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MARCH 2020 VOL. 16, NO. 2

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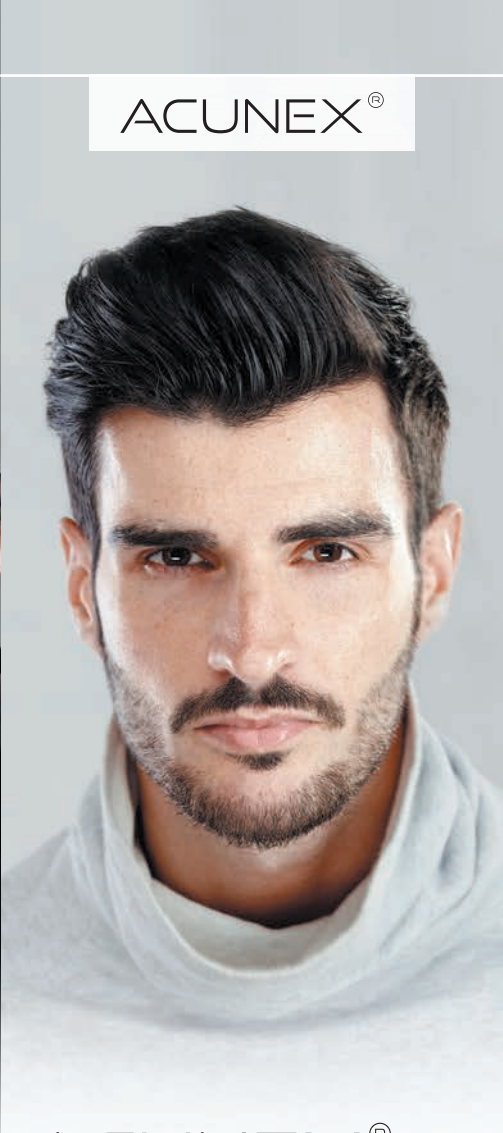

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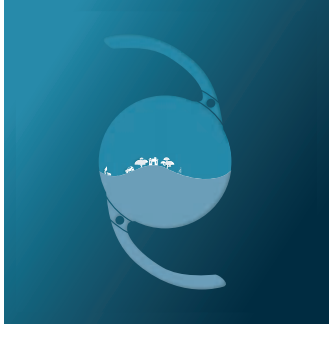

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GENE THERAPY

Studies target unilateral gene therapy injection

Research finds bilateral BCVA improvement

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GROUP EDITORIAL DIRECTOR
Sheryl Stevenson
SStevenson@mjhlifesciences.com

EDITOR
Caroline Richards
CRichards@mmhgroup.com

CREATIVE DIRECTOR
Robert McGarr

SENIOR ART DIRECTOR
Nicole Slocum

GRAPHIC DESIGNER
Jennifer Toomey

PUBLISHING / ADVERTISING

GROUP PUBLISHER
Leo Avila
LAvila@mmhgroup.com

EUROPEAN SALES MANAGER
James Tate
JTate@mmhgroup.com
TI: +44 (0) 2392 356 075

SALES OPERATIONS ADMINISTRATOR
Barbara Williams
BWilliams@mjhlifesciences.com
Tel: +44 (0) 151 705 7602

AUDIENCE DEVELOPMENT

AUDIENCE DEVELOPMENT MANAGER Kelly Kemper

CORPORATE

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Jeff Brown

Sycamore House, Suite 2
Lloyd Drive
Cheshire Oaks
CH65 9HQ

Tel. +44 (0) 151 705 7601

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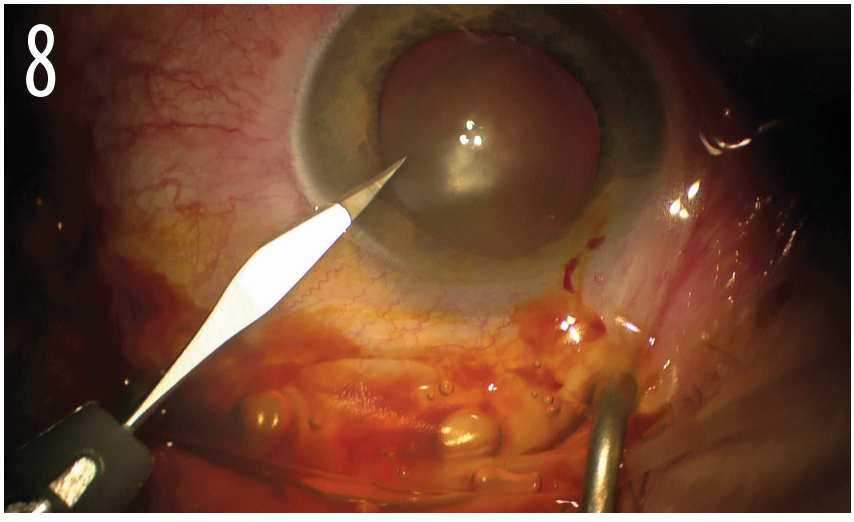

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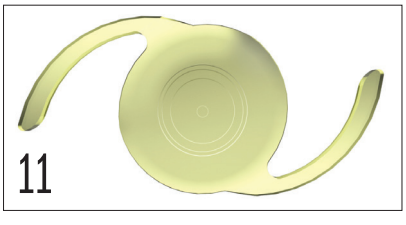


Gene Therapy

Paediatrics

How gene therapy is transforming the future of treating eye disease

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

Our cover story this month looks at gene therapy research that is uncovering key patient benefits. Gene therapy is a promising treatment strategy for Leber's hereditary optic neuropathy (LHON). Dr Patrick Yu-Wai-Man discusses how data from two clinical studies of LHON showed substantial visual improvements in patients with both disease durations of less than 6 months and between 6 months and 1 year. This could prove to be of particular interest to ophthalmologists.

In gene therapy, Dr Paulo E. Stanga also highlights how *AAV8-RPGR* gene therapy for X-linked retinitis pigmentosa showed early responses to treatment at 1 month with increased retinal sensitivity without retinal toxicity.

An expanded cataract and refractive surgery section highlights a discussion with Dr Burkhard Dick, who details several approaches to improving outcomes of cataract surgery, including a look at some available and emerging technologies.

Then, three specialists discuss the benefits that single-use surgical instruments offer over those that are reusable, including convenience, cost and consistent quality.

Also, Prof. David J. Spalton and Dr Mark Packer share how a new IOL offers optical qualities of a monofocal with minimal side effects, while at the same time providing true intermediate range of vision as with traditional extended-depth-of-focus (EDOF) lenses.

In the glaucoma arena, it goes without saying that the features that are paramount for any optical coherence tomography (OCT) instrument are image quality and the abilities to identify artifacts and interpret scans regardless of the desired structures to be viewed or the disease process involved. Dr Joel S. Schuman explains how the various commercially available devices work in different ways, and how understanding those differences may matter during evaluations.

Dr Felipe A. Medeiros tells us that structural evaluation with OCT and functional testing with visual fields should be used throughout the glaucoma disease continuum to detect progression.

Glaucoma is complicated, and it has finally been recognised that elevated IOP is not the only risk factor for progression. An entire menu of risk factors is now available, notes Dr Dale K. Heuer.

The area of retina continues to offer interesting options for ophthalmologists, and in this issue Dr Mark S. Humayun discusses bioengineering strategies that can help overcome challenges to achieving success, with advanced implants aiming to bioengineer the macula.

We also explore how research and development of dry AMD treatments could be expedited by a large-scale, collaborative and multidisciplinary approach.

Turning to cornea, Dr Clara C. Chan offers some pearls for managing ocular cicatricial disease. She notes that it requires a step-wise approach to secure the best results. The first step is keeping the inflammation under control. Without that control, the patient can slide down a path filled with hurdles to improving ocular health.

We close out the issue with a focus on paediatrics and a look at how a model based on simple birth characteristics may provide new, more efficient methods for predicting retinopathy of prematurity (ROP) in infants. A team of researchers led by Aldina Pivodic, MSc, found that this model compares favourably to other models currently in use, and has the benefit of being based purely on simple birth characteristics rather than complex longitudinal neonatal data, which is often inaccessible to ophthalmologists.

In addition, conducting examinations in uncooperative patients is challenging, especially in children. However, anterior-segment optical coherence tomography (AS-OCT), ultrasound biomicroscopy (UBM) and corneal topography have made that task easier in the paediatric population. Imaging technologies can be used in tandem with other clinical findings to design the best plan possible for each patient.

Thank you for reading.

Emerging technologies are improving outcomes of cataract surgery

Multiple innovations target postoperative refractive adjustment

By Cheryl Guttman Krader;

Reviewed by Dr Burkhard Dick

Dr Dick

Available and emerging technologies are addressing the need for solutions to the persistent problem of refractive surprises after cataract surgery, according to Burkhard Dick, MD, PhD.

Two multicomponent IOLs (PreciSight, InfiniteVision Optics; Harmoni Modular IOL, ClarVista) and the light-adjustable lens (LAL, RxSight) are now on the market in some countries, and four companies are developing approaches for inducing refractive index changes using a femtosecond laser, said Dr Dick, professor of ophthalmology, Ruhr University, and chairman, The University Eye Hospital Bochum, Bochum, Germany.

Light-adjustable lens

Sharing his personal perspectives on the light-adjustable lens, Dr Dick noted that there is now more than 10 years of clinical experience with this technology, and an upgraded version is now available commercially in Europe that is showing great success.

"A vast amount of experience underscores the value of this three-piece silicone lens whose refractive power can be changed within a few weeks after cataract surgery by specifically targeted UV irradiation," he said. "I consider the light-adjustable lens a great option to improve refractive outcomes and advance patient care."

The upgraded light-adjustable lens platform features added UV protection, is implanted with a proprietary injector that allows introduction through incisions ≤2.75 mm, and is adjusted with a new light delivery device. This offers improved ergonomics, a 10-fold reduction in retinal UV irradiance, and new optical patterns.

"The new platform allows for earlier noninvasive post-implantation adjustment and less lock-ins, and it can create an extended depth of focus pattern, induce negative asphericity, and be used to design individually adjustable mini-monovision," Dr Dick said.

The safety and performance of the new light-adjustable lens was investigated in a multicenter European study that enrolled 100 eyes of 50 patients with 0.5–3 D of preop keratometric astigmatism. The results demonstrated the safety and efficacy of the upgraded light-adjustable lens technology, Dr Dick said.

> 'I consider the light-adjustable lens a great option to improve refractive outcomes and advance patient care.'
>
> – Dr Burkhard Dick

"More than 70% of eyes achieved 20/20 or better UCVA, which represents a twofold improvement over the outcomes achieved with toric IOLs, and the accuracy to target refraction for spherical equivalent and cylinder was exceptionally high, matching LASIK outcomes," he pointed out.

"In addition, the incidence of both glare and halo were very low."

Multicomponent adjustable IOLs

Refractive adjustment with multicomponent adjustable IOLs is achieved by exchanging a front optic with a new component that corrects refractive error or better serves the patient's vision goals. The two available technologies differ in design.

The PreciSight multicomponent IOL is a dual optic platform that is implanted into the capsular bag. In contrast, the Harmoni Modular IOL uses a scaffold

IN SHORT

- ***A variety of approaches are commercially available or in development that allow refractive adjustment after cataract surgery, including changes in sphere, cylinder, asphericity and multifocality.***

that is implanted into the bag and a front exchangeable optic.

"My personal opinion is that because the multicomponent IOLs require a secondary procedure for power adjustment, they are best considered in situations where there is an increased likelihood of refractive change, such as in cases of paediatric cataract, progressive corneal pathology, or with vitreoretinal tamponade," Dr Dick said.

Laser-induced refractive index ange

Laser-induced refractive index change (LIRIC) is caused by multiphoton absorption of ultrashort laser pulses and can be performed in silicone, hydrogel, or dye-doped polymers but also in the cornea.

Clerio Vision, one company developing LIRIC technology, is focusing on the development of a device for refractive index modification in the cornea that could supersede LASIK and is the first company to demonstrate LIRIC of a living human cornea.

The company is also working on a bench top customisation device for contact lenses and investigating modification of IOL materials, according to Dr Dick.

Perfect Lens is another company working in the LIRIC space. It focuses on developing a device for *in vivo* IOL adjustment.

So far, the company has demonstrated IOL power adjustment in live rabbit eyes and the feasibility of adding or canceling IOL multifocality in a model eye.

