OCTOBER 2019 # 38

the Ophthalmologist™

Shared Vision

The essential and evolving relationship between ophthalmologists and optometrists

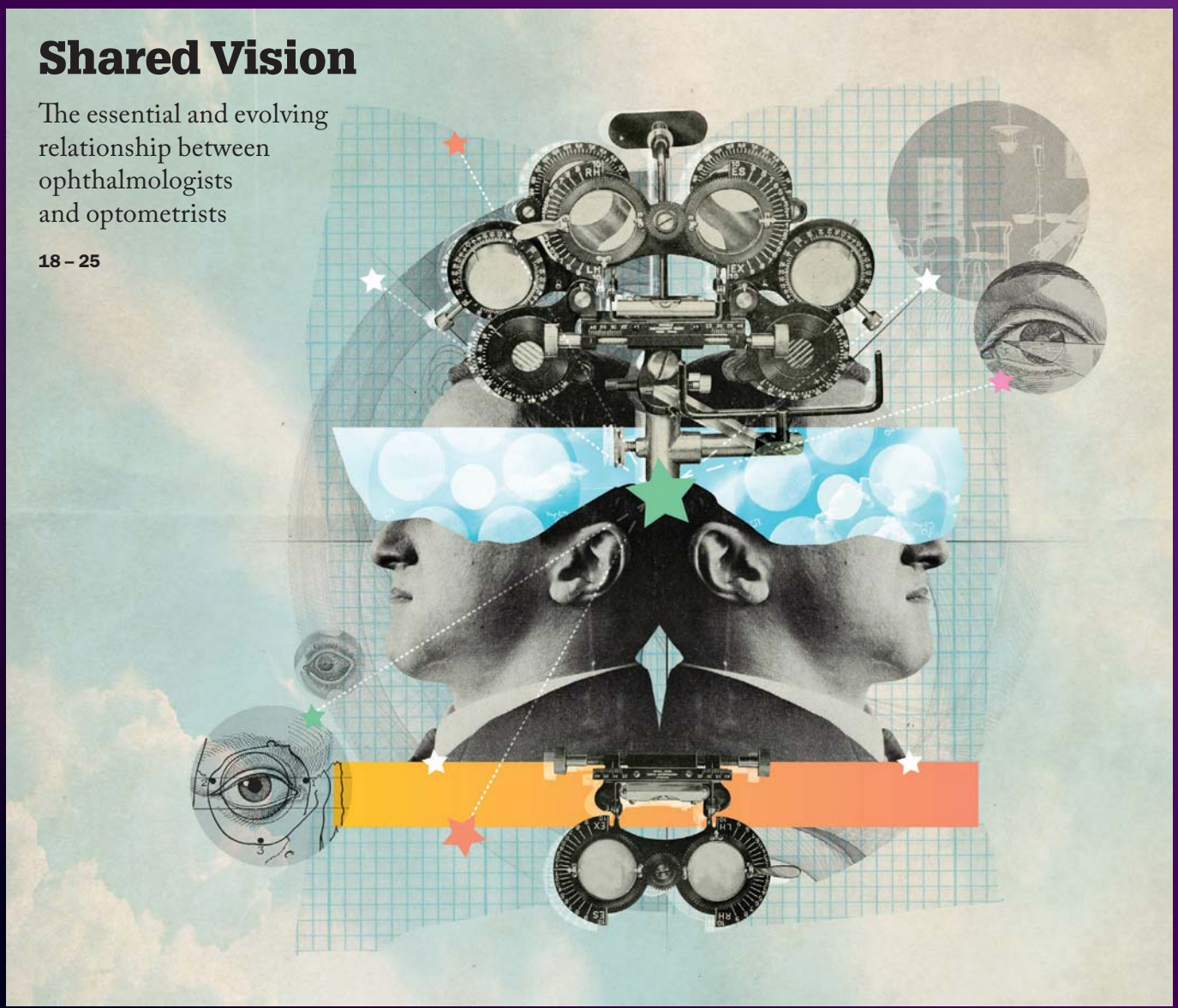

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Image of the Month

Is it Christmas Yet?

This month's image, taken with a slit lamp, shows a Christmas tree cataract. These cataracts are usually idiopathic or associated with myotonic dystrophy.

Credit: Martina David, ophthalmologist from Lohne, Germany

Do you have an image you'd like to see featured in The Ophthalmologist?
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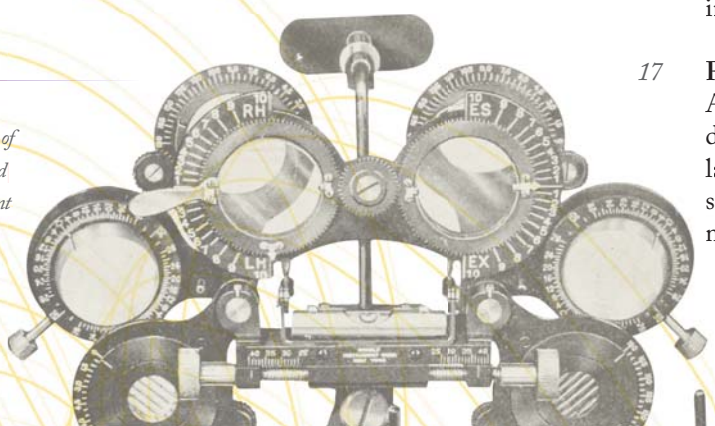
On The Cover

An entwined image of ophthalmologists and optometrists; the front line of eye care



the Ophthalmologist

DEXYCU®
(dexamethasone intraocular suspension) 9%

The first and only FDA-approved, single-dose, sustained-release, intracameral steroid for the treatment of postoperative inflammation[1-3]

With a single injection at the end of cataract surgery, anti-inflammatory efficacy begins as early as day 1 and continues through day 30[1]*

- The percentage of patients who received DEXYCU® (dexamethasone intraocular suspension) 9% (517 mcg) who had anterior chamber cell clearing on day 8 was 60% (n=94/156) vs 20% (n=16/80) in the placebo group[1]
- The cumulative percentage of subjects receiving rescue medication of ocular steroid or nonsteroidal anti-inflammatory drug (NSAID) at day 30 was significantly lower in the DEXYCU (517 mcg) treatment group (20%; n=31/156) compared to placebo (54%; n=43/80)[1]

*DEXYCU was studied in a randomized, double-masked, placebo-controlled trial. Patients received either DEXYCU or a vehicle administered by a physician at the end of the surgical procedure. The primary endpoint was the proportion of patients with anterior chamber cell clearing (cell score=0) on postoperative day 8.

INDICATION AND USAGE

DEXYCU® (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Increase in Intraocular Pressure

- Prolonged use of corticosteroids, including DEXYCU, may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision
- Steroids should be used with caution in the presence of glaucoma

Delayed Healing

- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids

Exacerbation of Infection

- The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures
- Use of a corticosteroid in the treatment of patients with a history of herpes simplex requires caution and may prolong the course and may exacerbate the severity of many viral infections
- Fungal infections of the cornea are particularly prone to coincidentally develop with long-term local steroid application and must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection

Cataract Progression

- The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts

ADVERSE REACTIONS

- The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis

Please see brief summary of full Prescribing Information on adjacent page.

References: 1. DEXYCU® (dexamethasone intraocular suspension) 9% full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. December 2018. **2.** Donnenfeld E, Holland E. Dexamethasone intracameral drug-delivery suspension for inflammation associated with cataract surgery: a randomized, placebo-controlled, phase III trial. *Ophthalmology.* 2018;125(6):799-806. **3.** Data on file. EyePoint Pharmaceuticals, Inc.

EyePoint™ PHARMACEUTICALS

480 Pleasant Street, Suite B300, Watertown, MA 02472

08/2019
US-DEX-1900120

DEXYCU (dexamethasone intraocular suspension) 9%,
for intraocular administration
Initial U.S. Approval: 1958

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE
DEXYCU (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Increase in Intraocular Pressure
Prolonged use of corticosteroids including DEXYCU may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma.

5.2 Delayed Healing
The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids.

5.3 Exacerbation of Infection
The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

5.4 Cataract Progression
The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

6 ADVERSE REACTIONS
The following adverse reactions are described elsewhere in the labeling:
- Increase in Intraocular Pressure *[see Warning and Precautions (5.1)]*
- Delayed Healing *[see Warnings and Precautions (5.2)]*
- Infection Exacerbation *[see Warnings and Precautions (5.3)]*
- Cataract Progression *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The following adverse events rates are derived from three clinical trials in which 339 patients received the 517 microgram dose of DEXYCU. The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis. Other ocular adverse reactions occurring in 1-5% of subjects included, corneal endothelial cell loss, blepharitis, eye pain, cystoid macular edema, dry eye, ocular inflammation, posterior capsule opacification, blurred vision, reduced visual acuity, vitreous floaters, foreign body sensation, photophobia, and vitreous detachment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
There are no adequate and well-controlled studies of DEXYCU (dexamethasone intraocular suspension) in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice and malformations of abdominal wall/intestines and kidneys in rabbits at doses 7 and 5 times higher than the injected recommended human ophthalmic dose (RHOD) of DEXYCU (517 micrograms dexamethasone), respectively *[see Data in the full prescribing information]*.

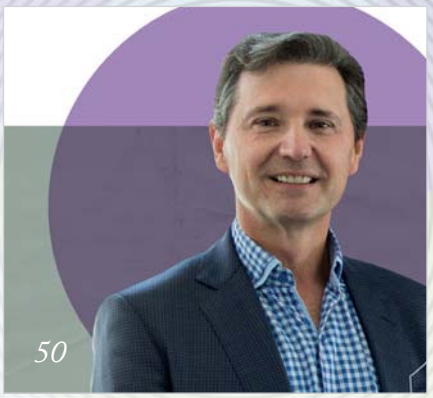
In the US general population the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation
Risk Summary
Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. There is no information regarding the presence of injected DEXYCU in human milk, the effects on breastfed infants, or the effects on milk production to inform risk of DEXYCU to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for DEXYCU and any potential adverse effects on the breastfed child from DEXYCU.

8.4 Pediatric Use
Safety and effectiveness of DEXYCU in pediatric patients have not been established.

8.5 Geriatric Use
No overall differences in safety or effectiveness have been observed between older and younger patients.

Manufactured for: EyePoint Pharmaceuticals US, Inc. Watertown, MA 02472



Feature

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Sitting Down With

the Ophthalmologist

ISSUE 38 - OCTOBER 2019

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Care to Join?

Shared ophthalmic care is needed, but patients' interests must always come before politics

Integrated, coordinated or comprehensive care – whatever we call it, it is increasingly clear that our aging populations desperately need health and social care professionals working together. Eye care is no exception, and with ophthalmologists struggling to meet growing demands, it is vital that the burden is shared among the wider health workforce. In the UK, ophthalmologists currently handle 10 percent of all outpatient appointments, but those numbers are set to grow, with a projected increase of glaucoma cases by 44 percent within the next 20 years, and the demand for cataract procedures predicted to rise by 50 percent over that period (1). Ophthalmic medical practitioners, nurses, orthopists, and, last but not least, optometrists, are all crucial pieces in this sizeable jigsaw puzzle. The common goals are clear: protecting vision and improving quality of life.

This month (and for the next few issues), we present various examples of where integrated support is already being applied to eye care – or where it is urgently needed.

Adam Mapani, ophthalmic nurse consultant, whom you may have spotted on our 2019 Power List, describes his experience of working in a setting where allied healthcare professionals play an integral role in delivering the best healthcare provision; they also educate practitioners around the world about implementing collaborative approaches (see page 16).

In our feature, Shared Vision (see pages 18-25), ophthalmologists and optometrists from Europe and North America describe their experiences of approaches that work well when it comes to joining forces, and suggest how the mutually beneficial relationships can improve even more in the future. But they also note the aspects of care that should not be shared. Mutual respect and working for the benefit of the patient should always win over prospects of financial gains or "turf wars." Though consensus is not always easy to achieve at the institutional level, our contributors regularly see successful examples of patient co-management and cooperation.

Appropriate regulation, education and training are all key to ensure that patient safety is not compromised when implementing aspects of integrated care into ophthalmic practice. But when done well – and responsibly – it represents a win-win-win solution, reducing ophthalmologists' burden, empowering healthcare professionals, and giving patients access to a support system that fully meets their needs.

Aleksandra Jones
Editor

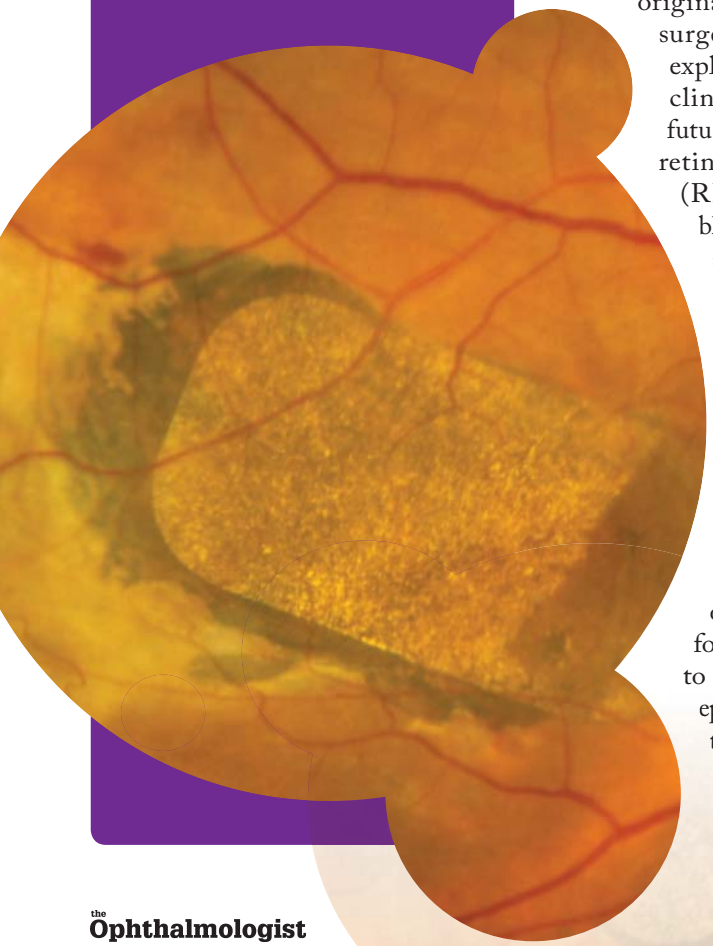
References

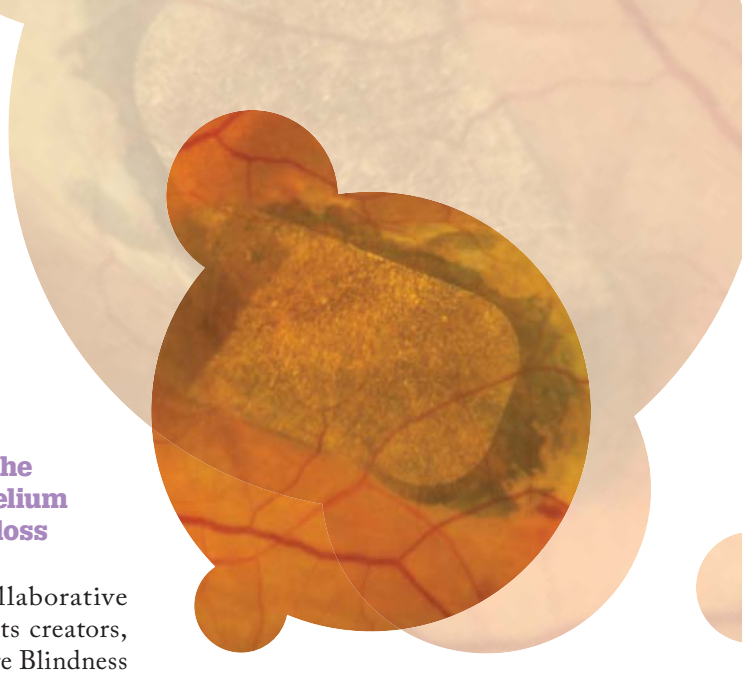
1. *The Royal College of Ophthalmologists, "The Way Forward Resources" (2017). Available at https://bit.ly/2kY1cWO. Accessed September 7, 2019.*

Upfront

Reporting on the innovations in medicine and surgery, the research policies and personalities that shape the practice of ophthalmology.

We welcome suggestions on anything that's impactful on ophthalmology; please email edit@theophthalmologist.com





A Promise Fulfilled?

The ongoing story of the retinal pigment epithelium patch for AMD vision loss

After many years of collaborative preliminary research by its creators, the London Project to Cure Blindness (LPCB) was officially launched in 2007, with the aid of a large charitable donation. This collaborative R&D initiative seeks to manifest the promise of embryonic stem cell technology in the fight against vision loss, and to devise specific medical treatments, tools and techniques alongside its ongoing scientific investigation. In an interview with The Ophthalmologist, one of the project's originators and ophthalmic surgeon Lyndon da Cruz explained the background, clinical trial success and future plans for the LPCB's retinal pigment epithelial (RPE) patch to reverse blindness in patients with severe wet AMD.

