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Ophthalmology Times EUROPE®

CUTTING-EDGE ADVANCEMENTS

MAY 2020 VOL. 16, NO. 4

NOW IN A PRE-FILLED SYRINGE:

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Eylea®40 mg/ml solution for injection in a vial & Eylea®40 mg/ml solution for injection in pre-filled syringe (aflibercept) Prescribing Information.

(Refer to full Summary of Product Characteristics (SmPC) before prescribing).

Presentation: 1 ml solution for injection contains 40 mg aflibercept. *Vial:* Each vial contains 100 microlitres, equivalent to 4 mg aflibercept. *Pre-filled syringe (PFS):* Each PFS contains 90 microlitres, equivalent to 3.6 mg aflibercept. **Indication(s):** Treatment of neovascular (wet) age-related macular degeneration (wAMD), macular oedema secondary to retinal vein occlusion (branch RVO or central RVO), visual impairment due to diabetic macular oedema (DMO) in adults and visual impairment due to myopic choroidal neovascularisation (myopic CNV). **Posology & method of administration:** For intravitreal injection only. Must be administered according to medical standards and applicable guidelines by a qualified physician experienced in administering intravitreal injections. Each vial or PFS should only be used for the treatment of a single eye. Extraction of multiple doses from a single vial or PFS may increase the risk of contamination and subsequent infection. The vial or PFS contains more than the recommended dose of 2 mg. The extractable volume of the vial (100 microlitres) or PFS (90 microlitres) is not to be used in total. The excess volume should be expelled before injecting. Refer to SmPC for full details. ***Adults:*** The recommended dose is 2 mg aflibercept, equivalent to 50 microlitres. For wAMD treatment is initiated with 1 injection per month for 3 consecutive doses. The treatment interval is then extended to 2 months. Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or further extended using a treat-and-extend dosing regimen, where injection intervals are increased in 2- or 4-weekly increments to maintain stable visual and/or anatomic outcomes. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly to a minimum of 2 months during the first 12 months of treatment. There is no requirement for monitoring between injections. Based on the physician's judgement the schedule of monitoring visits may be more frequent than the injection visits. Treatment intervals greater than 4 months between injections have not been studied. For RVO (branch RVO or central RVO), after the initial injection, treatment is given monthly at intervals not shorter than 1 month. Discontinue if visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment. Treat monthly until maximum visual acuity and/or no signs of disease activity. Three or more consecutive, monthly injections may be needed. Treatment may then be continued with a treat-and-extend regimen with gradually increased treatment intervals to maintain stable visual and/or anatomic outcomes, however there are insufficient data to conclude on the length of these intervals. Shorten treatment intervals if visual and/or anatomic outcomes deteriorate. The monitoring and treatment schedule should be determined by the treating physician based on the individual patient's response. For DMO, initiate treatment with 1 injection/month for 5 consecutive doses, followed by 1 injection every 2 months. No requirement for monitoring between injections. After the first 12 months of treatment, and based on visual and/or anatomic outcomes, the treatment interval may be extended such as with a treat-and-extend dosing regimen, where the treatment intervals are gradually increased to maintain stable visual and/or anatomic outcomes; however there are insufficient data to conclude on the length of these intervals. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly. The schedule for monitoring should therefore be determined by the treating physician and may be more frequent than the schedule of injections. If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, treatment should be discontinued. For myopic CNV, a single injection is to be administered. Additional doses may be administered if visual and/or anatomic outcomes indicate that the disease persists. Recurrences should be treated as a new manifestation of the disease. The schedule for monitoring should be determined by the treating physician. The interval between 2 doses should not be shorter than 1 month. ***Hepatic and/or renal impairment:*** No specific studies have been conducted. Available data do not suggest a need for a dose adjustment. ***Elderly population:*** No special considerations are needed. Limited experience in those with DMO over 75 years old. ***Paediatric population:*** No data available. **Contraindications:** Hypersensitivity to active substance or any excipient; active or suspected ocular or periocular infection; active severe intraocular inflammation. **Warnings & precautions:** As with other intravitreal therapies endophthalmitis, intraocular inflammation, rhegmatogenous retinal detachment, retinal tear and iatrogenic traumatic cataract have been reported. Aseptic injection technique is essential. Patients should be monitored during the week following the injection to permit early treatment if an infection occurs. Patients must report any symptoms of endophthalmitis or any of the above mentioned events without delay. Increases in intraocular pressure have been seen within 60 minutes of intravitreal injection; special precaution is needed in patients with poorly controlled glaucoma (do not inject while the intraocular pressure is ≥ 30 mmHg). Immediately after injection, monitor intraocular pressure and perfusion of optic nerve head and manage appropriately. There is a potential for immunogenicity as with other therapeutic proteins; patients should report any signs or symptoms of intraocular inflammation e.g pain, photophobia or redness, which may be a clinical sign of hypersensitivity. Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of vascular endothelial growth factor (VEGF) inhibitors. Safety and efficacy of concurrent use in both eyes have not been systemically studied. No data is available on concomitant use of Eylea with other anti-VEGF medicinal products (systemic or ocular). Caution in patients with risk factors for development of retinal pigment epithelial tears including large and/or high pigment epithelial retinal detachment. Withhold treatment in patients with: rhegmatogenous retinal detachment or stage 3 or 4 macular holes; with retinal break and do not resume treatment until the break is adequately repaired. Withhold treatment and do not resume before next scheduled treatment if there is: decrease in best-corrected visual acuity of ≥30 letters compared with the last assessment; central foveal subretinal haemorrhage, or haemorrhage ≥50%, of total lesion area. Do not treat in the 28 days prior to or following performed or planned intraocular surgery. Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last intravitreal injection. In patients presenting with clinical signs of irreversible ischaemic visual function loss, aflibercept treatment is not recommended. Populations with limited data: There is limited experience in DMO due to type I diabetes or in diabetic patients with an HbA1c over 12% or with proliferative diabetic retinopathy. Eylea has not been studied in patients with active systemic infections, concurrent eye conditions such as retinal detachment or macular hole, or in diabetic patients with uncontrolled hypertension. This lack of information should be considered when treating such patients. In myopic CNV there is no experience with Eylea in the treatment of non-Asian patients, patients who have previously undergone treatment for myopic CNV, and patients with extrafoveal lesions. **Interactions:** No available data. **Fertility, pregnancy & lactation:** Not recommended during pregnancy unless potential benefit outweighs potential risk to the foetus. No data available in pregnant women. Studies in animals have shown embryo-foetal toxicity. Women of childbearing potential have to use effective contraception during treatment and for at least 3 months after the last injection. Not recommended during breastfeeding. Excretion in human milk: unknown. Male and female fertility impairment seen in animal studies with high systemic exposure not expected after ocular administration with very low systemic exposure. **Effects on ability to drive and use machines:** Possible temporary visual disturbances. Patients should not drive or use machines if vision inadequate. **Undesirable effects:** *Very common:* Visual acuity reduced, conjunctival haemorrhage (wAMD phase III studies: increased incidence in patients receiving anti-thrombotic agents), eye pain. *Common:* retinal pigment epithelial tear (known to be associated with wAMD; observed in wAMD studies only), detachment of the retinal pigment epithelium, retinal degeneration, vitreous haemorrhage, cataract (nuclear or subcapsular), corneal abrasion or erosion, increased intraocular pressure, blurred vision, vitreous floaters, vitreous detachment, injection site pain, foreign body sensation in eyes, increased lacrimation, eyelid oedema, injection site haemorrhage, punctate keratitis, conjunctival or ocular hyperaemia. *Serious: cf. CI/W&P - in addition:* blindness, culture positive and culture negative endophthalmitis, cataract traumatic, transient increased intraocular pressure, vitreous detachment, retinal detachment or tear, hypersensitivity (during the post-marketing period, reports of hypersensitivity included rash, pruritus, urticaria, and isolated cases of severe anaphylactic/anaphylactoid reactions), vitreous haemorrhage, cortical cataract, lenticular opacities, corneal epithelium defect/erosion, vitritis, uveitis, iritis, iridocyclitis, anterior chamber flare, arterial thromboembolic events (ATEs) are adverse events potentially related to systemic VEGF inhibition. There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. As with all therapeutic proteins, there is a potential for immunogenicity. Consult the SmPC in relation to other side effects. **Overdose:** Monitor intraocular pressure and treat if required. **Incompatibilities:** Do not mix with other medicinal products. **Special Precautions for Storage:** Store in a refrigerator (2°C to 8°C). Do not freeze. Unopened vials and unopened syringe blisters may be stored at room temperature (below 25°C) for up to 24 hours before use. **Legal Category:** POM. **Package Quantities & Basic NHS Costs:** *Single vial or PFS pack:* £816.00 **MA Number(s):** EU/1/12/797/001-002. **Further information available from:** Bayer plc, 400 South Oak Way, Reading RG2 6AD, United Kingdom. Telephone: 0118 206 3000. **Date of preparation:** April 2020.

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Adverse events should be reported.
Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard**
or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc. Tel: 0118 2063500
Fax: 0118 2063703 Email: **pvuk@bayer.com**

EYLEA®
(aflibercept solution for injection)

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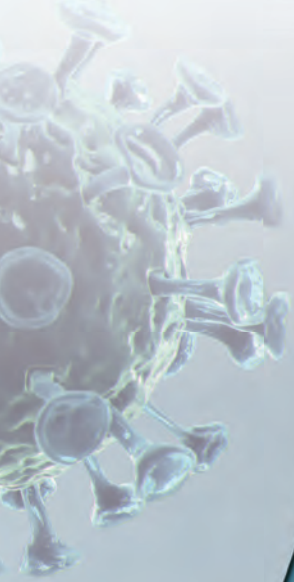
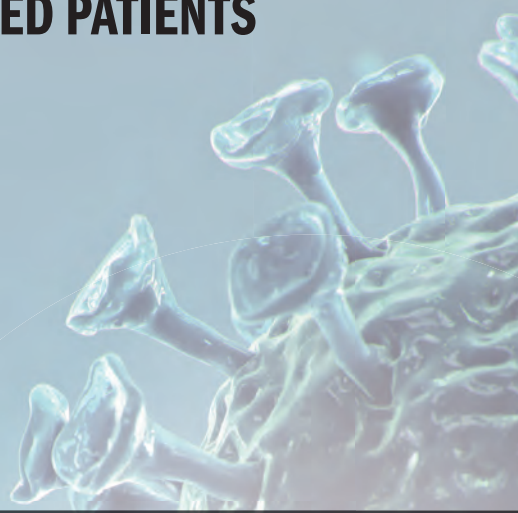


CORNEA

Researchers find low risk of COVID-19 transmission in tears

STUDY DID NOT DETECT VIRUS IN TEARS OF INFECTED PATIENTS



ISSUE HIGHLIGHTS

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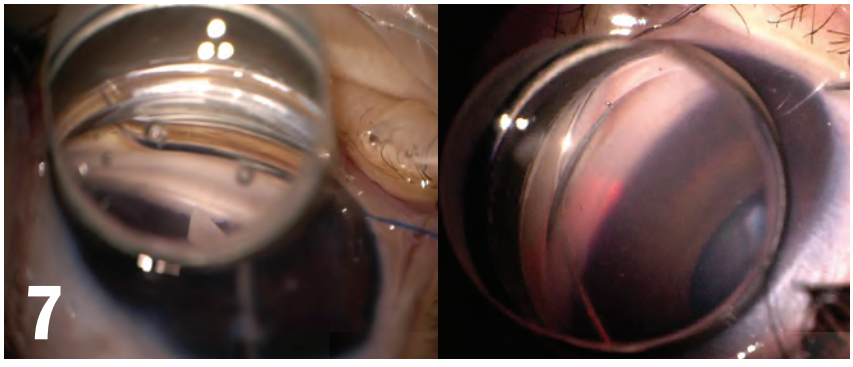
Glaucoma



