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Achieving up to 99% of patients within +/- 0.5 D post-op astigmatism.¹

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Image of the Month

A color fundus photography composite image of a morning glory disc anomaly in an 18-year-old. Image courtesy of Kevin S. Firl and Sandra Rocio Montezuma, Department of Ophthalmology & Visual Neuroscience, University of Minnesota.

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

Building a Bigger (Eye) Bank
Chris Hanna and Gregory Hageman share their experiences of working with the community to maximize eye tissue donation.

Sitting Down With

Malik Kahook, Slater Family Endowed Chair in Ophthalmology, Vice Chair of Clinical & Translational Research, and Chief, Glaucoma Service, Anschutz Medical Campus, University of Colorado.
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Determined to do Good

Ophthalmology mourns the loss of a leader who achieved many great things

I first met Peter Barry in September 2014. It was the last day of the ESCRS Congress in London, just after the “Best of the Best” review session. I was traveling home later, so I wasn’t wearing a suit – just wearing jeans, comfortable shoes, a clean shirt crumpled from being at the bottom of my suitcase all week, and a mildly disheveled brown tweed jacket. But I thought, what the hell, let’s go over and introduce myself to the great man. I’m forever glad I did.

A founding member of ESCRS back in 1991, and a past president and treasurer of the society, it’s fair to say that he played a great hand in building the ESCRS into the mighty organization it is today. Famously, he was responsible for the game-changing ESCRS postoperative endophthalmitis prophylaxis study. In his own words: “My primary interest was (and always has been) retinal surgery. In my job in the Eye and Ear Hospital in Dublin, I got distressed at the frequency of patients that were getting referred to me with postoperative endophthalmitis following cataract surgery – so that was the impetus to start the endophthalmitis study.”

This study demonstrated that intracameral antibiotics administered during cataract surgery significantly reduced the risk of postoperative endophthalmitis. Clinical practice was changed, and in the decade since the study’s publication, untold numbers of eyes have been saved from infection – in a large part, thanks to Peter’s determination. He was also behind the EUREQUO registry that allowed comparison of manual and femtosecond laser-assisted cataract surgery outcomes, providing robust evidence when there was little there before. In a time when a femtosecond laser is still the best part of €500,000, understanding just what that sort of capital investment will mean for patient outcomes is important. In the absence of head-to-head trial data, the EUREQUO registry represents the most robust dataset out there, and Peter, as the driving force behind it, deserves great credit. As a semi-objective metric of how ophthalmologists feel about that work, I last saw the EUREQUO data presented at the 2015 AAO annual meeting in Las Vegas. The presentation ended with the largest round of applause I’d seen all day.

The recent news of his death after a short illness was deeply saddening. I remember him as an impressive, charming man. I’m sure ophthalmology will, thanks to his achievements, remember him as a fearless leader, who tackled, head on, some of the field’s toughest challenges. I’d like to extend our sincerest sympathies to all of Peter’s family, friends and colleagues at this time.

Mark Hillen
Editor
Contributors

Gregory Hageman
A professor of ophthalmology and visual sciences, and executive director of a center for translational medicine, Gregory was raised in Central California, where his ancestors homesteaded as cotton farmers in 1885. Over the past quarter-century, Hageman has wondered mainly about the genetics and pathways involved in age-related macular degeneration, with great success. He has made major contributions to understanding the disease, briefed the US Congress on the subject on three occasions and founded two biotechnology companies. On page 48, Gregory and his colleague Chris Hanna explain how the Moran Eye Center and the Utah Lions Eye Bank work together – and with their local community.

Matteo Piovella
The current president of the Società Oftalmologica Italiana (SOI), Piovella founded the CMA: the Center for Outpatient Microsurgery based in Monza, back in 1992, where today, he serves as its Scientific Director. In addition to presiding over the SOI, Piovella is a member of the ISRS International Council, the ESCRs program committee, the council of the SOE, and was a founder member of the South-East European Society of Ophthalmology. Matteo presents his 8-year long term follow-up results of mixing-and-matching refractive and diffractive multifocal IOLs on page 38.

Paul McMenamin
Director of the Centre for Human Anatomy Education at Monash University, Sydney, Australia, and also head of the Ocular Immunology Group in the university’s Department of Anatomy and Developmental Biology, Paul and his team investigate a number of issues that relate to eye development and aging, and have a special interest in ophthalmic disease that may have an immune or inflammatory basis to their pathogenesis. Paul gives a lesson on convergent evolution with striking images of the retinæ of marsupials, on page 22.

Liliana Werner
Liliana is an Associate Professor of ophthalmology and a Co-director of the Intermountain Ocular Research Center at the University of Utah’s School of Medicine. Her research centers on the interaction between ocular tissues and different intraocular lens (IOL) designs, materials and surface modifications, including piggyback and phakic IOLs. She has written nearly 200 peer-reviewed articles and co-edited multiple textbooks on the subject, and is a popular speaker at major international congresses. On page 31, Liliana and her colleague Nick Mamalis illustrate the strange case of a patient with a calcified IOL in our Art of Eyes feature.
Ophthalmology Clinical Research Training Fellowship

Fellowship programmes are vital to the NHS. They enable participants to acquire new skills which complement their clinical practice; they promote and encourage innovative thinking; and inspire the next generation of ophthalmologists.

The Ophthalmology Clinical Research Training Fellowship is unique, in that it is the first example of a programme involving a royal college (Royal College of Ophthalmologists), the Medical Research Council (MRC), and a pharmaceutical partner (Novartis).1

The three-year fellowship is focused on ophthalmology research training in the UK and aims to foster a group of researchers dedicated to clinical ophthalmology. It’s designed to accommodate the dual clinical-research training career path by allowing fellows to spend some of their time on NHS sessions.

At Novartis, our vision for the UK is a future without sight loss. To achieve this, we cannot lose sight of tomorrow’s need and must create an environment that is conducive to continuous innovation.

We can’t do this alone. We are committed to innovating for future generations of patients and healthcare professionals by helping to develop the research leaders of tomorrow.

Novartis is investing in the future of ophthalmology, leading the way by sponsoring 20% of all industry supported ophthalmology clinical research in the UK.3 The co-funded Clinical Research Training Fellowship programme is another way that Novartis is demonstrating its commitment to improving eye care for future generations. Candidates from any area of ophthalmology can apply for the Ophthalmology Clinical Research Training Fellowship and applications in the areas of glaucoma, medical and surgical retina, paediatric ophthalmology and stem cells will be particularly welcome as the scheme aims to encourage clinical research in these particular fields.

