OZURDEX® (dexamethasone intravitreal implant) acts fast\textsuperscript{1,2} and lasts\textsuperscript{3–5} with less treatment visits compared with anti-VEGFs.\textsuperscript{5}

Effective DME treatment doesn’t have to be a burden.\textsuperscript{6}

Prescribing information can be found overleaf.

OZURDEX® is indicated for the treatment of adult patients with visual impairment due to diabetic macular oedema (DME) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy; macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO); inflammation of the posterior segment of the eye presenting as non-infectious uveitis.

The most commonly reported adverse events reported following treatment with OZURDEX® are those frequently observed with ophthalmic steroid treatment or intravitreal injections (elevated IOP, cataract formation and conjunctival or vitreal haemorrhage respectively). Less frequently reported, but more serious, adverse reactions include endophthalmitis, necrotizing retinitis, retinal detachment and retinal tear.

This advert is consistent with the UK marketing authorisation. Licences may vary by country, please refer to your local country SmPC.

DME, diabetic macular edema; IOP, intraocular pressure; VEGF, vascular endothelial growth factor.

OZURDEX® (Dexamethasone 700 micrograms intravitreal implant in applicator)

Abbreviated Prescribing Information

Presentation: Intravitreal implant in applicator. One implant contains 700 micrograms of dexamethasone. Disposable injection device, containing a rod-shaped implant which is not visible. The implant is approximately 0.46 mm in diameter and 6 mm in length. Indications: Treatment of adult patients: with macular oedema following either Branch Retinal Vein Occlusion (BRVO) or Central Retinal Vein Occlusion (CRVO), inflammation of the posterior segment of the eye presenting as non-infectious uveitis and visual impairment due to diabetic macular oedema (DME) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy. Dosage and Administration: Please refer to the Summary of Product Characteristics before prescribing for full information. OZURDEX must be administered by a qualified ophthalmologist experienced in intravitreal injections. The recommended dose is one OZURDEX implant to be administered intra-vitreally to the affected eye. Administration to both eyes concurrently is not recommended. Repeat doses should be considered when a patient experiences a response to treatment followed subsequently by a loss in visual acuity and in the physician’s opinion may benefit from retreatment without being exposed to significant risk. Patients who experience and retain improved vision should not be retreated. Patients who experience a deterioration in vision, which is not slowed by OZURDEX, should not be retreated.

In RVO and uveitis there is only very limited information on repeat dosing intervals less than 6 months. There is currently no experience of repeat administrations in posterior segment non-infectious uveitis or beyond 2 implants in Retinal Vein Occlusion. In DME there is no experience of repeat administration beyond 7 implants. Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs. Single-use intravitreal implant in applicator for intravitreal use only. The intravitreal injection procedure should be carried out under controlled aseptic conditions as described in the Summary of Product Characteristics. The patient should be instructed to self-administer broad spectrum antimicrobial drops daily for 3 days before and after each injection. Contraindications: Hypersensitivity to the active substance or to any of the excipients. Active or suspected ocular or periocular infection including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases. Advanced glaucoma which cannot be adequately controlled by medicinal products alone. Aphakic eyes with ruptured posterior lens capsule. Eyes with Anterior Chamber Intraocular Lens (ACOL), iris or transscleral fixated intraocular lens and ruptured posterior lens capsule. Warnings/Precautions: Intravitreous injections, including OZURDEX can be associated with endophthalmitis, intraocular inflammation, increased intraocular pressure and retinal detachment. Proper aseptic injection techniques must always be used. Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs. Monitoring may consist of a check for perfusion of the optic nerve head immediately after the injection, tonometry within 30 minutes following the injection, and biomicroscopy between two and seven days following the injection. Patients must be instructed to report any symptoms suggestive of endophthalmitis or any of the above mentioned events without delay. All patients with posterior capsule tear, such as those with a posterior lens (e.g. due to cataract surgery), and/or those who have an iris opening to the vitreous cavity (e.g. due to iridectomy) with or without a history of vitrectomy, are at risk of implant migration into the anterior chamber. Implant migration to the anterior chamber may lead to corneal oedema. Persistent severe corneal oedema could progress to the need for corneal transplantation. Other than those patients contraindicated where OZURDEX should not be used, OZURDEX should be used with caution and only following a careful risk benefit assessment. These patients should be closely monitored to allow for early diagnosis and management of device migration. Use of corticosteroids, including OZURDEX, may induce cataracts (including posterior subcapsular cataracts), increased IOP, steroid induced glaucoma and may result in secondary ocular infections. The rise in IOP is normally manageable with IOP lowering medication. Corticosteroids should be used cautiously in patients with a history of ocular herpes simplex and not be used in active ocular herpes simplex. OZURDEX is not recommended in patients with macular oedema secondary to RVO with significant retinal ischemia. OZURDEX should be used with caution in patients taking anti-coagulant or anti-platelet medicinal products. OZURDEX administration to both eyes concurrently is not recommended. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, consider evaluating for possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Interactions: No interaction studies have been performed. Systemic absorption is minimal and no interactions are anticipated. Pregnancy: There are no adequate data from the use of intravitreally administered dexamethasone in pregnant women. OZURDEX is not recommended during pregnancy unless the potential benefit justifies the potential risk to the foetus. Lactation: Dexamethasone is excreted in breast milk. No effects on the child are anticipated due to the route of administration and the resulting systemic levels. However OZURDEX is not recommended during breast-feeding unless clearly necessary. Driving/Use of Machines: Patients may experience temporarily reduced vision after receiving OZURDEX by intravitreal injection. They should not drive or use machines until this has resolved. Adverse Effects: In clinical trials the most frequently reported adverse events were increased intraocular pressure (IOP), cataract and conjunctival haemorrhage*. Increased IOP with OZURDEX peaked at day 60 and returned to baseline levels by day 180. The majority of elevations of IOP either did not require treatment or were managed with the temporary use of topical IOP-lowering medicinal products. 1% of patients (4/347 in DME and 3/421 in RVO) had surgical procedures in the study eye for the treatment of IOP elevation. The following adverse events were reported: Very Common (≥ 1/10): IOP increased, cataract, conjunctival haemorrhage*. Common (≥1/100 to <1/10): headache, ocular hypertension, cataract subcapsular, vitreous haemorrhage*, visual acuity reduced*, visual impairment*, abnormal visual fields, vitreous floaters*, vitreous opacity*, blepharitis, eye pain*, photopsia*, conjunctival oedema*, conjunctival hyperaemia. Uncommon (≥1/1000 to <1/100): migraine, necrotizing retinitis, endophthalmitis*, glaucoma, retinal detachment*, retinal tear*, hypotony of the eye*, anterior chamber inflammation*, anterior chamber cells/flares*, abnormal sensation in eye*, eyelids pruritus, scleral hyperaemia*, device dislocation* (migration of implant) with or without corneal oedema, complication of device insertion resulting in ocular tissue injury* (implant misplacement), (*Adverse reactions considered to be related to the intravitreous injection procedure rather than the dexamethasone implant). Please refer to Summary of Product Characteristics for full information on side effects. Basic NHS Price: £870 (ex VAT) per pack containing 1 implant. Marketing Authorisation Number: EU/1/10/638/001. Marketing Authorisation Holder: Allergan Pharmaceuticals Ireland, Castlebar Road, Westport, Co. Mayo, Ireland. Legal Category: POM. Date of Preparation: May 2019. UK/0288/2019

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ Adverse events should also be reported to Allergan Ltd. UK_Medinfo@allergan.com or 01628 494026

JOB CODE: INT-OZU-2050220
DATE OF PREPARATION: DECEMBER 2020

Allergan
an AbbVie company
New year, new set of CHALLENGES

Presbyopia, automation, cost-effectiveness: ophthalmologists predict 2022 trends
SPOT THE HIDDEN PREDATOR.

When it comes to retinal and choroidal vascular diseases, VEGF has always been the focus. But now we know that there is more than meets the eye.

Discover more at futureofvision.global/thewhitytonga
EDITORIAL ADVISORY BOARD

Ophthalmology Times Europe is the independent source of current developments and best practices in European ophthalmology. It is the balanced and unbiased forum for ophthalmologists to communicate practical experience, clinical knowledge, discoveries and applications, thereby promoting improvements to medical practice and patient health.

MISSION STATEMENT: Ophthalmology Times Europe is the independent source for current developments and best practices in European ophthalmology. It is the balanced and unbiased forum for ophthalmologists to communicate practical experience, clinical knowledge, discoveries and applications, thereby promoting improvements to medical practice and patient health.

S U B S C R I B E  A T  europe.ophthalmologytimes.com

europe.ophthalmologytimes.com
Collagen crosslinking provides corneal stability in young patients

Procedure is safe and effective to perform in this population, study shows

Dr Solin Saleh, who recently completed her paediatric ophthalmology fellowship at the Byers Eye Institute at Stanford University School of Medicine in California, United States, reported the findings at the American Society of Cataract and Refractive Surgery (ASCRS) 2021 annual meeting in July.

The study was designed by Dr Edward E. Manche, director of cornea and refractive surgery and Stanford University professor of ophthalmology. It consisted of a retrospective chart review of patients 22 years or younger who had undergone CXL for progressive keratoconus at the Byers Eye Institute during the previous 7 years. All CXL procedures were performed by Dr Manche.

The investigators evaluated the patient records to identify changes in visual and corneal parameters, including corrected distance visual acuity (CDVA) and maximum keratometry (Kmax) up to 2 years after CXL. Dr Saleh explained that the findings are important because although keratoconus is generally diagnosed during puberty, it can be more severe and progress more quickly when identified in younger children, who may need corneal transplantation if the disease is not addressed.

Dr Saleh reported that 86 eyes of 71 consecutive patients underwent CXL during the study. The patients ranged in age from 12 to 22 years (mean: 16.4 ± 2.5 years) at the time of surgery. Bilateral CXL was performed in eight patients. Of the study sample, 57 eyes had completed a minimum of 1 year of follow-up and 24 eyes had completed 2 years of follow-up.

Dr Saleh reported that the mean preoperative CDVA was logMAR 0.38 ± 0.32 (Snellen acuity 20/48), with mean postoperative CDVA of 0.29 ± 0.31 (20/39) and 0.31 ± 0.31 (20/41) at 12 and 24 months postoperatively. Compared with preoperative mean Kmax, there was an improvement of –0.8 D to a mean postoperative Kmax of 59.1 ± 9.1 D at 12 months and –1.3 D to 59.7 ± 8.8 D at 24 months.

The authors concluded that CXL was both safe and effective to perform in this young patient population. The procedure stabilised the cornea in these children and young adults, and in some cases the vision and the keratometry values improved. The authors urged surgeons to consider CXL for treating paediatric patients with early keratoconus to prevent ongoing disease progression, especially given the risk of visual morbidity in children.

By Lynda Charters

Reviewed by
Dr Solin Saleh
Dr Saleh

This article is adapted from Dr Saleh’s presentation at the American Society of Cataract and Refractive Surgery annual meeting. She has no financial interest in this subject matter.