Cataract & Refractive

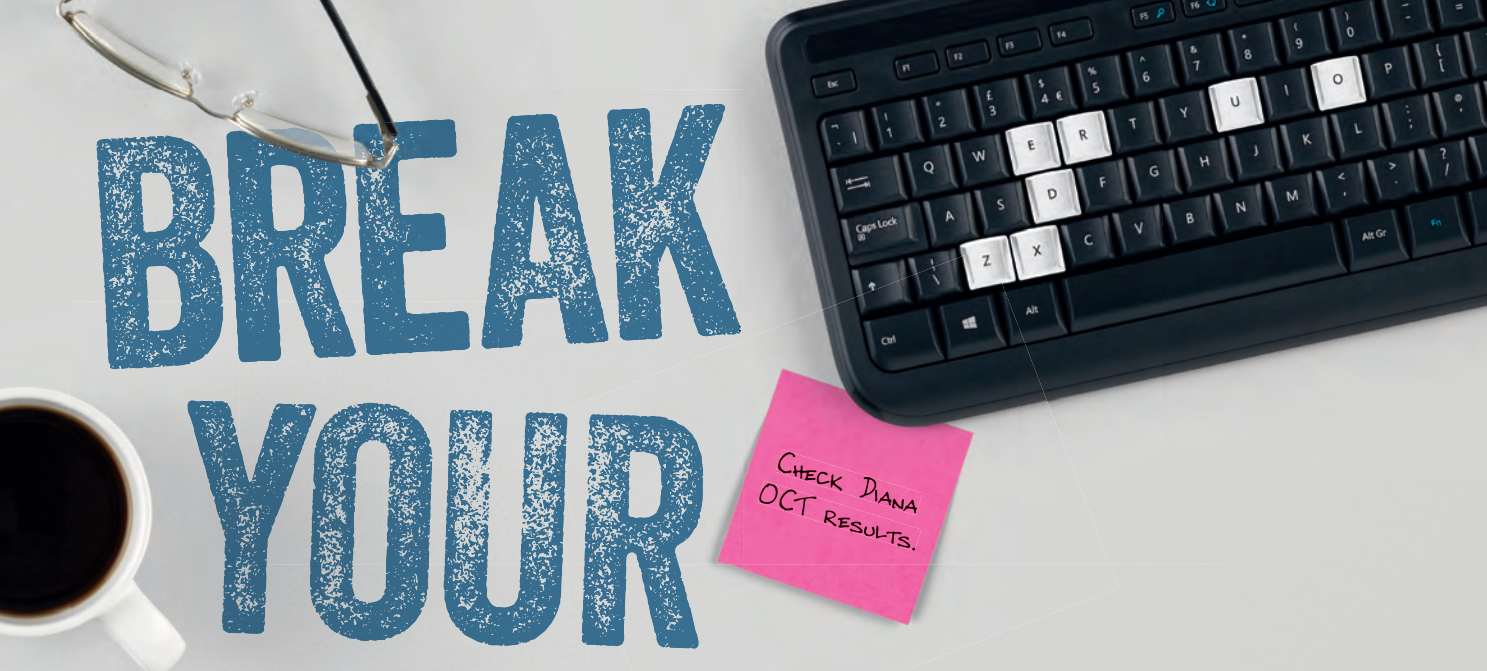
Retina

Cornea

Paediatrics

Gene Therapy

FOCAL POINT



BREAK YOUR ROUTINE

OZURDEX® has multiple modes of action,[1–3] a low treatment burden[4–7] and a manageable safety profile.[6–8]

TRY DIFFERENT LETTERS IN YOUR PRESCRIPTION FOR DME

Ozurdex®
(dexamethasone intravitreal implant) 0.7mg

DME, diabetic macular edema; OCT, optical coherence tomography. **1.** Nehmé A and Edelman J. Invest Ophthalmol Vis Sci 2008;49(5):2030–2038. **2.** Holekamp N. The role of corticosteroid implants in DME. Available at: http://retinatoday.com/2015/04/the-role-of-corticosteroid-implants-in-dme. Accessed March 2020. **3.** Campochiario PA *et al.* Am J Ophthalmol 2016;168:13–23. **4.** Malclès A *et al.* Retina 2017;37(4):753–760. **5.** Matonti F *et al.* Eur J Ophthamol 2016;26(5):454–459. **6.** Aknin I and Melki L. Ophthalmolgica 2016;235:187–188. **7.** Allergan. OZURDEX®. Summary of Product Characteristics. October 2019. **8.** Boyer SB *et al.* Ophthalmology 2014;121(10):1904–1914.

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 (ACIOL), 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/disturbance, vitreous detachment*, vitreous floaters*, vitreous opacities*, blepharitis, eye pain*, photopsia*, conjunctival oedema*, conjunctival hyperaemia. Uncommon (≥1/1,000 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

License and adverse events reporting may vary by country, please consult your local Summary of Product Characteristics. Date of preparation: March 2020 INT-OZU-2050058

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Ophthalmology Times EUROPE®

Springtime signals hope, providing inspiration for all

***Mike Hennessy Sr**, Chairman/founder of* Ophthalmology Times Europe*'s parent company, MJH Life Sciences*

As the spring days grow brighter, so, too, does the sense of new beginnings and inspiration among the global ophthalmic community. Never ones to rest, ophthalmologists are hard at work on advancing discoveries or treatments for their patients.

We begin with our glaucoma issue feature, in which Dr Yasmine M. El Sayed discusses how gonioscopy-assisted transluminal trabeculotomy (GATT) has been shown to be successful in the management of both primary and secondary open-angle glaucoma. Patient selection and management of expectations is key.

Next, we move on to surgical intervention for childhood glaucoma. Dr Alana L. Grajewski discusses a retrospective study, including 46 eyes of 41 patients, that supports the safety and effectiveness of single-incision *ab interno* trabeculotomy for treating childhood glaucomas, particularly primary congenital glaucoma.

Amid the coronavirus pandemic and with the world practicing social distancing, online learning takes on a new meaning. As Prof. Jorge Alio, Dr Almutez Gharaibeh and Dr Ahmed Khader share with us, the benefits include enhanced communication, flexibility and cost-effectiveness. The educational goal of e-learning is not to replace conventional hands-on experiences but to improve the quality of refractive surgery training worldwide, since learning is a non-stop process.

Turning our focus to retina surgery, clinical studies are under way to confirm the promising results obtained so far with subretinal implantation of human amniotic membrane plugs in the treatment of large and recurrent macular holes. Recent, novel surgical methods in the management of macular holes offer the chance to improve visual acuity in patients with large or recurrent holes who would otherwise be doomed to lose vision in the affected eye. Dr Emiliano Di Carlo and Dr Camilla Simini provide an update on surgical treatment approaches.

As the world continues to deal with the effects of the ongoing coronavirus pandemic, researchers are moving swiftly to learn more about COVID-19. On the cover of this issue, our cornea content includes research that shows there is little risk of viral shedding in the tears of patients with COVID-19. The National University Hospital Department of Ophthalmology, a high-volume ophthalmology centre in Singapore, offers an example of infection control measures implemented in the setting of COVID-19 infections that may be of value as other ophthalmology clinics begin to experience and plan for potential increases of COVID-19 risks.

In other news, a high number of corneal diseases only affect the inner layers of the cornea; that is, the Descemet membrane (DM) and endothelium. Until a few years ago, full-thickness corneal transplants—or penetrating keratoplasty (PKP)—typically took place, irrespective of whether the disease affected one or all layers. However, surgeons can now replace just the diseased parts with corresponding layers from healthy donor tissue in posterior lamellar corneal transplantation procedures. Caroline Richards, editor of *Ophthalmology Times Europe*, interviews Dr Lamis Baydoun on how corneal transplantation has changed—and what has been learned—since the introduction of Descemet membrane endothelial keratoplasty (DMEK).

In this issue, we also offer a look at the challenges of examining visual fields in children. According to Dr Mitchell Strominger, this work can be challenging, and optical coherence tomography (OCT) may be a good place to start. He explains that physicians should be aware that some children compensate for their visual field defects, with, for example, head turns related to visual field loss that are not related to strabismus.

Gene therapy coverage with Dr Cecilia Lee details how worse outcomes after development of endophthalmitis postoperatively are associated with the presence of bacteria and higher bacterial loads of pathogens other than *Staphylococcus epidermidis* as detected by whole-genome sequencing and quantitative polymerase chain reaction (qPCR).

Finally, amid all the seriousness of the worldly concerns, we take a break to appreciate all that is the eye. Erica Crompton walks us through *Pathos Ocularis—the Beautiful and the Curious*, a fascinating exhibition at the College of Optometrists in London that merges art with ophthalmology. The exhibition was due to close this month, but will be extended for a minimum of 6 weeks following the Museum's yet-to-be-determined reopening date after the coronavirus pandemic.

Pearls for conducting GATT in open-angle glaucoma

Moderate learning curve but safe and cost-effective method for lowering IOP

By Dr Yasmine M. El Sayed


Dr El Sayed

Gonioscopy-assisted transluminal trabeculotomy (GATT) is an *ab interno*, minimally invasive glaucoma surgery introduced by Dr Ronald Fellman in 2014.[1] It aims to circumferentially incise the inner wall of Schlemm's canal (SC), in order to connect it directly to the anterior chamber.

The procedure is performed through two clear corneal incisions, under gonioscopic view. An illuminated microcatheter or a prolene suture is introduced into SC through a goniotomy incision and threaded using 23 g microsurgical forceps, coursing circumferentially throughout the entire canal, until it reappears from the opposite cut end of SC. Both ends are then pulled out, creating a 360° incision, cleaving the entire trabecular meshwork (Figure 1).

GATT has been shown to be successful in the management of both primary and secondary open-angle glaucoma, particularly in steroid-induced glaucoma.[2] It has also demonstrated effectiveness in paediatric glaucoma and in eyes with a history of previous incisional procedures, including trabeculectomy and glaucoma drainage devices.[3]

Like most angle-based procedures, GATT requires the surgeon to be familiar with intraoperative gonioscopy and angle structures. These can be practised in a wetlab and/or intraoperatively after phacoemulsification. Once the surgeon is comfortable with goniosurgery, the procedure itself has a moderate learning curve. Once mastered, it becomes a safe and cost-effective surgical option to lower intraocular pressure (IOP), as well reduce dependence on glaucoma-lowering medications.

GATT carries several advantages:

- **It is minimally invasive – performed through two corneal paracentesis – and does not involve leaving a device inside the eye.**
- **It addresses the juxtacanalicular outflow pathway, known to have the highest resistance to aqueous outflow, thus restoring flow through the eye's natural drainage system, rather than creating an alternative pathway into the subconjunctival space.**
- **It does not violate the conjunctiva; hence, it does not compromise the results of any future bleb-based glaucoma surgeries. It also avoids the risks associated with bleb-based procedures, e.g., hypotony, infection and dysthesia.**
- **The 360° incision directs flow into more collector channels, especially through the inferonasal quadrant, which is known to have a higher distribution of collector channels.[4]**
- **It is a low-cost procedure, as it can be performed using a prolene suture.**

Patient selection

As with any surgical procedure, proper patient selection is key to success. Patients with a bleeding tendency, corneal opacities that impede proper visualisation of the angle, and eyes with narrow angles are poor candidates for GATT.

GATT may be avoided in poorly compliant patients with advanced glaucoma, where a trabeculectomy or tube surgery may have a better chance of putting the patient off medications.

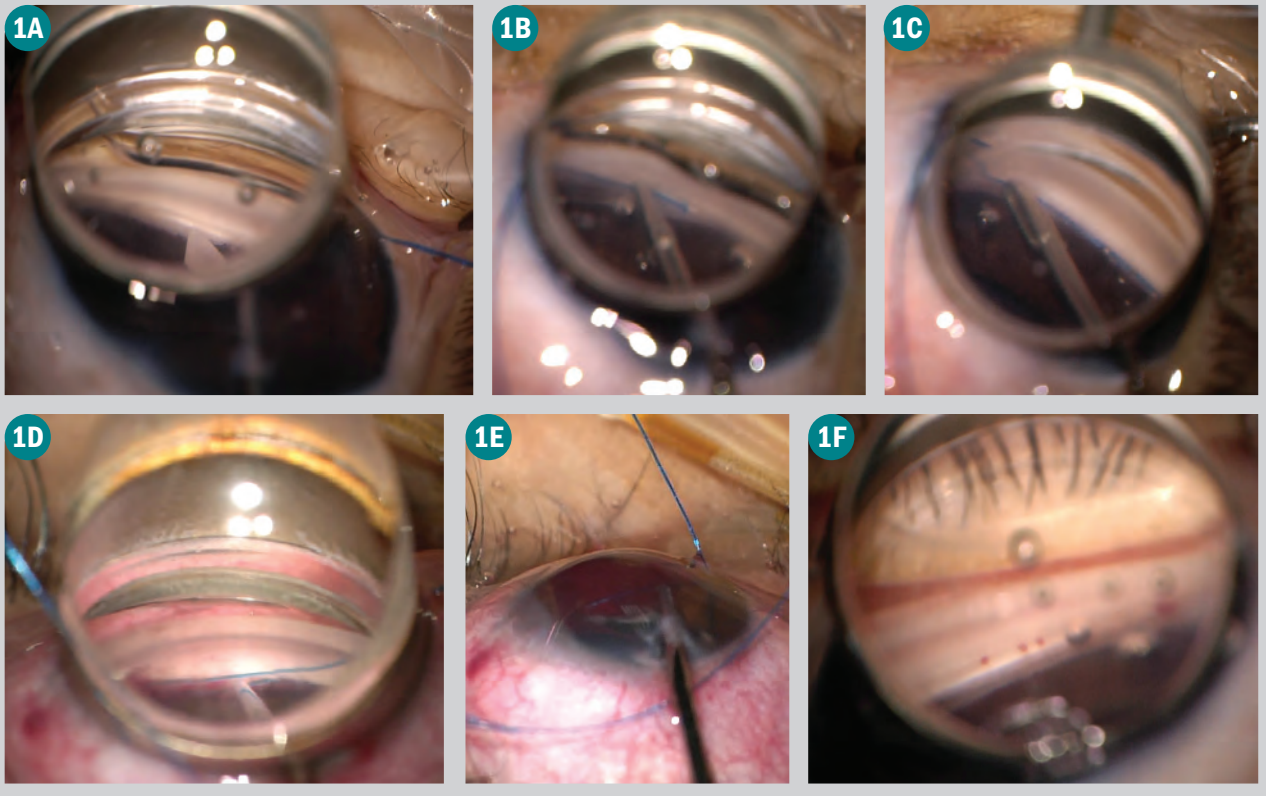
Managing expectations

GATT is expected to lower the IOP by around 30–50%,[5] and the number of glaucoma-lowering medications by one to two. There is some evidence that it is more effective in secondary compared with primary open-angle glaucoma.

