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Sstevenson@mjhlifesciences.com

Editor
Caroline Richards
CRichards@mjhlifesciences.com

PUBLISHING / ADVERTISING
Eurocare Sales Manager
James Tate
JTate@mjhlifesciences.com
Tel: +44 (0) 2392 356 075

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Paracelsus University Salzburg, SALK University Eye Clinic, Salzburg, Austria

John Hydrusko, Jr
Tel: +1 908 839 2065

JTate@mjhlifesciences.com

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“From an immunological perspective, the eye is the ideal target for gene therapy.”
—READ FULL STORY ON PAGE 30

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OZURDEX® is indicated for the treatment of adult patients with visual impairment due to diabetic macular oedema (DMO) who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy.

Real world evidence is collected outside of controlled clinical trials and has inherent limitations including a lesser ability to control for confounding factors.


OZURDEX® (Dexamethasone 700 micrograms intravitreal implant in applicator) Abbreviated Prescribing Information. Presentation: Intravitreal implant in applicator. One implant contains 700 micrograms of dexamethasone. Disposible injection device, containing a rod-shaped implant which is not visible. The implant is approximately 0.4 mm in diameter and 6 mm in length. Indications: Treatment of adult patients with macular oedema following cataract surgery (Intravitreal Injection Occulsion (IRVO)) 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 (DMO) 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. 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Patients should be monitored following the injection to permit early treatment in cases of infection or the need to remove an intraocular pressure or dot implant. The injection should 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 or 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 infections, are at risk of implant migration into the anterior chamber. Implant migration to the anterior chamber may lead to retinal detachment. Persistent severe cornual oedema could progress to the need for cornual 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) and increased IOP. Steroid-induced glaucoma 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 glaucoma simplex and not be used in active ocular herpes simplex. OZURDEX is not recommended in patients with macular oedema secondary to PVR with significant retinal October. OZURDEX should be used with caution in patients taking anti-capsular or anti-glaucoma medications. 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 new 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 minimised so no interactions are anticipated. Pregnancy: There are no adequate and well-controlled studies 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 temporary reduced vision after receiving OZURDEX due to intraocular 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 on day 6 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 (4/407 in DMO 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): increased IOP, cataract, conjunctival haemorrhage. Common (≥1/100 to <1/10): headache, ocular hypertenion, cataract subcapsular, vitreous haemorrhage, visual acuity reduced, visual impairment/diffusion, anorectal involvement, perianal abscess, perianal abscess, abdominal sensation in eye*, eyelid edema, cataract*, hypotony of the eye*, anterior chamber inflammation*, anterior chamber cells/flares*, abnormal vision*, abnormal sensation in eye*, anterior chamber infl ammation*, anterior chamber cells/flares*, abnormal vision*, posterior capsule tear*, visual disturbance, vitreous detachment*, vitreous fl oats*, vitreous opacities*/Behcet’s eye path*; photosensitivity; cataract; corneal deposits; conjunctival haemorrhage. Uncommon (≥1/1,000 to <1/100): migrane, necrotizing retinitis, endophthalmitis*, glaucoma, retinal detachment*, retinal tear*, history of the eye*, anterior chamber inflammation*, anterior chamber cells/flares*, abdominal sensation in eye*, posterior capsule tear*, visual disturbance, vitreous detachment*, vitreous fl oats*, vitreous opacities*/Behcet’s eye path*; photosensitivity; cataract; corneal deposits; conjunctival haemorrhage. Very uncommon (≥1/10,000 to <1/1,000): cataract*; posterior capsule tear*, retinal detachment*, vitreous detachment*, other visual disturbances, consider evaluating for possible causes which may include cataract, glaucoma or new diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids. Local adverse events were increased intraocular pressure (IOP), cataract and conjunctival haemorrhage. Other adverse events were reported. 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, 1 Festival Way, Brentford, West London, TW8 9DH. Legal Category: POM. Date of Preparation: May 2019.
Open the windows and enjoy the warmth of a spring-time breeze. That first-day-of-spring feeling awakens the senses and brings a fresh perspective to challenges old and new. We hope you enjoy reading about ophthalmology’s innovations this May.

Prof. Norbert Körber leads off this month’s Ophthalmology Times Europe with a look at a novel treatment paradigm for managing primary open-angle glaucoma. Ab-interno canaloplasty is suitable for patients with medication intolerance and non-compliance (page 7).

Our expanded cataract and refractive surgery section features a retrospective view on how techniques have changed almost beyond recognition over the past five decades. Dr Frank J. Goes reflects on a life at the forefront of ophthalmology, considering advancements in technology and the knowledge that has changed his practice and improved outcomes for patients (page 12).

Next, Dr Abha Amin shares some key learnings from adopting the Yamane method for intrascleral IOL fixation (page 18). Dr Joseph W. Fong and Dr Ahmed A. Sallam shed light on vitreous opacities and offer pearls for improving visualisation in eyes using retroillumination techniques (page 22).

In retina, Dr Quan Dong Nguyen highlights promising early data for an intravitreal diabetic macular ischaemia candidate. Best-corrected visual acuity improved slightly compared with baseline (page 26).

Turning to cornea, we hear from Dr Ritika Mullick on the missing link in the recognition of corneal abnormalities. New imaging modality reveals subtle changes in corneal collagen fibres (page 28).

In gene therapy, Prof. Albert Augustin tells us how ophthalmology is making waves in this space with modern techniques. Several approaches are tackling defective genes in ocular pathogenic pathways (page 30).

Our focal points article considers how cosmetic iris implants pose serious risks and are strongly discouraged. However, despite the potential risks, the surgeries are still performed. Dr Jorge Alio and Dr Francesco D’Oria break it down for us (page 32).

Lastly, Dr Carol L. Shields and her colleagues explore research for determining germline mutations in children with unilateral retinoblastoma. Their study focuses on ascertaining the risk of patients developing additional tumours (page 34).

Thanks, as always, for reading.

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

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INNOVATION KEEPS A SPRING IN OPHTHALMOLOGY’S STEP THIS SEASON

A portable solution for high definition slit-lamp imaging
A NEW TREATMENT PARADIGM with ab-interno canaloplasty for POAG

Technique suitable for patients with medication intolerance and the non-compliant

By Prof. Norbert Körber

Over the past decade, minimally-invasive glaucoma surgery (MIGS) has revolutionised glaucoma management, offering a myriad of advantages such as minimal disruption of the eye’s natural anatomy and physiology, a shorter recovery period and an enhanced safety profile.1,2

However, most MIGS approaches still alter the anterior chamber angle anatomy; for example, trabecular meshwork ablation using an electropulse or micro-trabecular bypass stents, which alter aqueous currents by creating an artificial pathway via one or two points of exit for aqueous humour.3,4

In our practice we use canaloplasty to improve the flow of aqueous throughout the entire 360 degrees of the conventional outflow pathway without redirecting aqueous currents to a single point of exit. It offers a comprehensive approach by addressing all aspects of potential outflow resistance in the trabecular meshwork, Schlemm’s canal and collector channel systems, with proven safety and long-term efficacy in peer-reviewed studies.5–7

The technique

Introduced in 2016, ab-interno canaloplasty is a physician-led refinement of traditional canaloplasty, entailing the intubation of Schlemm’s canal with a flexible microcatheter via a self-sealing, clear corneolimbal incision. This approach preserves the conjunctiva and thus can be used earlier in the treatment paradigm in cases of mild-to-moderate glaucoma. As an added benefit, it does not require a permanent implant in the eye.

We use the iTrack canaloplasty microcatheter (Nova Eye) and the iTrack Advance. With an illuminated fibre optic tip, both devices provide continuous location feedback and an internal guidewire mechanism that permits catheterisation of up to 360 degrees of the canal during a single intubation.

The ab-interno technique is based on the same principles as traditional canaloplasty and is defined as the 360-degree catheterisation of Schlemm’s canal to break obstructions and adhesions, followed by the subsequent viscodilation of Schlemm’s canal upon withdrawal of the microcatheter whilst injecting a high-molecular-weight hyaluronic-acid-based ophthalmic viscosurgical device (OVD).

This pressurised delivery of OVD dilates the canal, thus restoring the physiological aqueous outflow pathway. The tissue-sparing aspect of ab-interno canaloplasty allows future surgical options that rely on the preservation of the trabecular meshwork in patients who may

**Figure 1.**

| IOP at baseline and all postoperative visits following ab-interno canaloplasty. |
| Mean IOP (mmHg) |
| Pre-op (n = 27) | 19.85 | 14.98 | 15.58 | 14.71 | 14.56 |
| 12M (n = 26) | | | | |
| 24M (n = 25) | | | | |
| 36M (n = 21) | | | | |
| 48M (n = 18) | | | | |

Abbreviation: M, months; IOP, intraocular pressure
Cutting-edge Advancements
May 2022

ADDRESSING CHALLENGES IN GLAUCOMA MANAGEMENT

need further intervention as the disease progresses.