For more information, or to apply for the programme, visit mrc.ac.uk and search for “Jointly funded clinical research fellowship programme”. Or visit the links below

- http://www.mrc.ac.uk/skills-careers/fellowships/clinical-fellowships/jointly-funded-clinical-research-training-fellowship/

The deadline for applications is Thursday 8 September 2016.

References

1. Medical Research Council/The Royal College of Ophthalmologists/Novartis Research Fellowships

Manjit Mehat shares his fellowship experience

Manjit Mehat’s decision to become an ophthalmologist was inspired by witnessing cataract surgery as a medical student. He says: “It’s a very elegant procedure with a very small margin for error. Watching that procedure sowed the seeds of my career.”

Dr Mehat liked the combination of medical and surgical skills that ophthalmology offered. He was also motivated by the impact the work has on patients, “restoring sight or preventing blindness is an incredible cause to pursue.”

The focus of his research fellowship is stem cell biology: “It fascinates me. The field is evolving rapidly and I wanted to be part of it, so a clinical research fellowship seemed an ideal opportunity.”

He is currently investigating the potential of stem cells for retinal regeneration in conditions such as age-related macular degeneration and inherited retinal degenerations affecting children and young people.

Dr Mehat comments, “One of the real advantages of the fellowship is having clinician academics working with scientists, occupying that vital middle ground between bench and bedside. You work with people who have a deep understanding of both clinical medicine and the basic science of what goes wrong. This combination is essential for the advancement of medical science.”

His research looks at whether sight loss caused by the degeneration of the retina might be restored by transplantation of retinal cone and rod photoreceptor cells. Dr Mehat is expanding the number of healthy cells available for transplantation by promoting their growth in the laboratory from embryonic stem cells, testing the generated retinal cells in a host mouse retina and then transplanting them into human adult retinas.2

“My horizons have been well and truly broadened,” says Dr Mehat. “This programme is a unique experience. The way I now seek out answers has completely changed thanks to this fellowship. The programme has taught me to approach problems in a more analytical process that addresses the key question.”
2P-CXL: the Final Frontier?

Why settle for one-photon light absorption, when you can have two?

Ever since the first astigmatic keratotomy was performed over a century ago, ophthalmologists have known that changes in corneal biomechanics have refractive effects. Corneal collagen cross-linking (CXL) strengthens the cornea, and even it can be used for this purpose — for example, Avedro’s PiXL promises to correct refractive errors with selective cross-linking. But what’s next?

Researchers from the Wellman Center for Photomedicine at Massachusetts General Hospital have revealed two-photon CXL (2P-CXL) (1). The paper’s corresponding author, Seok-Hyun (Andy) Yun explains, “In optical imaging, two-photon microscopy has become very popular, and we wanted to take advantage of these benefits and use them to improve conventional CXL, which is based on one-photon absorption of UV light.” In their study, the team selectively stiffened bovine corneal tissue in three dimensions using just riboflavin and 810 nm light pulses from femtosecond laser (1).

“Two-photon excitation confines tissue cross-linking to only where the laser is focused. This allows us to cross-link an arbitrary region deep inside tissue,” noted Yun, adding that “the degree of stiffening was similar to that with conventional CXL.”

Central to the team’s research is in vivo Brillouin microscopy (2), which makes it possible to non-invasively visualize and characterize cross-linked regions. Yun explained, “Brillouin microscopy uses light to probe the mechanical properties of cells and tissues, and the principle relies on light scattering with spontaneous acoustic waves which are present in all materials.” Photons scattered by acoustic waves are sensitive to changes in compressibility and crosslink density, and local stiffening increases Brillouin frequency shifts, which are detected by high-resolution spectrometry (Figure 1).

There is room for improvement: the procedure currently takes one hour to cross-link 1 mm², but Yun believes that “this can be significantly improved with optimizations such as more efficient photosensitizers, laser pulses with higher peak powers, and optimized beam scanning patterns.”

The team hopes to develop 2P-CXL for refractive error corrections in myopic and post-cataract patients, and Yun envisages an expedited regulatory approval: “One advantage is that many femtosecond lasers are already approved for use in the clinic, and the safety of riboflavin has been studied.”

References
Ring in the Changes

Is a bimatoprost-eluting silicone ring a credible alternative to eyedrops?

In patients with glaucoma, every missed dose of topical antiglaucoma therapy means poorer IOL control and faster vision loss. Regimen adherence varies from patient to patient, and missing a dose now and then isn’t the end of the world. But IOP control often requires multiple drops, and the effect of missing doses can quickly add up. Naturally, anything that can support medication compliance will help patients preserve their vision for longer.

One approach that’s currently being investigated is a drug-eluting ocular insert ring (ForSight VISION5), which is placed on the upper and lower fornices of patients’ eyes (Figure 1). Comprised of a 1 mm bimatoprost-silicone matrix, the ring elutes therapeutic drug doses over a 6-month period. Results of a Phase II trial comparing the bimatoprost ring plus artificial tears with a placebo ring plus twice daily timolol 0.5% eyedrops in patients (n=130) with open-angle glaucoma or ocular hypertension controllable by monotherapy are now published (1). In this multicenter, randomized, double-masked trial, the primary efficacy measure was the difference in mean (diurnal) IOP change from baseline.

And the results? Over 6 months, reductions from baseline IOP ranged from 3.2 to -6.4 mmHg and -4.2 to -6.4 mmHg in the bimatoprost and timolol groups, respectively. The ring was well tolerated – at the end of the trial, 88.5 and 90.9 percent of patients still had the bimatoprost and placebo ring in place, respectively, and reported ocular discomfort rates were low for the bimatoprost (6.3 percent) and placebo rings (3.0 percent).

However, of the three diurnal time points on each of the three days of IOP assessment (at weeks 2, 6 and 12), the bimatoprost implant was non-inferior to timolol at only two of them. This may have been because the trial was underpowered to detect the observed treatment effect, and this will be addressed in later Phase III studies.

