CORNEA

Doing justice to corneal irregularities

Simple corrective procedures increase comfort, corneal clarity

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Recycling lenticules from SMILE
Reducing risks to see benefits

RETINA
Enter a new anti-VEGF agent
Practical use shows less-frequent dosing

GLAUCOMA
Macular OCT
Useful for examining RGCs and axons

PAEDIATRICS
Efficacy of atropine
Controlling myopia progression

GENE THERAPY
Zeroing in on LHON treatment
Appears promising for increasing BCVA
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The year 2020 is sure to be a momentous one for ophthalmology. For starters, this issue shines a spotlight on recent breakthroughs in retina. With the availability of a new anti-vascular endothelial growth factor (anti-VEGF) therapy, brolucizumab is a welcome treatment for patients, and it is the first new treatment for wet age-related macular degeneration in nearly a decade, Dr Joshua Mali tells us. For Dr Arshad Khanani, perhaps the greatest impact brolucizumab will have for both patients and physicians is a substantially reduced treatment burden.

The technologies used by retina surgeons are moving ahead at a rapid-fire pace. Dozens of new devices that are smaller (and sometimes larger), shorter, brighter and lighter have recently become commercially available with the hope of making surgeries easier and more efficient. This could prove to be a critical boost to your practice.

In cataract and refractive surgery, we also focus on lenticules, noting that those obtained during the SMILE procedure are safe to use to treat other corneal disease because there was no evidence of pathogens in the tissue.

Observation may be key to learning new techniques for small-incision cataract procedures. We will show you how the complication rates associated with cataract surgeries performed by residents provide approximate information about the learning curve but not about the individual’s competency.

On the cover, we take a look at how corneal irregularities can be treated and resolved without complicated surgery in some cases. Ophthalmologists find that epithelial basement membrane dystrophy or anterior BMD, Salzmann’s nodular degeneration and band keratopathy are frequent offenders in their practices. Dr Christopher Rapuano notes there are several techniques to identify these diseases, along with treatments that do not require complex surgeries.

Dr Wallace Chamon shares with us how the posterior corneal curvature has a greater effect on the total corneal power in keratoconus eyes than previously realised.

One issue faced by many patients is inflammation, and ophthalmologists may have an new weapon in their arsenal to combat the issue. The ability of a drug to penetrate into the ocular tissues is key to controlling inflammation, and fluorometholone acetate may fill that role for physicians.

Imaging of the macula using optical coherence tomography has become nearly indispensable in glaucoma clinical practice, and it is proving particularly useful for examining the RGCs and axons, the cells that are affected by the disease.

In glaucoma devices, Prof. Gus Gazzard talks about how a microstent provides stable IOP lowering in patients with primary open-angle glaucoma who underwent cataract surgery with stent placement or a standalone procedure.

Turning to paediatrics, results from many rigorous clinical trials demonstrate the efficacy of topical atropine for reducing myopia progression. Many more studies in populations around the world are ongoing.

Dr Ken K. Nischal advises that corneal collagen crosslinking should be offered to paediatric patients and developmentally delayed adults, and can be performed safely and with good outcomes using strategies for overcoming the intraoperative and postoperative issues that are unique to these populations.

In gene therapy, we look at two anti-VEGF gene therapies currently being investigated in clinical trials of patients with exudative age-related macular degeneration. According to Dr Szilárd Kiss, initial efficacy and safety results are encouraging.

Using gene therapy for Leber’s hereditary optic neuropathy (LHON) appears highly promising for increasing the best-corrected visual acuity in this patient population. There currently is no treatment for LHON, so we will be watching this topic closely.

The new year promises to be interesting for ophthalmology, and we will continue to give you key information to help you provide the best care possible for your patients.
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Retinal specialists are ushering in 2020 with a new anti–vascular endothelial growth factor (VEGF) therapy, since the FDA approval of brolucizumab (Beovu, Novartis) for the treatment of wet age-related macular degeneration (AMD) in the last quarter of 2019.

“[Brolucizumab] is a welcome treatment for patients, and it is the first new treatment for wet AMD in about 8 years,” said Joshua Mali, MD, vitreoretinal surgeon, private practice in Sarasota, FL, USA. “There has been a meticulous process to create a drug that provides advantages over currently available therapies for wet AMD,” Dr Mali added. “[Brolucizumab] maintains robust visual gains and provides superior retinal drying compared with aflibercept, with the potential for 12-week dosing intervals.”

