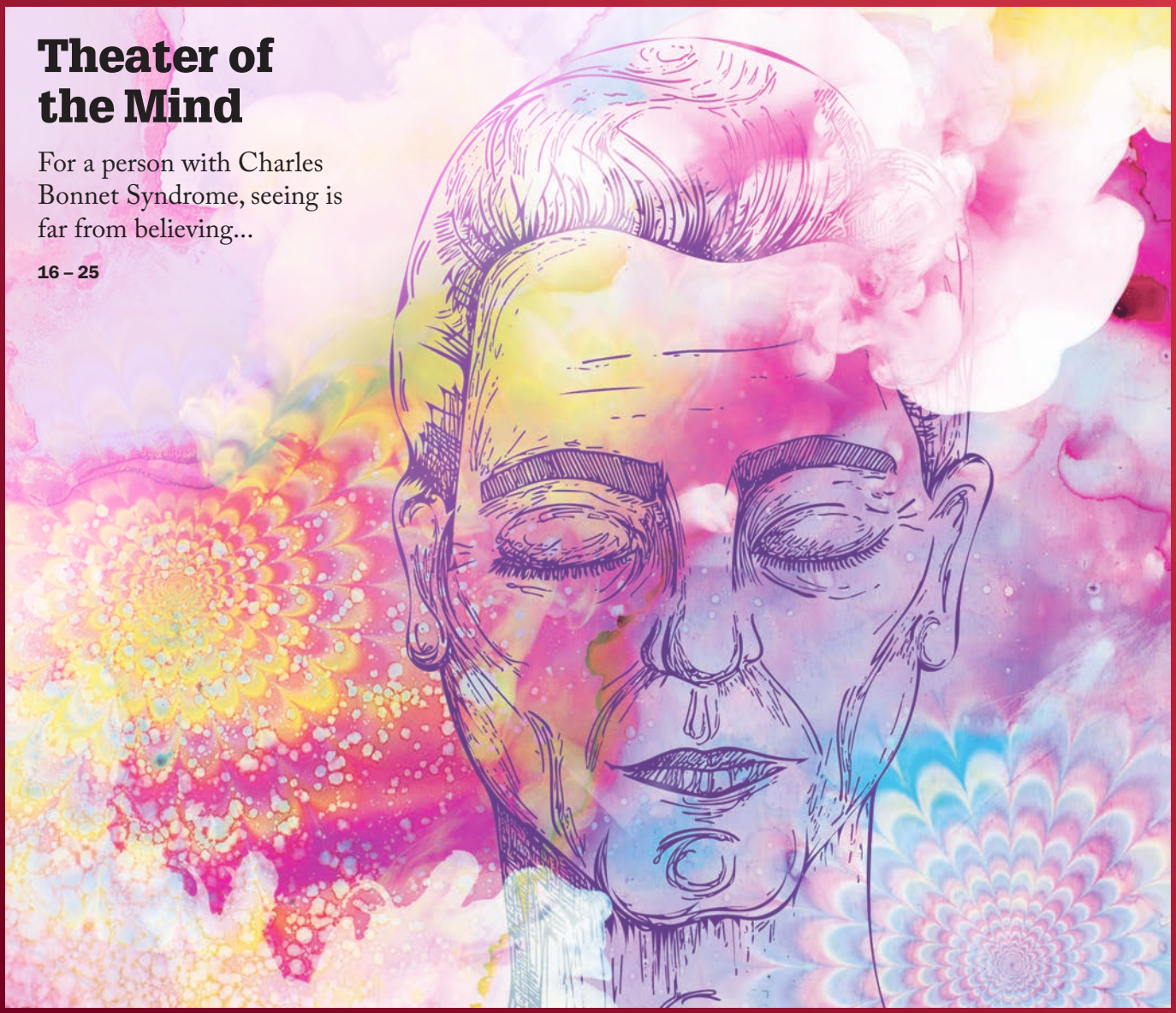
DECEMBER 2019/JANUARY 2020 # 40

# the Ophthalmologist™





## Theater of the Mind

For a person with Charles Bonnet Syndrome, seeing is far from believing...

xiidra® (lifitegrast ophthalmic solution) 5%

# THERE'S NO SWIITCHING THIS

## Xiidra is the only lymphocyte function-associated antigen-1 (LFA-1) antagonist treatment for Dry Eye Disease[1,2]

Xiidra, the first in a class of LFA-1 antagonists for Dry Eye Disease, is a prescription eye drop FDA-approved to treat both signs and symptoms of the disease.[1,3]

There's no substitute.[2,4] Check out patient resources, insurance coverage, and more at **Xiidra-ECP.com**


References:

**1.** Xiidra [Prescribing Information]. Lexington, MA: Shire US. **2.** TFOS DEWS II Research Subcommittee. Report of the Research Subcommittee of the Tear Film & Ocular Surface Society Dry Eye WorkShop II (2017). *Ocul Surf.* 2017;15(3):269-649. **3.** FDA approves new medication for dry eye disease. FDA News Release. July 2016. http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm510720.htm. Accessed July 12, 2016. **4.** Food and Drug Administration. Electronic Orange Book. http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/UCM071436.pdf. Accessed June 26, 2018.


### Indication

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

### Important Safety Information

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.

In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

**For additional safety information, see accompanying Brief Summary of Safety Information on the adjacent page and Full Prescribing Information on Xiidra-ECP.com.**



Shire

xiidra® (lifitegrast ophthalmic solution)5%

Rx Only

**BRIEF SUMMARY:**
Consult the Full Prescribing Information for complete product information.

## INDICATIONS AND USAGE
Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

## DOSAGE AND ADMINISTRATION
Instill one drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single-use container. Discard the single-use container immediately after using in each eye. Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

## CONTRAINDICATIONS
Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation.

## ADVERSE REACTIONS
### Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies 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. In five clinical studies of dry eye disease conducted with lifitegrast ophthalmic solution, 1401 patients received at least 1 dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had ≤3 months of treatment exposure. 170 patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5-25 % of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

### Postmarketing Experience
The following adverse reactions have been identified during postapproval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rare cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, and urticaria have been reported. Eye swelling and rash have been reported.

## USE IN SPECIFIC POPULATIONS
### Pregnancy
There are no available data on Xiidra use in pregnant women to inform any drug associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from pre-mating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear.

### Animal Data
Lifitegrast administered daily by intravenous (IV) injection to rats, from pre-mating through gestation day 17, caused an increase in mean preimplantation loss and an increased incidence of several minor skeletal anomalies at 30 mg /kg / day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg /kg /day (460-fold the human plasma exposure at the RHOD, based on AUC ). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg /kg /day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal No Observed Adverse Effect Level (NOAEL) was not identified in the rabbit.

### Lactation
There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

### Pediatric Use
Safety and efficacy in pediatric patients below the age of 17 years have not been established.

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

## NONCLINICAL TOXICOLOGY
### Carcinogenesis, Mutagenesis, Impairment of Fertility
*Carcinogenesis:* Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast.
*Mutagenesis:* Lifitegrast was not mutagenic in the *in vitro* Ames assay. Lifitegrast was not clastogenic in the *in vivo* mouse micronucleus assay. In an *in vitro* chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation.
*Impairment of fertility:* Lifitegrast administered at intravenous (IV) doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the recommended human ophthalmic dose (RHOD) of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female treated rats.

Shire

Manufactured for: Shire US Inc., 300 Shire Way, Lexington, MA 02421.
For more information, go to www.Xiidra.com or call 1-800-828-2088.

Patented: please see https://www.shire.com/legal-notice/product-patents
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| Comparison of Preloaded IOLs | | | |
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| Lens platform | 600C | Acrysof IQ | Tecnis1 |
| Injector | RayOne | UltraSert | iTec |
| Nd:YAG rate | 1.7%[1] | 7.47%[7] | 3.75%[7] |
| Miyata grade (Glistenings) | 0[2] (None) | 3[8] (High) | 0[12] (None) |
| ABBE value | 56[2] | 37[9] | 55[9] |
| Refractive index | 1.46[3] | 1.55[10] | 1.47[12] |
| Mean decentration | 0.08 mm[4] | 0.78 mm[11] | 0.27 mm[13] |
| Nozzle diameter | 1.65 mm[5] | 2.08 mm[5] | 1.86 mm[5] |
| Injector steps | 2[6] | 3[10] | 4[12] |

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[1]Mathew RG et al. Opthalmic Surg Lasers Imaging. 2010; 41(6): 651-55, [2]Rayner. Data on file. White paper, [3]Ferreira T et al. J of Refract Surg. 2019; 35(7): 418-25, [4]Bhogal-Bhamra GK et al. J of Refract Surg. 2019; 35(1): 48-53, [5]Nanavaty M et al. J of Refract Surg. 2017; 43(4): 558-63, [6]www.rayner.com, [7]Cullin F et al. Acta Ophthalmol. 2014; 92(2): 179-83, [8]Werner L. J of Refract Surg. 2010; 36(8): 1398-1420, [9]Zhao H et al. Br J Ophthalmol. 2007; 91(9): 1225-29, [10]www.myalcon.com, [11]Humbert G et al. Fr J Opthalmol. 2013; 36(4); 352-61, [12]jnjvisionpro.com, [13]Baumeister M et al. J of Refract Surg. 2009; 35(6): 1006-12

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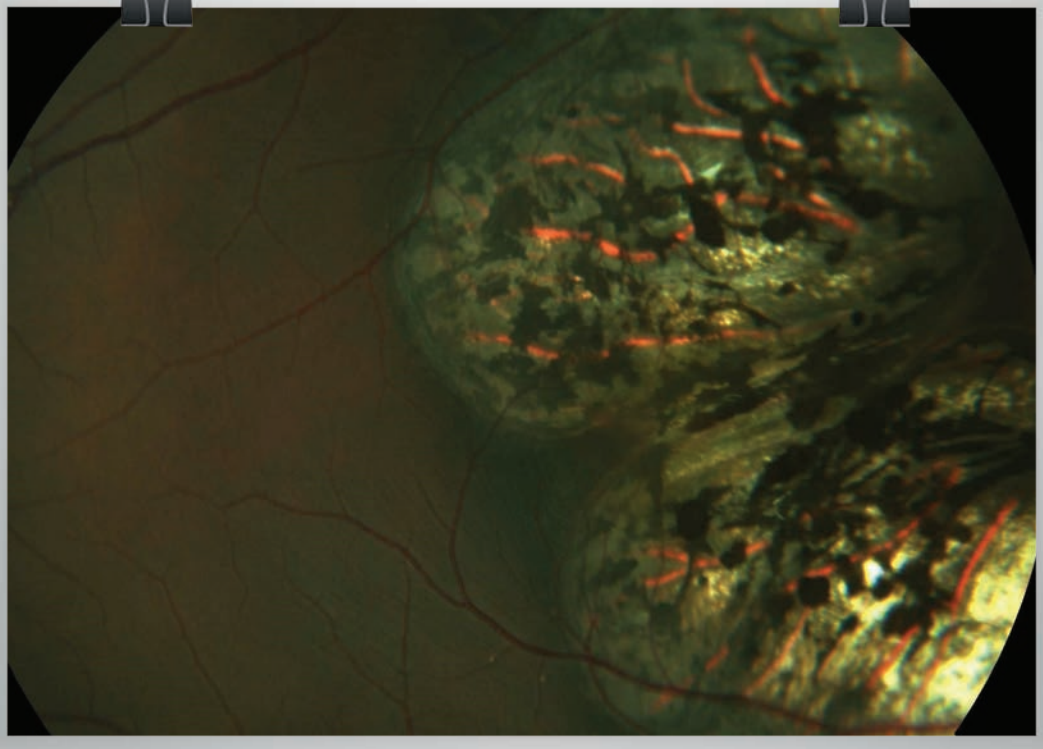
# Image of the Month



*Lava Flows*

This month's image shows posterior staphyloma. Staphyloma is the thinning of the sclera, to which the underlying pigmented tissue adds its color. Posterior staphylomas are often congenital or they manifest extreme myopia.

Credit: Channdarith Kith, Resident of Ophthalmology, University of Health Sciences, Cambodia.

Do you have an image you'd like to see featured in The Ophthalmologist? Contact edit@theophthalmologist.com

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*Artistic interpretation of the vivid, silent and often disturbing visions experienced by Charles Bonnet Syndrome sufferers*



## Feature



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## NextGen



## Sitting Down With



the Ophthalmologist
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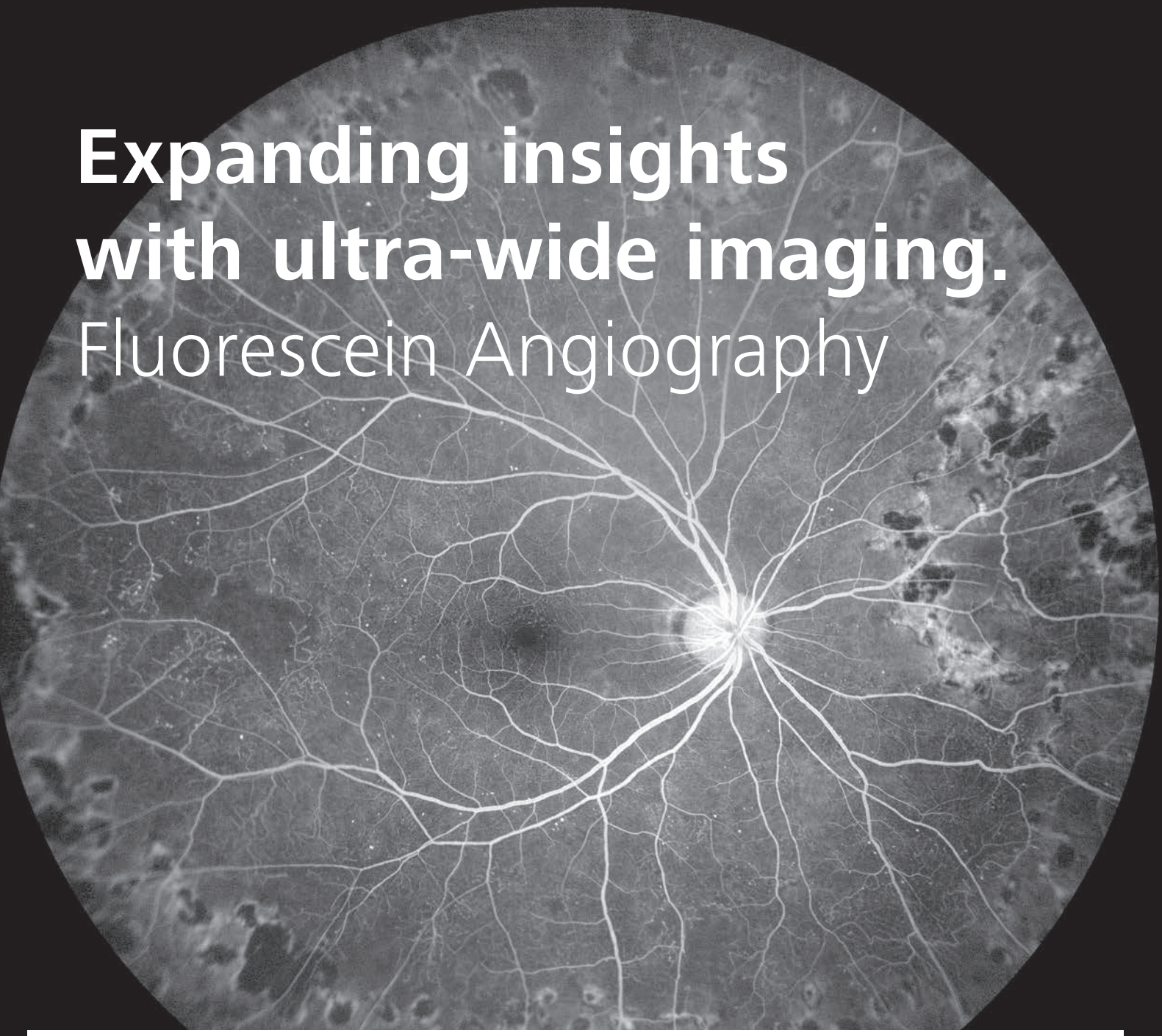
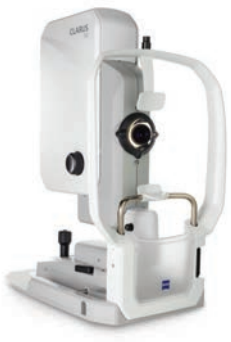
# Expanding insights with ultra-wide imaging.

## Fluorescein Angiography





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# Genetic Lottery

*When even the world's wealthiest economies struggle to fund gene therapies, we have a problem that demands disruptive solutions*



As this issue showcases, the field of ophthalmology is no stranger to innovation, cutting-edge science, or the adoption of new technologies. But when it comes to advanced therapies, innovation crashes into a daunting final hurdle: cost.

My friend – a pediatrician – recently announced that she is crowdfunding gene therapy treatment for her son. And it really brought the issue home. Zolgensma, a one-off treatment for spinal muscular atrophy (SMA), is the most expensive drug ever introduced to the market, at $2.1 million. The FDA approved the drug in the summer of 2019 for children under two years old – the crucial time to administer the drug, as 68 percent of children with SMA type 1 die before their second birthday (1). For my friend's infant, diagnosed at a few weeks old, the new therapy is a life-saving option. However, it is completely out of the family's financial reach; it is not currently reimbursed – or even approved – for use in the EU.

Gene therapies for inherited eye disorders are quickly becoming a reality, but here too the price tags are eye-watering. The recent NICE guidelines for Luxturna to be the recommended treatment for adults and children with RPE65-mediated retinal dystrophies in England and Wales are a welcome development (2) – even if the British NHS and the drug's producer, Novartis, haven't disclosed the exact details of the agreement. But what about patients elsewhere? In the US, Luxturna is not universally covered by insurance plans, and there is no currently accepted pathway for financing expensive gene therapies.

For many adults and children around the world, gene therapies are a distant dream; the sums of money required an abstract concept. My friend's crowdfunding campaign has raised 58 percent so far – she's a popular blogger and a well-known pediatrician. But on the same crowdfunding site, the faces of four other infants with SMA type 1 look up at me – and their parents' fundraising efforts are not looking as successful.