This comprehensive approach makes ab-interno canaloplasty an effective treatment modality in a variety of glaucoma patients, including those with mild-to-moderate open-angle glaucoma (OAG) and those who are intolerant, non-compliant or unresponsive to anti-glaucoma medication.

Ab-interno canaloplasty can be performed either as a standalone procedure or combined with cataract surgery. Various studies have documented long-term efficacy for reduction of both IOP and anti-glaucoma medication burden along with a satisfying safety profile and low risk of severe complications up to 36 months following surgery.3–10

Ab-interno limitations

The ab-interno technique is typically performed in cases of mild-to-moderate glaucoma and, to my knowledge, existing published literature does not incontrovertibly report clinical evidence with more advanced glaucoma stages. Furthermore, despite its minimal learning curve, familiarity with the gonio-prism is a known challenge of all the MIGS procedures. In addition, ab-interno canaloplasty can add up to 10–15 minutes of extra time to the traditional phacoemulsification procedure.

Experience as a surgeon

I was one of the first surgeons to use ab-interno canaloplasty in Europe and I recently presented the results of our retrospective, monocentric, consecutive case series using the ab-interno surgical technique at the 2021 European Society of Cataract & Refractive Surgeons meeting in Amsterdam and published the 4-year results.11

The study was conducted on 27 eyes of 22 patients with mild-to-moderate OAG experiencing insufficient IOP reduction or intolerance and non-compliance with glaucoma medication, also including a previously failed trabeculectomy. These patients underwent ab-interno canaloplasty with post-surgical follow-ups at 12, 24, 36 and 48 months.

The results were promising and demonstrated the efficacy of the procedure in reducing IOP and medication dependency, as well as patient complications. Mean IOP significantly declined by 30% from baseline ($P < 0.001$), and the reduction was sustained 4 years postoperatively, from 19.8 ± 5.2 mmHg at baseline to 14.6 ± 3.0 mmHg at the last follow-up.

A significant reduction in mean medication usage was evident 4 years postoperatively as well, from 1.92 ± 1.00 at baseline to 0.89 ± 0.83, and we were able to significantly reduce glaucoma medication dependence by the fourth year. Indeed, 4 years postoperatively, 39% of the eyes required no medication, compared with none at baseline, and 72.2% were using one medication or less (Figures 1 and 2).

No serious complications were documented throughout the duration of the study, except for a case of limited descemetolysis near the limbus, which resolved spontaneously within 2 months. We surmise this was due to slow withdrawal of the catheter resulting in local over-delivery of OVD in the canal and subsequent temporary detachment of the Descemet membrane. Overall, our results suggest that ab-interno canaloplasty is not only effective but also a safe surgical procedure.

Future plans in Europe

In 2022 we plan to start a prospective, non-randomised, multicentre...
TAKE-HOME MESSAGES

- Ab-interno canaloplasty is a stent- and implant-free procedure;
- It preserves trabecular meshwork tissue for subsequent procedures;
- It leads to a 30% average IOP reduction;¹²
- It is comprehensive—addresses all outflow pathway resistance points, including the collector channel ostia; and
- It can be performed in conjunction with cataract surgery or as a standalone procedure.

study across four investigational sites in Europe, to assess the efficacy, safety and quality of life outcomes of canaloplasty combined with phacoemulsification and performed via an ab-interno approach using the new-generation iTrack Advance, which has reengineered the previous microcatheter via a handheld injector design. This multicentre study, called CATALYST, will be performed over a 12-month period and will enrol up to 50 patients with mild-to-moderate uncontrolled OAG.

To sum up, in my experience, ab-interno canaloplasty offers significant versatility in real-world clinical practice and presents a useful tool in the glaucoma toolkit of comprehensive ophthalmologists and cataract surgeons, who typically see earlier-stage patients than their glaucoma surgeon peers. However, these encouraging results do not currently suggest that the technique can replace traditional glaucoma surgery or ab-externo canaloplasty, which we still use in our practice for more advanced glaucoma cases.

Ab-interno canaloplasty is effective in cases of controlled glaucoma, for patients who are intolerant or non-compliant to anti-glaucoma medications and thus have the treatment goal of reducing the number of medications required while maintaining IOP within target range, and possibly also delays the requirement for more invasive surgery and its subsequent increased risks and post-surgical complications.

**Prof. Norbert Körber, FEBO**

E: N.Koerber@gmx.de

Prof. Körber currently works at Augenklinik Köln and at the Clinica Oculistica, University-Hospital Padova, Italy. His areas of interest and expertise are cataract and glaucoma, with a special interest in canaloplasty. He has no financial or proprietary interest in any material or method mentioned but is the principal investigator for the CATALYST clinical study, which uses the product mentioned.

**REFERENCES**


By Florian Sutter, MD
Eye Clinic in Herisau and Appenzell, Switzerland

Minimally invasive glaucoma surgery (MIGS) has established itself in the modern glaucoma management algorithm as an option for effectively reducing intraocular pressure (IOP) with advantages of faster recovery and better safety compared to traditional glaucoma surgery. Most MIGS procedures, however, are indicated only to be used in combination with cataract surgery and have a modest IOP-lowering effect that makes them appropriate primarily for treating mild open-angle glaucoma. Within the MIGS category, HFDS® (Oertli Instrumente AG, Switzerland) stands out as an implant-free approach able to be performed by itself or combined with cataract surgery and offering impressive IOP-lowering potential that makes it a viable option for treating mild to moderate glaucoma.

HFDS® in brief
HFDS, which is an acronym for high-frequency deep sclerotomy, creates a deep sclerotomy in the angle underneath Schwalbe’s line and above the scleral spur. It is a minimally invasive, ab interno procedure, that is performed with a high-frequency diathermy handpiece optionally available with all Oertli surgery platforms (Catarhex 3®, Faros™, OS4™). The reusable HFDS glaucoma tip (Figure 1) penetrates approximately 1 mm into the sclera, extending through the pigmented trabecular meshwork, Schlemm’s canal and into the intrascleral collector channels. Therefore, the depth of the HFDS sclerotome addresses the highest outflow resistance in the conventional outflow pathway, the pigmented trabecular meshwork.

Surgical technique
HFDS is a simple and straightforward procedure with a relatively short learning curve that is also accessible to ophthalmic surgeons who are not glaucoma specialists. In my opinion, HFDS is easier to perform than other MIGS procedures since it does not require manipulation and proper positioning of any implant. Eliminating the use of an expensive implant, HFDS also offers a cost advantage. Adverse events after HFDS occur early, are generally mild, and are self-limiting or transient with minimal management. Its early postoperative safety minimises the number of necessary follow-up visits post HFDS. Because it leaves no foreign material in the eye, HFDS might also have a safety benefit long-term. In addition, HFDS can be repeated, and as a conjunctiva-sparing procedure, it does not preclude future penetrating glaucoma surgery. Performing HFDS does require the use of a direct or indirect gonioscopic lens for intraoperative visualization. Surgeons who are not familiar with this technique can easily acquire the necessary skill through wet lab training or with a dry lab kit available from Oertli.

I usually perform HFDS in patients undergoing cataract surgery where it adds just 3 or 4 minutes to the operative time. It is done after completing phacoemulsification and IOL implantation, and whatever anaesthesia was used for the cataract portion usually provides sufficient coverage for HFDS. The procedure is depicted in a surgical video (Figure 2) and online animation.

Documenting the outcomes
Studies appearing in the peer reviewed literature and results reported in other forums support the conclusion that HFDS is safe and provides effective and durable IOP control. Histological findings from HFDS-treated eyes examined postmortem showing that the sclerotomy remains open long-term corresponds with the procedure’s clinical longevity.

Pajic et al. published findings from longer-term follow-up of two patient cohorts treated with HFDS. One report included 53 eyes followed for 6 years after standalone HFDS done with only four deep sclerotomies.
Mean IOP was significantly reduced (42%; \( P < 0.001 \)) from 25.6 mmHg at baseline to 14.7 mmHg at 6 years; daily medication burden decreased from 2.6 to 0.5. At last follow-up, IOP was <15 mmHg in 53% of patients and <20 mmHg in 94% of patients.

The most common early adverse events were mild temporary IOP elevation (22.6%) that usually responded well to medication, and hyphema that disappeared within 2 weeks (11.5%). Cataract formation in nine eyes (17.1%), including three eyes with no change in visual acuity, was the only late side effect noted.