Edward E. Manche, MD
e: cornea@stanford.edu
Dr Manche has no financial disclosures related to this content.
'Tis the season to stay inspired

Mike Hennessy Jr, President & CEO of Ophthalmology Times Europe®’s parent company, MJH Life Sciences

’Tis the most wonderful time of the year… With each December issue, members of the Ophthalmology Times Europe® Editorial Advisory Board share their perspectives and predictions with editor Caroline Richards on what new developments and challenges will affect ophthalmology next year. Themes include a focus on cost-effectiveness and value for money alongside automation, regulatory concerns and climate change. Public policy is top of Board members’ minds as the COVID pandemic progresses, whilst refractive disorders and ocular surface disease remain at the forefront (page 6).

In cataract and refractive surgery, Dr Ben LaHood wraps up a three-part series on using toric IOLs. Part 1, published in the October edition of Ophthalmology Times Europe®, looked at patient selection and optimising biometry. Part 2, published in the November issue, covered the calculation of toric IOL sphere and cylinder power. In this final article in the series, Dr LaHood examines the perioperative period and provides postoperative troubleshooting (page 12).

In cornea, Mr David F. Anderson and Mr Aris Konstantopolous share their pearls for optimising vision in patients with keratoconus. They explain how topography-guided surface ablation improves qualitative and quantitative outcomes, they explain in their article (page 16).

Next, corneal collagen crosslinking (CXL) in paediatric and young adult patients with keratoconus can stabilise, and in some cases even improve, corneal keratomy and vision up to 2 years postoperatively, according to study results presented by Dr Solin Saleh (page 22).

In retina, we hear from investigators at Duke University, North Carolina, United States, on how optical coherence tomography (OCT) as well as OCT angiography ocular biomarkers may help diagnose Parkinson’s disease (PD). An imaging study revealed specific, associated retinal and choroidal changes. The investigators pointed out that, when the current findings are combined with the clinical history and other tests, the choroidal and retinal microvascular imaging results “may hold the potential to improve clinician confidence in the diagnosis of PD” (page 23).

Focusing on glaucoma, Dr Shan C. Lin notes how the advancements seen with some of the newer cyclophotocoagulation technologies are helping to improve outcomes. Benefits include better visualisation of ciliary processes and avoidance of tissue damage (page 28).

Several innovations are revolutionising surgical care in paediatric ophthalmology. Dr Janet L. Alexander recently presented a series of rapid-fire cases to discuss four such paediatric innovations: antenatal surgical planning to address congenital hereditary disease, endothelial keratoplasty, endocyclophotocoagulation to treat refractory glaucoma and ultrasound biomicroscopy as a tool for guiding complex cataract surgery. Techniques and technologies help to minimise complications and guide counseling and care, she says (page 30).

In gene therapy, Dr Janey Wiggs takes a look at identifying individuals at risk of glaucoma via genetics studies. Polygenic risk score allows multiple gene variants to be tested simultaneously, she says.

A high genetic burden defined by the primary open-angle glaucoma polygenic risk score is associated with earlier disease onset, higher IOP, thinner nerve fibre layer and a greater need for surgery (page 32). Such innovation will continue to inspire and serve the ophthalmic space well as we head into the new year. Thanks, as always, for reading this latest issue. Wishing you and yours a safe, happy and healthy holiday season.

Such innovation will continue to inspire and serve the ophthalmic space well.
Automation developments, pandemic backlogs and regulatory issues set to shape coming year

Editorial Advisory Board examines these and other eyecare themes as they look to 2022

As 2021 draws to a close, members of the Ophthalmology Times Europe® Editorial Advisory Board share their perspectives and predictions on new developments and challenges that will affect ophthalmology next year. Themes include a focus on cost-effectiveness and value for money alongside automation, regulatory concerns and climate change. Public policy is top of Board members’ minds as the COVID pandemic progresses, whilst refractive disorders and ocular surface disease remain at the forefront.

THOUGHTS ON REFRACTIVE ISSUES

PROF. PETO: One of the most common causes of visual loss is presbyopia and this causes loss of income for many as the population ages. There should not be anyone lacking appropriate pairs of reading glasses in Europe and yet this is still a major issue. There is a big divide between Western and Eastern Europe, and equity of access to basic services, such as a pair of glasses, should be the norm in today’s times.

PROF. ALİO: Despite the progress made with IOLs and laser procedures, presbyopia solutions still need to be better developed. An initial presbyope is not the same as a fully developed one and different treatments should be provided at different stages of the condition. This staging should probably be: pharmatherapy for the initial-intermediate presbyope, laser for intermediate cases and IOLs for advanced forms.

However, evidence to support each of the stages is lacking. PresbyLASIK is a technique that is not practiced by many but is very successful when properly indicated. IOLs are probably over-indicated today, sometimes being used in patients who are too young, and pharma-therapy does not yet exist.

Related to the previous point, accommodative lenses, rather than multifocal or extended depth-of-field (EDOF) lenses, should be the solution for pseudophakic presbyopia. The restoration of real accommodation is the physiological way to solve the issue but is still not properly accomplished.

Many unsuccessful attempts have been based on incorrect assumptions. The bag is probably not the best location to place a lens because the natural mechanism of fibrosis will probably cancel its effect. Sulcus implantation has been successful and is still under investigation.

Other mechanisms such as electronically-induced accommodation or refractive exchanges induced by pupil motility are a likely solution. 2022 should contribute to the further development of accommodative IOLs.

DR FAZIO: The debate continues as to which kind of presbyopia-correcting strategy is best overall or, at least, how to personalise the approach. Currently, there are seven types of advanced-technology IOLs available for the purpose: advanced monofocal; EDOF refractive; EDOF diffractive; sector bifocal; diffractive bifocal; trifocal; and extended near diffractive.

IN SHORT

Four members of the Ophthalmology Times Europe® Editorial Advisory Board consider the challenges and opportunities that lie ahead in Europe in 2022.
‘Minimonofocality’ could be added to the lens choice strategy to maximise the compensation of presbyopia. Studies comparing IOL types and strategies to ascertain their relative power and drawbacks are still lacking but remain urgent, for medico-legal reasons among others.

**PROF. PETO:** Capsulorhexis is one of the most important steps in cataract surgery. If it fails or is performed wrongly, it makes the patient a candidate for intraoperative complications or may negatively influence the performance of premium IOLs. Automatic capsulorhexis is a dream that will probably be accomplished in 2022.

**PROF. ALÍÓ:** Intrastromal lenticular corneal tissue implants, now available from several companies, should be promoted as they are clearly going to replace excimer lasers because of their lower maintenance costs, lack of duplicate technology for the same purpose (i.e., excimer plus Femto) and faster, less-invasive surgery.

**THOUGHTS ON CATARACT SURGERY**

**PROF. ALÍÓ:** Capsulorhexis is one of the most important steps in cataract surgery. If it fails or is performed wrongly, it makes the patient a candidate for intraoperative complications or may negatively influence the performance of premium IOLs. Automatic capsulorhexis is a dream that will probably be accomplished in 2022.

**DR FAZIO:** SMILE vs PRK vs LASIK vs phakic lenses: given a normal eye, with adequate corneal thickness and anterior chamber depth, and with −6 D myopia and 3 D cylinder, which technique would be the winner? Possible early and late complications, recovery time, precision and quality of vision all differ between the various strategies.

**THOUGHTS ON GLAUCOMA**

**DR FAZIO:** After a season of keen interest during which it seemed to be the only future of cataract surgery, laser-assisted phacoemulsification (FLACS) stopped being fashionable. Why, when the technique is beautiful and safe! Simply because, given the current IOL and phaco needle technology, clinical results are not sufficiently different from those of the standard phacoemulsification technique.

We are waiting for a complete set of new lenses capable of being inserted through an opening of less than 2 mm and phaco machines adapted to FLACS and capable of carrying out surgery through the same width of incision.

**PROF. ALÍÓ:** Myopia is the upcoming generation’s issue; more young people have it than we have seen in the current middle-aged/elderly population. It is a hidden disability, and the full economic impact will only be felt when this generation grows up. There might still be time to act, by encouraging young people to spend more time away from the screen and providing appropriate lighting in schools, and this process really should start imminently.

**THOUGHTS ON ARTIFICIAL INTELLIGENCE**

**PROF. HAFEZI:** The use of artificial intelligence (AI) in diagnostic equipment is the future of modern medicine. Although medical professionals cannot be replaced, AI-driven diagnostics will support and enhance the level of care provided to patients.

These future devices will be able to detect irregular corneas, for example, at a much earlier stage than we see today. The challenge that I see is to develop a way to capture ‘Big Data’ in a systematic way, to enable the machine-learning devices to process data.

Aside from publication politics and commercial interest, it is valuable to access large amounts of similar data because there are intricate ways to analyse and utilise such data sets, developing a model to support AI development in ophthalmology.

Eliminating the subjective approach with which doctors use current corneal
Corneal cross-linking is a rude technique.
—PAOLO FAZIO

PROF. ALIÓ: Even though it has been attempted only recently, corneal stromal regeneration has been successfully reported as feasible and extremely promising for the treatment of corneal dystrophies: results of the first clinical study were published in the American Journal of Ophthalmology, Cornea, IOVS and Experimental Eye Research. The combination of stem cells with acellular corneal tissue raises a new possibility for keratoconus, opacified stroma and other corneal diseases.

The same is happening with the corneal surface: clinical studies have demonstrated the possibility of using mesenchymal stem cells (the same ones as for the stroma) to reconstruct the ocular surface in a much better and cheaper way than using mucosal epithelium expanded cells.

Corneal endothelial regeneration is still only in its initial phases but the Japanese studies are promising. We hope that 2022 will be a year that sees all these projects progress and make impressive accomplishments.

PROF. HAFEZI: Prior to the 2000s, there was little-to-no mention of keratoconus in the literature. Fortunately, diagnostics have made significant advancements since then in terms of sensitivity, and irregular corneas can now be detected at a much earlier stage. Fast-forward two decades and you can see a number of prevalence studies claiming that keratoconus cannot be considered a rare disease.

However, the game has not yet been won. The challenge is that keratoconus has not yet been adopted as a public policy initiative. Every child should be screened, especially in regions with a high prevalence. Specifically, every child should have the right to be screened by qualified individuals using high-quality screening devices.

This initiative can only be realised if patients, patient organisations, medical professionals, industrial partners and governmental officials work together to increase awareness about the disease and propose feasible solutions for how best to screen school-aged children regardless of financial limitations.

DR FAZIO: I am convinced that we are overtreating some of our keratoconus patients with corneal cross-linking and undertreating others. Corneal cross-linking is a rude technique. We damage keratocytes, inducing opacities and long-term flattening effects in an unpredictable way.

In some cases, it seems the cornea continues to develop keratoconus despite treatment. We need ways to better titrate depth and amount of treatment and to personalise the amount of cross-linked corneal tissue.

PROF. HAFEZI: Anyone who has performed corneal cross-linking is aware that removal of the epithelium comes with several disadvantages and an increased risk for infection. The removal of the epithelium has been necessary until now to allow, firstly, enough riboflavin to penetrate the stroma and, and secondly, sufficient oxygen concentration in the stroma to maintain the cross-linking reaction.