Nevertheless, the bimatoprost ring was assessed under highly controlled clinical trial conditions where patients were compelled to be fully compliant with all dosing regimens. In the real world, the implant is being aimed at precisely those patients who struggle to do that. The ring has a large surface area – enough to carry a combination of ocular antihypertensive agents, and the fact that it can deliver drugs to the surface of the eye for an extended period with a high retention rate opens up the possibility that it might be used for the treatment of ocular surface disease, ocular allergy or post-surgical inflammation, all of which are under development. MH

Reference

The Future, in Sight

What can ophthalmologists expect from the aging baby boomer generation?

The year is 2050, and surviving baby boomers – born between the post-war years 1946 and 1964 – are now 86–104 years old. Has this aging population delivered the anticipated “demographic timebomb”? We summarize key results from a recent study forecasting the prevalence of visual impairment (VI) and blindness in the US up to 2050 (1).

• Estimated incidences of VI and blindness will increase, as will the proportion of patients aged 80 years or more.
• Women with VI and blindness will continue to outnumber men.
• Non-Hispanic whites are estimated to remain the largest ethnic population with VI and blindness.
• The second-largest ethnic population with VI will switch from African-Americans to Hispanic/Latino individuals, who are predicted to be the fastest growing US minority group.
• Florida and Mississippi will continue to be the states with the highest per capita prevalence of VI and blindness, respectively.
• The incidences of VI and blindness as a result of uncorrected refractive error (URE) are expected to rise, with incidences of VI almost doubling. RS

Conclusions

Between 2015 and 2050, the largest demographic groups for VI and blindness will be non-Hispanic white individuals and women.

Focusing screening programs on “at-risk” populations and areas are recommended.

Reference

Why do “open bag” IOLs reduce PCO?

Many attempts have been made over the years to help reduce the occurrence of posterior capsule opacification (PCO) after cataract surgery. Lens epithelial cells (LECs) are the target: anything that inhibits their migration to (and proliferation on) the posterior capsule will help. Square-edged IOLs were a great step forward; they formed a physical barrier to LEC migration – but alas, given enough time, that barrier will be breached.

Over the years, a number of approaches have been made, including capsular polishing, the bag-in-the-lens procedure, and leaving the capsular bag open. The latter seems to work… but people have always speculated why?

The hypothesis is this: unlike standard IOLs where the capsular bag “shrinkwraps” around the IOL, if the bag is open, it’s subject to greater irrigation by the aqueous humor, which washes away (or at least dilutes) the cytokines that promote LEC migration and proliferation. Eldred et al. (1) decided to test that hypothesis using human lens cell and tissue culture experiments.

Using donor eyes, with lenses hydrodissected out through a small capsulorhexis, the researchers created a “closed bag” preparation (see Figure 1a) that was placed in cell culture. To mimic the dilution of growth factors, they simply cultured the tissue preparation in different volumes of culture media (1.5 and 6 mL) and measured the proportion of the posterior capsule that was covered by cells. Volume mattered: after only 8 days of culture, posterior capsule cell cover was sparse in the 1.5 mL group, and non-existent in the 6.0 mL group, lending further credence to their hypothesis.

But if cytokines are at play, which ones are they? The team analyzed the media collected from the closed bag preparations: 24 cytokines were detectable in both the 1.5 mL and 6 mL cultures, but only nine were significantly reduced in the 6 mL culture (above and beyond that of simple fourfold dilution from the 1.5 mL culture). These were IL-8, IL-15, IL-12(p70), MCP-1, MIP-1β, IL-1ra, IL-10, IP-10 and VEGF.

There’s a human fetal lens epithelium cell line available, FHL 124, so the researchers’ next step was to assess the effect of each cytokine on the migration of FHL 124 cells. Ultimately, VEGF was identified as the likely culprit, as both the VEGFR-1 and -2 receptors are expressed in these cells, and their migration was significantly reduced when the VEGF-receptor antagonist, axitinib, was added to the culture medium. Further, axitinib reduced cell cover in their initial “closed bag” model – suggesting that VEGF is a survival or growth factor for human LECs.

So it looks like we have an explanation for why open-bag IOL use is associated with lower PCO rates – and it raises the question of whether the application of perioperative VEGF inhibitors to the capsular bag (perhaps as an IOL coating) might be another way of keeping those pesky LECs at bay. MH

Reference
PMID: 27076230.
The Diagnostic Dome

A new device could overcome the challenges of performing perimetry in infants

Visual field assessment in infants is hard... and perimetry is incredibly difficult (1). But it’s important information to have when visual field disorders or strabismus is suspected, and it can help identify and exclude those cases where infants present with an “eye turn”, receive strabismus surgery, but actually have congenital hemianopia.

What if there was an easier way?

The Pediatric Perimeter (1) is a hemispherical dome built out of steel rods to form 24 meridians (separated by 15°), that has an infrared (IR) camera at its apex, and is covered by black cloth (Figure 1). The infant is laid in the dome, and the infrared camera monitors their eye movements in response to LED stimulus patterns controlled by the clinician (Figure 1).

Does it work?

PremNandhini Satgunam of the L V Prasad Eye Institute in Hyderabad, India, and a lead member of the development team, explained that the perimeter has been used to successfully map visual field extent in both infants and toddlers. Further, it’s able to identify differences in the visual fields of infants with normal developmental milestones (NM) and those with developmental delay (DD). Five NM infants (mean age, 10.0±7.1 months) and 12 DD infants (mean age, 12.1±6.9 months) were assessed.

Although both groups displayed similar visual field extents, reaction times in DD infants were almost two times longer (Figure 2) – something that Satgunam ascribed to “potential
Infants with NM (n=4)  Infants with DD (n=8)

325 ms  627 ms

Figure 2. Median reaction time of infants with normal milestones and developmental delay measured during pediatric perimetry. DD, developmental delay; NM, normal milestones.

processing delays in afferent, efferent, or both systems.” The team also showed preliminary findings that the visual field isopter may differ between infants with NM and DD, but Satgunam comments, “we need to do a lot more normative database measurement before we can say anything for certain.”

If pediatric visual development is better understood, in both normal and DD children, as well as furthering knowledge to guide clinical practice, it may prevent unnecessary surgeries being performed on young children. MH

References
The *California* ultra-widefield (UWF™) imaging device was specifically designed for vitreo-retinal specialists and ophthalmologists. *California* includes a new UWF *optomap®* imaging modality, Indocyanine Green angiography (*icg*) while retaining Composite colour, Red-free, Autofluorescence (*af*) and Fluorescein angiography (*fa*), all offering UWF views of up to 200 degrees of the retina in a single capture.

