Glaucoma Association. Kuldev Singh is president of the American Glaucoma Society and an advisor to the International Society of Glaucoma Surgery. His research interests include glaucoma and cataract surgical trials, epidemiology, genetics and health care delivery in underserved communities. His clinical practice focuses on medical, laser and surgical management of glaucoma and cataract. Keith and Kuldev judge this year’s candidates for the Ophthalmologist’s Innovation Awards on page 19-25.
"My preferred stain in cataract surgery is VisionBlue®. I have tried other trypan blue solutions and they did not stain or contrast well." Dr Elena Barraquer - CEO Fundación Barraquer

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**Upfront**

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We welcome suggestions on anything that’s impactful on ophthalmology; please email mark.billen@texerepublishing.com

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**Culture Club**

A new tissue culture model of the retinal pigment epithelium may allow researchers to better understand the impacts of new interventions on the adult human retina

The retinal pigment epithelium (RPE) is one of the hardest-working tissues in the eye (if not the body), responsible for a multitude of functions, including nourishing the photoreceptors, elimination of metabolites, trophic factor production, the storage of retinal, and maintaining the blood-retinal barrier (1). It’s also a tissue that’s implicated in a multitude of disorders ranging from the well-known (like age-related macular degeneration) to the obscure (like monogenic retinal dystrophies and metabolic disorders). However, there’s one big issue that’s hindering the ability of vision scientists from understanding the RPE better: the lack of an appropriate tissue culture model.

This has meant that research involving RPE cell culture has mostly been performed using primary human fetal RPE cultures – a valuable model, as primary culture allows the retinal and choroidal sides of the monolayer to be manipulated and measured independently, and fetal human cells are close in function to the retina in its native state. One of the major drawbacks of using a fetal culture model is that it may not accurately represent the physiology of the adult retina. Researchers could overcome that obstacle by using adult human RPE cultures – but these tend to lose their native physiology over time, resembling fibroblasts more closely than epithelial cells.

So how can scientists in the cell culture room avoid that problem?

It turns out that not all adult human RPE cells are created equal. A particular subset can be reverted in vitro to a self-renewing, multipotent cell type known as the retinal pigment epithelial stem cell (RPESCs) (2). That discovery opened the door to developing an adult human RPE culture without some of the problems that have plagued previous attempts. A group of vision researchers from the United States have now developed a new tissue culture protocol for RPESCs, and have determined that the cells produced by their method preserve many key features of the adult RPE, including their morphology, electrophysiological properties, and gene and protein expression profiles (3). The researchers were even able to culture RPESCs from patients with macular degeneration, diabetic retinopathy and glaucoma, a success that may ultimately lead to “disease in a dish” models of various RPE-related disorders.

It’s too early to declare RPESCs the proverbial “better mousetrap” of RPE culture models. But so far, the authors feel that the new cells are promising as a useful model for diseases and disorders of the adult human RPE.

**References**

A Turbulent Transaction?

Pharmaceutical giants Pfizer and Allergan recently announced that they intend to merge (1) – or rather, Allergan is to perform a “reverse takeover” of Pfizer – and it’s one that would form the world’s largest pharmaceutical company. Both Pfizer and Allergan have eyecare portfolios, although Allergan’s is clearly more extensive than Pfizer’s – and both have ophthalmic products in their pipelines. According to clinicaltrials.gov, Pfizer and Allergan have 13 and 17 trials currently underway, respectively (see Figure 1), so it’s clearly a big deal for ophthalmology.

But the reverse takeover has prompted a significant amount of controversy. Media coverage has focused heavily on the tax implications. Although Pfizer, headquartered in the United States, was effectively taxed at 25.5 percent in the previous January–December fiscal year, a “takeover” by the smaller, Republic of Ireland-based Allergan could bring that rate to 18 percent. The move – termed “tax inversion” – can deliver Pfizer’s shareholders significant value (albeit at the expense of the US federal government’s tax receipts). This is not Pfizer’s first attempt to acquire a European company for what appeared to be tax inversion purposes; nearly two years ago (and after considerable media and US governmental hostility), UK-based AstraZeneca plc’s board of directors rejected Pfizer’s advances towards them (3).

If the transaction does go ahead, the company – to be renamed Pfizer plc – is expected to maintain Allergan’s legal domicile in Ireland, but maintain Pfizer’s New York operating headquarters and trade on the New York Stock Exchange. Pfizer’s chief executive officer Ian Read said that the merger would place the company “on a more competitive footing” with its non-US-based rivals (1).

References
What's Old is New (I)

Big data EMR mining (and some basic research) identifies a 50-year old drug that appears to protect against AMD development

The pharmaceutical industry, in some ways, has it tough. To take a drug from discovery to market takes on average 13.5 years and more than US$2 billion. But to take an existing, marketed drug and repurpose it for a new indication (remember, sildenafil was originally approved to treat angina) costs far less, and takes considerably less time.

The advent of “big data”(1) – in this case, the combination of electronic medical records (EMRs) and large amounts of processing power – has yielded Big Pharma a relatively inexpensive method of mining for drugs that might be worth further evaluation for a new application. And it looks like this approach has identified an existing drug that appears to be protective against AMD – both wet and dry (2). The drug? The antiparkinsonian agent, L-DOPA.

To be fair, this work wasn’t entirely done using brute-force processing power to interrogate a big EMR dataset for as many correlations as possible: the researchers from the University of Arizona who did the data mining already had an idea of where to look – having previously discovered a G protein-coupled receptor that L-DOPA binds and activates: GPR143 (3). Expressed in the retinal pigment epithelium, they found that GPR143 activation by L-DOPA increases the expression of a potent anti-angiogenic factor, pigment epithelium-derived factor (PEDF), and decreases the expression of vascular endothelial growth factor (VEGF).

The approach the researchers took to the EMR analysis was both simple and elegant. They examined the health records of 37,000 Marshfield Clinic patients, looking for those with AMD, those taking L-DOPA and those with AMD who received L-DOPA – and then determined the age at which patients developed AMD. They then took that approach to Truven MarketScan database’s ophthalmology records – which comprised 15,215,458 individuals – and found that L-DOPA use was highly significantly associated with a lower risk of developing AMD, and a lower average age of onset of the disease (Figure 1).

L-DOPA use isn’t without side effects, but if it’s an agent that can delay the onset of AMD, it is clearly something of great value – and the study authors view a clinical trial as the obvious next step in determining whether this drug from the 1960s has a future in this role. MH

Reference

What’s Old is New (II)

Placental growth factor inhibitors might show efficacy in treating dry AMD as well as wet. Might aflibercept be repurposed?

Dry age-related macular degeneration (AMD), unlike its neovascular cousin, has no effective therapies available today – bad news, especially as it comprises about 85 percent of AMD (1). To address this gap, researchers are focusing on the identification and verification of new treatment modalities in the lab. Recently, a group at Gifu Pharmaceutical University, Japan, observed a protective effect of placental growth factor (PIGF), a member of the vascular endothelial growth factor (VEGF) family, on a model of retinal neuronal damage in vitro (1). Seeing an opportunity to tackle dry AMD, the researchers opted to test this effect in a living mouse model (2).

Dark-adapted mice were injected intravitreally with 5 or 50 pg of PIGF-2 (the mouse isoform of the growth factor), either two hours before light exposure or immediately after. But electroretinograph and histological analyses revealed that, regardless of dose, PIGF was actually exacerbating
light-induced retinal damage, reducing a- and b-wave amplitudes (indicative of photoreceptor and neuron function, respectively) and decreasing the thickness of the outer nuclear layer. So the researchers changed tack, deciding instead to evaluate the validity of anti-PlGF agents. To do so, they administered either 0.1 or 1 μg of anti-PlGF-2 antibody into each eye of the mouse, which resulted in a partial protective effect against a- and b-wave amplitude reduction (an improvement of 60 percent with the lower dose and 80 percent with the higher), significant suppression of outer nuclear layer thinning (reductions of 57 and 66 percent, respectively), and improved cell-cell junctional integrity.

The results came as a nice surprise, as a drug that inhibits PlGF is already available for intravitreal use: aflibercept. Although aflibercept has not been clinically evaluated for the treatment of dry AMD, the study’s authors believe that “there is a very great likelihood that aflibercept will show efficacy in dry AMD.”

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References

Business In Brief
Glaukos submits iDose IND to the FDA, Allergan bimatoprost implant shows promise, and ALPHAEON makes three deals in as many weeks

- Glaukos submitted an investigational new drug application to the FDA for an intraocular travoprost implant that uses their iDose sustained delivery system (a hollow titanium container filled with drug, with a membrane cap that regulates drug release, that’s placed via a clear corneal incision into the anterior chamber. Glaukos will commence a 12-week Phase II trial comparing two travoprost elution rates with topical 0.5% timolol maleate.
- Interim results from Allergan’s Phase I/II trial of single-dose, sustained-release intracameral bimatoprost-eluting implant have yielded positive safety and efficacy results. Four months into the 24-month trial, 92 percent of patients with open angle glaucoma exhibited a decrease in IOP, and at 6 months, 71 percent of patients still had no need for either topical rescue or a second injection of bimatoprost. Not one of the 75 patients enrolled into the trial experienced serious adverse events.
- ALPHAEON, a self-described “social commerce company,” has announced an agreement to acquire LENSAR, makers of femtosecond lasers for use during refractive and cataract surgery. ALPHAEON has also entered into an agreement with PhysIOL, an intraocular lens manufacturer with a broad portfolio of products including an aspheric trifocal diffractive lens known as the FineVision. Together, the companies plan to develop and commercialize a specialized, ALPHAEON-branded trifocal lens. ALPHAEON’s chief executive officer, Robert E. Grant, has made it clear that dysfunctional lens syndrome is a new target for his company. Alphaeon has had a busy month – in mid-November, they announced the purchase of Integrity Digital Solutions LLC, an ophthalmology/optometry electronic medical records company.
Dodging the Downsides of Corneal Epithelium Debridement

A new matrix therapy agent may promote corneal healing after epi-off CXL, improving patient comfort and recovery times

Corneal collagen cross-linking (CXL) is a widely used method of halting keratoconus progression. The most appropriate technique is up for debate: whereas some patients are able to withstand the removal of the corneal epithelium for the procedure (“epi-off” – currently the most effective form), others might prefer the less invasive (but, despite many improvements in the technique, still less effective) “epi-on” method, where the corneal epithelium is left intact. The benefit of epi-on CXL is that healing is faster, less painful, and carries a lower risk of infections and visual disturbances.