A patient on single or a combination therapy may go off treatment after the surgery, but patients on more glaucoma medications will likely need to continue using some of their drops. So, if the patient

IN SHORT

Gonioscopy-assisted transluminal trabeculotomy (GATT) has been shown to be successful in the management of both primary and secondary open-angle glaucoma. Patient selection and management of expectations is key.



(FIGURE 1) **A. Creation of goniotomy incision. B. Insertion of prolene suture into SC through the goniotomy incision. C. Appearance of the suture inside SC. D. Suture end appearing from opposite side of SC. E. Suture ends pulled out, tearing the inner wall of SC circumferentially. F. Appearance of the cleaved angle under gonioscopic view with starting blood reflux from SC.**

(FIGURE 2) **Illuminated end of microcatheter seen in SC.**

(Images courtesy of Dr Hala Elhilali)

needs to go off treatment because of side effects or adherence issues, trabeculectomy may be a more appropriate option.

Although GATT is a minimally invasive procedure, one of its main drawbacks is the postoperative hyphema, which is quite common and can be agonising to the patient. I make sure patients understand that the blurring of vision may last for one or more weeks, that in the meantime they should assume a semi-sitting position during most of the day to help absorb the blood, and that there is a chance they may need an additional procedure to wash it out.

Intraoperative tips

GATT can be performed through either a temporal or superior approach. We prefer sitting temporally as it allows for easier, more comfortable positioning of the patient's head towards the nasal side, rather than in a chin-down position.

The patient's head, gonio lens and the surgical microscope should be positioned in perfect alignment. Fine tune the positioning until you optimise the angle view.

Circumferential incisions are easiest to achieve with 6/0 prolene sutures, as the suture passage is less likely to become interrupted. However, because of their smaller calibre. they may be less effective in IOP lowering. By contrast, 5/0 prolene tends to stop around 270° away from the original

goniotomy incision but, unlike 6/0 prolene and illuminated microcatheters, they can be pulled on if their path gets obstructed, thus tearing up the inner wall of SC without having to cut down over the interrupted end.

Cost is another consideration when choosing between suture and microcatheter-assisted GATT, with the use of a suture being considerably cheaper. When using a suture, surgeons should use a hand-held cautery to blunt out the tip, creating as small a knob as possible to avoid it from getting obstructed in SC.

The suture around the limbus should be placed circumferentially and a marker or the cautery used to mark the distance from its tip that corresponds to the circumference of the cornea. This helps to track the suture externally and predict its location if it stops proceeding.

The suture/microcatheter is inserted through a tangential paracentesis pointing towards the site of the goniotomy incision. One should avoid any limbal blood vessels when creating the paracenteses, as bleeding will impede visualisation by mixing with the Goniosol under the gonio lens.

Healon is used to fill the anterior chamber. Healon GV is the best gadget to tamponade blood. Operating with the patient in reverse Trendlenberg position also helps minimise the bleeding in eyes with excessive blood reflux from the angle.

In cases where SC cannot be easily located, such as in eyes with hypopigmented trabeculum or paediatric glaucoma, establishing temporary hypotony by allowing some aqueous to come out of the paracentesis may help to delineate the canal with the blood refluxing from the distal outflow channels.

A 1–2 mm goniotomy incision is created by a 23 g microvitreoretinal (MVR) blade. The posterior lip of the incision is pushed down to visualise and gain access into the canal and I often inject Healon into one side of the canal before cannulating it.

The suture/microcatheter often stops after passing through three quadrants (Figure 2), so if you are performing GATT through a temporal approach, insert the suture through the left end of the goniotomy incision when operating on the right eye and vice versa. This way, if it stops after 270°, you can locate it in the inferior quadrant, which is more accessible than superiorly.

It is important to make sure the anterior chamber is well pressurised throughout the procedure, and after the incision is created circumferentially. Before washing out the Healon, we place the surgical bed into Fowler's position, with the head tilted at 45–90°. Between 10 and 50% of the Healon should be left at the end of the procedure to tamponade the blood, stopping short of getting blood reflux from the angle.

Surgeons need to be ready with a back-up procedure in case GATT could not be performed intraoperatively. The most common culprit is excessive intraoperative bleeding. Back-up procedures include Kahook dual blade goniotomy, trabectome and ab-externo trabeculotomy. These can still be performed through two sites, on two-opposite quadrants, creating a more-or-less circumferential incision.

Postoperative course

As the filtration is still dependent on the drainage angle, there is still a chance of the patient developing an early steroid response. We only use a combination of antibiotic-steroid ointment at night and a NSAID eye drop for 2–3 weeks.

Patients need to keep their head titled at 30° until the hyphema resolves. In case the hyphema lasts for more than 1 week and is covering the pupillary area, you may inject air intracamerally on the slit lamp.

I find this useful since it moves blood away from the pupillary area, improving vision, and it helps the hyphema to settle and absorb. I have a low threshold to aspirate the hyphema, i.e., if it persists for more than 2–3 weeks, and even earlier for one-eyed patients if it is covering the pupil.

Barriers to success

Although SC surgery is a promising alternative to the relatively more invasive bleb-based procedures, some barriers to success remain to be addressed. The first is the risk of scarring.

Histopathological evidence suggests that, after incising the inner wall of SC, the trabecular meshwork undergoes a repair process, starting in the corneoscleral meshwork, followed by the endothelial and uveal meshwork. It is not yet clear which cases are more likely to scar. Factors such as ethnicity, type of glaucoma, lens status, and size and extent of the incision may influence the postoperative scarring of SC and remain to be studied. Developing drugs that can be injected intracamerally to halt the healing process may revolutionise the outcome of angle surgery, just as adjunctive antimetabolites have improved the success of trabeculectomy.

Another barrier to success is the health and patency of collector channels. Studies have shown that around one third of the resistance to outflow lies distal to the inner wall of SC. This resistance is even higher in advanced disease.

In cases where the collector channels cannot carry aqueous to the episcleral veins, a bleb-based procedure such as trabeculectomy or glaucoma drainage device implantation may be the only suitable option. Evaluation of this conventional outflow system is still evolving and may soon help us predict which cases are most suited for angle-based procedures.

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Surgical intervention for childhood glaucoma: A retrospective study

Study details safety and effectiveness with use of MIGS device

By Cheryl Guttman Krader;

Reviewed by Dr Alana L. Grajewski

Single-incision *ab interno* trabeculectomy with the Trab360 (SightSciences) provided safe and effective treatment for childhood glaucomas, according to the findings of a retrospective multicentre study.

The research, which was published in the January 2020 issue of the *American Journal of Ophthalmology*,[1] analysed outcomes from 46 eyes of 41 paediatric patients, who ranged in age from 1 to 325 months (median 12 months) at the point at which they underwent the minimally invasive glaucoma surgery (MIGS).

After a median follow-up of 14.5 months, median intraocular pressure (IOP) was reduced from 30 mm Hg (range 18–49 mm Hg) preoperatively to 18 mm Hg (range 5–40 mm Hg) after follow-up. Furthermore, the surgery was associated with a decrease in medication burden. Median number of medications fell from 2.5 (range 0–5) preoperatively to 1 (0–4) postoperatively.

Success, defined as postoperative IOP ≤24 mm Hg with or without medications, no additional surgery needed to control IOP and absence of devastating or severe complications, was achieved in two-thirds of eyes.

With eyes categorised by diagnosis, subgroup analyses showed the highest success rate was achieved in eyes with primary congenital glaucoma (PCG), which was also the most common diagnosis in the series (45.5%). Of 21 eyes with PCG, 81% met the criteria for success. Excluding three eyes with PCG that had undergone prior glaucoma surgery, the success rate was 83.3%.

Cyclodialysis occurred in two eyes (4.3%). One required surgical treatment and the other resolved spontaneously.

There were no other significant complications, according to the study.

Early research

The study authors pointed out that theirs is the first study to critically evaluate outcomes of the Trab360 procedure to treat childhood glaucomas. They observed that the success rates reported correspond well with those published previously for childhood glaucoma angle surgery.

Noting that the MIGS device used in the surgeries has been replaced by its manufacturer with new technology (OMNI Surgical System), the authors also suggested that the findings of the study could be generalised to any "sufficiently similar technique" of single-incision *ab interno* trabeculectomy.

However, they also noted that there is a learning curve for safe use of the Trab360 device and that the procedures were performed by surgeons with significant experience performing angle surgery in children.

More details

The children were operated on by one of four surgeons practicing at four different academic centres. Children needed to have sufficient corneal clarity to undergo the *ab interno* procedure.

To be included in the retrospective analysis, they were required to have at least 3 months of postoperative follow-up.

A variety of childhood glaucoma types were represented in the series. According to the study, subgrouping of the cases by diagnosis was based on the World Glaucoma Association's Childhood Glaucoma Classification System.

Aside from PCG, other diagnoses were glaucoma associated with a non-acquired systemic disease or syndrome (17%), juvenile open-angle glaucoma (13%), glaucoma following cataract surgery (11%),

IN SHORT

- ***A retrospective study including 46 eyes of 41 patients supports the safety and effectiveness of single-incision ab interno trabeculotomy for treating childhood glaucomas, particularly primary congenital glaucoma.***

glaucoma associated with an acquired condition (8.5%) and glaucoma associated with a non-acquired ocular anomaly (4%).

Researchers pointed out that success was achieved in 83% of eyes with juvenile open-angle glaucoma, 60% of those with glaucoma following cataract surgery, 50% of those with glaucoma associated with a non-acquired systemic disease or syndrome, and 50% of those with glaucoma associated with an acquired condition.

Neither of the two eyes with glaucoma associated with a non-acquired ocular anomaly achieved success.

Acknowledging that the numbers of eyes in each subgroup is small, the authors suggested that the MIGS procedure could be considered reasonable for the treatment of eyes with uveitic glaucoma or glaucoma after cataract surgery prior to resorting to a glaucoma drainage device, trabeculectomy or a cyclodestructive procedure.

The most common reason for failure was the need for additional surgery, either for IOP control or to address complications.

Of the 15 failures, 12 occurred within the first 3 months after surgery.

Safety considerations

The authors warned that good surgical technique and caution when operating on eyes with high-risk angles are critical to avoid cyclodialysis.

Both eyes that developed cyclodialysis had angle anomalies that could have made them susceptible to cyclodialysis cleft formation caused by placing traction on the trabecular meshwork.

Specifically, the authors urged caution performing the surgery in eyes with extreme bupthalmos, advanced uveitis or anterior segment dysgenesis, or if the angle anatomy is distorted, anomalous or obscured by peripheral anterior synechiae.

Conclusions

The authors acknowledged that the research was subject to the limitations inherent in a retrospective analysis. They also observed the need for cost analyses, but suggested that the cost associated with the device itself could be offset by its benefits relative to a 360° *ab externo* procedure for reducing operating time and duration of general anaesthesia exposure in children.

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Online ophthalmic learning in anterior segment surgery

Benefits include enhanced communication, flexibility and cost-effectiveness

By Prof. Jorge Alio, Dr Almutez Gharaibeh and Dr Ahmed Khader

Living in an era of vast technological development has shifted the way we learn. Teachers and students no longer need to be physically present at the same time and place, but can instead engage from afar and this form of online learning, or "e-learning", is increasingly becoming more the norm. Traditional learning still has an important role, however, and remains essential in maintaining the learning process.[1,2]

The concept of distance learning is not new; there is historical evidence as to its existence as far back as the 19th century, courtesy of Sir Isaac Pitman, who taught a system of shorthand in the 1840s for students living abroad, which was a method of exchanging mailing texts.[3]

There are many definitions for e-learning (also referred to as E learning, online training and online learning); however, broadly speaking, experts agree that it involves the electronic delivery of training or education and requires interaction with the Internet or other computer network via a computer or electronic device such as a mobile phone.[4-6]

Advantages of online learning

Many ophthalmologists seek continuous medical education in order to achieve personal growth and career development, especially when dealing with one of the most continuously advancing fields such as refractive surgery. However, for those with a full-time job or families, online learning becomes a particularly attractive proposition.

For instance, it allows them to take care of their home and children during the day and study at night, making distance learning highly advantageous over the traditional educational system.

Overall, the benefits of e-learning are many, including "cost-effectiveness, enhanced responsiveness to change, consistency, timely content and flexible accessibility".[5,6]

Moreover, e-learning technologies provide students with more control over the learning process in terms of content and pace of learning, which allows them to modify their experiences according to their individual learning objectives. E-learning also enhances communication between those engaging with it by making open discussion panels possible.

Since responses within e-learning can be made around the clock, students tend to be more highly motivated and more involved in the learning process[2]. In addition, there are no geographical barriers, making this style of learning accessible to doctors worldwide.

Disadvantages and challenges

Drawbacks of online courses include the limited emotional and personal interactions that take place, although this can be partially overcome by engaging in video conferences and live discussions.

Another consideration is the ongoing expenses incurred by students, whilst those who create and need to maintain the courses also need to set aside a budget.