Medicem is designing IOL material optimised for modification by a femtosecond laser and a device for in vivo IOL modification. To date it has found a material suitable for refractive index shaping that is expected to have potential for relatively high power change.

LicriEye (Merck) currently is developing polymers containing coumarin side groups to enable photo-induced adjustment of LIRIC. Its work is in an early stage of development.

DR BURKHARD DICK, MD
E: *burkhard.dick@kk-bochum.de*
This article is based on Dr Dick's presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Dick is a consultant to RxSight.

Single-use instruments: A preferred alternative to reusables

Three doctors, three countries, their key considerations

By Dr Martin Dirisamer, Dr Saj H. Khan and Dr Quentin de Bosredon


Dr Dirisamer


Dr Khan


Dr de Bosredon

Advances in technology and design have led to the development of reliable disposable instruments. In the past there was a question mark hanging over the quality of single-use instruments (SUIs), but now, surgeons are re-evaluating their options. Quality control is now excellent, as is the precision, safety and reliability of SUIs.

These instruments provide much more than convenience, as we will discuss in this article.

Key considerations when opting for single-use surgical instruments

MARTIN DIRISAMER, MD, PHD, FEBO
Cornea and refractive surgery specialist, Austria/Germany

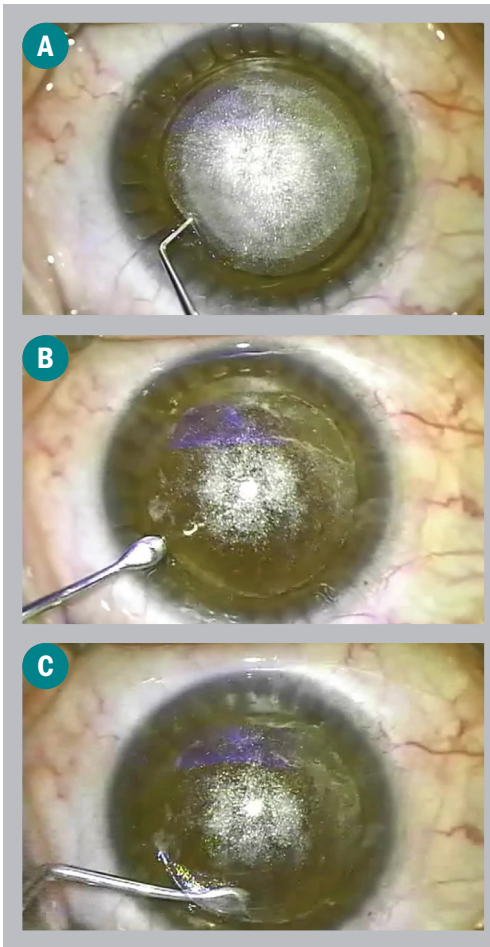
In my private clinic the patient demands quality. So, a quality instrument is of foremost importance for me. We have used single-use and reusable and instruments in the past. The main motivation to use SUIs has been the fact that I know the instrument will be always of a high quality. I will be certain to have a new flawless instrument every time I operate. With the disposable packed instruments, the tip will not be bent or blunt providing a precise sharp clean tool for surgery.

Especially when performing the small incision lenticule extraction (SMILE), I like to use the Reinstein Lenticule Separator (BVI Medical, Waltham, MA (BVI); Figure 1). It always comes in the same quality and I don't have to be concerned about the sterility of the instrument.

SUIs undergo quality control checks and regimental cleaning, ensuring I have a new, sterile quality instrument each time. The reliability that I have the best instrument of a high quality far outweighs any cost concerns.

In Austria and Germany, both single-use and reusable instruments are used, but the SUIs have been widely adopted.

Potentially, in the future, there may be a concern regarding the sustainability of environmental waste



(FIGURE 1) Reinstein Lenticule Separator (BVI) in use. *(Photos courtesy of Dr Dirisamer)*

IN SHORT

- ***Three specialists discuss the benefits that single-use surgical instruments offer over those that are reusable, including convenience, cost and consistent quality.***

with SUIs. But the SUI packs will surely save waste by using one package to envelope many items in a pack instead of every individual instrument being packaged. SUIs may appear like an environmental issue that is non-sustainable; however, when the life-cycle of a reusable instrument is considered, the cost of transportation to and from the sterilising centre, plus the carbon effect involved and the amounts of energy and chemicals used in the cleaning process, then SUIs can appear more attractive environmentally than the reusable instruments.

QUENTIN DE BOSREDON, MD, FEBO
Ophthalmic Surgeon, glaucoma, cataract, and premium IOL specialist, France

I find SUIs to be reliable instruments of high quality that are safe and avoid the whole sterilisation process. Quality and precision with good cutting abilities are evident in the SUIs I use at my practice in France.

The sharpness of the knives is a key advantage for me to attain the desired accuracy in the surgery. I have been using the single-use 2.2-mm double bevel (BVI) and the 15° side-port safety slit knives (BVI; Figure 2) in my practice. The knives have a shield, which is an excellent safety feature to prevent any needlestick injuries to the patient, staff, including to myself. These instruments are supplied in rigid cases for protection and safe disposal after use.

Appropriate reprocessing of reusable surgical instruments is paramount for safe and effective ophthalmic procedures. However, as a multi-step process involving collection, cleaning, disinfection, sterilisation, packaging, transportation and storage, ample opportunities exist for damage and loss of instruments, especially for ophthalmic surgical instruments.[1] This leads to additional activities for any hospital or clinic to regularly service, repair and even replace instruments damaged in the decontamination process. SUIs, therefore, present a solution to this monitory problem.

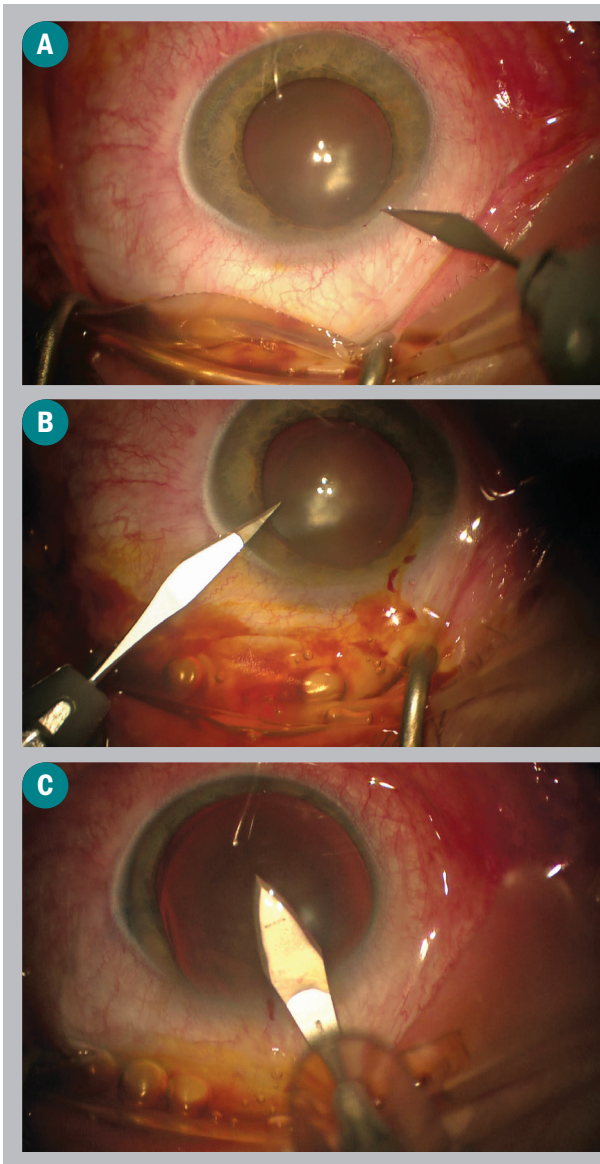
The financial cost comparison of single-use and reusable instruments is a comprehensive issue and a topic on its own. However, the complex reprocessing of surgical instruments bears a risk of additional costs caused by loss and damage, which can result in expensive instruments needing replacement or repair. This is only one example of the additional financial burden which can be dissolved by using SUIs. However, the environmental cost needs to be questioned.

SUIs are widely implemented in France. Possibly the new generation of surgeons may be concerned about SUI cost, but when this is weighed up against all the reprocessing costs, including costs of staff, loss and damage liabilities, SUIs become an appealing alternative to reusable instruments.

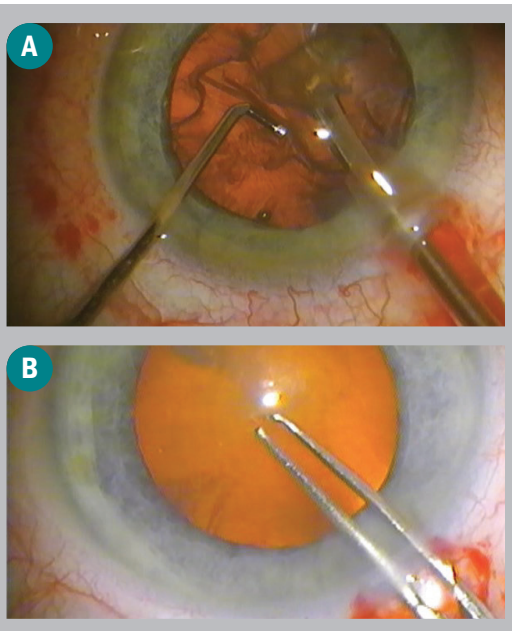
SAJ H. KHAN, MD, MBBS (LONDON), FRCSED (OPHTH)
Consultant Ophthalmic Surgeon, specialist in cataract, laser and lens-based vision correction surgery, UK

The main advantage I see with SUIs is that they eliminate a huge burden of the sterilisation process and the potential loss or damage that can arise during the cleaning process. When delicate reusable instruments return damaged, this leads to extra cost and can potentially compromise and sometimes even result in cancellation of the surgical procedure. It is not always possible to have a spare reusable instrument (they can be prohibitively expensive), but SUIs are much more accessible as they are cheaper. This also potentially makes it easier to trial small variations in instruments to find the optimal instrument for a particular surgeon—or else for a surgeon to request different instruments for different/infrequently performed procedures.

Reusable instruments that need to be sent away for sterilisation cause me concern as I need to be certain they are appropriately



(FIGURE 2) The single-use 2.2-mm double bevel (BVI) and the 15° side-port safety slit knives (BVI). *(Photos courtesy of Dr de Bosredon)*



(FIGURE 3) The single-use capsulorhexis forceps and the disposable Phaco Chopper/Mushroom Manipulator in use. *(Photos courtesy of Dr Khan)*

(FIGURE 4) Bolivia charity: day-1 post-op happy patient. *(Photo courtesy of Dr Khan)*

cleaned and returned safely. With SUIs, this concern is removed.

In standard cataract surgery I rely on the MICS single-use Capsulorhexis Forceps and the disposable Phaco Chopper/Mushroom Manipulator (BVI; Figure 3), because of their consistency.

Although changing over from reusable to single-use may take a small period of adaption, once the surgeon becomes accustomed to the instruments, they can possess additional benefits over the reusable. Everything I need for a procedure is provided in one disposable pack, from instruments and cannulae to drapes and swabs. This can save time in the operating theatre and resources such as staffing in a sterilising department. Staff don't have to open every piece of equipment/instrument separately, providing convenience and time efficiency for the surgeon and the entire team. This can lead to an overall increased theatre efficiency with reductions in set up time per procedure.

Another very important but easily overlooked benefit of the SUI over the reusable is the ability to take these instruments abroad for charity work. As the SUIs are cheap and there is no sterilisation required, they are ideal for unfunded charity environments often lacking access to adequate hygiene/sterilisation facilities (Figure 4).

In the UK, many ophthalmic surgeons are changing over from reusable to SUIs. There appears a definite shift in acceptance. I have used SUIs for over 7 years now and I would say in the last 5 years SUIs are both more popular than ever before and are being used in high-quality environments.

Conclusion

Collectively, all three of us have had experience with single-use and reusable instruments. Having utilised both, we find the SUIs overall very favourable. With SUIs, high-quality, safe and flawless new instruments are available for every procedure. SUIs provide a reliable alternative to reusable instruments.

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DR MARTIN DIRISAMER, MD, PHD, FEBO
E: *dirisamer@me.com*
Dr Dirisamer is a cornea consultant, University Eye-Hospital Munich, Germany, and co-owner of SMILE EYES Linz, Austria. Dr Dirisamer declares financial disclosures in Physiol and DORC.