Can you mitigate the downsides of removing the epithelium? At the moment, post-CXL treatment includes topical antibiotics, analgesics, artificial tears, and bandage contact lenses – but even taken together, these interventions can still leave patients in considerable discomfort during the healing period. Koray Gumus, a researcher at Erciyes School of Medicine in Kayseri, Turkey, decided to take a different approach – to try to reduce the time during which patients are at risk of pain and infection by focusing on faster healing after corneal de-epithelialization. Gumus developed a new type of matrix therapy agent known as ReGeneraTing Agent (RGTA), which consists of large, biodegradable nanopolymers. The polymers are designed to mimic the glycosaminoglycans damaged during epithelial removal, and act to help recreate an extracellular matrix microenvironment that should allow the corneal epithelial cells to heal faster.

Gumus tested RGTA in 30 eyes of 30 patients who received epi-off CXL and found that the healing time of RGTA-treated patients was significantly shorter than that of the control group – after two days, 83 percent of eyes in the RGTA group had healed completely, compared with 13 percent of eyes of patients in the control group (see Figure 1). The RGTA-receiving group also reported significantly lower ocular pain scores on days 0, 1 and 2; lower burning and photophobia scores on days 1 and 2; and lower stinging and tearing scores on days 2 and 3. The results still need verification in a larger population and longer follow-up data – but nevertheless, RGTA looks to be promising agent for promoting corneal healing and patient comfort after epi-off CXL. MS

Reference
1. MK Gumus, “A new matrix therapy agent (CACICOL20) for faster corneal healing following epi-off crosslinking with ultraviolet A and riboflavin”. Presented at AA0 2015; November 16, 2015; Las Vegas, NV, USA. Abstract #PA067.

Figure 1. Proportion of corneas with complete corneal epithelial cell healing two days postoperatively in either RGTA (left) or control (right) groups.
Corneal Anatomy: Lightning Strikes Twice

A specialized imaging technique has revealed two previously unknown structures of the cornea

News that a new part of the body—a layer of the cornea—had been identified back in 2013 was such a big story that it transcended the world of biomedical news and hit the mainstream media. It’s happened again: another new part of the human anatomy has been discovered—and again, it’s in the cornea (1).

Second harmonic generation imaging microscopy (SHIM) is an excellent method of producing extremely high-resolution images of certain (non-centrosymmetric) structures—one of which is collagen, the major structural component of the cornea. Researchers from the Albert Einstein College of Medicine in New York used SHIM on the cornea and managed to identify two new collagenous structures: a cribriform layer beyond the terminating loop of the limbal vasculature, and fibers connecting the peripheral cornea to the limbus (Figure 1).

“What makes this finding extra interesting is the proximity of these new structures to a stem cell region where we already perform limbal stem cell transplants to replenish the corneal epithelium when it is lost to disease or injury,” said study co-author Roy Chuck.

The researchers were led in the right direction by several previous studies that used X-ray diffraction (XRD) imaging to identify collagen fibrils anchored in the limbal region. But XRD can only detect the presence of a given material, and not its architecture, whereas SHIM was able to resolve the conformation of collagen fibers, thereby revealing these previously unknown structures at the submicron scale in the eye—the anterior limbal cribriform layer and its presumed anchoring fibers.

Although the function of these new structures remains unknown, the authors suggest a potential role in maintaining the stem cell and vascular surrounding environment in healthy corneas. The cribriform layer, which is composed of structural proteins like collagen and elastin, may also provide support to the region of the eye it underlies. “Hopefully we will be able to better understand the function of these newly discovered structures by monitoring their appearances in various disease states of the ocular surface,” said Chuck. JS

Reference
PMID: 26393473.
ATOM2: Low-dose Atropine Attenuates Myopia

5-year ATOM2 trial data confirms that 0.01% atropine is more effective at slowing myopia progression than 0.1% and 0.5% doses

Myopia is one of the world’s most common eye disorders, with a prevalence of about 40 percent in Europe (1) and the United States and up to 90 percent in developed Asian countries (2). It’s a dramatic increase from numbers seen only a few decades ago, and while the refractive consequences of high myopia are easily corrected, the disease state brings with it an increased risk of retinal detachment, macular degeneration, cataract and glaucoma. This is especially true for children with rapid myopia progression – so investigators based in Singapore decided to see if they could somehow slow the development of myopia pharmacologically.

To do so, they turned to a drug first isolated from deadly nightshade: atropine. The drug has been shown to inhibit the axial growth of the eye (3), directly combating the development of myopia. But when given at high concentrations, atropine can have unpleasant side effects such as blurry, light-sensitive vision (resulting from pupil dilation), allergic conjunctivitis and dermatitis (4). In an effort to avoid these consequences, the researchers investigated the potential of low-dose atropine to slow the progression of myopia while (hopefully) minimizing side effects (5).

The ATOM2 study began in 2006, with 400 children aged between six and 12 years being randomly assigned to receive a once-nightly atropine dose of either 0.5, 0.1 or 0.01% in a 2:2:1 ratio for a period of 24 months, after which atropine treatment was halted and children were monitored for a further 12 months. Children whose myopia progressed by –0.5 D or more during this washout period were restarted on atropine 0.01% for a further 24 months.

In a previous study of atropine use for myopia progression reduction, ATOM1, 1% atropine administration slowed myopia progression in children by 50 percent, compared with placebo (5). But when the first results of ATOM2 were published, the lowest dose of atropine proved most effective; children who received the 0.01% dose were less myopic at three years from baseline than those who received either the 0.1 or 0.5% doses.

More research is needed to determine which children are the best candidates for the treatment (as not all respond), and to establish the safest and most effective starting age and total duration of atropine therapy. The study’s lead investigator Donald Tan said, “Combined with other interventions, this treatment could become a great ally in preventing myopia from causing serious visual impairment in children worldwide” (7).

References
New horizons in treating severe keratitis in dry eye disease.

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- Concomitant therapy: Use with caution in patients with glaucoma, especially in those receiving concomitant beta-blockers which may cause eye irritation.
- Interactions with other medicinal products: Co-administration with eye-drops containing corticosteroids may potentiate effects on the immune system.
- Pregnancy and Breastfeeding:
  - Not recommended in women of childbearing potential not using effective contraception or during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. Benefits of treatment must be weighed against the benefits of breast feeding.
- Driving and using machines: Moderate influence on the ability to drive and use machines. If blurred vision occurs on instillation, the patient should be advised not to drive or use machines until their vision has cleared.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Santen UK Limited (Email medinfo@santen.co.uk or telephone: 0845 075 4863).
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The 2015 Innovation Awards Are Here

Ophthalmology is one of the most intense incubators of innovation in all of medicine. Competition is driving not just incremental improvements in products that you might expect, but also some big, game-changing leaps too. Here, we recognize a year’s worth of innovation. Apps, IOLs, imagers, lasers, devices and drugs – the latest and greatest are all here. But which one came out on top this year?
10. JENVIS Dry Eye Report
**A tool for quickly identifying the cause of dry eye**
*Produced by: OCULUS Optikgeräte GmbH and JENVIS Research Institute*

**Detail:** Dry eye disease is defined as a multifactorial disease which can cause reduced visual function, optical disturbances and discomfort. But its multifactorial nature means a successful diagnosis may need a combination of tests. The JENVIS Dry Eye Report (JDER) lets users gather all their findings in one overview: the combination of the Dry Eye Questionnaire (DEQ), results of a slit lamp examination, and the noninvasive measurements of the OCULUS Keratograph 5M complete the comprehensive dry eye analysis. The therapy – as well as the treatment plan – can be defined as text blocks so that they can be used and adapted easily for further applications.

**Impact:** Millions of people suffer from dry eye worldwide, and the JDER takes this into account and presents a tool for easy dry eye diagnosis. Providing a way to neatly arrange all findings including values, images, and videos enables easy comparison and integration of findings, the system combines screening and consultancy. The patient can then receive an easy-to-grasp print-out.

*One judge said:* “Dealing with patients with dry eye can be challenging, from diagnosis to dealing with regular repeat visits. Something that helps automate and speed the diagnostic part is to be welcomed.”

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9. Oertli SPEEP Mode
**Combining the benefits of the peristaltic and Venturi pump systems**
*Produced by: Oertli Instrument AG*

**Detail:** The SPEEP Mode is a form of peristaltic pump in which the characteristics are reversed – vacuum is controlled by the surgeon, whereas flow is maintained within preset limits. It works in accordance with Poiseuille’s Law, which governs flow rate in a tube. According to the law, vacuum (as controlled by the surgeon) increases flow rate (within preset limits) in a linear fashion.