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_Courtesy of Prof Paulo Stanga_  
Manchester Royal Eye Hospital, UK

_Courtesy of SriniVas Sadda, MD_  
Doheny Eye Institute

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The eye is a source of inspiration, both artistic and scientific. But irrespective of the instrument used, the structures examined, or whether the images are depicted by paintbrush, photography or precision instrument, beauty abounds.
"As an artist, working in a medical facility seeing both the eye’s fragility and its resilience provides a sense of the fleeting and the profound. The anatomical structures of the human eye are intriguing to me not only in their function but also their form. With artistic license (and a removal from context) these photographs become abstract, yet intimately familiar explorations of color and form.”

Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care and Owner, Kelly Aileen Photography, West Chester, PA, USA.
Swimming in a Blue Sea

Dendritic ulcer and unstable tear film after instillation of fluorescein.

Helena Prior Filipe, Department of Ophthalmology, Hospital of the Armed Forces, Lisbon, Portugal.

So Close and Yet So Far

One look at the displaced IOL and glaucoma implant shows that this eye might have seen an ophthalmologist or two.

Houston Sharpe III, Ophthalmic Imaging Specialist, UNC Kittner Eye Center, Chapel Hill, NC, USA.

Rubeosis Iridis

Fluorescein angiography of neovascularization of the iris.

Zachary Dupureur, Michael Tsipursky and Mary Bruce, Carle Foundation Hospital, Urbana, Illinois, USA.
Since 1998, the Miradas art contest has been run by the Jorge Alió Foundation, as a way of raising awareness and support for the prevention of blindness. Several winning paintings are featured here.

**Self Sight (Automirada)**
Top left
Sierra Barceló.

**S/T**
Bottom left
Luis Feito.

**Mirar Desde La Privacidad**
Top right
Jesus Lozano Saorín.

**¿Qué Miras?**
Bottom right
Josep Puigmarti.
El Cosmos Nos Mira  Top left
Polín Laporta.

Localización Al Cosmos De Gente Observando Un Ojo
Bottom left
Cristobal Toral.

Alegres Eran Mis Ojos  Top right
Paloma Navares.

Mirada Conclusente  Bottom right
Félix Revello de Toro.
Convergent Evolution: A Lesson From the Eye of Marsupials

Many ophthalmologists probably have a human-centric view of ocular anatomy. Indeed many likely think that all mammals have a retinal blood supply like ourselves - but of course this is not true. Many mammals, such as grazing animals, have fairly simple and thus thin retinae that do not have direct intraretinal vessels and rely on the choroid for all their nutrition. Now one would imagine that in species with retinal vessels, they would be arranged in approximately the same pattern in all mammals. Well it appears that when mammals split roughly 130 million years ago into eutherian (placental) mammals and marsupials, things got interesting...

Marsupials also have groups with simple retinae (including kangaroos, wombats, koalas and possums) and some with complex retinal functions (numbats, opossums and the Tasmanian devil) that evolved a retinal blood supply. However, as can be seen in this example of a South American opossum (Monodelphis domestica) (a) when one looks at their retina with a fundus camera it looks (at first) like a mouse retina (b). However if one looks closely at the fluorescein angiogram (arrow in (c)) one can see there are in fact two vessels and not one. Histology (d) shows that these pairs of vessels consist of an artery on the vitread aspect of the corresponding vein. This pattern can be seen in a flat mount of a retina that has been perfused with fluorescent dye (e). Here you can see the pairs of vessels and how they terminate in numerous hairpin loops. This pattern is completely different from placental mammals where capillaries form anastomotic beds and arteries/arterioles and veins/venules lie apart from one another except where they enter the eye at the optic nerve head.

So whilst the marsupials with complex retinal functional needs have solved the issue of providing a blood supply, they have used a different, double vascular pattern that is only seen in marsupial retinae and brains. There appears no obvious functional advantage to this pattern and it seems to be a classic example of convergent evolution.

Paul McMenamin, Director of the Centre for Human Anatomy Education, Monash University, Sydney, Australia.
Hyphema

Top left: This patient presented with hyphema caused by a rock striking the eye that was propelled by a weed whacker.

X Marks the Spot

Top right: This female patient presented with X-linked retinitis pigmentosa with symptoms including decreased night vision and mild glare. Female carriers often display a reduced electroretinogram signal, but tend not to develop other complications.

Tesla Coil

Bottom right: This wide-angle fluorescein angiogram shows severe proliferative diabetic retinopathy.

Beauty in the Breakdown

Bottom left: An inverted-color image of a patient with an iris defect and corneal scarring creates an image of immense beauty.

Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care and Owner, Kelly Aileen Photography, West Chester, PA, USA.
Well, There's Your Problem

Viewing this slit beam from the side gives a much better appreciation of the elevation of the cornea.

The infrared image shows an odd splotching pattern, but a quick glance with fundus autofluorescence displayed a completely different view of the pathology.

Houston Sharpe III, Ophthalmic Imaging Specialist, UNC Kittner Eye Center, Chapel Hill, NC, USA.
Choroideremia is a rare disease with a strong genetic component. Progressive vision loss results from degeneration of the retinal pigment epithelium, and the choriocapillaris is clearly demonstrated in this widefield fluorescein angiogram.

Joseph Territo, Ophthalmic Photographer, Retina Associates of Western New York, Rochester, NY, USA.
Retinal Nebula

Severe proliferative diabetic retinopathy with laser treatment.

Karen Gasperian, Ophthalmic Photographer at Retina-Vitreous Associates Medical Group, Los Angeles, California, USA.
Can You See Me Now?

Using bright diffuse lighting, a clear visualization is captured of this one day postoperative AC-IOL.

Houston Sharpe III, Ophthalmic Imaging Specialist, UNC Kittner Eye Center, Chapel Hill, NC, USA.

Deadeye

Experimental setup for puncture testing of full human cadaveric globe specimens.

Proximity Fuze

Color image of a patient’s fundus displaying torpedo maculopathy.

Karen Gasperian, Ophthalmic Photographer at Retina-Vitreous Associates Medical Group, Los Angeles, CA, USA.

Posterized Posterior Segment

Noninvasive visualization of the optic nerve head and peripapillary vascular network using OCT angiography.