A second study by Pajic et al. including 49 eyes treated with HFDS and cataract surgery showed similar benefits for reducing IOP and medication burden at 4 years of follow-up.² Surgeons in Egypt reporting data from 43 eyes followed for 9 months after standalone HFDS with six scleroto-

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**Conclusion**

HFDS, is a simple and straightforward, time- and cost-efficient MIGS procedure that is safe and provides significant, durable IOP reduction. As an appropriate choice for managing patients with moderate as well as mild glaucoma, HFDS has had a significant impact on my surgical management of glaucoma. Before I adopted HFDS, I would perform combined phacoemulsification/MIGS in only about 1 of 50 patients with both cataract and glaucoma because I only offered the combined procedure to individuals with mild glaucoma. Now, I am performing combined surgery in at least 1 in 20 patients because with HFDS I have confidence that I can also provide the benefits of IOP control and reduced medication burden to the larger group of patients with moderate glaucoma.

**REFERENCES**

I started my ophthalmology training in 1965 at Ghent University, Ghent, Belgium, in the department of Prof. Jules François, who was a man of many talents (author or co-author of 1,870 peer-reviewed articles; doctor honoris causa at 21 universities) and also a very didactic teacher!

Later, I founded the Ghent University clinic department of ultrasound, where I stayed some 15 years as a consultant. In 1968 I started a solo private practice in Antwerp, Belgium.

I have had the privilege to be a spectator, often a participant and sometimes a leader in the most important developments in ophthalmology over the 50-plus years since I started my ophthalmology career. It is my honour to share the most important learnings and developments with the reader.

Most of these happened during the first 30 years of my career. Indeed, except for the introduction of intravitreal anti-vascular endothelial growth factor injections, there have been no spectacular advancements in ophthalmology since then.

I observed, during those years, the birth of the IOL, the introduction of phaco-emulsification techniques and the use of lasers in the treatment of eye diseases and in refractive eye surgery. Vitreoretinal surgery has boomed and modern eye examination methods (OCT, retinal scans, topographic modelling) have improved and now help in making better diagnoses.

**Cataract surgery**

During my first years in ophthalmology, we worked with a head loupe (with a 6x magnification) and had to open the eye for cataract surgery with a von Graefe knife over 145°, remove the cataract with forceps and close the corneal wound with eight 6-0 silk sutures. The patient stayed in hospital for 5 days and recuperation of normal vision, after removal of the stitches and prescription of the very high hyperopic lens, took 7 weeks.

**Artificial IOL “miracle”**

The development of the artificial IOL—first implanted by the late Sir Harold Ridley at St Thomas’ Hospital in London in February 1950—changed the course of cataract surgery. However, it took several years before Ridley’s invention became widely accepted; I performed my first lens implant in the late 1970s. Before then, it made no sense to perform unilateral cataract surgery.

Indeed, the obligatory use of the very disturbing postoperative aphakic correction was only supported when used bilaterally. These high hyperopic (+12 D) glasses caused a 25% magnification of the image, which was not supported when prescribed unilaterally. These ugly glasses were also responsible for the very annoying roving ring scotoma called the “jack in the box phenomenon,” which made driving a car a very risky business.

Only when contact lenses for the correction of aphakia were introduced, towards the end of the 1970s, did it make sense to...
operate unilaterally, as the contact lenses created a magnification of only 6–8% and this difference could be supported by the other phakic eye.

**Phacoemulsification**

Once phacoemulsification became available, after the late Charlie Kelman's discovery in 1967, the corneal opening needed only to be 5 mm and then, after the introduction of foldable implants, 3 mm. Stitches were no longer needed because a scleral tunnel approach was already in use before foldable lenses became available.

In 1987, I mastered the technique during a course given by Dr Jim Little, an associate of Kelman, in Geneva, Switzerland. At that time there were only four surgeons in Belgium using this method. I recall that in the United States some time later, a wet lab on pig and rabbit eyes was organised in the ballroom of the Hilton Hotel. One hour later, a wedding party was held in the same room!

**Presbyopia-correcting lenses**

IOLs improved progressively over time. Tinted and UV-coated lenses became available and, from around 1990, presbyopia-correcting lenses (bifocal, trifocal and so-called accommodative lenses) were introduced.

The evolution continued and I became involved in many studies on foldable IOLs (Tecnis) and presbyopia-correcting lenses, and lectured on them at European and American meetings. The most difficult part was selecting the right patient for the right lens.

**Phakic IOL implantations**

The use of phakic IOL implantations in myopia and hyperopia became important in refractive surgery. Lenses included the Artisan lens, an iris-fixated lens first launched for cataract surgery and later also used for myopia and hyperopia correction in phakic eyes; the Verisyse IOL; and the Veriflex, which is the foldable IOL; all designed by Jan Worst from the early 1980s onwards.

The Artisan was initially referred to as the “worst” lens and so this was a difficult one to promote! I used to perform the surgery bilaterally in one session under topical anaesthesia so that the patient immediately obtained an excellent result. These surgeries gave me the most satisfaction.

**Continuous curvilinear capsulorhexis**

This technique, now used in every modern cataract surgery procedure, was unknown when I performed my first cataract surgeries. It was popularised simultaneously by Dr Howard Gimbel in Calgary, Alberta, Canada, and Prof. Thomas Neuhann in Munich, Germany, in 1983–1985, both of whom went on to publish their work in 1991.

I visited the two ophthalmologists, acquired the technique and have excellent memories of working with them during many American Academy of Ophthalmology (AAO) and American Society of Cataract and Refractive Surgery (ASCRS) courses.

**Buried corneal knots**

The use of a buried corneal knot when stitching up corneal wounds was also unheard of when I started cataract surgery. This technique, whereby the corneal silk stitches knot is reversed and buried in the stroma, was introduced in France by the late Jacques Charleux in the 1970s.

Before this innovation, the surgeon had to cut the stitches very short so that they did not cause too much irritation, which is somewhat difficult to imagine. Of course, nowadays, in most cataract surgeries the incision is so small that stitches are unnecessary.

**Freestanding centres**

Cataract surgery in a freestanding centre was undertaken for the first time in Arizona, US, in the 1970s, being unknown in Europe at that time. Of course I wanted to apply these new approaches in my practice: in 1984 I realised the first cataract surgery on an outpatient basis in the Benelux region (Belgium-Netherlands-Luxemburg) in my clinic in Antwerp.

**IOL power calculation**

Nowadays, a maximum error of 0.25 in the outcome of IOL power calculation seems achievable, but this was not always so. Ridley’s first two cases resulted in a postoperative refractive error because the refractive power of the material used was unknown and the importance of eye-length measurement had still to be discovered.

IOL power calculation formulas were progressively developed and improved. As American ophthalmologist Prof. Jack Holladay once said, surgeons have the best outcomes with their own formulas. Measurement techniques have
Measurement techniques have improved spectacularly from the starting point of a contact method that used A-scan biometry.

Botox
Botulinum toxin for the treatment of strabismus was introduced by the late Alan Scott in 1973. When I started using botulinum toxin type A for the treatment of blepharospasm in 1980, the condition
was still considered a psychiatric disease. At that time I had no idea that this treatment would become so widespread for so many other medical conditions as well as for cosmetic reasons.

After I had met Scott at one of the AAO meetings, I was able to order the product overseas. It was delivered in a protected lead container because one such a shipment could have killed a huge proportion of the citizens of Antwerp! The dry product was dissolved, diluted one million times and made ready for injection by our pharmacist.

It received US Food and Drug Administration (FDA) approval for strabismus and blepharospasm in 1989, and in 2002 it received FDA approval for the cosmetic applications as ‘Botox’ (Allergan).

Radial keratotomy
In 1970, Svyatoslav Nikolayevich Fyodorov (1927–2000), a surgical pioneer, was the first to discover that the curvature of the cornea, and consequently its refractive power, changed after it had been perforated by a traumatic impact. This was the start of radial keratotomy whereby 8–16 or sometimes 32 radial incisions were used to flatten the cornea, reducing myopia. Leo Bores brought this treatment to the US in the late 1970s.

I attended some courses during weekends in the US, then flew back to Europe and started practising the technique, but first I tested the extremely sharp diamond knife on rabbit eyes. I incised their corneas then placed the rabbits in my mother’s garden and checked how they were faring the following morning.

I found that they were happily jumping around and eating as if nothing had happened. This was proof for me that I had mastered the technique and could start operating on human patients.

Lasers
In 1985, I became acquainted with the first application of the excimer laser for refractive surgery. That year, eight European surgeons attended a session in Wangen, Germany, where it was demonstrated how the excimer laser (MEL 50) could improve the making of radial incisions.

Dr Stephen Trokel, who is regarded as being the first ophthalmologist to recognise the signifi-
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MY PREDICTIONS FOR THE FUTURE

1. Robotic surgery will be introduced in ophthalmology, as we are lagging behind in that area.

2. Artificial intelligence will bring new opportunities for cataract detection, grading and management, and also for keratoconus detection.