One of the oldest ways for riboflavin to effectively penetrate an intact epithelium is through iontophoresis. Although effective, iontophoresis is complicated, increases the time and costs of treatment, and is rather uncomfortable for both the surgeon and patient. For these reasons, few surgeons have adopted this mode of treatment.

Recent developments have shown that sufficient riboflavin concentration can be achieved using penetration enhancers. Oxygen goggles have been developed that allow a steady stream of oxygen during the cross-linking procedure. Although this method is effective, this additional device presents challenges: a raised level of complexity, the bulkiness of the equipment, and increased costs related to the goggles and required oxygen.

The challenge that I am facing is to find a safe and effective treatment protocol that can be adopted by medical professionals everywhere with little investment and a flat learning curve. Additional devices and complicated procedures limit the number of medical professionals who can provide the treatment. Access to treatment is imperative for patients, especially in regions with proven high prevalence.

Furthermore, if the treatment protocol is simple, patient risk decreases. So, a challenge I have is providing a means to enable an epi-on approach that is affordable, simple, safe and effective; without additional oxygen and without iontophoresis; ideally performed in an office-based manner.

The use of artificial intelligence in diagnostic equipment is the future of modern medicine.
—FARHAD HAFEZI
PROF. HAFEZI: There is confusion amongst colleagues regarding the use of the term ‘off-label,’ which applies to medical devices or pharmaceutical drugs that have been approved for clinical use in one indication but are used for another. An excellent example would be the off-label use of the intravitreal injection bevacizumab (Avastin, Genentech/ Roche). The drug has not been approved for age-related macular degeneration (AMD) but is registered for the treatment of colon carcinoma. Off-label use is generally legal.

However, use of non-CE-marked riboflavin is an example of something that does not constitute off-label usage. Several companies in the EU sell riboflavin solution that is not CE-marked and the use of such riboflavin is unlawful in any European clinic. What many surgeons do not realise is that they are forgoing their liability insurance when they use this low-grade, non-conforming formulation.

Even riboflavin pending a CE-mark is in clear violation. The purpose of the CE-mark is that a notified body declares that the medical device has met the General Safety and Performance Regulations of all current European Medical Device Regulations. Anything that is considered pending is not approved.

Often, non-conforming companies sell their riboflavin solution directly to surgeons at congresses. The reason for direct sales is because these companies cannot legally ship their product without having it be confiscated at the borders for non-compliance of regulatory requirements.

Aside from the commercial implications, the real problem is patient safety. I see many cases, even in Switzerland, of surgeons using non-CE-marked riboflavin solution. All too often, the illegal use of low-grade riboflavin solution leads to medical complications (ineffective/ shallow treatment, central scars and even corneal melting). So, ask yourself: are the savings really worth the risk?

To check, ask the manufacturer or supplier to provide a Free Sales Certificate, sometimes called a Certificate for Export. This certificate is only provided when the product is legally sold and distributed in an open market.

Another huge challenge is the looming antibiotic resistance that the World Health Organization has been warning us about for years. The time to start developing medical treatment strategies to combat bacterial infections without the use of antimicrobials is now.

Peer-reviewed publications on PACK-CXL, which stands for ‘photoactivated chromophore to treat keratitis-corneal cross-linking’, have grown exponentially in the past 5 years. Using PACK-CXL as an adjunct therapy along with antimicrobials to treat bacterial, fungal and mixed infections has been proven to be effective in shortening the time to healing and thus in reducing the number of follow-ups needed.

We have submitted for publication the results of our prospective multicentre study on the effect of PACK-CXL alone and have seen that in bacterial, fungal and mixed ulcers of up to 4 mm in diameter, a primary high-fluence PACK-CXL treatment is just as effective as antimicrobial therapy in terms of days to healing.

PROF. PETO: The COVID pandemic-related challenges we are likely to see in 2022 will largely depend on where people live and on how a given country is pulling through the crisis. The world’s population has been affected by entirely new ways of living. The level of uncertainty has been high and many of our patients have not been seen in a timely manner.

Dealing with serious complications of delayed presentation is becoming more common and unfortunately, people might lose their sight. Late presentation for AMD and diabetic retinopathy/maculopathy is quite common and patients at risk are juggling several appointments alongside conflicting advice about whether they should stay at home or attend the clinic.

Providing low-vision care to those who have already lost sight is a challenge, since many of these patients have become even more isolated during the pandemic. An appropriate level of care used to involve face-to-face consultations, discussions on special needs and teaching of new skills for everyday living. Although video or telephone consultations allow some level of care to be provided, these do not suit everyone and many patients do not have access to this, leading to further deprivation and isolation.

Sustaining our services will remain a challenge as many countries struggle with a low number of ophthalmologists carrying a high burden; trying to see the rising number of patients, teach the next generation of ophthalmologists, keep up with research and education and continue to thrive despite all the pandemic-related difficulties.

In addition, we will have to look at our services: where we are producing waste, whether we can reduce our footprint and how we can provide the best service to our patients. We cannot ignore our contribution to climate change any more but need to think about where our surgical waste goes and how we could use and re-use equipment better.
True measurements, fewer assumptions
ANTERION® is the definitive toolbox for refractive cataract surgery planning. It provides rich data from all refractive surfaces and integrates the measurements needed for predictable IOL power calculations.

Visualize your measurements with optimized swept-source OCT images. Benefit from advanced methods that make the difference in challenging eyes.

Uncover biometry with ANTERION: www.anterion.com
Toric IOLs for beginners

PART 3: What to consider during surgery and in the postoperative period

By Dr Ben LaHood

his three-part series on using toric IOLs in cataract surgery is designed to provide some practical tips for success. Part 1, published in the October edition of Ophthalmology Times Europe®, looked at patient selection and optimising biometry. Part 2, published in the November issue, covered the calculation of toric IOL sphere and cylinder power. In this final article in the series, I will examine the perioperative period and provide postoperative troubleshooting.

Preoperative marking

A toric IOL has maximum optical impact when aligned perfectly with the steep axis of the cornea. If it is a few degrees off, there is a decline in effect of astigmatic neutralisation. In general, most surgeons consider alignment within 10° to be accurate enough but in reality, a lot depends on the magnitude of astigmatism.

Misalignment of a high-power toric IOL can leave someone with a lot of residual astigmatism whereas misalignment of a very low cylinder power toric IOL may have a minimal effect. To align a toric IOL accurately, a reference mark must be used. There are many different methods of preoperative marking: ink markers, needle marking and even apps.

I prefer to use an intraoperative digital display system (Verion Digital Marker, Alcon or Callisto Eye, Carl Zeiss), not because these methods are more precise than manual marking but because they are more efficient and speed up the surgery. I do still make a manual mark on the eye in the sitting position prior to surgery as a back-up reference in case of difficulty with the digital system, but rarely need it.

Regarding manual marking, a single mark is adequate to align a Mendez ring. The human eye is incredibly good at halving things, so I will make a small mark inferiorly at the bottom of the cornea to split the cornea in half.

In the worst-case scenario, if your digital marking system fails, you have not pre-marked the eye and you still want to implant a toric IOL, I suggest that you can still safely do so. Simply look at the top of the cornea and identify the vascularised pannus. If you look at the midpoint of that pannus, this will be the midpoint vertically and you could drop a line down from that to halve the cornea.

If you look again at the widest point of the cornea...
and draw a line horizontally across it, you are going to give yourself an excellent surrogate marker; you could then use a Mendez ring and still be able to mark the axis to implant the toric IOL. You can safely use a toric even in this worst-case scenario.

**Surgical technique**

The surgical technique of toric IOL implantation differs from standard cataract surgery because of the preoperative marking and the rotational placement of the lens. The IOL injection is similar to cataract surgery but I recommend being primed and ready to rotate quite rapidly as the IOL is expanding.

**UNFOLDING**

The unfolding of the IOL is a prime time to get it into a good position. Many will suggest, if you are using a C-loop haptic, to put it 5° before where you want it so that you can nudge it into the final resting position when you are doing the next steps of surgery. If you are using a plate haptic IOL, you can put it exactly where you want it because you can nudge it in either direction very easily.

I do not use a capsular tension ring unless necessary due to zonular instability, even in high myopes. I find that toric lenses from the major manufacturers have good rotational stability, and the need to rotate is extremely low.

If you do find that you have over-rotated your toric IOL past its intended position, there is no shame in turning it around again. Take your time. Inject some more viscoelastic into the capsular bag and use two instruments to completely rotate the lens all the way back to where you want it.

If you wish to move just a few degrees in the opposite direction, it is possible but be wary of putting too much stress on the capsule. My tip is to slightly deflate the anterior chamber, which will allow easier “backwards” rotation of the IOL within the capsular bag.

**AT THE END OF THE CASE**

A key time that you may encounter a little IOL rotation away from its intended position will be at the end when you take the instruments out of the eye. Sometimes, if the incision has not perfectly sealed, shallowing of the anterior chamber will allow some movement of the toric IOL within the capsule.

I highly recommend being quick with your incision hydration, trying not to let the anterior chamber flatten and keeping things quite firm at the end of the case. This prevents setting up a cycle of IOL rotation, entering the eye, flattening the chamber and further movement, etc. I have noticed a major decrease in my need to hydrate the main incision after injecting the Clareon toric IOL with the AutonoMe injector and this has been helpful in leaving a stable anterior chamber at the conclusion of the case with little risk of early rotation.

If you notice any early rotation after you have finished the case, go back in and put the lens back where it needs to be. This is a lot easier to do while you are still in the operating theatre rather than seeing it the next day and wishing you had taken the extra few minutes.

**Postoperative assessment**

Postoperative care of a toric IOL patient is identical to that following any other cataract surgery. I recommend seeing the patient at 1 day, 1 week and 6 weeks postoperatively. On Day 1, I start to look for any early and significant rotation. If I notice a lens with significant malrotation, I take the patient directly back to the operating theatre and put the lens in the originally intended position.

If I notice on Day 1 that the lens is off by a few degrees, I am not concerned because the patient may be completely happy and it is fine to wait and see. Also, if the lens has moved a little, it means that it is not particularly stuck to the capsule and is a somewhat mobile. I would rather wait for the capsule to become more condensed so that if I do choose to rotate the lens, it is more likely to stay in that position long term.

**SUBJECTIVE REFRACTION**

At the 6-week postoperative appointment, I audit my results, looking at lens position both in terms of axial position and depth within the eye. This is also when I would perform an accurate subjective refraction.

If you find that you have over-rotated your toric IOL, there is no shame in turning it around again.

Even if the patient is happy, I recommend doing a subjective refraction. It will give you so much more information that you can use to improve your future results. I also take more optical biometry measurements for my records. These are handy if I want to consider any kind of toric rotation or lens exchange and provide me with postoperative anterior chamber depth.

If a patient has significant post-op astigmatic refractive error, I follow a structured decision-making tree by asking myself first whether the patient is happy. If the patient is unhappy, I want to do something for them. On the other hand, a happy patient with refractive error may be truly happy as they are or may prefer glasses anyway so do not try to fix things — instead, learn from what may have gone wrong in that case.