Shelley Mo, Toco YP Chui and Richard B Rosen, New York Eye and Ear Infirmary of Mount Sinai, New York City, NY, USA.
Segmentation of superficial vascular plexus in a neonatal mouse retina.

Sabine Uhles, Franco Revelant, Sabine Grüner, Guido Hartmann and Fethallah Benmansour, Ocular Discovery and Biomarkers, Roche, Basel, Switzerland.

Moon Through Trees

A strikingly high-contrast angiograph makes for an incredibly artistic image of the eye.

Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care and Owner, Kelly Aileen Photography, West Chester, PA, USA.
The Light of the Eye

This image was created in response to the Lawrence Ferlinghetti poem “Instructions to painters and poets”:

…and don’t forget to paint all those who lived their lives as bearers of light… paint the light of their eyes…

Gianpiero Actis, Eye surgeon and award-winning artist, Torino, Italy.

Eyelash Mites

Colored scanning electron micrograph of an eyelash hair growing from the surface of human skin; the tails of eyelash mites are seen protruding from the base. The eyelash mite or Demodex folliculorum is a parasite found in the follicles of the human face, mainly in the nose, cheeks and most especially the eyelash area.

Steve Gschmeissner, scientific photographer, Bedford, UK.
It’s Time to make a Move

The FEMTO LDV Z8 is now also available in the United States and Canada!

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The FEMTO LDV Z8 is CE marked and FDA cleared for the use in the United States. For other countries, availability may be restricted due to regulatory requirements; please contact Ziemer for details.
Coloboma

Top left: A patient with typical peripheral retinal coloboma.

Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care and Owner, Kelly Aileen Photography, West Chester, PA, USA.

Scleral Buckling Surgery

Bottom left: Ultrawide-field color image of the left fundus of a 58-year old female patient who underwent a scleral buckling surgery to correct a macula-off rhegmatogenous retinal detachment. The encircling band and 360° of moderate scleral indentation are visible.

A. Osman Saatci, Dokuz Eylul University, Izmir, Turkey.

Localized Calcification of a Hydrophilic Acrylic IOL

Some months after uneventful implantation of this hydrophilic acrylic IOL, the patient underwent further surgery for a retinal detachment repair, including vitrectomy with silicone oil tamponade. A few months later, the IOL exhibited a localized, central, round area of opacification on the anterior surface. Due to decreased visual function, the lens was explanted, and staining with alizarin red demonstrated that calcification caused the opacification.

IOL explanted by Robert Cionni and analyzed by Liliana Werner and Nick Mamalis, Salt Lake City, UT, USA.
Bird’s Eye View

The normal eye of a red-tailed hawk.

The Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW), USA. Further images can be found on the COPLOW Facebook page: bit.ly/COPLOW

A Dog’s Life

A dog eye with early-life trauma, which is believed to have happened prior to the eyelids opening at 12 days of life.

Image courtesy of COPLOW.
Illuminating Immunohistochemistry

Confocal microscopy imaging of rat retinal sections.

a. Double staining of a crushed optic nerve. Nerve fibers are stained in green, and the repulsive guidance molecule A is stained in red. The picture is taken 10 days after optic nerve crush directly at the crush site.

b. Triple staining of rat retina after optic nerve crush with cell nuclei in blue, GFAP-positive cells in green and repulsive guidance molecule A staining in red.

c. Triple staining of rat retina after optic nerve crush with cell nuclei in blue, nerve fibers and RGCs in green and repulsive guidance molecule A staining in red.

Sven Schnichels, Laboratory Head at the University Eye Hospital, Tübingen, Germany.

Helianthus

A pupil surrounded by a yellow-pigmented rich region of the iris, reminiscent of a sunflower.

Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care and Owner, Kelly Aileen Photography, West Chester, PA, USA.
The SPECTRALIS® system is an ophthalmic imaging platform with an upgradable, modular design. This platform allows clinicians to configure each SPECTRALIS to the specific diagnostic workflow in the practice or clinic.

Options include: OCT, multiple laser fundus imaging modalities, widefield and ultra-widefield modules, scanning laser angiography and OCT angiography*.

*Currently under development, not for sale yet.
In Practice
Surgical Procedures
Diagnosis
New Drugs

The SPECTRALIS® system is an ophthalmic imaging platform with an upgradable, modular design. This platform allows clinicians to configure each SPECTRALIS to the specific diagnostic workflow in the practice or clinic. Options include: OCT, multiple laser fundus imaging modalities, widefield and ultra-widefield modules, scanning laser angiography and OCT angiography*.

www.SPECTRALIS.info

*Currently under development, not for sale yet.

Lessons Learned
When it comes to mixing refractive and diffractive mIOLs, Matteo Piovella reflects on the past for a better future.
Lessons Learned

We've learned our lessons from mixing and matching the first generations of mIOLs. Applying them to current mIOLs should lead to success with today's multifocal lenses

By Matteo Piovella

When multifocal IOLs (mIOLs) were first introduced, the idea of giving my patients good vision without glasses really excited me. But as I soon discovered, first and even the second generations of presbyopia-correcting IOLs weren't without their limitations.

The variation patients experienced in their vision as their pupil diameter changed was a major challenge. At a pupil diameter of 3.0 mm, most mIOLs work very well. But our patients don't live in a static world – light intensity changes throughout the day and in different environments – so their visual experience with certain IOLs can change dramatically. Some designs also result in significant loss of light that is outside the range of vision at larger or smaller pupil sizes (as described in Table 1).

The other limitation of many of the earlier mIOLs was intermediate vision. Vision at about 70 cm is critical for many daily tasks, such as using computers or handheld devices like smartphones and tablets. Finding a way to overcome this limitation and provide truly spectacle-free vision for my patients was the reason I decided to try mixing refractive and diffractive mIOLs.

In Practice

At a Glance

• Early multifocal IOLs were something of a mixed bag – variations in vision caused by pupil diameter and problems achieving good intermediate vision made true spectacle-independence a challenge.
• The long-term data on mixing refractive and diffractive IOLs produced good results and revealed important lessons to apply to newer mIOLs.
• Refractive accuracy, achieving good near and intermediate vision, and careful patient selection are crucial factors to take into account.
• Surgeons who have achieved good results (despite the limitations of past mIOLs) should see even greater successes in the future.