Tell us about the RPE patch project.

Pete Coffey and I started the preliminary RPE project in the early 2000s, after melding his interest in retinal disease cellular therapies with my focus on surgical remedies for AMD. Our aim was to create retinal pigment epithelial cells that could be transplanted into patients with this condition. This was always the great hope of stem cell treatment and regenerative medicine in general: to create a part of someone and transplant it into them to repair damage from disease and restore function.

Over the past few years, we've been working together to both create the RPE cell layer or patch, and to develop the surgical trials, instruments and procedures necessary to actually put it into a human eye. We ran many preliminary surgical studies to determine the optimal installation time and tools for maximum therapeutic effect. We found that if we transplanted the RPE layer within the first six weeks after the sudden onset of vision loss, vision could be restored. All of this work led up to the two-patient trial that started in 2015, which enabled us to demonstrate clearly that our patients' vision returned (1).

Were you surprised by the trial results?

We were surprised and, of course, delighted to get such a clear signal of outcome from the first two patients. Usually when you're trying a totally new treatment, surgery and device, you just want to ensure it's safe and practical. Later, you look for indications that the surgery works, the cells go where needed and survive, and they produce at least a two-year visual recovery. But for us, this outcome is fantastic.

Why just two patients – and are there plans for more?
We planned to study the procedure in more patients, but we were delayed when Pfizer, the study sponsor, stopped the trial for commercial reasons; transferring the project back to UCL took around three years. So, hopefully by the end of this year, we will start the trial again and would hope to have implanted the patch in another six to eight patients in the coming year, in order to determine if the initial effect we saw is repeatable.

We've now submitted the two-year outcome data for the first two patients to publication, to show that the RPE patch is safe and stable, that the visual recovery persists, that the patients have no major systemic or ocular side effects and require only minimal local immunosuppression. The fact that patients don't have to take immunosuppression drugs for a long time is another benefit of this approach.

How do you expect the project to proceed from this point?
We'd like to confirm the vision restoration in a few more cases, and see the five-year follow-up data to make sure there's no tumor growth, major rejection or damage to the other eye. Then we'd like to do a pivotal study to show that in severe wet macular degeneration patients, this is a reproducible endpoint, and we finally have a way of restoring lost vision. After that, our second phase will be to look at treatments for early dry AMD patients.

Are there any other projects pursuing RPE technology?
A group in the USA is doing a sheet pigment epithelium transplantation trial, but they chose a patient group with severe dry degeneration, with no chance of good visual recovery. It was a pure safety study, but it seemed to indicate the persistence of cells and pigmentation, like ours did. In other trials, rather than arranging the cells in a sheet, researchers have injected them into the eye in suspension. Some of these trials showed that clumps of cells survived, but it was very difficult to document whether those were the same cells introduced or if they were even functional. Other researchers are looking at replacing pigment epithelial cells in different disease contexts, but they've been unable to show conclusive visual recovery so far.

References

1. *L da Cruz et al., "Phase 1 clinical study of an embryonic stem cell–derived retinal pigment epithelium patch in age-related macular degeneration", Nat Biotechnol, 36, 328 (2018). PMID: 29553577.*
2. *Nature Research Bioengineering, "A cell patch for the treatment of blindness" (2018). Available at: https://go.nature.com/2lJbZXc. Accessed September 2, 2019.*

Feast for the Eyes

Most people on extreme diets won't know what they are doing to their eyesight – until it's too late – so should ophthalmologists routinely ask their patients what they eat?

We know that diet can directly impact ocular health – indeed, we have known it for years. If the "eat your greens" commands we received as children weren't enough – and they often weren't – the Age-Related Eye Disease Studies (AREDS) has since put science into our plates of spinach. The first AREDS study, nearly two decades old, showed that AMD patients who take high doses of antioxidants and micronutrients (vitamins C and E, beta-carotene, zinc and copper) reduce their risk of progressing to advanced AMD by about 25 percent. Similarly, AREDS 2 suggested that some patients can benefit from supplementing their diet with high levels of lutein and zeaxanthin. In these studies, patients took very high levels of vitamin supplements; however, lower levels – such as those derived from a diet rich in, for example, leafy green vegetables – are also thought to reduce the risk of AMD (1). Furthermore, the influence of diet on ocular health extends beyond modulation of AMD risk; a quick glance through PubMed will reveal numerous studies suggesting a role for micronutrients in ocular disease – for example, glaucoma (2).

Mostly, however, the impact of diet seems relatively subtle – a modulation of progression here, a nudge in incidence rate there. But then, most people have relatively "normal" diets; upping their consumption of fruit and veg probably just shifts their position within the middle part of the bell-curve.

To see what can happen to the human eye in a truly nutrient-challenged environment, we must look to the extremes of eating. Case in point: a tragic, but exemplary, incident that received broad coverage in the UK media in the last couple of weeks, following its publication in a peer-reviewed journal (3). Briefly, a teenage boy complained of tiredness to his GP; he was known to be a fussy eater, but tests indicated normal BMI and no visible signs of malnutrition. Blood tests revealed anemia and low levels of vitamin B12; accordingly, the boy was prescribed B12 injections. Within a year, however, the patient was complaining of hearing loss and visual impairment. Sadly, his sight was lost before the true cause of his complaint was revealed: retinal starvation resulting from years of eating only chips, crisps and white bread, with the occasional addition of processed pork. Clinicians from the Bristol Medical School and Bristol Eye Hospital, UK, concluded that the unusually limited nature of his food intake had resulted in B12 deficiency, low levels of vitamin D, copper and selenium, high levels of zinc, reduced bone density – and severe optic neuropathy.

Denize Atan, Consultant Senior Lecturer in Ophthalmology, Bristol Medical School, UK, warns that diet-related optic neuropathy may become more prevalent as junk-food consumption – or a limited vegan diet – become more common. What should we take home from this? Perhaps that an investigation of dietary history should be included in any routine clinical examination – including initial ophthalmic consultations.

References

1. *National Eye Institute, "What the Age-Related Eye Disease Studies Mean for You" (2018), Available at: https://bit.ly/2lILP7a. Accessed September 9, 2019.*
2. *SC Sacca et al., "Substances of interest that support glaucoma therapy", Nutrients, 11 (2019). PMID: 30678262.*
3. *R Harrison et al., "Blindness caused by a junk food diet", Ann Intern Med, [Epub ahead of print] (2019). PMID: 31476767.*

Dextenza®
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- Insert can be removed via saline irrigation or manual expression, if necessary[2]
- Physicians rated DEXTENZA as easy to insert[3,4]*

VISIT BOOTH 2323 AT AAO 2019

INDICATION

DEXTENZA is a corticosteroid indicated for the treatment of ocular inflammation and pain following ophthalmic surgery.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

WARNINGS AND PRECAUTIONS

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during treatment.

Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

ADVERSE REACTIONS

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%); intraocular pressure increased (6%); visual acuity reduced (2%); cystoid macular edema (1%); corneal edema (1%); eye pain (1%) and conjunctival hyperemia (1%).

The most common non-ocular adverse reaction that occurred in patients treated with DEXTENZA was headache (1%).

Please see brief summary of full Prescribing Information on adjacent page.

*73.6% of physicians in Study 1, 76.4% in Study 2, and 79.6% in Study 3 rated DEXTENZA as easy to insert.

References: 1. Sawhney AS et al, inventors; Incept LLC, assignee. US patent 8,409,606 B2. April 2, 2013. **2.** DEXTENZA [package insert]. Bedford, MA: Ocular Therapeutix, Inc; 2019. **3.** Walters T et al. *J Clin Exp Ophthalmol*. 2016;7(4):1-11. **4.** Tyson SL et al. *J Cataract Refract Surg*. 2019;45(2):204-212.

Ocular Therapeutix™

Dextenza®

(dexamethasone ophthalmic insert) 0.4 mg
for intracanalicular use

BRIEF SUMMARY: Please see the DEXTENZA Package Insert for full prescribing information for DEXTENZA (06/2019)

1 INDICATIONS AND USAGE

DEXTENZA® (dexamethasone ophthalmic insert) is a corticosteroid indicated for the treatment of ocular inflammation and pain following ophthalmic surgery.

4 CONTRAINDICATIONS

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

5 WARNINGS AND PRECAUTIONS

5.1 Intraocular Pressure Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during the course of the treatment.

5.2 Bacterial Infection

Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection *[see Contraindications (4)]*.

5.3 Viral Infections

Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex) *[see Contraindications (4)]*.

5.4 Fungal Infections

Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate *[see Contraindications (4)]*.

5.5 Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Intraocular Pressure Increase *[see Warnings and Precautions (5.1)]*
- Bacterial Infection *[see Warnings and Precautions (5.2)]*
- Viral Infection *[see Warnings and Precautions (5.3)]*
- Fungal Infection *[see Warnings and Precautions (5.4)]*
- Delayed Healing *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation; delayed wound healing; secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera *[see Warnings and Precautions (5)]*.

DEXTENZA was studied in four randomized, vehicle-controlled studies (n = 567). The mean age of the population was 68 years (range 35 to 87 years), 59% were female, and 83% were white. Forty-seven percent had brown iris color and 30% had blue iris color. The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%); intraocular pressure increased (6%); visual acuity reduced (2%); cystoid macular edema (1%); corneal edema (1%); eye pain (1%) and conjunctival hyperemia (1%).

The most common non-ocular adverse reaction that occurred in patients treated with DEXTENZA was headache (1%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate or well-controlled studies with DEXTENZA in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, administration of topical ocular dexamethasone to pregnant mice and rabbits during organogenesis produced embryofetal lethality, cleft palate and multiple visceral malformations *[see Animal Data]*.

Data

Animal Data

Topical ocular administration of 0.15% dexamethasone (0.75 mg/kg/day) on gestational days 10 to 13 produced embryofetal lethality and a high incidence of cleft palate in a mouse study. A daily dose of 0.75 mg/kg/day in the mouse is approximately 5 times the entire dose of dexamethasone in the DEXTENZA product, on a mg/m^2 basis. In a rabbit study, topical ocular administration of 0.1% dexamethasone throughout organogenesis (0.36 mg /day, on gestational day 6 followed by 0.24 mg/day on gestational days 7-18) produced intestinal anomalies, intestinal aplasia, gastroschisis and hypoplastic kidneys. A daily dose of 0.24 mg/day is approximately 6 times the entire dose of dexamethasone in the DEXTENZA product, on a mg/m^2 basis.

8.2 Lactation

Systemically administered corticosteroids appear in human milk and could suppress growth and interfere with endogenous corticosteroid production; however the systemic concentration of dexamethasone following administration of DEXTENZA is low *[see Clinical Pharmacology (12.3)]*. There is no information regarding the presence of DEXTENZA in human milk, the effects of the drug on the breastfed infant or the effects of the drug on milk production to inform risk of DEXTENZA to an infant during lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DEXTENZA and any potential adverse effects on the breastfed child from DEXTENZA.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

17 PATIENT COUNSELING INFORMATION

Advise patients to consult their surgeon if pain, redness, or itching develops.

Ocular Therapeutix™

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Bitesize Breakthroughs

The latest research – in brief

1. Communication between the eye and the brain is clearly critical to our sense of sight. But the exact molecular mechanisms have been a source of speculation – until now. Using advanced mass spectrometry, a team at Scripps Research Institute has discovered how visual signals are distributed throughout the brain. The team identified upwards of 1,000 protein types that originate in the eye's retinal ganglion cells. They then watched how – and where – they traveled via the optic nerve in a living brain of a rat. The team evaluated the two major targets: the superior colliculus, which analyzes motion, and the lateral geniculate nucleus, which sends information to the visual cortex. Researchers found that similar proteins didn't always share a common destination, rather, many proteins were transported preferentially to one brain region, while some were transported to all of the regions studied. Though still in its infancy, the study expands accepted understanding of the visual system and, according to researchers, will hopefully lead to enhanced treatments in the future. Watch this space.

2. A collaboration between the University of Geneva and the École Polytechnique Fédérale de Lausanne may have answered the most fundamental question in ophthalmology: how is the retina formed? Sequencing more than 6,000 cells during embryonic development, the researchers did more than just uncover how – and why – certain neurons become associated with certain parts of the visual system; by predicting the sequential activation of neural genes, the team were able to reconstruct several differentiation programs, similar to lineage trees, showing how the progenitors progress to one cell type or another after their last division. They then conducted a secondary analysis, comparing the genetic diversity of two neuron populations – those associated with the left and right eye – discovering 24 genes that could play a key role in three-dimensional vision. The team hopes to continue their research, explaining that the more we know about the molecules needed to appropriately guide axons, the more likely we are to develop a therapy to treat nerve trauma.

3. We often hear of design mimicking nature – but sometimes it feels the other way round. Take the larval mantis shrimp – a crustacean that is able to simultaneously reflect and transmit light. How? Thanks to the crystal-like structure of its photoreceptors – natural analogs of the synthetic Fiber Bragg Grating, a visual filter used for monitoring in extreme environments. The similarity was discovered by researchers at The University of Minnesota while studying how vision informs and influences animal behavior, physiology and evolution. The team found that of the 17 families of mantis shrimp, only one – Nannosquillidae – possess these reflectors, believed to help detect bioluminescent targets. The filters are located within the rhabdom of larval compound eyes and selectively reflect a band of yellow light from a crystalline assembly of small, spherical units within the structure. While interesting in its own right, the findings open the door for even more exciting possibilities, as lead author, Kathryn Feller, explains: "The big question is what this new larval visual system can tell us about the evolution of adult mantis shrimp color vision, which is the most complex on the planet."

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In My View

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

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

Contact the team at edit@theophthalmologist.com

We're All in This Together

How allied health professions are making a difference in ophthalmology

By Adam Mapani, Honorary Clinical Teaching Fellow at UCL Department of Clinical Ophthalmology and Nurse Consultant at Moorfields Eye Hospital, London, UK.

Allied healthcare professionals (AHPs) play a significant role in the delivery of ophthalmic services for patients in the UK. The aging population, increase in disease prevalence, and emergence of new therapies have all created multiple challenges and opportunities for non-medical staff. For example, the medical retina landscape continues to evolve because of innovative treatments. The Way Forward project from The Royal College of Ophthalmologists (RCOphth) has indicated that the rise in medical retina patients is clearly going to stretch both ophthalmic services and the support structures that exist to help those with visual loss. Inaction is not an option. Changes to the way we deliver ophthalmic services are inevitable as the number of consultant ophthalmologists fail to match rising patient numbers.

Some aspects of the traditional roles of the ophthalmologist in the modern eye department have already been devolved. In the past decade, extended roles for AHPs in AMD and DME services have ranged from diagnostic, investigations interpretation and disease counseling to patient support, treatment and discharge. The macular clinics are protocol driven, making it safe and effective for AHPs to assume more responsibility. What's more, experienced, competent nurses often render a far higher patient satisfaction through full-circle treatment than when a patient's treatment is divided between nurses and doctors.

The nurse-led intravitreal injection case study serves as a model for a more cohesive approach, and has revolutionized patient care and the role of the ophthalmic nurse. Evidence in medical literature has consistently highlighted the importance of early diagnosis and intervention, finding that ophthalmic nurses have made a significant difference by reducing waiting times for injection treatments. More than that, safety outcomes and patient experience have both been reported as above the national average.

Moorfields has taken the training lead for setting up non-medical delivered injection service, training more than 500 AHPs nationally and internationally. Education delivery has had an impact as far afield as South Africa, Australia, the US, Singapore, Hong Kong, Ireland, Finland, Denmark and Northern Ireland. AHPs have taken the lead in driving innovation at busy outpatient clinics, with solutions that address long term follow-up challenges.

Other pathways – including diabetic eye disease – have established shared care models. Anecdotally, I have been part of this model, working with optometrists, diabetes nurse specialists and supervising consultant ophthalmologists. Our diabetes secondary assessment model is pitched towards patients presenting from retinal screening and consultant-led clinics.

Ophthalmic nurses play a vital role in disease prevention by promoting a healthy lifestyle, smoking cessation and disease stage counseling. By doing so, AHPs empower patients and improve health outcomes – something that has been recognized by Public Health England, the NHS and the RCOphth. In conclusion, AHPs make an enormous

contribution to the provision of ophthalmic care – but maintaining a certain level of quality, training and development is critical. Offering opportunities for career progression will improve retention, staff morale and job satisfaction, while succession planning, role modeling and inspirational leadership are essential to maintaining a stable workforce.

To read the full version of this piece, go to top.txp.to/all-in-this-together

FLACS Takes Flak

How does femtosecond laser-assisted cataract surgery really stack up against standard manual procedures?

By Anastasios Kanellopoulos, Director, Laservision Eye Institute, Athens, and Clinical Professor, Department of Ophthalmology, NYU School of Medicine, New York, USA.

When FLACS was first adopted in Europe, back in 2006, we had high hopes for this exciting new technology – unfortunately, these hopes have not been met. I say this from the perspective of 15 years' direct experience of the technique, during which time I have performed hundreds of procedures – including our combined femto and nanosecond laser cataract method, for which we received a video award at the 2015 ASCRS meeting. My opinion therefore has been formed by extensive personal experience of the FLACS method.