3. Concerning cataract surgery, a solution will have to be found to shorten the waiting lists. There are simply not enough ophthalmologists to perform these surgeries so technicians will have to be trained to perform routine cataract surgery. Then the ophthalmologist’s involvement will only be making the diagnosis, deciding which IOL should be used and dealing with complicated cases.

4. Bilateral cataract surgeries will be undertaken simultaneously and surgery will take place at an earlier age.

5. Cataract surgery will become possible without dilating the pupil, or by using short-acting dilating drops, to limit disruption for the patient.

6. Three-dimensional printing of IOLs individualised for a patient will be done in the operating room at the time of surgery.

7. Improvement of techniques will allow the surgeon to operate on a seated patient, much like a dentist’s chair.

Cancérate & refractive

The excimer laser for use in corneal refractive surgery, was present. However, we later realised that the incision approach was not the right one and that removing part of the cornea was a much better way. In 1992, after a European meeting in Brussels, I organised the first live refractive laser surgery with an excimer laser. This had never been done before anywhere in the world, but I did not realise that until later. Nearly all European and many American surgeons who were later to become famous in the discipline of laser refractive surgery were in attendance. Together with Prof. Dieter Dausch and some pioneers of excimer laser refractive surgery (members of the Carl Zeiss Academy), and later on Prof. Dan Reinstein, we lectured worldwide on the use of the excimer laser in ophthalmic refractive surgery.

At first we used the rather brutal technique of PRK, whereby the corneal epithelium was removed before the application of the laser. Healing took 3 days and was very painful. The use of a bandage contact lens relieved the pain and the switch to LASIK made it possible to treat both eyes in the same session and practically without pain. Later on, the femtosecond laser was introduced in my eye centre.

I was fortunate to have been involved in the first discussions, at the Zeiss Academy group in Barcelona, Spain, in 2008, where the idea of femtosecond lenticule extraction with a flap (FLEx) and, later on, SMILE was developed. “Mr SMILE,” Prof. Walter Sekundo, was at the forefront of this.

Nobody at that time could have foreseen that refractive laser eye surgery would become the second most-performed surgery on the human body, after cataract surgery.

Nd YAG laser

Other lasers (argon and krypton lasers) featured in ophthalmic treatment from 1970 onwards. Specifically, the introduction of the Nd-YAG laser after 1980 created a revolution in the treatment of posterior capsule opacification. Until then, this complication had had to be treated by a surgical incision of the opacified capsule.

Final wish

To round up my reflections by looking to the future now, my ultimate hope is that my colleagues experience still more improvements in the beautiful discipline of ophthalmology and that all patients have the possibility of accessing timely and speedy access to the eyecare they need.

Frank Joseph Goes, MD
E: frank@goes.be
Dr Goes is the founder of the Goes Eye Center in Antwerp, Belgium (www.drgoes.be), and is still active as a consultant at the centre. He has no relevant financial disclosures.
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Mastering the Yamane technique: Key learnings from first cases

By Dr Abha Amin

The Yamane technique, first described by Shin Yamane and colleagues, is of use for intrascleral IOL fixation when a patient is aphakic without capsular support. It sparked my interest since I was seeking a solution for cases where iris fixation was not an option.

The technique offers an elegant and effective way to fixate the IOL in complex cases. I have had the opportunity to perform it several times and my first few cases provided me with some key takeaways as well as offering a unique perspective to identify areas for further improvement.

Thorough preparation, including practising in two wet labs before the first case, is a must, and the learning curve with the Yamane technique can be steep. However, it is also short. And whilst mastering a method usually requires a large number of cases, I have achieved great outcomes quickly by going back and reviewing videos and analysing my early experiences.

Patient cases

I was referred a patient with a posterior capsule tear during cataract surgery whose IOL had slipped nasally half inside and half outside the bag. The patient could no longer see well because the optic edge was now in the centre of the visual axis.

IOL exchange was scheduled. The dislocated IOL was carefully removed from the capsular bag and then cut into three pieces using 19g Packer/Chang IOL cutters (MicroSurgical Technology [MST]) for atraumatic removal from the anterior chamber. Following IOL removal, I inserted a CT Lucia lens (Zeiss) and both haptics into the anterior chamber.

I then sutured the main incision (which was larger than usual because of the IOL removal) with the aim of avoiding excess fluid leakage and maintaining the pressure required for needle placement. I used a 23g Ahmed micro-grasper (MST) through the paracentesis for entry to grasp the haptics.

Placing the second haptic inside the anterior chamber made grasping and threading the haptic into the lumen of the needle much more challenging because the haptic slid into the angle. With hindsight, I should have left the trailing haptic outside of the eye; I will do so in the future.

In the next case, the patient’s lens had fallen into the posterior chamber during cataract surgery and the capsule was completely lost. During the pars plana vitrectomy and lensectomy, they endured a sector iridectomy. The patient presented to me with aphakia, no capsule, some loss of iris tissue and cystoid macular oedema.

I again elected to proceed with scleral fixation utilising the Yamane technique. This time, I used an AC maintainer included in the scleral IOL fixation solutions pack (SFP-1001, MST) to keep the eye firm. The needle placements went well, and there was no fluid egress even with the trailing haptic exposed through the primary incision. The procedure went smoothly and as planned. The trailing haptic can also secure the IOL from falling back into the vitreous cavity, especially in this case because there was no capsular support and iris tissue was missing.

I proceeded with the iris repair, which required suturing of the sphincter. I used 23g Ahmed micro-tying forceps (MST) to hold...
each edge of the tear as I passed the needle (10-0 prolene suture on CTC-6 needle) through to complete the repair.

At the end of the case, I saw that the IOL was not perfectly centred even though I had been careful with the scleral measurements, so I pulled the haptic to one side to centre the optic. I then trimmed the excess haptic material and mushroomed and reburied the tip. The IOL was perfectly centred and there was no tilt at all.

Learning points

Measurements and markings
Sometimes it can be difficult to mark accurately because the limbus is not always clearly defined. One can miss by half a millimetre due to difficulty in identifying a clear entry point. In this case, even though one marks at 2.5 mm, this may not actually be 2.5 mm from the limbus.

I believe this is what happened during the second case described above when I realised that the IOL was not well centred. One needle entered further from the limbus than the other, which affected the IOL positioning. Of note, each needle pass is performed by a different hand and at a different angle—it is difficult to be perfectly symmetrical but awareness of the issue certainly helps.

Visibility
To know exactly where the positioning and entry points are (2.5 mm posterior to the limbus and 2 mm across), I like to open the conjunctiva and measure directly on the sclera to see as much as I can. Surgeons who have experience with this technique can go through the conjunctiva, but I feel it is less stressful when you have better visibility to watch the needle pass under the sclera before making the turn.

The sclera can also be held to prevent the eye from rotating, which helps with the needle tunnelling. If going directly through conjunctiva, the scleral tunnel is not visible. Finally, when turning the needle to enter the eye, go deep and not shallow: turn and go straight down and then come back up to visualise the bevel of the needle.

Right versus left hand
Keep in mind that the needles will be passed by both hands and that each hand will act differently: one comes forward while the other goes back. There are going to be differences between your hand positions, which is not a big problem, but one need to be mindful of this and make adjustments to get the same result from both hands. This is something that can be practiced with simulation model eyes.

Fixation of the globe is very important; otherwise the eye rotates, so the hand positions should be thought out ahead of time.

Threading the haptic
One might think that the haptic should thread directly into the needle, but in my experience, it is the opposite: threading the haptic is much easier if the needle is aimed toward the haptic while holding the haptic still. I use the 30g thin-wall needles with specialist holders from the scleral IOL fixation solutions pack (MST), which allows for manoeuvrability and control during this delicate step. To manipulate the haptic, my preferred micro-instrument is the 23g Ahmed micro-grasper (MST), which is a versatile micro-instrument for the anterior chamber.

Equipment and IOLs
My final recommendation would be to choose your cases wisely and have retina support available. In addition, always prepare your equipment in advance.

I opt for the CT Lucia IOL (Zeiss) with PVDF haptics, which I find has the right proportion of flexibility and resistance to breaking. I also use the scleral IOL fixation solutions pack (MST), which includes the essential elements to perform the technique, including three 30g thin-wall needles with silicone hubs, two specialist needle holders, an AC maintainer, a marker and a calliper.

Conclusion
The Yamane technique can be easy to learn if one is prepared and well equipped. Even if things do not go perfectly the first couple of times, practice will help you learn from your mistakes and it will get easier!

Abha Amin, MD
E: Abha.Amin@wmchealth.org
Dr Amin is chief of complex anterior segment surgery at Westchester Medical Center, New York, United States. She has no financial disclosures relevant to this article.