DR QUENTIN DE BOSREDON, MD, FEBO
E: *quentindebosredon@gmail.com*
Dr de Bosredon is a consultant at Thiers Eye Clinic, Bordeaux, France and at Fondation Ophtalmologique Rothschid, Paris, France, and co-owner of Dr de Bosredon & Dr Giry, private practice, France. Dr de Bosredon declares no financial disclosures relevant to the subject matter.

DR SAJ H. KHAN, MD, MBBS (LONDON), FRCSED (OPHTH)
E: *admin@sajkhan.co.uk*
Dr Khan is a consultant in Caterham, East Grinstead and Croydon, UK, and director at Eye Law Chambers. Dr Khan declares he is a consultant for BVI.

Benefits of novel monofocal lens: Minimal glistening, glare or halo

New IOL provides diffractive extended depth of focus with fewer side effects

By Prof. David J. Spalton and Dr Mark Packer

Classified and CE-marked as a monofocal intraocular lens (IOL), the xact Mono-EDoF (Santen) delivers more than emmetropia at a single refractive plane. This new IOL also provides patients with extended depth of focus (EDOF), which results in good, uncorrected intermediate vision, without the level of visual side effects experienced with traditional EDOF and trifocal IOLs.

This new type of lens will mean surgeons can offer their patients more than standard monofocal vision correction after cataract surgery.

Here, we look at the conceptual framework underpinning this new IOL, as well as the bench-test study results.

What is the new IOL and how does it function?

The xact Mono-EDoF is an enhanced monofocal and is designed to provide good, uncorrected intermediate vision as well as excellent distance vision, with minimal glare or halo in contrast to "traditional" EDOF lenses.

The concept allows for the optical qualities of a monofocal with minimal side effects, while at the same time providing true intermediate range of vision as with traditional EDOF lenses.

This performance is accomplished through novel design. The posterior surface is refractive aspheric, while the anterior surface has three zones: a central refractive monofocal zone, a diffractive EDOF zone that has four rings on the surface, and then another refractive monofocal zone.

The diffractive zone is only 3.2 mm in diameter, which reduces the likelihood for glare and halo.

There is a broad single peak of focus rather than the bimodular peak seen with other EDOF lenses. This broad single peak of focus does not create the kind of dysphotopsia we see in diffractive lenses. Instead, the new IOL offers good intermediate vision and, although not promising near vision, it is comparable to a true monofocal in terms of dysphotopsia, halo, glare and contrast sensitivity.

As with any EDOF lens, lighting conditions are critical; people will read better in bright rather than dim light.

The lens offers increased independence from spectacles, specifically for distance and intermediate vision, although it's quite likely that patients will still require glasses for near work.

> This new type of lens will mean surgeons can offer their patients more than standard monofocal vision correction after cataract surgery.

Bench testing

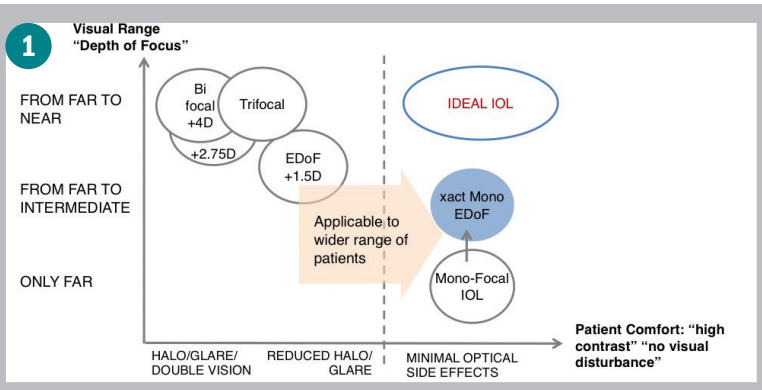
To assess the functionality of the xact Mono-EDoF, bench testing was conducted using a Trioptics OptiSpheric IOL Pro 2 bench and custom corneas matched to IOL asphericity.

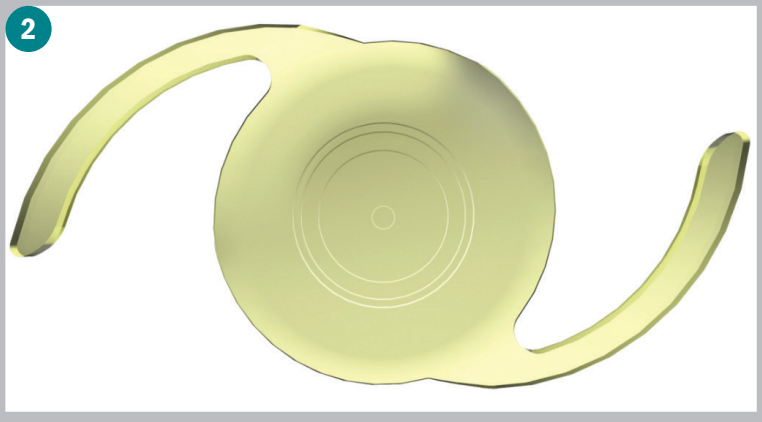
The sample pupil sizes (at the IOL plane) were 3.0 mm, 4.5 mm based on standard 550 nm wavelength.

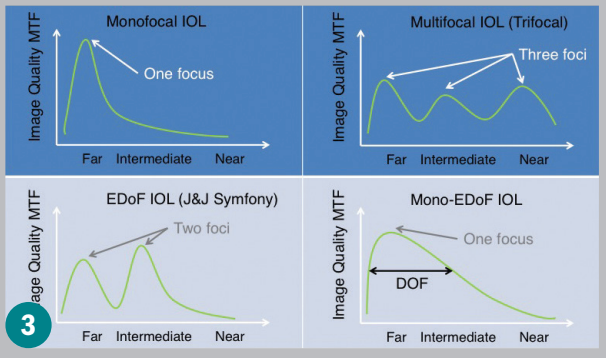
Spatial frequency was measured at 15 cycles/degree (50 lpmm) and 30 cycles/degree (100 lpmm), equivalent to 20/40 and 20/20, respectively.

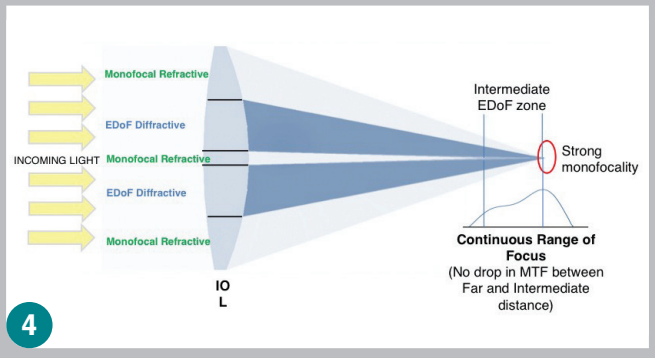
IN SHORT

- ***New IOL offers optical qualities of a monofocal with minimal visual side effects, including minimal glistening, glare or halo, while at the same time providing true intermediate range of vision as with traditional extended depth of focus (EDOF) lenses.***









(FIGURE 1) **The design concept of the xact Mono-EDoF. Minimal glare, glistening-free (due to the material used), minimal halos, and suitable to a broad spectrum of patients.**

(FIGURE 2) **The four diffractive rings in the new design. The IOL is made from Santen's proprietary, glistening-free hydrophobic material. The firmness of the material makes it resistant to scratching and pitting from YAG lasers or stretching when you inject it.**

(FIGURE 3) **Note that the new lens peaks at far distance and provides good intermediate distance image quality also on this animated through-focus MTF curve. It features a characteristic single elongated peak which extends into the myopic side, unlike other EDOF IOIs, which have bimodular peaks.**

(FIGURE 4) **Image illustrating the function of the new lens.**

(Images courtesy of Santen)

OPTICAL AND CLINICAL COMPARISON

Optical and clinical comparison with a conventional bifocal EDOF IOL found that the xact Mono-EDoF exhibited a continuous range of focus from far to intermediate. Contrast sensitivity was found to be equivalent to a monofocal IOL, and the new device had higher tolerance to the effects of decentration compared to a conventional EDOF IOL.

EFFECT OF TILT AND DECENTRATION

The effect of tilt and decentration on a novel EDOF IOL compared to conventional EDOF IOLs showed a high image quality through to 1.5 D depth of focus with the new design.

It was also relatively resistant to decentration and tilt in comparison to other EDOF IOLs.

Higher modulation transfer function (MTF) values and continuous range of vision is expected to result in higher levels of patient satisfaction, and with just four rings led to a very low incidence of dysphotopic symptoms.

Overall, bench testing showed the xact Mono-EDoF is less sensitive to tilt and decentration than other EDOF lenses.

SIMULATING REAL-LIFE VISION

Another evaluation performed was

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> This lens represents a revolutionary step forward in diffractive optics, ultimately improving patients' lives.

to simulate "real life vision" by mounting four cameras side by side on a car dashboard looking at the same object.

Here, a wet cell system with matching corneas was used and images were recorded under identical camera settings.

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This lens represents a revolutionary step forward in diffractive optics, ultimately improving patients' lives.

PROF. DAVID J. SPALTON, FRCS, FRCOPHTH
E: *profspalton@gmail.com*
Prof. Spalton is a Trustee of Fight for Sight, the vision research charity, a Trustee of the Elizabeth Frankland Moore and Star Foundation and a special adviser to the Ridley Foundation. He is a consultant adviser to a number of ophthalmic device and ophthalmic biotech companies, a medical adviser to Optical Express and a Director of UKISCRS.

DR MARK PACKER, MD, FACS, CPI
E: *mark@markpackerconsulting.com*
Dr Packer is chief medical officer for Cassini Technologies, BV as well as president of his own consulting company, Mark Packer MD Consulting Inc.

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OCT devices: The differences matter

Understanding variations between devices during ophthalmic evaluations

By Lynda Charters;

Reviewed by Dr Joel S. Schuman

Dr Schuman

Features that are paramount for any optical coherence tomography (OCT) instrument are image quality and the abilities to identify artifacts and interpret scans regardless of the desired structures to be viewed or the disease process involved. The various commercially available devices work in different ways, and understanding those differences may matter during evaluations.

In order to ensure image quality in spectral-domain OCT, the signal quality must be highest in the top third of the scanning window and the tissue must be as flat as possible. The condition of the ocular media, including a dry cornea, refractive errors, cataracts and vitreous opacities, adversely affect the image quality, according to Joel S. Schuman, MD, professor of neuroscience and physiology, neural science, and electrical and computer engineering, and chairman of ophthalmology, NYU Langone Medical Center, NYU School of Medicine, New York, USA.

According to Dr Schuman, acceptable signal strengths and quality scores vary among four of the most widely used OCT instruments: Cirrus (Carl Zeiss Meditec), Avanti (Optovue), Spectralis (Heidelberg Engineering) and Triton (Topcon). When acceptable images are not obtained, segmentation errors occur.

Blood vessel shadows are the products of every vessel containing blood. Mirror images or inverted images can result from the manner in which the image was acquired. Blinking artifacts, appearing as black bands across an image, indicate that the signal was interrupted during a blink or a segmentation error occurred, and eye movement artifacts can distort the shapes of the vessels, said Dr Schuman.

The health of the retinal nerve fibre layer (RNFL) is assessed in a circular area around the optic nerve head. This area of measurement can be used on any of the above-mentioned instruments. Some instruments provide a volumetric measurement that includes the tissue beyond the circle to determine the development of glaucoma as well as the shape and character of the abnormality, he said. When viewing the output from the devices, the abnormalities have a particular location and shape. "If the abnormality is normally located in a place where glaucoma generally develops along with a pattern normally seen in glaucoma, there is a high likelihood that the abnormality is glaucomatous," Dr Schuman explained.

Correlations between the superior and inferior thicknesses of the RNFL are shown by the devices. The Optovue and Triton machines show agreement between the nasal and temporal thicknesses of the RNFL. Spectralis, Triton, and Cirrus document floaters. Triton does not document inferior movement.

When evaluating glaucomatous progression over time, Cirrus contains the most complete glaucoma progression analysis software, says Dr Schuman. Data are obtained from the scanning circle and provide the average, superior, and inferior RNFL thicknesses and a trend analysis that describes if there is a significant difference from "no change" in the regression line.

The average changes in cup-to-disc ratio as well as RNFL thickness profiles over time and on a specific day also are provided. Another feature is a table of numerical values of the parameters highlighted for each visit with changes emphasised.