One of the first claims made for FLACS was that it mediated a capsulorhexis that was biomechanically superior to that provided by other methods. My view, however, is that the biomechanical rigidity of the FLACS capsulorhexis is not clearly superior to that provided by alternative methods.

Similarly, it has been widely suggested that FLACS permits much more precise centration than manual techniques, or even Zepto procedures, thanks to the "made-to-measure" trephination associated with intraoperative, anterior segment OCT technology. We should remember, however, that a FLACS capsulorhexis does not inevitably provide zero decentration: true, positioning often appears perfect in the immediate post-operative period, but capsule fibrosis and phimosis may gradually alter capsulorhexis shape and/or lens position over time. Consequently, the refractive data of these patients need to be evaluated at least a year after the procedure to achieve an accurate picture of the outcome.

Another claimed advantage of FLACS relates to the quality of the corneal incision, which is often said to be dramatically improved by femtosecond laser techniques. This, however, ignores less desirable aspects of laser-mediated corneal incisions.

My reservations regarding femtosecond lasers extend to their use in assisted astigmatic keratotomy as an adjunct to cataract surgery. This technique is supported by a significant number of clinicians, especially in the USA, but my impression is that astigmatic keratotomy incisions can be significantly misplaced when mediated by femtosecond laser – they may even approach the visual axis of the patient.

A particular FLACS-associated problem that frequently arises in our patient population is related to the effect of anesthesia. For the last eight years, we have performed all cataract procedures under a short duration, topical anesthetic. Specifically, we use 10 mL of 1 percent xylocaine, which we make up by a 1:1 BSS dilution of commercially available 2 percent xylocaine. This preparation effectively stops eye movements and sensation for about an hour and offers great comfort for the patient and safety for the procedure. Unfortunately, it makes subsequent use of a femtosecond laser impossible, since the peribulbar anesthetic invariably presents also as conjunctival chemosis, which prevents the patient interface effectively engaging the eye.

But what about outcomes? My own data are clear: visual acuity on day 1 post-surgery is far better with manual than with FLACS techniques, and very similar at one year after surgery. My conclusion is that FLACS has no clinical advantage over manual surgery, at least not in the cases I have treated.

Of course, there are reimbursement factors to consider and I realize that, in the US, opting for FLACS will turn a cataract procedure into a refractive procedure and alter the billing pattern accordingly, which may be economically advantageous for the practice.

In conclusion, at the risk of disappointing FLACS aficionados, I have to say that my experience of cataract surgery over 15 years is that FLACS is by no means definitively superior to manual techniques. Ethically, therefore – and to ensure the consistently good outcomes that are essential for a private practice to survive – I am unable to adopt FLACS as my routine method of cataract surgery at this point. I await further developments in femtosecond laser technology with interest!

The full version of this piece with references can be read here: top.txp.to/FLACS-takes-flak


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SHARED VISION

COMMON GOALS, NEW DIRECTIONS

Over the years, sharing care between ophthalmologists and optometrists has become the accepted standard – to the benefit of patients. But the process has not yet finished...

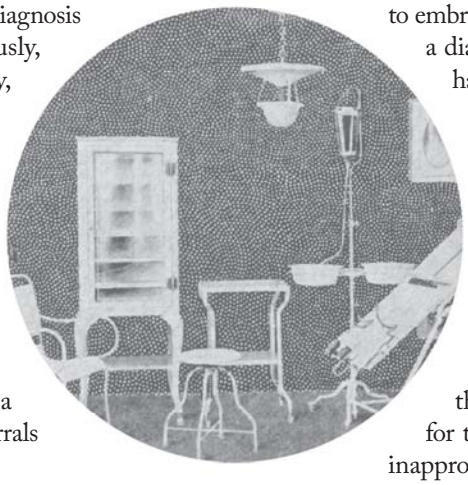
By Niall Patton

In my experience, the relationship between the ophthalmologist and the optometrist has evolved over the years. Since I began working in an NHS practice at the Manchester Royal Eye Hospital in 2008, specializing in cataract and vitreoretinal surgery, I have noticed that the care of the patient is seen very much as being in the hands of both: a shared care. Prior to this, the ophthalmologist would manage almost everything, from the pathology to the post-operative visits, before discharging them back to the optometrist. Now, I feel there is a much stronger relationship – more of a team approach.

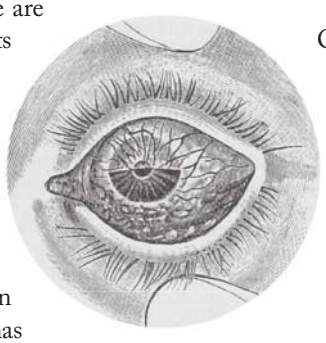
Frequently, patients who have had cataract surgery might see me for an initial appointment, but then further appointments will be with the optometrist. Today's optometrist does not simply dispense spectacles, but is wholly concerned with the health of the patient. And that's reflected in the range and sophistication of the comprehensive list of equipment you now find in a typical independent community optometrist's practice. To illustrate this, one of the most common examination tools we have for investigating retinal health and glaucoma is an optical coherence tomography (OCT) scanner. OCT scanners were only ever to be found in hospital environments. Now, most small independent optometrists have access. The use of OCT and imaging has enabled optometrists to extend services, from purely the visual field into other diseases areas; for example, diabetic screening.

"With greater access to specialist equipment, the quality of referrals and accuracy of diagnosis has become extremely high."

This transition has had a very positive impact on the ophthalmologist. Most importantly, the increased involvement of the optometrist has eased our workload – especially true for patients with glaucoma, where the optometrist has become very involved in the provision of their care. With the increased involvement and greater access to specialist equipment, the quality of referrals and accuracy of diagnosis has become extremely high. Previously, without access to imaging technology, a patient complaining of distorted or reduced vision could have suffered a wide range of diagnoses. Now, with an OCT scan at the point of care, the optometrist is able to correctly identify the underlying condition and refer on immediately to the correct person. This shift naturally leads to an acceleration in the delivery of appropriate care to the patient and a reduction in unnecessary referrals or referrals to the wrong service.



I believe that, in the future, there are even more activities that optometrists can take on. By way of example, we are particularly worried about post-operative retinal detachment. During a post-operative follow-up, clinicians are primarily concerned with ensuring the operation itself has been a success, for example, that the epiretinal membrane has been completely removed or the macula has closed. Checking for retinal detachment is a secondary consideration. As optometrists are now routinely examining and imaging the central macula and peripheral retina, they may well be able to take some of this workload away from the ophthalmologist in the future. It's not happening right now simply because there is not yet adequate additional training available to the optometrist; ophthalmologists are not yet sufficiently comfortable with discharging such patients back to the optometrist's care at an earlier stage. We may need some form of education, training and validation program that is accredited in a similar way to those currently available for glaucoma.



We should recognize that transferring these services to an optometrist also transfers additional responsibility. A reality that may deter some optometrists from taking on these additional duties – especially within an environment of increasing litigation. The optometrist will need training, continual support, and an ability to return the patient back to the hospital service should there be any inkling of a problem.

Technology and access to specialist equipment is not just improving for the optometrist of course. Artificial intelligence (AI) and advanced technologies are anticipated to reduce workload and improve patient care. It's another change that we will have to embrace in clinical practice. For me, AI is primarily a diagnostic tool, leaving the actual surgery in the hands of people – at least until robotics become sufficiently sophisticated! Algorithms are superior to individual skill after all and, if this benefits the patient, it should be encouraged.

The other question regarding the extent of an optometrist's remit is whether or not they could become prescribers of post-operative medicines, or broader medicines that would normally fall under the control of the ophthalmologist. I believe that while this may be another way of reducing workload for the consultant, many of these drugs would be inappropriate for prescribing by the optometrist as they are tightly connected with post-operative management. Obviously, there are also the formalities associated with being a registered prescriber, and this would require further training and monitoring.

Today we have a much more cooperative relationship between the ophthalmologist and optometrist than existed 10 or 20 years ago. There is no longer a feeling of "them" and "us." We do a much better job for the patient when we work together and, ultimately, we are both concerned with bringing better eye care to our patients.

Niall Patton is a Consultant Ophthalmic Surgeon at the Manchester Royal Eye Hospital and Optegra Eye Health Care clinic in Manchester, UK.

IN THE COMMUNITY, FOR THE COMMUNITY

Community optometrists are well placed to deliver high-quality eye care – with good education and training

By Clare O'Donnell

Ophthalmologists and optometrists are specialists in different, yet necessarily complementary disciplines, which has fostered a very positive relationship between the two. And that is particularly true for the community optometrist.

Healthcare is ever evolving, and we are continually challenging ourselves to find more efficient and effective ways in which we can deliver the highest quality patient care. Taking the provision of care into the community is a fundamental part of this endeavor – and ophthalmologists can benefit enormously from the skills of the community optometrist. We are looking at a valuable resource of highly skilled individuals working from well-equipped practices who are already familiar with the local patients. Moreover, their relationship with the patient is often very close, having been formed over a number of years.

I believe we can significantly improve our provision of secondary care by bringing it closer to patients and enabling them to receive effective follow-up closer to their homes. To achieve this, we should be looking at ways to support and up-skill our local optometrists in areas and practices to which they may not normally be exposed. It is important for the optometrist to have an oversight of the full patient pathway, from clinic to recovery. The positive interplay and good relations between the ophthalmologist and the optometrist will inevitably benefit our patients.

With this in mind, at Optegra Eye Health Care clinics, we offer further education and training to community partners, and I am keen to see this expand and move forward in a broader sense. So far, our events have been well received and enjoyed by both the participants and the trainers. Though we do design and deliver our own events, we are also receptive to organizing bespoke events, led by the requests and needs of the optometrist. For example, we might have a community partner who is particularly interested in the changes and advances in the treatment and care of macular degeneration. Equally and importantly, the topics may not be disease oriented. Some optometrists have expressed a desire to work with ophthalmologists to understand how we can deliver better referrals. In giving the optometrist a clearer view of what happens to the patient from the point of referral to coming back to the community practice, they are better equipped to understand the concerns and questions the patient may raise, improving their whole experience and promoting a positive outcome. We do ensure our events, where possible, are accredited and offer CET points, but our ultimate goal is to ensure people come along, see the latest technology, interrogate the patient journey, and come away with a better understanding of how to work together for the clear benefit of the patient.

I also firmly believe the interactions resulting from such gatherings foster stronger and more effective professional relationships. To me this is very important. In everyday practice, we see names and places on referral forms or records, but do not have the opportunity to simply chat in person. Our events facilitate this – and it leads to a closer and more open relationship.

With the roll out of national frameworks, including the national cataract pathways and, in the future, glaucoma and other sub-specialties, it is becoming increasingly important that we develop and foster a closer professional interaction between primary and secondary healthcare.

With this in mind, Optegra has developed specific partnerships with community optometrist networks. These start at the very beginning, with events run for trainee optometrists at university. For example, for a number of years now we have been running weekend educational events for final-year optometrists studying in Manchester. We spend the whole weekend with these students, running workshops where they practice their communication skills, become familiar with different diagnostic techniques and equipment and interrogating case-scenarios. Importantly, we also introduce the patient journey through the referral process and discuss the importance of informing the patient of the different choices they have during that process. We promote good-quality conversational techniques to ensure

the patient is properly informed and able to make an appropriate, personal decision. We also have programs across the UK that allow the student access to patients to discuss what happens after the optometrist has made a referral. This provides the student with a far deeper understanding of how the patient experiences their treatment, the impact and effect it may have on them and offers tools that the optometrist can use when discussing treatment options with a new patient. These experiences ultimately reassure the patient and provide a far better standard of care.

Once they have their degree, they will spend a year in pre-registration. During this year they are required to undertake additional training. We have become involved with this and are again providing weekend events that include lecture programs given by consultant ophthalmologists alongside more practical sessions. Vision Express (UK spectacle and contact lens seller who offers routine eye testing) is one of our main clients; the company sends all of its pre-registration optometrists to us for such training. For the more experienced optometrist, we host training and accreditation events that can also have practical aspects to them. Boots Opticians holds an annual CET meeting which we support by providing lectures on various ophthalmology topics – and they are always well received.

With the introduction of the new frameworks and pathways mentioned earlier, the relationship of the optometrist with secondary care is becoming more involved. This relationship has been in existence in some parts of the UK for some time now and we see that they work extremely well.

We are committed to continuing to deepen the relationship between the ophthalmologist and the optometrist, and to support further education and understanding. Not only do we work with independent optometrists, but we also interact with organizations responsible for designing educational content, such as OPEC. Why? Because we firmly believe secondary care in the community is not just appropriate, but hugely beneficial to the welfare of the patient.

Clare O'Donnell is a registered optometrist with over 20 years' experience. She is Honorary Senior Lecturer at University of Manchester and Head of Eye Sciences at Optegra in Manchester, UK.

SHARED OBJECTIVES, SINGULAR DEDICATION

Clearly established fields of expertise are important for a successful working relationship

By Elise Kramer

I studied optometry in Canada, and I currently practice in Florida, USA. By comparing my experiences of working in eye care in those two healthcare systems, I can clearly see how the relationship between ophthalmologists and optometrists differs in these two countries. Back in Canada, MD/OD collaboration was only just beginning, and it was only when I came to the States that I realized what this collaboration could and should look like. I was pleasantly surprised at the willingness of ophthalmologists to work with optometrists and their positive attitude to co-managing patients. The professions and their scopes are well defined here and doctors work together to achieve a common purpose.

In my practice, I have found the ability to refer patients to the best specialist in a particular area essential, and the referral system between ophthalmologists and optometrists seems to work very smoothly. I specialize in ocular surface disease and contact lens fitting, and I feel confident knowing that any cases outside the scope of my practice, such as glaucoma or retinal conditions, can be referred to my colleagues who focus on that particular area. Likewise, many ophthalmologists with patients who need specialized contact lenses will refer them to my practice.

"It is important to make sure that patients have a clear understanding of what each member of the health care team does – and why they are being referred to another specialist."

Co-management of patients is of vital importance for both the patients' wellbeing and for practice building. Patients with keratoconus or other corneal conditions that I refer to a corneal specialist, can then be referred back to me for continued care. There are many aspects of care that ophthalmologists could oversee, but given the limited time and resources they have, it may be more time- and cost-effective to refer those patients to optometric care. It is important to make sure that patients have a clear understanding of what each member of the healthcare team does – and why they are being referred to another specialist.

In Florida, as in most US states, surgical procedures can and should only be performed by ophthalmologists. It is important to know one's limitations, and regulations should clearly reflect that. When both professions can work together towards optimizing care and improving patients' quality of life, amazing things can happen.

Elise Kramer is a residency-trained optometrist at Miami Contact Lens Institute in Florida, USA. She specializes in ocular surface disease, keratoconus, refractive surgical complications, and regular and specialty contact lens fitting.

She reports the following relevant disclosures: BostonSight, Euclid Systems Corporation, Spectrum International and Visionary Optics.

FROM BOTH SIDES NOW

The remit of ophthalmologists and optometrists is not set in stone, it must evolve over time – and that will undoubtedly raise serious questions in both camps

By Kevin Waltz

I graduated from optometry school in 1981 and continued my education at a medical school, where I graduated six years later: I have seen eye care from the point of view of both an optometrist, and an ophthalmologist. More recently, I was the chairman of an ASCRS committee that tried to involve optometrists in ASCRS activities; sadly, the project did not turn out well, and the committee was disbanded. The debate between the two professions has been a politically challenging issue for decades. There are economic benefits of being able to perform surgical procedures or prescribe certain medications and, at the institutional level, things are not always amicable. There are currently four states in the US that allow optometrists to perform surgical procedures: Alaska, Kentucky, Louisiana and Oklahoma, but more states might join this group in the future. Once critical mass in a particular state is reached, legislation will follow. Less invasive procedures currently performed by optometrists might in time evolve into more complicated ones.

This relationship has been difficult throughout my 38-year career. In the early 1980s, optometrists wanted to get drug-prescribing privileges for diagnostic drops. The ophthalmology profession fought against this move by the optometric profession, but lost, and these days every US state allows optometrists to prescribe these drops. A similar process followed in the case of therapeutic drops, and now surgical privileges are on the table.

This situation is specific to the USA, of course. Depending on the particular country's regulation, education and training systems for both professions, practice varies greatly. Aiming at expanding a profession's privileges is a normal thing, provided it is done with patients' safety as the primary concern; in fact, some ophthalmologists are fighting to expand their profession into new fields, such as plastic surgery, which borders with oculoplastics. It is interesting to note that even though a profession might hold certain privileges, not all of its representatives use them. In the US, even though optometrists have fought for and won the ability to prescribe therapeutic medications, such as glaucoma drops or antibiotics, relatively few optometrists regularly prescribe these. Many practices have very successful working relationships between ophthalmologists and optometrists, with clearly defined specialty areas, and effective mutual referral systems.