SPEEP mode provides controllable holding force (vacuum), high efficacy, and controlled flow. The advantages of SPEEP mode in combined surgery include controlled lifting of epi-nucleus, aspiration of the cortex (especially when zonules are weak), detaching the posterior hyaloid, and working precisely in the periphery, with or without a detached retina.

**Impact:** SPEEP offers a controllable holding force without flow, and therefore no traction. In combination with the continuous flow-cutter, SPEEP mode is the ideal feature needed for vitreous shaving. Possible new applications could include membrane dissection, aspiration of membranes, aspiration of the subluxated lens particles, and aspiration of subluxated IOLs.

*One judge said:* “It’s a novel way to make phacoemulsification safer, which may be particularly useful in high risk eyes.”
8. Ikervis
**Ciclosporin eye drops for dry eye disease**
*Produced by: Santen*

**Detail:** Ikervis’ formulation was specifically developed to address unmet medical needs by improving ocular drug delivery, and combines the anti-inflammatory effect of ciclosporin with nanoemulsion formulation technology. The positively charged nano-sized droplets of the emulsion electrostatically adhere to the negatively charged mucins on the ocular surface, improving ocular retention and absorption. The lipids in the formulation support the stabilization of the tear film. Reduced droplet size means the surface area to volume ratio increases, meaning a greater total surface area of the emulsion is exposed to the ocular surface – this makes once-a-day dosing possible.

Ikervis is effective in reducing ocular surface inflammation and corneal damage, and is generally safe and well tolerated – even during long-term treatment.

**Impact:** Unlike artificial tears and lubricants, Ikervis addresses the underlying inflammatory processes of dry eye disease in patients suffering from severe keratitis. Its formulation allows for once-daily use, storage at room temperature, and a three-year shelf-life. It is the only approved ciclosporin eye drop in the EU today – bringing a new treatment option to patients with severe keratitis in dry eye disease who, until now, had no access to this class of therapy.

One judge said: “It’s Restasis for Europe, but the nano formulation is novel and looks like it could be a good drug delivery method.”

7. Kahook Dual Blade
**Micro-machined parallel blades designed to cleanly extract trabecular meshwork**
*Produced by: New World Medical*

**Detail:** The Kahook Dual Blade (KDB) is designed to precisely remove trabecular meshwork in complete strips, to allow for aqueous drainage through the natural outflow system of the eye. The device will help treat glaucoma, and simplify the collection of trabecular tissue for study.

Using precision micromachining and laser-cutting technology, the KDB is made from stainless steel, and engineered to excise trabecular meshwork (TM) tissue through a clear corneal incision as small as 1.2 mm. It features a tip to pierce the TM, a ramp that stretches as the KDB is advanced, and parallel blades that excise the stretched tissue. The heel is also precision engineered with rounded edges, in order to avoid damaging the outer wall of the canal of Schlemm’s canal. By excising the TM, the KDB is designed to allow aqueous to drain from the anterior chamber into the Schlemm’s canal and distal collector channels. Pre-clinical studies have demonstrated that the KDB leaves smaller leaflets than other widely used ab-interno trabeculotomy techniques.

**Impact:** This device will allow surgeons to treat glaucoma during a cataract extraction procedure, or as a standalone procedure, in a minimally invasive fashion. This will enhance patient safety, with lower cost compared with other devices in the minimally invasive category. The lower cost of entry will allow this device to be utilized around the globe, including in underserved areas, compared with electrically powered devices or, those made from titanium or similarly expensive metals. This product has the potential to democratize angle surgery from an economic perspective, without sacrificing precision. It will also allow researchers to finally analyze the trabecular meshwork of glaucoma patients – this tissue has long been theorized to be a major source of outflow resistance in patients with high pressure, but to date researchers have not been able to easily analyze the TM of their patients.
6. SmartPulse Technology
SmartPulse technology helps perfects corneal smoothness during corneal ablation, to optimize short-term clinical outcomes
Produced by: SCHWIND eye-tech-solutions

Detail: SmartPulse uses a sophisticate three-dimensional model—based on the structure of fullerenes—that realistically describes the curvature of the cornea, and which makes it possible to position the laser pulses more closely than has been achieved before. The latest measurement and analysis methods help make optimum use of the spot geometry. Using SmartPulse results in a very smooth stromal bed after the ablation process, with fast epithelial closure in surface treatments. This can enhance short-term outcomes by reducing residual roughness, and improves the smoothness of the residual bed without compromising the stability of long-term outcomes. SmartPulse technology improves patients’ visual acuity and quality in the early postoperative phase of all treatment methods, irrespective of whether flap technique, stromal, or surface ablation is used. The effect of a very smooth corneal surface is most evident with surface treatments, where neither a LASIK flap nor epithelium helps smooth the stromal surface before regeneration.

Impact: A recent multi-center evaluation with 1,000 eyes illustrated that SmartPulse provides excellent results, particularly in the early postoperative stage. All patients underwent TransPRK and the eight international surgeons involved in the study reported shorter recovery time of visual acuity, higher levels of postoperative visual quality, and shorter re-epithelialization in the patients they treated.

One judge said: “I am excited that this technology may allow surgeons to increase their use of surface ablation.”

5. BrainPort V100
A nonsurgical intervention to let the visually impaired “see with their tongue”
Produced by: Wicab Inc.

Detail: The BrainPort V100 is an oral electronic vision aid that provides electro-tactile stimulation to aid profoundly blind patients in orientation, mobility, and object recognition as an adjunctive device to other assistive methods, such as the white cane, or a guide dog.

The technology translates digital information from a wearable video camera into gentle electrical stimulation patterns on the surface of the tongue. Users feel moving bubble-like patterns on their tongue which they learn to interpret as the shape, size, location and motion of objects in their environment. Some users have described it as being able to “see with your tongue.”

Impact: The BrainPort V100 is a nonsurgical intervention that can be used by individuals with no vision, irrespective of whether they are congenitally blind, or have acquired blindness. The technology could allow blind people who cannot currently be treated to live more independently—and as BrainPort does not affect the eyes, this could be beneficial if future research offers better surgical or other therapeutic alternatives.

One judge said: “This innovation links the sensitivity of the tongue to the visual cortex. For visually disabled patients, it promises significant noninvasive help.”
4. Vula Eye Health Smartphone App
A smartphone app to connect healthcare workers with ophthalmic guidelines and advice
Produced by: William Mapham, Ophthalmology registrar, University of Stellenbosch, Tygerberg Hospital, South Africa

**Detail:** The Vula smartphone application provides healthcare workers with basic ophthalmic diagnostic guidelines, and connects them with an ophthalmologist who can provide advice, respond to queries, and accept referrals in real time.

Vula has the potential to bring specialist eye care to anyone, anywhere. Aimed at rural communities where access to specialist ophthalmic care is extremely difficult to obtain, the Vula app empowers community healthcare workers with decision making assistance, and access to specialist knowledge via their mobile phones. By equipping healthcare workers with the ability to conduct a basic ophthalmic examination, complete a standardized referral form, and access a local specialist for consultation and referral in real time, it ensures that eye conditions are appropriately managed and referred. The app can be used anywhere in the world, connecting healthcare workers with their local ophthalmologist.

**Impact:** Vula extends the reach of specialist eye care beyond the physical boundaries of the eye clinic. As a mobile platform, it can overcome the often poor traditional communication and transport infrastructure, taking advantage of the high penetration of mobile phones in even the poorest of communities.

**The judges said:** “A versatile program that has the potential to not only impact ocular health in developing countries, but also has the potential to make a significant impact in the developed world as well.”

“Apps like this hold the potential to simplify and make patient screening and referral more efficient — and looks like it could be of particular use in rural and inaccessible locales.”

3. LensAR Streamline Technology
The first femto cataract platform to automate several key steps of the procedure
Produced by: LenSAR, Inc.

**Detail:** The LENSAR laser system with Streamline is the first femtosecond cataract laser that can automate several key steps of surgical planning and delivery. It can integrate wirelessly with certain preoperative corneal topographers (like iOptics’ Cassini), and can perform iris registration, automatic cataract density imaging, and automatic customized fragmentation patterns. The system can perform anterior laser capsulotomies, lens fragmentation, and corneal and arcuate incisions, and its level of automation allows for integration into existing workflows without increasing procedure times.

**Impact:** The integration and automation the system offers has the potential to reduce errors that can occasionally arise from manual data entry and the issues that can arise from physically marking the eye preoperatively. This should increase accuracy and efficiency (and potentially visual outcomes too). This is the first system to fully automate and customize these important planning and execution steps of refractive surgery.

**The judges said:** “A significant advance in the way that femtosecond lasers can reduce risk with cataract surgery, as well as improve visual outcomes.”

“It’s a logical next step in terms of what femtosecond lasers offer, and soon all manufacturers will have to offer something similar.”
2. F4H5 WashOut
Amphiphilic surfactant for complications in silicone oil removal
Produced by: Geuder

Detail: F4H5 WashOut (perfluorobutylpentane – C4F9-C5H11) is a semifluorinated alkane that is able to dissolve silicone oil. F4H5 WashOut is similar to another solvent for silicon oil, F6H8 (perfluorohexylcane—C6F13-C8H17) but is more amphiphilic (i.e. both hydrophilic and lipophilic) and therefore a superior solvent for silicone oil. Crucially, F4H5 forms no potentially reactive structures, and should therefore ensure biocompatibility. F4H5 WashOut is able dissolve silicon oil in balanced salt solution at any mixing ratio – a situation where conventional surfactants have limited success.