For our sister publication – The Medicine Maker – the need to improve access to medicines (by reducing costs) is a regular discussion point. Here's hoping that the world's scientists, engineers, and leaders can find innovative ways of providing patients with the advanced therapeutics they so desperately need.

**Aleksandra Jones**
*Editor*

*References*

1. *SMA News Today, "SMA Life Expectancy and Disease Onset". Available at: bit.ly/2KMmLps. Accessed November 22, 2019.*
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# 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*

## Treating Active TED

### Thyroid eye disease may have met its match in teprotumumab

Recently presented Phase III clinical data show that teprotumumab significantly reduces double vision and improves the quality of life among patients with active thyroid eye disease (TED). Also known as Graves' ophthalmopathy, the progressive autoimmune disease attacks the tissues behind the eyes (causing them to bulge outwards) and the muscles in the eyes, which become inflamed and scarred. Not only can the disease cause significant visual impairment, leading to a reduced ability to perform daily tasks, but the resulting changes in patients' appearance can also affect mental health (1, 2).

Intriguingly, TED has only been shown to respond to pharmacotherapy in the "active" phase – characterized by inflammation and tissue expansion behind the eyes – which may last up to three years (3). The new data, presented at the American Society of Ophthalmic Plastic and Reconstructive Surgery's (ASOPRS) 50th Anniversary Fall Scientific Symposium, show that teprotumumab, a fully human monoclonal antibody (mAb), can reduce several devastating effects of TED.

The disease itself is caused by autoantibodies activating a signaling complex that is mediated by insulin-like growth factor 1 receptors (IGF-1R) in the orbit of the eye (4, 5). Teprotumumab works by targeting – and blocking – those receptors, eliminating the manifestation of the disease.

The drug is currently being reviewed by the FDA, with the Prescription Drug User Fee Act (PDUFA) date set for March 8, 2020. If approved, teprotumumab would be the first FDA-approved medicine for the treatment

of active TED. "Previously, patients might have been subjected to a variety of hydro-steroids and chronic treatments – and, later on, surgery. This would all be spread out over a five-year period. Now, this could potentially be condensed into one medical treatment with a series of infusions," says Raymond Douglas of Cedars Sinai Medical Center, lead investigator of the OPTIC study.

The results of the Phase III trial, which took place at leading centers in the US, Germany and Italy, were promising: 68 percent of patients saw an improvement of at least one grade in double vision, with further improvements seen in other measures, such as quality of life, and a significant benefit of teprotumumab on proptosis (bulging eyes).

Douglas adds, "The aim of potentially reversing the disease process and reducing the need for surgery was a particularly lofty goal – one that had never been attempted before. The biggest surprise was that the drug actually worked so well and was so successful."

*References*

1. *J Barrio-Barrio et al., "Graves' Ophthalmopathy: VISA versus EUGOGO Classification, Assessment, and Management", J Ophthal, 2015, 1 (2015). PMID: 26351570.*
2. *L Bartalena et al., "The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy", Euro Thyroid J, 5, 1 (2016). PMID: 27099835.*
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4. *RS Bahn, "Graves' Ophthalmopathy", N Eng J Med, 2010. PMID: 20181974.*
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# Timely Treatment for ROP

**Thanks to European approval of a new indication for Lucentis, preterm infants with ROP finally have a pharmacotherapeutic option**

Infants born with retinopathy of prematurity (ROP) – incomplete blood vessels in the retina – are at high risk of blindness-associated complications such as macular edema and retinal detachment. The disease is rare, but even so there are tens of thousands of ROP patients worldwide. Historically, treatment of these infants has been limited to laser-mediated ablation of abnormal retinal blood vessels; unfortunately, this inevitably results in damage to healthy tissue.

In recent years, the standard of care has been increasingly supplemented with off-label use of anti-VEGF drugs; the theory is that VEGF inhibition will suppress growth of abnormal vessels in the retina. "We'd seen reports (1) that suggested this approach seemed to be rather effective in ROP patients," says Dirk Sauer, Development Unit Head, Novartis Ophthalmology. "We thought we should do a proper trial to assess anti-VEGF efficacy and safety in this vulnerable population." Accordingly, Novartis sponsored the RAINBOW study, a randomized controlled trial which compared ranibizumab (Lucentis) with the laser ablation standard of care.

The result? RAINBOW confirmed that ranibizumab is safe and efficacious in ROP patients (2): in fact, patients treated with this anti-VEGF product were about twice as likely as laser-treated patients to have a positive outcome. Also, many more ranibizumab patients (80 percent) than laser patients (66 percent) responded very well to their treatment, although this effect just missed statistical significance

(p=0.0254). The anti-VEGF approach has other advantages too. "Importantly, ranibizumab doesn't destroy healthy tissue, which is probably its most significant advantage vis-a-vis laser therapy," says Sauer. By inhibiting the growth of abnormal vessels without damaging healthy tissue, Sauer suggests, the drug may achieve the goal of allowing normal development of visual function in ROP patients.

RAINBOW has now led to European approval for Lucentis use in preterm infants for the treatment of ROP with zone I, zone II or aggressive posterior disease, making ranibizumab the only approved pharmacological therapy in this indication.

So ROP patients in Europe at last have another treatment option: but what about the rest of the world? Sauer states that Novartis is seeking approval in other territories, including Australia, Canada and Switzerland; the intent, he says, is to achieve the same global reach for the ROP indication as Lucentis has for its other indications. A key question remains regarding the long-term benefits of anti-VEGF in ROP patients, and in this regard Sauer notes the five-year follow-up associated with RAINBOW: "We'll check the visual function of patients as they get older – our hope is that ranibizumab will be associated with better visual function development than laser, especially in the 80 percent of ROP patients who responded well soon after treatment." Final follow-up data should be available in 2023, notes Sauer, adding that interim data available to date suggest that the ranibizumab benefit is maintained for up to three years. Another question relates to the role of VEGF in normal development – might there be safety concerns relating to use of anti-VEGF therapy in young children? "We'll check other aspects of the development of these patients but we're not expecting any issues," says Sauer. "Systemic exposure to intravitreally administered anti-VEGF is really very low, and so far has shown no effect in terms of normal VEGF levels."

*References*

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2. *Clinicaltrials.gov, "RAINBOW Study: Ranibizumab compared with laser therapy for the treatment of infants born prematurely with retinopathy of prematurity – study results". Available at: https://bit.ly/2m8JjaD. Accessed September 4, 2019.*

# Cash Injection

**From a single cornea to a hundred or more cornea cell therapy transplant injections: is CorneaGen on course to end our dependence on donor tissue?**

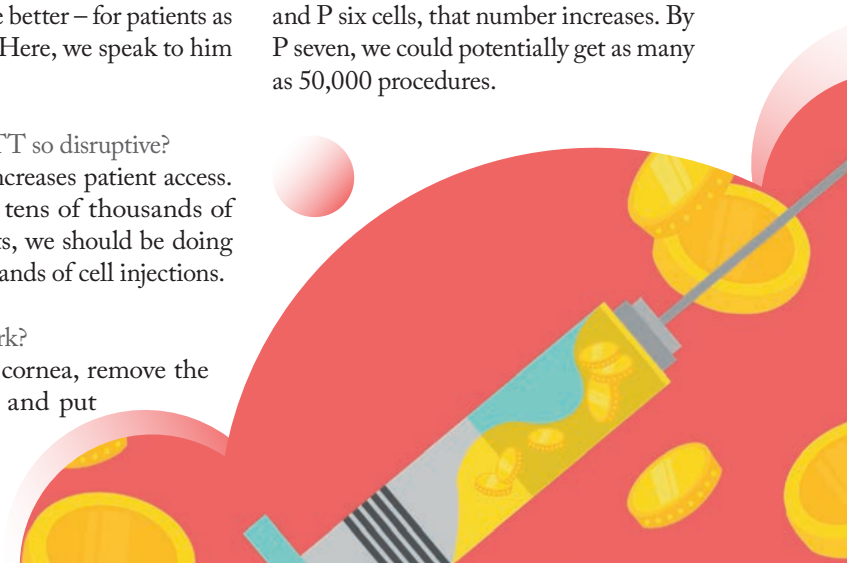
It would be an understatement to call CorneaGen well-capitalized. Since it was founded three years ago, the Seattle-based company has raised $10 million in Series A funding, $37 million in Series B funding, and accessed a debt vehicle of $25 million more. Its product? Corneal cell therapy transplantation (CCTT), capable of turning a single donated cornea into 100 or more sight-restoring treatments. How? By culturing human endothelial cells and injecting them into the anterior chamber of a blind patient's eye, eliminating the need for invasive corneal transplant surgery. The injected cells have been shown to safely restore sight within a month, and all patients who have taken part in clinical trials to date report clear, healthy corneas – a full year post-procedure. CorneaGen is currently creating a subsidiary in Japan to drive the regulatory approval process and initiate commercialization. CEO Monty Montoya claims the treatment will have the same effect on the cornea sub-specialty that phaco had on cataract surgery. In his own words: "CCTT will change the practice of medicine for the better – for patients as well as surgeons." Here, we speak to him to find out why.

### What makes CCTT so disruptive?

It exponentially increases patient access. Instead of doing tens of thousands of corneal transplants, we should be doing hundreds of thousands of cell injections.

### So how does it work?

We take a donor cornea, remove the endothelial cells and put them into a culture media that has the "secret sauce." The cells are expanded over multiple passes (the period of time in which they are cultured), with the high-quality cells being selected and then run again. With every pass, you multiply the cells available. Each pass takes around 45 to 60 days. In clinical trials, we used P three – third pass of cells – the number required to provide 100-plus procedures from a single donor cornea. When we use P four, P five and P six cells, that number increases. By P seven, we could potentially get as many as 50,000 procedures.



Is there a limit to the number of passes you can do?

In cell therapy, there is typically a limit of how far you can go as the cells don't seem to function as well. We feel confident that we will be able to expand to P four or P five cells in the future, but we will probably go to market, at least initially, with P three cells.

Did you expect the results to be so good?

You don't always expect 100 percent efficacy, so to have had that level of success through three phases of clinical trials is really positive. We have patients who are four and five years out and still have fantastic vision.

Why Japan?

The IP originated out of Kyoto Prefectural University of Medicine with Shigeru Kinoshita, who is the inventor and primary investigator. Because the therapy originated in Japan and is already through phase three clinical trials, it makes sense to finish them there. Hopefully the data that has already been generated from those clinical trials will help reduce the regulatory process we have to go through in the US.

Do you know when that process will take place?

Once we have taken the data from Japan, presented it to the FDA and begun to work out an agreeable pathway for us to go through – hopefully we will have the regulatory pathway with the FDA defined by the end of the first quarter of 2020.

Why CCTT over corneal transplants?

The efficacy of the procedure is much more powerful. Typically with any type of cornea transplant, endothelial cell count goes down over time until the patient ultimately needs another transplant or a re-graft. What we've seen in our studies is a stabilization of the endothelial cell count over all phases after the injection. At present, patients in our study are maintaining cells amazingly. Of course, we would expect this from patients who had the injection a few months ago, but patients from phase one and phase two still have great cell counts. The durability of the treatment is increased and we've had zero incidences of rejection, which is a big deal.

Another benefit is its practicality. Currently, when a patient has DMEK surgery, the physician puts an air bubble underneath the DMEK graft that holds it against the Descemet's membrane. For patients to have the best chance of success, they need to lie on their backs for three days – that is a long time to lie on your back. With a corneal cell injection, the patient only needs to lie face down for three hours. In the clinical trials, we would literally roll the patient onto a massage table after the procedure, where they could play with an iPad, text their friends or watch a video.

Another benefit is psychological. We have spoken to a lot of doctors and they tell us that patients typically undergo a significant amount of vision loss before they are willing to go through a transplant. Having a cell injection is a very different thing, and a lot more manageable mentally and emotionally. We expect to find patients prepared to access treatment a lot sooner with CCTT, making it a much earlier intervention rather than a last resort.

What is the ultimate goal for CorneaGen?

We are aiming to eliminate corneal blindness by 2040. If we are successful at CCTT, that will take care of half of it. It will also generate the resources for us to be aggressive and innovative in taking care of the other half, so I think it is definitely doable.

What would you like to work on in the future?

There are a lot of challenging ocular surface disorders – Stevens-Johnson syndrome, for example – but not a lot of fantastic curative treatments. Fortunately, the cornea is novel in that it doesn't have any blood vessels, which allows us to take advantage of advances like gene and cell therapy a lot earlier. These kind of therapies are going to be really critical for eliminating cornea blindness. We haven't tapped into that yet, but they are going to be important to us in the future.

# In My View

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

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

*Contact the team at edit@theophthalmologist.com*

## The Refractive Principle

**It is time for ophthalmology to embrace refractive surgery – for the sake of humankind**

*By Arthur Cummings, Consultant Eye Surgeon and Medical Director, Wellington Eye Clinic; Consultant Ophthalmologist at The Beacon Hospital, Dublin, Ireland*

In the words of Martin Luther King, Jr.: "I have a dream." Or should I say, we have a dream. "We" being the Refractive Surgery Alliance (RSA). The WHO estimates that 2.2 billion people live with some form of visual impairment and at least one billion people live with an impairment that could have been prevented, or is yet to be addressed, with refractive errors and cataracts being the leading causes (1). This one billion people includes those with moderate or severe distance vision impairment or blindness due to unaddressed refractive error (123.7 million), cataract (65.2 million), glaucoma (6.9 million), corneal opacities (4.2 million), diabetic retinopathy (3 million), and trachoma (2 million), as well as near vision impairment caused by unaddressed presbyopia (826 million). Uncorrected refractive errors dwarf the other causes of vision impairment. How can this be possible when the world has never been more prosperous, when poverty is on the decline, and when conditions are generally improving?

In some developing countries, spectacles are simply not available or don't work as intended (they get broken, sold, stolen or lost). For some, contact lenses are even less suitable. This is the first part of the story: the huge burden of uncorrected refractive error.

The second major challenge is how refractive surgery is viewed within ophthalmology. Our colleagues are not always aware of the strides that refractive surgery has made; they don't know that refractive surgery is safer than contact lens wear. Some even trivialize refractive surgery, claiming it's "easy" – a time filler squeezed between more important jobs,

*"The truth is that refractive surgery changes lives for the better at a much younger age, with economic, health and occupational benefits that accrue over a lifetime."*

a task subject to fly-by-night surgeons and medical tourism. They say it is simply not "serious surgery."

I could not disagree more. Refractive surgery is all about performance. The rest of our foundational knowledge and practice is about diseased-based approaches. We are programmed to view avoiding minimal loss as a better choice than pursuing gain. Daniel Kahneman, the Nobel Prize-winning economist and author, has performed many behavioral economics studies that bear this out. Therefore, we have health insurance for items like cataract surgery, glaucoma treatment and diabetic retinopathy treatment. We want to minimize loss. And we as a profession have done well with this admirable and important goal. Elective vision correction surgery, however, is not covered, as it is simply deemed to be cosmetic.

The truth is that refractive surgery changes lives for the better at a much younger age, with economic, health and occupational benefits that accrue over a lifetime. It has a value that is in the trillions of dollars in the developing world. Given the monumental improvements that refractive surgery can provide those with vision impairment due to uncorrected refractive error, we now have a mission. But first, we need to raise refractive surgery to the level that is required to make our mission achievable: excellent and safe outcomes at scale. And that means more formal and thorough training for refractive surgeons.

At the end of residency, young ophthalmologists are almost as far from being refractive surgeons as they were when they started. Being able to perform a LASIK procedure every now and then does not make one a refractive surgeon. It starts with a clear mindset: pursuing gain is a valuable and noble pursuit. It continues with another mindset: pursuing gain will take more discipline and commitment to excellence than does disease-based medicine. It requires training on how to deal with self-paying (and therefore much more demanding) patients undergoing elective surgery. The field of refractive surgery requires more of the time-honored features of a great doctor-patient relationship than almost any other discipline in medicine. Is refractive surgery different enough to warrant its own College of Refractive Surgery? We think it is. And that's step two: preparing the surgeons who will be needed to address the growing burden of refractive error.

How would such a college work? By focusing on three areas: curriculum development (and approval), accreditation, and impact assessment. The actual training would be provided by those following the approved curriculum – for example, the RSA – rather than the College itself, which would develop teaching materials and resources. The College would also oversee the surgical training with experts in the field – treating patients that otherwise couldn't afford refractive surgery with the most up-to-date treatments available. In short, experts get to teach, fellows get to learn, and the underprivileged and underserved get to see.

In fact, we are already working with large institutions to bring the benefits of refractive surgery to the underprivileged. With increasing awareness of how refractive surgery is changing the lives of so many, we hope the perception of refractive surgery may change – and thus encourage the youngest and brightest to choose refractive surgery as a career.

The need for a College of Refractive Surgery is not a divorce from ophthalmology, rather it is a response to the unique requirements of this ever-changing field. But it takes a lot to change the world. And this movement will require legislation, strategy, financial planning, execution, but, most of all, physician leadership – and many of you reading this are those leaders.

Consider this: the brain allots 60 percent of its resources to vision. The processing speed of vision is 100 times faster than that of hearing and smell, and 10 times faster than touch. We were made to see. Some in ophthalmology have made it their mission in life to allow people to see well without prosthetic aids, helping rid the world of this congenital defect.