The Spectralis provides a serial analysis of progression, the results of which are depicted in graphs and in different phases from a patient's scan. No statistical program is included to document significant progression changes.

The Optovue provides changes in both the ganglion cell count (GCC) and RNFL thickness. Changes in RNFL thickness are documented in a graph from baseline to the current day; significant changes in the GCC are highlighted in a table. For both parameters, the device provides a statistical test for trend.

For each machine, there is a floor effect: the point at which it can no longer measure the RNFL or the GCC. "Clinicians must be careful and not be fooled into thinking that the patient is stable, when in fact the RNFL is so thin that the machine cannot determine the glaucoma is worsening," Dr Schuman cautioned. "It is important to monitor both the RNFL and visual field when assessing glaucoma progression, especially in patients with moderate to advanced disease."

IN SHORT

- ***OCT detects abnormalities and progressive thinning of the RNFL better than measurement of the visual fields.***

DR JOEL S. SCHUMAN, MD
E: *joel.schuman@nyu.edu*

Dr Shuman is a consultant/advisor to numerous manufacturers of imaging instruments, holds patents for various technologies, and receives royalties for those technologies.

OCT is a key tool in determining glaucoma progression

Study demonstrates value as an adjunct for visual fields

By Cheryl Guttman Krader;

Reviewed by Dr Felipe A. Medeiros

Dr Medeiros

Glaucoma worsens slowly in most affected patients, but a substantial number show at least moderate progression over time based on monitoring with optical coherence tomography (OCT) and visual fields.

Although OCT can detect progression across all stages of disease, the findings from OCT and standard automated perimetry (SAP) frequently disagree. Therefore, it is essential that patients with glaucoma be followed for progression using both modalities, according to Felipe A. Medeiros, MD, PhD, Distinguished Professor of Ophthalmology, and Joseph AC Wadsworth Endowed Chairman, Duke University School of Medicine, Durham, NC, USA.

These recommendations are based on findings from analyses of data collected in the Duke Glaucoma Registry Study from over 27,000 eyes of over 14,000 patients with glaucoma or suspected glaucoma.

During follow-up, which ranged to almost 9 years, this large patient cohort had undergone more than 100,000 tests with spectral domain (SD) OCT.

"We believe our undertaking is probably the largest analysis of longitudinal SD OCT and SAP results to date," Dr Medeiros said. "Visual field testing remains the primary method of assessing glaucomatous progression. The findings of our study are helpful for understanding where OCT is useful."

In analysing the data, eyes were categorised as having slow, moderate, fast or catastrophic change over time based on average annual change in SAP or average retinal nerve fiber layer (RNFL) thickness change criteria. For example, eyes with <0.5 dB/year change in SAP or <1 µm/year loss of average RNFL were classified as experiencing slow change.

Dr Medeiros explained that the cut-off of <1 µm/year was chosen to define slow change based on findings of a study that looked at the impact of normal aging on change in RNFL thickness. Data from healthy subjects showed that the 95% confidence interval for age-related loss was up to 1 µm/year.

Analysing the data in the Duke Glaucoma Registry showed that ~30% of eyes experienced moderate or faster glaucomatous progression over time.

IN SHORT

Structural evaluation with OCT and functional testing with visual fields should be used throughout the glaucoma disease continuum to detect progression.

When the subjects were grouped by glaucoma severity, it was found that, in the group with early glaucoma at baseline, SD OCT detected many more eyes that were progressing fast than did visual fields.

Among subjects who had severe glaucoma at baseline, the proportion identified as having fast or catastrophic progression was approximately the same using SD OCT and visual fields. The eyes identified by the two tests, however, were not the same.

"We found that most eyes identified as having fast or catastrophic progression by OCT would have been classified as showing slow or moderate progression by their visual fields and vice versa," Dr Medeiros said. "This result drives our conclusion that both structural and functional tests should be used throughout the disease continuum to monitor for progression in patients with glaucoma."

Although changes noted on serial OCT scans may indicate disease progression, clinicians must consider whether the change is the result of worsening glaucoma or has some other cause. A case of a patient with vitreous traction illustrates this point. Here, OCT imaging showed a decrease in RNFL thickness superiorly over time, but it was attributable to a region of vitreous traction that was pulling on the RNFL. The change disappeared after the traction was released.

Dr Medeiros concluded that different OCT instruments evaluate progression differently, but it is always essential to consider whether change is glaucoma-related.

DR FELIPE A. MEDEIROS, MD, PHD

E: *felipe.medeiros@duke.edu*

This article is based on a presentation by Dr Medeiros at the American Academy of Ophthalmology's Glaucoma Subspecialty Day meeting. Dr Medeiros is a consultant to and receives research support from Carl Zeiss Meditec and Heidelberg Engineering.

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Predicting glaucoma progression: More than meets the eye

Risk calculation to determine management, treatment and follow-up

By Lynda Charters

Glaucoma is complicated and it has finally been recognised that elevated intraocular pressure (IOP) is not the only risk factor for progression. An entire menu of risk factors is now available. Dale K. Heuer, MD, enumerated all the factors that can be considered easily by physicians when evaluating their patients in the Shaffer-Hetherington-Hoskins Lecture Keynote address titled "Risk Factors for Glaucoma Progression" at the Glaucoma 360 annual meeting.

"Every patient should undergo risk calculation to determine management, treatment and follow-up," Dr Heuer, retired professor and chair of ophthalmology, Medical College of Wisconsin, Milwaukee, USA, said. The frequency of visits and testing is important and facilitates the advisability of escalating or de-escalating treatment, adjusting target IOPs and perhaps reducing costs.

IOP remains the biggest risk factor that is treated; the Early Manifest Glaucoma Trial (EMGT) reported that the 77% of patients were more likely to have glaucoma progression. Predictive analysis showed that in patients who were evaluated at 6, 12 and 18 months with IOPs under 14 mmHg were less likely to progress, and those tested at the same time points with IOPs over 17 mmHg were more likely to progress. Another consideration may be the peak pressure of a patient; and physicians should pay attention to outlier IOPs as indicators of risk.

Central corneal thickness, a non-modifiable risk factor and the most robust factor in the development of glaucoma, is the most significant fact in patients with high IOPs. It alerts physicians to a greater risk of ocular hypertension to primary open-angle glaucoma.

Patients with pseudoexfoliation syndrome, also a non-modifiable risk factor, alerts physicians to the risk of open-angle glaucoma progression. These patients were more than two times likely to progress compared with those without this syndrome. Dr Heuer pointed out that it is easy to identify.

Optic disc haemorrhages are also another entity to look for, he noted. The Collaborative Normal Tension Glaucoma Study found that the presence of optic disc haemorrhages translates to almost a three-fold greater risk of progression of glaucoma. Another interesting observation was that lowering IOP after a disc haemorrhage can slow the rate of change, which emphasises the importance of treatment. Patients with disc haemorrhages and normal tension glaucoma or open angle glaucoma had a three- to six-times greater risk of progression and are in a higher risk category, as reported in a study from The Netherlands.

The presence of beta-zone parapapillary atrophy increases the risk of progression over two-fold, according to the New York Eye and Ear Infirmary. A later study from Korea reported a three-fold increase in the risk of progression on optical coherence tomography (OCT) images with signs of damage inferiorly.

Interestingly, low blood pressure (BP) is a problem, with a 42% increase in the risk of glaucoma progression when systolic BP was 25 mmHg.

Other factors in progression may be age and poor follow-up adherence. Depth-enhanced OCT and OCT angiography may be able to measure bowing of the lamina cribrosa. Less physical activity, nocturnal dips in the diastolic BP, sleep apnea and systemic perfusion pressure are possible modifiable risk factors. A family history can alert physicians to a greater risk of primary open-angle glaucoma and normal tension glaucoma, and also provides another opportunity to identify other individuals at risk of glaucoma.

IN SHORT

- ***Elevated IOP is not the only risk factor in glaucoma progression. Identifying other modifiable risk factors can help physicians treat patients.***

DR DALE K. HEUER, MD
E: *dheuer@mcw.edu*
Dr Heuer is retired professor and chair of ophthalmology, Medical College of Wisconsin, Milwaukee. Dr Heuer has/has no financial interest in this subject matter.

Bioengineering puts a focus on retinal degeneration

Varied approaches giving physicians vision-restoring options for patients

By Cheryl Guttman Krader;

Reviewed by Dr Mark S. Humayun

Dr Humayun

There are many challenges to achieving success with advanced implants aiming to bioengineer the macula, according to Mark S. Humayun, MD, PhD.

Dr Humayun also offered a brief update on two projects that he has been leading to restore vision in patients with retinal degenerative disease – implantation of a bioelectronic epiretinal visual prosthesis (Argus II Retinal Prosthesis System, Second Sight Medical Product) for end-stage retinitis pigmentosa and subretinal implantation of a bioengineered retinal pigment epithelial (RPE) monolayer (California Project to Cure Blindness-Retinal Pigment Epithelium 1 [CPCB-RPE1], Regenerative Patch Technologies) for advanced dry age-related macular degeneration (AMD).

"Both bioelectronic and nanoscale scaffold approaches require a safe and effective abiotic-biotic interface with the ocular tissue," said Dr Humayun, Cornelius Pings Chair in Biomedical Sciences and professor of ophthalmology and biomedical engineering, director of the USC Ginsburg Institute for Biomedical Therapeutic and co-director of the USC Roski Eye Institute, Los Angeles, USA. "As we look to leverage improvements in energy sources, materials, 3D printing, and nanoscale fabrication along with growing interest of larger, traditionally nonmedical corporate partners bodes well for future development of these technologies."

IN SHORT

- ***Strategies for bioengineering the macula include both implantation of a visual prosthesis and retinal pigment epithelial transplantation.***

(FIGURE 1)
A patient uses the Argus II Retinal Prosthesis System to participate in archery as an instructor looks on. *(Photo courtesy of USC)*

Visual prosthesis

The epiretinal visual prosthesis has been implanted in 35 centres around the world in almost 400 eyes. It is FDA approved for implantation in the United States in patients who have light perception vision OU secondary to retinitis pigmentosa. In the European Union, the device is approved for use in patients with hand motion vision OU from retinal degeneration.

The device consists of extraocular components (a video camera attached to glasses and a video processing unit) and an intraocular implant consisting of an implanted microchip as well as an electrode array that is placed epiretinally.

"Function of the device requires close approximation of the electrodes to the retina, and intraoperative OCT guidance has made it easier for achieving this goal," Dr Humayun explained.

The approach is designed to ultimately allow blind people to be able to read and recognise faces. In its current version, it mainly serves to improve patients' orientation and mobility. By doing so, the epiretinal prosthesis still provides significant benefits because it permits re-engagement in activities of daily living therefore increases well-being.

"Patients implanted with the prosthesis report that it has allowed them to walk safely within a crosswalk, locate doors and windows, detect and track other people, and sort light and dark clothes," Dr Humayun said. "With the prosthesis they feel more socially connected and some patients have been able to participate in recreational activities such as bowling, archery, and even skiing."

Initially, the best visual acuity achieved with the implant was 20/1,200. However, thanks to software enhancements and better surgical placement, function has improved to 20/480, and it can reach 20/200 with digital zoom. Dr Humayun reported that the team is now working to provide color vision that will help patients with object recognition at lower resolutions.

> 'Both bioelectronic and nanoscale scaffold approaches require a safe and effective abiotic-biotic interface with the ocular tissue.'
>
> – Dr Mark S. Humayun

RPE transplantation

Multiple approaches are being investigated for RPE transplantation to restore vision in patients with advanced dry AMD.

Dr Humayun and colleagues are working with a polarised monolayer of human embryonic stem cell-derived RPE on a non-biodegradable, synthetic parylene scaffold.

"Injecting a cell suspension is technically easier," he said. "Transplantation of RPE as a confluent sheet on a supportive scaffold, however, assures that the cells adhere with the proper orientation that is critical for survival and growth factor production by the RPE."

According to Dr Humayun, his research team has spent five years working on the development of an erodible substrate for the RPE sheet, but then turned to use of parylene, which is non-erodible polymer with a Class VI USP rating (highest biocompatibility rating) that has a history of more than 30 years of use in implantable devices in other parts of the body.

"Maintaining molecular diffusion across these biomimetic membranes is very important," he explained. "We were trying to mimic Bruch's membrane in that regard, and our studies show we have come very close."