Impact: Tamponades like silicone oil and perfluorocarbon liquids (PFCL) are today’s gold standard in modern vitreoretinal surgery. But although they are necessary, and can positively impact clinical results, there are also potential side effects, such as emulsified oil, unwanted mixtures of silicone oil and PFCL, and residual oil that remains in the eye. This situation can entail unwanted clinical manifestations, including glaucoma, inflammation and formation of fibrosis, and proliferative vitreoretinopathy, so it’s important to eradicate silicon oil completely to avoid risking these complications.

Increased use of PFCL and silicone oil, as well as increasingly smaller incision sizes (which can make it more complicated to completely remove the vitreous, as well as inducing tamponades) can increase the incidence of adverse effects – making a biocompatible, effective detergent a necessity.

The judges said: "This is a very clever chemical solution to a difficult problem." “Touches upon an unmet clinical need. Persisting postoperative oil and perfluron remnants might cause toxic and visual problems. This innovation seems to solve that.”

The Judges

**Florian Kretz**
Eye Clinic Ahaus-Raesfeld Rheine, Ahaus, Germany

**Keith Barton**
Moorfields Eye Hospital, London, UK

**Kuldev Singh**
Stamford School of Medicine, Palo Alto, California, USA

**Michael Koss**
Goethe University, Frankfurt-am-Main, Germany

**Michael Mrochen**
IROC Science, Zürich, Switzerland

**Bill Trattler**
Center for Excellence in Eye Care, Miami, Florida, USA
**1 Harmoni Modular IOL**  
A two-piece IOL designed to adapt to, and accommodate changes in, refractive needs  
*Produced by: ClarVista Medical, Inc.*

**Detail:** The HARMONI modular IOL system is designed to improve upon existing IOL designs, by having the flexibility to exchange the optic component at any time – without manipulation of the capsular bag or the base component. HARMONI's base component enhances structural support of the capsular bag, in order to help deliver more predictable post-procedural outcomes. The base component is designed to securely receive the optic component using traditional surgical tools and techniques, and the optic component can be of monofocal, toric, advanced multifocal or extended depth-of-focus designs – and can be exchanged post-operatively without manipulation of the base or the delicate capsular bag.

The two-piece design means that the base plate has the potential to maintain a consistent position within the capsular bag – and that the addition of the optic portion of the IOL to the base plate should attain a more predictable position within the eye. The effective lens position can therefore be better predicted, allowing for improved outcomes. If the desired power is missed, the fact that the optic portion of the IOL can be easily exchanged allows for a safer and more predictable enhancement than current IOL designs permit. In the case of toric misalignment, realignment should also be safer and easier than current IOL designs.

**Impact:** The HARMONI Modular IOL system is designed to produce a more predictable lens position, and allow for refractive care to be provided over the patient’s life, even if changes in lifestyle or pathology create the need for a different refractive solution, as it will allow patients to upgrade their IOL as better technologies arise.

The HARMONI allows for easy adjustment of IOL power, addition (or subtraction) of toricity, IOL rotation by exchange, or manipulation of the modular component of the optic in these two-piece component IOLs. It is also potentially very important for pediatric cataract patients, who experience changes in eye power as the eye grows.

**The judges said:**

“It would be amazing to be able to swap IOL optics with a small operation to tweak refractive error, without having to unembed the haptics. An easy winner.”

“The ability to change the optic without touching the haptics could revolutionize cataract surgery.”

“The concept of postoperative IOL adjustment is very appealing.”

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For more information, please contact: Patricia Ishak (patricia.ishak@bayer.com)
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For more information, please contact: Jennifer Pluim (jennifer.pluim@bayer.com)

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For more information, please contact: Melissa Chen Montes de Oca (melissa.chenmontesdeoca@bayer.com)
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Small Incision Femtosecond Refractive Lenticule Assisted CXL in Corneal Ectasia

Hemlata Gupta and colleagues describe how they apply SMILE lenticules to thin corneas before performing CXL.

Anti-Spin Doctor

Florian Kretz recounts his experiences with the Miniflex toric IOL to date. The lens claims to achieve minimal postoperative rotation… is this what Flo found?
Small Incision Femtosecond Refractive Lenticule Assisted CXL in Corneal Ectasia

CXL is effective in slowing and halting keratoconus and corneal ectasias – but the thinnest corneas can’t receive it, so we propose a new way of bringing CXL to those that need it most

By Hemlata Gupta, Mahipal S. Sachdev, Deepa Gupta, Ritika Sachdev and Gitansha Sachdev

Keratoconus is a non-inflammatory progressive corneal thinning and ectasia of unknown etiology in which the cornea assumes a conical shape. It is associated with irregular astigmatism, central corneal scarring and progressive myopia resulting in impaired visual acuity (1). Although there are a number of treatment options – from contact lenses to keratoplasty – before the advent of corneal collagen cross-linking (CXL) with UV light and riboflavin, none were able to alter the natural course of the disease (1,2). CXL, however, has shown that it has the potential to be disease-altering; it acts to increase the cornea’s biochemical strength and can slow – or even halt – the progression of the disease (3,4,5). Nevertheless, it is not a panacea – there are limitations on what the technique can achieve and on whom.

Currently, the most effective form of CXL is the Dresden protocol (3) – photosensitizing the cornea with iso-osmolar riboflavin (0.1% solution in 20% dextran) for half an hour and then exposing to UV-A radiation (370 nm, 3 mW/cm²) for an additional half hour. However, it’s important to note that the effects of the riboflavin and the UV-A irradiation are restricted to the anterior ~300 μm of corneal stroma (3,6,7). Continual application of riboflavin and a stromal thickness of at least 400 μm are both critical to the procedure, as the combination of the two prevent the UV-A irradiation used during the process from penetrating into sensitive ocular tissues like the deep stroma, corneal endothelium or even the crystalline lens (6,8,9). But one of the hallmarks of keratoconus and other corneal ectasias is the thinning of the cornea, and this means that many patients with advanced disease have corneas that are too thin for safe cross-linking. One method is to swell the corneal epithelium with hypo-osmolar riboflavin beforehand, bringing its thickness to the minimum 400 μm, as described by Farhad Hafezi’s group (10). However, this procedure is less effective than the Dresden protocol CXL, and this might be due to artificially swollen corneas not behaving like non-swollen ones during the procedure. It’s also possible that the decreased relative collagen concentration in the stroma makes CXL less effective – and Hafezi’s group suggest that taking this approach in any cornea thinner than 330 μm may be inadvisable (11).

Another option is transepithelial or “epi-on” CXL, which was introduced to prevent the complications associated with epithelial debridement – principally pain, haze and an increased risk of infection. Though researchers have reported statistically significant improvements in visual and topographic parameters (12,13) with epi-on CXL, the current evidence shows

Figure 1. A cross-sectional view of the steps of our technique. a. The femtosecond laser separates the lenticule of the myopic patient, b. The lenticule is extracted through the small incision, c. The lenticule is placed on the de-epithelialized corneal surface, with the thickest part of the lenticule (1) placed over the thinnest part of the cornea (2).
that the traditional epi-off methods are still more effective, and endothelial cell toxicity associated with the transepithelial solutions used remain a concern. Recently, Kymionis et al. (14) performed customized pachymetry-guided epithelial debridement in two patients with progressive keratoconus. They performed a central 8 mm epithelial debridement, but preserved a small localized island that corresponded to the thinnest or steepest area. Although this technique has some advantages – preventing local stromal dehydration, blocking excess UV-A in the most sensitive region – it fails to strengthen the thinnest regions that most require cross-linking, and concerningly, an anterior segment optical coherence tomography (AS-OCT) and confocal microscopy study has demonstrated stromal haze and the demarcation line in areas corresponding to de-epithelialized stroma – things that were not evident in areas with an intact epithelium (15).

Finally, a highly innovative approach has also been suggested is the use of riboflavin-soaked bandage contact lenses to artificially increase the corneal thickness for CXL (16). Unfortunately, originality has its drawbacks, as it’s impossible to customize the thickness of the lens, different materials have varied hydration states and UV-A transmission properties, and the lenses may adhere unevenly to the stromal bed, causing the riboflavin to pool.

Sadly, what this means that there’s a significant population of patients with corneal ectasias that have progressed beyond the point where they are able to receive a truly effective intervention – CXL. It’s an issue I’ve encountered in my own practice, and one that’s prevalent in many developing countries. It’s also a particular problem in Asian countries, where keratoconus arises earlier and is diagnosed later – so many of our patients have already progressed beyond the limits for safe CXL.

This might not be the case for much longer. We have devised a new method for increasing the intraoperative corneal thickness: using refractive lenticules extracted from eyes undergoing small incision lenticule extraction (SMILE) surgery for myopia (without astigmatism).

How do we do it?
SMILE is a novel refractive surgery that involves the extraction of a femtosecond laser-constructed corneal lenticule through a single small incision without raising a flap (17). The lenticular thickness depends upon the refractive error of the patient, but is greatest at its center and decreases toward the periphery (18). We’ve devised a new technique that takes advantage of the extracted lenticule, which is added onto the ectatic corneal surface after epithelial debridement to tailor stromal expansion for performing CXL in thin and ultrathin cornes. Using a lenticule allows us to increase corneal thickness by adding tissue with the same biological and absorptive properties; we can also place the lenticule over the apex of the cone to augment thickness where required and enable the remaining stroma to be cross-linked normally.

We performed CXL using our modified technique in seven eyes, each of which had documented progression of keratoconus with steepening on corneal topography over a period of one year. Pachymetric analysis revealed a corneal thickness of less than 400 μm...
at the area of maximum steepening. The procedures were planned along with SMILE surgeries on patients with moderate myopia and no astigmatism. Based on the technique described by Shah et al. (17), SMILE using a VisuMax femtosecond laser (Carl Zeiss Meditec AG) was performed under topical anesthesia. The refractive lenticule, 6.2 mm in diameter with an estimated central thickness of 110 to 120 μm, was extracted intact for use in CXL corneal augmentation – and the femtosecond cuts were so precise that the lenticule was highly likely to form a stable assembly when placed on a de-epithelialized cornea.