*"The need for a College of Refractive Surgery is not a divorce from ophthalmology, rather it is a response to the unique requirements of this ever-changing field."*

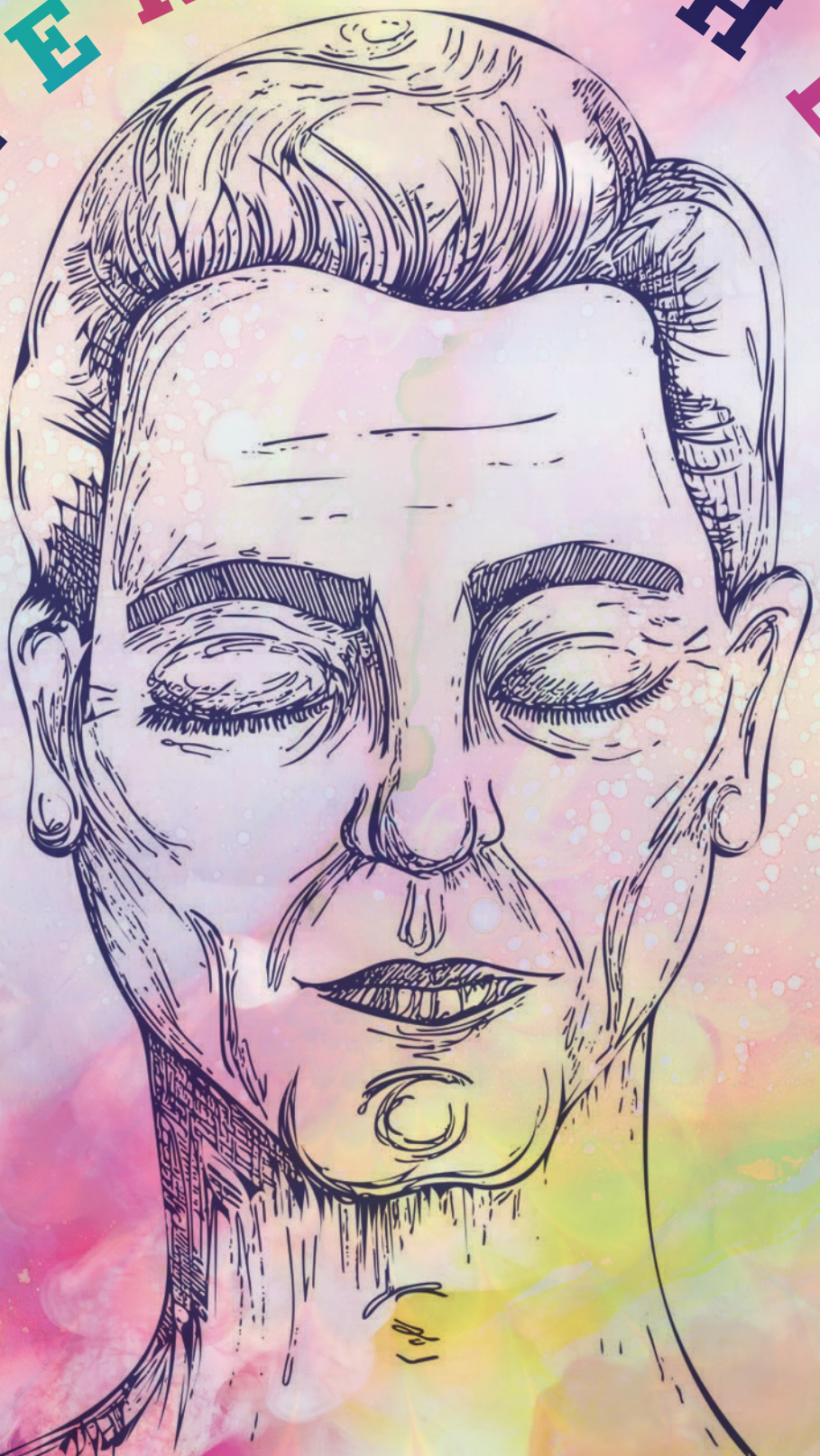
I see myself involved in this endeavor for the rest of my career – and I consider it an enormous privilege. I invite all those who share this mindset to join the RSA* and help make our dream a reality.

** RSA members currently come from 26 countries around the world, there are > 350 of us and it is completely funded by its members with no financial support from any other source. See www.refractivealliance.com to learn more.*

*Reference*

1. *World Health Organization, "Blindness and vision impairment" (2019). Available at: https://bit.ly/2CwpC1l. Accessed November 11, 2019.*

# THEATER of THE Mind



Charles Bonnet Syndrome (CBS) is an orphan condition, first fostered by Dominic ffytche at King's College London. In 2015, I launched the charity Esme's Umbrella at the British House of Commons to raise awareness of CBS, as well as funds for research into this disturbing side effect of sight loss.

*By Judith Potts*

When my mother, Esme, finally confided in me about the faceless people sitting on her sofa, the gargoyle-like creature that jumped from table to chair, and the Edwardian tear-stained street child who seemed to follow her everywhere – not to mention the times the room or garden morphed into an alien place – I had absolutely no idea what could be wrong with her.

Despite advancing glaucoma, Esme lived a happy, independent life and much enjoyed completing the cryptic crossword in her daily newspaper. In that case, surely these "visions" – as she called them – were not caused by dementia? Yet, the word occurred to both of us and hung heavily in the air. With a huge stroke of luck, I discovered a tiny paragraph buried in the health pages of a newspaper about a condition that produced vivid, silent, visual hallucinations and was caused by loss of sight. It was written by a young man called Matt Harrison, but it could have been written by Esme.

With enormous relief, I called her ophthalmologist. To my surprise, he refused to discuss CBS or tell me why he had never warned us that her diminishing sight could bring with it such a distressing condition. As I have said since – during presentations at various events – forewarned is forearmed. How could he not agree? I realize now that he probably knew very little about CBS and, possibly, thought that it would fall into a different medical specialty – even though it was caused entirely by a condition that fell into his remit. Likewise, Esme's general practitioner (GP) had never heard of CBS, and was very skeptical about its existence. The optometrist had no knowledge of the condition, but – to be fair to him – he did become very interested when I was in a position to explain it all.

At that time, I knew nothing about Eye Clinic Liaison Officers – indeed, I suspect the Yorkshire eye clinic, which Esme attended, did not have such a person – nor Rehabilitation Officers for the Visually Impaired. I had only a vague understanding of the charities in the eye sector. With a desperate need to find some help, I was forced to do what lay people are always told not to do: I consulted the Internet. There, I found Dominic ffytche at King's College London, who is the sole, globally-acknowledged expert in CBS. Now Reader in Visual Psychiatry, he has just been announced by Expertscape as the number one in the world for visual hallucinations of all types.

ffytche confirmed that Esme was, indeed, living with CBS, and broke the news that there were no medical specialists to whom I could take her, nor any suitable medication. He stressed that this was not a mental health issue but, for Esme, could only be treated with reassurance and coping strategies. He had developed an eye

"IT WAS EVIDENT THAT THE CBS COMMUNITY WAS HUNGRY FOR INFORMATION – AND THE OPPORTUNITY TO JOIN TOGETHER FOR A DAY."

exercise which, for some people, dispelled the hallucination and, subsequently, I collected many others from the CBS community – all can be found on the website www.charlesbonnetsyndrome.uk.

I was appalled that such a disturbing yet extremely common condition could be ignored by mainstream health professionals, and only touched on during ophthalmology and optometry training. Recently, I received an email from an ophthalmologist in Canada, who had been trained in the UK. He had just read my article on CBS, and he confessed – with great embarrassment – that he was unaware of the condition and astonished that it had not featured in his training. I know that GPs in the UK receive just a few hours on ophthalmology in their course, but I had assumed that every ophthalmologist and optometrist would be aware of such a serious side effect of sight loss.

I had many questions for Dominic ffytche, and my consternation grew when he told me that CBS was not exclusive to adults: children and young people with compromised sight could develop it too (see Box: CBS in Pediatric Patients).

Although it was glaucoma that had taken more than 60 percent of Esme's vision, CBS can be caused by loss of sight from any eye disease, including tumors, stroke, accidents, diabetes, or another condition that damages the optic nerve. It had been thought that CBS vanished after 18 months, but ffytche's work proved otherwise.

At the time, I was writing a Health Column for The Telegraph and, determined to give the subject a wider audience, I began to include CBS along with my usual subject of cancer. I found myself inundated with emails from people who were either relieved to discover that they were not necessarily experiencing a mental health issue, were seeking more information about CBS, or just wanted to tell their stories.

It was one of these stories that persuaded me to stop hesitating, and launch an awareness campaign. The email came from a reader in the USA. She told me she had read everything I had written about CBS, and realized, to her horror, that her mother – much against the will of the family, but on the advice of the doctor – had been unnecessarily admitted to a dementia unit because she was hallucinating. No one in the unit had heard of CBS, so there was nobody to reassure her mother that the perceived worms and slugs writhing on her food and in her drink were not real. She stopped eating and drinking, with inevitable, tragic consequences. Her daughter said she would never forgive herself.

I launched Esme's Umbrella on 16 November, 2015, at the House of Commons, with the support of The Help and Information Service (TH&IS), and with Dominic ffytche as my Medical Adviser. The date has been accepted as the official CBS Awareness Day and each year there has been a special event to mark the occasion.

Never having run a campaign of any sort (and far outside my comfort zone), I was spurred on by the torment of Esme's final years and that of so many others to whom I was speaking on my helpline, which had been set up for me by TH&IS. Callers' descriptions of their hallucinations were gathered by TH&IS, building up a database – until new data protection regulations (GDPR) called a halt. Last year, the call volume became so high – too many for me to answer alone – and I had to relinquish my Helpline to the Eye Health Team at the RNIB (the number is +44 (0)20 7391 3299). However, I am always happy to return calls or refer people to the CBS Buddy Helpline at Retina UK.

To mark the first year of Esme's Umbrella, SELVIS – the eye charity in south London – offered to host an event. We were nervous about how many people would turn up – would anyone appear? The day proved that my decision to launch a campaign had been entirely correct. The room filled with people from the CBS community – many of whom had never spoken to another person with the condition and had thought they, alone, lived in a world of hallucinations. For health and safety reasons, we had to turn people away at the door. It was evident that the CBS community was hungry for information – and the opportunity to join together for a day.

Witnessing the evident delight of the group and how enthusiastic they were to help push the campaign forward, the next step I took was requested by them: to start some Esme Room Support Groups. The question was: where and how? In the end, I decided to ask all the local low vision charities around the UK to host these events, at which people living with CBS – and their families and friends – could meet over a cup of tea and exchange experiences and coping strategies. In the same way as English National Ballet's "Dance for Parkinson's" project has opened up a social world for people with that condition and their caregivers, my plan is for the Esme Rooms to evolve into proper CBS hubs, offering information, support and practical advice about CBS and sight loss in general. If funding

allows, these hubs could also include counseling, mindfulness and free complementary therapies. Esme Room Support Groups would help inform improved social support. The Esme Rooms, which are already up and running, report great success in relieving the stress of living with CBS – for patients and caregivers.

It is not just those for whom CBS hallucinations are part of their everyday life that need support. Family caregivers describe how the intangible nature of the hallucinations – and their frequency – produce such a feeling of isolation within the relationship. They know that CBS is not a mental health condition, but having to constantly reassure someone that there is no dog, no hole in the floor or no fire, can be very wearing. It is vital that these caregivers are not forgotten.

London City University has produced a research survey for eyecare professionals: "Caring for the Carers" (1). The writers asked for my input and CBS is included. There is also a follow-up survey directly targeting caregivers themselves (2).

Though care and support for those whose lives have been affected by both sight loss and CBS was at the forefront of my campaign, it was also very obvious that I needed to begin by raising awareness of CBS across the whole healthcare profession and out in the community.

Starting with the Royal College of Ophthalmologists, I visited its President, Mike Burdon. He was hugely supportive and invited me to speak in his session at the College's Congress in May 2018. It seems that, though ophthalmologists have always been aware of CBS, many did not appreciate how it negatively affects those who develop it and how it can impinge on relationships with family and friends.

I suspect that one of the reasons ophthalmologists have not all felt the need to offer a warning or information about CBS, was that their patients – afraid that the hallucinations heralded a mental health issue – said nothing. Or, the clinicians only heard about benign, beautiful images seen by their elderly patients and assumed, wrongly, the hallucinations were only linked to aging and macular degeneration. Consequently, it was not considered a problem. I asked Michel Michaelides, Consultant Ophthalmic Surgeon at Moorfields Eye Hospital in London, if he agreed with my conclusion. He does, and adds, "Several factors may contribute, including patient stigma, timing of symptom onset, and the eye-examination focus of ophthalmology/optometry assessments."

Michaelides is well aware of CBS, but I still find myself having to correct some ophthalmologists who are of the opinion that the condition is somewhat "fanciful." I assure you: it is not if you live with it. One person whose normal vision is partial and blurred, told me that he woke to find a large tiger sitting beside him. The beautiful colors of the tiger's coat were sharp and clear – but so were the teeth and saliva.

Another problem was that CBS was not included in previous

## ICD11 AND CBS

The World Health Organization oversees the International Classification of Diseases (ICD) that provides a standardized taxonomy used by healthcare systems all over the world. Major revisions are released approximately every 20 years to reflect changes in clinical practice and disease understanding. Like previous versions, ICD 11 is arranged as a series of coded sections and subsections. Diseases of the visual system (09) contains a section Impairment of Visual Function with a subcategory for Subjective Visual Experiences. These include seven specific categories, such as visual discomfort, hemifield losses, and transient visual loss.

Last on the list is 9D56 Visual Release Hallucinations with the illustrative description: "Charles Bonnet syndrome, also called visual release hallucinations, refers to the experience of complex visual hallucinations in a person who has experienced partial or complete loss of vision. Hallucinations are exclusively visual, usually temporary, and unrelated to mental and behavioral disorders." There is acknowledgment that visual hallucinations also have other causes, with schizophrenia and primary psychotic disorders specifically excluded from the visual release hallucinations category.

Although a small acknowledgment, this represents a major advance in the recognition of CBS. The scheme used over the last two decades (ICD10) included Visual Disturbances and Blindness (H53-54) with a subsection on Subjective Visual Disturbances (H53.1), where visual hallucinations were specifically excluded. Instead, visual hallucinations were coded in the symptoms and signs involving cognition, perception, emotional state and behavior (R40-R46) as R44.1 – Visual Hallucinations, thus disconnecting visual hallucinations from eye disease and not allowing for the possibility of CBS as a clinical entity. In the version used through the 1980s and 1990s (ICD9) visual hallucinations are not even mentioned in the scheme.

versions of WHO's taxonomy of diseases and conditions and not mentioned by name in its recent revision. It was only referred to as "visual release hallucinations." And that is why I began my crusade to include Charles Bonnet Syndrome as a condition in its own right. With the help of August Colenbrander, ophthalmologist and senior scientist at Smith Kettlewell Eye Research Institute in the USA, and Andrew Dick, Professor of Ophthalmology at the University of Bristol in the UK, I succeeded. CBS and visual release hallucinations are now listed in WHO's ICD 11. And that represents a huge breakthrough; the NHS has no excuse not to exact its duty of care to people living with CBS. As Andrew Dick comments: "I believe it is now timely for the NHS to recognize CBS in line with the WHO diagnostic classification. To benefit patients, an initial action would be academic – to provide evidence of the extent of the problem – contemporaneous to NHS funding to support pathways for diagnosis, treatment and support."

GPs and hospital doctors are rarely aware of CBS. If a patient confides the reason for a broken bone – avoiding the sudden appearance of a snake, flames or a Lilliputian-sized army – misdiagnosis is on the cards. The patient is ushered down the mental health pathway, wasting clinicians' time and medication – all precious NHS resources.

Much time and money would be saved if the NHS Falls Prevention Unit included CBS as a reason to be very careful as you move around the house. I always suggest checking with a cane to see if the image is real. Guide dogs are a great help because even the best trained dog would react if a rat ran across the room or a weary Second World War soldier appeared. Even cats – as I told one distressed caller – would not stay around if a waterfall suddenly flowed from the ceiling. However, it is not always easy to think logically at that moment.

I asked my own GP, Joanna Cheung, if she had heard of CBS.

"THE PATIENT IS USHERED DOWN THE MENTAL HEALTH PATHWAY, WASTING CLINICIANS' TIME AND MEDICATION – ALL PRECIOUS NHS RESOURCES."

She says, "When Judith first mentioned CBS to me at the end of a routine GP consultation, I toyed with the idea of using the 'trying to look wise with a knowing nod' technique, but in the end confessed to knowing nothing at all about it. And that is the response from the majority of GPs. I thought it must be a rare condition (as I hadn't heard of it), but figures show over 100,000 cases in the UK, and these are just the formally diagnosed patients."

Actually, Dominic ffytche estimates there are one million people living with CBS in the UK. A straw poll by Renata Gomes, Head of Research at Blind Veterans, concluded that three quarters of her veterans lived with CBS – and probably more, but "stiff upper-lips" prevented them from confiding in anyone. It can only be very roughly estimated how many patients are living with the

# CBS IN PEDIATRIC PATIENTS

*Mariya Moosajee, Consultant Ophthalmologist at Moorfields Eye Hospital and Great Ormond Street Hospital for Children in London, UK, on BOSU and the need for evaluation of pediatric CBS patient numbers*

## AT WHAT AGE IS CBS TYPICALLY DETECTED/ IDENTIFIED?

CBS typically affects older people, reflecting the mean age at which common underlying conditions, such as AMD, diabetic retinopathy and glaucoma, cause loss of vision. The reported prevalence ranges in adults are 0.4-30 percent, but no formal epidemiological studies exist.

However, we know that CBS can occur at any age. We have focused on the elderly and the distressing situation where they experience visual hallucinations but are unaware of CBS, and hence fear that they are mentally ill or suffering from dementia. But the impact of such visual hallucinations for a child can be equally psychologically damaging, resulting in fear, mental health and behavioral issues. Overall, we need to raise awareness of CBS in children and adults amongst ophthalmologists, GPs, and all those working in the sight loss sector with patient contact.

## WHAT EXPERIENCE DO YOU HAVE WITH PEDIATRIC PATIENTS WITH CBS?

I have not met any pediatric patients with CBS so far, but I don't think that up until recently I had been asking or warning parents about visual hallucinations. In addition, it is important to consider the age of the child, as they may have a pretend play friend/pet, or have poor or distorted vision, so they describe odd imagery based on their condition and level of sight. Many of the children I see have genetic eye diseases and over 60 percent can have systemic features including developmental delay and learning difficulties. All these components can make it difficult to assess CBS in this cohort.

## IS ANY DATA ON CBS BEING GATHERED NOW? WHAT COULD IT BE USED FOR?

My research team is in the process of commencing the first prospective epidemiology study across the UK for CBS in children, funded by the Thomas Pocklington Trust. I hope that as a result of this work, ophthalmologists will see the condition on the card, and it will trigger them to start asking patients about it – inadvertently raising awareness.

In 2018, the Royal National Institute for the Blind (RNIB) reported that 25,000 children aged between 0–16 years were registered sight impaired in the UK. If we establish the incidence, sight loss conditions associated with CBS and the level of vision, this will help both ophthalmologists and pediatricians change practice by informing families about CBS, and how to cope with these visual hallucinations. For extreme cases, we will be able to offer the correct management, such as referring to child psychiatry.