As background, the FDA approval was based on the results of the Phase III HAWK and HARRIER 2-year clinical trials that placed brolucizumab head-to-head with aflibercept (Eylea, Regeneron Pharmaceuticals).

The key finding was that, in both study arms, at 48 weeks and 2 years brolucizumab achieved its primary endpoint and was found to be noninferior to aflibercept regarding the best-corrected visual acuity (BCVA).

“An important point to consider is that the dosing of the two drugs was quite different, with aflibercept dosed every 4 weeks for three loading doses with subsequent extension to every 8 weeks,” according to Dr Mali, who is also founder and chief executive officer of Mali Enterprises. “In contrast, brolucizumab was dosed every 4 weeks for three loading doses and then extension to every 8 or potentially 12 weeks based on the assessment of the disease activity.”

Other relevant findings, Dr Mali pointed out, were that the visual gains achieved with brolucizumab were noninferior to those achieved with aflibercept at the two time points, but with longer treatment intervals in most patients; about 56% of patients in the HAWK trial and 51% in the HARRIER being treated with brolucizumab were maintained on 3-month dosing during the first year.

In addition, the central retinal thickness in patients receiving brolucizumab in both study arms decreased more compared with aflibercept at both week 16 and years 1 and 2, he noted.

“Retinal fluid is a critical indicator of disease activity in patients with wet AMD and how they are responding to treatment,” he said. “The presence of fluid is also an extremely important factor in the determination of BCVA.”

Safety profiles of the two drugs were similar. A difference was seen in inflammation between brolucizumab and aflibercept (4% and 1%, respectively).

Impact in clinical practice

Brolucizumab is a single-chain antibody fragment and is a smaller molecule compared with other anti-VEGF formulations that are currently available, according to Arshad M. Khanani, MD, MA, clinical associate professor, University of Nevada, Reno School of Medicine, NV, USA.

“The small size of the molecule and the 6-mg injection results in a relative molar dosing of about 12 times compared with aflibercept,” Dr Khanani said. “This is what accounted for the greater drying of the retina compared with aflibercept in the HAWK and HARRIER Phase III studies.”

For Dr Khanani, perhaps the greatest impact from brolucizumab for both patients and physicians will be a substantially reduced treatment burden. “Patients with neovascular AMD require treatment anywhere from every 4 to 8 weeks,” he said. “When considering the real-world outcomes, the gains in vision are minimal, about eight to 12 letters, compared with the results in the clinical trials. This speaks to the unmet

IN SHORT

Brolucizumab, a single-chain antibody fragment, is a smaller molecule compared with other available anti-VEGF therapies, and could decrease treatment burden.
need for durable agents that last longer to decrease the treatment burden.”

Another factor, he noted, is many patients still have active disease despite monthly injections. These patients have persistent fluid and a high need for anti-VEGF therapy. Two weeks after an injection, the retina is dry, but by 4 weeks, the fluid returns.

“Having a more potent drug to control the disease in a patient with a higher VEGF load is a big advantage,” he said.

In his clinical practice, brolucizumab fulfills two needs for patients. He starts treatment-naïve patients with the more durable brolucizumab to control the disease for a longer period. For his previously treated patients who have persistent fluid on monthly injections, their regimen can be switched to brolucizumab to dry the retina and better control the disease. Patients receive three loading doses of the drug followed by two doses at 8 or 12 weeks based on the HAWK and HARRIER trials.

“Even if patients had been previously treated for AMD, they can be treated according to this schedule, but they may not need the loading doses if the retina is dry after one injection,” Dr Khanani said.

He has not observed any significant adverse events in his patients so far, either in trials or his clinic after approval. “As with any new drug, we need to watch for any adverse events that can develop in patients who are receiving treatment,” he said.

Patients are encouraged about the increased time between treatments, thus lessening the burden on them and their families, he noted.

“We have not had a new drug for these patients since 2011 when aflibercept was approved. It is exciting for our patients and for physicians to have this new drug that is more durable than the available drugs and achieves better drying of the central retina and better control,” Dr Khanani concluded.