REFERENCE
Taking visual field analysis to a higher level with the iCare COMPASS automated perimeter

**BY KAWEH MANSOURI, MD**

Visual field testing to identify functional damage is an essential component of the diagnostic evaluation for glaucoma detection and monitoring. Full threshold testing with automated perimetry is the gold standard for identifying and quantifying glaucoma-related functional damage and can be done using different perimeters that are based on various technologies.

Combining perimetry, fixation loss correction, and confocal TrueColor fundus imaging with patient- and technician-friendly features, the COMPASS Automated Perimeter with active Retinal Tracking (Centervue Spa, a company of iCare Finland Oy; Vantaa, Finland) is a unique tool that takes visual field testing and interpretation to a higher level.

**iCare COMPASS functions and features**

**Visual field testing**

Automated perimetry with COMPASS is fully compatible with standard 24-2, 30-2 and 10-2 visual field testing containing age-matched databases of retinal sensitivity in normal subjects. In addition, COMPASS offers SupraThreshold and Quick SupraThreshold testing for rapid visual field loss screening. Done using the standard 24-2 test grid, the SupraThreshold test takes approximately 2 to 3 minutes per eye. The Quick SupraThreshold test using an optimally reduced 24-2 grid is even faster, taking just 30 to 90 seconds per eye and allowing testing of both eyes sequentially using the “OU” option.

Visual field testing with COMPASS is done using Active Retinal Tracking. During the examination, continuous and automated tracking of eye movements by infrared scanning of the retina provides real-time compensation for fixation losses and assures that the stimulus position is correct. Perimetric stimuli are automatically repositioned prior to and during projection based on the current eye position. Stimuli lost due to blinking are automatically repeated and do not interrupt the test.

**TrueColor confocal imaging**

COMPASS generates 60° confocal images of the retina in three modalities: TrueColor, infrared and red-free. By combining a confocal engine with a white light LED source to illuminate the retina, COMPASS generates fundus images that are sharp, high contrast, and natural in colour. High quality images are obtained even in eyes with media opacity because of the confocal technology. Registration between the retinal image and retinal sensitivity threshold allows a direct correlation between visual function and retinal anatomy.

**My clinical perspective**

Visual field testing and acquiring high resolution, true colour images of the fundus and optic nerve head are essential when evaluating patients with glaucoma. Not only does COMPASS address both needs in a single time-saving examination, but it also generates a superimposed image that shows a precise overlap between areas of depressed sensitivity and areas of the retina with indications or source of defects, some of which cannot be seen with optical coherence tomography only.

The opportunity to simultaneously perform perimetry testing and fundus imaging is by itself a great benefit of COMPASS compared to standard automated perimeters, but its active retinal tracker further distinguishes COMPASS from standard automated perimeters that cannot actively compensate for eye movements during testing. The retinal tracking technology serves to increase test precision by measuring sensitivity at specific retinal locations with high topographic accuracy. Thus, it ensures accurate correlation between function (i.e. retinal threshold values) and structure (retinal appearance) and decreases test-retest variability. I believe that active retinal tracking brings added value for improving the clinical accuracy of visual field tests, their interpretation in general and especially in eyes that have several pathologies at different stages, and the reliability of detecting glaucomatous progression.

In addition, because active retinal tracking automatically positions stimuli correctly on the retina, despite fixation losses, blinking or movements of the eye or head, and since lost stimuli are repeated automatically, patients can blink, close the eye, or rest and continue without loss of data and technician involvement during COMPASS visual field testing. This decreases stress and fatigue in patients, is convenient for the operator, and decreases the need for retakes due to unstable fixation.

Multiple other features of COMPASS make visual field testing operator-friendly, easier for patients, and more efficient. Designed with auto-focus that compensates for spherical refractive errors between -12 D and +15 D, COMPASS avoids the need for using trial lenses to perform visual field testing. Auto-focus therefore eliminates the potential for lens rim artefacts that can result in test misinterpretation and also saves time.

Further enhancing workflow efficiency, visual field testing with the iCare COMPASS is done without mydriasis for pupils larger than 3mm. Consequently, there is no delay waiting for the pupil to dilate nor any need to wait for the eye to adjust after a flash of light. As another time-saving feature, cleaning of the COMPASS is quick and simple because it has

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a smooth, narrow, convex design, lacks any sensitive structures, like a bowl, and has no trial lens assembly. The machine’s surfaces can be easily disinfected using only an alcohol wipe. This ease of decontamination holds increased importance because of COVID-19. All of these contributors to efficiency more than compensate for the slightly increased duration of combined visual field testing/fundus imaging with COMPASS compared to standard automated perimeters.

**Clinical case**
Figures 1 and 2 show the COMPASS printout and fundus image from one of my patients. The fixation plot in the printout (bottom left) shows that the patient had unstable fixation, but even in this situation it was possible to obtain a reliable visual field with adequate false positive and false negative indices as well as an MD of -2.68. The COMPASS fundus image revealed a significant peripapillary atrophy (as shown in the red-free image and in the zoomed ONH colour image) that is well represented as an enlarged blind spot on the visual field. The printout also shows a single focus in the superonasal visual field that needs to be confirmed by repeat testing. By providing excellent visual field test repeatability, COMPASS will enable the determination of whether the defect is an artefact or represents an early sign of glaucomatous damage.

**Conclusion**
I find that COMPASS brings many benefits to clinical practice. It is the first automated perimeter that can perform standard visual field tests using a real-time retinal tracker while simultaneously delivering ultra-high resolution confocal TrueColor fundus images. In addition, it saves time in many ways and makes visual field testing more patient- and technician-friendly for many reasons. In a study where patients underwent perimetric evaluation with both the Humphrey Field Analyzer and COMPASS, results of a post-test interview showed the participants had a strong preference for the COMPASS examination. Importantly, our own technicians give very positive feedback about their experience with this unique diagnostic device. Finally, I give COMPASS high ratings as a clinician because with its capabilities and benefits, COMPASS enables me to optimize patient care by helping me detect glaucoma and its progression accurately and early.

Dr. Mansouri is a consultant ophthalmologist, Clinique de Montchoisi, Lausanne, Switzerland, and adjunct professor, Department of Ophthalmology, University of Colorado Anschutz Medical Campus, Denver, Colorado. Dr. Mansouri is a consultant to iCare. CENTERVEU S.P.A., ICARE FINLAND OY are parts of REVENIO GROUP and represent the brand iCare.
Shedding light on vitreous opacities during cataract surgery

Physicians offer pearls for improving visualisation in eyes using retroillumination techniques

By Lynda Charters; Reviewed by Dr Joseph W. Fong and Dr Ahmed A. Sallam

Cataract surgery can be difficult to perform when dense vitreous opacities are present, due to the absence of the red reflex. Even when cataract surgery is combined with vitrectomy, this difficulty still exists because, in many cases, the view is too poor to permit vitrectomy to clear the vitreous opacities before removal of the cataract.

Dr Joseph W. Fong and Dr Ahmed A. Sallam, both from the Harvey & Bernice Jones Eye Institute at the University of Arkansas for Medical Sciences in Little Rock, Arkansas, United States, shared their pearls for improving the visualisation in these eyes using retroillumination techniques that include a 25-gauge chandelier or a light pipe.

**Retroillumination configurations using the chandelier**

The doctors described two configurations using the 25-gauge chandelier. In the first, the chandelier was directed down towards the vitreous. In the case being demonstrated, the patient had a dense vitreous haemorrhage due to diabetic retinopathy. Dr Fong advised that the view can often be improved in this scenario by extinguishing the room and microscope lights and by depending only on the retroillumination provided by the chandelier.

In a second case, Drs Fong and Sallam demonstrated the view achieved when the chandelier was directed horizontally or towards the lens. “Directly illuminating the lens from behind provides the surgeon with crisp and detailed visualisation of the lens structure and is often very helpful in cases where vitreous haemorrhage is very dense,” Dr Fong said.

**Retroillumination via light pipe**

In another case of a patient with a dense vitreous haemorrhage from diabetic retinopathy, Dr Fong showed how to maximise use of the light pipe. As in the previous case using the chandelier, maximum visualisation was achieved when the lights from the microscope and rooms were turned off.

**In short:**

Use of a chandelier or a light pipe can overcome the problems posed by various types of vitreous opacity.
Dr Fong explained that a light pipe has an advantage compared with a chandelier because an experienced vitreoretinal surgeon has real-time control over the position of the light pipe at all times intraoperatively. However, use of the light pipe means that the surgeon has to perform the procedure using one hand, which is a major disadvantage.

The surgeon does have the option of removing the light pipe to chop the nucleus using both hands. After the chop procedure is completed, the light pipe can be re-inserted to facilitate a better view of the cortex to be removed.