Moreover, participants need to have a good sense of self-discipline and time management in order to follow course timelines, which indeed may interfere or overlap with working hours or night times as they may take place in countries with different time zones.[5,6] These factors can make compliance with attendance more challenging.

Another challenging feature of e-learning is that surgical skills have to be acquired by observation rather than through a hands-on approach available with traditional methods of teaching. A lack of reliable assessment after each lecture or course can be another issue with e-learning programmes.

IN SHORT

- ***The educational goal of e-learning is to not to replace conventional hands-on experiences but to improve the quality of refractive surgery training worldwide, since learning is a non-stop process.***

Table 1. ***Traditional and e-learning approaches***

	TRADITIONAL LEARNING	E-LEARNING
Discussions	• Face-to-face discussions take place. • Students might feel less free to express their opinion or provide feedback when they are in close proximity to each other. • Responses are usually made in real-time.	• Learning occurs through discussion board, e-mails or video chat. • Students may feel freer and more confident in expressing opinions and providing feedback. • Responses can be provided at all times of the day.
Learning process	• The presence of the whole class is almost essential. • The students are not involved in inquiry-based education, which is an active form of learning, but rather they perform assignments given by the teacher. • There is a fixed curriculum. • Direct student–teacher interaction makes the learning process active. This is the most distinguished characteristic of traditional education.	• The learning process takes place either in groups or by the individual student. • The learning is strongly related to the real world, and the subject material is rich and includes information in variable formats. • There is a more flexible and dynamic curriculum.
Role of educators	• Educators are mostly working as content distributors. • Educators play a major role, especially in surgical specialties as supervisors on surgical training.	• Educators do not serve solely as distributors of content, but become facilitators of learning and assessors of competency. • Blended-learning strategy can be applied by allowing direct supervision at peoples' place of work by senior doctors.
Motivation	• The students may feel less enthusiastic because they recognise the subject matter as being distant to them.	• Motivation can be higher as students feel as though they are related and more connected to the learning process.
Cost	• There are higher tuition fees, travel costs and a need for infrastructure.	• It is more cost-effective due to lower travel and labour costs, reduced institutional infrastructure and the possibility of expanding programmes using modern educational technologies.
Convenience	• Requires physical attendance at set times and places. • The timetable and duration of lectures are all scheduled. This helps make students more disciplined. • Learning materials are usually provided during the sessions and are not always available online afterwards.	• Online learning does not require physical attendance. • Learning process is self-paced. • Students are not bound by time and place because courses are available 24/7 and they can study wherever suits them. • One can read materials directly online or download them for reading later.

E-learning in ophthalmology

Continuous medical education is considered compulsory for ophthalmologists to ensure that knowledge and skills are regularly updated. Due to growth in educational technologies, the e-learning resources that have become available to ophthalmologists worldwide has significantly increased.

Examples of major providers are: the International Council of Ophthalmology, the American Academy of Ophthalmology, the Asia-Pacific Academy of Ophthalmology, and Cyber Sight. Moreover, social media (such as Facebook, Twitter and LinkedIn) play some role in providing medical news feeds.

However, it is important to build the most effective online courses and provide

a trusted source for continuous ophthalmic education, especially in subspecialty training with known syllabuses and flexible timelines.

E-learning in cataract and refractive surgery

We are still facing some limitations and scarcity in the field of refractive training, especially in relation to residents and young ophthalmologists. Most of their knowledge is provided through humble training or some courses they attend during international or regional conferences.

This is where online courses are important, since they provide in-depth theoretical training with flexible timelines without the need to leave their jobs and families. Such courses are given by the most prominent and well-respected figures in the field.

Moreover, these courses are not biased towards certain technologies. Such bias might be seen in other workshops or courses that are provided by companies wishing to highlight their products and any new technologies in the field of refractive surgery.[7] Therefore, we can spread healthy practice policies and provide unbiased answers to ophthalmologists everywhere.

Refractive surgery online training programmes

There are four online courses in refractive surgery that were designed specifically to provide intensive specialty training, with a diploma or certificate awarded at the end of the course:

1) The Scientific Methodology in Cataract, Refractive Surgery and Corneal diseases, Miguel Hernández University, Alicante (Spain)[8], is a 25-credits programme containing six modules, which are conducted over the period of one academic year. The course is two semesters long, and an official university certificate is issued on its completion.

The material for this course is prepared by a team of national and international professors and consultant ophthalmologists, providing a comprehensive learning channel that covers all aspects of modern refractive surgery science.

The expected average of weekly educational activity required is 6 hours, depending of the learning base of the student; communication with the teaching faculty can take place at any time via email or direct communication to cover any difficulties the student may face.

One and a half years after the course began, the results were encouraging, with over 100 students enrolled worldwide.

Interaction with students was maintained through weekly forums and the practical parts were covered through 1-week mini-fellowships offered only for Spanish ophthalmologists. However, it was found to be very time-consuming for academic staff.

2) The Cataract and Refractive Surgery (Theory) – Postgraduate diploma (PGDip), an online postgraduate course offered by Ulster University[9] is over 2 years long. This programme has been designed in cooperation with The Royal College of Ophthalmologists' standards and is the only endorsed RCOphth refractive surgery course that is completed entirely online in the UK.

Through this platform, students are offered the chance to learn the latest highly advanced and revolutionary technologies in refractive corneal and lens-based surgeries.

3) Students undertaking a Master of Medicine (Cataract and Refractive Surgery) at the University of Sydney[10] need to complete 48 credit points in order to obtain their degree. The course consists of 36 credit points of core units of study in addition to 12 credit points of research thesis.

Core units include studies in ophthalmic anatomy, ophthalmic optics, refractive surgery and practical refractive surgery.

The online component of the course includes lectures from internationally recognised corneal and refractive surgeons and interactive online discussions with coordinators.

Students are also offered the opportunity to attend a week of hands-on training through workshops and wet labs at the Sydney Eye Hospital as well as undertaking placements in accredited refractive surgical centres.

4) The European Society of Cataract and Refractive Surgeons (ESCRS)[11] provides over 30 hours of interactive, assessed and accredited e-learning content, including surgical videos, diagrams, animations and quizzes.

Cataract surgery, refractive surgery and corneal surgery courses are available as follows:

A) Cataract surgery. There are seven courses, including phacodynamics, the techniques and technology used in phacoemulsification, postoperative refractive outcomes and the management of endophthalmitis.

B) Refractive surgery. These six courses include refractive surgery, biomechanics and optics of the cornea, preparing for and performing LASIK, approaches to treat presbyopia and surface ablation techniques.

C) Cornea. These six courses including corneal diseases and dystrophies, diagnostic methods and a range of surgical procedures.

Other educational resources

There are other educational resources that do not end up providing professional certificates but contribute in major parts in scientific online resources. Examples include:

1) Cyber Sight[12], developed and delivered by international

ophthalmology experts, offers free online courses in ophthalmology, as well as a library containing a lot of hot topics discussed through live webinars, lectures and quizzes on subjects including cataract, glaucoma, paediatric ophthalmology and uveitis.

In addition, with 'cyber sight consult' you can contact 150 international experts who are standing by to help anyone who needs second opinions.

Certificates earned contribute to Continuing Medical Education/ Continuing Professional Development (CME/CPD) credits, and all of the courses are optimised for mobile devices.

2) Wills Eye Hospital[13]. The department of Continuing Medical Education provides more than 100 courses in all eye subspecialties throughout the year.

On Friday mornings weekly during the Chiefs round, the residents at the hospital present at least two unknown cases on different topics to attending staff, and other interested colleagues can attend through live webinars.

These excellent courses can be accessed free of charge on the website portal Wills Eye Knowledge, which also offers updates for glaucoma surgery, anterior segment surgery, orbital surgery, cataract surgery and retinal surgery.

3) 15-20 Institute[14]. The 15-20 Institute is a medical hospital ophthalmology training platform in France which has more than 3,000 registered users and 35,000 connections to platforms both in the country and abroad.

Meetings take place on Thursdays monthly, and are hosted by a different specialist each time who discusses various subjects in ophthalmology.

In 2018, ten courses were offered, including four sessions of live surgeries in the operating theatre.

The institute also provides attendees with seminars and discussions as well as valid certificates that add more to their CME hours in cornea, cataract, glaucoma, surgical and medical retina, oculoplasty and neurophthalmology, and ophthalmic emergencies.

Further developments and outlook

Although e-learning has many advantages, there is still scope for improving the experience for students willing to engage with it. For example, learning could be made to be more adaptive, with courses tailored more to each specific student according to his or her specific learning needs and capabilities.

In addition, learners' interactions with each other could be enhanced, with greater collaboration helping to increase levels of satisfaction and knowledge for students. And the role of the teacher needs to be truly transformative, so that they do not just distribute content but really facilitate the learning process and take an active part in assessing attendees' performance[8].

Again, it is important to bear in mind that e-learning is not intended to replace traditional methods. The educational goal is to improve the quality of refractive surgery training worldwide because learning is a non-stop process.

We believe that research should be directed towards studying both the effectiveness and limitations of online courses in refractive surgery so that any drawbacks can be overcome as it continues to develop as a learning modality. However, we have to keep in mind that surgical skills are still the core of ophthalmology practice and should be always secured through hands-on training.

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Making the transition to SMILE has benefited my patients and my practice

By Robert T. Lin, M.D.

I first became interested in small incision lenticule extraction or SMILE® (Carl Zeiss Meditec AG) about four years ago. I was intrigued by the possible advantages of a procedure that provided equivalent visual outcomes to LASIK, but without its principal drawbacks in terms of flap creation and postoperative dry eye. After researching further and reading all the key peer-review studies concerning SMILE as well as discussing with many international colleagues who had already made the transition to SMILE, I became convinced that this represented a clear advance on LASIK and could serve as a catalyst of growth for my practice, 95% of which is devoted to refractive surgery.

After travelling to China in 2017, I was able to observe Lenticule Extraction being performed with SMILE on the VisuMax® (Carl Zeiss Meditec AG), and I was further convinced that this was a technique which would prove a valuable addition to my practice. I performed my first SMILE surgery in 2018 and witnessed firsthand how it delivered excellent outcomes and a smooth postoperative experience for my patients.

From that point onward, my practice became more and more SMILE oriented. It was almost a natural progression as I became convinced of the benefits of this solution and became more proficient at performing the surgery. My practice includes twelve offices in California which is a very competitive market for refractive surgery. We have been in business since 1999 and have built up a successful and well-known practice with significant market share in the industry. In that time, I have performed over 60,000 LASIK procedures, and even underwent successful LASIK surgery myself, so opting to embrace a new refractive surgery procedure was not a decision that I took lightly.

MAKING THE CHANGE

The refractive surgery market in the United States is LASIK dominated, and there is very little awareness of SMILE or any other alternative options. From my perspective, there had to be a really clear benefit to my patients in making the transition to a SMILE-dominated practice. I think that has to be the starting point for any change: the surgeon has to believe 100% in the procedure and have total confidence in the visual outcomes it will deliver for his or her patients.

Based on the international experience with SMILE, I felt that I could get excellent results for my patients and I diligently learned the technique. The learning curve is not too steep and surgeons can attain LASIK-like results very quickly. I think most surgeons will be comfortable performing SMILE once they have performed a few procedures, but will continue to get even better results with more cases if they are critically evaluating their techniques and outcomes.

However, we do not recommend performing SMILE until the surgeon has a thorough understanding of the VisuMax laser. My advice for starting with SMILE is to follow the ZEISS SMILE onboarding process accompanied by a regional clinical application specialist from ZEISS. This proprietary laser system can also be used to create a flap, just as in LASIK procedures, under a very low-pressure system. This means that patients are much more comfortable during the procedure. I would recommend following the ZEISS onboarding process by doing about 50 cases of the flap procedure prior to starting SMILE just to become more familiar with the laser.

As part of the learning process, it is important to be diligent and to watch the videos of other surgeons as well as record your own performance. I watched every single one of my videos after my initial surgeries to see how we can possibly improve in order to get the best possible results. Technically SMILE is slightly more difficult than LASIK, but it is still much easier than cataract surgery. If you are diligent and persevere you will get these excellent results in the early post-operative period. The bottom line is that it may take a little bit of time to master the procedure, but the return on investment can be huge for your practice. The reduced enhancement rates and increase in patients makes learning the new procedure worth it.

RETHINKING THE BUSINESS

Making the transition to SMILE entailed much more than a surgical decision – it essentially meant overhauling our practice management from top to bottom. It involved everything from developing appropriate marketing and educational materials to staff training and customer care. This is where ZEISS was very supportive, helping with all the key aspects of practice development including staff training, customer service and

marketing in order to ensure that SMILE was fully integrated into our practice and that everyone understood their role in relation to this new technology. The ZEISS Practice Development Consulting (PDC) was very beneficial in helping us fine-tune our marketing strategy and in drawing up a business plan to facilitate regional educational events in both northern and southern California for optometrists. This led to many educational events over the last few years to include educational evenings, continuing education events, multiple optometrists undergoing the procedure with SMILE themselves, and an increase in overall practice revenue through new co-management leads and treated cases.