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Advances in the technologies used by retina surgeons are moving ahead at a rapid-fire pace. Dozens of new devices that are smaller (and sometimes larger), shorter, brighter and lighter have recently become commercially available with the hope of making surgeries easier and more efficient.

David R. Chow, MD, FRCSC, detailed several new tools for physicians to consider adding to their practices. Dr Chow is assistant professor of ophthalmology, University of Toronto, St. Michaels Hospital, Toronto Retina Institute, North York, Canada.

**Vitrectomy cutters**

A number of new vitrectomy cutters are now available to retina surgeons.

Bausch + Lomb has introduced a bi-blade dual-port vitrectomy cutter with an innovative dual-blade design that features a cut rate of 15,000 cuts/minute and is available in three gauges: 23, 25 and 27. The instrument can increase balanced saline flow by 230% and increase vitreous flow by 180%.

Bausch + Lomb has also developed the Vitesse hypersonic vitrectomy probe that boasts a new cutting concept in that the needle is mounted to a piezoelectric ultrasound transducer that vibrates harmonically, resulting in a cut rate greater than 1 million cuts/minute.

This instrument has been used in more than 200 procedures throughout the globe, covering a wide range of vitreoretinal pathologies. It can effectively remove vitreous, lens material, membranes and silicone oil.

Alcon is offering the Hypervit Dual-Blade vitrectomy probe. This cutter is capable of 20,000 cuts/minute. This instrument has a beveled-tip design, which lets it move up to 50% closer to the retinal surface; it is available in 25 and 27 gauge.

A new prototype probe, the multiport vitrectomy cutter, features an outer sleeve that can be rotated to expose three ports. “This exposure of the additional ports facilitates higher flow rates,” Dr Chow said.

**Cataract and vitrectomy systems**

Dutch Ophthalmic Research Center (DORC) announced pending upgrades to the Eva cataract and vitrectomy system.

Firstly, the footswitch has been redesigned and now has integrated laser control with improved ergonomics.

The second improvement is in the 27-gauge light output, which improves output by 65%, and a new LED module adds another 30%, which allows optimal 27-gauge light output.

The company is also marketing a 27-gauge ultra-short vitrectomy kit that includes a trocar/cannula that is 25% shorter, a vitrectomy probe that is 25% shorter and 60% stiffer, and a light pipe that is 20% shorter and 65% brighter.

NGenuity with Datafusion has been integrated into the Constellation platform (Alcon). This innovation allows real-time display of the Constellation parameters on a monitor.

**Infusion system**

Bausch + Lomb has developed the Freeflow infusion device, which is an infusion line that is placed over the infusion cannula to maximise the internal diameter of the cannula. This improves flow rates by

‘This exposure of the additional ports facilitates higher flow rates.’

– Dr David R. Chow

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**IN SHORT**

- For surgeons, the attention to detail in new technologies being offered today is allowing them to perform safer, more efficient procedures.
up to 40% and will be useful with the bi-blade vitrectomy probe to maintain infusion at high flow rates.

**Internal limiting membrane stain**

DORC is currently trying to bring Brilliant Blue dye to the US market. The dye is currently being reviewed by the FDA.

“This is potentially the first FDA-approved staining agent for identification of the internal limiting membrane [ILM] intraoperatively,” Dr Chow commented.

**Subretinal injection devices**

Three new subretinal injection devices are becoming available this year. Altaviz is releasing a microvolume injector with dose guidance; it is a self-powered stand-alone device for use in stem-cell and gene therapy.

Besides providing visual and audible dose guidance, the injector also allows Bluetooth connectivity that displays the progress of the injection and the metrics.

Another injector, from MedOne, is the Nano Cannula, a 48-gauge metal beveled-tip cannula that is specifically designed for use in subretinal procedures.

Vortex has designed the Nano Subretinal Gateway Device, which is designed to be used in the absence of a vitrectomy. This injector includes a 28-gauge needle, designed for transscleral injections, with an extendable beveled-tip 41-gauge flexible cannula that facilitates injections into the subretinal space.

**Forceps device**

Larger and smaller forceps handles have been introduced by Alcon, which have been designed for use by surgeons with large or small hands.

The Stiff Dex (Katalyst) is a 19-gauge telescoping stiffening sleeve on a 27-gauge forceps, which allows the forceps to have a much stiffer profile.