“The chandelier and light pipe are both great options to achieve retroillumination and optimal visualisation during these challenging cataract surgeries,” Dr Fong said. “Using the chandelier has an advantage over the light pipe in that the surgeon can use both hands throughout cataract surgery. This frees the surgeon from concerns about the position of the light source and facilitates his or her concentration on the details of the challenging surgery.”

Use of the light pipe means that the surgeon has to perform the procedure using one hand.

Another challenging surgical scenario is encountered in cases of active endophthalmitis. Dr Fong demonstrated insertion of a light pipe into a trocar to retroilluminate the lens during the capsulorhexis. The light pipe was then inserted through the limbal side port to illuminate the lens during phacoemulsification.

“These retroillumination techniques can be used to conquer cataract surgery when many different types of vitreous opacities are present,” Dr Fong concluded.

Joseph W. Fong, MD  
E:jfong32@gmail.com

This article is adapted from Dr Fong and Dr Sallam’s presentation at the American Academy of Ophthalmology Annual Meeting in New Orleans, Louisiana, US. Drs Fong and Sallam have no financial interests in any aspect of this report.

Ahmed A. Sallam, MD, PhD  
E:ASallam@uams.edu

A chandelier is directed horizontally toward the lens.  
(Image courtesy of Dr Joseph W. Fong)
Patient education has a fundamental role in cataract surgery success and patient satisfaction. So that patients can apply and benefit from the information they are given, it must be delivered in an understandable manner and remembered throughout the cataract surgery journey.

The ZEISS EYEGUIDE patient app was developed as a modern tool for educating patients and helping them stay compliant during their cataract surgery journey (Figure 1). Its content includes text, video, and graphic information about vision, cataract, and cataract surgery, as well as a patient-customizable reminder tool for appointments and medication. In addition, using the online EYEGUIDE Customizer Tool, practices can easily personalize the app’s content by incorporating their own pre- and post-operative checklists, articles, or links to information about the clinic, the surgeons, intraocular lenses, and other technology offerings.

At Precise Vision, we had already developed a variety of printed and digital materials for patient education. However, we thought that the EYEGUIDE app could add value as both a complement and supplement to our existing tools. Early experience with the app is already validating our expectations.

**Why did you decide to adopt EYEGUIDE?**

**Dr Kretz:** Patients undergoing cataract surgery represent a heterogeneous population, and different approaches may be needed to be successful educating and communicating with this diverse group. EYEGUIDE has features that make it appealing to different types of patients. Patients who are younger or technologically savvy are accustomed to and like using mobile apps for information and as assistive tools. The app also addresses obstacles faced in educating older individuals who can benefit from support given by family or caregivers. I have often seen older patients struggling to read printed educational materials, and then it remains unknown if they understand the information or go on to share it with others who can assist them. The app is a wonderful tool where everyone can access the educational materials. It addresses the problem of older patients misplacing printed brochures or failing to understand or just not remembering information they received verbally. With checklists provided by the clinic and reminders customizable by the patient, the app is also a great tool for reminding patients of their eyelid regimen, which is in my opinion critical for optimizing surgical success.

**Nicole Kretz:** We were interested in using EYEGUIDE because it seemed to offer a host of benefits. Patients undergoing cataract surgery may feel anxious about the procedure and its outcome, but these concerns can be diminished if patients are trusting of their provider and have knowledge that makes them well-prepared for the process. The app addresses both of these areas because it allows patients to gain information about their surgery, their surgeon, and the clinic through a single easily accessible platform. EYEGUIDE’s customization tool that allows practices to include information about their clinic and its team is also helpful because I believe this type of knowledge builds patient trust and comfort and ultimately increases their satisfaction with the surgery journey.

**How did you find the process of customization and implementation?**

**Nicole Kretz:** I designed and customized the content of the app and found it was easy. I added...
information about cataract surgery, our clinic, and our surgeons. I also incorporated videos, images, forms, and links to our podcasts and YouTube videos. Many of the resources we included were newly created based on searching the Internet for frequently asked questions and staff input on questions received from patients and tips on how we could make the whole cataract surgery journey harmonious for patients.

**How has the app been received by patients, family members, or caregivers?**

**Dr Kretz:** Many cataract surgery patients are very technologically savvy regardless of age, and those with a mobile phone were all interested in the app. Of the patients who did not have a mobile phone, most were happy to take the flyer we had about the app to give to their family. Feedback from patients, family members and caregivers who have used the app has been positive. Equally important, we have not gotten any calls with questions from individuals who were experiencing problems using the app.

**Nicole Kretz:** It is my impression that patients are more trusting of the content of the EYEGUIDE app than they are of information about cataract surgery they might find online or through an app store because EYEGUIDE is an app that is recommended by their provider rather than being something created by an unknown source.

I’d like to share an unexpected encounter I had with the son of one of our patients. The gentleman is a newspaper agent, and while I was meeting with him to discuss advertising in his paper, I mentioned that we had an app for cataract surgery patients. The newspaper agent told me that his mother had undergone cataract surgery at our clinic and that because of the app, he felt more confident as a family member being able to assist his mother during her journey. He remarked that in the past he would only be able to talk with his mother about information she could remember. The ability to refer to and discuss the materials on the app with his mother allowed him to help her make clear decisions about the surgical procedure, follow all of the preoperative instructions and tips, use her eye drops as directed, and keep her postoperative appointments.

**What internal feedback have you had about the app?**

**Nicole Kretz:** The app has been very well received by our refractive managers who have remarked that it is a great addition to the tools they are using. They have commented about the quality of the educational material and the value of articles about our practice. Our team members also note that patients who used the app seemed to be more confident going into their surgery. We might expect that this will lead them to have a more positive impression of their experience overall.

**Have you noticed any other impact of the EYEGUIDE app in your practice?**

**Dr Kretz:** The app has had a positive effect on workflow efficiency. Patients who installed the app before their preoperative consultation visit accessed and partly filled out online intake forms, and that saves time in the clinic.

As another benefit relating to efficiency, the overall in-clinic counseling process is shortened when patients use the app because they are well-informed about cataract surgery and their options for pseudophakic correction. In addition, patients who choose premium lenses and femtosecond laser-assisted cataract surgery have information about these options available to share and review with their family members before they come for their operative visit.

**What take home message do you have for cataract surgeons about the EYEGUIDE app?**

**Nicole Kretz:** It is a wonderful and useful tool to share with patients and their family members or caregivers. According to our experiences, the app delivers information that is important for helping patients make decisions about their surgery and have a successful outcome. It is a tool that patients can access when they are relaxed and comfortable at home and together with family members so that they can make decisions with trust and confidence.

**Dr Kretz:** I concur. With its open approach to presenting information about our practice, our staff, the surgery, and surgical options, I believe the EYEGUIDE app makes patients feel more at ease and comfortable with their decisions and their surgery, and it is my personal opinion that its tools for increasing patient compliance can contribute to a successful outcome.

Needless to say, implementing the app involves some effort. However, the amount of effort required is not that much and it truly goes a long way in the right direction.

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**Nicole Kretz and Dr Florian Kretz**

are Managing Directors, Precise Vision Augenärzte, Headquarter Rheine, Germany.

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Promising early data with intravitreal DMI candidate
In study, best-corrected visual acuity improved slightly compared with baseline

By Lynda Charters;
Reviewed by Dr Quan Dong Nguyen

A recent Phase 1/2a trial of an intravitreal treatment designed to treat diabetic macular ischaemia (DMI), BI-X (Boehringer Ingelheim), found the candidate to be well tolerated with no dose-limiting events and no drug-related adverse events, according to Dr Quan Dong Nguyen, a professor of ophthalmology at Byers Eye Institute at Stanford University School of Medicine in Palo Alto, California, United States.

DMI is defined as any disruption in retinal vascularity within the superficial and/or deep retinal plexus as seen on optical coherence tomography angiography, and it is a complication of diabetic retinopathy (DR). Currently, there is no treatment available that can prevent or stop progression of DMI. Dr Nguyen pointed out that the development of a treatment is important because it is a common complication that can have a profound impact on a patient’s vision.

BI-X works as an anti-ischaemia modulator of the human protein, semaphorin 3A, which blocks revascularisation in ischaemic retinas.

The HORNBILL Study
DMI patients enrolled in the Phase 1/2a study had previously been treated with laser for DR. The study has two parts, or ‘phases’, and all subjects treated with BI-X have received one intravitreal dose of the drug.

Single-rising-dose (SRD) phase
The non-randomised, open-label section of the study is complete. Three cohorts received 0.5-, 1- or 2.5-mg doses of the therapy; the cohorts included three, three and six subjects, respectively. The primary endpoint was the number of dose-limiting events, and the secondary endpoints were the numbers of drug-related and ocular adverse events.