The optometrists were really excited that there is now a procedure that has no flap, as they have been concerned about flap-related complications and incomplete healing. Due to less cornea nerve disruption the cornea has the potential to stay stronger with SMILE which showed less dry eye symptoms post-operatively in my clinics.

Overall, the ZEISS PDC was very helpful and a real collaboration that enabled us to grow our market share in a very competitive landscape. I think the Practice Development Consulting is something that definitely helps the culture of the company. We are a 95% refractive surgery practice. There are many practices that are not as focused as we are, and they would probably benefit even more from the ZEISS PDC expertise. This is because some basic features that the PDC offers would make a major difference for a less focused clinic. For us, what it did was supplement the training that we were already doing and took it to the next level. We were already at a very high level and the PDC just raised the bar a bit higher. ZEISS really exceeded my expectations in terms of the back-up and support services they offered at all stages of the transition to SMILE. They were very accommodating and were very responsive to any questions I had. The clinical trainers were always available whenever they were needed and service support was also on hand to field queries and ensure that everything was and still is running smoothly. In terms of marketing support, ZEISS was very helpful letting us know the type of strategies that worked in other successful markets. The PDC also helped with our overall customer service and how to improve sales conversion. A practice needs to have that type of support when incorporating a new technology, and it proved very beneficial for us.

REAPING THE DIVIDENDS

We were also able to introduce SMILE gradually, launching it first in our northern California office where the LASIK volume was not as high. Having observed the excellent outcomes and positive patient feedback we also incorporated it in southern California. Confidence is key in making the transition work. The more the surgeon performs SMILE surgery, the more confident he or she becomes with the technology. This confidence transmits to the staff and the patients as well once everyone sees the first-rate results that are being obtained with SMILE time after time. Our clinic used to be almost exclusively LASIK. About 90% of our patients today that qualify for either LASIK or SMILE, choose to undergo surgery with SMILE. The other 10% percent that don't opt for SMILE usually do so for financial reasons, as we charge slightly more for SMILE. We explain to them that this new technology required considerable investment, and that we have had to re-train our staff, create new marketing materials, and invest in new technology. This is why it is about 10% more expensive than a LASIK procedure.

The key is to build trust and for the patient to have confidence that you want the best for them. At the consultation, we tell them LASIK is an excellent procedure and explain how it differs from SMILE, and the pros and cons of each approach. Patients will then usually ask which solution we recommend, and we tell them that we recommend SMILE based on our experience, the results we have obtained, and the potential advantages it offers. Now that we have performed a critical mass of procedures with SMILE the patients are posting their amazing experience and patients are asking for SMILE and not LASIK.

Moving our practice to SMILE has turned out to be an excellent decision for our patients and ultimately our business. Our results are consistently excellent with a higher percentage of patients obtaining 20/15 uncorrected vision after SMILE than they achieved preoperatively with glasses or contact lenses. The results are also very predictable and stable over the long term as borne out by studies in the peer-reviewed literature. Our LASIK enhancement rate is about 1%, while that for SMILE touch-ups is only about 0.2%. As word spreads about the visual outcomes we have been achieving, we have seen a definite increase in demand.

I estimate that SMILE has increased our revenue by at least 20%. However, the real reward is seeing just how happy our patients are after their SMILE surgery. Converting to SMILE for purely financial reasons is probably not a viable strategy. Surgeons need to do their research and to really understand what the benefits are for their patients. Once they believe in that, and start to see the results, everything else will follow, including financial success.

Dr Robert T. Lin founded IQ Laser Vision in 1999 and has successfully performed more than 60,000 refractive procedures over the past 20 years. Dr Lin received his undergraduate education from UC Berkeley and medical training at UCLA. He completed his ophthalmologist residency at the prestigious Jules Stein Eye Institute at UCLA where he is currently an Assistant Clinical Professor.

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Human amniotic membrane in the surgery of recurrent macular holes

Transplanted membrane stimulates retinal ingrowth, improves visual acuity

By Dr Emiliano Di Carlo and Dr Camilla Simini

Dr Di Carlo

Dr Simini

Macular holes (MHs) are tears in the retina's fovea centralis, and can be acquired, acute or subacute, spontaneous or traumatic. They can cause the severe deterioration of eyesight if left untreated. Since our clinical practice in the ophthalmology unit of the Städtisches Klinikum in Karlsruhe is one of the largest medical centres in the southwest region of Germany, we encounter and treat a significant number of patients affected by this disorder.

Recent, novel surgical methods in the management of MHs offer the chance to improve visual acuity in patients with large or recurrent holes who would otherwise be doomed to lose vision in the affected eye.

Following a short overview of MHs, this article provides an update on surgical treatment approaches.

The first description of MHs dates back to Hermann Knapp in 1869,[1] who reported them as resulting from direct blunt ocular trauma. Patients with MHs without a history of eye trauma were increasingly observed, and by 1970, only 5–10% of them were ascribed to trauma, with the rest considered idiopathic.[2] Presently, the vast majority of MHs are attributed to vitreomacular traction.[3]

Clinical suspicion is confirmed by slit-lamp fundoscopic examination, which shows a well-defined round or oval lesion in the macula with yellow-white deposits at the base.[1] Optical coherence tomography (OCT) confirms the diagnosis and allows the lesion to be classified into one of Gass' four stages.

Surgical approaches

Ophthalmologists Neil E. Kelly and Robert T. Wendel described the first modern surgical approach to MHs in 1991. This technique is still used today and is standard procedure for holes under 400 µm in diameter.

The procedure consists of the following stages:

- **An extensive 23- to 27-gauge pars plana vitrectomy;**
- **Detachment of the posterior vitreous cortex with internal limiting membrane (ILM)-peeling;**
- **Epi-retinal membrane (ERM) peeling around the hole and thorough fluid–gas exchange (gas tamponade);**
- **Followed by postoperative face-down positioning.[4]**

The preoperative diameter of the MH plays an important role in choosing the best surgical technique and in predicting postoperative closure of the hole and visual outcome.[5,6] It is therefore advisable to consider the need to accurately measure the width of each hole with an OCT caliper before choosing the surgical approach. Indeed, for all types of vitreoretinal surgery, a good preoperative strategy helps to achieve the best outcome.

> For all types of vitreoretinal surgery, a good preoperative strategy helps to achieve the best outcome.

A study published in *Ophthalmology* in 2010 described the classic ILM-flap technique,[7] and it was subsequently revised in 2015, when the temporal-inverted-ILM-flap technique was introduced. With this method, following core vitrectomy and dye staining, the ILM is not completely removed from the retina but is left in place, attached to the edges of the MH. This ILM remnant is then inverted to cover and fill the MH. Finally, fluid–air exchange is performed.[8]

According to another study, which compared the use of inverted ILM-flap, free-flap and conventional

IN SHORT

- ***Clinical studies are underway to confirm the promising results obtained so far with subretinal implantation of human amniotic membrane plugs in the treatment of large and recurrent macular holes.***

ILM peeling, although all techniques showed a tendency towards visual improvement, the inverted-flap technique seemed to induce a faster and more significant recovery in the short term.[9]

From our point of view, despite the optimal anatomical results, it remains unclear as to how good a substrate the ILM-flap is for the remodelling of the neuro-sensitive retina, given the fibrogenic potential of the ILM plug and the uncertainty as to the role fibrotic proliferation may play in restoring visual function.

Until recently, our surgical approach for large and recurrent MHs was to inject autologous whole blood of the patient into the macular defect: a three-port 23-gauge pars plana vitrectomy was undertaken and the central portion of the retina coloured with indocyanine green. ILM peeling then took place with the help of scraper and thumb forceps.

A partial fluid–air exchange followed, as well as the injection of one to two drops of blood.

After aspiration of excessive fluid and blood, the surgery was completed with a low-density silicon oil tamponade.

Anatomical results using this technique were relatively satisfying but functional ones controversial.

Interestingly, Purtskhvanidze et al. compared both anatomical and functional success when using platelet concentrate or whole blood to induce closure of persistent MHs. Their results indicated that the former approach seemed to give better results.[10]

In particularly large or recurrent MHs in which the ILM has already been removed during previous surgery, transplantation may offer a solution to close the holes. A study published in 2016 reported using the lens capsule in an attempt to close MHs, with promising results.[11]

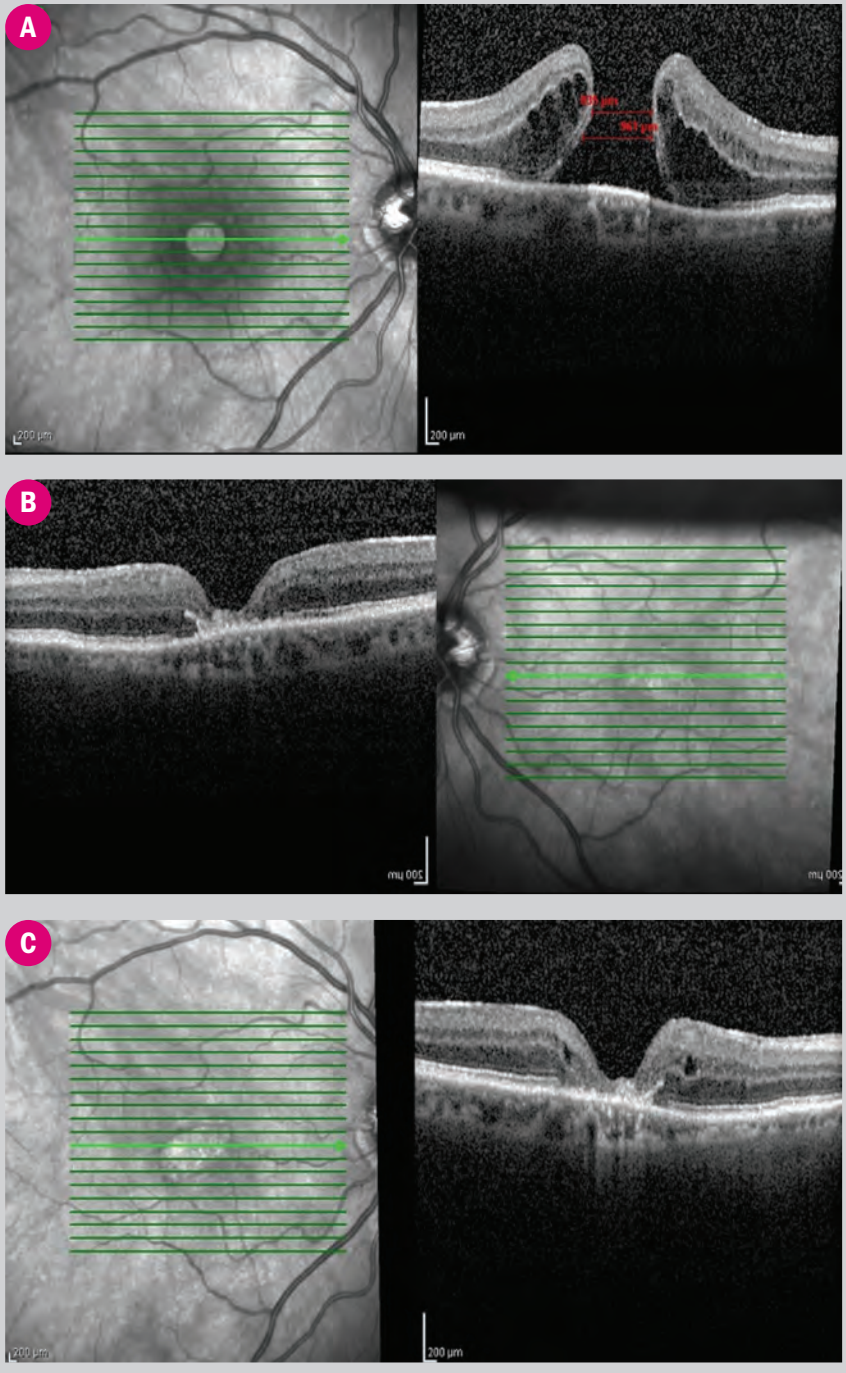
Another autologous transplant was then introduced. It consisted of a neurosensory peripheral retinal transplant, followed by tamponade: either silicone oil tamponade, or short-term perfluoro-n-octane heavy-liquid tamponade. Anatomical results were good but success in postoperative visual acuity was limited.[12]

The use of amniotic membrane

A novel, less invasive alternative to autologous tissue transplantation in the surgical treatment of large and recurrent MHs is the use of human amniotic membrane (hAM) transplantation (or implantation). With this method, the lens capsule and the peripheral retina of the affected eye are left intact. A plug of lyophilised or cryopreserved hAM is used instead of the patients' tissues to repair the MH.

Use of hAM in medicine is not new. Applications of hAM in medicine in general, and in surgical ophthalmology in particular, have been reviewed.[13] Until 2018, the use of hAM in clinical ophthalmology had been confined to the ocular surface.

In one study published in 2018, hAM patches were placed via an intraocular approach to repair large and recurrent MHs.[14] Interestingly, from a historical point of view, repair of MHs with hAM had already been attempted in the mid 20th century, with a surgically



(FIGURE 1) **A. OCT macula of a 77-year-old patient after PPV, MP, gas tamponade; 2 months after surgery, the macular hole persisted, with a diameter of 961 µm, VA: 20/200. B. OCT macula 2 months after PPV with implantation of amniotic membrane gas tamponade: the macular hole is closed C. OCT macula 5 months after surgery, VA: 20/100** *(Images courtesy of Städtisches Klinikum in Karlsruhe)*

complicated retro-bulbar approach in 1957 and in 1964.[15,16]

Animal and *in vitro* experiments preceded present day clinical use of hAM. Experiments carried out in pigs' eyes showed the effect of transplanted amniotic membrane on subretinal wound healing.