## HOW DO YOU THINK THIS TYPE OF DATA COULD BE COLLECTED IN A COORDINATED MANNER?

In the UK we have the British Ophthalmological Surveillance Unit (BOSU) based at our Royal College of Ophthalmologists, which provides an active surveillance system involving all UK consultant ophthalmologists via a monthly reporting card scheme. They collect incidence data on rare diseases. Ophthalmologists will indicate that they have seen a new case of CBS, BOSU will notify the research team, and they will collect patient details through a questionnaire.

## WHAT PRECONCEPTIONS EXIST FOR CBS AMONG OPHTHALMOLOGISTS?

Some preconceptions are that it only affects adults and it is temporary – so, after complete sight loss, it stops. But we now know there are cases where it lingers, and I have heard from adults who experienced visual hallucinations as a child, and it really affected them psychologically. They never told their parents at the time or spoke of it due to fear; they found it hard to delineate from reality and imagery.

## DO YOU THINK PERCEPTIONS HAVE CHANGED, AND ARE THEY LIKELY TO CHANGE IN THE COMING YEARS?

Judith Potts' Esme's Umbrella campaign has succeeded in raising awareness amongst health care professionals and patients alike. CBS is definitely talked about more; I know of several visually impaired community groups that have discussed this topic over coffee and unearthed how common this condition is, providing a sense of comfort to those affected. Raising awareness is great; the next job is to determine how prevalent this syndrome is and how we can tackle the severe cases, and manage patients appropriately.

condition around the world.

As Andrew Dick says, we need proper prevalence studies. It is hard enough for children who are told that their eye condition means they will lose their sight, but if no one understands CBS and warns them, it becomes a lot harder. I suspect there are many pediatricians with no idea that the children with low vision in their care could also be living with CBS. Indeed, I was thanked by a Developmental Vision Pediatrician – who had heard me speak – for alerting her to the possibility.

Everyone whose sight is diminishing – no matter what age – must be warned that CBS might develop.

I asked Kirsty James – now the Campaigns Officer for the RNIB in Wales – what happened to her. She says, "When I was 13, I was told I would go completely blind from Stargardt's Disease. I was so frightened, especially as we were not told anything about the condition and had to look it up for ourselves." CBS was never mentioned and it was when she was living on her own, after university, that the condition kicked in. "There would be cars outside the flat on a cobbled street much too narrow for any traffic; I saw steps down that weren't there or the gravel would suddenly appear to be a river in full flow," she says. "Once, I looked down and saw blood all over the floor. I thought my guide dog's paws were bleeding." She told no one about her "strange visions," and feared she was "going mad." It was only when she met a low-vision specialist who asked her if she had heard of CBS, that she learned what was happening to her. She told me: "I just cried and said, 'So I'm not going mad?' I remember feeling a huge relief that I didn't have a mental health problem: it was an eye condition."

CBS Awareness Day last year was celebrated at Moorfields Eye Hospital in London. The hospital gave me a lecture theater in its Academy, and it was there I hosted the world's first CBS Patient Day at which the CBS community were joined by ophthalmologists, doctors, researchers, ECLOs, ROVIs, medical students, and representatives from the eye charities.

"EVERYONE WHOSE SIGHT IS DIMINISHING – NO MATTER WHAT AGE – MUST BE WARNED THAT CBS MIGHT DEVELOP."

One of the speakers was Amit Patel, who was a trauma doctor before a hemorrhage in both his eyes robbed him of sight. Not only has he had to come to terms with his new reality, but he has developed CBS. His hallucination is particularly terrifying. It is of a young woman, covered in blood, mud and tears. Amit says, "She stands in terrifying silence and she follows me everywhere – on the train, on the tube, in the street. My wife has even heard me shouting at her in my sleep." Amit's guide dog, Kika, has begun to sense before the hallucination occurs. She warns Amit by placing her head on his lap and remaining there until the hallucination vanishes.

This intrigued me, and I approached Claire Guest, the CEO of the Medical Detection Dogs' charity. These amazing canines had featured in my Telegraph Column very often. Not only are they able to correctly detect cancer through their extraordinary sense of smell, but they are also able to alert their owners when medication – for conditions like Addison's disease, epilepsy or diabetes – is required. I asked Guest if she thought it was possible that Kika could do this. Her answer was a very firm "yes" and then another "yes" to my next question: would she do some research to establish the change in Amit's body that Kika is detecting? If we could feed that information into the research in Newcastle (see Researching CBS box), who knows what we might find?

For those who might not have heard of the charity, I asked Guest to explain the two sides of Medical Detection Dogs' work. She began by describing the current disease-detection work: "Medical Detection Dogs (MDD) is a world-leading charity training dogs, pioneering both medical assistance and disease detection. The work is committed to carrying out empirical research to improve operations and to inform future medical technologies. To further this aim, MDD is currently working on a range of NHS approved clinical trials, exploring dogs' ability to locate urological cancers, and is also researching the volatile detection of the malaria parasite and Parkinson's disease."

For CBS, it would be the medical assistance detection that would be needed, and Guest went on to explain how that would fit the CBS research. She said: "The other arm of MDD, Medical Alert Assistance Dogs, uses olfactory alerting ability for day-to-day support for people living with chronic conditions. The Assistance Dog is trained to alert its carefully-matched human partner to an oncoming emergency episode by detecting a change in his or her odor as their health condition changes; for example, a complex type 1 diabetes attack. There is anecdotal evidence that dogs may be aware of an oncoming visual hallucination in individuals with CBS, and so they could potentially be trained to alert and give a warning. MDD wishes to explore this further, train and partner the first dog, and collect data in relation to the reliability and impact of this canine intervention."

Research delving into CBS only began in the 1990s when Dominic ffytche showed the first interest in the condition (along

*Judith Potts with Amit Patel, and his dog, Kika.*

with other causes of visual hallucinations) since Charles Bonnet documented his grandfather's hallucinations in 1760. With funding from the Thomas Pocklington Trust, Fight for Sight (which holds my Restricted Fund) and the National Eye Research Centre, Esme's Umbrella has a research team at Newcastle University, working with ffytche. This research project is nearing its end and the results will be known in the spring of 2020. Shockingly, these are the only two centers hosting CBS medical research in the world. Even in the USA, which has the deep pockets of its medical foundations and universities, there is still no CBS research. My invitation to the ophthalmology department at Stanford University in California, to be the USA's lead in CBS research, was declined. However, Fight for Sight has put out a call for another researcher. Funded by the money I have managed to raise and matched by Blind Veterans, CBS research will continue next year. We do not know, yet, where it will be or what specific aspect of CBS will be researched, but it is good to know that someone will be taking another step towards treatment and a cure.

Listening to the clinical psychologist who represents Esme's Umbrella in the USA – Gary Cusick – it is evident that exactly the same scenario is playing out on the other side of the Atlantic. Gary Cusick works exclusively with the visually impaired (not a role we have in the UK, but one which would be welcome) at the McDowell Centre in Louisville, Kentucky – a comprehensive state

## RESEARCHING CBS

*Kat da Silva Morgan, PhD Researcher at the Institute of Neuroscience, Newcastle University, UK*

At Newcastle University, we are investigating how the activity levels of the visual part of the brain are different in people who experience CBS and hallucinations, compared with people with eye disease who do not. Based on the deafferentation hypothesis, which suggests that loss of sensory information from the eyes may result in compensatory hyperexcitability and disinhibition of the visual cortex, the study aims to investigate changes in the visual cortex by examining markers of cortical activity, such as blood flow and neurotransmitter concentrations. Using this information may allow researchers to further interrogate the mechanisms that precipitate into the occurrence of visual hallucinations in CBS.

Building on this work, researchers at Newcastle University are investigating a novel therapy for patients experiencing CBS, which uses non-invasive brain stimulation as a treatment for hallucinations in an ongoing placebo-controlled crossover trial informed by a pilot study conducted in collaboration with King's College London. The trial aims to assess the therapeutic benefits of inhibitory non-invasive electrical brain stimulation applied over consecutive days to target specific areas of visual cortical hyperactivity in CBS, and its subsequent effects on visual hallucinations.

Using both patient reports of changes to the subjective nature of their visual hallucinations and neurophysiological observations of changes to brain activity, the findings of this study will help inform further, larger scale, treatment studies in CBS.

rehabilitation center for people with every type of blindness or visual impairment. He says, "Clients typically do not talk about what they are seeing, perhaps for fear of being thought psychotic. I have been working with Esme's Umbrella for the last year, answering questions regarding CBS from family members, clients and vision professionals in North America. CBS is still relatively unknown and may be mistaken for hallucinations seen in dementia patients. As the baby boomer generation of the USA reaches the age when macular degeneration develops, it is vital that CBS be understood."

Not only do we need Gary Cusick's role to be replicated in the UK, but we also need specialist CBS nurses. Modeled on the way Macmillan nurses care for people who receive a cancer diagnosis, CBS nurses would do the same – liaising with ECLOs, ROVIs, GPs, sensory services, optometrists and ophthalmologists too, for the benefit of everyone in the family. Not being a charity, Esme's Umbrella is not in a position to fund these nurses but, potentially, one of the large charities could step in.

David Probert, Chief Executive of Moorfields, comments, "CBS can have a significant psychological impact on patients who are also having to deal with the impact of losing a vital sense. The condition is poorly understood across the healthcare world and there is no clear treatment nor support service that is universally available to support people with CBS. It is important to support efforts to improve the care available for these patients, and Moorfields is proud to support this initiative."

TH&IS commissioned the first CBS information video, which is available on the website, and is working now to make Dominic ffyche's training course for nurses and anyone interested in qualifying as CBS carers interactive online; the course will carry CPD points.

Obtaining a referral to ffytche's specialist national service for CBS has never been easy – mostly because the need to clone him is paramount – but now there are two new requirements in the Individual Funding Request process. The first is proof of exceptionality or rarity and the second asks for evidence of clinical effectiveness and previous treatment. As CBS is neither exceptional nor rare, and as there has been no research and no medication available, CBS patients fall at the first two fences. It is clear that the IFR is not fit for CBS purpose.

What would work? To have CBS included as part of specialist ophthalmologist services, so patients can access ffytche – and other doctors, yet to be appointed – through NHS commissioning. The complexities of achieving this are manifold and almost unintelligible to someone not familiar with the specialized terminology of NHS England.

Studies and research on treatment options are few. Michel Michaelides explains, "There are no studies of how CBS is managed by ophthalmology services in the UK. Clinical impression is that most ophthalmologists will explain the symptoms, reassure and signpost for further support. If CBS is clinically significant, it might be referred to a neurologist/neuro-ophthalmologist rather than be treated in a general ophthalmology clinic. There is no high-quality clinical trial evidence for the treatment of CBS."

> "AS THE BABY BOOMER GENERATION OF THE USA REACHES THE AGE WHEN MACULAR DEGENERATION DEVELOPS, IT IS VITAL THAT CBS BE UNDERSTOOD."

The words "clinical impression" and "might" illustrate the problem.

A few steps to create the much-needed medical and support pathway would save the healthcare system and social services millions. Giving evidence to the Minister for Loneliness, I explained how people living with severe CBS can find it impossible to distinguish between what is real and what is not. Eventually, they are too distressed and frightened to leave their homes – where they will require the input of social services. Others, who can no longer tolerate the terrifying or sexually explicit images, contemplate suicide. At the moment, if I speak to someone in this distressed state, I have to rely on the local low-vision charity to send an outreach worker on a visit, or suggest a phone call to the Samaritans. CBS needs to be included in The Campaign to end Loneliness.

Meanwhile, I am extremely grateful for all the help and support I receive from the ophthalmic sector as a whole – clinicians, nurses, ELCOs, ROVIs, and the charities. Insisting, quite rightly, that CBS needed a wider audience, Sandra Ackroyd and Tracy Atkinson from Sight Support Hull and East Yorkshire hosted an Information Day at York College in April of this year for me, and another is planned for Charles Bonnet's 300th birthday on March 13, 2020.

As readers will be well aware, media coverage of sight loss issues is low down on the health journalists' priority list. And yet, this is the sense that most people least want to lose. Unless there is a surgical breakthrough that restores sight, very little is written about the effect of a sightless world on everyday life. There is confusion,

too, in the public's mind between eye disease and conditions for which people wear glasses.

When I was a young actress, I appeared in an American play called Butterflies are Free, which is about a blind musician. I played his girlfriend and remember well the rehearsal days. The director insisted that the whole cast wore blindfolds all day, during lunch and coffee breaks too, so that we all gained some understanding of living in a sight-skewed or dark world. I will never forget the fear and helplessness that instantly took over – and that was only for a short time. When CBS appears, the loneliness and isolation already being experienced, is compounded by anxiety and depression, which often follow as quality of life takes a further downturn.

However, there is now considerable light at the end of the tunnel – not least from Rupert Bourne, Consultant Ophthalmic Surgeon at Cambridge University Hospitals, and Professor of Ophthalmology at Anglia Ruskin University, who encapsulates everything I am trying to achieve. He understands entirely the need for patients to receive a warning and for specialist nurses. Discussing CBS with me, he says, "One of the key features of CBS is that patients are fully or partially aware of their complex visual hallucinations that occur in the presence of vision loss. Given that the proportion of those with vision impairment who do experience CBS may range from 5 to 27 percent, it is beholden on clinicians, nurses and AHPs, like optometrists, to enquire about these symptoms, as it is quite possible that the prevalence may actually be much higher because of the stigmatization and fear of confiding, or of being considered mentally ill by relatives or health professionals. Correctly diagnosing CBS provides reassurance to the patient, but also means that the needs of the patient can be better assessed and managed. My clinical specialization is glaucoma, and when one asks about CBS symptoms in patients with glaucoma and vision impairment, I am always surprised how many patients do affirm these hallucinations and how often this has not been recognized by either the patient, the carer, or the clinical team. I think that enquiry about CBS symptoms should be a routine part of the history-taking by members of the clinical team and, often, this is best done by a nurse with awareness of CBS in advance of seeing the doctor or optometrist. Given that CBS may evolve during a patient's clinical follow-up, it is important to continue making enquiries at subsequent visits rather than presume symptoms will not appear after the first visit, when often the history-taking is most comprehensive."

CBS remained with my mother, Esme, for the rest of her life. Her confidence disappeared, as did her joie de vivre. She became exhausted with the constant need to "shunt her brain into another gear" to remove the hallucination – and then only temporarily. Waving her arms, sweeping the gargoyle off the table or clapping her hands took over her days. This was 10 years ago, but little has changed for the CBS community.

In 2020, no one should be left to cope alone when their life has been dramatically and negatively altered by what Charles Bonnet himself described as "the theater of the mind."

*Judith Potts is a health writer and founder of Esme's Umbrella – Awareness Campaign for Charles Bonnet Syndrome.*

## CBS PATHOPHYSIOLOGY

*Dominic ffytche, Reader in Visual Psychiatry at the Department of Old Age Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK*

Although CBS is linked indirectly to eye disease, the underlying mechanism occurs in the brain. Visual cortical hyper-excitability is a response to reduced neural input to the visual cortex as a result of retinal or visual pathway disease or reduced light transmission within the eye (such as cataracts or corneal opacity). In neurophysiological terms, the mechanism is referred to as deafferentation; in psychological terms it is referred to as "release" – the term adopted by ICD11. Visual cortical hyper-excitability results in spontaneous increases in neural activity experienced as CBS hallucinations. Functional imaging studies capturing the spontaneous increases have shown that the visual content of a hallucination depends on the location of the neural activity: if occurring in cortex specialized for faces, the hallucination is of a face, if in cortex specialized for objects, it is of an object. Cortical hyper-excitability also leads to increased background neural activity and enhanced responses to visual stimulation. These changes are only present for patients with CBS and it remains unclear why some patients with impaired vision develop cortical hyper-excitability while others do not.

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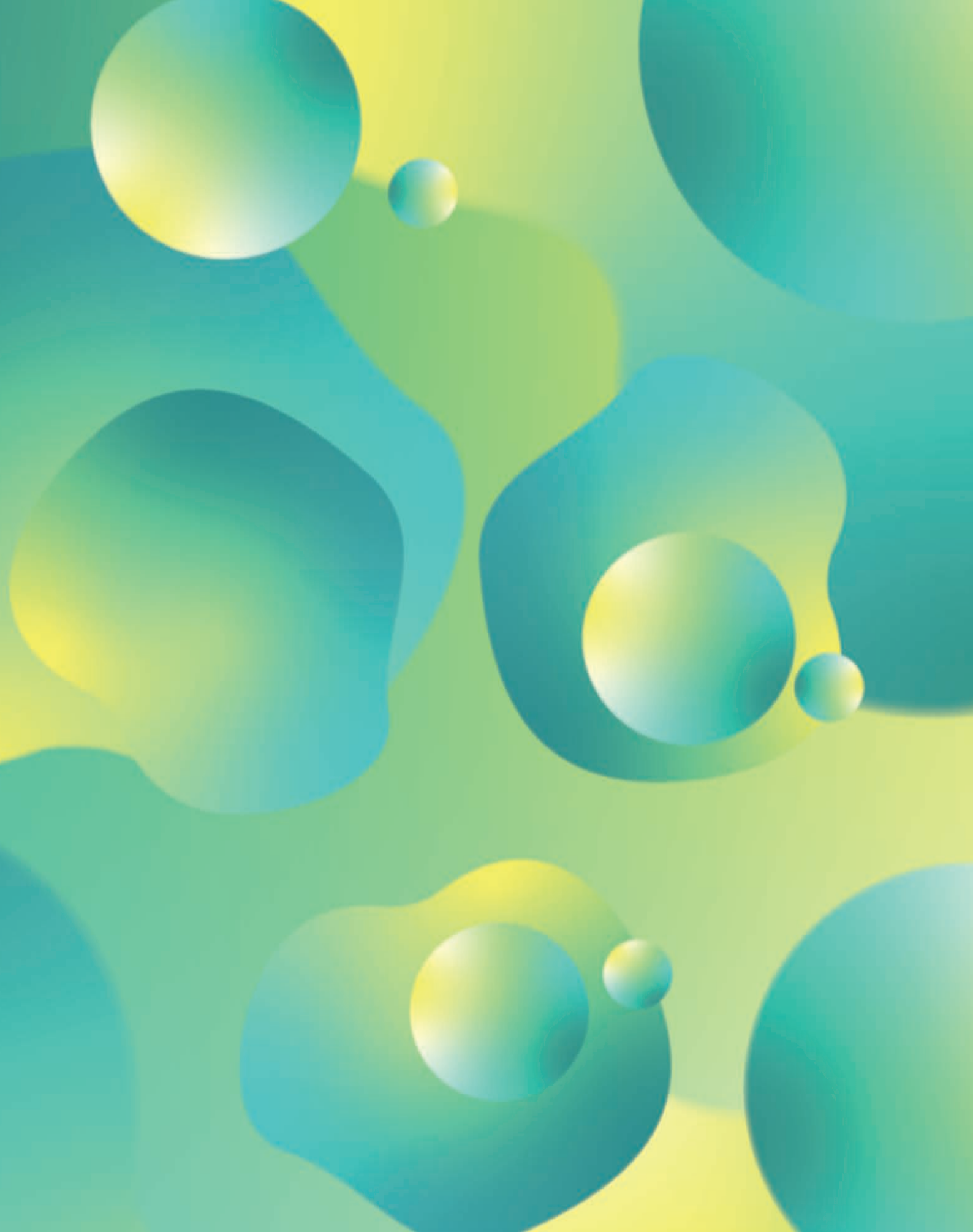
2. *City of London University, "Exploring support for family members and friends of people with visual impairment" (2019). Available at: https://bit.ly/2DckRtO. Accessed November 22, 2019.*


# THE INNOVATORS 2019

The field of ophthalmology is constantly breaking new ground. As one of the most inventive fields in medicine, ophthalmology is often at the forefront of cutting-edge technologies and treatments. Here, some of the leading innovators from the ophthalmic space present their latest offerings: from imaging and diagnostics, through software, to refractive surgery and glaucoma care.