From my vantage point

My personal relationship with optometrists is a very positive one. I work with them a lot, and I believe they are critical to the delivery

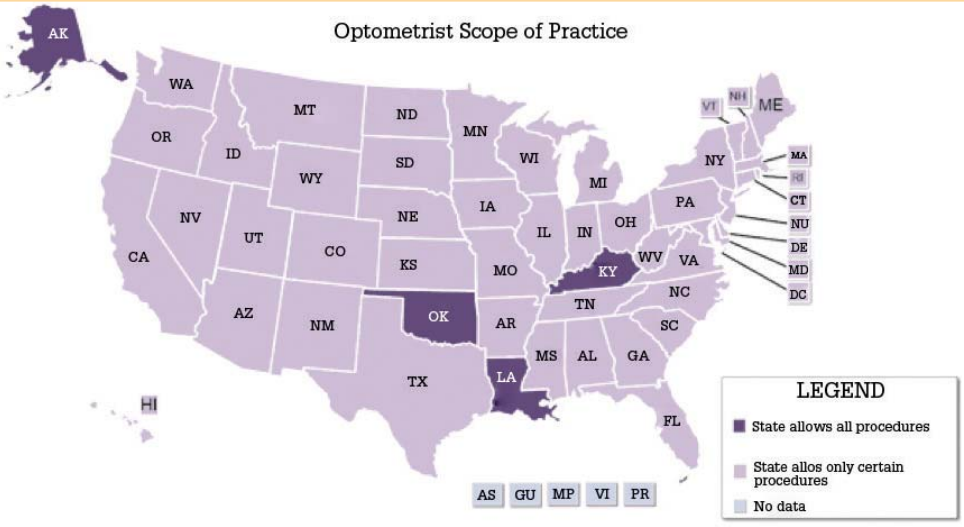


Figure 1. Optometrist scope of practice: surgical procedures. Source: American Optometric Association.

of eye care in the US. It would be impossible to deliver the care that people need without optometrists. There is no question in my mind that they should be a vital part of the team, the question is: what role they play in that team, including the exact scope of their activities. There is a whole spectrum of specialties among the optometrists I regularly work with, and some of my optometrist colleagues are of the opinion that they should be performing some surgical procedures, like their colleagues in some parts of Europe, or in the US states mentioned earlier.

Currently, a lot of responsibility in the USA is devolved to individual practices. Outside of state regulation, they have autonomy to decide whether specific types of surgery are done by the surgeon, or by a physician assistant, who receives mostly technical training around how to do the surgery and has little experience compared with a doctor, but is legally allowed to do surgery or administer intravitreal injections under a surgeon's license. This is specified in the practice's protocols, but it is ultimately the surgeon who is liable. It's just one example of how physician assistants and nurse practitioners are taking on more and more responsibility in eye care to assist in the delivery of care.

Over the horizon

Over the next two or three decades, we are not expecting to have more ophthalmologists trained and practicing than we have today. Demands from an aging society, on an other hand, are steadily growing: we are projected to have twice as much work in 20 years' time as we do now. With so few practitioners expected to do so much, new scenarios have to be developed. The UK, which suffers from tremendous pressure of intravitreal injections volumes, is exploring the possibility of nurse practitioners administering injections. Such reports create a stir among US ophthalmologists, but it is simply addressing the burden of work under which our profession finds itself. In time, our delivery systems must be adjusted to match the available workforce with the needs of the population.

What I believe optometrists require is the cognitive process behind examining a patient – seeing the big picture. And that is actually more complex and in some ways more difficult than learning how to do a YAG laser procedure. The ability to perform complex processes is important, but knowing which complex process to apply is vital.

Kevin Waltz is President of Ophthalmic Research Consultants, and Chair, Board of Directors for Central American Eye Clinics.

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US optometry practice, prescriptive and surgical authority timeline (1, 2).

1961 A bill is introduced by Pennsylvania optometrists to authorize the use of ophthalmic diagnostic pharmaceutical agents – it is defeated.

1971 First DPA Law passes in Rhode Island, giving specifically authorization to optometrists for using ophthalmic drugs for diagnostic purposes. (By 1989 all states and DC had DPA laws)

1973 Optometrists in North Carolina are authorized to use and prescribe pharmaceutical agents for diagnostic and therapeutic purposes.

1976 First TPA Law passes in West Virginia, permitting the use of therapeutic drugs by optometrists. (By 1998 all states and DC had TPA laws)

1981 US Congress expands optometric coverage under Medicare to enable reimbursement for procedures performed on aphakic patients.

1986 Medicare parity legislation allows optometrists to be reimbursed for health-related services performed on non aphakic patients. The law became effective in April 1987.

1998 Oklahoma enacts the first state law specifically authorizing the use of lasers by optometrists for certain treatment purposes.

2005 Oklahoma regains the right to use lasers after losing it.

2011 Kentucky optometrists are allowed to perform certain injections and laser procedures under new legislation.

2014 Louisiana becomes the third state to allow optometrists to perform surgical procedures.

2017 Under Alaskan House Bill 103, optometrists in the state can perform anterior segment laser procedures, including YAG capsulotomy, SLT and LPI.

CLEAR ADVANTAGES ULTRA-WIDEFIELD IMAGING WITH HD FLUORESCEIN ANGIOGRAPHY

The ZEISS CLARUS 700 is the first fundus camera to combine an ultra-widefield of view with True color high-resolution imaging. And now it comes with a full suite of imaging capabilities – including fluorescein angiography – and advanced features to collect the best image, every time.

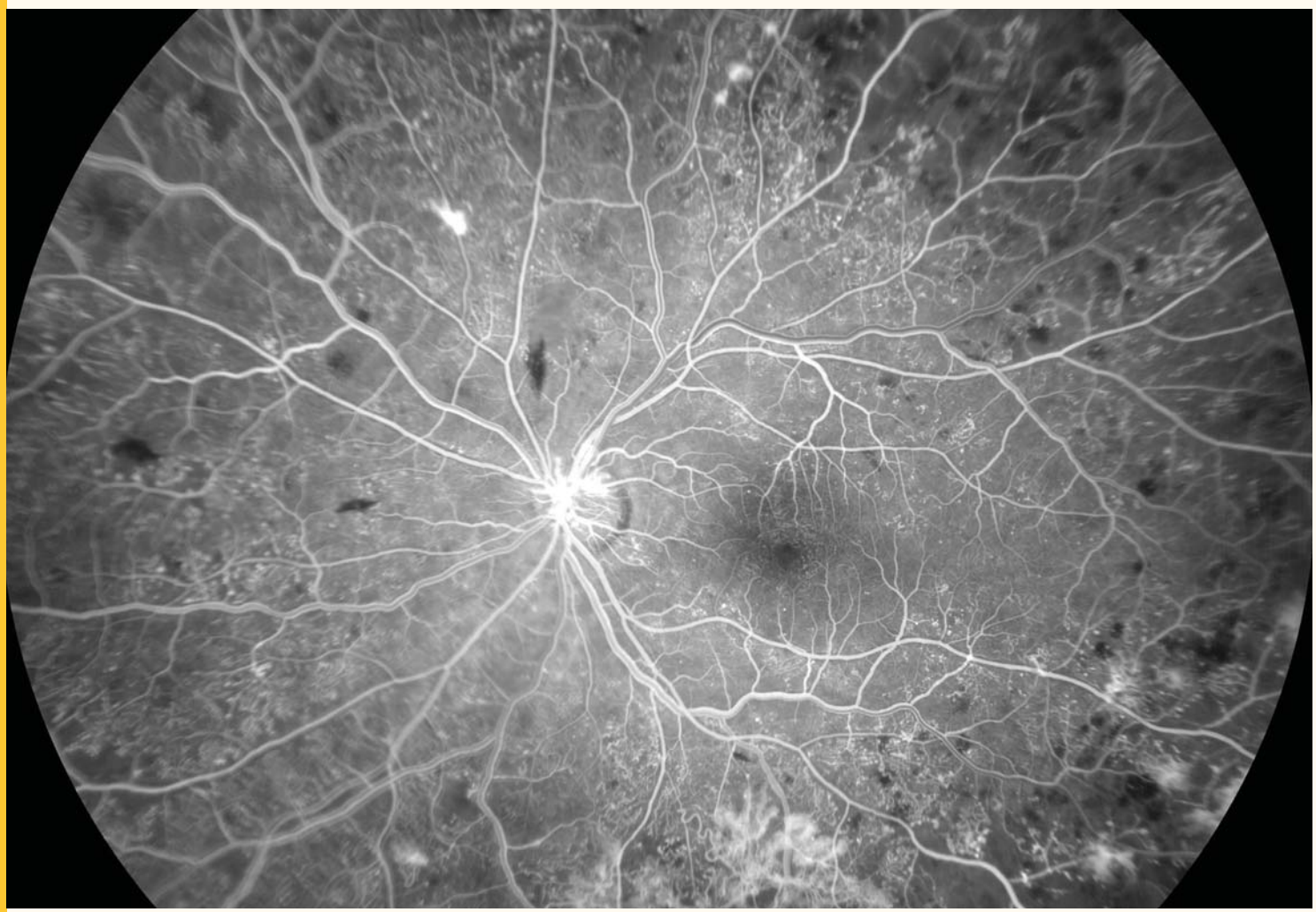

Figure 1. Widefield Fluorescein Angiography image of a central vein occlusion.

Legacy ultra-widefield retinal imaging systems require separate devices to capture images of the periphery on the one hand, and, on the other, high-definition color images of the optic nerve head. A far better option is to meld the two capabilities in a single instrument – as ZEISS has done with CLARUS 700 – so that clinicians can retrieve high-resolution pictures of the retina from macula to far periphery in one coordinated system.

True color

The CLARUS 700 is powered by Broad Line Technology: an innovative technology that illuminates only a small portion of the retina at any one time. This approach limits scatter and reflections, and thus enables the user to visualize high-resolution details over a wide field. This is not possible with classic fundus cameras, which illuminate the whole field simultaneously. Furthermore, by sequential illumination with broad spectrum red, green and blue LEDs, Broad Line Technology captures images that closely resemble fundus colors as seen under direct clinical observation, thereby facilitating diagnostic analysis.

Comprehensive capabilities

The recent addition of ultra-widefield high-resolution fluorescein angiography to the CLARUS capability set aids in visualization of vascular structures of the retina and the choroid. Fluorescein angiography may permit earlier identification of the more severe forms of diabetic retinopathy, and reveals non-proliferative diabetic retinopathy signals that may not be visible in color images. Beyond this, CLARUS 700 has a comprehensive suite of imaging modalities. These comprise of: infrared; red channel separation (reveals choroid in more detail); green channel separation (provides excellent contrast of retina, especially for vasculature and hemorrhages); blue channel separation (increases visibility of anterior retinal layer); FAF blue (helps reveal geographic atrophy); FAF green (can expose dry AMD); stereo imaging (for stereoscopic fundus evaluation); and views of the external eye. Together, these give the clinician unparalleled differential diagnosis capabilities, and may be employed together without compromising image quality.

Figure 2. True Color Montage of a central vein occlusion.

Advanced features

CLARUS 700 utilizes algorithm-based technology to take the pain out of image processing:

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In Practice

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Swimming Against the Current

The trials and tribulations of developing a cure for infectious corneal disease

By John Dart

Acanthamoeba keratitis (AK) is a rare infectious corneal disease. But although incidence is low (1 in 100,000 in the EU), it has potentially devastating consequences. In the UK keratoplasty is required in 25 percent of affected eyes (1), blindness (<3/60 acuity) results in 25 percent of eyes and no light perception or enucleation in 2 percent (2). Six to seven percent of UK contact lens users have bilateral infection (1, 3). In countries with a high prevalence of contact lens use, over 85 percent of cases of AK infection stem from wearing contacts, but it can also occur after corneal trauma, particularly in rural environments. AK is on the rise in developing economies and there is no approved drug to treat this disease. Through the systematic study of AK at Moorfields and the UCL Institute of Ophthalmology, including laboratory, epidemiological and clinical research, we have identified avoidable risk factors, developed better techniques for diagnosis, and introduced and developed a class of disinfectants – the biguanides – as topical anti-amoebic therapy.

At a Glance

- *A systematic study of Acanthamoeba keratitis (AK) has identified risks associated with contact lens hygiene, contaminated water, and swimming or showering while wearing contact lenses*
- *Introducing polyhexanide therapy has had a dramatic effect on patient outcomes*
- *Research into AK has had a profound impact on developing new guidelines and regulations for contact lenses and developing new standards of care around the world.*

Hygiene above all

We first established that an epidemic of cases of AK had developed in the UK in contact lens users in the 1990s. Users of the then newly-introduced monthly disposable contact lenses were at particular risk due to the association of these lenses with (subsequently withdrawn) chlorine-based disinfection systems (4). We subsequently showed in two national surveys of AK that the disease was up to 20 times more common in the UK than has been reported elsewhere, and that the incidence was increased in hard water areas; a previous clinical study had shown that limescale build up on domestic taps in hard water areas, harbored Acanthamoeba, probably by providing the mixed microbial microenvironment that the organism favors (3). We then demonstrated that genetically identical organisms, present in their contaminated domestic roof tank supplied water, had infected a high proportion of AK patients (5). We have shown that good contact lens hygiene practice is critical to the prevention of AK, including regular disinfection of lenses and lens case hygiene, or the use of daily disposable lenses, which eliminates the need for lens disinfection and contact lens case use. In addition to hygiene, we have identified the risks of exposure to contaminated water by showering and swimming while wearing contact lenses (3, 6). In 2018, we published an incidence and case control study which has identified a current UK outbreak and some new risk factors, including a contact lens solution containing Oxipol, which was consequently withdrawn as a result of our findings (6). This solution was the only readily modifiable risk factor identified and, since its withdrawal, the numbers of AK cases treated at Moorfields has substantially reduced.

Additionally, our research has demonstrated that diagnosis and treatment within three weeks of onset improves outcomes (7). We were also the first to investigate the value of the identification of Acanthamoeba DNA by PCR as the most sensitive and specific method for the diagnosis of AK, since confirmed by several other independent studies (8). We have also investigated the use of confocal microscopy, another widely used imaging technique for diagnosis, particularly in the USA. We performed a masked multi-observer study and measured the sensitivity and predictive value of this technique and the resulting potential for misdiagnosis (9).

Cleaning the pool

Acanthamoeba is notoriously difficult to treat; the cerebral disease has a high mortality rate. In the eye, disease persists because the cysts are resistant to most antimicrobials. When we recognized the epidemic of cases in the UK, there was little in terms of really effective treatment apart from the use of a diamidine – but resistance was high. As a result, patients needed therapeutic corneal transplant surgery but outcomes were poor with high morbidity. Responding to this serious issue, we collaborated with a protozoologist Simon Kilvington, who suggested polyhexamethylene biguanide (PHMB) – also known as polyhexanide – a swimming pool disinfectant to which the encysted form of Acanthamoeba was susceptible. In 1992, we first described the use of topical PHMB as therapy (10) and then followed this up with clinical studies that showed a dramatic and beneficial effect on outcomes (11). PHMB was rapidly taken up worldwide and is currently recommended as first-line treatment by the Centers for Disease Control and Prevention in the USA and the Royal College of Ophthalmologists in the UK (12, 13).

The success of polyhexanide as a therapy was also recognized by the award of an EU grant of more than €4 million to the Orphan Drug for Acanthamoeba Keratitis (ODAK) project in 2012 which was designed to carry out the laboratory and clinical studies required to license PHMB as a medicine. Another biguanide, chlorhexidine, has also been introduced, building on our early work. There are no other anti-amoebics available that are consistently effective against the encysted from of the organism.

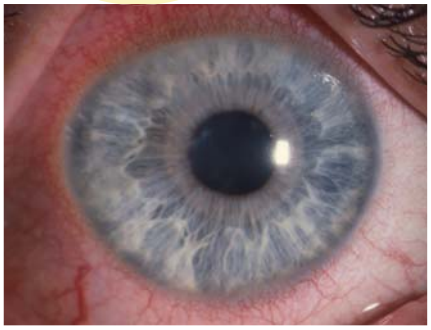
The ODAK Acanthamoeba keratitis randomized controlled treatment trial, the last package in the ODAK program of work, started at the end of 2017 and there are six sites in Europe (three in the UK, two in Italy and one in Poland). We have recruited over 100 of the 130 subjects required by the study and expect to complete recruitment at the end of 2019.

AK impact

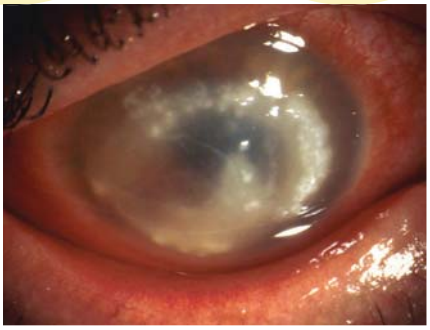
The British Contact Lens Association's Guide for Practitioners now makes several references to our research on risk factors in relation to swimming, extended-wear contact lenses and hygiene related to contact lens cases. Our work has been incorporated into contact lens packaging and led to disposable contact lens cases being supplied with bottles of contact lens solution. Our demonstration that chlorine-based solutions are not effective against AK has led to such solutions being removed from the market – both in the UK and US. PCR for diagnosis of AK is becoming widely used in routine diagnostic laboratories (14). The sensitivity of this technique is between 85 and 95 percent (culture is up to 60 percent), with 100 percent specificity. Our clinical studies have identified the importance of early diagnosis and introduction of appropriate therapy (within three weeks of onset) as the major predictor of disease outcomes, since corroborated by independent studies (15).