We performed our CXL operations under aseptic precautions as follows:

1. The patient’s eye is cleaned and draped.
2. Proparacaine 0.5% is instilled three times at five-minute intervals, 15 minutes prior to the procedure.
3. The central 8 mm of corneal epithelium is debrided with a blunt spatula.
4. Intraoperative pachymetry determines the required thickness of the refractive lenticule.
5. The central area of the lenticule (corresponding to the optic zone of the donor eye) is placed over the apex of the cone so that the thinnest area of the cone corresponds to the thickest area of the lenticule (Figure 1).
6. The augmented stromal thickness is confirmed to be by intraoperative ultrasonic pachymetry to be at least 400 μm.
7. Instill one drop of riboflavin (0.1% solution) every five minutes for 30 minutes, using slit lamp examination to confirm the presence of yellow flare in the anterior chamber and ascertain adequate penetration of the dye.
8. Apply UV-A radiation (365 nm, with an irradiance of 3 mW/cm²) at a distance of 5 cm for 30 minutes. Continue instilling one drop of riboflavin every five minutes while irradiating.
9. Once irradiation is complete, peel the refractive lenticule from the stromal bed.
10. Irrigate the corneal surface with normal saline.
11. Apply a bandage contact lens to be removed on the fifth postoperative day.

In our patients, the refractive lenticule showed increased rigidity after CXL, and histopathological examination revealed cross-linking (Figure 2). In addition to the bandage contact lens, the patients received postoperative medications including gatifloxacin 0.3% eyedrops four times daily for seven days, loteprednol acetate 0.5% eyedrops three times daily for 20 days, and hypromellose 0.3% eye drops six times daily for 45 days.

How did it work?
In all seven eyes, we saw an even demarcation line indicative of successful cross-linking (19). The epithelium healed completely within three to five days of the procedure, after which bandage contact lenses were removed. We noted no intraoperative or postoperative complications in any of our patients, and we were able to demonstrate corneal stability by topography at the one-year follow-up (Figures 3 and 4). Mean Kmax decreased from a preoperative value of 56.9 D to 55.7 D at one year postoperatively. Specular microscopy.
revealed no significant endothelial cell loss. For these early procedures, we performed SMILE and CXL one after another in adjacent operating rooms to maintain sterility. A method for sterile preservation of myopic lenticules would allow them to be stored after SMILE for CXL procedures at a later date, as well as enabling more widespread use of our lenticule CXL method. Overall, the technique was highly successful in our initial test cases – but of course, we still need to conduct long-term studies to further establish the efficacy and feasibility of our procedure.

References
The Anti-Spin Doctor

Implanting a toric IOL during cataract surgery is great way of dealing with a patient’s corneal astigmatism – but off-axis rotation of the IOL can erode those benefits. One IOL claims to achieve minimal postoperative rotation. Can it?

By Florian Kretz

Every cataract and refractive surgeon hears the same thing from patients: that they want to be spectacle-free after cataract surgery. The introduction of (what’s now a wide range of) premium intraocular lenses (IOLs) has made surgeons able to achieve that in most patients. But astigmatism still poses problems. Traditional monofocal IOLs correct the spherical equivalent of refractive error, but not pre-existing corneal astigmatism – and as 20–30 percent of patients have astigmatism of 1.25 D or greater (1). That’s a significant proportion of patients. There are essentially two options in such cases: limbal relaxing incisions (LRIs) – a tried and tested method of correcting corneal astigmatism during cataract surgery, but one that also carries a risk of infection and can cause damage to the cornea (2,3). The other option is toric IOLs, which are often more costly relative to monofocal IOL implantation plus LRIs, but have a better safety profile and offer more predictable results (4,5).

The evolution of IOL design
IOL design continues to evolve and every manufacturer is trying to improve upon their existing designs. For example, square edges on the posterior edge of the IOL’s posterior face help reduce posterior capsule opacification (PCO); aspheric optic designs should eliminate spherical aberration; better haptics help with IOL centration and rotational stability; and there’s always a push to minimize the incisions made to the cornea during surgery below 2 mm, as this minimizes surgically induced astigmatism. The Miniflex Toric IOL (Mediphacos) claims to tick all of these boxes – and so we decided to evaluate it. But in terms of ensuring patients are satisfied and remain spectacle-free after surgery, it’s important to ensure that the IOL is aligned along the correct axis to correct the astigmatism, and that it stays correctly aligned after surgery. There are a number of factors in an IOL’s design that can promote rotational stability – principally, the total diameter of the IOL and the design of the haptics (6–8). To minimize optical torsion and tilting, the Miniflex Toric has a large overall diameter (12.5 mm), self-centering double haptics, and step-vaulted haptic angulation to keep the haptics in parallel alignment with the optic at all times. Data published to date indicate that no patient who has received one has experienced rotation greater than 7° (1).

Our experience
In cooperation with the International Vision Correction Research network, I and my colleagues at the University of Heidelberg are currently conducting our own clinical analysis of the IOL. To date, 19 eyes (14 patients; mean age 69±9.6 years) have received the IOL as part of cataract surgery. Preoperatively, our patients’ UDVsAs ranged from 1.3 to 0.24 LogMAR, and corrected distance visual acuities (CDVAs) ranged from 1.10 to 0.20 LogMAR, with preoperative cylinder ranging from −3.48 D to −0.16 D. All patients were implanted with the Miniflex Toric lens with a sphere ranging from 15.0 to 29.0 D and a cylinder of 1.5 to 6.0 D. Target refraction was emmetropia in all but one patient (in whom the target refraction was −2.5 D). At postoperative day one, patients’ UDVsAs ranged from 0.5 to 0.20 LogMAR and their CDVAs from −0.7 to −0.20 LogMAR. Of course, the study is still underway – but longer-term follow-up data from our first three patients (see Box) further support the idea that this IOL significantly reduces refractive error and has good rotational stability.

Cyclorotation and IOL power calculations
These early successes are a good sign, but we can’t rely on the IOL alone to...
appropriately address astigmatism. To avoid lens misalignment and achieve accurate results, we need to consider cyclorotation (rotation of the eye around the line of sight), axis marking, intraoperative alignment and accurate toric IOL power calculation. Key considerations with regard to cyclorotation include head posture, change in fixation distance, monocular versus binocular viewing, and sitting versus supine position. In my practice, I always mark the axis of alignment with the patient awake and sitting upright. I make sure that the head and upper body are straight, and then I mark the cylinder axis using a pendulum marker. Toric IOL power calculation requires a little more data – not only biometry, but also an assessment of corneal topography. I always make sure I get three comparable keratometry results before proceeding, and to improve accuracy, I ask patients to refrain from wearing contact lens for at least two weeks beforehand. Because there have been reports of different K readings with different keratometers (9), I also recommend that ophthalmologists measure the corneal radius, rather than relying solely on D-values.

Thus far, my findings indicate that patients with corneal astigmatism of at least 0.75 D benefit from toric IOLs. Although we still need data from longer follow-up, early results in my patients suggest that the Miniflex Toric IOL prevents rotational instability, affords excellent visual outcomes, and may help to increase post-surgical spectacle independence in patients with both cataract and astigmatism.

Florian Kretz is a consultant ophthalmologist and research fellow at the IVCRC and the David J Apple International Laboratory for Ocular Pathology at the Department of Ophthalmology, University Hospital Heidelberg, Germany, research coordinator for the International Vision Correction Research Centre Network (IVCRC.net), Heidelberg, Germany and one of the lead surgeons at the Eyeclinic Ahaus-Raesfeld-Rheine (Gerl Group), Ahaus, Germany.

References
Ocular surface: what’s new?

Highlights from Laboratoires Théa’s Satellite Education Program, “Ocular Surface: What’s New?” held on October 8, 2015, at the 7th EVER Congress, Nice, France.

Dry eye disease (DED) is a particular burden for both doctor and patient alike. There are three principal reasons behind this: high prevalence (up to 100 million people worldwide are thought to be affected by DED to some degree), many causes (autoimmune, environmental, drug adverse events, and ocular and systemic disease) with multiple forms (principally aqueous-deficient and evaporative). From the ophthalmologist’s perspective, the presence of DED precludes patients from receiving surgery, complicates recovery after surgical procedures, and can present with symptoms of discomfort, visual disturbance, and tear film instability – leading to patients who are constantly unhappy with how their eyes feel.

DED is frequently characterized by increased osmolarity of the tear film and inflammation of the ocular surface, which, without intervention, can ultimately result in permanent damage. Poor eyelid hygiene or impaired function of the meibomian glands can also cause or exacerbate inflammation and ocular surface damage. Because of DED’s many and multifactorial etiologies, there’s a wide range of therapeutic options in use – from lubricants to immunomodulators, and treatment needs to be individualized to each patient. However, it’s clear that DED-induced perturbations in tear film – no matter what the cause – lead to increased inflammation and visual disturbances. This supplement aims to document the issues involved in DED; its causes, its effect on the tear film – and vision – and how this situation can be improved with topical eyedrops containing a bioprotectant like trehalose. (see page 2).

A new paradigm in dry eye disease

Christophe Baudouin, Professor and Chairman of the Department of Ophthalmology, Quinze–Vingts National Ophthalmology Hospital, Paris, France.