The synthetic membrane (scaffold), CPCB-RPE1, is very easy to handle. After positive results were achieved in preclinical testing investigating the safety, survival, and functionality of the transplant and the feasibility of its subretinal implantation, a phase I/IIa clinical trial was launched enrolling patients with AMD-related geographic atrophy. The initial ten patients were required to have BCVA of 20/200 or worse, and subsequently patients with better vision (20/80 or worse) were eligible.

The surgery involves creation of a subretinal pocket, hydrodissection of the retina overlying the region of the geographic atrophy, and insertion of the CPCB-RPE1 through a small retinotomy.

Custom-created tools are used to introduce and position the implant. Perfluorocarbon (PFC) heavy liquid flattens the retina overlying the implant.

The retinotomy is closed, air-fluid exchange performed, the PFC is removed, and then either expansile gas or silicone oil are instilled into the vitreous cavity.

Conclusion

The study has enrolled 16 subjects to date. The preliminary results that made the cover story of *Science* magazine showed that the implant helped patients regain the ability to fix on small targets and that OCT showed similarly good integration of the implant with the host retina.

"Results from 1 year of follow-up are being collected," Dr Humayun concluded.

DR MARK HUMAYUN, MD, PHD
E: *humayun@med.usc.edu*
Dr Humayun is an equity owner and holds patents for Second Sight Medical Products and Regenerative Patch Technologies and is a consultant to Regenerative Patch Technologies.

Dry AMD for non-retina specialists

Success requires change of approach

By Michelle Dalton

Age-related macular degeneration (AMD) is the leading cause of blindness worldwide among the elderly, and its prevalence is expected to increase as the population ages.[1]

There are two forms of this sight-stealing disease: dry AMD and wet AMD. Although wet AMD is chronic and incurable, the disease is manageable with anti-VEGF injections. Vision can be maintained, or even improve, with consistent, regular, anti-VEGF treatment. Both forms of AMD involve a complex interplay of pathogenic factors, including genetics and lifestyle risk factors such as smoking. Research thus far has failed to decipher how these various factors interact in dry AMD and success in doing so would require a large-scale, collaborative and multidisciplinary approach.

To address this issue, a large-scale, collaborative, systems-biology approach is needed to expedite the discovery of treatments for dry AMD—a leading cause of blindness among people 65 and older for which is there is no treatment—according to a report by a working group of scientists appointed by the National Advisory Eye Council (NAEC).[2] The NAEC is a 12-member panel that guides the National Eye Institute (NEI), part of the National Institutes of Health. The NAEC charged the working group to assess the state of research on dry AMD and to propose directions for future research.

"The working group thoroughly assessed what is known about dry AMD pathobiology, and the recommendations will be informative for considering future NEI research priorities to align with promising pathways for discovering

IN SHORT

- ***Research and development of dry AMD treatments could be expedited by a large-scale, collaborative and multidisciplinary approach.***

therapeutic targets," said NEI Director, Paul A. Sieving, MD, PhD.

Further understanding risk factors

There are multiple genetic and environmental factors at play in the development of AMD. More than 40 genetic variants have been associated with AMD, including APOE, CHF, and HTRA/ARMS2. The discovery of these gene variants have helped identify potential therapeutic targets, and gene-therapy clinical trials are currently underway for the treatment of the wet subtype.[3,4]

"We propose that researchers utilise a systems-biology approach, integrating the big data available from clinical registries and various fields of biology known as 'omics' to develop better models and ultimately treatments for patients with this blinding disease," said report co-author Joan W. Miller, MD, chair, Harvard Medical School Department of Ophthalmology, Boston, MA, USA.

"This approach would integrate basic, genomic, preclinical, medical, pharmacological and clinical data into mathematical models of pathological processes at different stages of dry AMD in order to ask how relevant individual components act together within the living system," Dr Miller said.

Development of new imaging technologies

Standard-of-care imaging for AMD diagnosis, classification of disease severity, and the evaluation of treatment efficacy currently include colour fundus photographs, optical coherence tomography (OCT), and OCT-angiography. Handa et al. suggest that new imaging technologies could help identify preclinical risk factors or currently unknown AMD subtypes that may impact disease progression and treatment efficacy by allowing physicians to see cellular and subcellular structures at different disease stages. For example, "when used with a scanning laser ophthalmoscope and OCT, adaptive optics systems can visualise individual cones, changes in rods, RPE [subretinal pigmented epithelial], and SDD [subretinal drusenoid deposits] in dry AMD," the researchers write.

Other novel imaging modalities suggested include polarisation-sensitive OCT, fluorescence lifetime, and hyperspectral fluorescence. They note, however, that more data and larger clinical trials are needed to confirm the utility of these new imaging technologies, as existing trials have been in small study populations with variable follow-up.

"To advance our understanding, we must identify imaging biomarkers of early changes that reflect AMD pathobiology, predict disease progression and/or treatment response, and correlate with molecular markers that are relevant in both animal models and humans," they conclude.

Precision medicine through clinical trials

Much like in patients with cancer, Handa et al. believe dry AMD can and should be treated through personalised, precision medicine. To do so, they advocate for individually tailoring computer models to assess a person's potential risk for developing dry AMD, progression rate, and potential response to treatment.

For this to be effective, however, the group acknowledged that drugs must first be developed for the dry AMD population through robust clinical trials. They further recommend partnering with pharmaceutical companies to developing these trials, with patients followed closely long-term.

Finally, patients with dry AMD should be encouraged to donate their eyes to science after they die to further research efforts.

With these efforts and approaches, Handa et al. hope to expedite the research and development of dry AMD treatments.

> 'This approach would integrate basic, genomic, preclinical, medical, pharmacological and clinical data into mathematical models of pathological processes at different stages of dry AMD.'
>
> – Dr Joan W. Miller

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DR JOAN W. MILLER, MD

E: *joan_miller@meei.harvard.edu*

Dr Miller did not indicate any financial interests relevant to the subject matter.

DR PAUL A. SIEVING, MD, PHD

E: *pas@nei.nih.gov*

Dr Sieving did not indicate any financial interests relevant to the subject matter.

Pearls for management of ocular cicatricial disease

Controlling inflammation key to successful treatment strategy for patients

By Lynda Charters;

Reviewed by Dr Clara C. Chan

Dr Chan

Patients with severe cases of ocular surface disease can be some of the most challenging in ophthalmology, and cannot be treated with a "cookbook" approach. Often, these patients require a physician to pull out all the stops in the treatment armamentarium.

The first step is keeping the inflammation under control. Without that control, the patient can slide down a path filled with hurdles to improving their ocular health.

According to Clara C. Chan, MD, FRCSC, FACS, assistant professor of ophthalmology, University of Toronto, Canada, and medical director, Eye Bank of Canada, Ontario Division, the importance of the conjunctiva cannot be overemphasised.

"The tissue allows for monitoring of inflammation," she said. "The goblet cells, which secrete the mucin layer of the tears, are a hallmark of healthy conjunctival tissue. When goblet cells are identified on the corneal surface, it is diagnostic of limbal stem cell deficiency (LSCD)."

> 'When goblet cells are identified on the corneal surface, it is diagnostic of limbal stem cell deficiency (LSCD).'
>
> – Dr Clara C. Chan

In addition to LSCD, other sequelae of conjunctival inflammation can occur, including goblet cell loss, mucin deficiency, symblephara formation, loss of the fornices and end-stage surface keratinisation, Dr Chan pointed out.

The salvage options are very difficult once patients have run the gauntlet of these ocular insults.

Dr Chan explained that eyes with chronic conjunctival inflammation and total LSCD have the worst prognosis with any surgical intervention.

"The sequelae of LSCD are daunting, and include conjunctivalisation, visual loss, chronic pain with persistent epithelial defects, photophobia, red eye and corneal transplant failure," she said.

Patients with more than 50% LSCD and active conjunctival inflammation, such as those with Stevens-Johnson syndrome, mucous membrane pemphigoid (MMP) and recent chemical or thermal injury, can expect the worst outcomes.

Following a step-wise approach, as discussed here, can help to give patients with ocular cicatricial disease the best results.

Treatment steps

Good history-taking is mandatory for identifying some of the ocular offenders in plain sight that can be overlooked, such as topical formulations with preservatives and glaucoma medications that can damage the ocular surface with chronic use.

In addition, a medical history of atopy, graft-versus-host disease and Stevens-Johnson syndrome can create cicatricial changes on the ocular surface. The physician should also be alert to a history of infections, i.e., herpes simplex virus and adenovirus; trauma from chemical/thermal injury or radiation; and inflammation from rosacea and chronically treated refractory blepharitis.

The presence of a disease such as MMP with ocular involvement is not always evident initially and the condition of the ocular surface—the persistence of inflammation—can escape the control of the treating physicians. Determining the aetiology of the inflammation clearly is important to keep it in check.

Dr Chan pointed out that MMP can be misdiagnosed and managed as blepharitis for years (stage 1). With no improvement, a biopsy of the abnormal conjunctiva is performed (stage 2).

Continues on page 26 : ***Pearls***

IN SHORT

- ***Ocular cicatricial disease requires a step-wise approach to secure the best results.***

Providing spectacle independence for a young adult patient with cataract and astigmatism

By Nick Kopsachilis, MD, PhD

CASE HISTORY

A 19-year-old female patient presented with severe posterior subcapsular cataract in both eyes. Her medical history included asthma and irritable bowel syndrome, and her cataract was believed to be induced by the corticosteroids she had been using to manage her health problems.

Visual acuity was 6/18 unaided OD, improving to 6/12 with pinhole, and 6/18 unaided OS, improving to 6/9 with pinhole. Refraction was -3.00 -1.75 x 10° OD and -2.50 -1.50 x 4° OS. The rest of the ophthalmic findings, including OCT scan of the macula, were normal.

We decided to perform cataract surgery with bilateral implantation of the AT LARA toric 929MP IOL (Carl Zeiss Meditec; Jena, Germany). Biometry measurements were obtained with the IOLMaster 700 (Carl Zeiss Meditec; Jena, Germany). Keratometry and higher order aberrations of the cornea were also measured with a Scheimpflug imaging device. In addition, a Dell type questionnaire was completed to assess whether the patient was suitable for the AT LARA lens. IOL power calculation was done using the ZEISS IOL Calculation Service (Figure). The selected IOL powers were 25.50 SE 2.00 cyl OD and 25.50 SE 2.50 cyl OS, which were predicted to result in a postoperative SE that was closest to the target of emmetropia.

The patient underwent bilateral simultaneous cataract surgery under general anaesthesia. Axis alignment reference marks were placed at 0° and 180° preoperatively at the slit lamp, and correct alignment of the IOL was checked intraoperatively using a Mendez gauge.

At 3 weeks after surgery, refraction was -0.25 -0.25 x 178° OD and -0.25 -0.50 x 10° OS. Unaided binocular visual acuity was 6/6 at distance, N12 at 30 cm, and N10 at 60 cm; binocular distance BCVA was 6/5. The patient reported that she was thrilled with her outcome because she could see and read without glasses after surgery.

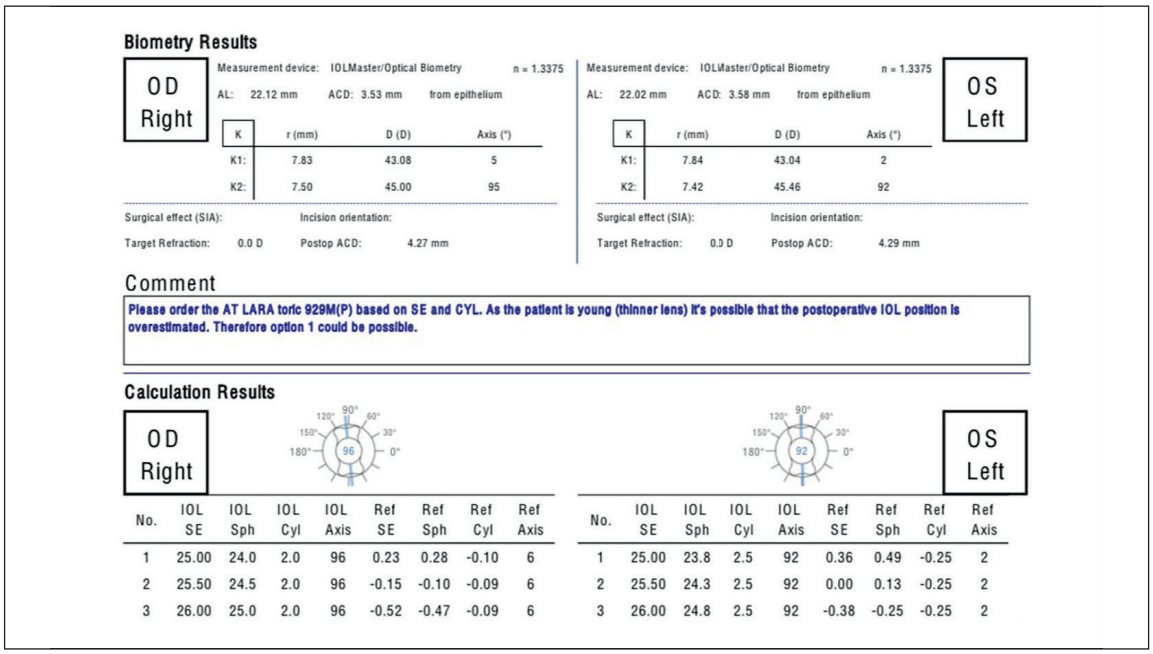
DISCUSSION

The ZEISS portfolio of IOLs encompasses a variety of lens designs that give cataract surgeons the opportunity to meet the range of goals for functional uncorrected vision postoperatively that are encountered in today's patient population. For the typical cataract surgery patient who is older than 60 to 65 years of age, I tend to prefer an AT LISA trifocal IOL (Carl Zeiss Meditec; Jena, Germany) because these patients often are interested in good uncorrected vision for reading at a shorter distance of 30 cm. The patient in this case, however, was a young adult with a priority for good intermediate vision to work at the computer, read on a tablet device, and use her cell phone. Because of its properties, the AT LARA toric 929MP IOL was an excellent choice for this patient.