“The other limitation of many of the earlier mIOLs was intermediate vision. Vision at about 70 cm is critical for many daily tasks.”
Long-term lessons
I now have eight-year results of the mix-and-match approach in 52 patients (32 female and 20 male, 104 eyes). The average age of the patients studied was 69.33 ±11.35 years, and all returned to the clinic annually for follow-up examinations.

These patients all had a refractive mIOL (ReZoom, Abbot Medical Optics) implanted in one eye, and a diffractive multifocal (Tecnis Multifocal, Abbott Medical Optics) implanted in the other. Patients with pupils >5.0 mm in dim light were excluded from the study, because the lens used in this study does not perform well at larger pupil sizes. Eyes with astigmatism of more than 0.50 D were also excluded.

So far, the results I’ve seen are very promising – eight years postoperatively, the best-corrected visual acuity (VA) outcomes of these patients are stable, with no variation. Mean manifest refraction spherical equivalent (MRSE), which is a useful way to demonstrate postoperative refractive results, was approximately -0.25 D, and has been very consistent throughout the eight-year follow-up period (see Figure 1).

Finally, and most importantly, patient satisfaction was very high.

This method isn’t perfect though, as monocular near vision was J3 to J5 at all time points – which is not as good as our typical experience with bilateral diffractive multifocal IOLs. However, with both eyes open, 94 to 95 percent of patients said they could function without glasses at intermediate distance, which was the goal of mixing these two different IOL types in the first place.

Top tips for refractive success
Today, we have new and better options...
“The patients in this study were very happy with their vision following IOL implantation, because they achieved plano results that allowed them to have great distance vision.”

The patients in this study were very happy with their vision following IOL implantation, because they achieved plano results that allowed them to have great distance vision. In refractive cataract surgery in general, and when using mIOLs in particular, performing precise biometry and excellent surgery, in order to get a plano result, are crucial steps.

Some years ago, Jack Holladay explained the relationship between pupil size and quality of vision (1). With a small pupil (<5.0 D), minor residual error of -0.50 D after surgery has little effect on VA, and the patient will still have VA of about 20/24. But that same amount of residual error provides a theoretical best acuity of only 20/30 if the pupil is 7.0 mm, which is possible in younger refractive lensectomy patients. With a diffractive mIOL, the penalty doubles, meaning that just -0.50 D of residual error can reduce vision by a full two lines — something that most patients will definitely notice. If you combine residual error with larger pupils in a mIOL patient, you’re creating a recipe for dissatisfaction and complaints.

“Get a plano result.” This might be a direction that is easy to give and difficult to follow, but make no mistake that it is absolutely mandatory for spectacle-free vision, and a happy patient.

<table>
<thead>
<tr>
<th>Pupil diameter</th>
<th>Near</th>
<th>Intermediate</th>
<th>Far</th>
<th>Outside range of vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>ReZoom 2.0 mm pupil</td>
<td>0%</td>
<td>17%</td>
<td>83%</td>
<td>0%</td>
</tr>
<tr>
<td>ReZoom 5.0 mm pupil</td>
<td>30%</td>
<td>10%</td>
<td>60%</td>
<td>0%</td>
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<tr>
<td>ReStor 2.0 mm pupil</td>
<td>40%</td>
<td>0%</td>
<td>40%</td>
<td>20%</td>
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<tr>
<td>ReStor 5.0 mm pupil</td>
<td>10%</td>
<td>0%</td>
<td>84%</td>
<td>6%</td>
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<tr>
<td>Tecnis MF (+4) 2.0 mm pupil</td>
<td>41%</td>
<td>0%</td>
<td>41%</td>
<td>18%</td>
</tr>
<tr>
<td>Tecnis MF (+4) 5.0 mm pupil</td>
<td>41%</td>
<td>0%</td>
<td>41%</td>
<td>18%</td>
</tr>
</tbody>
</table>

Table 1. Light distribution by pupil size in refractive and diffractive IOLs.
vision, again highlighting the importance of this gap in older technology.

3. Know your technology – and know your patients

Although today’s presbyopia-correcting IOLs are more forgiving and have fewer visual tradeoffs than the lenses we had eight years ago, it’s just as important now as it was then to understand how they work, and to carefully select patients who will benefit from these lenses.

For example, it is very unlikely that you’ll achieve a good result using a mIOL with a patient with ≥0.75 D of corneal astigmatism – you need to correct the astigmatism with incisional or laser ablation methods, or perhaps opt for a toric lens instead.

Understanding the degree to which new lenses are pupil dependent, and how that might affect visual performance for patients with unusually large or small pupils is another consideration. A big disadvantage of the refractive lens used in this study is that it may not provide high quality far vision in patients with larger pupil sizes, because of an increase of halos. In my practice, we have decided not to implant them in patients with pupils of diameters greater than 5.0 mm.

Past lessons for future success

Through different focal points, better optics, and new light distribution strategies, newer generation IOLs are beginning to address the challenges of intermediate vision and pupil independence that previously made it necessary to take a mix-and-match approach. They may also be able to address some of the additional challenges we see with mIOLs, such as reduced contrast sensitivity, and reduced available light.

I believe that these new technologies will allow many more patients to take advantage of presbyopia-correcting IOLs. And even though previous generations of these lenses had some downsides, surgeons who have learned from the challenges and limitations of the IOLs of the past, and achieved successful outcomes despite them, are likely to find even greater success in the future.

Matteo Piovella is Medical Director of CMA (Centro Microchirurgia Ambulatoriale) in Monza, Italy, and serves as President of the Italian Ophthalmological Society.

Reference
When changing your IOL makes a big difference.

**ZEISS CT LUCIA**

During the statistical evaluation of implantation times, carried out by the David J Apple International Laboratory for Ocular Pathology, International Vision Correction Research Centre (IVCRC), Department of Ophthalmology, University of Heidelberg, Chairman: G.U. Auffarth, MD, PhD, FEBO., comparing the ZEISS CT LUCIA and the Alcon AcrySof® (SN60WF), the ZEISS CT LUCIA performed with a total implantation time of 70 seconds versus the Alcon AcrySof® (SN60WF) with 90 seconds. The ZEISS CT LUCIA showed a faster centration after insertion in the capsular bag with less manipulation required, compared to Alcon AcrySof® (SN60WF). The measured implantation steps included: insertion, injection, unfolding and centration.

When changing your IOL makes a big difference.