If you examine the patient and...
find the lens is exactly where you intended yet they still have some residual refractive error, you may ask yourself what you have done wrong, but the answer is likely nothing. Either the patient had significant change in their surgically induced astigmatism or their initial biometry was not quite right. This is now a situation that needs a little further investigation before treatment decisions can be made.

You simply need a subjective refraction and measurement of the axis and pseudophakic anterior chamber depth, along with knowledge of the sphere and cylinder power of the implanted toric IOL. Working out whether you can rotate the IOL to fix the residual astigmatism or if an IOL exchange may be needed can seem daunting.

You will need to use an online tool to help you with this, but a good rule of thumb is that if the spherical equivalent of the subjective refraction is close to zero then you should be able to rotate the current IOL into a more optimal position for the patient. Ultimately, the patient will have to decide whether they want to have another surgical procedure so that you can rotate the IOL or whether they can have laser treatment to the cornea.

My preference is to rotate the lens to a better position to get rid of the residual astigmatism if I can, and it is a simple solution. My colleague Dr Michael Goggin and I created an app called Toric Pro.1 Other calculators include astigmatismfix.com and the Barrett RX formula. All these resources can tell you whether you can rotate the lens for a better residual refractive outcome.

There will be some patients who do not want to undergo surgery again and there will be some eyes that you will not want to re-enter. Perhaps they had unstable zonules or it was a difficult operation. For these cases, laser vision correction can be a safe and effective option.

Again, the most important thing in this situation is an accurate subjective refraction as this is what will be used in planning the laser surgery. Most people will know a friendly laser surgeon who is happy to help with such cases.

One of the most important points to make about re-rotating an incorrectly positioned IOL is that it is not appropriate to simply put the IOL at the originally intended position if it is not there already. Once you have made an incision and implanted a toric IOL, you have changed the eye. Surgically induced astigmatism has altered the shape and you now know how deep the toric IOL sits.

You have new information and a new subjective refraction to work with. Do not be tempted to just go in and put the IOL back unless on Day 1 there is a large rotational change from intended. In this scenario, I think it is reasonable to go back and reposition, often with the added security of a capsular tension ring.

Going back in
If at any stage you do have to go back inside the eye, it can be particularly stressful because you want to get it right this time and because this is not a common procedure. My suggestion, if going back into the eye early, is to free up the lens and take a minimalist approach.

Use a little viscoelastic but do not fill the bag. Rotate the lens to its new position — and I always gently press or tap the IOL against the capsule to maximise contact between optic material and capsule.

If going back into the eye much later, when capsular fibrosis has sandwiched the IOL in place, take your time and be kind to the zonules. I recommend putting a needle between the IOL and the capsule edge before visco-dissecting the two apart.

There are times when an IOL simply cannot be completely removed and haptics must be left inside the bag. It is always good to have a sulcus and anterior chamber IOL option on standby in case there are any complications with this relatively tricky procedure. Also, remember that if you find yourself having difficulty rotating a previously implanted toric IOL, there is no harm in backing out and deciding that the safest course of action is to instead perform laser vision correction surgery.

Conclusion
I would like to encourage surgeons to implant toric IOLs more frequently. The tips and advice I have given in this series of three articles will help you plan for success and to be prepared for the rare occasions you must deal with failure.

Success is all about doing all the small steps well and minimising the chance of error. You will have to be a little more pedantic about reviewing preoperative results and considering postoperative data but the improvement in patient results will be worth it.

REFERENCE
1. toricpro.com

BEN LAHOOD, MBCHB, PGDIPOPH, FRANZCO
e: benlahood@gmail.com
Dr LaHood is an ophthalmologist specialising in refractive cataract and laser surgery in Adelaide, Australia. His research and teaching focus on the management of astigmatism. He is a consultant to Alcon and Zeiss.

Read Part 2 of Dr LaHood’s IOL series
AOP 2022
INTERNATIONAL EDITION N°33
JANUARY 7 & 8
PALAIS DES CONGRÈS • PARIS – FRANCE

TO START FRESH 2022!
JOIN THE 1ST OPHTHALMOLOGICAL & PHYSICAL EVENT

REGISTER NOW ON AOPCONGRESS.COM
Corneal collagen crosslinking (CXL) to increase corneal biomechanical strength has become the standard of care for eyes with the progressive disease keratoconus. The procedure is very effective at halting the ectatic process and thus reducing the risk for eventual corneal transplantation.

Because of the corneal flattening that occurs with CXL, patients can also benefit from some improvement in uncorrected and best-corrected visual acuity (UCVA and BCVA). Nevertheless, irregularity of the anterior corneal surface persisting despite CXL limits the improvement to visual acuity (VA) and is also associated with higher order aberrations (HOAs) that degrade the quality of vision.

The efficacy of the Athens Protocol, combining partial topography-guided photorefractive keratectomy (PRK) and CXL for stabilising keratectasia and improving VA, was first reported in the literature in 2010 and its long-term benefits have been shown in eyes with 10 years of follow-up.\(^1,2\)

Although many investigators have reported on their experience with combined topography-guided PRK and CXL to treat eyes with keratoconus, widespread knowledge about its effects on HOAs is more limited.\(^3\)

We have been performing partial topography-guided surface ablation with CXL for visual rehabilitation and stabilisation of eyes with keratoconus. Our experience shows the benefits of using the surface ablation technique for regularising the anterior corneal surface, reducing HOAs and improving visual function.

**Treatment rationale**

The HOAs that are predominantly elevated in eyes with keratoconus are vertical and total coma.\(^4,5\)

Coma is associated with a “comet-like” blur of the perceived image\(^6\) and it can be particularly disabling for patients. Spectacles and contact lenses correct errors in sphere and cylinder in eyes with keratoconus and thus improve VA, but these do not address HOAs.

HOAs can be reduced with a wavefront-guided corneal ablation, but this technique is not the most appropriate for treating eyes with keratoconus because of limitations such as the challenge of obtaining a reliable wavefront map. Corneal topography, which is a static measurement, provides more reproducible data, and topography-guided PRK reduces HOAs by regularising the anterior corneal surface.

Ablation depth with excimer laser treatment is limited in eyes with keratoconus because of their thinner and inherently biomechanically weaker corneas; therefore the aim of the treatment is not to reach emmetropia but to normalise the anterior surface. The treatment results in improved BCVA secondary to the induced reduction in coma and reduction in spherical equivalent of manifest refractive error.\(^7\)

**Our approach**

We perform subjective refraction and cycloplegic refraction according to our standardised protocols, with a focus on measuring the complete astigmatic error. Because of the inability to obtain an accurate clinical refraction in eyes with keratoconus, especially for moderate to advanced disease, we rely greatly on topographic imaging for the data.

To fully characterise the corneal surface, we use both a Scheimpflug topographer (Pentacam HR, Oculus) and a Placido imaging modality (ATLAS 9000, Carl Zeiss). Dual imaging also allows us to analyse HOAs with both Zernike and Fourier reconstructions. To evaluate the axis of the vertical coma and correctly identify the axis of astigmatism with Scheimpflug-based imaging, we turn off all HOAs except those related to coma (N8, N9, N18 and N19).

The topography scan and the irregularity data map generated by the 22 Placido discs of the ATLAS

---

**IN SHORT**

- Partial topography-guided surface ablation, combined with corneal collagen crosslinking when visual acuity is still quite good, optimises prognosis for the patient with keratoconus.
9000 are transferred to the dedicated treatment planning station (CRS Master, Carl Zeiss) for the excimer laser (MEL 90, Carl Zeiss). The optical zone, treatment refraction and Z axes are adjusted to keep the ablation depth to 50 μm maximum.

The treatment begins with alcohol-assisted epithelial removal using 20% alcohol applied for 40 seconds. The ablation excimer pattern is then applied by the MEL 90. Mitomycin C 0.02% is applied to the ablated corneal surface with a soaked sponge for 30 seconds followed by copious irrigation with chilled balanced salt solution.

This is followed by the cross-linking procedure. Riboflavin 0.1% saline, HPMC (VibeX Rapid, Glaukos) is applied every minute for a total of 10 minutes. Ultraviolet-A light (10 mW/cm²) is delivered for 4.5 minutes, corresponding to a total energy of 2.7 J/cm².

Postoperative management includes a bandage contact lens, topical dexamethasone 0.1% and topical ofloxacin 0.3% for 2 weeks. The following case highlights our approach and how it improves refraction, UCVA and coma.

**Case study**

A 39-year-old man presented with an interest in having laser vision surgery to correct his low myopia. He reported that he was managing with contact lenses and spectacles, but he found those options inconvenient because he was in the military.

The patient’s refraction was −0.75/−1.75×155 logMAR 0.00 OD and −0.75/−0.50×20 logMAR 0.00 OS. Slit-lamp evaluation showed a few corneal guttata. There were no other abnormal findings on clinical examination.

On corneal topography, the front surface axial curvature maps for both eyes showed vertical asymmetry that strongly suggested keratoconus (Figure 1). Total HOA root mean square (RMS) was 0.617 μm OD and 0.601 μm OS (Figure 2).

Minimum corneal thickness was 545 μm OD and 543 μm OS. Treatment with topography-guided PRK plus CXL was recommended and the patient consented. Figure 3 shows the planned ablation patterns. The ablations were done with a 6.5 mm optical zone and expected depths of 37 μm OD and 25 μm OS.

Complete corneal re-epithelialisation was achieved at the 1-week follow-up visit. At 3 weeks, there was no evidence of corneal haze or other adverse sequelae, and the patient’s UCVA had improved to logMAR 0.22 OD and 0.24 OS.

At 3 months after the procedure, the patient’s UCVA was logMAR 0.00 OD.
and logMAR 0.50 OS. Visual acuity in the left eye improved to logMAR 0.00 with a refraction of –1.25/–0.50×113.

Corneal topography showed normalisation of the axial curvature maps OU, no evidence of ectasia and a small amount of regular astigmatism OS (Figure 4). Total HOA RMS had decreased to 0.445 μm OD and 0.447 μm OS (Figure 5), providing further evidence of the treatment’s benefit for regularising the anterior corneal surface.

The patient underwent an enhancement excimer laser procedure in the left eye at 12 months after the initial treatment, with an excellent result. At his last available follow-up, 6 weeks after the enhancement, UCVA in the left eye was logMAR 0.10. The patient was very satisfied with his visual outcome.

Early detection of keratoconus allows CXL to be performed when VA is still reasonably good and optimises prognosis for the patient. As in this case, patients with early keratoconus causing decreased vision often present for a refractive surgery consultation that enables diagnosis of their corneal disorder. The good outcomes that can be achieved for patients with keratoconus highlight the need to consider the implementation of screening programmes for this condition, as diagnosis and treatment at early stages can achieve excellent unaided acuities.

This case also highlights the efficacy of the topography-guided PRK procedure for normalising the anterior surface of the cornea and reducing coma in eyes with keratoconus. Recent reports substantiate its benefit for improving visual quality.1,7,8

We have also used topography-guided surface ablation techniques successfully for visual rehabilitation in eyes with irregular astigmatism and elevated HOAs related to conditions other than keratoconus, including in eyes with a history of trauma or infectious keratitis.