The Reddy end-grasping forceps (Bausch + Lomb) features microserrations with a long grasping platform and a window for visualisation.

The Sharkskin internal limiting membrane (ILM) forceps (Alcon) features laser-ablated microstructures—10×10×5-μm teeth—that point towards the grasping edge, which increases the kinetic friction between the forceps and tissue.

A second feature is a conforming platform that reduces by 50% the indentation force needed to grasp the ILM. Both features increase grasping ability.

**Chandelier system**

Vitreq now has the 29-gauge Spotlight directional chandelier system that uses a unique fixation system to the drape above the patient’s brow to direct a wide-view light beam with a 29-gauge trocar cannula.

**Cannulas**

A membrane-peeling cannula (Katalyst) has burrs on the lateral edges to cut the ILM and a spatula shape with active extrusion to engage and remove the ILM flap. After removing the membrane, the same cannula is used to perform an air/fluid exchange.

MedOne is reintroducing the 27-gauge VFI Cannula with a Luer lock, which is the only all-metal 27-gauge oil-injection device. It has very thin walls to maximise the internal diameter of the cannula for speedy oil injection.

A 38-gauge cannula designed by Carl Claes, MD, has a 38-gauge tapered tip that is available in 23 or 25 gauge that is used to drain or close macular holes under silicone oil with active extrusion.

**Portable laser**

The new FDA-approved Leaf Ultracompact Green Laser (Norlase) weighs 3 pounds and connects to a slit lamp without any external cables. The laser is controlled wirelessly by a tablet.

**New microscope**

Alcon is now offering the Luxor Revalia Ophthalmic Microscope that incorporates an objective lens placed above the light source, allowing enhanced depth of field, and three LED options for personalisation of the illumination quality: warm, cool or mixed white.

**Scleral depressors**

Vortex Surgical now has the EDD (external drainage and depression), a scleral depressor that includes a retractable 28-gauge needle that is 2.4 mm long and can be connected to active extrusion.

The third scleral depressor, Sclerex from Natalia Vila, is a mechanical scleral depression device that attaches to a lid speculum.

**New needle design**

Lyubomyr Lytvynchuk, MD, designed a needle to perform intravitreal injections. It has a solid tip that may require less force during injection, and a proximal injection port that may reduce the amount of cellular tissue that is dragged into the eye during injections.

**Conclusions**

An array of new technologies are available that allow retina surgeons to perform procedures more safely and efficiently, with better surgical outcomes.

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This article was adapted from Dr Chow’s presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Chow has no financial interest in any aspect of this report.
Recycling lenticules from SMILE: Reducing risks to see benefits

Proper processing of materials can result in low infection, rejection risks

By Lynda Charters; Reviewed by Dr Fengju Zhang

The use of lenticular tissue acquired during the SMILE procedure seems to be the same with a minimal risk of infection, and the risk of rejection can be reduced by using an appropriate preservation method.

Myopia has an extremely high incidence in China, and as a result, numerous patients undergo the SMILE procedure, according to Fengju Zhang, MD.

“Because of this, we have accumulated many transparent lenticules after the surgeries and they are being reused in a number of corneal procedures, such as patching corneal perforations and correcting hyperopia, keratoconus, and ectasia after LASIK,” said Dr Zhang, from the Beijing Tongren Eye Center, Beijing Tongren Hospital, and the Beijing Ophthalmology and Visual Sciences Key Lab, Capital Medical University, Beijing City, China.

However, the recycling of this tissue does not come without inherent risks. Possible infections that can take hold include herpes simplex virus (HSV), which can be latent in corneal stromal tissue for an extended period as well as bacteria, fungi and Acanthamoeba that may be lurking in the normal conjunctival sac, she explained.

Another potential problem is immunological rejection following implantation of the lenticules.

One Chinese study reported that, at the 1-year follow-up of 29 cases (53 eyes) that underwent allogeneic corneal stromal lenticule implantation to treat hyperopia, rejection of the tissue occurred in three eyes (5.66%) of two patients, Dr Zhang noted.

Clinical trial

In light of these complications, Dr Zhang and colleagues undertook a study to detect pathogens and antigens in the fresh lenticules obtained during the SMILE procedure.