# SEEING MORE WITH THE FIRST DIGITAL MICROSCOPE

*The ARTEVO® 800 from ZEISS: a paradigm shift in ophthalmic visualization*

A new era of visualization has begun with the ZEISS ARTEVO 800. Unveiled at the ASCRS meeting in May 2019, this first-of-its-kind digital microscope is now commercially available in both the US and Europe.

Developed in partnership with more than 300 ophthalmic surgeons, the digital microscope can be used as an imaging, information, and teaching tool in cataract, corneal, retinal, and glaucoma surgery.

The DigitalOptics™ technology produces a stereoscopic 3D image viewed using passive polarized glasses, which boasts 25 percent higher resolution than competitor modular systems (1). The 55-inch 4K monitor provides viewers with a natural-color impression of the surgical field and can be positioned anywhere in the operating room, providing the surgeon with a comfortable position and the rest of the team with a clear view. Data, such as intraoperative OCT, cataract assistance functions, and phaco vitrectomy values, as well as patient information and operating room settings, can be overlaid onto the active image without blocking the surgeon's view of the eye.

If the surgeon wants to use oculars at any point, a sterile knob can redirect a portion of the light to them. The screen remains in operation so other people in the room continue to see what the surgeon sees. However, speaking at the microscope's launch, Peter Stalmans, an ophthalmic surgeon from University Hospitals in Leuven, Belgium, who has used ZEISS digital visualization technology in operations on more than 1,000 eyes, commented that he had not needed to look through oculars in the past year and a half.

The device transmits 25 percent more light than conventional optics (2) so surgery can be performed at a reduced light intensity, providing the possibility of more comfort for the patient.

The depth of field is exceptional. More of the eye can be kept in focus so valuable surgical time is not spent on refocusing. For any adjustments that are necessary, a foot control pedal allows surgeons to control the microscope without interruption.

The ZEISS ARTEVO 800 integrates seamlessly with the ZEISS Cataract Suite to allow surgeons to access data and images from the cloud, with a one-click transmission to facilitate the process.

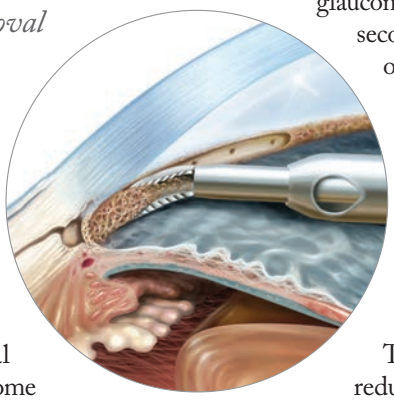
With 170 years of experience at the forefront of optics, ZEISS has set a new standard with the ZEISS ARTEVO 800 digital microscope. It's not just a digital system bolted on to a conventional set up, but an innovation that has been built from the ground up to smoothly integrate digital technology into optics specifically designed for surgery. Visualization, information, comfort, and workflow in the operating room have all evolved to meet the needs of the modern surgeon in a modern world.

*References*


1. *Measured comparing the number of vertical T V lines of a 4K 3D monitor with polarization using a resolution test chart ISO 12233 from Esser. Comparing the ZEISS ARTEVO 800 to a competitor's system on the same monitor with yields 1000 T V lines resolution for the ZEISS ARTEVO 800, and 800 T V lines resolution for the competitor's system.*
2. *Based on transmission calculation. Data on file. Increased optical transmission together with light sensitive ZEISS ARTEVO 800 cameras result in light reductions of up to 85 percent (according to Peter Stalmans).*

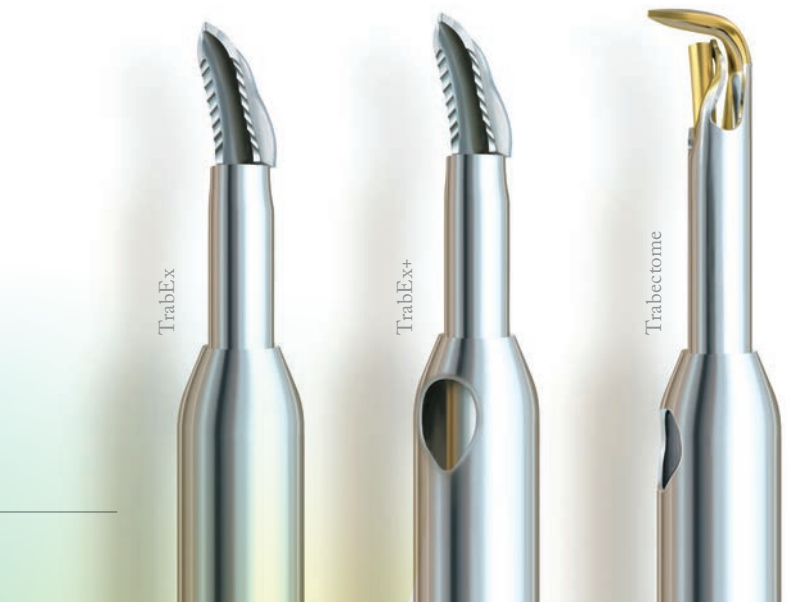
# EXCISIONAL GONIOTOMY, SIMPLIFIED

*Introducing the trailblazing line of MST Excisional Goniotomy devices: Trabectome, TrabEx and TrabEx+, designed for the complete removal of diseased trabecular meshwork*



The number of glaucoma patients is expected to exceed 88 million by the end of 2019 (1); the need for minimally invasive surgical glaucoma treatments has never been greater. Fortunately, pioneering surgical company MST has the answer: a range of excisional goniotomy devices. Commercially available in over 56 countries, the MST Excisional Goniotomy portfolio consists of the Trabectome and TrabEx product lines, designed to increase aqueous outflow and promote enduring intraocular pressure (IOP) reduction through the removal of diseased trabecular meshwork (TM)*. These devices facilitate complete edge-to-edge TM removal, providing lasting exposure of collector channels.

TrabEx boasts laser-sharpened, serrated blades that have been precision-engineered to cut, rather than tear, to facilitate safe, efficacious TM removal, while TrabEx+ adds the additional benefit of I/A for increased visibility during surgery. The Trapezoidal shape of the TrabEx blades, customize the excision to varying patient anatomies and TM's.




Notably, Trabectome uses electro-surgical ablation, rather than cautery, to completely fragment the diseased TM. All three devices also feature a rounded heel that guides the devices around the anatomical arch of Schlemm's Canal.

"The MST excisional goniotomy devices are the premier option for minimally invasive surgical glaucoma (MIGS) treatment," states Erik Bonn, Director of Commercial Development at MST. "These devices are indicated for a range of clinical scenarios: the management of pediatric or adult mild, moderate, or severe glaucoma; open or narrow angle glaucoma; primary or secondary glaucoma; as well as pseudoexfoliative or non-pseudoexfoliative glaucoma. This allows users of Trabectome and TrabEx to treat a wide range of patients."

How does that translate to the clinic? According to data collected over seven years – very well. Trabectome has proved to be a highly efficacious and easy-to-use surgical platform; clinical studies show that a significant majority of patients who had Trabectome surgery experienced a sustained IOP reduction to ≤21 mmHg – at least a 20 percent improvement from the IOP baseline – with no need for additional glaucoma surgery (2). The knock-on effect is that the Trabectome also results in a significant reduction in glaucoma medication use, which helps negate patient compliance issues (2).

MST's desire to improve on the results of existing MIGS devices has paid off. In its excisional goniotomy line, MST has provided a premium offering for the removal of diseased TM. By simplifying excisional goniotomy, Trabectome, TrabEx, and TrabEx+ make it easier for glaucoma and cataract surgeons alike to treat a broad range of patients – without the need for more invasive procedures (such as trabeculectomies and aqueous shunts). MST will continue to innovate in the glaucoma space and extend its complex surgery offering, delivering on its promise to improve vision for patients worldwide.

*For more information visit microsurgical.com.*

** TrabEx and TrabEx+ were formerly known as "Goniotome" and "Goniotome + I/A." Their product names are scheduled to take immediate effect in the US and April 2020 in Europe.*

*References*

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# BRINGING GLAUCOMA MANAGEMENT HOME

*The Icare HOME tonometer enables 24-hour IOP monitoring – any time, any place*

Experts predict that glaucoma – the second leading cause of global blindness – will affect 79.6 million people by 2020 (1). Lowering IOP is currently the only proven method for preventing or slowing down the condition. And that's why it is crucially important that ophthalmologists are able to accurately detect fluctuations in eye pressure to ensure treatments are effective – and that patients are complying with recommended regimens. However, the time, effort and cost of IOP monitoring mean that it's not possible for ophthalmologists to measure IOP with optimum frequency in the clinical environment, during office hours. Does this matter? Yes – given the high probability that important IOP peaks could be missed, leading to a worsening of the condition.

The Icare HOME tonometer offers patients and ophthalmologists an easy-to-use method for 24-hour IOP monitoring outside of the office environment, providing doctors with real-world diurnals in as little as a week. Developed by Icare Finland, a global leader in handheld tonometry, the device uses a rebound technique for measuring eye pressure that is barely noticeable; a very light, sterile probe makes momentary contact with the cornea, and then rebounds. The technology makes the Icare HOME the first tonometer that does not require any anesthetic, drops or air puffs for use outside the doctor's office. The HOME measures the deceleration of the probe and contact time, and uses a patented algorithm to calculate the IOP measurement. This puts the technology of the Icare clinical tonometer in the hands of a patient. Afterwards, the user can send the IOP measurements to a healthcare professional via the Icare CLINIC in a secure HIPAA compliant cloud for review and analysis.

The device includes automatic OD/OS recognition technology – an intelligent positioning assistant that guides correct alignment of the tonometer – and an automatic measurement sequence feature that can switch between "series" and "single" modes. Approved by the FDA over two years ago, the Icare HOME now qualifies for reimbursement via remote physiological monitoring. CMS classify these as permanent category 1 codes.

Regular – at-home – monitoring provides more reliable IOP information to the ophthalmologist, enabling them to better personalize treatment to each patient. The ophthalmologists benefit from improved clinical efficiency, and the treatment process is more convenient for patients. Moreover, by putting tonometry into the hands of patients, the Icare HOME could help improve patient engagement and therefore increase treatment compliance.

*For more information, see the FAQ: www.corcoranccg.com/products/faqs/rpm-icare-home-tonometer-icare*

*Reference*

1. *HA Quigley and AT Broman, "The number of people with glaucoma worldwide in 2010 and 2020", Br J Ophthalmol, 90, 3 (2006). PMID: 16488940.*

# THE NEW GENERATION: ELECTRONIC IOLS

*Restoring vision using a smart, active intraocular lens for cataract surgery*

SAV-IOL (Swiss Advanced Vision) is working towards the world's first active, electronic intraocular lens implant for cataract surgery through the R-TASC Project. This new lens represents a real leap forward in vision restoration: smart, real-time autofocus.

Current IOLs on the market suffer from optical compromises, including a limited visual accommodation range, loss of light or unwanted visual disturbances. One of the last unexplored terrains in the IOL field is the use of an active lens, which overcomes the optical limitations of traditional passive lenses.

SAV-IOL is striving to meet this challenge with the R-TASC Project by designing an innovative lens that is equipped with an autofocus system able to detect the distance of objects in its visual field. Mimicking the human lens, the autofocus system sends signals that trigger micro-pumps to alter the curvature of the optical membrane through liquid displacement – in real time; in fact, the process occurs at 0.2 seconds, a speed equivalent to the accommodation of a healthy human eye.

The design of an active system clearly requires careful consideration when it comes to the power source – especially in the eye. In the case of R-TASC, the device is powered by solar energy coupled with induction technology, which effectively charges the lens during use, reducing the need for patient interaction.

The lens is sited in front of the iris and, in the case of natural lens removal, is fitted alongside a monofocal lens. SAV-IOL has plans to develop an "app" that allows the lens to be modified remotely after surgery (for calibration, pre-set accommodation modes, and more).

The R-TASC project comes off the back of a short but fast-paced history of innovation. In 2016, SAV-IOL launched its first lens – a premium IOL with a patented extended depth of focus (EDOF) optical technology called "Instant Focus." In 2017, came Lucidis – an affordable refractive EDOF IOL that was very well received by the market. Following on from this success, Harmonis, a customizable EDOF IOL with an online configurator, was launched in 2018. In September 2019, SAV-IOL released specialized toric versions of Lucidis and Eden IOLs to correct astigmatism, completing its current portfolio of products.

By bringing active lenses to patients in a market that has yet to see progress in this area, SAV-IOL is securing its position as a true pioneer. And, despite being in development, R-TASC is much more than a pipedream; SAV-IOL is currently looking for an investment to raise the capital required to bring this lens to the market – and that will be a major step forward for the whole IOL field.

*For more information visit sav-iol.com.*

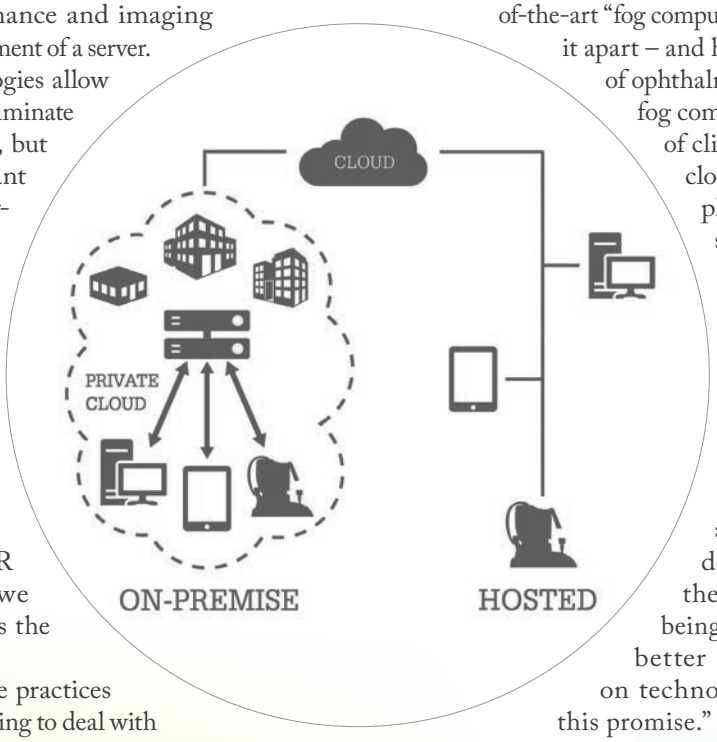
# FOG COMPUTING: MEETING CURRENT AND FUTURE NEEDS

*The newest release from EyeMD EMR Healthcare Systems harnesses fog computing architecture to deliver a system without compromise – significantly disrupting the ophthalmic electronic medical record marketplace in the process*

The pros and cons of different electronic medical record (EMR) systems can cause confusion and leave practices with a difficult choice to make… Client/server systems allow practices to achieve superior performance and imaging capabilities but require management of a server. Browser-based cloud technologies allow access from any browser and eliminate the need to manage a server, but come at the cost of significant limitations inherent in browser-based systems. Unfortunately, many ophthalmology practices do not have the in-house expertise to fully understand the impact of selecting one solution over the other. And yet they are forced to make technology infrastructure decisions that will have an effect throughout the lifetime of the practice. EyeMD EMR simply asked, why can't we develop a system that merges the benefits of both?