Biguanides (PHMB and chlorhexidine) with or without a diamidine (propamidine or hexamidine) have become the standard of care for this condition around the world (16). We have also formulated the only available guidelines both for the management of persistently culture positive cases (about 5 percent of our series) (17)

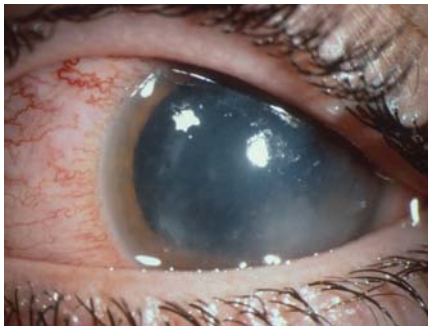
"When we recognized the epidemic of cases in the UK, there was little in terms of really effective treatment apart from the use of a diamidine – but resistance was high."



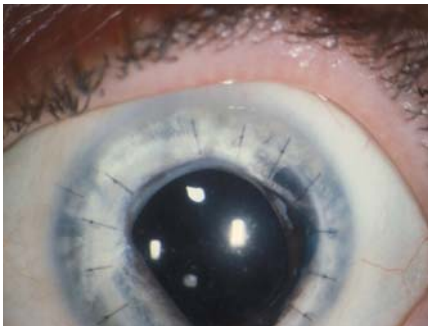
Early AK example.



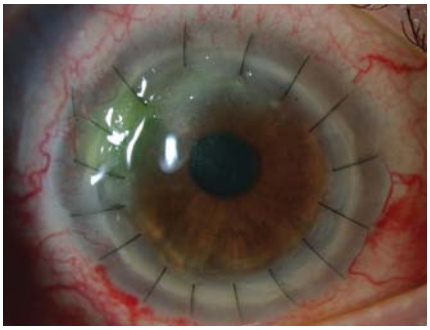
AK screlatitis pre-treatment.



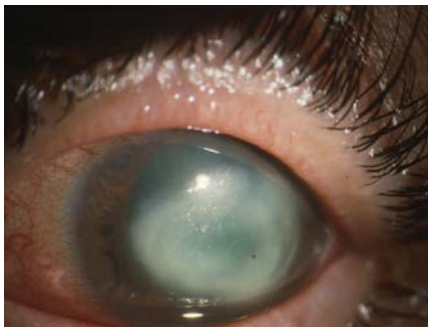
Early stromal AK.



Eye post PK.



PK recurrence.



Severe AK example.

and for the management of the severe scleral inflammation that is associated with the disease, but unrelated to direct invasion of organisms – the major reason for enucleation at our center. Here, the treatment involves the use of systemic immunosuppressive therapy and effective topical anti-amoebic therapy (18).

I am proud to say that our work over the years has had a profound impact on the prevention, diagnosis and treatment of AK today – and into the future.

John Dart is a Consultant Ophthalmic Surgeon at Moorfields Eye Hospital, London, UK.

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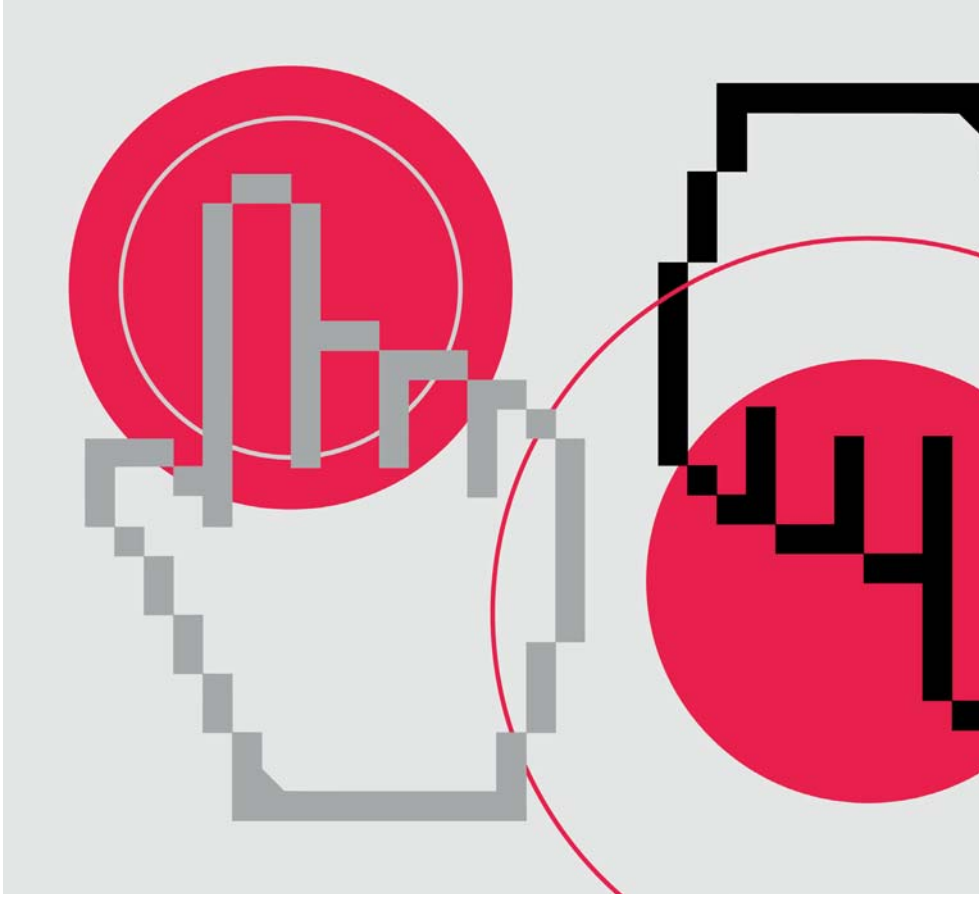
Finger on the Pulse

In favor of micropulse transscleral cyclophotocoagulation for glaucoma mild – and wild

By Nir Shoham-Hazon



As the only fellowship trained glaucoma and advanced anterior segment specialist (GAASS) in the province of New Brunswick, Canada, I see many patients who have traveled great distances to reach my practice. This scenario can create logistical challenges in following a condition that requires close monitoring, not to mention that long-term success in managing glaucoma often depends on timely escalation of therapy. Because many of my glaucoma patients are followed locally by a comprehensive ophthalmologist, there may be delays between the documentation of IOP elevation or disease progression and the patient coming back to my office for an evaluation. Even if a new intervention is performed during this follow-up, it may be some time before it effectively lowers the pressure.

An overall trend in glaucoma is the increasing popularity of procedural interventions, ranging from laser to minimally invasive surgeries. Generally speaking, this development has reduced the need to rely on patients instilling drops on a routine basis, while also offering advantages for avoiding IOP fluctuations. There are several options within the category of procedural glaucoma interventions, and some of them may be more advantageous in terms of follow-up protocols.

In my practice, the addition of the micropulse transscleral cyclophotocoagulation (MP-TSCPC) procedure with the MicroPulse P3 probe and the Cyclo G6 Glaucoma Laser (Iridex) has proven to be a safe, effective and reliable approach for lowering IOP. The vast majority of patients who travel to see me and have been treated with MP-TSCPC are able to perform their follow-up with a local comprehensive ophthalmologist, only returning to my clinic if further intervention is warranted. Because it differs from traditional cyclodestructive procedures, MP-TSCPC treatment has also proven to be a versatile option for a diverse range of patients in my practice.

From mild to wild

Cyclodestructive procedures have historically been reserved for more advanced glaucoma – most typically for refractory cases or individuals with poor visual prognosis. The classic thinking has been that because these treatments damage the secretory epithelium of the ciliary body, they should be used as a last resort to reduce aqueous production before opting for incisional drainage procedures. The procedure with the MicroPulse P3 probe is different in this regard. As the name implies, MP-TSCPC is unlike traditional transscleral cyclophotocoagulation, which is performed with a continuous wave laser. MP-TSCPC uses energy that is delivered using a 31.3

At a Glance

- *Micropulse transscleral cyclophotocoagulation (MP-TSCPC) has proven to be a safe, effective and reliable approach for lowering IOP*
- *Unlike other interventions, MP-TSCPC delivers energy in a 31.3 percent duty cycle, allowing tissue to cool between each application, so there is minimal impact on target tissue and a reduced risk of injury to adjacent ocular tissue*
- *MP-TSCPC can be used early in the disease course and requires minimal medication, reducing the reliance on anti-inflammatory drops post-procedure*
- *It can also be used on a wide range of glaucoma severity, not just those in the most advanced stages of disease progression.*

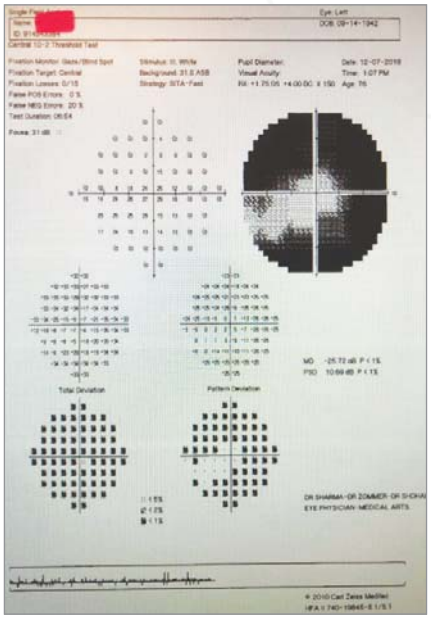


Figure 1. Left eye visual field. 10-2 central field, depicting advanced glaucoma stage.

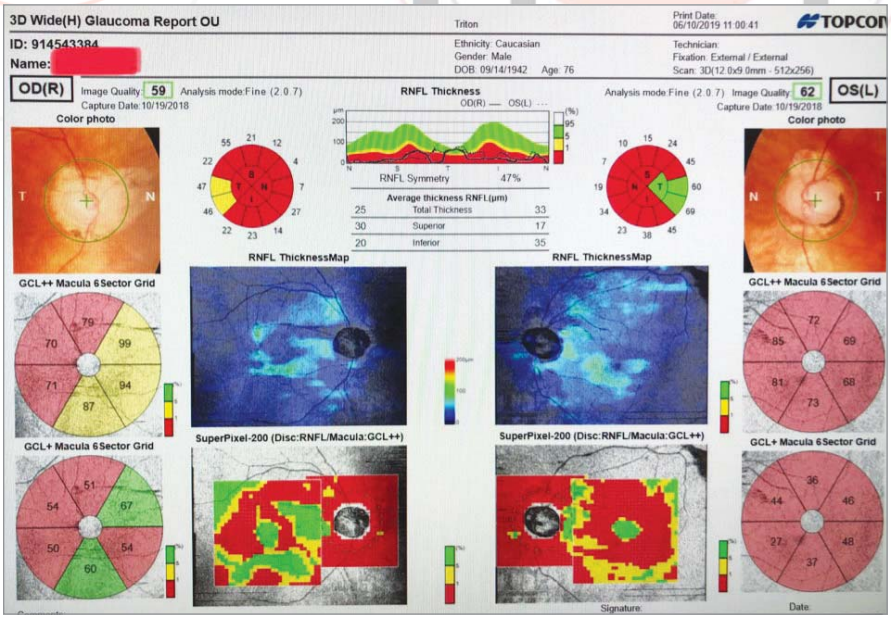


Figure 2. Glaucoma report of OCT - depicting severe thinning of the RNFL as well as advanced ganglion cell layer loss.

percent duty cycle (0.5 milliseconds on, 1.1 milliseconds off), thereby allowing the tissue to cool between each application. As a result, there is minimal impact on target tissue and a reduced risk of injury to adjacent ocular tissue. Because there is no remnant scarring, MP-TSCPC is also repeatable if the target pressure is not achieved after the first application.

In various clinical trials, MP-TSCPC has been shown to achieve up to 30 percent reduction in IOP with reduction of an average of one medication (1, 2, 3, 4). Interestingly, most of the current literature with this modality is in patients with relatively high baseline IOP, suggesting enrolled patients had more severe glaucoma at the time of treatment. Though cyclophotocoagulation reduces production of aqueous humor, there is a possibility that MP-TSCPC may also increase uveoscleral outflow. With this is mind, MP-TSCPC could be an option for a wider range of patients than has been suggested in studies. Personally, I have used MP-TSCPC on patients with what I would call mild to wild glaucoma – and for good reason. It is safe and effective without yielding major impact on the target tissue, and it's repeatable if necessary. It makes as much sense for a patient on two to three drops with uncontrolled pressure or those who cannot manage drop therapy but who are not yet indicated for frank glaucoma surgery (penetrating filtration surgery or MIGS) as it does for those patients with neovascular glaucoma. With regard to patients who travel to see me, I have found that I can intervene early in the disease course with MP-TSCPC to get the pressure under control, and then have them followed locally with low medication requirement, reducing the reliance on anti-inflammatory drops post-procedure.

I learned an interesting lesson with my first few cases of MP-TSCPC. Initially, I would prescribe a steroid and a nonsteroidal anti-inflammatory, and ask patients to return in two weeks – which is what I would have done had the treatment been performed with a continuous wave laser. Despite some of these patients not using their drops, I found no signs of active inflammation when I saw them again. As a result, I now only rarely use an anti-inflammatory protocol after a MP-TSCPC treatment, and plan for the first follow up at five or six weeks. This significant change has had a positive impact on my patients' daily lives, particularly for those who have to travel long distances to see me.

Shifting the paradigm

Achieving and maintaining the target pressure is the primary objective of treating glaucoma. In the past, adding drops or escalating to surgery were the best options for patients who were out of range. Fortunately, we now have a variety of procedural options that allow us to achieve that goal while also considering quality of life factors, such as the convenience of the treatment and follow-up protocol. As a result, the treatment paradigm for glaucoma has slowly shifted to the point where we can now safely and effectively intervene at earlier stages, with implications for achieving the target pressure sooner while delaying the need for more invasive approaches. Though there are many options

for doing so, the unique manner in which laser energy is delivered with the MP-TSCPC procedure results in relatively little destructive effect to the ciliary processes and surrounding tissue, in turn yielding a safe and effective procedure with little post-procedure inflammation. Because of these characteristics, it is widely applicable across a range of glaucoma severity – from mild to wild.

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He reports the following financial disclosures: Allergan, Bayer, IOPtima, Iridex, Novartis, Neomedix.

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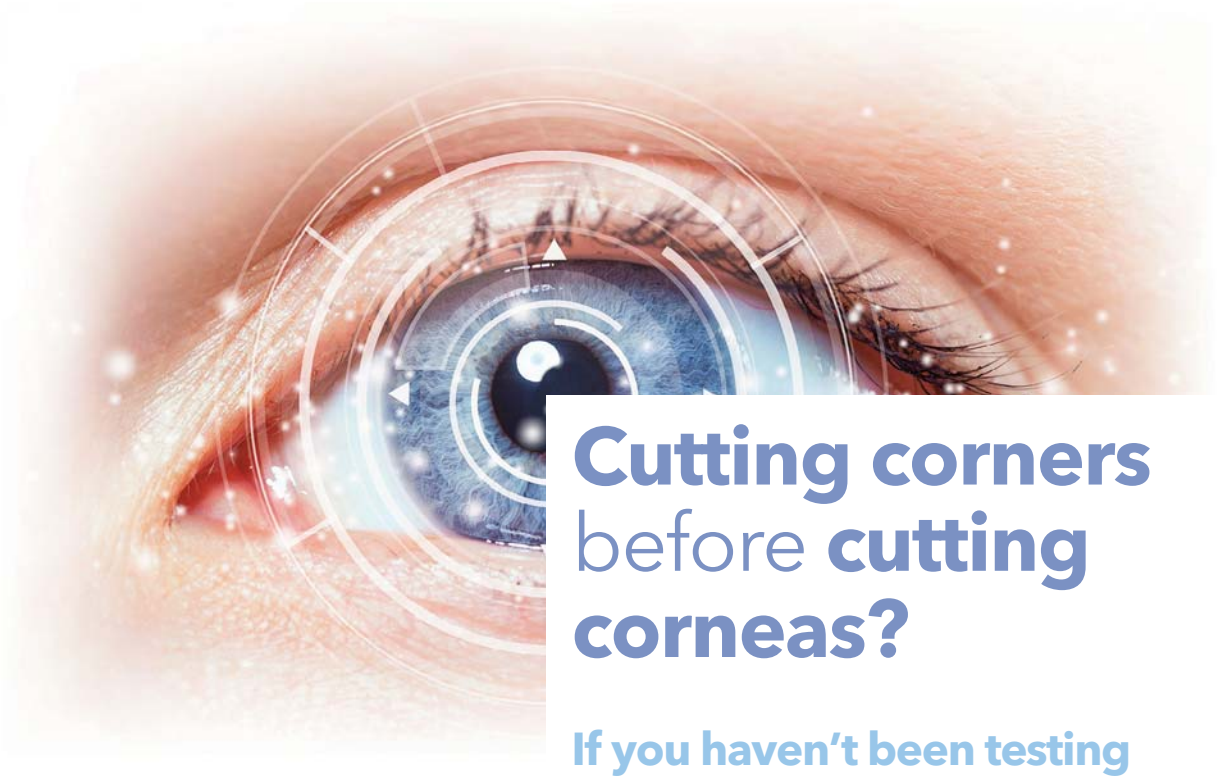
Figure 3. Nir Shoham-Hazon performing MicroPulse on a patient.