A total of 167 patients who underwent the SMILE procedure from October 2018 to April 2019 were chosen randomly. Those included had no systemic diseases, no history of use of systemic hormones or immunosuppressive drugs, no ocular diseases except for a refractive error, and no history of ocular surgery or trauma. Patients had a stable refractive with no change exceeding 0.5 D annually for 2 years.

Patients also could not have used soft spherical contact lenses within 1 week, toric soft contacts and hard contacts within 2 weeks, or orthokeratology lenses within 3 months before surgery.

Any eyes with or suspected of having corneal ectasia, moderate to severe dry eye, severe meibomian gland disease, or an allergy induced by contact lenses were excluded.

SMILE lenticules were collected in 128 eyes of 64 patients with myopia. The donor specimens from each patient were divided into two groups in order to detect pathogens: specimens from 64 eyes (32 left and right eyes) and specimens from 64 eyes (32 left and 32 right); in the latter group, each specimen was divided into three pieces.

In the first group of 64 eyes, polymerase chain reaction (PCR) was performed to detect HSV-2; in the second group of 64 eyes, cultures were carried out to identify bacteria, fungi and Acanthamoeba, Dr Zhang recounted.

The investigators also undertook another experiment to identify antigens.

Lenticules were collected during SMILE from 132 eyes of 103 patients with myopia and divided into three groups of 44 specimens each: the fresh group, the −78°C glycerol preservation group, and the 0.1% sodium dodecyl sulfate (SDS) group. All specimens were subjected to immunohistochemistry, western blot analysis, transmission electron microscopy (TEM), transmittance and nanoindentation.

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Lenticules obtained during the SMILE procedure are safe to use to treat other corneal diseases because there was no evidence of pathogens in the tissue. The risk of rejection can be lowered by using the −78°C pure glycerol preservation method.
'The –78°C pure glycerol preservation is an ideal method to reduce the expression of antigen in human corneal stromal lenticules.'

- Dr Fengju Zhang

**Pathogen and antigen detection**

PCR showed negative results in all cases for detecting HSV-1 and HSV-2, bacteria, fungi, and Acanthamoeba in both patients with and without a history of contact lens wear.

Regarding antigen detection, in the fresh group, immunohistochemistry showed a positive result for detection of HLA/B/C and HLA-DR. No positive results were seen in the –78°C glycerol preservation and the 0.1% SDS groups.

Western blotting analysis reflected the immunohistochemistry findings. TEM showed collagen fibrils were very regular in the fresh group and the nuclei were intact; in the –78°C glycerol preservation group, the collagen fibrils were regular but the interiors of the nuclei were destroyed; and in the SDS group, the both elements were completely destroyed, Dr Zhang noted.

Regarding transmittance, in the fresh and –78°C glycerol preservation groups, the specimens were transparent, with average transmittance values of 89.32% and 87.94%, respectively; however, in the SDS group the transmittance value was lower at 82.09%.

The nanoindentation curves showed the highest Young’s modulus values in the fresh and glycerol groups, with values of 49.21 and 60.6 kPa, respectively, compared with 24.26 kPa in the SDS group. Human corneal stromal lenticules from SMILE have a low risk of infection for reuse, Dr Zhang said.

“HLA-I and HLA-II antigens were all expressed in human corneal stromal lenticules from SMILE, and there is a risk of transplant rejection for reuse,” she said. “An ideal method to reduce the expression of antigen in human corneal stromal lenticules is by using –78°C pure glycerol preservative.”

**Diving deeper**

In discussing the negative pathogenic findings of the study, Dr Zhang said the study subjects were young and healthy with no systemic or ocular diseases.

“Previous studies have reported that HSV-1 was detected mainly in the limbal tissue, while the corneal stromal lenticules were located within the central 6.5-mm diameter of the anterior stroma, which brings us to an advantage of the SMILE procedure,” she said.

**‘WIDEFIELD’ IMAGING**

The International Widefield Imaging Study Group has released recommendations for classifications and guidelines for defining “widefield” and “ultra-widefield” imaging. Though ultra-widefield is the new standard of care for fundus imaging in patients with retinal vascular diseases, no standardized definition existed.