Amniotic membrane modified choroidal neovascularisation after mechanical damage to Bruch's membrane and seemed to behave as a basement membrane substitute for the proliferation of retinal pigment epithelium (RPE).[17] *In vitro*, it was demonstrated that RPE cells cultured on hAM had an epithelial phenotype and secreted growth factors essential for retinal homeostasis.[18]

A 2018, prospective, consecutive case-series described positive results when hAM was implanted in eight patients who had large recurrent MHs. All patients had already undergone pars plana vitrectomy with ILM peeling and gas tamponade. The hAM was delivered cryopreserved from a human tissue bank and was defrosted intraoperatively before insertion.

In all patients, OCT at 1 week postoperatively showed MH closure with neurosensory retina overfilling the hAM. Best corrected visual acuity improved from 1.48±0.49 logarithm of the minimal angle of resolution (logMAR), (20/800) preoperatively to 0.71±0.37 logMAR (20/100) 3 months postoperatively, and to 0.48±0.14 logMAR (20/50) 6 months after the procedure. No ophthalmological adverse events were seen during follow-up.[14]

In a further study, hAM was used in ten patients with high myopia and MHs associated with retinal detachment who had undergone at least one pars plana vitrectomy. Half of the patients received silicon oil and half 10% octafluoropropane as tamponade at the end of surgery.

Silicon oil was removed 2 months after surgery. Results were very satisfying since retinal re-attachment

was achieved in all patients and visual acuity improved from 1.73 logMAR to 0.94 logMAR after 6 months.[19]

It appears that hAM is well tolerated. The possibility of hAM rejection has also been considered. In 1999, subretinal implantation of hAM in a rabbit model caused no evidence of inflammation or rejection.[20]

In the wake of these results, we started implanting amniotic membranes in patients who had large or recurrent MHs. However, a few of the steps in our surgical approach differs from that described by the aforementioned study: like them, we use a 23-gauge access but unlike their approach, we do not use a chandelier, so the method is not bi-manual. The amniotic membrane is managed with a crocodile forceps.

A partial fluid–air exchange takes place, leaving a minimal amount of fluid at the foveal level in order to facilitate the manoeuvre of insertion of the amniotic plug. Implantation of the membrane may be facilitated by the use of a Tano scraper. No perfluorocarbon (PFCL) is used. Surgery is completed with fluid–air exchange and, finally, wash-out with perfluoropropane takes place.

The best possible outcome, in terms of anatomical results as well as visual acuity, is achieved when patients are able to remain in a face-down position for several days. In those who have physical disabilities or high comorbidities and who are, therefore, unable to hold the face-down position for a long time, silicon oil is used to keep the amniotic membrane in place after insertion.

Conclusions

Clinical studies are currently underway to confirm the promising results obtained so far with subretinal implantation of hAM plugs in the treatment of large and recurrent MHs. It seems that, in addition to anatomical success, the amniotic membrane stimulates retinal ingrowth and leads to improvements in visual acuity.

For this reason, we think attempts should be made to further the understanding of this novel technique in order to analyse its capability to restore visual function. We would suggest an accurate comparison of preoperative and postoperative measured parameters such as visual field assessment and electroretinogram exams, which can validate this technique. In conclusion, we would affirm that the implantation of amniotic membrane may offer new hope in restoring vision in patients with an otherwise grim outlook.

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Researchers find low risk of COVID-19 transmission in tears

Study did not detect the coronavirus in tears of infected patients

By Lynda Charters

Day after day, new information is added to the current knowledge about the severe acute respiratory syndrome COVID-19 virus and how it works. While it currently is clear that the virus is transmitted in droplets spread through coughing and sneezing by infected patients, a new study found that the virus does not seem to be present in the tears of those patients.

"Transmission through infected ocular tissue or fluid has been controversial. It is hypothesized that the nasolacrimal system can act as a conduit for viruses to travel from the upper respiratory tract to the eye. Hence, ocular tissue and fluid may represent a potential source of [the virus]," the investigators said.

> In the study under discussion, there was no evidence of COVID-19 shedding in tears throughout the course of the disease.

Before appearances in Europe, North America, South America and Africa, Singapore experienced local transmission in multiple clusters across the country.

The National University Hospital Department of Ophthalmology, a high-volume ophthalmology centre in Singapore, offers an example of infection control measures implemented in the setting of COVID-19 infections that may be of value as other ophthalmology clinics begin to experience and plan for potential increases of COVID-19 risks.

Armed with this knowledge, ophthalmologists may be able to balance the infectious disease risks with continuing care for ophthalmology patients during this period, prompting this perspective of infection control strategies at the National University Hospital Department of Ophthalmology, Singapore.

First author, Ivan Yu Jun Seah, MBBS, and colleagues from the National University Hospital and several other institutions in Singapore set out to determine in a prospective study if the virus is transmitted in tears by assessing for its presence using quantitative reverse transcription polymerase chain reaction (RT-PCR).

In this study, the investigators collected 64 tear samples from 17 patients with the virus at different time points following the onset of the initial symptoms (range: days 3–20).

The samples were collected from both eyes of the patients using Schirmer's test strips over the course of the study.

In total, 12, 28 and 24 samples were obtained during the first, second and third weeks of the initial symptoms, respectively, and then analysed by RT-PCR.

All patients had tested positive for the infection by RT-PCR analysis of nasopharyngeal swabs.

The patients were assessed for ocular symptoms that included red eye, tearing blurred vision, discharge and colour desaturation, the investigators reported, which are the ocular symptoms manifested by other coronaviruses that infect humans and animals.

Patients were also assessed for other symptoms of COVID-19 that included fever, cough, shortness of breath, rhinorrhea and sore throat. No patients presented with ocular symptoms.

During the hospital stay, one patient developed conjunctival injection and chemosis. A total of 14 patients presented with upper respiratory symptoms that included cough, rhinorrhea and sore throat.

IN SHORT

- ***According to a research team, there is a low risk of viral shedding in the tears of patients with COVID-19.***

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Findings

"All patients tested negative for COVID-19 on viral isolation and RT-PCR," Dr Seah reported. The findings were reported in *Ophthalmology*.[1]

The authors reported that they are unaware of any other study that compared viral shedding in tears with the results of nasopharyngeal swabs during the course of COVID-19 infection, although a previous study reported positive results, but the virus could not be successfully isolated.[2]

Dr Seah pointed out that, in the study under discussion, there was no evidence of COVID-19 shedding in tears throughout the course of the disease. A previous study had shown that the viral load in nasal and throat swabs are elevated for about 2 weeks from the onset of the viral symptoms.[3] The time points at which the tears were sampled in the current study covered the 2 weeks of active infection, and all tear samples tested negative even when the nasopharyngeal specimens continued to test positive.

"Patients with symptoms of upper respiratory tract infections did not demonstrate any viral shedding in tears, suggesting that the hypothesis of the lacrimal duct as a viral conduit may not be true," the investigators commented.

They also pointed out that only one patient developed ocular symptoms and there was no evidence of virus in the tear samples, thus "suggesting that transmission through tears regardless of the phase of infection is likely to be low."

However, the investigators issued the caveat, i.e., that "COVID-19 has been known to infect cells via ACE2 receptors", and they noted that further studies are needed to prove the presence of ACE2 receptors on corneal and conjunctival cells. In addition, more studies are warranted to determine the association between serum viral load and viral shedding in tears.

As more information about COVID-19 emerges, these measures likely will continue to undergo revision to try to ensure eye care services can be provided safely. Meanwhile, these measures may serve as a starting point for those beginning to consider this new threat for ophthalmology practices, especially in areas where the number of cases may climb rapidly in the near future.

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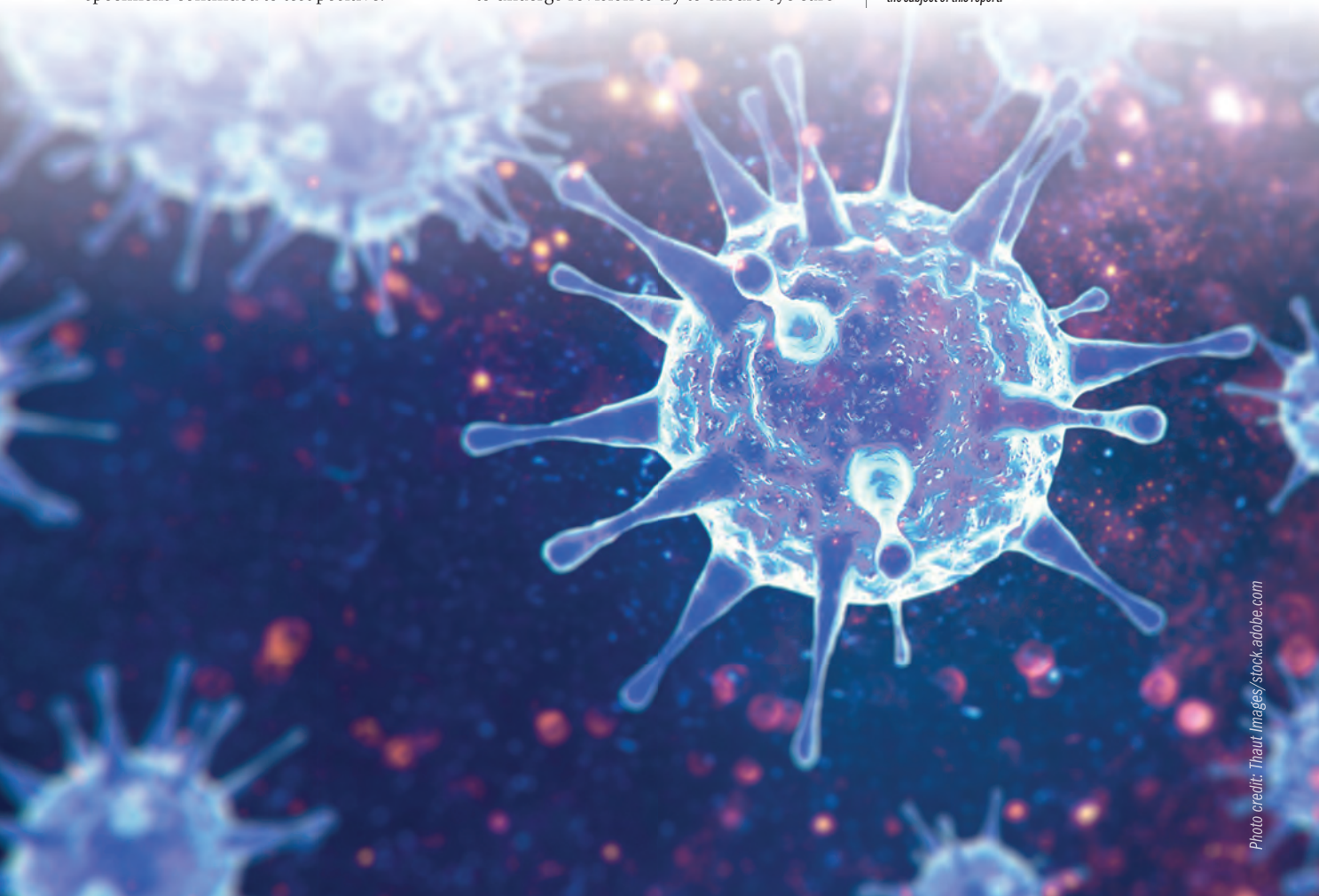

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Being the 'boss' of the graft

An interview on how corneal transplantation has changed since DMEK

Caroline Richards, editor of Ophthalmology Times Europe®, *interviews Dr Lamis Baydoun on how corneal transplantation has changed—and what has been learned—since the introduction of Descemet membrane endothelial keratoplasty (DMEK)*

Dr Baydoun

A high number of corneal diseases only affect the inner layers of the cornea, that is, the Descemet membrane (DM) and endothelium. Until a few years ago, full-thickness corneal transplants—or penetrating keratoplasty (PKP)—typically took place, irrespective of whether the disease affected one or all layers. However, surgeons can now replace just the diseased parts with corresponding layers from healthy donor tissue in posterior lamellar corneal transplantation procedures.

Dr Lamis Baydoun, former head of academy and corneal surgeon at the Netherlands Institute for Innovative Ocular Surgery (NIIOS) in Rotterdam, has been heavily involved in developments with posterior lamellar keratoplasty and the most recent type of corneal surgery to spring from this, Descemet membrane endothelial keratoplasty (DMEK). At NIIOS, she taught dozens of surgeons across the world how to perform DMEK surgery, and her research continues to push the field forward.

» WHO INVENTED DMEK?

Gerrit Melles is the founder of NIIOS and is regarded the 'Pope' of lamellar endothelial surgery. For 100 years, corneal surgeons performed only full-thickness penetrating keratoplasty—there was no other option to treat patients who have only one diseased layer.