Regardless of the indication, patients need to be consented appropriately to establish realistic expectations for the outcome, depending on the severity of their condition and including the high probability of needing more than one laser treatment. In our experience, patients who elect to undergo the surgery are gratified by their improved visual quality.

REFERENCES


(FIGURE 2) Preoperative Zernike HOA analysis OD (top) and OS (bottom).

(FIGURE 3) Planned ablation patterns OD (top) and OS (bottom).


(FIGURE 4) Normalisation of the anterior corneal surface OD (left) and OS (right) at 3 months after topography-guided PRK combined with prophylactic CXL.

(FIGURE 5) Postoperative Zernike HOA analysis OD (left) and OS (right). (Images courtesy of Mr Anderson and Mr Konstantopoulos)
CASE OF THE MONTH

Setting a new standard in cataract surgery safety

By Jens Jordan, MD

Cataract surgery with phacoemulsification has been recognized for many years to be one of the safest and most effective surgical procedures. Nevertheless, there has been continued effort on the part of our industry partners to develop advances in technologies that will further increase surgical success.

In September 2021, a new phacoemulsification system came onto the market – the QUATERA® 700 from ZEISS (FIGURE 1). Before it became commercially available, I had the opportunity to use the new device in a wet lab setting operating on enucleated porcine eyes. Then, after it was approved for human use, I used the QUATERA for 3 days at my surgery center. I will need more experience with the device before I can fully appreciate all of its features. Based on my initial limited experience, however, I can state conclusively that I was impressed by its performance for providing unsurpassed anterior chamber stability in challenging cases. Being able to work in a controlled intraocular environment made me feel comfortable and relaxed, and by the end of the first day I was looking forward to operating again with the ZEISS QUATERA 700.

Quiet and controlled anterior chamber

The device is built with a number of new features. However, its ZEISS patented QUATTRO® Pump represents its most remarkable asset, distinguishing the ZEISS QUATERA 700 from other phacoemulsification machines in its design and performance for controlling fluidics.

Differing from venturi and peristaltic pumps, the QUATTRO Pump directly controls both infusion and aspiration and operates via four syringe-like chambers that provide synchronous exchange of infusion and aspiration (FIGURE 2). Sensors directly measure actual irrigation and aspiration flow and automatically compensate for incisional leakage to maintain the pre-set target IOP independent of vacuum limit or IOP level. The QUATTRO Pump enables rapid stabilization of free flow state IOP after occlusion break in about 200 ms (Data collected by Carl Zeiss Meditec), and consequently I did not experience surge.

Watch the Video

FIGURE 2. Optimizing safety with the QUATTRO Pump

The QUATTRO Pump is designed to keep the anterior chamber stable throughout surgery, and at least in my early experience, it achieves this goal. During the days when I had the QUATERA at my center I used it on all scheduled patients. This unselected cohort represented the full spectrum of routine and challenging cases that are encountered in clinical practice and included eyes with hyperopia and a shallow anterior chamber, small pupils, pseudoexfoliation, and cataracts with very hard nuclei. In all of the procedures, including those that tend to be stressful situations themselves, and even if
there was fluid outflow from the main or side-port incisions, I felt very comfortable because I encountered no incidences of anterior chamber shallowing, forward bulging of the posterior capsule, or excessive turbulence.

Working in this controlled environment gave me the confidence to use presets for my fluidics settings that are higher than my usual settings in order to increase my efficiency in more complicated cases, such as in eyes with a hard nucleus, pseudoxfoliation or miotic pupil. At first I operated with my standard vacuum of 330 mmHg and flow rate of 33 cc/min. After several cases and with the knowledgeable guidance of my manufacturer’s representative, I felt comfortable that safety would not be compromised by higher settings. Setting the machine for a rapid rise in vacuum and up to 625 mmHg and for 60 cc/min for flow improved efficiency while the anterior chamber remained stable. The ZEISS QUATERA 700 provided stable non-phaco suction for chopping the nucleus and good “grabbing” of fragments along with controlled anterior pulling of the fragments for emulsification. There also seemed to be less iridal movement during surgery.

A brief glance at other features

The ZEISS QUATERA 700 also has Automated Ultrasound Power on Demand, meaning that ultrasound is delivered only when it is needed. Unlike with other phaco machines, when operating with the QUATERA there is no need to repeatedly use the foot pedal to control ultrasound power. With Power on Demand, ultrasound is only provided when full occlusion is detected, and ultrasound is deactivated when the occlusion breaks, thus, reducing the ultrasound energy to a minimum. Although I feel that I will need more time to fully understand how best to work with Automated Ultrasound Power on Demand, I was able to appreciate how it could provide improved fragment followability and more efficient surgery. In fact I was surprised in some cases by how little energy was used. Reducing ultrasound power use during cataract surgery can lead to greater safety, minimize corneal endothelial cell stress, and enable faster visual recovery.

The ZEISS QUATERA 700 also has a dual-linear foot pedal that allows surgeons to easily control ultrasound energy, and I especially enjoyed this feature that is lacking on the machine I have been using. Another design element of the new phaco machine that I and my entire team liked a lot is that the phaco screen integrates the microscope view, which allows the OR staff to see what the surgeon sees. By having a real-time perspective of how the surgery is progressing, the OR nurse can anticipate the next steps and have the necessary instruments ready as soon as the surgeon is about to ask for them, enabling OR workflow efficiency. As with all new equipment, staff needs thorough introduction to the system and on-screen menu management. Yet, after receiving training, the OR personnel found system initiation of the QUATERA before each operation and handling of its on-screen menu easier compared to other machines.

The ZEISS QUATERA 700 is also capable of digital integration with the IOLMaster® and CALLISTO eye® (both Carl Zeiss Meditec AG). It allows surgeons to see patient data from the IOLMaster displayed on the QUATERA screen and to have integrated workflow of the CALLISTO eye assistance function and phaco steps for full control of the surgical workflow from one sterile cockpit. This digital integration of technology brings important benefits from streamlining cataract surgery workflow and reducing human input errors.

Conclusion

It is usual to experience some stress and apprehension when operating on patients with equipment that is new and unfamiliar. For that reason, it was amazing to me how quickly those feelings disappeared during my initial experience using the ZEISS QUATERA 700 because of how well it handled fragments and maintained anterior chamber stability in a variety of situations. Not only did I look forward to the next day’s surgical schedule at the end of my first and second days using the new device, but I missed it after the 3-day trial ended. When I returned to using my own phacoemulsification system I had the feeling that I was going back to driving an older car that lacks the comfort and safety benefits of the latest vehicles.

The ZEISS QUATERA 700 offers many options for finetuning settings that provide the opportunity to optimize the surgical efficiency and safety in various surgical scenarios. After using the machine during just a short testing period, I was able to determine fluidics settings that I felt were excellent for my technique. Different cataract surgeons use different techniques and have different preferences for phacoemulsification settings. As with all new machines, as surgeons begin to use the QUATERA, they will need professional help and some time to learn how to program it and find settings tailored to their preferences and needs. Having had a limited testing period, I still need more experience with the new machine to understand how best to use it. Considering the control and safety it provides, I expect that when I resume on the road that takes me on my learning curve with the ZEISS QUATERA 700, I will have an enjoyable and rewarding journey.

Prof. Dr. Jens Jordan
is in private practice in Frankfurt/Main, Germany.
He is a consultant to Carl Zeiss Meditec.

Media placement sponsored by Carl Zeiss Meditec AG
Collagen crosslinking provides corneal stability in young patients

Text: Collagen crosslinking (CXL) in paediatric and young adult patients with keratoconus can stabilise, and in some cases even improve, corneal keratometry and vision up to 2 years postoperatively, according to study results presented by Dr Solin Saleh.

Dr Saleh, who recently completed her paediatric ophthalmology fellowship at the Byers Eye Institute at Stanford University School of Medicine in California, United States, reported the findings at the American Society of Cataract and Refractive Surgery (ASCRS) 2021 annual meeting in July.

The study was designed by Dr Edward E. Manche, director of cornea and refractive surgery and Stanford University professor of ophthalmology. It consisted of a retrospective chart review of patients 22 years or younger who had undergone CXL for progressive keratoconus at the Byers Eye Institute during the previous 7 years. All CXL procedures were performed by Dr Manche.

The investigators evaluated the patient records to identify changes in visual and corneal parameters, including corrected distance visual acuity (CDVA) and maximum keratometry (Kmax) up to 2 years after CXL. Dr Saleh explained that the findings are important because although keratoconus is generally diagnosed during puberty, it can be more severe and progress more quickly when identified in younger children, who may need corneal transplantation if the disease is not addressed.

Dr Saleh reported that 86 eyes of 71 consecutive patients underwent CXL during the study. The patients ranged in age from 12 to 22 years (mean: 16.4 ± 2.5 years) at the time of surgery. Bilateral CXL was performed in eight patients. Of the study sample, 57 eyes had completed a minimum of 1 year of follow-up and 24 eyes had completed 2 years of follow-up.

Dr Saleh reported that the mean preoperative CDVA was logMAR 0.38 ± 0.32 (Snellen acuity 20/48), with mean postoperative CDVA of 0.29 ± 0.31 (20/39) and 0.31 ± 0.31 (20/41) at 12 and 24 months postoperatively. Compared with preoperative mean Kmax, there was an improvement of ~0.8 D to a mean postoperative Kmax of 59.1 ± 9.1 D at 12 months and ~1.3 D to 59.7 ± 8.8 D at 24 months.

The authors concluded that CXL was both safe and effective to perform in this young patient population. The procedure stabilised the cornea in these children and young adults, and in some cases the vision and the keratometry values improved. The authors urged surgeons to consider CXL for treating paediatric patients with early keratoconus to prevent ongoing disease progression, especially given the risk of visual morbidity in children.

By Lynda Charters; Reviewed by Dr Solin Saleh

SOLIN SALEH, MD
Email: solinaleh@stanford.edu
This article is adapted from Dr Saleh’s presentation at the American Society of Cataract and Refractive Surgery annual meeting. She has no financial interest in this subject matter.

EDWARD E. MANCHE, MD
Email: cornea@stanford.edu
Dr Manche has no financial disclosures related to this content.
OCT/OCTA ocular biomarkers may help diagnose Parkinson’s disease

Imaging study reveals specific, associated retinal and choroidal changes

By Lynda Charters;
Reviewed by Dr Sharon Fekrat and Dr Dilraj S. Grewal

There is no single diagnostic test for Parkinson’s disease (PD), and neurologists often rely on the patient’s response to drugs to differentiate the disease from conditions with similar symptoms. However, investigators at Duke University, North Carolina, United States, have taken a step towards establishing an adjunctive approach in a study utilising retinal imaging for diagnosis.

Dr Cason B. Robbins of the Department of Ophthalmology at Duke University School of Medicine in Durham, North Carolina, US, was the lead author of the study. He was joined by Dr Sharon Fekrat, professor of ophthalmology, and Dr Dilraj S. Grewal, associate professor of ophthalmology.