Go to Europe.OphthalmologyTimes.com/ComingTermsImaging

**KEYS TO ASSESSING TRUE CROSSLINKING OUTCOMES**

A novel method of noninvasively evaluating the outcomes after crosslinking is under development. The software that can be plugged into existing topographers will become commercially available in the near future. “We have numerous topographers available, but what are we missing?” asked Gairik Kundu, MBBS, MS.

Go to Europe.OphthalmologyTimes.com/KeysCrosslinking

**SIMULATOR HELPS PATIENTS ‘SEE’ BEFORE IOL IMPLANTATION**

A visual simulator that provides patients the experience of vision with multifocal IOLs (mIOLs) before actual implantation may help to manage patient expectations, according to Dr Susana Marcos. This innovation arose out of the scaling down of technologies that originated in astronomy into a system useful to ophthalmologists.

Go to Europe.OphthalmologyTimes.com/SeeSimulator
Keys to manual small-incision cataract surgery techniques

ICO-OSCAR assesses novice surgeon skills to learn, perform particular tasks

By Lynda Charters

The number of surgeries performed during residency training varies from institute to institute, and this can raise the question: How many surgeries are adequate to ensure patient safety and good outcomes after cataract surgery?

The complication rates associated with cataract surgeries performed by residents provide approximate information about the learning curve but not about the individual’s competency. The International Council of Ophthalmology’s Ophthalmology Surgical Competency Assessment Rubric (ICO-OSCAR) facilitates an objective assessment of the surgical skills of a novice surgeon for performing a particular surgical task.

Rajesh Vedachalam, MBBS, highlighted the results obtained using the ICO-OSCAR in an analysis of the learning curve. Dr Vedachalam, from the Department of Cornea, Aravind Eye Care, Puducherry, India, presented the study findings on behalf of Aravind Haripriya, MBBS.

Observation is key
Dr Vedachalam pointed out that more manual small-incision cataract surgeries (MSICS) are performed in India during residency training compared with phacoemulsification, and are associated with lower complication rates (1.75% versus 8.2%) among novice surgeons.

Dr Haripriya and colleagues conducted a prospective cohort study in which they sought to predict the average number of surgeries required for a resident to gain competency in MSICS using ICO-OSCAR. All residents who started residency training at the Aravind Eye Hospital were included. The first 15 procedures and every tenth case thereafter were assessed using ICO-OSCAR, Dr Vedachalam explained.

The ICO-OSCAR scoring tool contains 20 objectives, and scores each surgical step. The total score is then evaluated. In this study, all surgical complications were documented during the step at which it occurred. A form was completed regarding various factors that may have affected the surgical outcome to determine their effect on the learning curve. The investigators compared the preoperative and postoperative visual acuities for significant differences, Dr Vedachalam explained.

Twenty residents (mean age, 27.8 years) were included in the study, and two were excluded for excessive absences. Of the 18 remaining (11 women, seven men), 15 had previous surgical experience with other surgeries.

‘The positive factors predictive of higher ICO-OSCAR scores are female gender and previous general surgery experience.’

– Dr Rajesh Vedachalam

A total of 2,021 surgeries were performed between September 2016 and May 2018. Surgical complications developed in 62 (3.06%) procedures, with posterior chamber opacification and zonulysis the most common complications.

“This complication rate is much lower than in other studies,” Dr Vedachalam pointed out.

Twenty-eight (1.38%) patients underwent second surgeries. The mean best-corrected visual acuity at follow-up was 20/20.

Positive factors in the surgical outcome
Two factors were found to have a positive impact on the surgical outcome: watching videos of MSICS or observing surgeons perform before operating and the confidence level or mood of the surgeon.

Other influential factors included wet lab practice

IN SHORT

» Factors that positively affect the performance of residents during surgery are using a simulator preoperatively and maintaining a positive outlook.
performed on a simulator and the laterality of the patient’s operated eye.

When the relationship between the ICO-OSCAR score and potential predictive factors was analysis, the number of surgeries performed and simulator practice both had significantly higher scores ($P<0.001$ for both comparisons).

‘Simulator practice before surgical training is correlated with better scores.’

– Dr Rajesh Vedachalam

Other positive factors were previous general surgical experience ($P=0.002$) and female gender ($P=0.04$). Eye laterality had no role in improving the OSCAR score, a finding that was in contrast to other studies.