The results of Dr Melles' experiments and his first surgeries opened up the field of endothelial keratoplasty. This started with deep lamellar endothelial keratoplasty (DLEK), then Descemet stripping (automated) endothelial keratoplasty (DSEK/DSAEK) and, finally, DMEK, the latest and most precise innovation, where you can practically restore the normal corneal anatomy.

» HOW HAVE OPHTHALMOLOGISTS' PERCEPTIONS OF DMEK CHANGED OVER TIME?

Many corneal surgeons were reluctant to adopt it at first. They were very uncomfortable with the technique and the graft itself, and perceived several obstacles.

Firstly, it was very difficult to recover the DMEK graft from a donor cornea. Secondly, the possibility of the graft unfolding during surgery incited fear in learning this technique because every time the delicate graft is touched, the corneal endothelial cells that are required to clear the cornea may be damaged.

The management of a new post-operative complication such as graft detachment (i.e., separation of the DMEK graft from the posterior stroma) was another concern. Patients faced complications that just did not occur with full-thickness penetrating keratoplasty (PKP) transplants, so surgeons felt they were far more comfortable remaining with the older technique.

However, over the longer term, the benefits of DMEK over all previous keratoplasty techniques were so overwhelming that the method could not be ignored any more—you could actually reach a level of visual outcomes that were comparable to those seen following lens or even refractive surgery!

We had some very happy patients following the procedures. And when the patient is happy, of course, us doctors are also very happy.

» WHAT ARE THE CHALLENGES FOR OPHTHALMOLOGISTS WHO ARE NEW TO THE PROCEDURE?

It is worth mentioning that the technique is now becoming much easier to master. Dr Melles first performed the surgery in 2006, so we have 13 years of experience to draw on, and during this time period we developed a standardised procedure and learnt how to handle the graft and complications better.

However, it is, of course, a challenge for surgeons starting out with performing DMEK. This is why courses are offered in Rotterdam: to teach surgeons tips and tricks, and help them to get over common obstacles, thus enabling them to adapt to DMEK surgery more quickly.

The main issue beginner surgeons have is knowing which graft side is the right side up. This is a key step for a successful surgery, and certain intraoperative signs can help indicate the correct graft orientation.

An intraoperative OCT (iOCT) may be a useful tool during the DMEK learning curve to visualise graft orientation and positioning. Once the surgeons are familiar with the technique and the surgical set-up, they do not necessarily need to use it, although it may remain a helpful tool in eyes with very, very edematous corneas.

» WHICH DISEASES ARE BEST TREATED WITH DMEK?

The answer to this is: all diseases that concern the corneal endothelium.

So, the cornea normally consists of five layers. Going from the outside to inside, you have: the epithelium; the Bowman layer; the stroma; the Descemet membrane; and finally the endothelium—and these final two layers are replaced in endothelial diseases.

There is one disease—Fuchs endothelial corneal dystrophy—which is very common and effectively treated with DMEK, showing outstanding results.

Then there is bullous keratopathy, which usually occurs when corneal endothelial cells are damaged during certain eye operations; for example, during surgery to treat glaucoma or remove cataracts. This is another disease that is well treated with DMEK.

» WHAT SHOULD PATIENTS EXPECT WHEN THEY ARE TOLD THEY NEED LAMELLAR CORNEAL SURGERY SUCH AS DMEK?

Patients can expect a minimally invasive treatment. Rather than excising the whole cornea and having the eye open during surgery, the surgeon will make only minimal, small incisions, entering the eye with small instruments to remove the diseased layers before inserting a healthy donor graft.

Following this, the surgeon unfolds the graft before attaching it with an air bubble to the posterior stroma of the patient.

This was actually how this surgery became so successful: previously, the graft was attached with sutures. These sutures can irritate the eye and induce inflammation, leading to possible transplant rejection.

Attaching the graft with an air bubble eliminates this problem, providing patients with a less traumatic surgery, and, after that, faster rehabilitation with better visual outcomes.

From our experience at NIIOS, the graft can detach in about 10% of cases; however, not all cases may need a re-bubbling procedure. In my experience, graft detachment has become a controlled complication.

» WHAT LESSONS HAVE YOU LEARNT SINCE THE FIRST PROCEDURE WAS PERFORMED?

What I have learnt is to no longer be afraid of the graft! This is something that at first is quite frightening. You are afraid of touching the graft and fearful because it behaves how it wants to behave. However, with experience, you realise that you can tell it what to do, and in most of the cases it will do what you want.

I have also learnt that not every surgery that is difficult necessarily ends up producing a bad result (it is often the other way around)—it can be surprisingly good even though it was a difficult surgery. These are mysteries that we still need to understand.

» WHAT ARE THE BENEFITS OF QUARTER-DMEK SURGERIES?

Quarter-DMEK surgery was invented at NIIOS and the first series was recently published. The surgery was offered to patients with central Fuchs dystrophy and not those with bullous keratopathy. The rationale for this is as follows.

Fuchs dystrophy is a disease that sometimes only causes central guttae with mild or localised corneal oedema, but still-functioning peripheral endothelial cells. So, in a similar way to how Dr Melles invented DMEK, to offer a selective treatment for the patient that only treats the diseased endothelium and DM, we took that thinking a step further. We asked: is standard DMEK, with its 9.0 mm descemetorhexis (i.e., removal of the DM and endothelium) and round 8.5–9.5 mm graft, really the most selective treatment for all forms of Fuchs dystrophy?

If you have a patient with Fuchs disease but only central guttae that cause visual disturbances such as stray lights during activities such as driving, it would seem sensible to remove just this small diseased central portion and provide the person with a small graft piece for quick visual rehabilitation while sustaining his/her own peripheral cells. This is the idea with quarter-DMEK; you can use endothelial donor tissue more efficiently, hence instead of one standard graft, you can recover four quarter DMEK grafts from one donor cornea.

Endothelial keratoplasty brought us new understandings in cell biology and physiology. Further innovations are possible because of how the endothelial cells react and how they migrate after DMEK surgery. It is not just simply a case of placing some graft tissue in the eye: much more than this takes place.

» WILL YOU BE ABLE TO USE PATIENTS' OWN CELLS TO TREAT CERTAIN DISEASES IN THE FUTURE?

Potentially, yes. A lot is happening in this field at the moment. For example, in 'Descemet stripping only' or 'Descemet stripping without endothelial keratoplasty' for Fuchs disease, foreign tissue is not used, so there is no transplant. As a consequence, there is no risk of tissue rejection and so you avoid the problem of repeated transplants.

In this procedure, surgeons remove the DM and the endothelial layer in the centre of the cornea, which allows the cells from the periphery to migrate inwards to the centre and clear up the cornea.

However, we still don't know which cases should be treated without a transplant (and still profit from this treatment with fast visual recovery), so we currently feel that if we transplant a smaller quarter DMEK graft just in the centre of the optical axis and use it for these kinds of patients, then we will have combined the benefits of the migration approach, use less graft tissue with the chance of further reduction of rejection, and still give the patient fast visual rehabilitation.

In addition, a lot of research is being carried out on approaches with cell injections and cell carriers. I think we will still be doing some DMEKs for a couple of years, but it is likely such innovations will shake up the field again.

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The challenges of examining visual fields in children

Technologies may ease the diagnostic burden in paediatric cases

By Lynda Charters;

Reviewed by Dr Andrew G. Lee

The biggest challenge in visual field testing is recognising when a child may have a visual field defect. A number of symptoms may be clues, including difficulty finding words, difficulty reading as evidenced by missing words or hemifield slip, difficulty during tests as the result of skipping letters, not reading an entire line, or only seeing one number of the Ichihara test when there actually are two.

Dr Mitchell Strominger, professor of ophthalmology and paediatrics, Renown Medical Center, University of Nevada Reno School of Medicine, Reno, Nevada, United States, believes that physicians should be aware that some children compensate for their visual field defects, with, for example, head turns related to visual field loss that are not related to strabismus.

"They may have head turning or head thrusting toward the nonseeing field or use touch to help navigate around," said Dr Strominger.

Some children can have associated motor or sensory deficits; for example, children with cerebral palsy may have a hemiparesis on the side of the visual field deficit.

Children with a known central nervous system abnormality that includes perinatal stroke, encephalomalacia, periventricular leukomalacia, craniopharyngioma, pituitary adenoma or optic pathway glioma, or a known systemic or genetic abnormality, such as neurofibromatosis, should undergo visual field testing, Dr Strominger pointed out.

Other indications for visual field testing are the presence of retinal abnormalities and anterior visual pathway congenital disorders.

Options in visual field testing

Many options are available that can be used to evaluate the visual fields, each with limitations. Visual field testing generally is done binocularly and monocularly. However, Dr Strominger noted that, if a patient has a bitemporal defect, testing should be done monocularly because the defect may not be apparent when binocularly testing is done.

Confrontation visual field testing, in which the child is shown toys and the clinician monitors the responses, is the most basic procedure that has not changed markedly over the decades.

Using the saccadic technique, a confrontation test, the clinician moves objects in front of young children in order to observe the saccades; in older children, counting fingers or the red object test can be used.

Arc perimetry is an old and time-tested technique during which babies can be tested with the use of a flashing light to evaluate the child's response to the light.

Goldmann perimetry is another testing method, in which a light moves from the periphery to the centre of a hemisphere. The child signals when he or she detects the light by tapping on a buzzer; this method works best with cooperative patients.

The Humphrey visual field analyser, the latest technology, is another option, but its use is extremely difficult in small children, Dr Strominger noted.

Contribution of OCT

Optical coherence tomography (OCT) can provide valuable information about the nerve fibre layer. Dr Strominger advises doctors to also measure the ganglion cell layer.

"The ganglion cell layer provides a lot of information that might not be available if only the nerve fibre layer is assessed," he said.

Specifically, in a patient with café au lait spots and glioma, the visual field deterioration was progressing. OCT performed in this patient showed that the glioma was progressing along with a decrease in the nerve fibre layer over time.

Monitoring ganglion cell loss is informative. In a

IN SHORT

- ***Assessing the visual fields in young patients is challenging. OCT may be a good place to start.***

Photo credit: rotozey/stock.adobe.com

child with a suspect visual field, in whom assessing the nerve fibre layer may not provide a great deal of information, the ganglion cell layer may shed some light on the retinal status.

Dr Strominger described a patient with binasal ganglion cell loss secondary to a suprasellar lesion, who was diagnosed with bitemporal hemianopsia.

In another case, in which a change in vision in the right eye was found, the bilateral vision was 20/20. The right eye appeared to have a subtle change in the visual field. Analysis of the nerve fibre layer on OCT showed a good structural appearance; however, a small ganglion cell loss was apparent in the left eye.

"This defect is seen more and more often in patients with demyelinating disease," Dr Strominger said. "The visual acuity can be completely normal, the colour vision may be good, but there is a decrease in the ganglion cells."

In a patient with left homonymous hemianopsia, OCT showed a corresponding loss of ganglion cells with a lesion in the occipital lobe.

"Patients are being identified with retrograde axonal degeneration that can be identified by evaluating the ganglion cell layer," he said. "In cases in which a visual field examination cannot be performed and in which ganglion cell loss is found, physicians should be concerned about a posterior defect."

In a similar case, the patient had a superior quadrantic defect; the nerve fibre layer was normal on examination but the ganglion cell layer was defective and corresponded to that defect. The patient was diagnosed with post-lateral geniculate disease.

In commenting on the importance of OCT, Dr Strominger noted that the nerve fibre layer thickness should be affected in anterior visual pathway disorders except in some cases with demyelinating disease in which the ganglion cell layer only may be affected.

"Some ganglion cell loss can be seen in retrograde axonal degeneration. OCT can be easier to perform in children and the findings can correspond to visual field defects," Dr Strominger explained.

Technologies on the horizon

Saccadic vector optokinetic perimetry uses fixation targets and an eye tracking device to monitor real-time eye movement responses to visual field stimuli. The system includes separate patient and examiner displays, the eye tracker and a height-adjustable table.

A head-mounted eye tracking perimeter (Virtual-Eye, BioFormatix Inc.) device capable of vector analysis is under development.

While many options are available to assess the visual fields in young patients, Dr Strominger generally starts with OCT because of the wealth of information that the technology provides. Performing Humphrey visual field testing can be useful in cooperative patients. Some newer technologies in the pipeline may soon add to the ophthalmologist's armamentarium in this challenging patient population.

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Endophthalmitis detection by whole-genome sequencing and qPCR

Cultures not sensitive enough to detect endophthalmitis pathogens

By Lynda Charters

Worse outcomes after development of endophthalmitis postoperatively are associated with the presence of bacteria and higher bacterial loads of pathogens other than *Staphylococcus epidermidis*, as detected by whole-genome sequencing (WGS) and quantitative polymerase chain reaction (qPCR).

The incidence rate of endophthalmitis that develops after intravitreal injections is low, but more and more injections are being administered annually in the US and the rate of endophthalmitis is climbing. However, the current gold standard, cultures, seems less than adequate: the Endophthalmitis Vitrectomy Study (*Arch Ophthalmol.* 1995;113:1479-96) found that only 69.3% of cases were culture-positive, leaving the rest with no aetiological diagnosis.