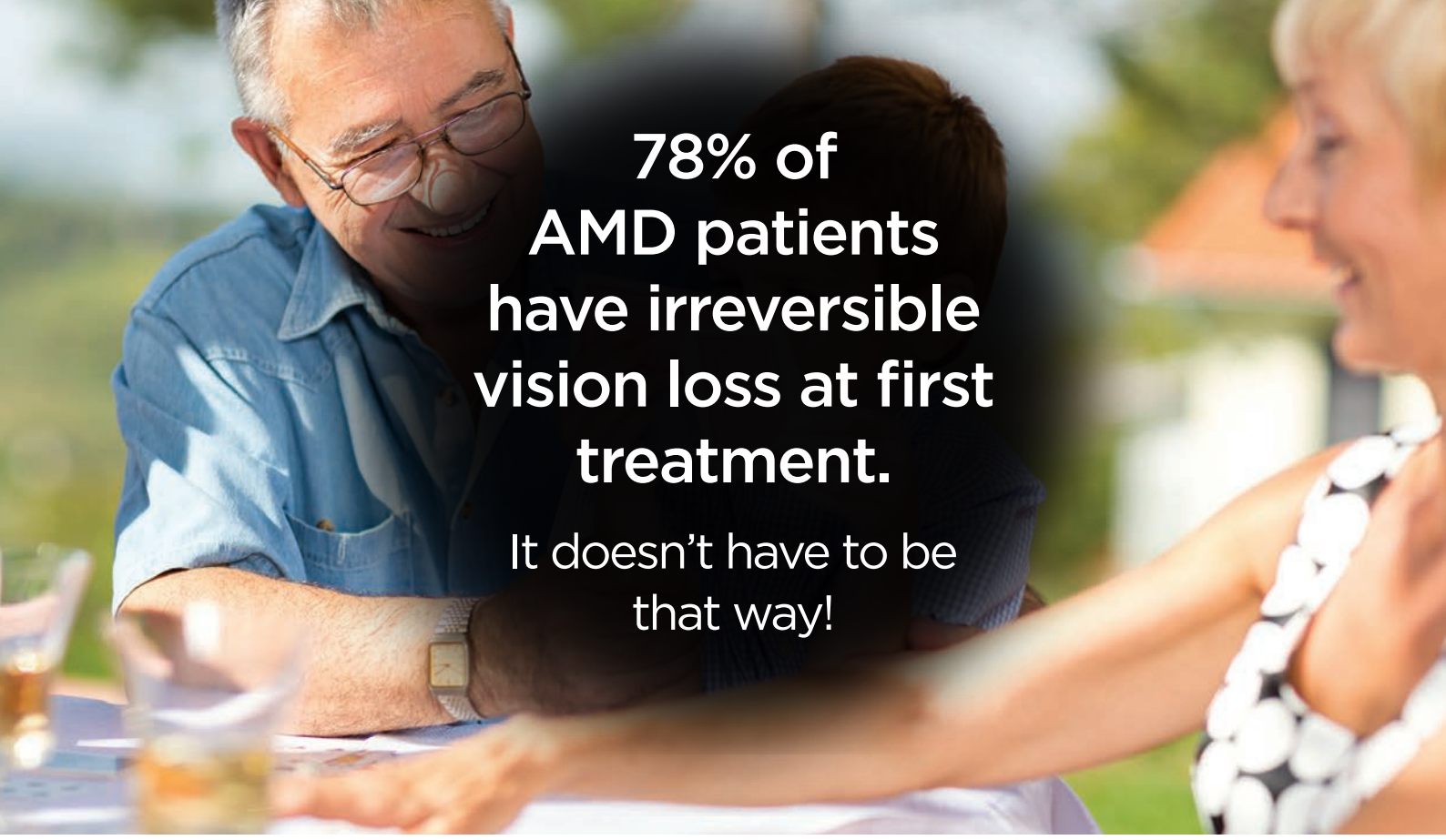
"We recognized that some practices wanted to move away from having to deal with a server, but we knew that moving to a browser-based system would negatively impact the performance and capabilities of our Client/Server system," says Abdiel Marin, CEO of EyeMD EMR. "The result was EyeMD EMR 2.0."

The new system's technological innovations, including state-of-the-art "fog computing architecture" are what sets it apart – and helps better address the needs of ophthalmic practices. In simple terms, fog computing combines the benefits of client/server and browser-based cloud systems into one superior platform, giving practices a system with the power and flexibility to adapt to current and future needs.




But the company has already set its sights on the future. Marin adds, "Although our products and services help practices improve workflow efficiencies and assist in the medical decision process, we believe the future lies in our products being able to help doctors become better doctors. We are working on technologies that will deliver on this promise."

*For more information visit eyemdemr.com.*

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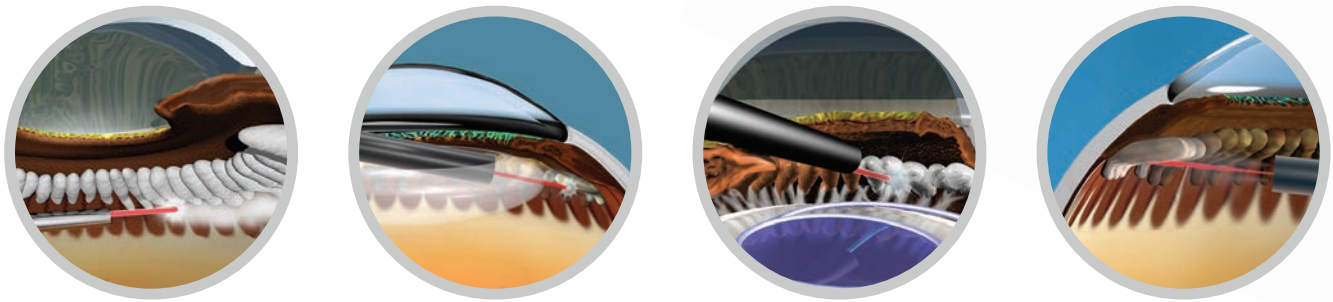
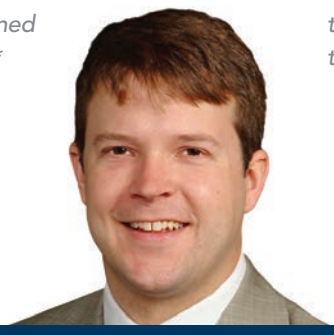


*"ECP-Plus is an effective treatment for refractory and ultra refractory glaucoma. Our 2 year data shows outstanding sustained IOP lowering and medication reduction."**

— Brian Francis, MD, MS



*"Combining ECP with a variety of other MIGS procedures allows me to offer a balanced therapy that is tailored to each patient."*

— Nathan Radcliffe, MD

**endooptiks.com**

**bvimedical.com**

*Tan, J.C.H., Francis, B.A., Noecker, R., Uram, M., et. al. Endoscopic Cyclophotocoagulation and Pars Plana Ablation (ECP-Plus) to Treat Refractory Glaucoma. J. Glaucoma, May 14, 2015. doi:10.1097/IJG. 278



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# In Practice

*Surgical Procedures*
*Diagnosis*
*New Drugs*

# In and Out

## Could combining inflow and outflow procedures be a new strategy for combating glaucoma?

*By Philip Bloom*

The most common first-line medical treatment for glaucoma is a prostaglandin analog eye drop. In addition to prostaglandins, beta-blockers, alpha-adrenergic agonists, carbonic anhydrase inhibitors and other traditional medications, we now have new pharmacologic additions, such as nitric oxide-donating compounds, Rho-kinase inhibitors and a variety of fixed combination options. In total, there are around nine different classes of glaucoma medications from which physicians mix and match to get a patient to their target intraocular pressure (IOP). An effective and useful strategy is to combine medications with different mechanisms of action to achieve an additive effect.

Although pharmacologic treatment remains the backbone of glaucoma therapy, there has also been incredible innovation and growth in the surgical device arena. Some of the procedures, such as the iStent Trabecular Micro Bypass (Glaukos), have safety profiles that arguably compare favorably to the side effects of topical medications. And yet, though it is common for a patient to be on a number of topical medications, it is not common practice to combine more than one minimally invasive glaucoma surgical procedure (MIGS) to achieve the same end. I would argue that this strategy should be considered more frequently.

*"Although pharmacologic treatment remains the backbone of glaucoma therapy, there has also been incredible innovation and growth in the surgical device arena."*

### At a Glance

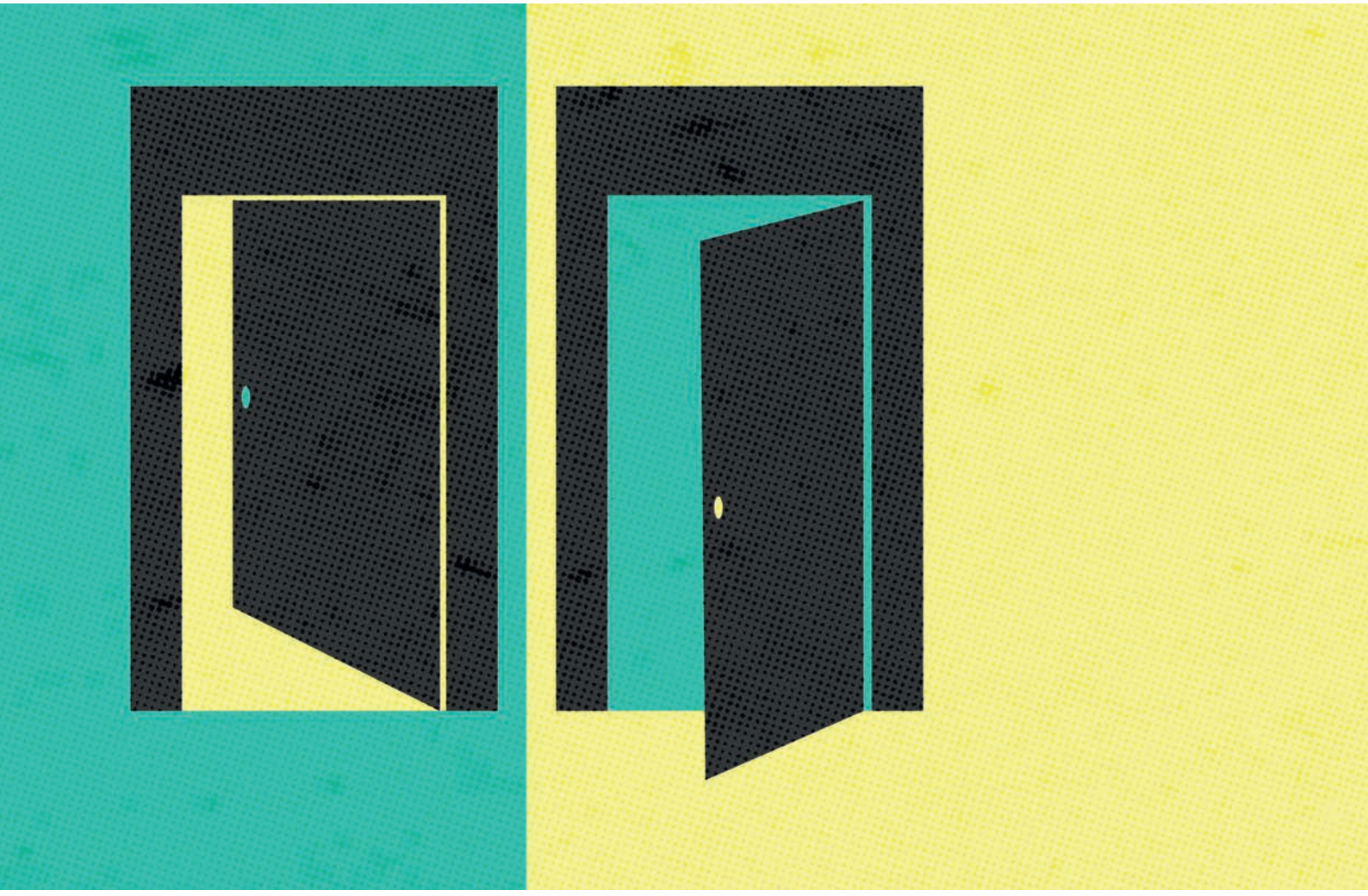
- *Although pharmacologic treatment remains the backbone of glaucoma therapy, there has also been incredible innovation and growth in the surgical device arena, not least MIGS*
- *While it is common for a patient to be on a number of topical medications, it is not common practice to combine more than one MIGS procedure to achieve the same end – though perhaps it should be*
- *Combining procedures – such as ECP with the iStent (3) – makes sense; there is a growing body of real-world experience, both in terms of efficacy and safety*
- *Though a practice still very much in its infancy, combining procedures should be given the same consideration afforded to the combination of pharmaceutical agents with different mechanisms of action.*

### Affirmative action

In the same way that we combine topical hypotensive drops to impact inflow and outflow in a sequential approach to strengthening therapy, we can combine MIGS procedures to augment IOP control; this can be in the form of multiple similar devices or by combining devices with different mechanisms of action. The procedure I have performed most commonly to reduce aqueous inflow is endoscopic cyclophotocoagulation (ECP). The ab interno procedure shrinks and effaces the ciliary processes in a controlled and titratable manner, resulting in an effective reduction of aqueous humor production. A review of several published studies of ECP shows a reduction in IOP between 18 percent and 47 percent in patients across the spectrum from moderate to severe disease states (1).

I feel that it is most beneficial to treat a full 360 degrees of the ciliary epithelium, applying laser both to the ciliary processes and the intervening crypts. I use the EndoOptiks E2 laser and endoscope system (Beaver-Visitec International, Inc.); I prefer a curved probe, which allows me to treat approximately 270 degrees through a single incision, then treat the remainder of the ciliary ring via a second incision. The laser is generally set between 200 and 300mW and the ciliary processes are treated sufficiently to cause them to shrink and whiten, but not to pop. Though the safety profile is favorable (2), it is necessary to plan for inflammation following ECP. An intracameral steroid at the completion of the procedure is ideal, and I generally prescribe frequent post-operative steroid drops and topical NSAIDs as well.

In combination with ECP to reduce aqueous production, it is possible to use any of a number of MIGS procedures



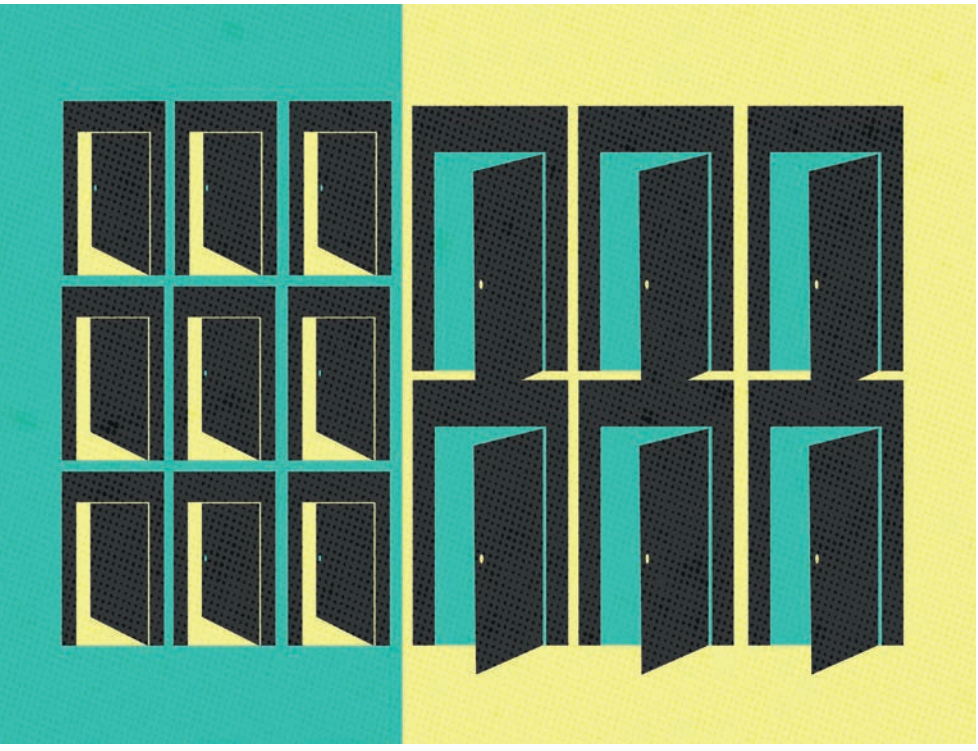
aimed at improving aqueous outflow. iStent and Hydrus microstent (Ivantis) can augment trabecular outflow, while Trabectome (Neomedix) or Kahook Dual Blade (New World Medical) can be used to remove trabecular meshwork to bypass the traditional outflow pathway. The rational combination of ECP with the iStent has already been described in the literature (3); there is a growing body of real-world experience with both techniques in terms of both efficacy and safety.

## iStent and beyond

The release of the iStent inject has only increased adoption and success with this device. The iStent inject system deploys two separate stents, increasing the probability of accessing the collector channels. Studies have shown that placement of multiple stents does positively titrate treatment (4), and the new device also eases implantation with a direct, perpendicular approach to the trabecular meshwork, rather than circumferential; iStent designs continue to evolve in an attempt to further improve efficacy. The Hydrus microstent also aims to improve the traditional outflow system, dilating and scaffolding Schlemm's canal to augment outflow of aqueous humor. The 8-mm-long Hydrus spans an entire quadrant, potentially providing access to numerous collector channels in this region, but there is not as much clinical experience with this newer device as with iStent.

Goniotomy performed using the Trabectome lowers IOP by selectively removing the trabecular meshwork and inner wall of Schlemm's canal from 90 to 120 degrees of the nasal angle. This device uses a micro-electric cautery system. The Kahook Dual Blade is a similar, minimally invasive but single-use approach, providing aqueous direct access to the collector channels and distal outflow system by removing a section of trabecular tissue procedure.

The suprachoroidal space provides a further potential drainage route, analogous in some ways to the uveo-scleral outflow route promoted by some



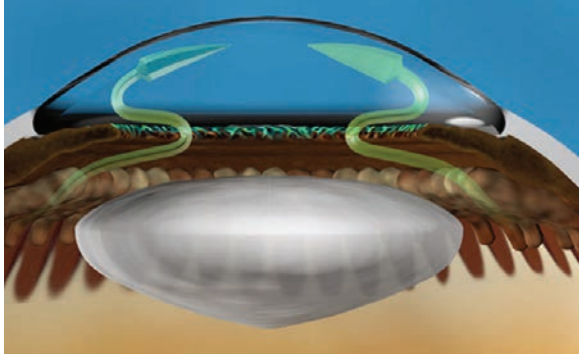


Figure 1. ECP is an aqueous inflow reducing procedure. Combining ECP with other outflow procedures offers a balanced surgical solution for the patient that follows the same line of thinking used when offering inflow and outflow medications.

medications. The CyPass (Alcon) was the first device to work in this way but has recently been withdrawn over concerns regarding adverse effects on the corneal endothelium. For some clinicians, this setback sounded a precautionary note over widespread early adoption of new technologies, though for most experienced surgeons, it merely reinforced the need for a full and candid discussion of the risk-benefit ratio of any form of surgical intervention.

Evidently any surgical procedure has risks, but MIGS procedures generally have fewer serious complications than traditional penetrating surgery, making them more attractive for both patients and surgeons than a trabeculectomy, at least in the early stages of treatment. When we combine one of these new approaches to increasing aqueous outflow with ECP, still the only widely-available treatment to decrease aqueous production and secretion, we have highly effective glaucoma treatment with an excellent safety profile.