Inflammation is a ubiquitous mechanism in ocular surface diseases, but sometimes it can be difficult to identify, even in situations where it plays a key role. For example, in many cases of DED, there are no signs of clinical inflammation – no redness or swelling can be observed, and often no pain is felt – just a sensation of dryness or grittiness. Nevertheless, subclinical inflammation as evidenced by cytokine and lymphocyte presence, is one of the four key mechanisms of DED and a significant contributor to its pathophysiology, along with tear hyperosmolarity, apoptosis and tear film insufficiency and instability. These mechanisms form the basis of the “vicious circle” hypothesis (see Figure 1).

Tear hyperosmolarity is a significant contributor to inflammatory activation in DED. Hyperosmolarity induces inflammatory cytokines such as CCL2 and IL-8; in a mouse model of DED, an antagonist to CCR2 – the CCL2 receptor – decreased monocyte infiltration into the cornea. Damaged or dysfunctional corneal nerve signaling (which can result from corneal surgery, congenital factors, and even from dry eye itself), can also contribute to the pain and inflammation patients with DED experience. Once established, this inflammation can lead to the keratinization of the meibomian gland orifices, leading to blockage, dropout, and ultimately meibomian gland dysfunction (MGD). We now know that DED is not restricted to the ocular surface – with the involvement of nerves, mucosa and even the immune system, there’s much more going on behind the scenes – and it’s time to begin addressing those aspects of the disease.

Figure 1. The four target areas contributing to the pathophysiology of DED are tear film instability, tear hyperosmolarity, apoptosis and inflammation. The “vicious circle” is primarily driven by hyperosmolarity and tear film instability, but can be entered at any point (1). LPS: lipopolysaccharide; MGD, meibomian gland dysfunction; MMP, matrix metalloproteinase.
Even now, there’s no shortage of targets for blocking inflammation: we use steroids, antibiotics, essential fatty acids, and even topical cyclosporine. But in the race to do so as effectively as possible and with as few side effects as possible, treatment options like trehalose – a bioprotectant that acts at multiple points of dry eye’s vicious circle – could be a good alternative.

The MEIBUM survey: a closer look at the eyelids

David Díaz-Valle, Section Chief, Ocular Surface Unit, San Carlos Clinic Hospital; Madrid, Spain.

One significant cause of DED is MGD, which can result in tear film alteration, symptoms of eye irritation, inflammation, and ocular surface disease. It’s the main cause of evaporative DED (which comprises 49–58 percent of all dry eye) and is typically diagnosed by examining a patient’s symptoms, clinical signs, meibography (see Figure 1), and gland expression.

To better understand the management of MGD, a study known as MEIBUM (Management of Eyelid Disorders By Ophthalmologists in Usual Medical Practice) was conducted at clinics across nine countries in Europe. In the first three countries completed (Poland, Spain and Germany), a total of 4,884 patients (mean age 57.5, 63 percent female, 80 percent with pre-existing eye disorders) have been surveyed thus far. Of those patients, 92 percent presented with at least one DED-related symptom, and 78.7 percent showed evidence of eyelid disease. Ultimately, 55 percent of patients were diagnosed with MGD and 64 percent with DED.

The fact that over half of non-selected patients have MGD with negative impact on their daily vision- or contact lens-related activities shows that it’s a significant concern in the clinic. It impacts on patients’ quality of life, their professional and personal activities, and even on their perceived visual acuity and overall satisfaction. There’s also a significant correlation (p<0.001) between MGD and dry eye – which is unsurprising, as MGD is the main risk factor for DED. It’s therefore vital to evaluate the eyelids and free margin in every patient, as many exhibit some degree of MGD and would benefit from treatment by eyelid hygiene and artificial tears.

What is trehalose?

Trehalose is a naturally occurring bioprotective disaccharide molecule present in organisms from bacteria to crustaceans – but not in mammals (5). It acts as a protector against environmental stress (6), chiefly through osmoregulation (preventing water leakage from the cytoplasm). It also preserves cell integrity by stabilizing membrane lipids, protecting proteins, inducing autophagy (to renew cell material), and decreasing apoptosis and inflammation.

Trehalose: a natural bioprotector

Trehalose is able to suppress structural changes due to dehydration – likely by hydrogen bonding with protein surfaces to maintain their conformation and activity (7), and now its bioprotective effects are being applied to DED. It can protect corneal cells from desiccation (9), apoptosis (10), accelerate their healing (11) and restore and maintain the osmotic balance of the ocular surface (12,13). The availability of eyedrops containing both sodium hyaluronate and trehalose, capitalizing on the components’ lubricant and bioprotectant properties, are clearly an advance in the treatment of DED.
In DED, there is often a discordance between clinical signs and functional ones like dryness or the sensation of itching, burning or foreign bodies (see Table 1). In moderate DED, for instance, there may be weak or absent corneal staining and moderate tear-film breakup time (TBUT), but many subjective and difficult-to-quantify visual complaints due to tear film instability.

The most powerful refractive surface of the eye is the interface between air and tears – so the state of the lacrimal tear film can clearly affect the eye’s refractive index. In DED, when the tear film thickness decreases in an irregular manner, the result can be a significant impact on patients’ optical quality as determined by scattering and aberrations (see Figure 1). An irregular alteration of the tear film, as seen in DED, dramatically changes the refractive power of the cornea and can lead to visual acuity decreases of greater than 1.0 D, as well as significant increases in higher-order aberrations.

Of note, the tests most commonly used to diagnose DED – fluorescein staining and TBUT – are subjective, in that no strict correlation exists between their results and optical quality in DED. What’s needed, then, are tests that can dynamically visualize corneal tear film quality, like the Ocular Quality Analysis System (OQAS), a “double pass” aberrometer that also generates an ocular scattering index (OSI) by screening a projected point source on the retina after two passes through the eye.

Because tear film irregularity has such a significant impact on optical quality, tear film substitutes can decrease the mean OSI (and the variability of it) and improve contrast sensitivity, visual quality and tear film stability. This is why it’s important to evaluate DED using both eye and visual symptoms, use both classical and new tools to examine the impact of the disease, and consider tear film substitutes with a long residence time as a treatment to improve optical quality.

Table 1. Clinical evaluation of minimal, moderate and severe DED. *Conjunctival.

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<th>Minimal DED</th>
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<td>Visual signs</td>
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<td>Staining*</td>
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Figure 1. The effect of the lacrimal tear film on refractive index. In DED, an irregular decrease in tear film thickness (bottom right) affects the eye’s optical quality and can affect aberration measurement (2).

Figure 2. OSI is measured at half-second intervals to plot ocular scatter over time in a. normal eyes and b. severe DED. Variation in OSI indicates a patient’s disease severity (2).

New treatment to improve tear film thickness in dry eye disease

Leopold Schmetterer, Section Head, Department of Clinical Pharmacology, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna; Vienna, Austria.

The eye clinic at the Medical University of Vienna’s Department of Clinical Pharmacology has a custom-built optical coherence tomography (OCT) imaging system prototype that is capable of detecting tear film changes on the order of 50 nanometers – a threshold that is far more sensitive than any commercially available system. That system has been used to compare the thicknesses of the tear films of patients with and without DED and evaluate the impact of topical artificial tear application to these eyes.

In a randomized, double-masked, controlled parallel group study, 60 DED patients received a single dose of either preservative-free sodium chloride 0.9% (Hydrabak®), preservative-free sodium hyaluronate (HA) 0.15% (Hyabak®), or preservative-free HA 0.15% + trehalose 3% mg/mL (Thealoz Duo®). HA
drops increased tear film thickness as compared to sodium chloride over a four-hour period, and combining HA with trehalose was even more effective (4).

The question is: how do these results on tear film thickness relate to what is seen in the clinic? To answer that, a multicenter, randomized, investigator-masked, parallel group Phase III clinical trial was conducted to demonstrate the noninferiority of Thealoz Duo® (HA 0.15% + trehalose 3%) to VISMED® (HA 0.18%) in treatment of DED (5). 105 patients with moderate-to-severe DED (OSDI ≥18) and at least one eligible eye (global ocular staining grade 4–9 on the Oxford scheme and at least one eligible eye (global ocular staining and at least one eligible eye (global ocular staining grade 4–9 on the Oxford scheme and at least one eligible eye (global ocular staining grade 4–9 on the Oxford scheme and at least one eligible eye (global ocular staining grade 4–9 on the Oxford scheme and at least one eligible eye (global ocular staining grade 4–9 on the Oxford scheme) were randomized, investigator-masked, parallel treated with Thealoz DUO® or HA three to six times daily for six consecutive days (Figure 1b) and in the OSDI score at three months (see Figure 1c). At the conclusion of treatment, Thealoz Duo® also yielded significantly better investigator and patient satisfaction reduces inflammation and apoptosis and induces autophagy (7).

Why does adding trehalose increase efficacy? One likely reason is because trehalose is a bioprotectant that not only provides osmoregulation, but also stabilizes the membrane lipid bilayer, protects proteins, reduces inflammation and induces autophagy.

Ultra-high-resolution OCT provides a new and effective method of determining tear film thickness in DED patients and has allowed ophthalmologists to verify that preservative-free HA 0.15% + trehalose 3% offers a longer residence time on the ocular surface. The clinical study that compared Thealoz Duo® with HA has also shown that both drugs yield similar improvements in ocular staining, but that Thealoz Duo® offers significantly greater improvements in OSDI score, symptom severity, and patient and investigator satisfaction. Some or all of these may be related to trehalose's mechanisms of action – in particular, its natural bioprotection.