In addition, the culture-positive rates may be even lower in endophthalmitis that develops following intravitreal injections: among 23 cases of endophthalmitis analysed following 27,736 injections, 16 cases were found to be culture-negative (*Ophthalmology* 2011;118:2028-34).

According to Dr Cecilia Lee and colleagues, as "the prognosis of endophthalmitis appears at least partially dependent on the causative organism, the high rate of culture-negative cases suggests a need for a more sensitive modality for pathogen detection."

In light of this, Dr Lee et al. conducted a prospective cohort study in which Mid Atlantic Retina, the Retina Service of Wills Eye Hospital, PA, USA, and the University of Washington, WA, USA, participated. Consecutive patients were enrolled who had a clinical diagnosis of endophthalmitis after any intraocular procedure or surgery, within 6 weeks of presentation. On the day of recruitment, all patients underwent either intraocular fluid biopsy or pars plana vitrectomy. qPCR for specific pathogens and WGS were performed.

Fifty patients (52% men; mean age, 72 years) were enrolled. Following qPCR and WGS, 24 cases were culture-positive. "WGS identified the cultured organism in 76% of the culture-positive cases and identified potential pathogens in 33% of the culture-negative cases," said Dr Lee, who is from the Department of Ophthalmology, University of Washington. Findings were published on behalf of the Endophthalmitis Study Group in the *American Journal of Ophthalmology* (2020; doi: 10.1016/j.ajo.2020.03.008).

The most frequently cultured organisms were *S. epidermidis* followed by other *Staphylococcus* and *Streptococcus* species.

Median bacterial load was 3.32 (mean, 53.50; range, 0.028–480) in the culture-positive cases. In WGS-positive but culture-negative cases, median bacterial load was 1.44 (mean, 2.04; range, 0.35–6.19).

Visual outcomes in cases with *S. epidermidis* endophthalmitis did not differ from those in pathogen-negative cases; however, patients who tested positive for other organisms had worse visual outcomes. Visual acuity (VA) levels were worse at months 1 and 3 in cases that had higher baseline bacterial DNA loads of pathogens other than *S. epidermidis* detected by WGS. Interestingly, the bacterial load of *S. epidermidis* did not seem to affect the outcomes, the investigators reported.

qPCR identified Torque teno virus in 49% of cases, which correlated with a higher rate of secondary pars plana vitrectomy and retinal detachment. Merkel cell polyomavirus was identified in 19% of cases.

The authors concluded that the culture/molecular pathogen testing status (for bacteria and virus) as well as the baseline VA has prognostic significance for clinical outcomes, including the VA and secondary vitrectomy in endophthalmitis. "Molecular studies provide more extensive and sensitive characterisation of pathogens and have the potential to allow for improved treatment paradigms," they wrote. "Further development of rapid, point-of-service molecular diagnostics and subsequent prospective randomised controlled clinical trials will allow for testing of new paradigms for risk stratification and individualised treatment for endophthalmitis."

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Dr Lee has no financial interest in the subject of this report.

The beautiful and the curious: Artwork of ocular pathologies

Artist merges scientific and artistic expertise with own experience of dry eye

By Erica Crompton;

Reviewed by
Miss Iluá Hauck da Silva
and Mr Neil Handley

(FIGURE 1) ***Stigmata*: an example of the artist's work with anatomical and pathological symbolism.**

Almond shapes, long eyelashes and interesting irises—in particular those with several colours and patterns: these are what make beautiful eyes, according to artist and glassmaker Iluá Hauck da Silva. "However," she says, "ultimately it is the intensity and sincerity of gaze which makes a pair of eyes beautiful: eyes that sparkle with enthusiasm and love, and that overflow with tears when emotion takes over. The ability to candidly and transparently express feelings is definitely the most fascinating and beautiful quality eyes have."

The crux of Miss Hauck da Silva's practice is to visually investigate the human condition, and she specialises in works of anatomical and pathological symbolism (see Figure 1). It is eyes, specifically, that she has dedicated her latest work to, following her artist-in-residence at the College of Optometrists in London, UK in 2019. At the College's museum—the British Optical Association Museum—she has created a fascinating modern-day cabinet of eye-related curiosities, complete with drawings, photographs, digital images and glass objects, all of which can be viewed by the public.

In producing *Pathos Ocularis—the Beautiful and the Curious*, the title of the exhibition, Miss Hauck da Silva took inspiration from the Museum's collections, as well as from medical, scientific and historical research she conducted in the College library (which contains literature on the eye and optical science dating back to the 15th century). She combined her research findings and artistic expertise with facets of her own experience with eye disorders.

IN SHORT

- ***Pathos Ocularis—the Beautiful and the Curious*, is a fascinating exhibition at the College of Optometrists in London that merges art with ophthalmology.**

(FIGURE 2) ***Eyeconography*: Chalice-like platters of glass eyeballs, their shiny surfaces vying for attention, invite visitors to consider ocular pathologies at rather gruesome stages.**

Glass eyeballs feature largely in the exhibition. In *Eyeconography* (Figure 2), an antique silver dish designed to look like a chalice holds a dozen or so exquisitely made but not so healthy-looking eyeballs—each a glossy white with irises in vivid blues, oranges and greens—and some with a double pupil or iris, to represent the double vision that the artist has herself experienced.

Drawing on experience

Describing her experience with diplopia, Miss Hauck da Silva told *Ophthalmology Times Europe*: "I suffered from diplopia as a result of sixth nerve palsy, which occurred due to the fact that I had an infection in my petrous bone [which I had] for at least 6 weeks before my sixth nerve was affected. In a way, I am glad I had diplopia because it was the symptom that urged me to seek help at Moorfields Eye Hospital [London]. Double vision was rather disorienting and deeply concerning—I remember feeling very fragile and vulnerable."

Once hospitalised at Guy's Hospital, London and medicated, Miss Hauck da Silva's diplopic symptoms quickly subsided, but it took at least 3 months for the movement in her right eye to return to normal. Ever since the infection, she has suffered from dry eyes and photophobia, which worsen if she has to work on a computer for long periods of time, use her mobile phone a lot or travel on public transport. She finds these symptoms both "uncomfortable and frustrating".

Miss Hauck da Silva is also an art historian and considered Saint Lucy, the patron saint of the blind in Roman Catholicism, when producing the show. "When I first saw the Museum's cabinet drawers full of glass eye models representing ocular pathologies in advanced stages, I immediately made a connection with Saint Lucy's eyes on a plate, her principle iconography, which suddenly resonated very differently with me," she described.

"I was compelled to think of people from bygone eras who would leave votive offerings or ex-voto on altars dedicated to Saint Lucy either in hope to be cured or in gratitude for having been cured. Such people could have been suffering from those advanced ocular pathologies represented in the glass models—glaucoma, cataract or an eye infection—when there was no medical treatment for such conditions. It must have been truly awful!"

She added: "This called into question the role of the cult of saints before the advent of modern medicine, and how our attitudes towards illness and cure have changed since then. This is why, in my *Self-portrait as Saint Lucy* (Figure 3), instead of eyes I have placed images of the medication that cured me from acute diplopia on the plate, conflating the religious and the scientific."

According to Miss Hauck da Silva, the most validating moment of her art residency was when she first told Neil Handley, curator at the Museum for the past 22 years, that whilst doing research in the Museum's library, she had come across a chapter in a book that had been written by the very doctor who had treated her when she suffered from diplopia/sixth nerve palsy. This is when Mr Handley said she should make her work about the illness she had, since sharing her personal experience would potentially make it easier and more interesting for viewers to relate and engage with the show.

Mr Handley, who has a background as an historian of science and medicine, first encountered the artist as a visitor to the Museum. "Her obvious interest in our collections, coupled with fortuitous timing—it had been 7 years since our last artist-in-residence—meant she was an obvious person to approach," he said.

"Her work is also very visual, but not abstract, which suits the general flavour of our displays, which our founder John Sutcliffe instigated as far back as 1901 (we are the oldest optical museum in the world). Sutcliffe commented that he wanted there to be eyes looking at you from every corner of the professional headquarters (then at a different location, but we've continued the theme in our present building) so that no one who crossed the threshold could be in any doubt as to the subject matter of the optometry profession," he added.

"It's appropriate, therefore, that Iluá's exhibition is in the reception area, making it the first thing that visitors to the College see."

Mr Handley explained that all the College's exhibitions are a challenge,

(FIGURE 3) **In the artist's version of the Self-portrait as Saint Lucy, eyes on a plate have been replaced with the medication that cured her from acute diplopia.**

because they have to operate on a very small scale due to their location in what were formerly domestic premises, albeit a pair of very nice Georgian town houses. He said: "Our first-ever artist-in-residence, Derek Ogbourne, produced a 'micro' exhibition within a single pull-out drawer, whereas our second, Patrice Moor, produced an exhibition comprising just three works, placed strategically at intervals within the permanent display."

He added: "I decided to offer Iluá one entire display case, but she was governed by its dimensions and the fact that all the works would have to be displayable in the horizontal position. Iluá obtained great insight from holding discussions with our Clinical Adviser at the College, Mr Daniel Hardiman-McCartney. It was a learning journey for her as much as for us, in that she learned a lot more about her own eye condition and how others have coped with eye disease or visual impairment over the centuries."

For Mr Handley, the lived experience that manifests in the exhibition is a highlight. He says: "I like the assemblage of pieces collectively entitled *Dry Eyes* [see Figure 4]. The aim was to represent, in artistic form, just what experiencing an eye condition feels like. That's quite a challenge, but Iluá has succeeded; just looking at the pieces is painful."

"Their rough, gritty surface texture took multiple firings to perfect and it was quite a lengthy process to achieve the end result, in the same way that treatment for a medical condition can often take a long time and bring its own pain in the process." For this piece, the artist chose to move away from anatomically correct eyes to a two-dimensional form inspired by ancient Egyptian imagery.

Although her story is told ultimately as a positive one of recovery, Miss Hauck da Silva pointed out: "I wanted to include the word pathos in the exhibition title, as in many languages it evokes suffering and pain, and thus prompts empathy/compassion in the viewer for the sufferer."

The Museum hopes that visitors to this show will respond to both the beauty and the curious nature of the exhibits. These concepts are not mutually exclusive. Some of the imagery may subvert commonly accepted notions of beauty, and some of the most curious things, including pathological conditions, can convey a strange beauty of own.

It is often suggested that the works of art in an exhibition will 'speak for themselves'. For this show, Mr Handley said he wanted to allow the voice of the artist to be heard much more explicitly—and the College has certainly succeeded in this, for these exhibits 'see for themselves'.

The exhibition will be available to visit by appointment at The College of Optometrists, London, once the lockdown restrictions currently in place due to the COVID-19 pandemic have been lifted. For more information, visit www.college-optometrists.org.

(FIGURE 4) ***Dry Eyes*: by creating a gritty surface, the aim was to artistically represent what it's like to experience an uncomfortable or painful eye condition.** *(Photos courtesy of the College of Optometrists, London, UK)*

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Mr Handley is the current curator of the British Optical Association Museum and the first full-time museum professional to hold the post.

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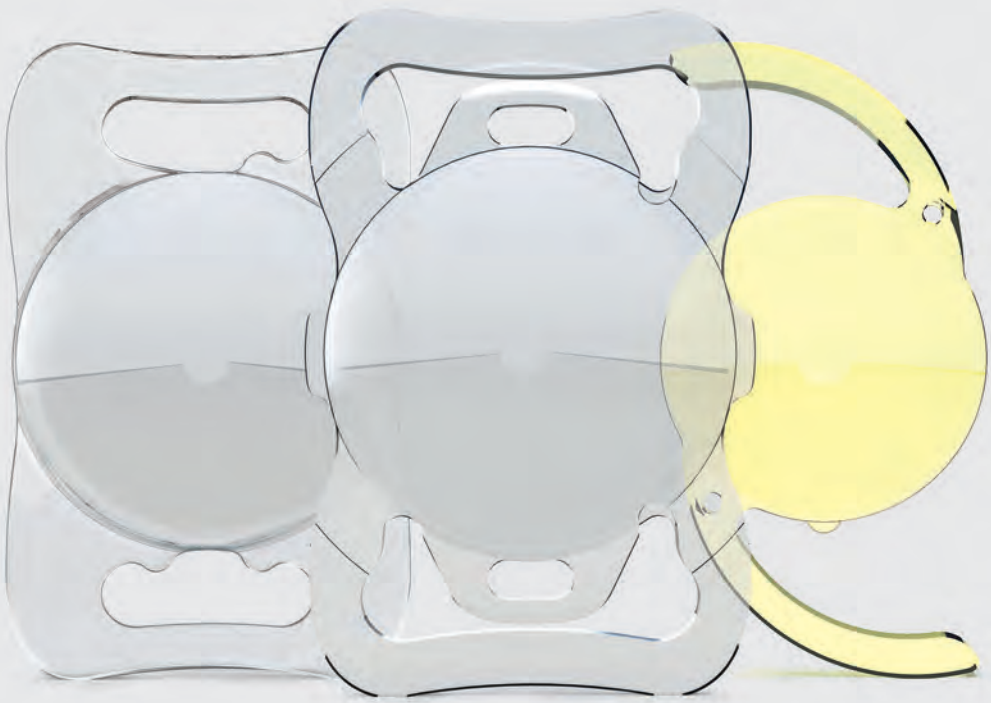

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