The AT LARA toric 929MP IOL is a hydrophilic acrylic lens with hydrophobic surface properties. It has an aberration neutral optic with an extended depth of focus design that provides excellent visual acuity over a wide range from far to near intermediate distances and satisfactory near vision for most patients.[1] It also features patented Smooth Microphase Technology that is designed to minimize visual symptoms of halos and glare. In addition, it has advanced chromatic optics for increased contrast sensitivity. For that reason, I believe that the AT LARA may be considered for patients who are interested in presbyopia correction but who have some ocular comorbidity associated with reduced contrast, such as glaucoma, epiretinal membrane, or a history of LASIK, that creates concern about their visual quality outcome using a multifocal IOL.

The AT LARA IOL is also designed to maintain stable outcomes postoperatively. The optic features a 360° anti-PCO ring and square edge design to reduce the rate of posterior capsule opacification. In addition, its plate haptic platform creates four points of contact in the capsular bag. As reported in the peer-review literature and observed in my own clinical experience, this design confers excellent rotational stability that is critical for good visual function with a toric IOL.[2] I implant approximately 500 premium IOLs every year and have never had to perform a secondary procedure to rotate an AT LARA toric IOL.

Preoperatively, I always assess lifestyle, vision preferences, and follow strict guidelines (Holladay Report Interpretation Guideline) in order to achieve the highest quality of care. Furthermore I always ask my patients to complete the New Dell Questionnaire in order to assess their needs and expectations from surgery.



Biometry Results

OD Right

Measurement device: IOLMaster/Optical Biometry n = 1.3375
AL: 22.12 mm ACD: 3.53 mm from epithelium

K	r (mm)	D (D)	Axis (°)
K1:	7.83	43.08	5
K2:	7.50	45.00	95

Surgical effect (SIA): Incision orientation:
Target Refraction: 0.0 D Postop ACD: 4.27 mm

OS Left

Measurement device: IOLMaster/Optical Biometry n = 1.3375
AL: 22.02 mm ACD: 3.58 mm from epithelium

K	r (mm)	D (D)	Axis (°)
K1:	7.84	43.04	2
K2:	7.42	45.46	92

Surgical effect (SIA): Incision orientation:
Target Refraction: 0.0 D Postop ACD: 4.29 mm

Comment

Please order the AT LARA toric 929M(P) based on SE and CYL. As the patient is young (thinner lens) it's possible that the postoperative IOL position is overestimated. Therefore option 1 could be possible.

Calculation Results

OD Right

No.	IOL SE	IOL Sph	IOL Cyl	IOL Axis	Ref SE	Ref Sph	Ref Cyl	Ref Axis
1	25.00	24.0	2.0	96	0.23	0.28	-0.10	6
2	25.50	24.5	2.0	96	-0.15	-0.10	-0.09	6
3	26.00	25.0	2.0	96	-0.52	-0.47	-0.09	6

OS Left

No.	IOL SE	IOL Sph	IOL Cyl	IOL Axis	Ref SE	Ref Sph	Ref Cyl	Ref Axis
1	25.00	23.8	2.5	92	0.36	0.49	-0.25	2
2	25.50	24.3	2.5	92	0.00	0.13	-0.25	2
3	26.00	24.8	2.5	92	-0.38	-0.25	-0.25	2

Figure. A power calculation service from ZEISS uses a proprietary formula that can include measured posterior cornea astigmatism.

Vision outcomes following cataract surgery depend on achieving the desired refractive target. While there are multiple factors determining success, the outcome in this case and the results in a published series show excellent refractive predictability with the AT LARA IOL.[1]

I usually use the IOL power calculation tool integrated in the IOLMaster 700 for surgical planning. For toric IOL cases, the software uses the Barrett Toric formula that provides excellent refractive outcomes because it accounts for posterior corneal curvature and lens position.[3] On the advice of my ZEISS sales representative, I sent the biometry for this young patient to ZEISS for an analysis by the company's power calculation team. This service uses a proprietary formula, also available as Z CALC Online IOL Calculator, that considers posterior cornea curvature values and unique circumstances that can make patients outliers in the general cataract surgery population.

I sometimes use intraoperative digital guidance for toric IOL positioning. It was not available in this case, but through my vast experience with toric IOLs, I have found manual marking at the slit-lamp to be a very reliable method for achieving accurate axis alignment. Patients are instructed to look with the fellow eye at a distant target that is at head height. Using the rotator switch, the slit light of the slit-lamp is turned on to the steep astigmatic meridian in the orthograde position. Then, the two tips of the astigmatic meridian are marked with a marking pen, where the slit light crossed at the limbus 180° away.

CONCLUSION

Cataract surgery patients are a diverse group with respect to their ocular condition and aims for postoperative vision. In all cases, a comprehensive preoperative examination and thorough patient counselling are important to guide surgical decisions and set appropriate patient expectations.

The young adult patient in this case was interested in spectacle independence after cataract surgery, had particular needs for excellent intermediate vision, and required astigmatic correction to achieve the desired outcome. Implantation of the AT LARA toric 929MP IOL proved effective for achieving this patient's satisfaction.

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Mr Nick Kopsachilis is a Cornea Consultant Ophthalmic Surgeon and Clinical Lead in Ophthalmology at East Kent Hospitals University NHS Foundation Trust, Kent, England, where he performs complex corneal, cataract, and refractive cases. Nick has completed his training in Germany and his subspecialty training in UK's leading ophthalmic hospitals including Moorfields Eye Hospital and King's College Hospital in London. Nick has a keen interest in research and has published over 60 peer reviewed papers.

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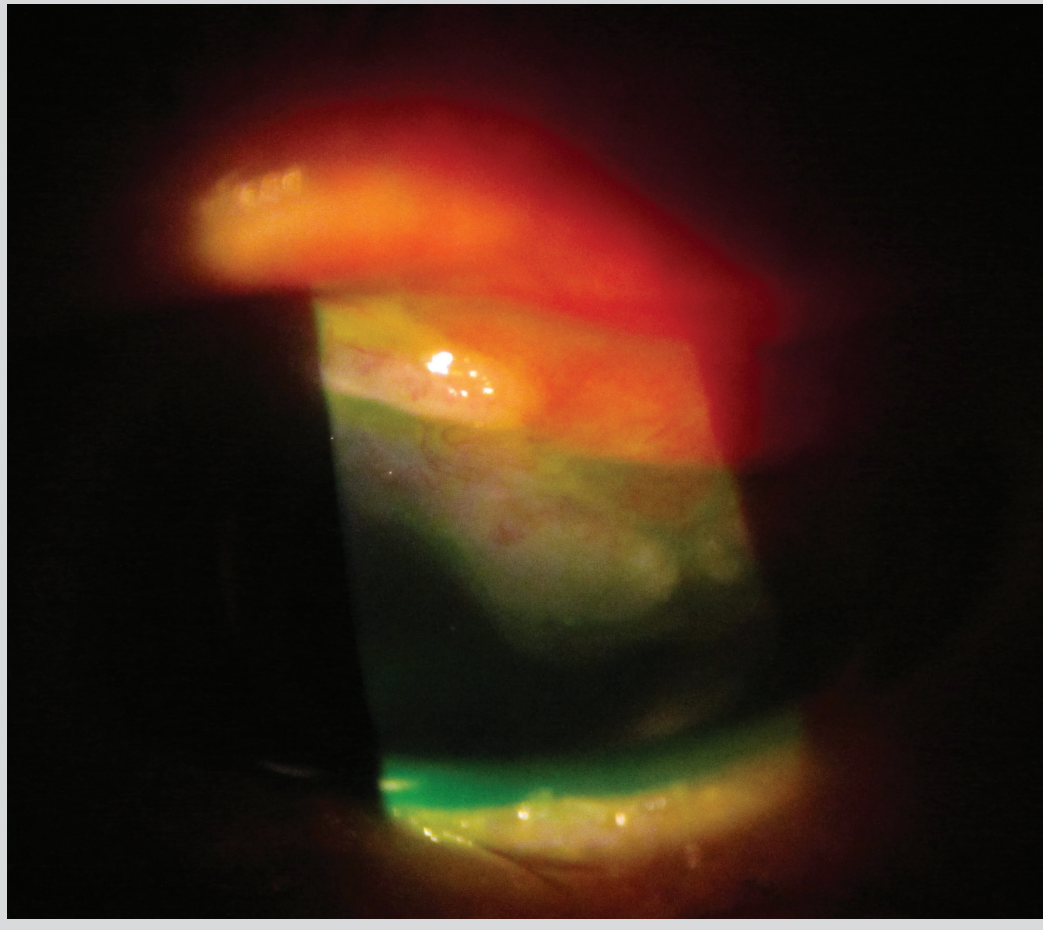

(FIGURE 1) A key step in treating ocular cicatricial disease is keeping inflammation under control.
(Photo courtesy of Dr Chan)

PEARLS

(Continued from page 23)

Symblephara forms (stage 3) and end-stage keratinisation (stage 4) develops with resultant poor prognosis. Patients need systemic immunosuppression to control the inflammation.

Patients often need a combination of long- and short-term treatments to optimise the ocular surface. Examples of such treatments are lubricants, anti-inflammatory drugs, nutritional support, management of lid margin disease, adjunctive therapy such as punctal plugs, environmental changes, elimination of agents that are toxic to the ocular surface, changes in systemic medications, and scleral contact lenses, among others.

Six steps to success

- **STEP 1** in managing patients with cicatricial disease is optimisation of glaucoma with early placement of a tube shunt and eliminating the toxicities from glaucoma medications.

- **STEP 2** involves correcting lid abnormalities such as entropion, trichiasis, exposure, keratinised lid margins, and lagophthalmos. If left uncorrected, reconstructive efforts will have a poor prognosis, Dr Chan commented.

- **STEP 3** calls for suppressing ocular surface inflammation and autoimmune responses. This can be accomplished with topical instillation of treatments or systemic therapies.

"This can take months or years to achieve," she emphasised.

Patients with chemical burns treated with inflammatory suppressive measures do much better sometimes up to a decade after the insult with this approach.

Chan noted, "have revolutionised how I manage these patients. Often, this is the point at which we can stop and not need to go on with other interventions."

Two commonly used scleral contact lenses used in Dr Chan's patients are the prosthetic replacement of the ocular surface ecosystem (PROSE, Boston Foundation for Sight) and the impression-molded EyePrintPro (EyePrint Prosthetics), a clear device that is custom fitted onto the eye surface.

Dr Chan described the case of a 21-year-old patient with monocular vision who had Stevens-Johnson syndrome and was fitted with the EyePrintPro and achieved a best-corrected visual acuity of 20/30 in his functioning eye.

"We did not have to do stem cell transplantation, avoided systemic immunosuppressive therapy, and his vision has been maintained for 10 years," she said.

- **STEP 5** involves ocular surface stem cell transplantation in which either the limbal stem cells or the conjunctiva can be transplanted for patients for whom the previous steps failed.