References
3. D. Diaz-Valle, “MGD MEIBUM study”. Presented at the 7th EVER Congress; October 8, 2015; Nice, France.
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Benchmarking Endophthalmitis

Analysing the last five years of literature tells us who’s published what in endophthalmitis, and gives us an idea of where the field is heading.
Benchmarking Endophthalmitis

What does analysis of the last five years of literature on endophthalmitis tell us about the priorities of the field, and the contributors to it?

By Mark Hillen

Endophthalmitis — the purulent inflammation of the intraocular fluids — is never a good sign, and typically arises because of infection. There are a number of types – exogenous (which comprises both acute and chronic postoperative forms, traumatic, filtering bleb-associated, and post-intravitreal injection-arising) and endogenous, with acute postoperative endophthalmitis being the most common form.

But what are your peers’ thoughts on the matter? What are they reading? Where is the research heading? We decided to benchmark the last five years of PubMed-listed literature on the topic. We asked:

• What are the major topics for the field?
• Which journals have the greatest impact?
• How is the knowledge available online?
• What type of articles are being published?
• Who are the most prolific authors?

PubMed was searched for “endophthalmitis”, with results limited to the last five years. The data were analyzed in Microsoft Excel 2013.
Fee or Free?

Just over one in every three articles is available online, free of charge. However, 6 percent of articles are, even now, unavailable via the web.

Top 20 Journals
(by number of Publications)

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<td>Retina</td>
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<td>J Cataract Refract Surg</td>
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<tr>
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Publications per year

- 2011: 317 publications
- 2012: 345 publications
- 2013: 342 publications
- 2014: 347 publications
- 2015*: 372 publications

*year to date

Top 20 journals (by Impact Factor)

- Arch Ophthalmol: 7.008
- Ophthalmology: 6.17
- J Clin Microbiol: 4.232
- Am J Ophthalmol: 4.021
- Retina: 3.96
- Retin Cases Brief Rep: 3.96
- Invest Ophthalmol Vis Sci: 3.661
- JAMA Ophthalmol: 3.318
- Clin Experiment Ophthalmol: 2.973
- Clin Ophthalmol: 2.826
- Int J Ophthalmol: 2.773
- Curr Opin Ophthalmol: 2.638
- J Cataract Refract Surg: 2.552
- Br J Ophthalmol: 2.525
- Acta Ophthalmol: 2.512
- J Glaucoma: 2.427
- Cornea: 2.36
- Curr Eye Res: 1.897
- Eye (Lond): 1.663

Impact Factor
**Article categorization by number of publications**

- **Case report/series**: 783
- **Comparative/observational study**: 430
- **Review**: 230
- **Comment/Editorial**: 142
- **Basic science/preclinical**: 57
- **Multicenter study**: 44
- **Editorial**: 25
- **Guideline**: 7
- **Other**: 2

**Most common additional search terms**

- **Fungal**: 70.3%
- **Postoperative**: 42.5%
- **Intravitreal**: 41.5%
- **Injection**: 31.5%
- **Intravitreal**: 30.3%
- **Cataract**: 29.6%
- **Vitrectomy**: 28.1%
- **Prophylaxis**: 25.3%
- **Endogenous**: 15.7%
- **Thrombolytic**: 13.4%
- **Candida**: 10.8%
- **Klebsiella**: 5.9%
- **Sterile**: 4.2%
- **Other**: 3.7%
Lighting the Way for Corneal Cross-Linking
Nikki Hafezi discusses the work of the non-profit organization Light for Sight – including bringing a family from Tajikistan to Iran in order get their son who had Down syndrome and keratoconus the treatment he needed.
Lighting the Way for Corneal Cross-Linking

The Light for Sight foundation provides ophthalmologists around the world with CXL training and ensures that no young patient must go without treatment

By Nikki Hafezi

Keratoconus, the progressive thinning and bulging of the cornea, is one of the most common causes of severe visual impairment in young people. A disorder that affects as many as one in every 1,500 people, keratoconus can lead to focusing difficulties, higher-order aberrations and corneal scarring. But it's possible to reduce the impact of this potentially debilitating disease with proper diagnosis and early corneal collagen cross-linking (CXL) treatment to halt its progression. The best time to treat keratoconus is early in the disease, before significant changes in corneal shape and thickness take place – but to do this, we must overcome two obstacles: one, the lack of routine systematic screening for children and adolescents, and two, a lack of childhood keratoconus awareness among health care professionals.

Although research has shown that eye rubbing and hormonal influences both increase the prevalence of keratoconus, one of the highest documented incidence rates is among the Down syndrome population. Thanks to increased expression of collagen genes on chromosome 21, patients with Down syndrome often show altered collagen characteristics – typically an unusual degree of laxity and elasticity. In ophthalmology, the collagen of the cornea shows similar characteristics – and in the cornea, hyperelasticity presents as the thinning and deformation typical of keratoconus. As many as one in 67 patients with Down syndrome has keratoconus, an incidence over 20 times higher than that of the general population.

With the knowledge that awareness presents an obstacle to early treatment, and that the Down syndrome population has a higher prevalence of keratoconus, my colleagues and I founded Light for Sight – a nonprofit organization whose mission is to combat preventable blindness among

“At a Glance

- Keratoconus, a progressive disease that involves corneal thinning and bulging, affects a significant portion of the population, particularly in patients with Down syndrome
- The disease is best treated early, but a lack of screening and awareness often prevents this
- Light for Sight’s mission is to increase keratoconus awareness among healthcare providers and ensure that children and adolescents have access to treatment
- The foundation accomplishes this goal by making connections, providing training, and seeking industry support – an ongoing task

“We chose the name Light for Sight to reflect that goal – a reference to the use of ultraviolet light to perform CXL, the only surgical intervention proven to arrest progression of keratoconus.”
children and adolescents with keratoconus. We chose the name Light for Sight to reflect that goal – a reference to the use of ultraviolet light to perform CXL, the only surgical intervention proven to arrest progression of keratoconus. Light for Sight has been operating for over four years and has brought keratoconus awareness and treatment to both specialized patient groups and the public.

Taking treatment to Tehran
Down Syndrome International, a patient organization based in London, contacted us on behalf of one of their members. The Tajikistani family has a son with Down syndrome and suspected keratoconus. They knew that he needed ophthalmic care to preserve his already limited sight, but they had no access to a corneal specialist. Time was of the essence, and traveling would be difficult due to political conditions and visa requirements – so Light for Sight began by locating corneal surgeons near Tajikistan. The foundation ultimately contacted Hassan Hashemi, head of the Noor Eye Institute in Tehran, Iran.

Hashemi recommended that the family travel to his clinic’s headquarters in Tehran, rather than one of the subsidiaries in Afghanistan, so that he could provide the best possible care. But that raised another obstacle – they had extremely limited funds for travel, lodging and treatment. When Hashemi heard this, the Noor Eye Institute didn’t stop at providing treatment; not only did the clinic still accept the patient, but it also agreed to cover all of his medical costs. After his treatment, the mother wrote, “I don’t know how to thank everyone who helped. [My son] felt sick, ate poorly, and did not sleep well. Now he sleeps well, which is most important. […] He is much more responsive than before with gestures.”

Despite all of the geographic, political and financial barriers, the Light for Sight ambassadors were able to step forward and support the wellbeing of patients and their families. “All of the many people who made the connections to the hospital in Iran, all of the people who donated money, an enormous thank you for helping us,” said our patient’s mother. And that’s the goal of our foundation: to provide services to those who might not otherwise have access, so that we can eliminate keratoconus as a cause of treatable vision loss. Thanks to the generosity and philanthropic spirit of our
ambassadors, we were able to achieve that goal with our Tajikistani patient.

Advocating for awareness
One of the newest Light for Sight ambassador groups is also one of our most active. Led by Miltos Balidis, director of corneal and refractive services at Protipo Ophthalmiatrio in Thessaloniki, Greece, the team created a media campaign to increase the awareness of eye problems – including keratoconus – among the Down syndrome population. They strategically launched the campaign on March 21st, World Down Syndrome Day.

The team contacted national television outlets and other media sources to bring more awareness to their work. They organized a mini-symposium in Thessaloniki on the launch date, inviting international corneal experts to speak on their area of expertise. The program was split into a scientific session, mainly focused on keratoconus and CXL, and an accessible session for health care providers, patients and their families. Conducted at the office of the regional Down syndrome patient organization, television and radio stations translated, recorded and broadcast the ophthalmologists’ presentations and the question-and-answer sessions. The audience consisted of Down syndrome patients and their families, vision healthcare specialists and general healthcare professionals. And the campaign didn’t stop there – the Thessaloniki-based group have now been invited to three local schools to screen children and adolescents for keratoconus.

“The foundation also works in Tanzania, where it focuses on bringing new resources to a population with limited access to specialized vision care.”
“Training the trainers” in Tanzania

Light for Sight’s mission isn’t limited to patients with Down syndrome. The foundation also works in Tanzania, where it focuses on bringing new resources to a population with limited access to specialized vision care. Sheraz Daya, the chairman and medical director of London’s Centre for Sight, initially approached Light for Sight to ask what he could do to support our international efforts. He also mentioned that he was about to leave for his annual trip to Tanzania, where he visits Comprehensive Community Based Rehabilitation in Tanzania (CCBRT) to examine and treat patients. He also mentioned that he was about to leave for his annual trip to Tanzania, where he visits Comprehensive Community Based Rehabilitation in Tanzania (CCBRT) to examine and treat patients. The hospital, which initially started as a rehabilitation center for patients with cataract, is now the largest indigenous provider of disability services in the country – and we immediately saw an opportunity to bring CXL to our Tanzanian colleagues.