According to Dr Nguyen, the best-corrected visual acuity (BCVA) improved slightly compared with baseline in the subjects assigned to 1 and 2.5 mg of BI-X. No dose-limiting, drug-related or serious adverse events occurred. Three subjects experienced ocular adverse events: specifically, subconjunctival haemorrhage and ocular hyperaemia, both in the 0.5-mg cohort.

One vitreous detachment occurred in the 2.5-mg cohort. Four procedural-related adverse events occurred: subconjunctival haemorrhage, ocular hyperaemia and temporary intraocular pressure increase in the 0.5-mg group, and mild pain after the procedure in the 2.5-mg group.

The findings in the three cohorts were similar. The main take-aways from the SRD study were that BI-X was well tolerated by subjects with DMI in all three dosing cohorts and that the BCVA showed signs of improvement compared with baseline in the 1-and 2.5-mg cohorts.

Multiple-dose phase
In the second, ongoing, single masked and randomised part, the BI-X cohort (20 subjects) will receive three 2- to 5-mg doses separated by 4-week intervals and 10 subjects are to receive sham injections.

The primary endpoint is the number of drug-related adverse events; the secondary endpoints are the number of ocular adverse events and the changes from baseline in the foveal avascular area size, BCVA and central retinal thickness.

“Discovering a treatment for DMI is a major challenge for many clinician-scientists, as DMI can lead to significant visual loss, even if the diabetic macular oedema is well controlled,” Dr Nguyen concluded. “It is our hope that BI-X can be among the first successful treatments for this devastating complication of DR.”

Quan Dong Nguyen, MD, MSc, FARVO
E: ndquan@stanford.edu
This article is adapted from Dr Nguyen’s presentation at the American Academy of Ophthalmology Annual Meeting. Dr Nguyen has received research funding from Boehringer Ingelheim.
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The missing link in the recognition of corneal abnormalities

New imaging modality reveals subtle changes in corneal collagen fibres

By Lynda Charters; Reviewed by Dr Ritika Mullick

Polarisation-sensitive optical coherence tomography (PS-OCT) is a functional extension of the conventional form of OCT and exploits the polarisation properties of light. According to Dr Ritika Mullick, a fellow in cornea and refractive services at Narayana Nethralaya Hospital, Bangalore, India, this imaging modality can aid the early recognition of disease-related changes before they can be seen topographically.

Dr Mullick explained that the human eye is known to have polarisation-altering tissues; using an ultra-high-resolution PS-OCT helps us to study the form birefringence caused by the underlying fibril structures in the corneal stroma. This, in turn, can enable users to detect subnormal distribution of collagen in corneal disorders.

In a clinic setting, this technology can demonstrate both normal corneal biomechanics and clear-cut cases of abnormalities, such as the development of post-SMILE ectasia.

Development of PS-OCT
The technology is especially useful in what Dr Mullick describes as “confusing” cases, which comprise about 35% of those that pass through her clinic. For example, upon examination, one patient had a thin cornea but no keratoconus; another had a suspicious presentation, but the biomechanics were normal; and yet another had normal topography but suspicious biomechanics.

This raises the question: should physicians rely on the corneal topography or the biomechanics in such cases?

This question spurred the development of PS-OCT, which can image the spatial distribution of fibril structures and their orientation.

As Dr Mullick explained, “The arrangement of collagen fibres in normal corneas exhibits a checkered pattern centrally. In the images, the presence of dark blue/purple indicates the least phase retardation: that is, the least alteration of polarised light, due to the uniform arrangement of the collagen fibres. This indicates a very healthy cornea.”

When corneas are diseased, however, irregular organisation of the collagen fibres can be seen, with more alteration of the polarised light; this indicates higher phase retardation, as seen by the warmer colours in the image.

Corneal study
Dr Mullick and her colleagues studied 50 healthy corneas, 50 with keratoconus and 35 suspicious corneas prospectively. Patients underwent corneal tomography, corneal biomechanics and epithelial mapping, biomicroscopy, fundus evaluation and refraction.

The evaluations were followed by PS-OCT. The results were categorised based on the topographic and biomechanical analyses followed by in vivo analysis of the phase retardation (PR) distribution. The Belin-Ambrosio enhanced ectasia display (BAD) software, which helps in the early detection of subclinical keratoconus changes, was used with the inbuilt Oculus HR Pentacam camera system.

Dr Mullick provided some examples of representative cases. She reported
that the in vivo imaging by PS-OCT showed normal topography in two cases, but another case yielded a suspicious BAD deviation value (BAD-D). However, the checkered arrangement in the centre of the image indicated that the two corneas were healthy and therefore would be suitable candidates for refractive surgery.

A third case had normal BAD-D and suspicious biomechanics; this patient had a partial loss of the checkered arrangement. In this case, refractive surgery was deferred. The fourth case had a thin cornea and no keratoconus, but there was partial loss of the checkered arrangement.

In the fifth and sixth cases, with keratoconus and post-SMILE ectasia, respectively, there was a complete loss of the checkered arrangement, which indicated that these were weak ectatic corneas with weak collagenous arrangements.

This approach has facilitated the ability to diagnose disease earlier before it becomes apparent on topography. "PS-OCT can clearly identify differences in collagen fibre distributions between healthy and keratoconic corneas. Suspicious corneas had a unique distribution of collagen, which indicated early changes before they were detected on topography,” Dr Mullick commented.

She added: “The imaging technology can help diagnose keratoconus even in cases that have normal or borderline suspicious topography findings, and therefore can be an excellent screening modality.”

The technology can also be used to screen candidates for refractive surgery; identify forme fruste keratoconus; monitor keratoconus progression or follow cross-linking outcomes; perform post-graft imaging; or diagnose retinal disorders.

Ritika Mullick, MBBS, MS
E: drritikamullick@gmail.com
This article was adapted from Dr Mullick’s Subspecialty Day presentation at the 2021 American Academy of Ophthalmology annual meeting, New Orleans, Louisiana, United States. Dr Mullick has no financial interest in this subject matter.

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Making strides in eyecare with modern gene therapy techniques

By Prof. Albert Augustin

According to the clinicaltrials.gov database, there are around 2,000 gene therapies currently under investigation worldwide in many areas of medicine. In recent decades, the discipline has rapidly evolved.

Whilst the focus of most gene therapies has so far been on rare diseases, many additional drugs/products are currently being studied to treat disorders such as cancer, as well as genetic and infectious diseases. And around 20 gene therapies are already available in the United States, having received Food and Drug Administration (FDA) approval.

The are several available approaches in gene therapy. We can replace a disease-causing gene with a healthy gene or deactivate a gene that is not functioning properly. In addition, a modified or completely new custom-designed gene can be introduced to treat a disease.

The basic principle is to target missing or faulty genes in monogenic diseases. Usually the “gene therapy drug” is given only once; it carries an instruction to change the sequence of one or more proteins. This change is necessary if those essential proteins are produced in a faulty manner: either they are not produced in sufficient quantities or the catalysis process controlled by the protein is not working correctly.

Major pathobiochemical or pathophysiological pathways have been investigated intensively. Gene therapy products include plasmid DNA and viral or bacterial vectors; in a subset of diseases, cells are extracted, genetically modified and then re-introduced into the body, however, more commonly a viral vector is used, which entails eliminating the virus gene and using its ability to penetrate the cell to safely deliver the new information.

From an immunological perspective, the eye is the ideal target for gene therapy, which thus makes it likely that, in the future, highly successful gene therapy approaches will lead to cures for certain diseases of the eye.

Retinal diseases

In 2017, voretigene neparvovec-rzyl (Luxturna, Spark Therapeutics) became the first FDA-approved ocular gene therapy. Also approved in Europe (since 2018), it is used to treat certain inherited retinal diseases such as RPE65-related Leber congenital amaurosis or retinitis pigmentosa.

As mentioned already, gene therapies focus on monogenetic diseases. The approach becomes much more complicated for diseases with many pathways involved, such as age-related macular degeneration (AMD). Hence, current methods focus on gene augmentation and/or suppression to enhance or reduce the production of a molecule that plays a crucial role in the pathogenesis of the disease.

In wet AMD, this is vascular endothelial growth factor (VEGF). Its...
antibody (anti-VEGF) needs to be applied on a monthly basis, which may lead to both clinical and adherence problems. One way to overcome this is to employ a surgical intervention such as the implantation of a slow-release device. An alternative would be the augmentation of anti-VEGF production using a genetic approach.

One candidate that is currently being studied is RGX-314 (Regenxbio). This drug is delivered subretinally or suprachoroidally. It contains a novel adeno-associated viral vector (AAV8) and is currently in development for wet AMD, diabetic retinopathy and other retinal diseases.

As described above, the cells are transfected, which delivers the information to produce a protein. This protein is designed to neutralise VEGF and, by doing so, modify the pathway for the formation of new leaky blood vessels and retinal fluid accumulation.