**ZEISS CT LUCIA** – monofocal IOL

**Controlled unfolding and faster centration compared to AcrySof® IQ**

Thanks to its special lens design and specific properties, ZEISS CT LUCIA® smoothly unfolds without the haptics sticking to the optic to enable faster centration with less IOL manipulation.

**Small changes can make a big difference.**
Benchmarking Cataract

We mined the last five years of the clinical cataract literature to uncover who is publishing what, where, and the impact that it has made.
Benchmarking Cataract

Two years ago, we benchmarked the clinical cataract literature. What’s today’s state of play?

By Mark Hillen

Cataract surgery continues to advance, not only in lens design, but also in terms of surgical instruments. From femtosecond lasers, improved IOLs and smarter phaco platforms, the field evolves continuously.

To generate some insight into the past and future of cataract surgery, we asked the following questions:

• Who has published the most?
• Who has had the greatest impact?
• What are the big topics being discussed?
• Is this knowledge available online?

To provide the answers to these questions, a literature analysis was performed.

PubMed, was searched for cataract, with results limited to the last five years, in humans (for a clinical focus). The data were analyzed in Microsoft Excel 2013.

Top 20 journals by number of publications

Publications per year*

<table>
<thead>
<tr>
<th>Year</th>
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*Only complete year datasets were included

Top 20 topics

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<td>Cataract</td>
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<td>Visual Acuity</td>
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<td>1970</td>
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<tr>
<td>Phacoemulsification</td>
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<tr>
<td>Aged, 80 and over</td>
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<tr>
<td>Postoperative Complications</td>
<td>1247</td>
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<tr>
<td>Retrospective Studies</td>
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<td>Prospective Studies</td>
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<td>Refractive Errors</td>
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<td>Lenses, Intraocular</td>
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<td>Treatment Outcome</td>
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<td>Cornea</td>
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<td>Vision Disorders</td>
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Language

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<td>Japanese</td>
<td>36</td>
</tr>
<tr>
<td>Other</td>
<td>108</td>
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</tbody>
</table>
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Building a Bigger (Eye) Bank
Chris Hanna and Gregory Hageman share their experiences of engaging with the community to encourage organ donation to the Utah Lions Eye Bank.
Building a Bigger (Eye) Bank

Making ocular research tissue widely available is achievable – if you approach it in the right way

By Chris Hanna and Gregory S. Hageman

Remarkable advances in our understanding of the genetic and biological foundations of a number of major human ocular diseases have derived from studies of donated human eyes. As an example, early morphological and immunohistochemical studies of human eyes provided the first evidence that aberrant function of the complement system at the level of the RPE-choroid interface plays a key role in the etiology of age-related macular degeneration (AMD). Importantly, these studies led to the identification of an association of a common risk haplotype of the Complement Factor H (CFH) gene with AMD (1–4).

According to a recent article in The Ophthalmologist, the number of eyes donated for research has declined over the last decade (5). But is it because (as was suggested) of fewer people being willing to donate their eyes? A recent study (6) confirmed that this was the case with some people, but apparently others would donate, but labor under the mistaken assumption that their eyes were “too old or unhealthy to be of any use.” The majority, however, simply hadn’t considered donating their eyes, because they hadn’t been made aware of the possibility.

Our ingredients for success

Communication has been the most important component of our successful partnership. At an operational level, it is critical that the overall need of tissue is established early in any partnership, as this dictates many of the partnership’s parameters. Once the need is established, we have learned that it is imperative that research institutions provide financial support to their eye bank partner. There are significant costs related to the acquisition of human eyes – and this is a number of key ingredients that lead to successful and long-lasting partnerships, such as the one created here in Salt Lake City between the John A. Moran Eye Center (JMEC), the Sharon Eccles Steele Center for Translational Medicine (SCTM) and the Utah Lions Eye Bank (ULEB).

At a Glance

- Research institutes and eye banks must work closely together to secure a good pipeline of donor eyes and tissue
- All collaborating institutes need to recognize that organ harvesting and eye banking have significant costs – and fund accordingly
- Communicating clearly with potential donors and their families is the key to unlocking globe donation
- It’s vital to feed back to the donors’ families: let them know what their precious gift is doing to advance medicine and vision science
The ULEB and JMEC/SCTM at the University of Utah have created one of the most productive research tissue placement systems in the United States. How? A decades-long partnership where money has been spent building and maintaining not only a robust tissue collection and processing program, but also supporting public outreach and education programs that center on eye donation. This last part is key. Together, we partner in educating potential donors, their families, caregivers, hospital staff members, local ophthalmologists and the general public about donation and the importance of ocular tissue to scientific discovery and the future of medicine. These educational activities are ongoing and are a critical component of this successful partnership. The JMEC/SCTM and ULEB use social media, community events and newsletters as platforms to educate and inform the public about the importance of tissue donation to research, often with Moran’s real-life research breakthroughs as examples.

Keep the message simple
We have learned that simple messages – like “tissue can be used for research even if it’s not suitable for transplant” and “tissue derived from older individuals with and without eye disease are precious gifts” – are important to communicate. It’s here where our long-established partnership pays dividends: ULEB employees are exquisitely skilled in having delicate conversations with patients and their families, and Moran scientists and physicians call upon them regularly to help communicate donation options and needs. Feedback to donor families is equally important and both partners strive to ensure that this occurs – for example, SCTM staff members are in contact with the majority of donor families, often leading to the participation of the donor’s family members in other research studies.

So far so good
The symbiotic arrangement between the ULEB and JMEC/SCTM has been wonderfully productive. The Moran Eye Center provides physical space and salary support, subsidizing ULEB’s efforts and helping them to expand (the ULEB recently built a new, state-of-the-art center with an increased capacity for receiving and processing tissue). In return, Moran scientists and clinicians have access to higher-quality, lower-cost tissue than they would from out-of-state eye banks. The ULEB provided 11,381 eyes to researchers between 2012 and 2015, and in 2015 was the fourth highest in terms of research tissue placed in the US. For SCTM, the ULEB has provided 3,401 fresh globes (i.e. tissue recovered within five hours) since 2010. The significance of fresh tissue is vitally important for Moran scientists and clinicians due to the fact that significant cell death occurs once blood circulation in the body ceases, meaning that it’s imperative that most tissue is provided within a short timeframe to enable scientists and researchers to glean the best, most accurate results from their experiments.