Light for Sight worked with industry partners to obtain a CXL device. Thanks to a generous donation from the (former) IROC Innocross AG, we were able to provide a lamp for CCBRT. The goal was not just to provide care – Sheraz was there to train his local colleagues on the device during his trip and then leave it with the hospital so that they could provide CXL as a part of routine patient care after his departure. During his 2013 trip to Tanzania, Sheraz was able to screen 45 cornea patients, perform nine corneal grafts, and lead a full-staff training session so that the work could continue in his absence.

What did we learn from this experience? First, that training others to perform CXL, or any procedure, will have a more lasting effect than simply providing the treatment; and second, that you should never be afraid to ask for industry support for humanitarian initiatives that show promise and long-term benefits.

We’re pleased with the impact that Light for Sight has had so far in raising awareness of, and bringing treatment to, keratoconus patients. But the work never ends with a mission like ours, so we hope to continue providing CXL training and treatment to ophthalmologists, patients and families for many years to come.

Nikki Hafezi is the co-founder of Light for Sight 21, managing director of GroupAdvance Consulting GmbH and the CEO of EMAGine AG, and is based in Zug, Switzerland.
Berneck’s Brothers Beyond

Sitting Down With... Christoph and Thomas Bosshard, Oertli Instrumente AG, Berneck, Switzerland.
Self-financed. Family-owned. How do you compete in an international arena against some very big players in a very high-tech industry?

It’s a constantly changing environment, and we have to continuously adapt. Regulation is one example. We’ve had to invest heavily in our quality systems, in response to FDA-mandated quality assurance processes and increasingly stringent CE regulations, and this has meant that we’ve had to find other ways of reducing costs – such as adopting lean production methods.

Another issue is bundling. Larger companies have the ability to sell many of their products together as bundles, which is clearly something that we cannot do. But although this may seem like a disadvantage, our local dealers have complementary products in their portfolio that they can bundle with our equipment, letting us stay competitive.

What are the advantages?

Our company is family-run, and we sell through a network of independent dealers. This plays an important role in our success. In most markets, we have very long-lasting relationships with our dealers, who in turn have strong personal relationships with their local customers – which gives us a great customer base, founded on trust and long-term connections. We don’t have to answer to shareholders, which means we can put less focus on producing short term profits, and focus on the bigger picture – we don’t have shareholders grilling us on our profit and loss figures every three months!

Frankly, we love to compete against the big multinationals! We believe engineering and manufacturing our own machines, instruments and consumables (rather than outsourcing it) brings a number of advantages: tight control of our products, reliability, and we can be more responsive to market trends and the needs of our surgeon customers. It enables us to be a very attractive alternative to the big players.

Mergers and acquisitions happen frequently in the eye care industry – how have you avoided it?

We believe having no shareholders, banks, or leveraged business model behind us makes us stronger. Although there are many mergers going on, there is still space for independent companies to thrive, and many customers value our independence. Actually, the more we see mergers, the more encouraged we feel – it means that increasingly, we stand out from the crowd.

“We think it’s gone from a vendors’ market to a buyers’ market, and products aren’t as distinct from each other as they were before.”

How has the market changed in the last few decades?

We think it has changed significantly, moving from scattered local and national entities, both scientific and commercial, to a truly global discipline and market. Small, local manufacturers have given way to multinational organizations, and surgical procedures have become far more standardized. As well as the introduction of new surgical and diagnostic tools, we think the use of sterile consumables, and the dramatic increase in regulations, have resulted in the biggest changes in the way that ophthalmic surgery is performed.

In marketing, we think it’s gone from a vendors’ market to a buyers’ market, and products aren’t as distinct from each other as they were before. This makes it easier to switch between products, which we think has resulted in a decrease in brand loyalty. I also believe that cataract surgery has become more and more of a commodity, and is now far more consumer-orientated. Walking through the big international congresses, you don’t see medical device exhibitions anymore – they have become big marketing trade shows.

You make a big deal out of being Swiss. Why?

Here, we have access to a highly committed and qualified labor force who put a lot of love into what they do. We can work in an environment that is predictable and politically stable, with a fair taxation system and without major hurdles in terms of government rules. We think the result is excellent engineering and quality, which many Swiss companies are known for, so manufacturing here is very important to us.

What’s your approach to staying ahead of the game?

You need to constantly scan the market and keep talking to your partners, and your customers, to see what the unmet needs are – this is a great way to get new ideas. And it’s important to remember that innovation doesn’t need to be a huge, unexpected epiphany – we think of it as a continuation of small, daily improvements, can all add up to a big step forward.
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**Product Name:** TAPTIOOM® 15 micrograms/ml + 5 mg/ml eye drops, solution in single-dose container. **Composition:** One drop (about 30 µl) contains about 0.45 micrograms of tafluprost and 0.15 mg of timolol. One single-dose container (0.3 ml) of eye drops contains 4.5 micrograms of tafluprost and 1.5 mg of timolol. Please refer to the Summary of Product Characteristics (SmPC) for a full list of excipients.

**Indication:** Reduction of intraocular pressure in adult patients with open angle glaucoma or ocular hypertension who are insufficiently responsive to topical monotherapy with beta-blockers or prostaglandin analogues and require a combination therapy, and who would benefit from preservative-free eye drops. **Posology and method of administration:** Recommended dose is one drop in the conjunctival sac of the affected eye(s) once daily. Not to exceed one drop per day in the affected eye. Not recommended in children or adolescents (under the age of 18). In renal or hepatic impairment use with caution. To reduce systemic absorption, patients should be advised to use nasalconalr occlusion or close the eyelids for 2 minutes after instillation. Excess solution should be wiped away to reduce the risk of darkening of eyelid skin. If more than one ophthalmic product is used, five minutes should separate their administration. Contact lenses should be removed before instillation.

**Contraindications:** Hypersensitivity to the active substances or to any of the excipients. Reactive airway disease including bronchial asthma, or a history of bronchial asthma, severe chronic obstructive pulmonary disease. Sinus bradycardia, sick sinus syndrome, including sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker, Overt cardiac failure, cardiogenic shock. **Warnings and Precautions:** Before initiating treatment, patients should be informed of the possibility of eyelash growth, darkening of the eyelid skin and increased iris pigmentation related to tafluprost. These changes may be permanent, and lead to differences in appearance between the eyes if only one eye is treated. Similar cardiovascular, pulmonary and other adverse reactions as seen with systemic beta-adrenergic blocking agents may occur. The incidence of systemic adverse reactions after topical ophthalmic administration is lower than with systemic administration. Caution should be exercised when prescribing TAPTIOOM® to patients with cardiac or severe peripheral vascular disorders eg Raynaud’s disease or syndrome. Use with caution in patients with mild/moderate COPD and in patients subject to spontaneous hypoglycemia or liable diabetes. Beta-blockers may mask signs of hyperthyroidism and block systemic beta-agonist effects such as those of adrenaline. Anaesthetists should be informed when a patient is receiving timolol. Patients with a history of severe anaphylactic reaction may be more reactive to repeated challenge with such allergens and be unresponsive to the usual doses of adrenaline used to treat anaphylactic reactions. The known effects of systemic beta-blockers may be potentiated when TAPTIOOM® is given concomitantly. The use of two topical beta-blockers is not recommended. Patients with corneal disease should be treated with caution as ophthalmic beta-blockers may induce dry eyes. When timolol is used to reduce elevated intraocular pressure in angle-closure glaucoma, always use a miotic. Caution is recommended when using tafluprost in aphakic patients, pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, and in patients with known risk factors for cataract, macular edema or uveitis. Please see the SmPC for further information. **Interactions with other medicinal products:** Potential for hypotension / marked bradycardia when administered with oral calcium channel blockers, beta-adrenergic blockers, anti-arrhythmics, digitals glycosides, parasympathomimetics and guanethidine. Please refer to the SmPC. **Pregnancy:** Do not use in women of childbearing age/potential unless adequate contraceptive measures are in place. **Breast-feeding:** It is not recommended to breast-feed if treatment with TAPTIOOM® is required. Driving and using machines: If transient blurred vision occurs on instillation, the patient should not drive or use machines until clear vision returns. **Undesirable Effects:** Conjunctival/ocular hyperaemia occurred in approximately 7% of patients participating in clinical studies with TAPTIOOM®. Other common side effects include: eye pruritus, eye pain, change of eyelashes (increased length, thickness and number of lashes), eyelash discolouration, eye irritation, foreign body sensation, blurred vision, photophobia. Adverse reactions that have been seen with either of the active substances (tafluprost or timolol) and may potentially occur also with TAPTIOOM® include: increased iris pigmentation, anterior chamber cellularity, iritis/uveitis, deepening of eyelid sulcus, hypertrichosis of eyelid, exacerbation of asthma, dyspnea, allergy, angioedema, urticaria, anaphylaxis, hypoglycemia, syncope, ptosis, bradycardia, chest pain, palpitations, oedema, cardiac arrest, heart block, AV block, cardiac failure. Please also see the SmPC. **Ovulation:** Treatment should be symptomatic and supportive. **Special Precautions for Storage:** Store in a refrigerator (2°C - 8°C). After opening the foil pouch keep the single-dose containers in the original pouch and do not store above 25°C. Discard open single-dose containers with any remaining solution immediately after use. **Package quantities and basic NHS cost:** 30 x 0.3ml single-dose containers £14.50. **Product Licence Holder:** Santen Oy, Nittyharakatu 20, 33720 Tampere, Finland (PL 16038/0012) **Price:** 30 x 0.3ml single-dose containers £14.50. Date of Authorisation: 30/10/2014 POM Date of Prescribing Information: 31/05/2015

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**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.** Adverse events should also be reported to Santen UK Limited (Email medinfo@santen.co.uk or telephone: 0845 075 4863).