Both approaches, subretinal and suprachoroidal, are surgically challenging. However, the suprachoroidal method, which our group used for the application of other drugs more than a decade ago, has been redesigned and appears to be a safe way to apply such a drug.

The positive interim results of two trials of RGX-314 (AAVIA and ALTITUDE) using in-office suprachoroidal delivery were presented by Dr Robert L. Avery at the most recent meeting of the American Academy of Ophthalmology. The studies are including wet AMD and diabetic retinopathy patients without centre-involved diabetic macular oedema.

Another drug candidate in development is ADVM-022 (Adverum Biotechnologies), an adeno-associated virus vector encoding aflibercept. Results to date have shown that a single intravitreal administration of ADVM-022 is able to provide a safe and effective long-term treatment option for both wet AMD and diabetic macular oedema.

Looking at dry AMD, the approach is similar. Rather than focusing on genes that are responsible for the disease, we are trying to produce or antagonise factors that are part of the pathogenetic cascade. Inflammation has been shown to play a crucial role in the pathogenesis of dry AMD.

One way to tackle inflammation is by increasing the production of complement factor I (CFI), also known as C3b/C4b inactivator (a protein that regulates complement activation). Doing so has been shown to reduce complement activity and thereby inflammation.

About 3% of patients suffering from dry AMD have CFI mutations, with lower CFI levels giving a higher risk of dry AMD. GT005 (Gyroscope Therapeutics) is an AAV2 vector that delivers a plasmid construct expressing normal CFI; it is currently under investigation with promising results and no significant side effects so far, although the drug does need to be applied subretinally.

Proceeding with caution in a new era

As described, clinical studies of promising ocular gene therapies are underway. However, safety remains a concern in this area of therapeutic medicine, where retinal pigment epithelium (RPE) changes and inflammatory reactions can take place. Thankfully, there have been some reports that these potential side effects can be successfully controlled by topical steroids.

Until now, only patients who have been heavily pre-treated have been included in trials. As well as the need to conduct intensive safety assessments, before these new gene therapy approaches can be used on a regular basis in real-world settings, Phase 3 trials need to be completed and surgical procedures taught.

And so, while we are entering a new era of drug therapy, with gene therapy having the potential to change the way many diseases are treated (which is good news for our patients), there is still much work ahead. Both drug safety and drug delivery issues present major challenges that need to be addressed.

One promising future approach lies in the CRISPR-Cas9 gene-editing tool, which has recently been introduced for the treatment of a hereditary human disease. It functions rather like a molecular scissor to snip parts of the DNA: in this way, we can insert, delete or modify genes.

After identifying the defective genes, this exciting technology will provide the next step in gene therapy. We are already underway and have identified the defective genes in other hereditary diseases. Thus, this new technology will first be used in diseases with a clearly defined genetic signature.

Prof. Albert Augustin, MD
E: albertjaugustin@googlemail.com
Dr Augustin is professor of ophthalmology and chairman of the Department of Ophthalmology at the Karlsruhe Municipal Hospital, Germany. He has no financial disclosures related to this article.
Cosmetic iris implants pose serious risks to patients and are strongly discouraged, according to Dr Jorge Alio and Dr Francesco D’Oria, both from Vissum Alicante Miranza Group and the Miguel Hernández University of Elche in Alicante, Spain. However, despite the potential risks, the surgeries are still performed.

The currently available models are the NewColorIris (Kahn Medical Devices) and BrightOcular (Stellar Devices). The NewColorIris, a silicone iris diaphragm with six rounded flaps in the periphery to hold the device in place, has a diameter that ranges from 11 to 13 mm and a pupillary aperture of 3.5 mm and thickness of 0.16 mm. The BrightOcular, which is held in the eye by five triangular flaps in the periphery, comes with diameters ranging from 11.5 to 13.5 mm and thicknesses of 0.16 and 0.18 mm; the authors reported that the posterior face has grooves to facilitate aqueous flow.

Dr Alio and Dr D’Oria conducted a retrospective study of the medical records of five patients (10 eyes; age range, 27–46 years) who had received one of the devices (two with NewColorIris and eight with BrightOcular). The patients had been referred to the Vissum Instituto.
Oftalmológico de Alicante for complications associated with the latest models of the implants, which had been available for 6 years.

The authors reported that all the devices had been explanted 1–60 months after the surgeries (Figures 1 and 2). The mean endothelial cells density was $848 \pm 227.5$ cells/mm$^2$. Corneal transplantations had to be performed in 30% of eyes; in other words, two eyes had a Descemet membrane endothelial keratoplasty and one eye had a penetrating keratoplasty.

Three other patients were advised that they would need a corneal transplant. Nine of the 10 eyes developed ocular hypertension and a filtering surgery was needed in two cases. Early development of cataract was a common complication, with 40% of the patients—who were a mean age of 36 years—requiring cataract surgery.

In a representative case, a 37-year-old woman who had a cosmetic iris implanted in both eyes returned 2 years later with problems in her left eye. This patient had a dramatic endothelial cell loss of $1,163$ cells/mm$^2$ (Figure 3).

Following referral, iris atrophy was seen superiorly. The investigators said that the endothelial cell density was relatively conserved after explantation, at $1,054$ cells/mm$^2$. The cosmetic implant of the other eye also had to be removed for similar reasons.

Neither of these commercial devices had been approved by the United States Food and Drug Administration or received a CE mark, but they continued to be implanted. Newer models have not been improved and cause the same complications to develop as the previous models.

“Patients with cosmetic iris implants have a high risk of definitive loss of vision and other serious complications that should be described to patients before implantation,” Dr Alio concluded. “Implantation of cosmetic [iris] implants should be considered today as malpractice in the light of available evidence.”

Jorge L. Alio, MD, PhD
E: jialio@vissum.com

Francesco D’Oria, MD
E: francescodoria91@hotmail.it

This article is adapted from Dr Alio and Dr D’Oria’s presentation at the 2021 American Academy of Ophthalmology annual meeting in New Orleans, Louisiana, United States. Dr Alio and Dr D’Oria have no financial interest in this subject matter.
Determining germline mutations in children with unilateral retinoblastoma

Study focuses on ascertaining the risk of patients developing additional tumours

By Lynda Charters;
Reviewed by Dr Carol L. Shields

The greatest likelihood of a germline mutation in patients with a unilateral retinoblastoma occurred in patients who were 1 year of age or younger versus those older than 1 year, as well as in a subset of patients 3 months and younger versus those between 3 and 12 months of age. This finding was presented by Dr Carol Shields, chief of the Ocular Oncology Service at Wills Eye Hospital in Philadelphia, Pennsylvania, United States.

Dr Shields and her colleagues conducted a retrospective case series to evaluate the likelihood of germline retinoblastoma in children with solitary unilateral retinoblastoma. She explained that the goal of the study was to determine the risk of patients developing more of these tumours—that is, the risk for a germline mutation.

“It is important to know the germline status because the patients are at risk of developing multiple bilateral retinoblastomas, pinealoblastoma and secondary cancers,” Dr Shields said. “These can lead to blindness and death.”

Germline mutation study

The investigators retrospectively reviewed 482 consecutive patients who presented with one unilateral retinoblastoma and were later found to have a likely germline tumour. The latter was defined as a family history of retinoblastoma; development of bilateral disease and/or new tumours; and the gold standard: i.e., a documented germline on genetic testing.

A comparative analysis was then completed based on the following patient age groups: 0–1 year, 1–2 years, 2–3 years and older than 3 years. The results showed that in children aged 0–1 year who presented with one unilateral retinoblastoma, 29% had a germline mutation (odds ratio 2.96). When compared with children older than 3 years, 9% had a germline mutation. This difference reached significance (P = 0.001).

Among children who were 12 months or younger with one unilateral retinoblastoma, Dr Shields reported that in the youngest of these (aged 0–3 months), 61% had a germline mutation. When they were compared with those aged 9–12 months, the percentage dropped to 22%. This difference was significant (P = 0.009).

“It is clear that the youngest children with a unilateral retinoblastoma are at the greatest risk for a germline mutation,” Dr Shields said. In the other age groups—aged 3–6 months, 6–9 months, 12–24 months, 24–36 months and older than 36 months—the respective percentage of germline mutations was 20%, 24%, 17%, 8% and 9%.

“Of the 482 consecutive patients with a solitary unilateral retinoblastoma who were seen at the Ocular Oncology Service at the Wills Eye Hospital, we found a significant decreasing risk for a germline mutation based on the older patient age at presentation,” Dr Shields concluded.

Carol L. Shields, MD
E: carolshields@gmail.com

This article is adapted from Dr Shields’ presentation at the American Academy of Ophthalmology 2021 annual meeting in New Orleans, Louisiana, United States. This presentation received the Best Poster award. Dr Shields has no relevant financial disclosures.
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