Symblepharon and ankyloblepharon lysis can be performed, and the fornix can be re-formed to facilitate wearing of therapeutic contact lenses.

The Boston Keratoprosthesis (Kpro type 1) can be implanted if there are contraindications to systemic immunosuppression, Dr Chan noted.

A number of types of stem cell transplants are available.

Conjunctival limbal allograft or autograft are indicated for mild/moderate disease.

Keratolimbal allografts use cadaver donors and are reserved for moderate and severe disease in the absence of suitable donor.

These grafts serve as complete barriers to conjunctivalisation, and are secured with glue and sutures and re-epithelialise between 1 and 3 months postoperatively, according to Dr Chan.

A combination approach, i.e., the Cincinnati Procedure, uses both live and cadaver tissue.

"This provides greater replenishment of goblet cells as well as a 360-degree limbal stem cell barrier," she explained.

- **STEP 6** is the final step—optical corneal transplantation. The surgical choices are deep anterior lamellar keratoplasty, penetrating keratoplasty, Kpro type 1 if the previous two fail, or Kpro type 2 if Kpro type 1 fails.

"The patient must have ongoing surveillance for glaucoma, infection, corneal melt, retinal detachment, sterile vitritis, endophthalmitis, or extrusion," Dr Chan advised.

> 'A step-wise approach with a multi-disciplinary team is needed for ocular surface reconstruction in ocular cicatricial diseases.'
>
> – Dr Clara C. Chan

Pearls

According to Dr Chan, symblepharon formation may indicate that much more is going on as in the case of a patient referred for a biopsy to rule out MMP. The biopsy uncovered squamous cell carcinoma.

Symblepharon after epidemic keratoconjunctivitis also can be associated with binocular diplopia with side gaze.

After dry eye and inflammation were addressed, the symblephara were freed and an amnion graft placed into the conjunctival defect and fornix.

The key to success is to allow conjunctival reepithelialisation before symblephara re-forms.

Keratolimbal allograft segments can be used to treat symblephara that form as the result of mechanical and iatrogenic trauma, such as orbital floor fractures, tree branch injuries, and blepharoplasty gone awry.

Dr Chan described an unusual case in which uneventful cataract surgery was complicated by symblepharon formation to the wound, postoperatively.

The patient reported eye pain, fatigue, severe weakness, abnormal complete blood count, and bone marrow biopsy that resulted in an ultimate diagnosis of leukaemia, which was the underlying cause for paraneoplastic pemphigus, which requires treatment of the malignancy and immunosuppressive therapy.

"A step-wise approach with a multi-disciplinary team is needed for ocular surface reconstruction in ocular cicatricial diseases," she concluded. "Therapeutic scleral contact lenses can delay or obviate the need for surgery."

Biopsy acute symblepharon to rule out squamous cell carcinoma and MMP. MMP can be a paraneoplastic manifestation.

DR CLARA C. CHAN, MD, FRCSC, FACS
E: *clarachanmd@gmail.com*

This article is based on Dr Chan's presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Chan has received prior honoraria or research funds from Alcon, Allergan, Bausch + Lomb, Johnson & Johnson, Labtician Thea, Santen, Shire, Tearlab, and Zeiss.

Studies target unilateral injection of a gene therapy vector for LHON

Research finds bilateral visual improvement, possibly via transfer of viral vector

By Lynda Charters;

Reviewed by Dr Patrick Yu-Wai-Man

Dr Yu-Wai-Man

Two clinical studies of Leber's hereditary optic neuropathy (LHON) showed substantial visual improvements in patients within the first year of disease. The improvements resulted from a unilateral injection of a gene therapy vector (GS010) and, remarkably, the viral vector seemed to be carried over to the untreated eye. The mechanism of action for these unexpected results needs to be clarified with further experimental work.

LHON is the most common cause of mitochondrial blindness, with a minimal prevalence of one in 30,000 people. It primarily affects young adult men, with a peak age of onset in the third decade of life. It is invariably a bilateral disorder in which the fellow eye becomes affected within 3–6 months of disease onset in the first eye. Both eyes are affected simultaneously in about 25% of patients, according to Patrick Yu-Wai-Man, FRCOphth, FRCPath, BMedSci, MBBS, PhD, an academic neuro-ophthalmologist with faculty positions at the University of Cambridge, Moorfields Eye Hospital, and the UCL Institute of Ophthalmology, in the UK.

Three primary mutations within the mitochondrial genome cause about 90% of cases worldwide, namely, m.3460G>A, m.11778G>A and m.14484T>C. The m.11778G>A mutation is the most common by far, accounting for over 70% of affected individuals. Unfortunately, most affected patients remain legally blind, with vision worse than 1.3 logarithm of the minimum angle of resolution (logMAR) or 3/60 in Snellen equivalent. Given the poor prognosis, there is an urgent clinical need to identify effective treatments for this blinding optic nerve disease.

"Gene therapy is obviously a very attractive treatment option, because the underlying pathophysiology is due to an insufficient amount of the wild-type protein," Dr Yu-Wai-Man said. "Therefore, if the defective gene is replaced, we should be able to rescue the retinal ganglion cells (RGCs), preserving function and improving the visual prognosis." He described the principles of allotopic gene expression, which involves inserting the mitochondrial gene of interest, in this case *MTND4*, into the nuclear genome with a modified viral vector. The wild-type protein produced has a specific mitochondrial targeting sequence that directs it to be imported into the mitochondrial compartment.

The use of an intravitreal injection is a big advantage for this treatment approach as it is a relatively straightforward procedure that provides direct access to the inner retina. Previous preclinical work indicates that allotopic expression is able to rescue the RGCs from the deleterious effects of the m.11778G>A mutation.

Clinical trials

RESCUE and REVERSE are two studies sponsored by GenSight Biologics. The RESCUE study included 39 subjects with the m.11778G>A mutation who have had the disease for 180 days or less. The REVERSE study included 37 subjects who had lost vision for 181–365 days. In both studies, one eye was treated with the gene therapy vector (GS010) and the contralateral eye received a sham treatment.

The primary endpoint of the RESCUE study was the difference between the GS010-treated and sham-treated eyes at 48 weeks, with the hope of finding a difference between the eyes of 15 or more letters on the ETDRS chart. Other parameters of visual function were assessed, including optical coherence tomography (OCT) imaging and patient-reported quality-of-life measures.

Among the 39 patients (31 men) in the RESCUE study, vision was lost for an average of 4 months and the average best-corrected visual acuity (BCVA) just before treatment was 1.29 logMAR. During the first 48 weeks, vision continued to decrease in both eyes of each patient to reach a nadir. The primary endpoint was not met.

IN SHORT

- ***Gene therapy is a promising treatment strategy for Leber's hereditary optic neuropathy.***

(FIGURE 1)
Researchers performed a quantitative polymerase chain reaction assay at three months to detect and quantify the viral vector DNA in various parts of the eye and brain.
(Photo courtesy of Adobe Stock/Sergey Nivens)

"Interestingly and unexpectedly, vision started to improve bilaterally from week 48 to week 96 in both the GS010-treated and sham-treated eyes," Dr Yu-Wai-Man said. "In fact, at week 48, vision had already begun recovering from the nadir." By week 96, vision in the GS010-treated eyes improved by a mean of 26.3 letters from the nadir, while, in the sham eyes, vision improved by 22.8 letters.

A responder analysis was conducted, defined as an improvement of 10 or more letters if the patient's BCVA was on-chart at its lowest point, or the ability to read a minimum of five letters if the VA was off-chart at its lowest point. Based on this definition, the responder rate was 63.2% in the RESCUE study. To put this into perspective, the responder rate was 27.9% in a retrospective natural history study of LHON.

In the REVERSE study, the same unexpected bilateral improvement in vision was also observed. Using the same responder analysis that had been conducted for the RESCUE study, 67.6% of patients achieved a clinically relevant visual recovery in BCVA.

Non-human primate study

To help determine the basis for the bilateral response, a study with non-human primates was undertaken to evaluate the biodistribution of GS010. A unilateral injection of GS010 was administered in cynomolgus monkeys. A quantitative polymerase chain reaction (qPCR) assay was performed at 3 months to detect and quantify the viral vector DNA in various parts of the eye and brain.

Three animals were treated with an injection of GS010 in the right eye and one control animal received a placebo intravitreal injection in the right eye. In the treated animals, viral vector DNA was detected in all ocular tissues, but not in the tears of the injected eyes. In the fellow uninjected eyes, vector DNA was found in the anterior segment, optic nerve, retina, optic chiasm, optic tract and the lateral geniculate nucleus, but not in the visual cortex.

There was, therefore, evidence pointing towards the transfer of the viral vector from the injected to the contralateral uninjected eyes. This observation needs to be confirmed and it remains to be determined whether there is a diffusion pathway via the optic chiasm.

Conclusions

According to Dr Yu-Wai-Man, the data from the GenSight trials showed a continuous bilateral improvement in BCVA from week 48 to week 96.

"This improvement in BCVA was significant: GS010-treated eyes had a 26-letter average increase compared with the nadir in RESCUE and a 28-letter increase in REVERSE," he concluded. "More than two-thirds of the combined number of participants in the RESCUE and REVERSE studies experienced a clinically relevant recovery from the lowest level of BCVA compared with 28% of patients in a retrospective natural history study."

DR PATRICK YU-WAI-MAN, FRCOPHTH, FRCPATH, BMEDSCI, MBBS, PHD
E: *py237@cam.ac.uk*
This report was designated Best Paper in Session at the American Academy of Ophthalmology 2019 annual meeting. Dr Yu-Wai-Man is a consultant to GenSight Biologics.

Gene therapy offers treatment for X-linked retinitis pigmentosa

Research finds the highest doses had best responses with no retinal toxicity

By Lynda Charters;

Reviewed by Dr Paulo E. Stanga

Dr Stanga

Treatment of X-linked retinitis pigmentosa (XLRP) with *AAV8-RPGR* gene therapy has been proven effective, with durable improvements in vision as early as 1 month post-treatment.

This rare disease accounts for 10–20% of RP worldwide and affects mostly males. Most cases (70%) are from *RPGR* mutations, and 60% of those are mutations in *RPGR*-ORF15, causing blindness at an earlier age than other forms (median 45 years).

Disease progression occurs in stages: nyctalopia manifests in the early stage, peripheral visual field constriction in the middle stage, and central visual deterioration and visual loss in the end stage, according to Paulo E. Stanga, MD, professor of ophthalmology and retinal regeneration, Manchester Royal Eye Hospital and University of Manchester, UK.

The RPGR mutations cause abnormal transport across the cilium, where RPGR is located, causing photoreceptor death. Dr Stanga et al. devised a treatment to correct the full length of *RPGR*-ORF15 mRNA. "We aim for yields of high expression levels that are four times higher than the expression levels of the wild-type *RPGR*," he explained.

Dr Stanga and colleagues are conducting a 2-year dose-escalation clinical trial of men ≥18 years with genetically confirmed XLRP. All had active disease that was visible bilaterally in the maculas. The study included six cohorts with different levels of affected vision: 1, better than light perception; 2 and 3, 34–73 Early Treatment Diabetic Retinopathy Study (ETDRS) letters; and 4–6, >34 ETDRS letters. The primary endpoint was the incidence of dose-limiting toxicities and treatment-emergent adverse events. Secondary endpoints were the changes in microperimetry, visual stability and changes in the ellipsoidal zone on spectral-domain optical coherence tomography.

Patients underwent a surgical procedure that included creation of a bleb followed by injection of the virus vector within the bleb.

The investigators evaluated the early effects of changes in the retinal sensitivity in the central retina using microperimetry (Maia, Centervue). The central 16 retinal loci represent 8 degrees of vision; an improvement of five of the central 16 loci equals a 30% improvement in the central visual field. An improvement of 7 dB represents five times greater light sensitivity, he explained.

IN SHORT

- ***AAV8-RPGR gene therapy for XLRP shows early responses, with increased retinal sensitivity without retinal toxicity.***

Dr Stanga reported that there was a significant improvement in microperimetry in six of the 12 treated eyes in cohorts 3–6 that occurred at 1 month after vector injection; these cohorts received therapeutic doses. Cohorts 1 and 2, which received subtherapeutic doses, showed no changes.

Cohort 3 showed a mean improvement in the mean retinal sensitivity of 5–6 dB in the central 16 retinal loci between the treated and untreated eyes. The improvement became apparent at 1 month and remained relatively stable at 3 and 6 months.