Case example

A recent case of a 76-year-old man with advanced primary open-angle glaucoma (Figures 1 and 2) demonstrated the benefits of MP-TSCPC. In addition to an eye condition, the patient was in poor health, which presented a challenge when it came to frequent monitoring examinations. His ocular history included a previous trabeculectomy and, at the time of the visit, his IOP was 20 mm Hg, which was above his target pressure. He stated he was having difficulty tolerating his ocular medications. The patient was on a combination drop (beta-blocker and carbonic anhydrase inhibitor) taken twice daily and a prostaglandin analogue at bedtime. Due to his overall medical condition and extent of his disease (remaining 5 degrees of fixation on visual field), I determined that the patient was not a good candidate for frank filtration surgery and that additional medications would not be helpful. The decision was made to offer MP-TSCPC using the MicroPulse P3 probe and the Cyclo G6 Glaucoma Laser (Iridex). After a single treatment, pressure was lowered to 11 mm Hg. When we saw him next, I was able to stop one of his bottles and he has maintained the target IOP with a stable visual field for over one year.

Why use MP-TSCPC for this patient? First, there was a need to quickly gain control of the pressure and typically patients have a rapid response to MP-TSCPC. I usually do not alter the settings on the unit (2000 mw, five passes per hemisphere, 80 seconds); in cases where I want to achieve a little more pressure lowering – especially in treatment enhancements – I start treatment in the inferior hemisphere, move to the superior and then re-treat the inferior a second time. This process allows me to titrate the treatment without adjusting the settings. The second reason is that the previous trabeculectomy, as well as his frail health, limited the viability of performing a surgery. Needling this filter ran the risk of destabilizing the IOP in a fragile nerve, while longstanding hypotony or IOP elevation might snuff out his optic nerve completely. Moreover, additional medications would likely be unsuccessful if his current regimen was already problematic. Thus, the non-incisional, minimally invasive nature of MP-TSCPC represented a more favorable approach.



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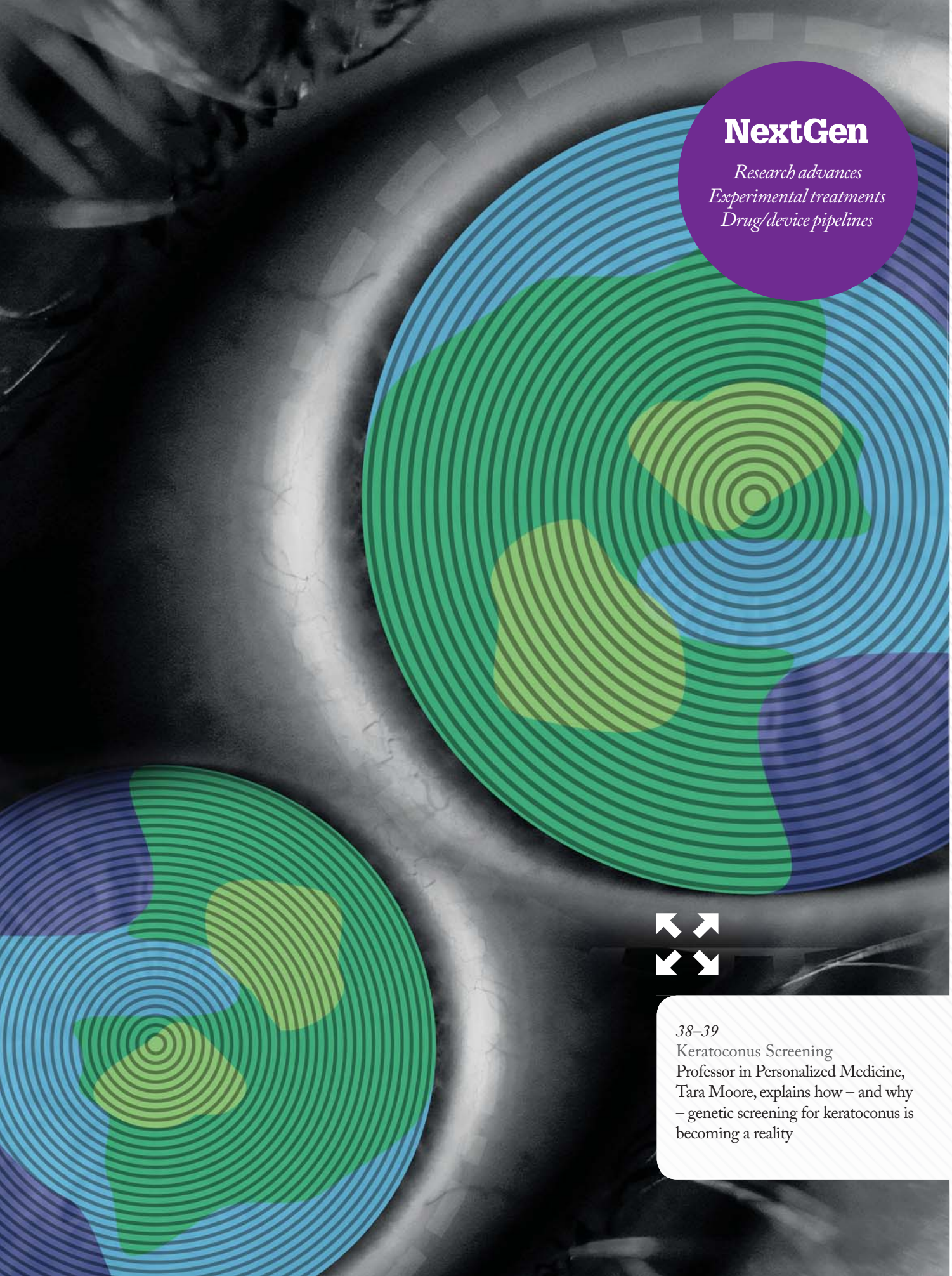


NextGen

Research advances
Experimental treatments
Drug/device pipelines

Keratoconus Screening

Genetic screening for keratoconus is becoming a reality

By Tara Moore

Eyes may appear perfectly normal, yet be predisposed to serious conditions – some of which can be triggered by medical intervention. It follows that the ability to screen for such predispositions would be very useful, particularly where elective surgery is being proposed. Keratoconus (KC) is a classic example – if you are offering a patient refractive surgery to achieve spectacle-free vision, you want to be certain that the eye is not predisposed to KC. Also, if you are looking for early indicators where family history exists, or in patients with corneas with high dioptric values or astigmatism, you want to be able to catch them as early as possible. But is KC screening a realistic option?

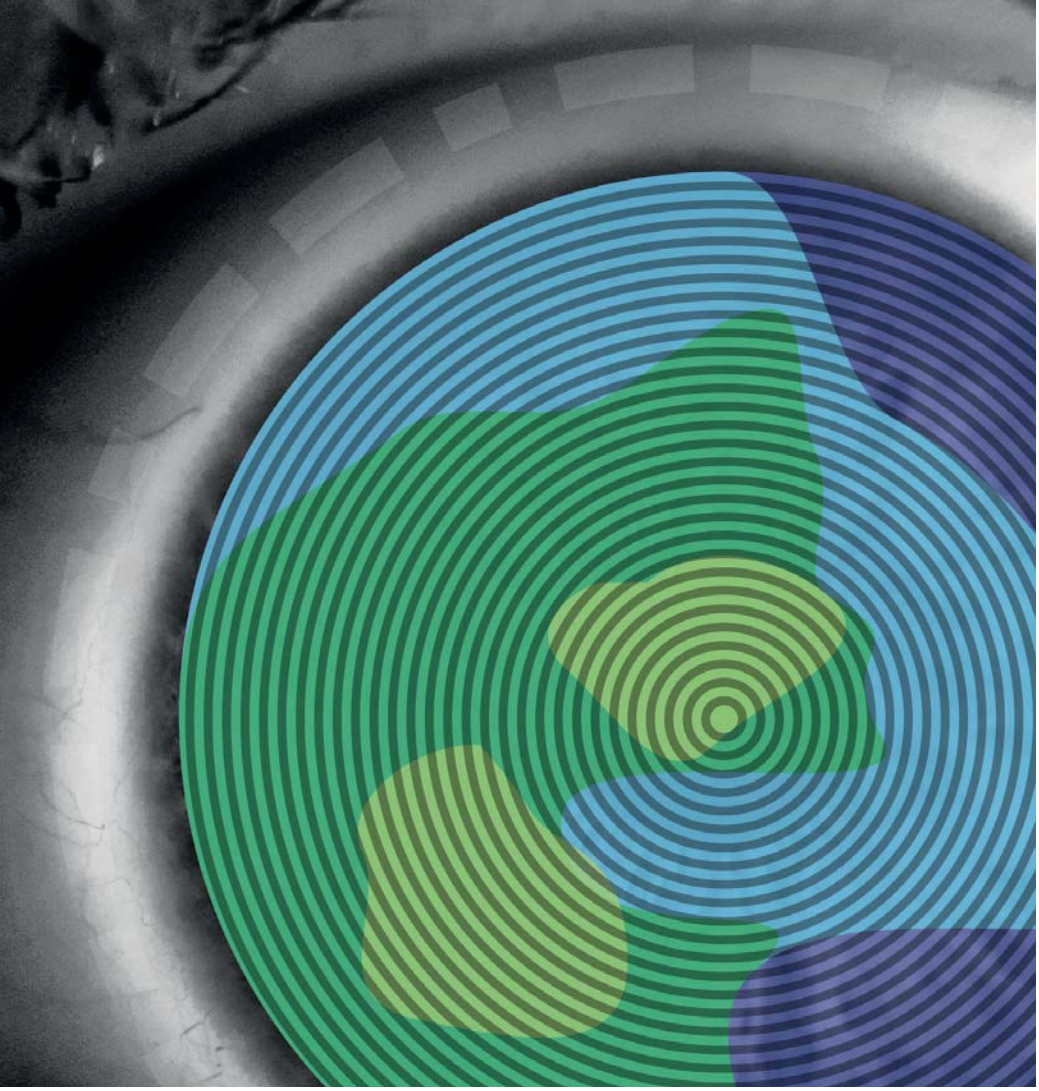
At a Glance

- *Surgeons planning refractive surgery should be certain that the patient does not have a predisposition to keratoconus*
- *Genetic testing for corneal dystrophy is widespread, but keratoconus is a much more complex condition*
- *The research into keratoconus genetic screening is promising, and data will become more precise as more information is included*
- *The ultimate goal is to develop a test available for every potential keratoconus patient, which will become an inexpensive industry standard.*

Important considerations

To answer that question, we can look at some other disorders where genetic screening is now the norm. Corneal dystrophy, like KC, can be triggered by refractive surgery or injury to the cornea; unlike KC, however, genetic testing for corneal dystrophy is increasingly widespread. This is because corneal dystrophy is a well-characterized monogenic inherited disorder, and screening is therefore very simple: we know that if the patient has no keratoepithelin mutations, we can safely proceed with the surgery. But KC is far more complex than corneal dystrophy; can we develop a useful screen for this condition? I think we can; consider, for example, breast cancer, the genetic complexity of which is not dissimilar to that of KC. We know that mutations in the BRCA gene are strongly associated with an increased risk of breast cancer. It is also true, however, that not all breast cancers have a known genetic etiology, and only some of those that do will fall into the BRCA camp. Nevertheless, BRCA screening is useful to guide treatment choices in breast cancer management.

Given the above, it doesn't seem unreasonable to expect that we will get to a similar position with genetic screening for KC, and we are certainly actively working towards that goal. The research is still at an early stage, but it is promising – we've already found over 300 variants within 75 genes that are strongly associated with KC. The data will only get better as we look at more and larger populations of KC patient DNA, and as we add hundreds of genes – and thousands of mutations – to our screening panels. It is particularly important to include, as we are doing, a broad range of ethnicities in this work,



because our experience is that the genes and mutations most commonly implicated in KC differ from population to population. This kind of information is very important for us at Avellino Labs – if we're going to develop a genetic test to be used in a given geographical area, we need to be sure that it will catch the mutations typical of the people in that area.

Looking to the future

Our long-term goal is to develop a product that could be used to screen every patient potentially at risk for developing KC, where there is a genetic component to their disease manifestation. Testing could include those with family history, contact lens or refractive surgery candidates, and those patients with corneal shapes that are steep or questionable upon exam, especially those for whom KC diagnosis is equivocal. Of course, providing a universal KC test at a price that is both commercially viable and acceptable to the market will require economies of scale – and that is what we are working towards. We want the test to become a standard that physicians agree upon, and not be prohibitively expensive. Genetic testing has not had consistent success in the eye care industry, but to get an idea of the likely adoption pattern of a KC test, we should look to the uptake of the genetic test for corneal dystrophy test. At first, many surgeons were resistant to the product; they would claim, for example, that they didn't need a genetic test for the corneal dystrophy because they "know it when they see it." But now, as more physicians are seeing patients with the disease, they're increasingly accepting that actually it's better to confirm than not, especially as the patients themselves are more aware of availability of genetic testing. Patient health and safety are always the primary concern, but as genetic testing for conditions becomes more mainstream for all areas of healthcare, screening will eventually help reduce litigation risks.

Today, our focus is on the benefits to the patient. A genetic screening test allows early identification of at-risk patients, which empowers both the physician and the patient with information, allowing better treatment decisions, avoiding the more complex KC procedures – transplantations and so forth – by choosing specific vision correction procedures or getting the patient into a monitoring program and using treatments like cross-linking. Even simple lifestyle changes, like actively managing inflammation and making the patient aware of the dangers of eye rubbing, can help reduce progression in patients.

Mainly due to an increased awareness of the prevalence of KC in the world, we expect to see a much faster uptake for the KC test than what we saw for the corneal dystrophy test. In fact, it's difficult to find reasons not to apply a KC genetic test.

Our genetic test will screen for particular KC-associated genes and mutations that are specifically associated with KC. As with any genetic test, physicians and patients need to work together with a genetic counsellor to understand the implications of the data that is being provided, and how it may change over time. Overall, the advancement of precision medicine and use of Artificial Intelligence tools in eye care is something to be excited about, and as physicians use them more in their practice they will become more comfortable having these types of discussions with patients. Ultimately, that will mean better care through earlier detection of at-risk patients, due to errors they carry in their DNA, which I know physicians are excited about.

Tara Moore is Professor of Personalized Medicine, Ulster University, Northern Ireland, UK and Chief R&D Officer, Avellino Labs, San Francisco, USA.

* Not commercially available yet

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The Business of Innovation

Ahead of the Ophthalmology Innovation Summit 2019 at AAO, we dig into market trends and the latest advances

By bringing together clinical, capital and corporate leaders – all key stakeholders in the development and commercialization of novel technologies and therapies – the Ophthalmology Innovation Summit (OIS) has a clear objective: to act as an innovation accelerant, helping convert conceptual sparks into glowing success.

The brainchild of ophthalmologist and venture capitalist Emmett Cunningham (Blackstone Life Sciences) and experienced conference producer Craig Simak, OIS fully sprang into life when two further venture capitalists – William Link of Versant Ventures/Flying L Partners and ophthalmologist Gil Kliman of InterWest Partners – came on board to co-chair the initial programs. OIS had found a recipe for success.

The flagship "OIS@AAO" began in 2009 and – a decade on – will attract 1,200 leaders in ophthalmology with the common goal of addressing unmet vision needs. For 2019, the full-day (6:45am–6:30pm) program on October 10 covers everything from the game-changing technologies of today and tomorrow, to opportunities and challenges for healthcare leaders, to markets updates – not to mention a "Keynote Conversation" between Alex Gorsky, Chairman & CEO of Johnson & Johnson, and summit co-chair Link.

Here, we ask seasoned OIS experts to get us up to speed for OIS@AAO with notable approvals, business trends, and a glimpse of how the innovators of the future are being forged.

FDA CDER Update: The Latest Approvals

By Gary Novack, PharmaLogic Development

Over the last six months, only four products were approved (see Table 1). And though none were new chemical entities in the USA, they do represent new therapeutic options for American patients and eye care specialists. There are relatively few fixed-dose combinations available in the USA to lower intraocular pressure, and thus the Rocklatan approval represents a regulatory milestone.