Dr Robbins evaluated the retinal microvascular and choroidal structural changes in the eyes of patients with PD. The investigators used enhanced-depth optical coherence tomography (OCT) as well as OCT angiography (OCTA), both non-invasive technologies, to evaluate patients who had received a clinical diagnosis of PD, in order to identify differences between patients with PD and healthy controls.

The investigators noted indications from previous study results that cerebral small vessel disease may be a potential risk factor for development of PD, and PD has a higher prevalence of cerebral ischaemic lesions.

Study outline and findings

Participants were enrolled at the Duke Neurological Disorders Clinic. The 69 patients (124 eyes; mean age 71.7 years) had received an established clinical diagnosis of PD. The study also included 137 cognitively healthy controls (248 eyes; mean age 70.9 years). All the patients underwent OCT and OCTA.

The investigators assessed the superficial capillary plexus vessel density (VD) and perfusion density (PFD) within the Early Treatment Diabetic Retinopathy Study (ETDRS) 6 × 6-mm circle, 6 × 6-mm inner ring and 6 × 6-mm outer ring, and the foveal avascular zone. They also measured the thickness of the retinal nerve fibre layer; the macular ganglion cell/inner plexiform layer and the central subfield; the subfoveal choroidal thickness; total choroidal area; luminal area; and choroidal vascul arity index (CVI).

The results showed that when compared with the healthy sex- and age-matched controls, the VD and PFD were significantly lower in the patients with PD in the 6 × 6-mm ETDRS circle (P = 0.3 and P = 0.4, respectively) and in the 6 × 6-mm inner ring (P = 0.003 and P = 0.004, respectively).

The total choroidal area and luminal area were larger in the patients with PD (P = 0.1 and P = 0.2, respectively). The CVI was lower in the patients with PD. The results did not show differences in the retinal nerve fibre layer or ganglion cell layer thickness or the subfoveal choroidal thickness; the latter finding differs from the results of some other studies.

The investigators pointed out that, when the current findings are combined with the clinical history and other tests, the choroidal and retinal microvascular imaging results “may hold the potential to improve clinician confidence in the diagnosis of PD.” They added that the findings demonstrate the need for further research into retinal imaging as a potential novel biomarker for individuals with neurodegenerative diseases such as PD.

“Future long-term studies that characterise the natural history of microvascular and structural retinal changes in individuals across the clinical spectrum of PD [are] warranted,” they concluded. “Such studies may help clarify whether these imaging findings may be useful as biomarkers for the onset of PD.”

REFERENCES
Treating Hyperopia with SMILE: A clinical study

By Walter Sekundo, MD, PhD

The overall prevalence of hyperopia in the European population is estimated at approximately 35% and is higher among middle to older age adults compared to their younger counterparts. For hyperopes seeking refractive surgery, LASIK is more likely to be considered for younger individuals than a more invasive lens exchange or phakic IOL procedure. Despite advances in techniques and technology, however, efficacy, safety, predictability, and stability outcomes with hyperopic LASIK fall short of those achieved with myopic LASIK.

SMILE has advantages compared with LASIK, including less risk for postoperative dry eye and avoidance of LASIK flap-related complications. While the development of SMILE for hyperopia has faced challenges, modifications in the lenticule profile, optical and transition zone sizes, nomograms, and laser energy settings led to improved outcomes as reported in studies conducted at my center and in Nepal.

The promising results achieved with these refinements supported the initiation of an international multicenter registration trial for SMILE to treat hyperopia and hyperopic astigmatism using the VisuMax femtosecond laser (Carl Zeiss Meditec AG; Jena, Germany). The final report from the study, which demonstrates efficacy, safety, and predictability of the procedure, is currently undergoing regulatory review. Hopefully, approval of the hyperopic SMILE is on the near horizon. Meanwhile, engineers at ZEISS Medical Technology guided by customer input were redesigning the company’s femtosecond laser. Introduced in September 2021, the new VISUMAX 800 is a significant advance in many ways that include particular benefits for performing hyperopic SMILE® treatments.

SMILE FOR HYPEROPIA during clinical trials:

I was one of eight principal investigators in the hyperopic SMILE study and have the honor of being its coordinating investigator. The final analysis includes data from 374 eyes of 199 patients enrolled at centers in Europe, China, and India.

Eligible patients had up to 6.00 D of hyperopia and 5.00 D of cylinder, a predicted postoperative refraction ≤51.0 D, and CDVA 20/25 or better in the treated eye(s). The study participants represented a heterogeneous population with respect to age and refractive error. Mean spherical equivalent for the study eyes was 3.20 ± 1.48 D with a range from +0.25 to +6.50 D.

Using fairly low energy (of 25 to 27 nJ and 4.5 μm spot/track distance), the VisuMax femtosecond laser was programmed as follows: 8.8 to 8.89 mm diameter cap with a thickness of 120 μm, 25 μm central lenticule thickness, 6.3 mm optical zone, 2 mm transition zone, and a 2 to 4 mm incision for lenticule removal.

The efficacy and safety results were good and equal to or better than those achieved in recent studies of hyperopic LASIK. Importantly, serial data from planned follow-up visits showed the refractive and visual outcomes of hyperopic SMILE were stable between 3 and 12 months.

CASE HISTORY

More details of the results from the hyperopic SMILE registration trial are forthcoming. The following case describing one of my patients highlights the efficacy and safety of the procedure.

The patient was my operating room head nurse—a 58-year-old woman who decided she no longer wanted to wear glasses for near vision. She was a low hyperope with minimal astigmatism, and while assisting me during a hyperopia SMILE treatment, she asked me if she could be treated as well. Having assisted during thousands of SMILE cases, she was very familiar with the procedure, and she fulfilled all inclusion criteria. I treated her in 2019, and the procedure was planned to provide micro-monovision with targets determined through testing with Reinstein’s PRESBYOND testing protocol.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preop</th>
<th>Postop</th>
<th>Target refraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>OD refraction</td>
<td>+1.25 -0.5@85°</td>
<td>-1.0 -0.75@50°</td>
<td>-1.0 D</td>
</tr>
<tr>
<td>OD CDVA/UVA</td>
<td>1.25/0.8</td>
<td>1.25/0.32</td>
<td></td>
</tr>
<tr>
<td>OS refraction</td>
<td>+0.75 -0.25@85°</td>
<td>-0.5 -0.5@100°</td>
<td>-0.75 D</td>
</tr>
<tr>
<td>OS CDVA/UVA</td>
<td>1.25/0.8</td>
<td>1.0/0.8</td>
<td></td>
</tr>
<tr>
<td>Binocular UNVA</td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
</tbody>
</table>

Table 1. Preoperative and 12 months postoperative data

As shown in Table 1, the patient’s refractive and visual outcomes were excellent, and she achieved her goal for glasses-free vision.
Figure 1 displays the patient’s preoperative, postoperative, and differential topography maps that show excellent centration and steepening of the central cornea after the surgery. Furthermore, the patient was extremely happy with her outcome. She reported not needing to wear glasses for distance or near and was somewhat amazed when she found herself capable of threading a 10-0 nylon suture without her glasses. Remarkable to me as well was her ability to assist in the OR without glasses even in the lower light setting of a vitrectomy procedure.

**SMILE FOR HYPEROPIA with VISUMAX 800** - overcomming the challenges

While positive results were achieved in the hyperopic SMILE study, the procedure still has some challenges. Accurate centration is important for any refractive surgery procedure and is especially critical for hyperopic treatments. In addition, the technique requires creation of a large lenticule so that use of the M-contact glass is mandatory. However, hyperopes tend to have smaller eyes, and with a laser treatment time of 35 seconds, there is increased potential for suction loss during the procedure. In fact, the rate of suction loss in the multicenter trial was 1.34%. The VISUMAX 800 addresses these issues and brings additional safety.

The possibility for suction loss can be expected to decrease with the VISUMAX 800 because it is 3 times faster than the current VisuMax and completes the SMILE hyperopia protocol in just 12 seconds\(^\text{5}\). The shorter procedure time reduces stress for the patient and surgeon alike. Moreover, with the new patented computer-assisted centration function (CentraLign\(^\text{6}\)) achieving a perfect centration is no longer an art. It becomes a science. We know that centration of an eye might slightly differ depending on the pupil size (photopic versus scotopic). OcuLign\(^\text{6}\), a new function featuring in VISUMAX 800 enables cyclotorsion adjustment which is done through digital rotation of the cutting pattern, adding value for astigmatic corrections. And while acquiring images for the cyclotorsion adjust-

ment system, the surgeon can even choose the illumination level in order to define the perfect centration mark.

As other benefits, the VISUMAX 800 femtosecond laser is a mobile device and has a much smaller footprint than the VisuMax. It features two screens – one used for data management and the other that can be used to observe the surgery. The data management screen has a very user-friendly interface, and the heads-up display of the second screen offers better ergonomics for the surgeon and the opportunity for the surgical nurse to visualize the procedure. The VISUMAX 800 is still equipped with an optical infinite resolution microscope. The VISUMAX 800 was also designed for improved workflow efficiency. It is integrated with other devices and software platforms through the DICOM-based FORUM system as central archive. Because data management and treatment planning are centralized, treatment planning can be conveniently done outside the OR using Refractive Workplace (Carl Zeiss Meditec AG)\(^\text{7}\) and then seamlessly sent to FORUM for transfer to the laser.

**CONCLUSION**

SMILE for hyperopia and hyperopic astigmatism has become truly feasible. As soon as the procedure receives regulatory approval, it is expected that the hyperopic SMILE module will be released for the VISUMAX 800. This state-of-the-art femtosecond laser not only brings benefits that are especially suited to achieve good results with hyperopic SMILE, but its features make it a valuable addition for any surgeon performing corneal laser vision correction procedures.

---

**Dr. Sekundo** is Professor and Chairman, Department of Ophthalmology, Philippa University of Marburg, Marburg, Germany. He is a consultant to Carl Zeiss Meditec AG.

Media placement sponsored by Carl Zeiss Meditec AG
Retina experts recently gathered virtually for the Ophthalmology Times Europe® and Modern Retina® Podcast Series to discuss findings from studies on the treatment for neovascular age-related macular degeneration (nAMD) and diabetic macular oedema (DMO) presented at the 39th annual meeting of the American Society of Retina Specialists.

Drs Carl Regillo and Carl C. Awh highlighted results from ARCHWAY, the pivotal trial that supported the recent United States Food and Drug Administration approval of ranibizumab injection (Susvimo, Roche), previously called Port Delivery System with ranibizumab (PDS) 100 mg/mL, for the treatment of nAMD in patients who have previously responded to at least two anti-VEGF injections. Dr Regillo is director of the Wills Eye Retina Service and professor of ophthalmology at Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, US, and ARCHWAY study investigator. Dr Awh is in private practice with Tennessee Retina, Nashville, Tennessee, US.

Patient selection
The two retina specialists also provided their perspectives on patient selection for the new nAMD therapeutic option, noting that, like the patients enrolled in ARCHWAY, candidates for the ranibizumab implant would be individuals who have shown benefit with prior anti-VEGF injections. “I think initially, it wouldn’t be first-line therapy,” said Dr Awh.