## Consider combining

It behooves those planning healthcare to ensure that any new procedures are both clinically- and cost-effective before widespread adoption, particularly in areas of nationally funded health services. When considering clinical and financial benefit, some have expressed concerns over the cost of MIGS outflow procedures compared to their efficacy, especially when stacked up against the relatively low cost of topical drugs in the UK. In this regard, it is important to consider not just high device costs (iStent, Hydrus) but overheads, such as initial setup (ECP, Trabectome), and savings afforded by using MIGS, consequent upon reduced need for follow up consultations compared with traditional surgery (trabeculectomy or tubes).

MIGS in general, and ECP in particular, are enjoying a quiet crescendo as surgeons realize that they can add these procedures to phacoemulsification in patients with combined cataract and glaucoma for little extra cost; indeed, if one factors in reduced need for follow-up consultations compared with trabeculectomy, MIGS procedures may work out ultimately to be more cost-effective.

Combining MIGS inflow and MIGS outflow procedures is still very much in its infancy in Europe, and I acknowledge that it is not currently widely accepted. But when it comes to evaluating efficacy, I believe that combining an inflow and an outflow procedure should be given consideration in a manner analogous to the combination of pharmaceutical agents with different mechanisms of action.

*Philip Bloom is a Consultant Ophthalmologist for the National Health Service, UK.*

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# A NOD to Affirm Performance

**Surgeons need to know if they are making the cut – and that requires expensive, time-consuming performance appraisals. But it doesn't need to be that way. The Royal College of Ophthalmologists National Ophthalmology Database (RCOphth NOD) Audit can provide richer outcomes analysis than any single individual or institution could ever achieve – and at less cost.**

*By John Sparrow*

We all like to know how well we're doing – and we are increasingly obliged to ensure that we have that knowledge to hand. Indeed, performance assessment – as measured by patient outcomes – is now a key part of ongoing professional development for surgeons. But measuring performance criteria can be onerous; even a local audit in a representative group of patients is very time consuming, especially if it involves accessing and analyzing hard copies of medical records. Furthermore, medical time is expensive; it just doesn't make economic sense for each surgeon to spend hours analyzing their own performance.

## *At a Glance*

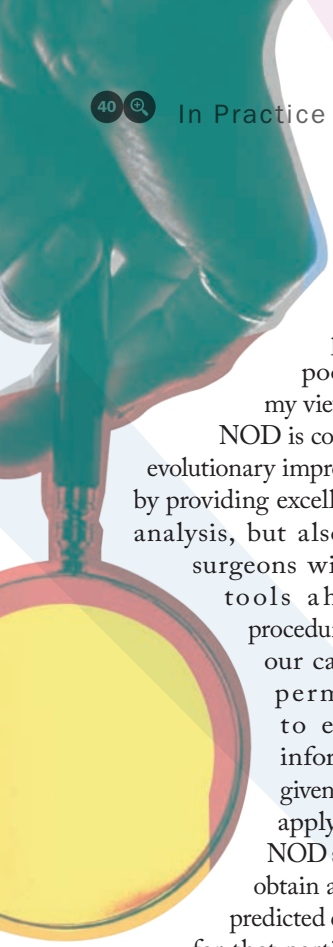
- *Increasing adoption of electronic medical records throughout the NHS provides opportunities to improve outcomes via data analysis*
- *The RCOphth NOD Audit is capitalizing on this information source to assess cataract patient outcomes per center and per surgeon throughout England and Wales*
- *By virtue of the richness of these data, the Audit can also employ statistical models to identify high-risk patients, enabling them to be allocated to more experienced surgeons*
- *Future developments include expansion of the Audit into other parts of the UK and into non-cataract ocular conditions.*

### Deep analysis, fair appraisal

The RCOphth NOD Audit exists to provide performance analysis for ophthalmic surgeons, at least for those who use electronic medical records (EMRs). Obviously, this saves surgeon time – and reduces costs to the NHS – but there is far more to the RCOphth NOD Audit than that. Because we have outcomes data from all over the country, we can present individual surgeon performance measures in the context of peer performance; understanding comparative positioning can be very informative. At the same time, we provide richer analysis, resulting in more accurate appraisal: in particular, we can allow for risk when assessing surgical outcomes. For example, if a surgeon's case-list is skewed towards complex, difficult operations, the RCOphth NOD Audit would take account of that by adjusting for the complication risk associated with those patient profiles (see Figure 1). In practice, the adjustment gives credit to surgeons who take on difficult cases, rather than penalize them through an outdated appraisal process that can only record good or bad outcomes. In other words, the RCOphth NOD Audit creates a level playing field.

### Wider coverage, better outcomes

As the Audit has become better established over the last 10 years, its coverage has increased: our most recent report is based on data from over 100 cataract surgery centers in England and Wales, comprising about 218,000 cataract operations for the reported one year period – which is over half the cataract procedures performed in the targeted geographical area (1). During this period we have seen changes in surgeon behavior, resulting in better outcomes – not least, an almost 40 percent reduction in the overall complication rate from 2010 to 2018, which translates to



over 3,000 fewer patients with poor outcomes. In my view, the RCOphth NOD is contributing to this evolutionary improvement, not just by providing excellent retrospective analysis, but also by providing surgeons with informative tools ahead of their procedures. In particular, our calculator facility permits surgeons to enter clinical information about a given patient, and then apply the RCOphth NOD statistical model to obtain an estimate of the predicted complication risk for that particular procedure in that specific patient. This in turn allows high-risk cases to be directed to the most experienced surgeons, while more straightforward cases can be allocated to the trainees. And that's the true power of the Audit; it focuses minds, and makes surgeons more aware of the need to be very careful in certain high-risk cases. Ultimately, the Audit benefits patients, which is what makes our work so important.

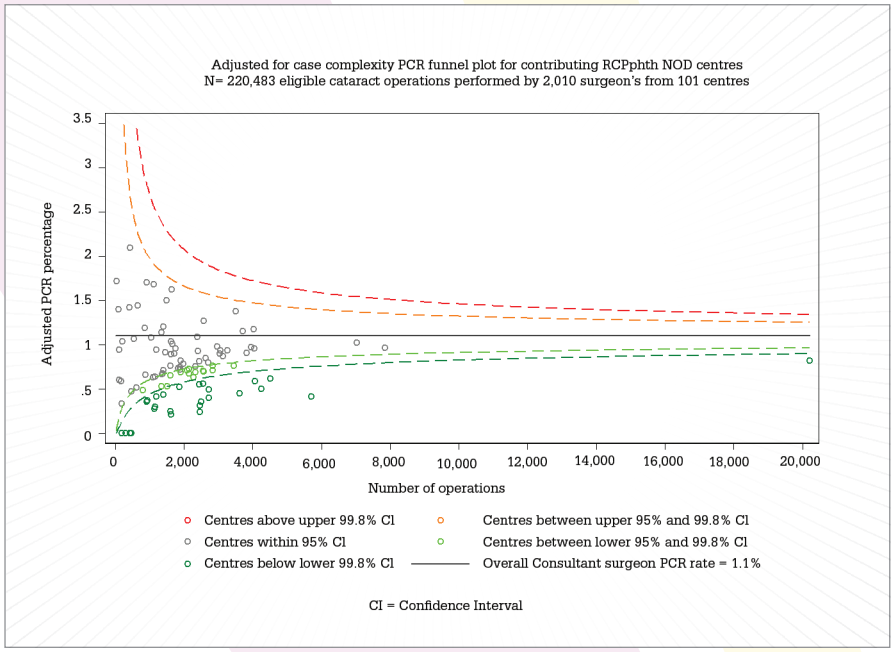



Figure 1A. Case complexity adjusted PCR outcomes for individual surgeons with lines of acceptable practice for the period 1 September 2017 to 31 August 2018.

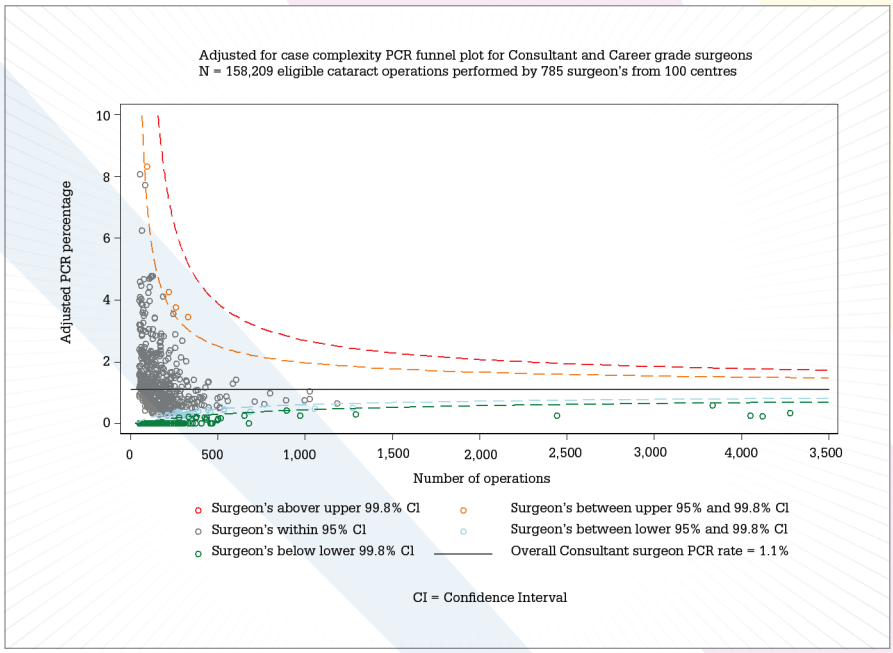



Figure 1B. Case complexity adjusted PCR outcomes for participating centres with lines of acceptable practice for the period 1 September 2017 to 31 August 2018.

## Evolving capabilities

To date, the Audit has focused on cataract surgery outcomes, but the plan is to extend our analysis to other conditions, with an initial focus on areas that practicing ophthalmologists have told us are most important to them. In general, for those hospitals that use EMR systems, we would be able to analyze and report on other procedures just as we do for cataract surgery; you could say our cataract surgery audit is a proof of concept.

In fact, we have already taken the first steps towards broadening our remit: namely, feasibility studies on the application of our methodology to age-related macular degeneration, glaucoma, diabetic retinopathy and retinal detachment surgery. Some of these reports are freely available on the NOD website (2). We will first focus on AMD. Why? It's high volume, very expensive, and extremely important to patients and healthcare providers alike. And consider this: the UK NHS spends an estimated £500 million per year on AMD drugs – and doesn't know what the outcomes are! That is clearly unacceptable; unfortunately, the NHS prefers not to fund a RCOphth NOD AMD audit at present, despite our proven ability to implement this kind of outcomes analysis. Perhaps that's a reflection of the current

budgetary environment.

Glaucoma is another area I'd really like to target, not least because it happens to be a particular interest of mine. But this will be a challenging condition to include in the Audit – unlike cataracts, where treatment periods are relatively short, glaucoma is lifelong, and its management goes on for extended periods, typically 15 to 20 years. And that means each patient is likely to have significant hospital records – and, very often, much of those records will be in paper form. Just to enter all that information into an EMR would be a significant task – a point illustrated by our pilot study on auditing glaucoma treatment via the RCOphth NOD. We looked at the single measure of visual field preservation among patients attending five glaucoma centers, and found that it was possible to link clinical data with relevant visual field outcomes, but that there were issues with regard to IT implementation and to getting older medical records entered into the EMR. We concluded that a comprehensive RCOphth NOD Audit for vision preservation in glaucoma is not a short- or even medium-term goal – it will take 10 or 20 years.

But the real barrier to the evolution of the Audit is the availability of funding. When we started this initiative, we had no external resource – we were just enthusiasts doing something we thought worth doing. Later on, we attracted some financial support which we used to employ a statistician; we continued to build up our expertise in that piecemeal way until we received five-year funding from the Healthcare Quality Improvement Partnership (HQIP), the intent of which was to get the Audit established. These funds have now run through, so we are looking into other sources of support; for example, from participating centers and lens implant manufacturers. We've had encouraging responses from many centers who recognize the benefits of participation in the audit and are willing to pay a subscription, as well as some positive discussions and contributions from lens manufacturers. Furthermore, there might be a benefit to the cessation of HQIP funding in that, in future, we will be able to include Scotland and Northern Ireland in the Audit – we couldn't do that while in receipt of HQIP monies. So Northern Ireland will be included in the RCOphth NOD from 2020, and we're planning on how and when to get Scotland to participate too. However, until we get money in the bank, we are in survival mode.

## Post survival

Assuming that funds are not limiting, what does the future hold for the RCOphth NOD Audit? Firstly, I look forward to being able to report on all the cataract surgery being done throughout the UK, including Scotland and Northern Ireland. This wider audit will allow us to provide ever better guidance for surgeons and reassurance for patients – and, I believe, it will enable us to show patients that it doesn't matter which hospital they choose for their cataract procedure, because all NHS eye surgery departments are doing well. And that, I think, is a very important message. Secondly, I anticipate that expansion into non-cataract conditions, such as AMD – and eventually glaucoma, will enable us to ensure that these patients are also getting the right treatment and the best outcomes. But regardless of what the future holds, I am delighted with what we have done with the RCOphth NOD Audit to date. We are now international leaders in the ophthalmology auditing field; though I admit this is partly due to our single NHS system, in which many patients are treated in EMR-compliant treatment centers. In these participating hospitals the RCOphth NOD has the capability to access to the entire record of each patient – which provides us with a richness of data that other countries, with other systems, simply cannot match.

Others have started to move in the same direction as the RCOphth NOD – for example, the Intelligent Research in Sight (IRIS) Registry in America – but, I understand, with only mixed success. We in the UK are very fortunate to have a dataset that is both very large and very rich; it's what enables us to provide unique advantages to ophthalmological services stakeholders, such as adjusting for complexity on a case-by-case basis. No other large-scale audits can offer that kind of benefit.

*John Sparrow is a Consultant Ophthalmologist at the Bristol Eye Hospital, an Honorary Professor at the University of Bristol, UK and the Clinical Lead for the Royal College of Ophthalmologists NOD Audit.*

*He is the chief investigator for an NIHR funded cataract research program (RP-PG-0611-20013).*

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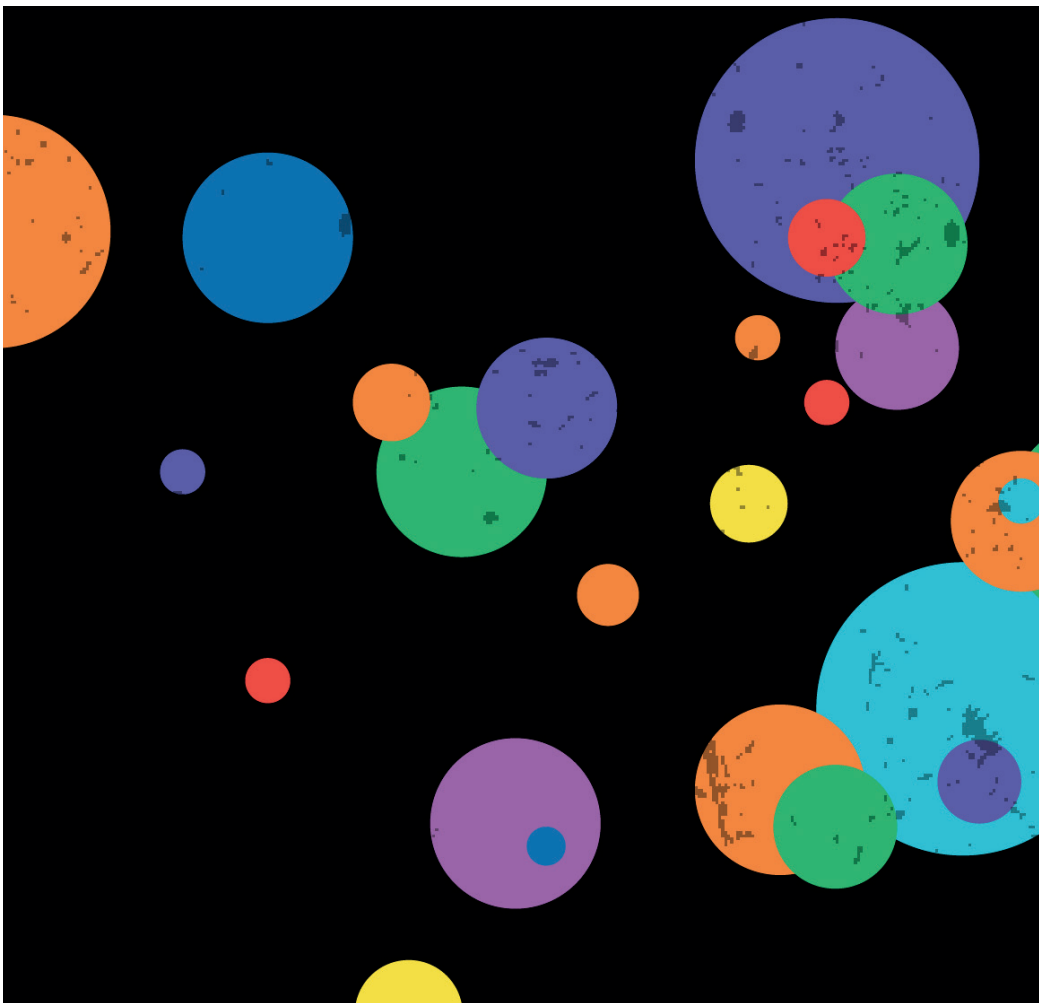
# Quantum Leap?

## Electrical stimulation of neural responses can significantly improve outcomes for retinitis pigmentosa patients

*By Jim Taylor*



While I have been involved in ophthalmology since 1999, my career in the medical device industry started with CAT scanners, as well as ultrasound machines and other devices in fields including cardiology, critical care and anesthesia. I migrated into ophthalmology in the laser therapeutic space as President of Coherent Medical, and have been in the field ever since. I'm now at a point in life where I try to spend my time only on developing new technologies that will make a significant difference to patients – opportunities that can truly change healthcare for the better. With some recent innovation, where might we find such step-change opportunities in ophthalmology today?