Drug name	*Registered Name – NDA/BLA*	*Indication*	*Company*	*Date Granted*
Loteprednol etabonate	LotemaxSM	0.38% in new formulation to treat post-operative inflammation and pain following ocular surgery	Bausch + Lomb	Feb 22, 2019
Tetracaine	Tetracaine	Local anesthesia	Bausch + Lomb	Mar 12, 2019
Netarsudil/ Latanoprost	Rocklatan	Fixed dose combination to reduce intraocular pressure in glaucoma and ocular hypertension	Aerie	Mar 12, 2019
Acyclovir	Avaclyr	Topical formulation for treatment of acute herpetic keratitis (dendritic ulcers) in patients with herpes simplex (HSV-1 and HSV-2) virus.	Fera	Mar 29, 2019

Table 1. Original NDA/BLA approvals, listed in order of approval from February 1, 2019 through August 31, 2019. Center for Drug Evaluation and Research, Office of New Drugs, Division of Transplant and Ophthalmic Products.

OIS Index Update

By Michael Lachman, EyeQ Research

The OIS Index of ophthalmic stocks turned in a flat performance over the six months between March 1 and September 1, 2019, outperforming the NASDAQ Biotechnology Index (-8.7 percent) but lagging an index of medical device stocks (+10.2 percent) and the overall US stock market (+4.0 percent).

Despite the flat six-month performance overall, declining stocks in the OIS Index outnumbered advancing stocks by a 2-to-1 margin. It was a particularly challenging period for small cap ophthalmic stocks. Among the 19 companies in the index with market capitalizations below $300 million as of July 1, 14 stocks declined by 20 percent or more, including nine stocks that declined by at least 40 percent.

OIS Index September 1, 2019

1,046.33

Index Performance (% Chg.)	3 Months	6 Months	1 Year
OIS Index (OIS)	**0.9%**	**-0.2%**	**-10.5%**
NASDAQ Biotechnology Index (NBI)	3.0%	-8.7%	-15.8%
US Medical Device Index (IHI)	13.0%	10.2%	13.4%
US Market: Russell 3000 (R3000)	5.9%	4.0%	-0.6%

Powered by EyeQ Reseach

Figure 1. OIS Index Performance Table.

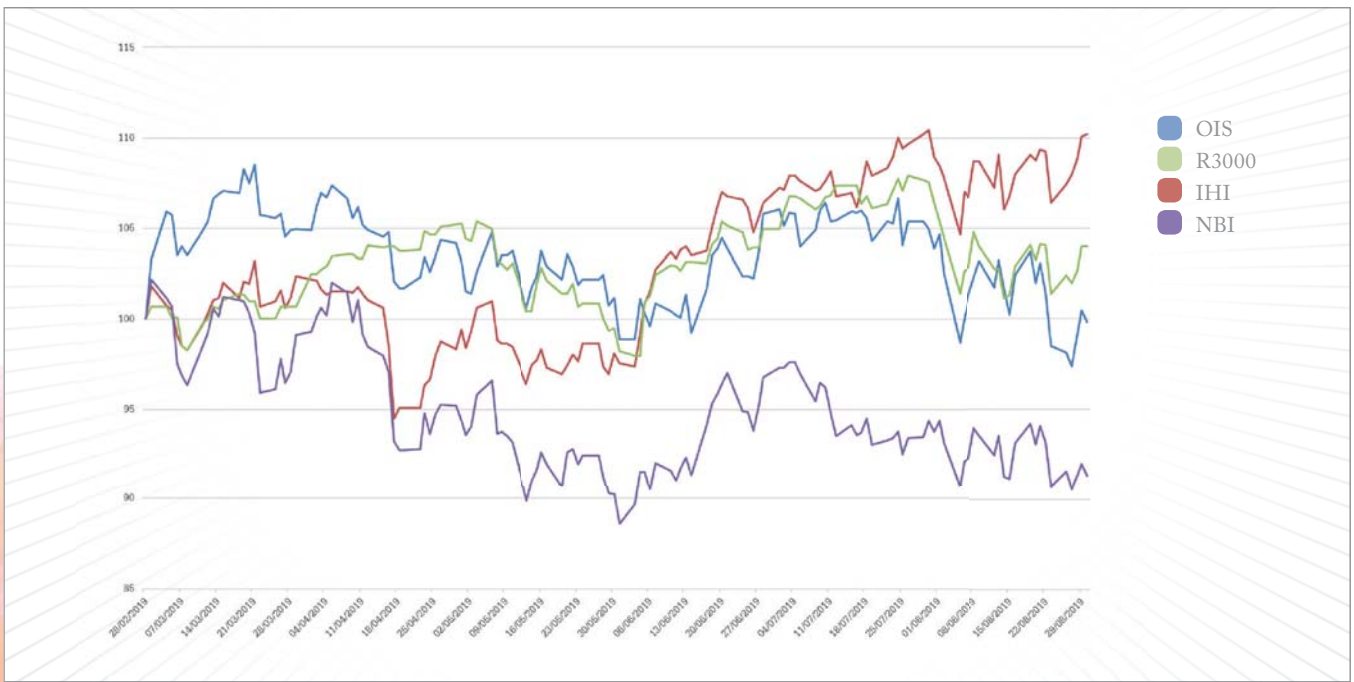

Figure 2. OIS Index: Six-month performance.

OIS six-month market movers

Opthea +356 percent on positive clinical data from the company's Phase 2b wet AMD trial

Adverum Biotechnologies +155 percent on progress in the company's Phase 1 wet AMD gene therapy trial

Avedro +95 percent on positive operating results and an announced acquisition by Glaukos

Apellis Pharmaceuticals +92 percent on progress in Phase 3 geographic atrophy trials and in non-ophthalmic programs

Carl Zeiss Meditec +41 percent on strong financial reports and raised revenue and earnings expectations

Aerie Pharmaceuticals -54 percent following the stock's strong run-up in advance of Rocklatan FDA approval

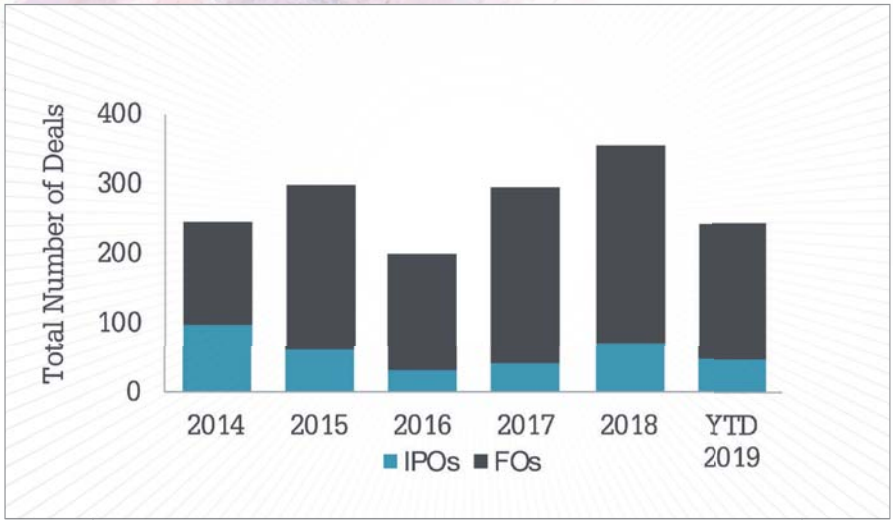

Figure 3. Life science equity financings.

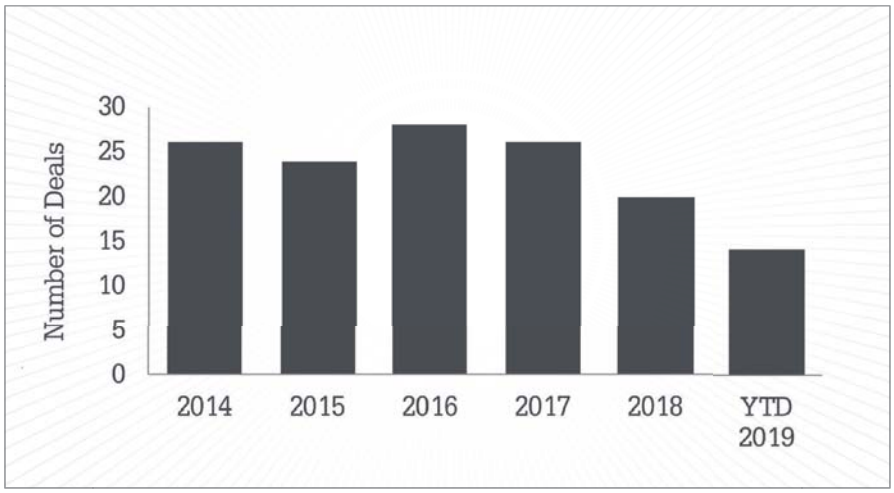

Figure 4. Public company life science M&A.

Date	*Deal type*	*Target*	*Counterparty*	*Deal value ($M)*
Apr 2019	Spinoff / IPO	Alcon	Novartis	28,000*
May 2019	M&A	Xiidra	Novartis	5,300
June 2019	M&A	Allergan	Abbvie	63,000
Aug 2019	M&A	Avedro	Glaukos	500

Table 2. Recent ophthalmology transactions.

**Market capitalization as of 4/9/2019 (the first day of trading following their spinout of Novartis)*

Source: Piper Jaffray Equity Capital Markets, Company Filings, FactSet. Data as of 9/10/2019.

Public Markets Update

By Udit Patel, Piper Jaffray

Life science overview

- The year 2019 is on pace for a record number of financings, with 48 initial public offerings (IPO) and 196 follow-ons (FO) completed to date raising a total of $28B (see Figure 3).
- IPOs have performed well, up 17 percent on average.
- Approximately $300M of equity financing has been raised for ophthalmology companies in 2019 YTD, across 1 IPO and 4 FOs.
- Acquirers continue to favor commercial stage targets, which account for 10 out of the 14 public acquisitions in 2019 (see Figure 4).
- Ophthalmology's landscape continues to shift with Shire/Takeda exiting the space, the Alcon spin out, and now the acquisition of Allergan (see Table 2).

FDA CDRH Update

The Ophthalmology Innovation Fellowship: How Stanford University and CDRH are partnering to deliver the next wave of innovators

Lee Kramm (ClinReg Consulting Services) interviews 2018–2019 fellow Frank Brodie, Vitreoretinal Fellow, Department of Ophthalmology, Duke University

What led you to apply for Stanford's Ophthalmology Innovation Fellowship?
Something that I enjoyed during my residency at UCSF was trying to find solutions for problems I encountered in clinic. I developed a wearable position tracker and alarm for patients who had to position after retinal surgery, a method for developing custom glasses for children with craniosynostosis, and an approach to stimulate the retina through a congenital cataract in hopes of forestalling amblyopia.

The Stanford Ophthalmology department has an impressive reputation for devising and developing new technologies and bringing them all the way to clinical care. Mark Blumenkranz personally has an incredible track record in this respect. I had gotten to meet him a few times and, in addition to being a fantastic clinical teacher, he's known for being a terrific mentor, so this was a significant draw. Additionally, being part of the Stanford community was an exciting prospect as innovation seems to be in the DNA across the campus and the program allows for the flexibility to engage in outside classes and research. Finally – and very importantly – the program offers the unique opportunity to work with the FDA on a variety of projects and provides an in-depth education on the regulatory process.

Which subjects are covered?

The fellowship focuses on how to take an idea, develop and test prototypes, assess commercial viability, and understand and plan the regulatory pathway. You meet regularly with David Myung and Blumenkranz, who provide insight and mentorship. Additionally, they each have deep and broad connections in the scientific and medical device communities, so you can meet, get advice from, and collaborate with leaders in the field throughout the year. In addition to this central project, the fellow spends considerable time at the FDA, in my case, a week in the fall, a few days in the early spring and then again at the end of the academic year. While at the FDA, you both learn general concepts of regulatory science for ophthalmic devices as well as those specific to your fellowship project. In addition, I was fortunate to be able to participate in the planning of the FDA spring workshop "Forum on Laser Based Imaging." Finally, I took the graduate level Biodesign capstone course in which we worked in teams to develop novel technologies; we had speakers across diverse backgrounds addressing topics, such as raising capital, IP strategy and clinical trials design. Overall, it was an unbelievable year that touched on nearly every aspect of medical innovation and product development in ophthalmology.

What key concepts did you take away from the fellowship regarding premarket/postmarket regulatory science while at the CDRH with Malvina Eydelman and her staff?

As a clinician we always consider the risk benefit ratio in terms of a single patient and treatment; however, I found this concept needed to be adapted to the clinical development and regulatory process as well. And that requires a determination of what features of a device pose the greatest potential risk and how we can ensure those who might be the first humans to use it potentially stand to benefit the most.

I also gained an appreciation for how clarity and specificity on the label for a device are paramount. It is the lens through which an entire FDA submission is viewed, so clearly defining the population and for what condition the device is intended is critical in developing a regulatory plan.

What did you find most surprising about FDA's regulation of medical devices?

I was impressed and grateful, as a user of these devices, for the incredible rigor of preclinical testing that devices undergo prior to first in-human trials. Though many of these tests are standardized for certain devices, such as IOLs, I also admired the flexibility to adapt tests and development of new ones to fit specific product attributes that might be novel.

What positives (or negatives) did you observe?

I was incredibly impressed by the team at the FDA. They were not only deeply knowledgeable within their fields, but eager to find and support products that could help patients. They were motivated to work with applicants in developing a path forward for their products. Additionally, because they have seen such a huge number of products and clinical data, though they cannot specifically reference specific files in leveraging historical experience, any advice they give comes from it.

In clinical practice, we use a variety of products off-label – not in the manner they were approved by the FDA. For example, almost none of the current IOLs are approved for sulcus placement, yet three-piece lenses are routinely placed in the sulcus without complication. Unfortunately, this makes the development of products based on sulcus placement difficult to evaluate as the IOL would first need to be approved for sulcus use. The FDA is increasingly open to using real-world data; one example being the IRIS Registry by American Academy of Ophthalmology, as supporting data in regulatory evaluation, so it will be interesting to see how this comes to play with off-label use of devices.

What can the industry do better to facilitate the FDA's work?

I spent a lot of time learning about the various new programs the FDA is developing to support device innovation and expedite approvals for products. These include the Breakthrough Pathway, Early Feasibility Studies, and Humanitarian Device applications. I think these all offer tremendous opportunities for companies to engage the FDA in the development of truly novel products and advance meaningful innovation.

The pre-submission process allows any applicant to have discussions with the FDA on a broad range of topics prior to a formal submission. This incredibly valuable opportunity allows companies to understand and respond to regulatory concerns before going too far down the development and clinical trials pathway.

OIS@AAO takes place Thursday, October 10, 2019 at the Hilton San Francisco Union Square. For more information and to register, please visit ois.net/ois-aao-2019

Residency to Retirement: Part One

Key financial success factors for ophthalmologists at every career stage... starting with fellowships

By David B. Mandell and Carole C. Foos

In writing this two-part article, we faced a significant challenge: how to select a handful of key success factors to building and protecting an ophthalmologist's finances. As advisors to physicians for decades, we know that there are many other important planning areas, including retirement modeling, asset protection and estate planning, that we simply did not have the space to discuss. In this article, we will focus on selected topics for young physicians, namely managing student loan debt, protecting a multi-million-dollar asset and beginning a financial plan.

At a Glance

- *Rising education costs mean it is not unusual for young ophthalmologists to begin their careers with six-figure debt*
- *There are three things residents can do for a more financially secure future: manage student loan debt, protect a multi-million-dollar asset and begin a financial plan*
- *Physicians in their early career can reduce tax by maximizing contributions to qualified retirement plans and considering non-qualified plans (if they work in private practice) and using both pre-tax qualified retirement plans and after-tax IRAs (if they are employed)*
- *It is also useful to employ a financial advisor to avoid any potential pitfalls and secure the best chance of a comfortable retirement.*

1. Residency and fellowship

Manage Student Loan Debt

Given the rising costs of medical education and the expenses of living during residency and fellowship, it is not unusual for young ophthalmologists to be staring at six-figure debt loads as they embark on their careers. Unless addressed properly, such debt burdens may dramatically affect real savings, retirement planning and even credit worthiness later in life.

Try to Avoid Capitalization

Although sometimes unavoidable, student loan costs typically balloon the highest during residency due to a process called capitalization; the addition of unpaid interest to the principal balance of your loan. The principal balance of a loan increases when payments are postponed during periods of deferment or forbearance and unpaid interest is capitalized. Sometimes, it is difficult to avoid capitalization during residency due to a high cost of living. However, if possible, paying some or all of the interest during residency will allow the young physician to significantly slow runaway capitalization of their debt burden. Income-driven repayment plans have recently become a solution for allowing repayment of student loan interest during residency with much more affordable monthly payments. One such example is the Revised Pay As You Earn (REPAYE) program offered through the Department of Education. With REPAYE, the federal government covers 50 percent of all interest above the monthly payment amount during repayment. To illustrate, a resident making $55,000 a year has a student loan of $164,000 at 6 percent interest. If the loan is deferred until completion of residency and fellowship, the monthly payment just to cover interest would be $824, under a typical 10-year repayment plan. Under REPAYE, the resident would only have to pay $300 per month while the Federal government would cover $262 of the monthly interest. Although some interest will still capitalize, the amount is much more tolerable.