“We also found that surgeons who performed micro hand movement activities, such as those during piano playing or eating with chop sticks, did not perform better during surgery,” Dr Vedachalam said.

The research indicated 119 surgeries were needed to reach competency to achieve a competency score of 80. For a score of 90, 172 surgeries were required.

Other such studies have assessed the numbers of surgeries required as indicators of experience and the complication rates, and the reoperation rate, but did not assess surgical competency of the surgeons or the learning curve, Dr Vedachalam noted.

“We believe that the measure of competency as measured by the objective ICO-OSCAR in each surgical step and the surgeons’ ability to perform surgeries independently are important and that assessment of competency and learning curve is a strength of our study,” he said.

Dr Vedachalam pointed out that using the ICO-OSCAR tool, a minimum of 119 MSCIS surgeries is recommended to achieve competence with a score of 80 and above.

**Conclusion**

“The positive factors predictive of higher ICO-OSCAR scores are female gender and previous general surgical experience,” he concluded. “Simulator practice before surgical training is correlated with better scores. Residents find that observing surgeries and being in the right frame of mind are useful for better surgical performance.”

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This article is based on Dr Vedachalam’s presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Vedachalam has no financial interest in any aspect of this report.
Corneal irregularities: Detection and treatment to avoid complex surgery

Simple corrective procedures increase patient comfort, corneal clarity

By Lynda Charters; Reviewed by Dr Christopher J. Rapuano

For many ophthalmologists, epithelial basement membrane dystrophy (EBMD) or anterior BMD, Salzmann’s nodular degeneration, and band keratopathy are frequent offenders in clinical practices. Today, there are numerous techniques to identify these diseases, along with treatments that do not require complex surgeries.

**EBMD**

EBMD is characterised by reduplicated epithelial basement membrane that causes loose adherence of the corneal epithelium to the stroma leading to recurrent painful erosions and/or irregular astigmatism on slit-lamp examination that may or may not be apparent on corneal topography or K readings.

However, clinicians should be alert to irregular astigmatism, according to Christopher J. Rapuano, MD, because it affects vision. In addition, if a cataract or refractive surgery is being considered, it can result in inaccurate K readings and incorrect IOL power calculations, affect the postoperative quality of the vision, and worsen postoperatively, causing significantly decreased vision.

When diagnosed postoperatively, these issues become the surgeon’s problem, noted Dr Rapuano, chief of the Cornea Service, Wills Eye Hospital, and professor, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, USA.

Detecting EBMD can be tricky in some cases, but Dr Rapuano explained that fluorescein staining will often make it readily apparent. When deciding whether to treat, he shared some pearls.

“If there was no negative staining or irregularity on topography or K readings centrally, then the problem probably does not require treatment,” he explained. “Consider treating if the patient is symptomatic or awaiting cataract or refractive surgery and wait about 6 weeks before rechecking the biometry twice to ensure the stability.”

Treatment can consist of epithelial debridement alone, or debridement in conjunction with diamond burr polishing or excimer laser phototherapeutic keratectomy (PTK). The process of debridement includes removal of all loose or irregular epithelium and basement membrane with a cellulose sponge or blade.

Dr Rapuano said he likes to perform diamond burr polishing, which begins with epithelial debridement. He then uses a 5-mm diameter diamond-dusted burr to polish Bowman’s layer uniformly over the entire cornea for about 5–6 seconds to ensure that all reduplicated basement membrane has been removed.

According to Dr Rapuano, some patients who undergo this procedure may have transient haze postoperatively that can be alleviated with steroids.

The key when performing excimer laser PTK, after debridement, he advised, is treating the entire epithelial defect with a uniform ablation of only about 5 μm.

**Salzmann’s nodular degeneration**

This pathology presents a creamy white mild to moderately elevated lesion often in the peripheral cornea, but occasionally is seen centrally. It can be associated with EBMD and can cause dry eye symptoms and irregular astigmatism despite a peripheral location.

Dr Rapuano advised treating in the presence of any centrally located irregular astigmatism. If the patient is awaiting a cataract or refractive surgery, he also suggested waiting about 6 weeks after treatment before rechecking the biometry before any surgery.