Dr Regillo agreed, but added, “The way we are going to use this device [in practice] may or may not be different than the clinical trials.” Dr Regillo also noted that the requirement for an operating theatre procedure would influence patient selection so that initially the focus would be on patients who have a high-frequency injection need.

Their discussion included a review of some modifications made during clinical development of the product in the implantation and refill-exchange technique, and they discussed the training and learning curve for the procedures. “It’s important to know that no surgeon will walk into the operating room and just know how to do this procedure without a lot of preparation,” Dr Awh said.

Dr Regillo observed that the implantation procedure is unique, but not difficult. “I think any vitreoretinal surgeon can do this operation and do it well,” he said. Ongoing trials investigating the PDS for treating wet AMD, DMO and diabetic retinopathy were also described, and Drs Awh and Regillo shared their thoughts on forthcoming approaches for
reducing the injection burden for patients with nAMD. Anticipating multiple novel options, Dr Regillo described the future for managing wet AMD as “super bright.”

**Faricimab clinical study data**

Drs Caroline R. Baumal and Karl Csaky discussed outcomes of pairs of Phase 3 studies evaluating the efficacy and safety of Roche’s monoclonal antibody faricimab for the treatment of nAMD (TENAYA and LUCERNE) and DMO (YOSEMITE and RHINE). Dr Baumal is a retina specialist at New England Eye Center, Tufts Medical Center, in Boston, Massachusetts, US. Dr Csaky is in practice with the Retina Foundation of the Southwest in Dallas, Texas, US.

Both doctors remarked on the trial designs that included treatment approaches emulating what is done in the clinic. “Then we can take the data from these trials and really apply it to our day-to-day practice,” Dr Csaky said.

The results from the pivotal trials showed that, as a treatment for both wet AMD and DMO, faricimab was non-inferior to aflibercept in the primary endpoint analysing change from baseline best-corrected visual acuity (BCVA). Importantly, the findings also highlighted the durability of the investigational agent’s treatment benefit, which Dr Csaky explained is accounted for by its dual inhibition of VEGF and angiopoietin-2.

In the nAMD studies, 45% of patients assigned to faricimab were able to be treated every 16 weeks and approximately three-quarters could be treated every 12 weeks without harm in terms of vision, Dr Csaky said. Dr Baumal reported that in the DMO trials, over 50% of patients were controlled with faricimab injected every 16 weeks and over 70% were being treated every 12 or every 16 weeks.

Noting that there is always concern about unexpected side effects with new treatments, especially when they are administered to patients who can be systemically fragile, Dr Baumal said that the absence of unusual adverse events or cases of serious inflammatory conditions among faricimab-treated patients was a very encouraging sign.

Closing with their perspectives on the future of retinal disease management, Drs Baumal and Csaky agreed that pharmacotherapy will remain at the forefront. They suggested, however, that it might involve delivery modes other than direct intravitreal injection or use of a device for sustained drug release.

**Understanding real-world outcomes**

Studies discussed by Drs Parisa Emami-Naeini and Theodore Leng analysed information extracted from large databases to investigate real-world use of anti-VEGF treatment for nAMD and DMO and outcomes. Dr Leng is director of clinical and translational research at Stanford University, Stanford, California, US. Dr Emami-Naeini is director of the uveitis service at UC Davis Medical Center, Sacramento, California.

Dr Emami-Naeini and colleagues used the Vestrum Health database to examine maintenance of driving vision in patients being treated with anti-VEGF agents. They identified treatment-naïve patients with driving vision (BCVA of 20/40 or better in the better seeing eye) at their index visit when they started on the intravitreal drug therapy.

The study found that both for the DMO and AMD cohorts, the number of injections received during the first year was the main factor associated with the ability to maintain driving vision over the follow-up period. Race, gender, insurance type and location (rural vs urban) were not deemed to be predictive variables in the study.

Using the American Academy of Ophthalmology’s IRIS Registry dataset, Dr Leng and colleagues analysed data for patients receiving anti-VEGF injections for nAMD who had >2 and up to 6 years of follow-up. The results of this study showed better vision at each follow-up time point, the longer they stayed on anti-VEGF therapy.

Drs Leng and Emami-Naeini observed that results in the real world can be very different than those seen in clinical trials for reasons that include differences in the characteristics of their respective populations and follow-up. As an example, they cited a study reporting that only 50% of patients seen in a retina clinic would qualify for enrollment in even the most inclusive clinical trials. Furthermore, these ineligible patients were shown to have worse visual outcomes than their counterparts whose characteristics would have allowed their entry into the registered trials.

“We need to study the real-world outcomes because we live in the real world,” Dr Leng said. He stated that information from real-world studies identifies gaps in care between what clinicians believe they are doing based on evidence-based medicine and reality. Therefore, it helps clinicians to modify the way they are treating patients and how they are communicating with them about what they could do to stay engaged in their care, Dr Leng said.

Both Dr Leng and Dr Emami-Naeini expect the time is coming when real-world data will be incorporated into the regulatory pathway and used to complement clinical trial data in the management of patients in clinical practice.

*The podcasts can be heard online, at: europe.ophthalmologytimes.com/view/updates-from-asrs-2021*

*Produced in partnership with Roche.*
Newer CPC laser technologies are improving glaucoma outcomes

By Lynda Charters; Reviewed by Dr Shan C. Lin

Ophthalmologists have seen a progression in cyclophotocoagulation (CPC), with each generation of the technology becoming more doctor- and patient-friendly. Dr Shan Lin, a glaucoma specialist at the Glaucoma Center of San Francisco in California, United States, recently described some of the latest advancements in the treatment.

Transscleral cyclophotocoagulation (TCPC) was developed first, but it has its limitations. In some cases, the treatment is unable to reach the targeted tissue because the tissue is not visible. In addition, the surrounding structures can potentially be damaged. Excessive treatment using TCPC can also occur and cause an audible popping and explosion of the ciliary processes and pars plana, which can result in inflammation such as cystoid macular oedema (CMO).

The G-Probe Illuminate Delivery Device (Iridex) has helped to address these problems. This technology uses a diode laser to treat the ciliary processes through the sclera and reduces the intraocular pressure (IOP) by decreasing aqueous production.

“This latest generation of the technology allows identification of the ciliary process locations either before or at the time of treatment,” Dr Lin said. He explained that the locations of the ciliary processes can vary among the different ocular quadrants and among different patients with glaucoma. He cited a study reporting that they can range from 2–5 mm behind the limbus.

**Endoscopic visualisation**
Endoscopic CPC is a newer technology that facilitates direct visualisation of the ciliary processes as they are being treated. Probes with different gauge sizes (18, 19, 20 and 23 gauge) are available for this intraoperative procedure. In addition, the availability of curved probes allows the treatment of a larger area within the same incision, according to Dr Lin.

A typical procedure, as he described, is one performed in a pseudophakic patient through a limbal approach. “The goal is to cause shrinkage and whitening of the ciliary processes,” he said.

A study of endoscopic CPC in 68 patients, which included a range of glaucoma types, found that the IOP decreased from approximately 27 mm Hg preoperatively to 17 mm Hg postoperatively. In addition, the numbers of medications needed decreased from approximately three to two.

The complications associated with endoscopic CPC included fibrin exudate (24%), hyphaema (12%), CMO (10%), vision loss (6%)—due to CMO in most cases—and choroidal detachment (4%).

**Short pulse technology**
MicroPulse is the newest of the technologies. It controls the thermal effect by “chopping” a continuous wave of the energy beam into repetitive short pulses interrupted by relaxation times, which makes for less thermal damage to the targeted area. Dr Lin explained that the technology is also thought to stimulate biological factors, such as cytokines and growth factors, at the treatment area.

The Cyclo G6 Glaucoma Laser with the MicroPulse P3 probe (Iridex) is a transscleral procedure designed to deliver laser energy in a pulse pattern to avoid excessive damage to the tissues. It also differs from the G-Probe in that the treatment is aimed...
at the pars plana rather than the ciliary processes and involves a slow sweeping motion along the superior and inferior limbus rather than the discrete spot placement of the G-Probe.

An advantage of this new technology is that it can be performed either in an ophthalmologist’s surgery or in the operating theatre. Dr Lin said that he prefers performing the procedure in the latter location, for increased control and patient comfort.

In addition, there are no pops involved with the treatment. However, Dr Lin noted that the sweeping motion should avoid the 3 and 9 o’clock positions. “Having slower sweeps with the MicroPulse facilitates better uptake of the laser and efficacy,” he explained.

A study with follow-up of almost 7 years reported the long-term efficacy and durability of this treatment. The authors reported a 43% reduction of IOP at 78 months in 14 patients and a concomitant reduction in medications from 1.8 to 1.1. A number of treatments were needed, with an approximate average of 4.5, to achieve IOP lowering.³

Dr Lin also presented the results of MicroPulse technology in a retrospective analysis of 54 patients with a baseline IOP of 24 mm Hg, 75% of whom had primary open-angle glaucoma. Postoperatively, the average IOP was 17 mm Hg ($P = 0.0002$).

Success in this study was defined as IOP lowering of 20% or more with or without medications; this criterion was met in 68% of patients. Seven of the eyes required re-treatment. The potential complications of the technology include rare, unexplained visual loss; hypotony; ocular inflammation; and CMO.

In anatomical assessments using ultrasound biomicroscopy, there were no observable changes comparing before and after treatment. Iridex also recently introduced a new Rev-2 probe with a footplate that helps with limbal alignment, improves tissue coupling for better laser delivery, makes the technique easier to perform and potentially has fewer complications.

**Conclusion**

“Diode TCPC with the G-Probe is usually reserved for blind, painful eyes and is now available with transillumination. Endoscopic CPC can be useful in some cases; however, there are risks associated with penetrating surgery,” Dr Lin concluded.

```
```

REFERENCES


SHAN C. LIN, MD

This article is adapted from Dr Lin’s presentation at the Glaucoma Research Foundation’s 25th Annual Glaucoma Symposium. Dr Lin is a consultant to Iridex.

**Subscribe for practical tips and valuable resources**

“Micropulse TCPC is useful for patients with refractory glaucoma, with less inflammation and possibly less risk than with diode laser. In addition, the new REV-2 probe is now available.”

**VIEW MORE GLAUCOMA CONTENT ONLINE:**

A Phase 3 clinical extension study of a bimatoprost implant (Durysta, Abbvie Inc.) showed that patients had sustained lowering of their IOP for 2 years or more with no additional treatment and no changes in their visual fields.

The previous results of the Phase 1 and 2 clinical studies of the implant showed that the duration of the IOP-lowering effect had extended beyond the expected period of intraocular drug bioavailability.
Several innovations are revolutionising surgical care in paediatric ophthalmology, according to Dr Janet L. Alexander, an assistant professor of ophthalmology and paediatrics at the University of Maryland School of Medicine in Baltimore, Maryland, United States.

Speaking at the Women in Ophthalmology 2021 Summer Symposium, Dr Alexander presented a series of rapid-fire cases to discuss four such paediatric innovations: antenatal surgical planning to address congenital hereditary disease, endothelial keratoplasty, endocyclophotocoagulation (ECP) to treat refractory glaucoma and ultrasound biomicroscopy (UBM) as a tool for guiding complex cataract surgery.