"Unless addressed properly, debt burdens may dramatically affect real savings, retirement planning and even credit worthiness later in life."

Next step, refinance

One of the simplest methods for reducing the burden of student loan debt is refinancing through a private lender when starting practice. Refinancing is a relatively easy way to not only consolidate student loans into one lump sum, but also lower the interest rate considerably. Although the physician may give up certain loan protections inherent to federal student loans and income-based repayment models, the upside of refinancing is typically a dramatic reduction in student loan interest rate. It is not uncommon to see interest rates lowered by two or three percent, an amount that may significantly reduce the cost of debt over a ten-year span. For example, a $268,000 loan paid back over 10 years at 6 percent interest would require a monthly

payment of $2975.35, with $89,042 in total interest. The same loan at a 4 percent rate would cost $2713.37 per month, with $57,604 in total interest.

2. Protect a million-dollar asset

While student loans are generally a depressing topic for young ophthalmologists, the prospect of already owning a million-dollar asset is exciting, if not astonishing. Many of them, with little savings, may ask: "What million-dollar asset? I am in severe debt!" The answer is that they have actually built a significant asset that needs protecting – the value of their future incomes. It should not be surprising that the present value of an ophthalmologist's future income is substantial. Let's assume that an ophthalmologist is offered a starting salary of $300,000, including benefits. Assuming this physician plans on practicing for 30 years (and 3.5 percent inflation), the present value of this annual income is $5,517,613, even if that doctor never makes more than $300,000 per year, including inflation. Most people would think an asset this valuable is worth protecting.

The Need for Disability Insurance

Disability income insurance is essential for two reasons. One, because of the physical nature of their work, ophthalmologists who perform surgeries and other procedures have a relatively higher risk of disability than other professionals like attorneys or CPAs; and two, the disability of the physician income-earner can be more financially devastating to a family than premature death. In the case of death, the deceased earner is no longer an expense to the family. Yet, if the breadwinner suddenly becomes disabled, he or she still needs to be fed, clothed and cared for by medical professionals or family members. Thus, with a disability, income is reduced or eliminated and expenses increase. And that is why disability income insurance is so important – and is the number one tool for young ophthalmologists to implement. Further, young ophthalmologists with financial dependents – typically, children, spouses or other family members – need to focus on protecting their future income value, not only against disability, but also against death. For this reason, life insurance is the second most important tool we recommend for young physicians.

3. Begin a financial plan

Student loan repayment tactics and disability and life insurance are simple tools. While implementing them independently can be effective, it is best to create a longer-term financial plan that considers these two areas and several others, including tax reduction, retirement planning, education planning and budgeting. Within a multidisciplinary financial plan, different tools and tactics fit together in a holistic manner and encourage the physician to visualize long-term financial goals. This focus is crucial because it provides motivation for systematic saving, allowing the young ophthalmologist to capitalize on the powerful benefits of compounding interest. As Albert Einstein said: "Compound interest is the eighth

wonder of the world. He who understands it, earns it; he who doesn't, pays it."

Early Career

Implement tax-reduction tactics, choose an investment advisor wisely

The following two key success factors are applicable to all physicians, but it behooves every young ophthalmologist to focus on them early in their careers.

Tactics to reduce taxes for ophthalmologists in private practice

1. *Maximize contributions to qualified retirement plans ("QRPs").* A QRP for a private practice may be in the form of a defined benefit plan, profit sharing plan, money purchase plan or 401(k). Properly structured plans offer a variety of benefits: tax deductions for contributions to a traditional QRP, tax-deferred growth of funds within the QRP and (if non-owner employees participate) the funds within a QRP enjoy superior asset protection.
2. *Consider non-qualified plans ("Non-Q Plans").* Many private practice physicians want to save significantly for retirement but are limited by the funding rules of QRPs and the employee costs. Non-qualified plans can be the solution for many doctors. Because these plans are not subject to QRP rules, Non-Q Plans do not have to be offered to any employees. Further, even among the physician-owners, there is total flexibility. For example, one doctor can contribute a maximum amount, the next partner could contribute much less, and a third physician could opt out completely. The main drawback to Non-Q Plans is that contributions are not tax deductible. However, they can be structured for tax-free growth and tax-free access in retirement, like a Roth IRA. In fact, a Non-Q Plan can be an ideal long-term tax hedge against a QRP.

Tactics to Reduce Taxes for Employed Ophthalmologists

1. *Maximize contributions to employer's QRP.* Physicians who are W-2 employees can often participate in their employer's QRP, which allows them to defer income by contributing to the plan. As employees themselves, these physicians are not negatively impacted by the costs for employees, as are owners in private practices. Further, they may receive some type of contribution match from their employer, making the plan even more attractive.
2. *Use after-tax IRAs, when possible.* Under the 2019 limits, doctors can defer up to $6,000 per year ($7,000 per year if they are 50 or older) into a traditional IRA. Ophthalmologists who are not covered by a workplace retirement plan may deduct pretax contributions; those who are can make non-deductible or partially deductible contributions (depending on their earned income and filing status). While Roth IRA contribution limits are the same as traditional IRA limits, most ophthalmologists earn income that exceeds the adjusted gross income limits for Roth IRAs and are therefore not allowed to contribute directly to a Roth IRA. Doctors can often implement a "backdoor Roth IRA" by contributing to a traditional IRA and then converting the traditional IRA to a Roth IRA. (Note: This tactic requires careful planning to avoid unnecessary taxation. The help of an experienced advisor is crucial.) Roth IRAs can be very beneficial to long-term retirement planning because funds in a Roth IRA grow tax free and can be withdrawn tax free during retirement.
3. *Use life insurance as a retirement plan, when appropriate.* As above, Roth IRA contributions are after-tax, but the balance grows tax-free and can be accessed tax-free in the future. Many physicians are surprised to learn that, if managed properly, a permanent life insurance policy behaves the same way. "Permanent" life insurance includes whole life, universal life,

variable life and equity-indexed life insurance policies. Regardless of the product type, the cash value of such policies grows tax free and can be accessed tax free during the insured's life – a tax treatment that has remained stable for over 100 years. For many ophthalmologists, this type of tax planning tool makes sense in their overall financial plan.

Choose an investment advisor wisely

All physicians, including ophthalmologists, want to invest well for their retirement and avoid potential pitfalls. However, the topic of investing (in general) and working with financial advisors (specifically) is a complex one. One fundamental question for an ophthalmologist to ask: does a particular investment professional, or do they not, owe the physician-investor a fiduciary duty? If they do, this factor alone does not guarantee the achievement of one's investment goals. But, if they do not, the advisor is simply not required to work in the doctor's best interests. Despite this simple fact, the unfortunate truth is that many ophthalmologists work with financial professionals who can legally put their own interests above their physician clients. Here are two key questions that physicians should ask a prospective or current financial advisor to determine where they stand on this fundamental issue:

Question #1. As an advisor, do you owe me a fiduciary duty as a client, or are you held only to a "suitability" standard?

Per above, this may be the most important question of all. For those not in the industry, this may seem like a subtle difference; however, the result can have a substantial impact on the client.

Example: Client A contacts his broker and expresses an interest in investing $50,000 in US growth stocks. The broker invests the client assets in Fund XYZ, which charges a sales load of 5.75 percent with operating expenses of 0.68 percent annually. The client will immediately pay a one-time fee of $2875 on the trade on top of the recurring fund-management fee. In this case, the suitability standard has been met. Client B contacts his Registered Investment Advisor (RIA) with the same request. The investment advisor purchases an exchange-traded fund (ETF) with a gross expense ratio of 0.18 percent and pays a commission of $8.95 on the trade. This client pays his RIA a management fee of 1 percent of the assets, which equates to $500 per year on $50,000. The advisor has met the fiduciary standard. In our very realistic example, the front-loaded fees paid by client A are significant enough that it would require a commitment of approximately nine years to this fund family before that commission is equal to the sum of advisory fees paid by client B.

Question #2: Can you provide me a detailed explanation of all the ways you are compensated?

Does an ophthalmologist's advisor receive commissions on any of the investments they recommend? Beyond commissions, compensation can come from sales charges on mutual funds or from a higher operating expense on a specific class of funds. Further, private equities, structured notes, hedge funds, and non-traded real estate investment trust (REIT) can offer various fee arrangements that may not be transparent. A RIA operating under the fiduciary standard may be able to offer the same investment at a lower cost simply because they are not taking a cut before your money goes to work for you.

Example: Client A is approached by his broker to invest in a non-publicly traded REIT. The client sends in a check for $100,000, and the security is priced at $10 per share, so the client receives 10,000 shares. The broker receives a 7 percent commission from the REIT sponsor. Client B is approached by his RIA to invest $100,000 in the same privately held REIT. The advisor charges a 1 percent management fee and does not accept compensation from the REIT sponsor. In this scenario, the commission is returned to the RIA client in the form of a reduced purchase price for the shares. Client B receives a discounted price of $9.30 from the sponsor and is able to purchase 10,752 shares of the same REIT with his $100,000 investment. Client A would have to hold the investment for approximately seven years before his 7 percent commission matches the sum of fees paid by client B to his advisor.

Takeaway tips

These success factors are crucial for young ophthalmologists in residency and fellowship, and later, as they continue on in their careers. The points we have listed are just a few of the many components of a comprehensive wealth management plan – one that can play a significant role in helping physicians achieve their long-term financial goals. In part two of this article, we will discuss success factors for ophthalmologists further along in practice and those approaching retirement.

David B. Mandell is an attorney and author of more than a dozen books for physicians. He is a partner in the wealth management firm OJM Group, where Carole C. Foos is also a partner and lead tax consultant.

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Refractive Revolutionary

Sitting Down With… Arthur Cummings, Consultant Eye Surgeon and Medical Director, Wellington Eye Clinic; Consultant Ophthalmologist at The Beacon Hospital, Dublin, Ireland

What inspired you to become an ophthalmologist?

I have always wanted to be a doctor and that has never changed, despite being exposed to other opportunities. After completing my medical degree, I was conscripted into the army – as all South African young men were at the time – and ended up working in urology. I enjoyed it so much that I decided to specialize in it. Coincidentally, my best friend had landed up in ophthalmology and having known each other for years, he persuaded me to spend a day with him in the eye clinic. I know it's a cliché, but the rest is history. One look at the iris through the slit-lamp and I was sold – hook, line and sinker.

How has ophthalmology changed over the course of your career?

The technological advances are the most obvious. In ophthalmology, and especially refractive surgery, they seem to change at a furious rate. Other changes include more women entering the specialty – a very welcome development – and patient expectations rising dramatically, especially in the elective fields of cataract and refractive surgery. As the technology develops, so do the expectations, so to be a successful cataract and refractive surgeon today, you need to be a bit of a psychologist and an entrepreneur, too.

What are your career highlights so far?

I have had so many positive things happen to me that it's very difficult to pinpoint any one highlight. I would say that cumulatively, the following chronologically correct events have all had an impact to the point where the more obvious achievements are noted, and one appears to be an "overnight success."

Making the decision to specialize in refractive surgery and relocate to Ireland to a clinic doing refractive surgery was very likely the start of this journey. Being introduced to WaveLight very early on in their history and developing a lifelong relationship that today is still very dear to me also played a significant role. Meeting Guy Kezirian, who was doing the FDA trial for the WaveLight, and learning from him that trying to achieve a perfect outcome for every LASIK patient was just as admirable as closing a retinal hole. Working with Michael Mrochen, developing a lifelong friendship and, along the way, collaborating on multiple projects has been life-changing for me.

However, the cherry on the cake has been the appointment to the board of directors of Alcon Inc., as they spun-off from Novartis in April 2019 to become the world's largest ophthalmology company. The process started in August 2018 and I have still not completely processed the fact that it happened. I am on a learning curve that is very exciting, and I am grateful beyond words to the Alcon leadership for entrusting me to this role. I am determined to help grow the market, to help encourage their innovation quest and bring the benefits of modern ophthalmology to more people.

What are your current projects?

There are a few innovations that I am involved with, either through clinical trials or as a member of a medical advisory board. Vivior, the producers of the Vision Behaviour Monitor (VBM), comes to mind first. This technology is going to revolutionize how we treat our patients, allowing us to make choices based on objective lifestyle data and provide the most appropriate refractive correction by means of presbyopia correcting IOLs or blended vision laser vision correction.

What do you think will be the next big step in the field of eye surgery?

There are a few exciting technologies either completing clinical trials or just entering clinical trials that are very promising indeed and have the ability to revolutionize current practice. Adjustable IOLs, either light adjustable (already proven technology) or those that still need to be proven clinically. LIRIC (laser-induced refractive index change) may provide refractive power change to the cornea, IOLs or a contact lens – all without shape or thickness changes. Developments in femtosecond laser technology may see the cataract being removed with irrigation and aspiration after the femtosecond laser, without the need for phaco. There are also some technologies on the horizon that may replace phaco with light-based handpiece solutions altogether. Artificial intelligence is going to become a bigger part of our lives and decision-making will become easier in terms of screening, making therapeutic decisions and selecting IOLs.

How do you see the field of robotic surgery changing in the near and far future?

Any maneuver that requires precision and repeatability (such as capsulorhexis and other aspects of cataract surgery) has the potential to be improved upon using robotic technology. If robotics can help improve outcomes and make procedures safer for patients in a cost-effective manner, we have no option other than to embrace them. Eventually, many of our procedures may be performed by robotic devices – of course, surgeons will be required to operate them and manage any complications. This may improve productivity, as clinicians can perform surgery faster and more effectively. I see robotics playing a role in the diagnostic space, too. Today we have so many diagnostic devices, instead of having patients move from device to device for measurements, we may see more innovative solutions by having the devices move to the patients. Sounds like science fiction? It's not. Just watch this space.

To read an extended version of this interview, go to top.txp.to/refractive-revolutionary

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Indications and Important Safety Information

Rx Only

TECNIS SYMFONY® EXTENDED RANGE OF VISION IOL

INDICATIONS: The TECNIS Symfony® Extended Range of Vision IOL, Model ZXR00, is indicated for primary implantation for the visual correction of aphakia, in adult patients with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model ZXR00 IOL is intended for capsular bag placement only. **WARNINGS:** Patients with any of the conditions described in the Directions for Use may not be suitable candidates for an intraocular lens because the lens may exacerbate an existing condition, may interfere with diagnosis or treatment of a condition, or may pose an unreasonable risk to the patient's eyesight. Lenses should not be placed in the ciliary sulcus. May cause a reduction in contrast sensitivity under certain conditions, compared to an aspheric monofocal IOL; fully inform the patient of this risk before implanting the lens. Special consideration should be made in patients with macular disease, amblyopia, corneal irregularities, or other ocular disease. Inform patients to exercise special caution when driving at night or in poor visibility conditions. Some visual effects may be expected due to the lens design, including: a perception of halos, glare, or starbursts around lights under nighttime conditions. These will be bothersome or very bothersome in some people, particularly in low- illumination conditions, and on rare occasions, may be significant enough that the patient may request removal of the IOL. **SERIOUS ADVERSE EVENTS:** The most frequently reported serious adverse events that occurred during the clinical trial of the TECNIS Symfony® lens were cystoid macular edema (2 eyes, 0.7%) and surgical reintervention (treatment injections for cystoid macular edema and endophthalmitis, 2 eyes, 0.7%). No lens-related adverse events occurred during the trial.

TECNIS® MULTIFOCAL FAMILY OF 1-PIECE IOLs

INDICATIONS: The TECNIS® Multifocal 1-Piece intraocular lenses are indicated for primary implantation for the visual correction of aphakia in adult patients with and without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire near, intermediate, and distance vision with increased spectacle independence. The intraocular lenses are intended to be placed in the capsular bag. **WARNINGS:** Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the Directions for Use that could increase complications or impact patient outcomes. Multifocal IOL implants may be inadvisable in patients where central visual field reduction may not be tolerated, such as macular degeneration, retinal pigment epithelium changes, and glaucoma. The lens should not be placed in the ciliary sulcus. Inform patients about the possibility that a decrease in contrast sensitivity and an increase in visual disturbances may affect their ability to drive a car under certain environmental conditions, such as driving at night or in poor visibility conditions. **PRECAUTIONS:** Prior to surgery, inform prospective patients of the possible risks and benefits associated with the use of this device and provide a copy of the patient information brochure to the patient. Secondary glaucoma has been reported occasionally in patients with controlled glaucoma who received lens implants. **ADVERSE EVENTS:** The rates of surgical re-interventions, most of which were non-lens related, were statistically higher than the FDA grid rate for the ZLB00 (+3.25 D) lens model. The re-intervention rate was 3.3% for both the first and second eyes in the ZLB00 group.

ATTENTION: Reference the Directions for Use for a complete listing of Indications and Important Safety Information.

REFERENCE: 1. DOF2018CT4021. Johnson & Johnson Surgical Vision, Inc; 2018.

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