The will is there!
We propose that the key issue at hand is not that “the number of people willing to donate their eyes for research purposes has been falling.” Our experiences have taught us that patients who are educated about tissue donation are willing to donate for both transplant and research; and that families are comforted that their loved one gave a lasting gift of sight, whether for today or for tomorrow. People are more than willing to donate their eyes! The challenge of increasing the availability of ocular tissue lies with the creation of robust partnerships, commitment of time and staff, active cooperation and communication, financial investment, promotion, education and, importantly, feedback to all who have participated in the donation and acquisition of these precious tissues. The eye donation program here in Utah has been a resounding success because of these key ingredients.

Chris Hanna is the Executive Director of the Utah Lions Eye Bank and Gregory S. Hageman, is the John A. Moran Presidential Professor and Executive Director of the Sharon Eccles Steele Center for Translational Medicine at the University of Utah Moran Eye Center in Salt Lake City.

References
Better by Design

Sitting Down With... Malik Kahook, Slater Family Endowed Chair in Ophthalmology, Vice Chair of Clinical & Translational Research, and Chief, Glaucoma Service, Anschutz Medical Campus, University of Colorado, USA.
You're an inventor. How do the ideas come—are they the result of lots of discussions, or are they just rays of inspiration entering the brain?

Rays of inspiration often come from many discussions and collaborations. I am part of the Chandler-Grant lineage of glaucoma-trained ophthalmologists, and their original teachings espoused the importance of being a clinician-scientist, and working collaboratively. I remember David Epstein, who was also trained by Chandler and Grant, explaining to me on a long drive one day that all I need to do is listen to my patients to hear what problems are most in need of solving. I think it’s clear that I am a product of my environment, and I see my translational research as an integral part of who I am as a caretaker of patients.

You hold quite a few patents—what advice do you have for other ophthalmologists hoping to make their idea a reality?

The single most important piece of advice I can give is to never give up. Persistence is the magic that takes a fleeting idea and pushes it towards a reality. Of course, nobody can do this kind of work in a vacuum. Finding a mentor who can help guide your path through the minefields of prototype building, patent applications, fundraising and clinical trials is extremely important. My final piece of advice centers on the idea of the “Go No-Go” decision. During the invention process, we always consider if what we are building is meeting our expectations, and if our original idea still holds promise. Sometimes we have to be honest with ourselves and come to the difficult realization that our idea is either not as novel or as practical to implement as we had originally thought.

Have you worked on a drug or device that you thought was going to be the next big thing…and it wasn’t?

More often than not, yes. I have many devices sitting on the shelf that I thought would be “the next big thing” but ended up being leap-frogged by another technology, or just not working as expected. But sometimes something special happens, and our product concept becomes a reality and helps patients around the globe. Two examples of this are the Kahook Dual Blade and the Harmoni Modular IOL System.

What would you consider your greatest career highlight so far?

I have received a tremendous amount of satisfaction from launching products that were born in the lab. It is hard to top that feeling, especially because the joy is shared with so many close friends and colleagues. One achievement, not related to research, that comes to mind is my work with many other talented clinicians, including Joel Schuman, on developing the 5th edition of Chandler and Grant’s Glaucoma textbook.

What is your current research focus?

My device lab focuses on several aspects of treating ophthalmic diseases, ranging from glaucoma treatment devices to novel IOL materials and designs. We have also started new programs centered on drug delivery and ocular surface disease therapies with transformative potential. These are high risk and high reward projects that are in early clinical studies, but I hope we can share more details in the coming year.

What’s exciting you about ophthalmology right now?

The current atmosphere of innovation coupled with a refusal to accept the current state of affairs in ophthalmic care is very exciting. Multiple technologies are now coming to the market that we could only dream of when I was in residency, for example, next generation femtosecond laser technology. It is worth noting that industry leaders in ophthalmology are significantly changing their approach to R&D and how they interact with small companies and inventors, and this is providing more opportunities to partner and impact patient care in a more meaningful way.

Where do you see yourself in 10 years? I hope that my day-to-day work life will be much the same—I enjoy seeing patients and performing surgery. I feel that our device development infrastructure at the University of Colorado has matured to the point that we can focus on game-changing technology using an effective system. This was a decade-long effort, and I hope we can enjoy the fruits of our labor for the next decade and beyond. I do see myself getting more involved with different aspects of our startup companies, including learning more about the business side which I find tremendously interesting. I am sure the next 10 years will hold some surprises, and I hope to find opportunities to continue to grow professionally.

Any advice for the Malik Kahook of 10 years ago?

If I could make a call to myself 10 years ago, I would simply say: “The ahead might seem long, but the lessons learned and life experiences are well worth the effort.”

An extended version of this interview is available online at: top.txp.to/issues/0616/701/
NEW in Glaucoma

THE NEXT STEP FOR PRESERVATIVE-FREE POWER

- Powerful IOP lowering reductions of up to 40% vs baseline
- Low level of hyperaemia (7%)
- One preservative-free drop once-daily

Product Name: TAPTQIOM® 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 (eyes) once daily. Not to exceed one drop per day in the affected eye. Not recommended in children or adolescents (under the age of 16). In renal or hepatic impairment use with caution. To reduce systemic absorption, patients should be advised to use nasoalarinal 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 TAPTQIOM® 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 hypoglycaemia or liable diabetes. Beta-blockers may mask signs of hypothyroidism and block systemic beta-agonist effects such as those of adrenaline. Anxa2asthetists 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 TAPTQIOM® is given concomitantly. The use of two topical beta-blockers is not recommended. Patients with conaval 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 cystoid macular oedema or iris/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 guanethidines. 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 TAPTQIOM® 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 TAPTQIOM®. 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 TAPTQIOM® include: increased iris pigmentation, anterior chamber cells/flares, iritis/uveitis, deepening of eyelid sulcus, hypertrichosis of eyelid, exacerbation of asthma, dyspnea, allergy, angioedema, urticaria, anaphylaxis, hypoglycaemia, syncope, ptosis, bradycardia, chest pain, palpitations, oedema, cardiac arrest, heart block, AV block, cardiac failure. Please also see the SmPC. Overdose: 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 0.3 ml single-dose containers £14.50. Product Licence Holder: Santen Oy, Nittyhaankatu 20, 33720 Tampere, Finland (PL 16030/0012) Price: 30 x 0.3 ml single-dose containers £14.50. Date of Authorisation: 30/10/2014 POM Date of Prescribing Information: 31/05/2015

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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References:

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