**Antenatal surgical planning**

One case involving a child born with Norrie disease highlighted the value of antenatal surgical planning to enable intervention prior to complications. A 30-year-old woman in her second trimester of pregnancy presented with carrier status for *NDP* mutation.

Amniocentesis confirmed foetal *NDP* mutation, and the ultrasound showed no foetal retinal detachment. Labour was induced at 34 weeks’ gestation for early retinal treatment.

As well as having Norrie disease, the baby was diagnosed with bilateral vitreous haemorrhages at birth, and underwent bilateral treatment with intravitreal anti-vascular endothelial growth factor therapy and peripheral retinal laser. Six months later, both eyes demonstrated robust light perception vision with an attached retina.

Dr Alexander noted that the case was a reminder that it is never too early to start antenatal surgical planning. “Prenatal surgical planning requires proactive and timely genetic testing to identify surgical candidates, counselling for female carriers of high-risk genetic traits, and involvement of geneticists and genetic counsellors,” she said.

**Endothelial keratoplasty**

Dr Alexander discussed the benefits and drawbacks of descemet stripping automated endothelial keratoplasty (DSAEK) versus penetrating keratoplasty (PK) with reference to a case involving a 4-year-old child who presented with a cloudy cornea 2 years after undergoing cataract surgery. The child received a diagnosis of bullous keratopathy and underwent DSAEK.

“Compared to PK, DSAEK is associated with stronger wound integrity, less astigmatism and faster visual recovery. It also avoids the need for stripping of the host endothelium in paediatric eyes,” Dr Alexander said. “However, DSAEK graft positioning can be very difficult in paediatric patients, and complications such as graft folds; detachment and dislocation; pupillary block; endothelial immune rejection; and steroid response can occur.”

**ECP for glaucoma**

There are advantages to choosing ECP over transscleral ciliary ablation to treat refractory glaucoma in paediatric patients, according to Dr Alexander. She presented a case involving a 7-year-old child who had sustained a traumatic cataract, then presented with 20/250 vision and elevated intraocular pressure (IOP) despite maximal medical treatment, selective laser trabeculoplasty and goniotomy.

The most remarkable feature of ECP is that it is minimally invasive and has a more favourable safety profile compared with the trans-scleral technique. “For example, phthisis in the absence of retinal detachment occurs in over 30% of eyes treated transsclerally but in less than 1% of eyes that undergo ECP,” Dr Alexander said. Other advantages of ECP include avoidance of late infectious complications,
such as wound leak and endophthalmitis. However, ECP has a modest success rate and its benefit is short-lived. Outcomes data show that it effectively reduces IOP in about 30% of eyes, and about half of those eyes maintain IOP control for 1–2 years. In addition, ECP can lead to the serious complications of hypotony, retinal detachment and vision loss.

**ECP effectively reduces IOP in about 30% of eyes.**

**Imaging for paediatric cataract**

According to Dr Alexander, preoperative evaluation with UBM enables cataract surgery planning and helps to prevent intraoperative surprises. Dr Alexander demonstrated these points with several case examples.

In one case, a 1-month-old child presented with bilateral cataract, but cataract surgery was postponed for 3 months whilst the child underwent treatment for comorbid heart failure. Repeat imaging prior to the scheduled cataract surgery showed that crystalline lens thickness had decreased dramatically over time. Dr Alexander said that knowledge of the absorbed cataract had guided appropriate surgical techniques.

“Cataract surgery planning with UBM allows surgeons to evaluate IOL position, the lens periphery and the ciliary body,” she said. “Importantly, it allows us to avoid surprises, including absorbed cataract, foreign bodies, masses, cysts or membranes.”

Other cases involving uveitic cataracts showed how imaging with UBM can document pathology that might complicate cataract surgery and can inform the surgical approach. Dr Alexander presented a series of eyes in which UBM revealed the presence of a cyclitic membrane, pupil synechiae and calcified plaque on the anterior capsule.

Dr Alexander concluded by observing that quantitative UBM is an innovation that further enhances the clinical utility of this procedure. Quantitative UBM uses algorithms to analyse the images and generates information that helps clinicians interpret the images. The algorithms are also capable of suggesting clinical diagnoses and prognostic features, such as the risk of complications.

**Fundus photo 1 month following laser treatment for Norrie disease.** (Image courtesy of Dr Janet L. Alexander)
Identifying individuals at risk of glaucoma via genetics studies

Polygenic risk score allows multiple gene variants to be tested simultaneously

Genetic investigations have garnered a wealth of information about glaucoma. The findings have pinpointed specific genes involved in early-onset familial disease with autosomal dominant or recessive inheritance, as well as genetic risk factors for common glaucoma types with complex inheritance patterns.

Speaking at a recent ophthalmology conference, Dr Janey Wiggs, the Paul Austin Chandler Professor of Ophthalmology, Harvard Medical School, Massachusetts, United States, defined the major goals of genetic research as being to identify at-risk individuals and to use knowledge about disease-causing genes to develop novel therapies.

She reported how current studies have set out to evaluate the risk and clinical outcomes in primary open-angle glaucoma (POAG) based on development of a polygenic risk score (PRS) applied to data in genome-wide association studies (GWASs).

**POAG genetics and risks**
The contribution of any single genetic variant to POAG is only small; multiple gene variants are needed to increase both the risk of disease and adverse outcomes. According to Dr Wiggs, to assess the risk, multiple variants must be tested simultaneously using a tool such as the recently developed PRS.

The PRS score determines the total number of genetic risk variants for each person, and individuals in a population are scored according to the number of DNA risk variants they have. Those with the highest number of variants have the highest genetic burden, which is likely to have the greatest impact on the risk of developing POAG and the outcome.

In analyses, the outcomes of individuals with the highest PRS (highest percentile) are often compared with the overall population distribution or with individuals who have the lowest genetic burden. Dr Wiggs said that to develop this valuable tool, two requirements must be met: a GWAS that is large enough to facilitate identifying all potential variants to be included in the PRS, and the availability of computational methods that can manage large data sets and create the score.

**Individuals in the TOP 10% of the PRS had a 15 TIMES greater risk of developing disease.**
A high genetic burden defined by the primary open-angle glaucoma polygenic risk score is associated with earlier disease onset, higher IOP, thinner nerve fibre layer and a greater need for surgery.

**Consortium**
The International Glaucoma Genetics Consortium (IGGC), which comprises investigators from around the world, was formed to complete the GWASs to identify all genetic risk variants for POAG. Each research group contributed their clinical and genetic data from POAG cases and controls.

A trans-ancestry meta-analysis was performed using all data sets; this resulted in the identification of 127 chromosomal regions significantly associated with the risk for POAG. Dr Wiggs said that each region contains hundreds to thousands of genetic variants individually associated with disease risk.

Dr Wiggs reported that all the information from the participating groups worldwide was used to create a POAG PRS, which was applied to different populations and data sets to evaluate the clinical outcomes. When the investigators evaluated the impact of the PRS on disease risk, they found that individuals in the uppermost decile (the top 10% of the PRS) had a 15 times greater risk of developing disease compared with those in the lowest decile.

Dr Wiggs said: “This supported the concept that the PRS is associated with greatly increased risk.” In addition, individuals with the highest genetic burden as defined by the PRS experienced the onset of disease 5–10 years earlier than individuals in the bottom PRS distribution.

**Further applications**
An association has been identified between PRS and increased intraocular pressure (IOP). A recent Australian study showed that individuals with the highest PRS had higher IOP throughout the day, which was especially true in the morning, and those individuals with the highest PRS had increased IOP spikes.

“These results suggested that home tonometry would be useful in patients with high PRS to accurately assess the IOP burden,” Dr Wiggs said. The highest PRS is also associated with ageing, thinner retinal nerve fibre layers and the proportion of patients requiring trabeculectomy to control IOP.

One recent study into myocilin-related glaucoma, conducted on individuals belonging to the UK Biobank, reported that mutations in the MYOC gene can cause juvenile OAG and early POAG, and that the most common mutation in carriers was found to be MYOC p.Gln368Ter.

The study identified 200 carriers of this gene who had IOP measurements and fundus photographs. The goal was to determine the disease rate (penetrance), diagnosis rate and effect of the POAG PRS among mutation carriers.

Dr Wiggs reported that the PRS reflected both the disease penetrance and severity; this finding supported the use of PRS in optimising risk stratification among carriers of MYOC p.Gln368Ter mutation. “People who were mutation carriers were much more likely to have evidence of disease as defined by elevated IOP and disc-defined glaucoma if they were also in the high PRS percentiles,” she said.

Moreover, among patients with glaucoma who were mutation carriers, those in the highest percentiles were far more likely to have received a diagnosis, suggesting that having the myocilin mutation and a high PRS causes more severe disease that is evident to the patient.

Another study involving the UK Biobank, to assess the association of increased caffeine consumption and the PRS interaction with IOP and the risk of POAG, found that caffeine only caused IOP elevations in patients who had the highest PRS. The individuals who had raised IOP levels resulting from higher caffeine intake also had a greater risk of glaucoma.

The main takeaways from this line of research are that a large GWAS made the development of a PRS for POAG possible. A high genetic burden defined by the POAG PRS is associated with disease onset that is earlier by 10–15 years, higher IOP, thinner nerve fibre layer and a greater need for surgery. As Dr Wiggs noted, the PRS can modify disease outcomes due to other genes, such as MYOC, and can interact with environmental factors to influence the level of disease risk.

**REFERENCES**

**IN SHORT**
- A high genetic burden defined by the primary open-angle glaucoma polygenic risk score is associated with earlier disease onset, higher IOP, thinner nerve fibre layer and a greater need for surgery.
UPDATES FROM ASRS 21
PODCAST SERIES
Conversations with eyecare leaders about the latest developments in retina.

EPISODE 1
The FDA-Approved Port Delivery System
A reflection on this major advancement and milestone: the system’s course through clinical trials, benefits from reducing current treatment burdens, and next steps to optimise real-world outcomes.
CARL C. AWH, MD, FASRS • CARL D. REGILLO, MD, FACS

EPISODE 2
Real-World Use of Anti-VEGFs and Outcomes in AMD, DMO
Reviewing insights drawn from studies using two comprehensive retina databases, including differences in outcomes between trials and clinics, the importance of first-year injections, effects of switching therapies, and COVID-related impacts.
PARISA EMAMI-NAEINI, MD, MPH • THEODORE LENG, MD, PHD

EPISODE 3
Faricimab Clinical Study Data to Date
A review of two pairs of Phase III trials respectively, assessing the safety and efficacy of faricimab in the treatment of patients with AMD and DMO.
CAROLINE R. BAUMAL, MD • KARL CSAKY, MD, PHD

Listen Now
COLORED UP

GALILEI ColorZ. ENABLING EXCELLENCE.
The versatile diagnostic platform for refractive, therapeutic and cataract surgery planning.

www.ziemergroup.com/galilei

The GALILEI G4 ColorZ and GALILEI G6 ColorZ are CE marked and FDA cleared. For some countries, availability may be restricted due to regulatory requirements. Please contact Ziemer for details.