According to Dr Stanga, these changes in retinal sensitivity differed from those observed in untreated eyes in the central 16 retinal loci. The untreated eyes showed decreases in retinal sensitivity over time.

The microperimetry heat maps also reflected the changes in the treated eyes with enlargement of the sensitive areas.

The investigators also reported that they also determined that the gene therapy with *AAV8-RPGR* for XLRP was generally well tolerated.

No patients left the study and no dose-limiting toxicities were readily apparent. Transient inflammation developed in the higher cohorts that responded to systemic steroid therapy. Two ocular adverse effects were related to the procedure or drug.

DR PAULO E. STANGA, MD

E: *p.stanga@retinaspecialist.co.uk*

This article is based on Dr Stanga's presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Stanga has no financial interest in this subject matter.

Simplified model for predicting retinopathy of prematurity

Ophthalmologists can use readily available data to predict ROP in infants

By Laird Harrison

A model based on simple birth characteristics may provide new, more efficient methods for predicting retinopathy of prematurity (ROP) in infants. ROP is a sight-threatening disease common in infants with a gestational age (GA) of ≤31 weeks. It is a serious enough problem that standard procedure in Swedish hospitals is to screen all infants born before 31 weeks: a costly approach since each screening must be performed by a specially trained ophthalmologist and it is often stressful for infants. Yet, between 2008 and 2015, only 5.7% of those infants screened for ROP required treatment.

A team of researchers led by Aldina Pivodic, MSc, a researcher at the University of Gothenburg in Sweden, wanted to see if they could avoid unnecessary screenings by using a predictive model for ROP risk based on simple birth characteristics alone. They conducted a study of 7,286 Swedish infants with a GA of 24–30 weeks born between 2007 and 2017. Their findings were published in *JAMA Ophthalmology.*

The researchers used a Poisson regression, a type of statistical model, to analyse time-varying birth characteristics (e.g., postnatal age, birth weight, sex, GA) and important interactions to develop an individualised predictive model for ROP, which they titled the Digital ROP (DIGIROP)-Birth model.

They found that this model compares favourably to other models currently in use, and has the benefit of being based purely on simple birth characteristics rather than complex longitudinal neonatal data, which is often inaccessible to ophthalmologists.

Researchers validated their model internally by screening 85 infants for ROP and comparing results with those predicted by their model. The screening results were 100% consistent with those of the study. They estimated that DIGIROP-Birth could have avoided 11% of screenings in the cohort analysed.

The model was also validated against four external models—the Children's Hospital of Philadelphia ROP (CHOP-ROP), Omaha ROP (OMA-ROP), Colorado ROP (CO-ROP), and Weight, Insulin Like Growth Factor 1, Neonatal ROP (WINROP)—by applying each model to data on 1,485 American infants.

IN SHORT

- ***Simple birth characteristics, including birth weight and sex, can predict ROP as efficiently as complex longitudinal models.***

The new model performed well. Applying the same cut-off, DIGIROP-Birth and CHOP-ROP both achieved a sensitivity of 99.0%. Specificity was 48.9% for the new model versus 44.4% for CHOP-ROP. At a 97.8% sensitivity, DIGIROP-Birth had a specificity of 58.1% (22.4% for OMA-ROP). At a sensitivity of 96.8%, its specificity was 49.3%, while that of WINROP was 35.8%. At a 98.4% sensitivity, DIGIROP-Birth had a specificity of 47.9%, whereas CO-ROP was 10.5%.

In addition to developing a model based on simple birth characteristics, researchers were able to determine that some birth characteristics are more useful than others in predicting ROP treatment. Pivodic and colleagues noted that, "postnatal age rather than postmenstrual age was a better predictive variable for the temporal risk of ROP treatment".

Pivodic's team concede that their study does have some limitations. "Infants born at GA less than 24 weeks could not be included in the prediction model because of the lack of a reference algorithm for birth weight, preventing BWSDS calculations. Given the small sample size, only a simple model could be developed for these infants, resulting in low predictive ability."

However, they are confident that their model will help diagnose and treat ROP, stating: "The DIGIROP-Birth model is an accessible online application that appears to be generalisable and to have at least as good test statistics as other models that require longitudinal neonatal data, which are not always readily available to ophthalmologists".

ALDINA PIVODIC, MSC
E: *aldina.pivodic@stat-grp.se*
Pivodic did not indicate any proprietary interest in the subject matter.

Making the most of imaging in examination of paediatric patients

Technologies help determine nature of anatomic abnormalities, level of severity

By Lynda Charters;

Reviewed by Dr Phoebe D. Lenhart

Dr Lenhart

Conducting examinations in uncooperative patients is challenging, especially in children. However, anterior-segment optical coherence tomography (AS-OCT), ultrasound biomicroscopy (UBM) and corneal topography have made that task easier in the paediatric population.

These technologies are helpful in children because they can determine the nature or level of severity of anatomical abnormalities, facilitate following a pathology over time, which aids in surgical decision making and formulating the optimal management plan, and shed light on the prognostic implications, according to Phoebe D. Lenhart, MD, associate professor of ophthalmology, Emory University School of Medicine, Emory Eye Center, Atlanta, GA, USA.

AS-OCT

Dr Lenhart described the case of a 12-year-old boy with long hair that continuously hit him in the eye, causing a large corneal scar. AS-OCT noted the presence of a central nodule with a very irregular surface that involved the anterior third to half of the cornea, resulting in the diagnosis of a large Salzmann's nodule. AS-OCT in this case also aided visual rehabilitation by facilitating the customised design of a scleral contact lens that incorporated multiple OCT data points and ensured the safety of the cornea.

Orthokeratology patients can also benefit from the use of AS-OCT, as it can confirm how well the lens fits. Orthokeratology lenses have a reverse geometry to conventional contact lenses, and provide apical flattening and midperipheral corneal steepening to correct the peripheral hyperopic retinal defocus.

In the youngest patients and patients who are developmentally delayed, AS-OCT can also be beneficial in the operating room with the patients under anaesthesia. She demonstrated that, in an early attempt to use the technology, she was able to obtain a great deal of information about the depth of a pathology, which in this case were progressive corneal keloid lesions in a 1-year-old boy.

The technology also helps the surgeon gauge incisional depths as in a patient with limbal dermoid.

"This helps do the cleanest job possible and also minimises the risk of unexpected entry into the anterior chamber," she noted.

In some cases in which AS-OCT may be attempted, larger lesions can cause extensive shadowing, and the posterior cornea may not be visible. A good surgical result was obtained in a 5-year-old girl when AS-OCT was used in the operating room to determine the plan to excise the lesion, Dr Lenhart reported.

Integrated AS-OCT technology also allows surgeons to visualise anterior segment procedures through the surgical microscope.

UBM

"While UBM is not the most current technology, in some cases it is the most useful—in cases of anterior segment dysgenesis or complete corneal opacification—because it provides visualisation when visualisation is otherwise impossible," Dr Lenhart said.

Work by Nischal et al. has even demonstrated errors in clinical phenotyping in almost half of cases of anterior segment dysgenesis.[1] Cases that were misdiagnosed as sclerocornea actually had high-frequency ultrasound characteristics of Peters anomaly.

Knowledge about whether a patient has iridocorneal or lenticulocorneal adhesions may make the difference in the success rates of keratoplasty, which differ markedly according to type of anterior segment dysgenesis, she said. The success of grafts with only iridocorneal adhesions can be as high as 80–90%, while success rates are much lower in eyes with lenticulocorneal adhesions.

IN SHORT

- ***Imaging technologies can be used in tandem with other clinical findings to design the best plan possible for each patient.***

Corneal topography

Keratoconus can be easily diagnosed in most cases, but is challenging in others. Dr Lenhart recounted the an 11-year-old boy with acute hydrops in the right eye. AS-OCT showed severe corneal thinning and bowing in the left eye. In other cases, diagnosis is more difficult because the cornea in early keratoconus can appear normal during a slit-lamp examination.

Dr Lenhart said she likes to use the Pentacam (Oculus) because it allows images to be obtained quickly in young or uncooperative children. The instrument provides an axial curvature map, anterior and posterior float map, and a pachymetry map, all of which show the corneal peaks and troughs using colour coding compared with normative databases. Using the information garnered from both the corneal topography and the clinical examination, a diagnosis of keratoconus can be reached and the degree of keratoconus can be differentiated in the same patient, because different degrees of severity will determine appropriate treatment.

The axial curvature map of a 14-year-old boy showed severe paracentral steepening in the right eye (flat and steep keratometries, 65 D and 67 D, respectively). Pachymetry showed central corneal thickness of 415 µm, which was thin in the area of steepening. The anterior and posterior float maps showed paracentral bulges suggesting elevation. This boy had advanced keratoconus. He was referred for cross-linking in the left eye but had a corneal transplant in the more severely affected right eye.

Conclusion

"All of these technologies should be used together with other clinical findings to design the best plan possible for each patient. Delays in diagnosis and treatment can lead to amblyopia in younger children and visual loss," she concluded.

REFERENCE

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DR PHOEBE D. LENHART, MD
E: *phoebe.lenhart@emory.edu*

This article is based on Dr Lenhart's presentation at the American Academy of Ophthalmology's 2019 annual meeting. Dr Lenhart has no financial interests related to the topic of this report. Some of the imaging modalities used in children are off-label.

Oculus celebrates 125th anniversary

As Oculus Optikgeräte GmbH celebrates its 125th anniversary in 2020, the company marked the occasion with a special programme for representatives of the media last month at its Wetzlar, Germany, headquarters. Following a reception and company tour offering a glimpse behind the scenes, attendees enjoyed lunch and a presentation on the company's history with Senior Partner Graduate Engineer Rainer Kirchhübel.

Significant innovations noted in its portfolio include the Keratograph 5M device. The JENVIS Pro Dry Eye Report is designed to support dealing with dry eye. Measurements are presented in an easy-to-understand way.

The company also reflected on recent milestones in 2019 that included the start of construction for new manufacturing facility, Oculus Surgical Inc., in Port St. Lucie, Florida, USA. In addition, the company celebrated the world premieres of the devices Pentacam AXL Wave and Myopia Master, as well as the founding of Oculus Instruments Ltd. in Birmingham, Great Britain, for direct distribution to retina specialists in the UK and Ireland.

As the company marks the milestone at various events throughout the year, one of the early highlights was a presentation of its 125-year history at its Opti 2020 booth.

For more information, go to www.oculus.de

Exonate, Janssen collaborate to develop eye drop for retinal vascular disease

Exonate, an early-stage biotechnology company, announced that it has entered into a strategic collaboration agreement with Janssen Pharmaceuticals Inc., one of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Through the collaboration, Exonate will work with Janssen Research & Development LLC scientists to develop an eye drop treatment for retinal vascular diseases such as wet AMD and DMO by using mRNA targeted therapies. Exonate has developed small molecules that inhibit the production of pro-angiogenic vascular endothelial growth factor (VEGF) through the selective inhibition of serine/threonine-protein kinase (SRPK1)-mediated VEGF splicing.

The agreement was facilitated by Johnson & Johnson Innovation.

"I am absolutely delighted to enter this strategic collaboration with Janssen. We are looking forward to successfully developing a novel treatment for retinal neovascular diseases," said Dr Catherine Beech, CEO of Exonate.

For more information, go to www.exonate.com

LumiThera to expand research into diabetic retinopathy for Valeda Light Delivery System

LumiThera Inc. announced it has initiated further studies with the University of Wisconsin-Milwaukee to establish the use of its Photobiomodulation platform in diabetic retinopathy (DR).

"Recent research in our labs in both preclinical and clinical areas have indicated potential in treating diabetic edema with PBM," said Janis Eells, PhD, professor, University of Wisconsin-Milwaukee. "Our work shows that early PBM benefits in reducing the detrimental effects of high glucose on retinal cells and early human data is now starting to show benefits in the clinical setting."

"The results from Dr Eell's lab point to the multiple cellular benefits of treating the disease early and PBM would be an alternative approach for treatment of early disease," said Clark E. Tedford, PhD, president and CEO of LumiThera. LumiThera was granted a CE mark to commercialise the Valeda System in European Union for the treatment of ocular diseases including dry AMD.

The company previously announced that the National Institutes of Health and division of the National Eye Institute have provided a $2.5M grant to support the LIGHTSITE II multi-centre clinical trial to lead to US approval for dry AMD.

The company is enrolling two multicentre trials, one in the European Union and one in the US, for dry AMD. The entry into DME provides a second major ocular disease platform for the Valeda system.

For more information, go to www.lumithera.com

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