### *At a Glance*

- *Dysfunction and death of retinal cells, and consequent vision loss, can be inhibited by direct electrical stimulation of vulnerable cells in the visual pathway*
- *We achieve this effect not by invasive, bulky implants that generate unnatural visual stimuli, but by intravitreal injection of a colloidal suspension of nanoparticle devices that support natural vision*
- *These "quantum dots" diffuse into the retina where they transduce visible light energy into electricity, thereby triggering action potentials in adjacent neural cells and preserving function*
- *Our initial field of focus is retinitis pigmentosa; we are following encouraging Phase I results with a controlled, 15-patient clinical trial, expected to be complete by the end of 2020.*

### Quantum shift

The answer to that question lies partly in the shifting demographics of emerging markets (aging populations will increasingly suffer from age-related, back-of-the-eye diseases) and partly in an appreciation of the direction of research throughout the last 20 years (which, with a few worthy exceptions, has been heavily directed at refractive, front-of-the-eye conditions). Going forward, the next 20 years will see much of the research efforts focused on the retina – and that is why I am working on the ophthalmological application of nanoparticles known as quantum dots (see box: Quantum dots).

The rationale behind our approach is very simple. In many retinal diseases, cellular degeneration and vision loss involve dysfunction or death of photoreceptors and/or associated neurons in the visual pathway – but you can inhibit this process, and maintain functionality, by directly triggering activity in visual

*"I'm now at a point in life where I try to spend my time only on developing new technologies that will make a significant difference to patients."*

pathway neurons. We achieve this via intravitreal injection of quantum dots. It's an entirely new approach to the retinal implant concept, and it is potentially applicable to any condition associated with retinal degeneration. So how does it work? Briefly, it's a sophisticated take on an idea that was around well before Mary Shelley wrote Frankenstein – namely, electrical stimulation of neural responses.

Prior to the use of quantum dots, the electrical innovation approach relied on invasive, retinal implants: for example, the Second Sight "Argus" device. But these types of retinal prostheses have some fundamental drawbacks: the invasive nature of the implantation procedure limits their use to patients who have lost almost all vision, and the nature of the device is such that it presents the brain with a stimulus that the visual system must learn to interpret. Our approach, by contrast, involves the application of a suspension of quantum dots. The size and construction of these particles are such that they easily diffuse into and across the retina, assisted by the natural processes of the eye which move the vitreous through the retina. In effect, we are using the vitreous as a reservoir to supply quantum dots to visual neurons.

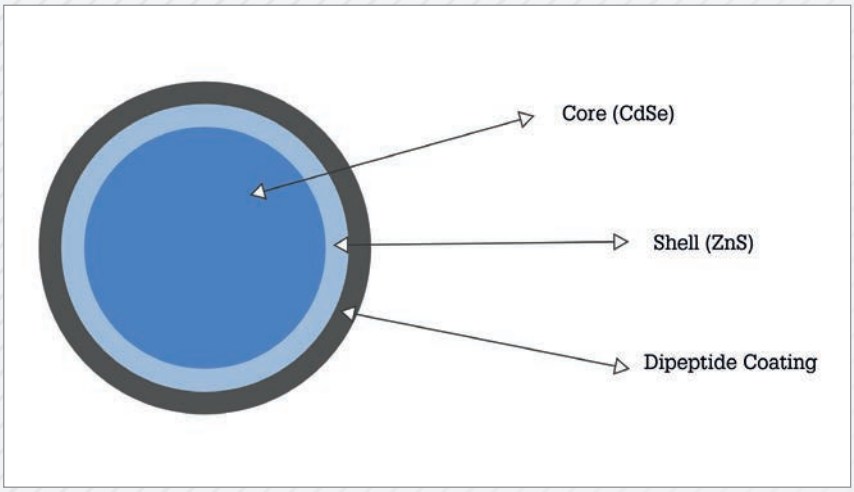
## Quantum effect

The quantum dot mechanism of action is strikingly simple. While in the retina, the nanoparticles are stimulated by visible light entering the eye – and if a quantum dot is stimulated while it is in close proximity to a neural cell, it triggers an action potential in that cell which is interpreted as vision by the brain. Thus, the effect of photovoltaically active nanoparticles diffused throughout the retina is to electrically stimulate a large range and number of neuro-retinal cells. This form of direct stimulation has been reported (1-3) to prevent cell death in the ganglion cell layer, inner nuclear layer and outer nuclear layer, the latter of which contains photoreceptor cell bodies.

In this way, administration of photovoltaic quantum dots to the retina may preserve the function and extend the lifetime of photoreceptor-dependent neurons, thereby arresting the visual decline associated with degenerative diseases of the retina. Furthermore,

## Quantum dots

- Nanoscale-sized, biocompatible semiconductor crystals
- Exhibit photovoltaic response – conversion of light into electricity – when illuminated by particular wavelengths
- Optoelectronic properties change as a function of size, shape, material and coating: hence, Quantum Dots can be designed such that they are excited only by particular wavelengths in the visible light range
- Voltaic response therefore can be fine-tuned to correspond to light of strictly defined wavelength
- Quantum Dot technology developed by 2C Tech (Irvine, USA) is based on a cadmium-selenium crystalline core encapsulated in a zinc sulphide shell, which is itself coated by a hydrophilic dipeptide
- This design supports formulation as a colloidal solution, protects the metallic elements from oxidative damage, and enhances efficiency of photovoltaic response
- In vivo injection is followed by diffusion and eventual elimination by normal biological processes




this effect may be achieved without the invasive surgery required for fixed, permanent implants – all that is needed to administer quantum dots is a standard intravitreal injection, just like the millions already given to AMD patients across the globe. Moreover, the injected aliquot can be very small – a volume far less than that of a sharpened pencil point holds over 12 trillion quantum dot nanoparticles!

The original work on quantum dot-mediated electrical stimulation of visual neurons was carried out by Jeff Olson at the University of Colorado. Using the Royal College of Surgeons rat model of inherited retinal degeneration, he showed that quantum dots could enhance cell survival and visual function (4). Subsequently, our preliminary, open-label clinical trial in Mexico assessed the safety of quantum dots in 20 patients with severe RP-associated vision loss. No significant treatment-related adverse events were recorded; one person had a heart attack, which was unrelated to treatment, and another had self-resolving injection-site inflammation, which is not unusual for the intravitreal administration route. But, perhaps more interestingly, 78 percent of the patients reported subjective improvements in visual function: for example, brighter and clearer vision. One patient said she'd been able to cook dinner for the first time in seven years; another reported that he'd been able to walk down the street without stepping in so many puddles. And when there was an effect, it was rapid – benefits were seen within weeks, if not days. These are anecdotal accounts, of course, and the trial was not controlled, but they are nevertheless suggestive of an encouraging quantum dot effect. It's worth noting that these patient accounts were independent; they were not in communication with each other.

### Joining up the dots

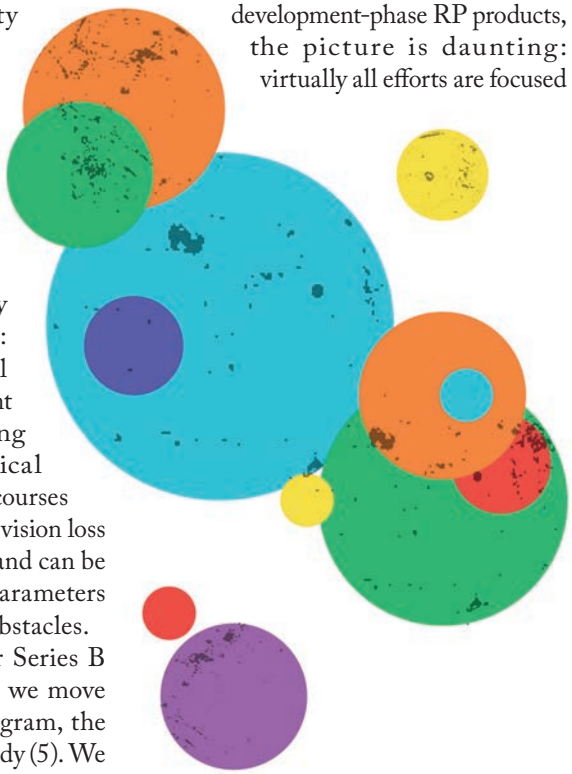
These data on the potential efficacy of quantum dots supported our recent fundraising activities. We've now had two phases of Series B funding: the first allowed us to address a number of questions regarding the design of a controlled clinical trial, and the second will pay for the trial itself. A key outcome from the first of these two phases was obtaining the regulator's agreement that although an injectable quantum dot product looks like a drug, it is, in fact, a device. This is because there is nothing "pharmacological" about quantum dots – they don't bind to or otherwise engage cells, they just provide electrical stimulation on their way through the retina. Another key

point was that we were eligible for the FDA Early Feasibility Study pathway, which means we have a relatively low-cost route for early clinical studies. Basically, this pathway is the FDA's way of encouraging companies to conduct early trials in the US rather than in other countries. Thirdly, the FDA agreed with our proposal to use functional vision – navigation of a mobility course – as a clinical end-point rather than solely relying on visual acuity and other similar standard endpoints. Our mobility course was developed by Ora and is conceptually similar to the one used by Spark Therapeutics, which resulted in the company getting clearance for its product. The ORA mobility test is a sophisticated design: it can be configured to control lighting in a variety of different physical locations, enabling efficient multi-center clinical trial use. Ora-VNC mobility courses accommodate various types of vision loss as well as different severities, and can be customized with regard to parameters such as color, contrast, and obstacles.

The second tranche of our Series B will support the company as we move forward with our clinical program, the US-based Early Feasibility Study (5). We intend to engage three sites; at present, we are confirming the arrangements, and carrying out the final phases of preclinical work – demonstrating that the product batch is non-toxic, for example. Getting this work completed will be the last hurdle to jump through before being granted investigational device exemption by the FDA, which we must have prior to initiating our controlled, 15-patient clinical trial in early 2020. We expect to have the final data by the end of 2020. Overall, the clinical development will be relatively straightforward – one byproduct of addressing an unmet need where there are no other therapies makes our trial far less complex.

## Quantum of solace

At this point, we are entirely focused on retinitis pigmentosa (RP) – it is a highly unserved market and RP patients desperately need effective therapeutic options. Even if you include development-phase RP products, the picture is daunting: virtually all efforts are focused on gene therapy or stem cell therapies. When you consider that there are more than 40 gene defects associated with RP, and that each defect could require development of a separate gene or cell therapy, it is clear that these approaches are unlikely to provide a near-term alternatives for most RP patients. Our hope is that the quantum dot approach will offer a substantive and reasonably near-term therapeutic choice.



The simplicity of our approach also provides significant advantages compared to other alternatives, namely that the treatment is injected as opposed to undergoing invasive surgery. With that said, the quantum dot RP therapy will not be a single-shot cure – we would expect the treatment to be repeated, perhaps three to four times a year, somewhat less than anti-VEGF therapy for AMD. However, there are benefits to the temporary nature of the quantum dot effect: you don't have to explant anything if it doesn't work; if something better comes along, you can just stop treatment; and if something complementary is developed, there is the possibility of additive or synergistic therapeutic effects. We believe we are on the road to providing a meaningful option to a population of patients who have been underserved for far too long.

*Jim Taylor is President and CEO, 2CTech Corp, San Francisco, USA.*

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# Crossing (Corneal) Borders

**Sitting Down With… Audrey Talley Rostov,** Director of Cornea, Cataract and Refractive Surgery, Northwest Eye Surgeons and Global Medical Director, SightLife, Seattle, USA

What inspired you to become an ophthalmologist?

I don't think there was a single reason – it's more a combination of factors. In medical school, I had the opportunity to do a research fellowship. I started in one lab but funding changed, so I needed to find an additional research opportunity. I ended up doing a research fellowship in ophthalmology at the Massachusetts Eye and Ear Infirmary, where I studied endophthalmitis.

Initially, I was coming at it from more of an infectious disease/molecular biology standpoint, but then, as I started to learn more about ophthalmology, I simply fell in love with it. I enjoyed the combination of outpatient medicine and having the opportunity to do surgery – I'm very surgically orientated – and I didn't really enjoy inpatient medicine very much. But mostly, it was realizing what a difference you can make to someone's quality of life. I would say that's what really drew me to ophthalmology.

What would you be doing if you weren't an ophthalmologist?

I guess if I wasn't in ophthalmology but still in medicine, I would either be in dermatology or plastic/reconstructive surgery. But if I wasn't in medicine at all, maybe I would be a yoga instructor! Every day, first thing in the morning, I do some sort of workout, whether it's running or cycling or spinning. And then in the evenings I do yoga. Sometimes we do mini yoga sessions in the operating room between cases! I think I'd enjoy being a yoga instructor: I love to work out and I like the opportunity to try and motivate people.

Where did you train – and who are your mentors?

I did my residency at Washington University in St Louis, Missouri. The person who really kindled my love of cornea – my sub-specialty being cornea, cataract and refractive surgery – was Jay Pepose. He's an amazing teacher and a great researcher; he's also extremely ethical and has a great sense of humor. I really credit him with sparking my interest in cornea.

I then did a fellowship with Dick Lindstrom at Minnesota Eye Consultants. Dick has been a mentor to me ever since, he is just an amazing individual. He taught me about combining clinical practice with clinical research, being innovative, the importance of involvement with industry for innovation – and incorporating that into clinical practice, as well as further honing my surgical skills and teaching me how to come up with original solutions.

What are your career highlights so far?

One of my highlights from early on in my career was the opportunity to train where I did – and to have Dick as a fellowship director and mentor. Aside from that, it is the global work that I do. I work with SightLife – a global health organization committed to eliminating corneal blindness worldwide – where I have served as Associate Global Medical Director for the last few years. I'm now on the board of SightLife and I also serve as the Global Medical Lead between the Global Medical Director and the board. In this role, I've been very involved with surgeon training and curriculum development worldwide. In particular, I've developed a curriculum for training surgeons in certain techniques, such as endothelial keratoplasty, DMEK, DSEK, as well as other corneal transplant techniques.

We've trained hundreds of fellows across the world – and now many of these people are training others. We really go for sustainability in our program. It is not just about mission trips where people go and do surgery and then leave; it is really more about teaching and training. Going back to India and seeing people that I've trained participate in workshops where they train other surgeons has been incredibly rewarding.

Tell us more about the humanitarian work you have been involved in.

About 10 years ago, I was invited to give a keynote speech in Mumbai but, shortly before I left, terrorist bombs went off, and the event was cancelled. I had already purchased airline tickets, booked the time off, and my husband was going with me as well, so we decided that we would go anyway and just change our itinerary.

*"We've trained hundreds of fellows across the world – and now many of these people are training others."*

At that point, SightLife was just branching out into global work, so I asked if there was any way I could add some value. I ended up training a surgeon in PK and DSEK, back when endothelial keratoplasty was only just being adopted. She was the only surgeon for a catchment area of a couple of million people and it was clear that she just didn't have the means to go and get training. It made me realize that although there were some amazing surgeons in India, there weren't enough resources to train enough of them to

Credit: Margot Duane.

serve the entire population. After that, we started looking at the whole cornea ecosystem – not just training surgeons, but also making sure there are enough corneas available, ensuring quality of tissue, distribution, and building capacity. We have been working on that for the last decade.

Over the last couple of years, SightLife has also embarked on a prevention program following a proof-of-concept study done by the Proctor Foundation. The study looked at using female community healthcare volunteers in rural Nepal to diagnose and treat early corneal injuries; a lot of blindness in developing countries is caused by secondary infection from a relatively minor injury that is not treated. Even as we're trying to treat the 12 million corneal blindness cases that exist, about a million people are becoming blind every year, so it makes it hard to catch up. The prevention program looks to train additional community healthcare volunteers and, so far, it has been incredibly successful. These women are able to treat and resolve 96 percent of the injuries that they are faced with, helping eliminate corneal blindness.

Has access to eye care in developing countries improved over the last decade?
It's definitely looking better, especially in terms of additional surgeon training. Another important factor is policy, and that's why at SightLife we work with governments in India and Nepal, to help with the implementation of healthcare policy.

It's great to see that the landscape is really improving and more patients are able to get access to care. But there is still so much more work to be done.

What projects are you working on right now?

I'm helping with additional curriculum development, not just for corneal surgeons, but also for general ophthalmologists, as well as optometrists. There are always new techniques to learn, so we want to make further changes to the DMEK curriculum in developing countries, as well as creating a keratoconus curriculum.

On the home front, I do a lot of work with femtosecond lasers and femtosecond laser keratoplasty techniques – it's a big research interest of mine. I've also been doing a lot of work on cross-linking for keratoconus.

How do you see the field changing in the future?

Techniques are obviously becoming less and less invasive. And corneal treatments are becoming much more bespoke and focused on specific problems, compared with 10 years ago, when we used to perform full thickness keratoplasty for all diseases. For example, in endothelial keratoplasty, if there is a problem with endothelial layer, we can now just replace that layer.

Within corneal surgery, I think we should be looking to cataract surgery and aiming to provide not just functional vision, but take it to a more refractive level. Years ago, cataract surgery was just about restoring functional vision. Now, with modern IOLs, we can provide patients with a better range of vision and, therefore, a better quality of life. I find it really exciting to correct someone's astigmatism and restore their vision to unprecedented levels. There is still a lot of work to be done, but I think one of the most exciting things that you can do in ophthalmology is to help people go beyond simply functional vision, and perform a truly refractive procedure. My hope is to take corneal transplant surgery to that level as well.

*"Don't forget that our end goal is to take are of patients and what we're doing is really a privilege."*

What advice do you have for ophthalmologists at the beginning of their career?

You've made a good choice! It's an extremely rewarding profession and my advice would be to find something you really like to do and get very good at it. Don't forget that our end goal is to take care of patients and what we're doing is really a privilege. I think it's also important to remember about self-care. You can only be a good doctor if you also care for yourself. Try to avoid burnout by doing daily exercise, knowing your limits, and remembering to find balance in your life.

I think I'd also remind new ophthalmologists that it is OK not to love everything that you're trained in, but it is important to keep learning. I was recently at an institute in Bangalore, India, where they had a quote above the doors to their study and research area, which read: "The most dangerous phrase is 'because we've always done it that way.'" I love that. It is extremely important to be a life-long learner.


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