The treatment options include lamellar keratectomy using a blade with or without diamond burr polishing. In some cases, he noted, the nodules will easily peel off of Bowman’s layer and leave a
smooth surface. In cases in which the underlying stroma remains unsmooth, he performs excimer laser PTK with or without mitomycin C (MMC).

If PTK is performed, he usually uses MMC. During this procedure, he advises using a blade to remove the nodules and subepithelial fibrosis and then smooth the surface with PTK. MMC 0.02% should be applied on an 8-mm sponge for 60 seconds and then irrigated with 30 cc of saline.

**Band keratopathy**

This pathology, which appears as a white calcium deposit, is frequently related to chronic inflammation but may be idiopathic.

If located centrally, the vision can be affected. However, if elevated and in the periphery vision also can be affected. In cases when it is elevated or irregular, it can cause patient discomfort.

Dr Rapuano advised performing a workup to determine the etiology.

The treatment is ethylenediaminetetraacetic acid (EDTA) chelation. The key point in this procedure is removal of the epithelium over all of the calcium using a number 15 blade or Tooke knife.

The presence of any epithelium will prevent absorption of the EDTA. Diluted EDTA 3–4% should be applied to the calcium on a cellulose sponge or cotton-tipped applicator for 10–45 minutes until the calcium has dissolved.

“Corneal irregularities and opacities are common and they can affect comfort, clarity and corneal curvature, making it especially important to diagnose before cataract and refractive surgeries,” Dr Rapuano concluded.

“There are numerous techniques to identify them, and there are excellent treatment options for clinically relevant pathology.”

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This article is based on Dr Rapuano’s presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Rapuano has no financial interest in any aspect of this report.
A relationship exists between the posterior and anterior surfaces of the cornea, such that the posterior surface diminishes the power of the total cornea.

A ratio is believed to exist between the anterior and posterior powers of the cornea that varies from 0.8 to 0.9 in normal eyes. In keratoconus, a progressive eye disease, the normally round cornea thins and begins to bulge into a cone-like shape. The cone shape of the cornea deflects light as it enters the eye on its way to the retina, causing distorted vision in patients.

Wallace Chamon, MD, explained that the ratio is used to estimate an artificial refractive index for the cornea that compensates for the posterior surface of the cornea with its real refractive index of 1.376. Smaller indices are used to compensate for the negative power of the posterior that ranges from 5 to 7 D.

However, in order to calculate the ratio in the refractive indices, some presumptions must come into play, namely, that the factor between the two surfaces is a constant factor in all kinds of eyes, regardless of whether they are normal or not and the cornea has a constant thickness, said Dr Chamon, adjunct professor of ophthalmology, Department of Ophthalmology and Visual Sciences, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil, and volunteer clinical faculty, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, IL, USA.

“With these assumptions, there is good accuracy in determining the total corneal power by measuring only the anterior surface of the cornea,” he said.

While that last statement has been a consistently held belief, Dr Chamon and his colleagues challenged both presumptions. He was joined in his research by Rafael Kobayashi, MD, Felipe M. C. Taguchi, MD, and Ibraim V. Vieira, MD.

Regarding keratoconic eyes, Dr Chamon pointed out that the progression of thinning of the cornea differs from that in normal eyes and that progression is more aggressive toward the apex or the thinnest part of the cone.

According to Dr Chamon, when comparing maps of thinning progression, ophthalmologists can see clearly that a keratoconic eye does not follow the progression of thinning in normal eyes.

“However, if we assume that the keratoconus begins with the thinning of the cornea and leads to progression to a steeper cornea, we have to assume that the ratio has changed because with corneal thinning, the posterior curvature will increase.”

‘Keratoconic corneas present a different anterior:posterior ratio, with a greater effect of the posterior interface.’

– Dr Wallace Chamon

Pointing to examples

As an example, Dr Chamon demonstrated that in a normal eye based on Gullstrand’s theory, the anterior surface has 7.7 mm of curvature, leading to 43.05 D using the refractive index of 1.3315. The posterior cornea would have 6.8 mm of curvature.

In contrast, in a keratoconic eye with an anterior surface curvature of 7.7 mm, the posterior curvature would be even steeper at 6.00 mm. In the normal eye, the ratio would be 0.883 compared with 0.857 in the keratoconic eye.

The posterior corneal curvature has a greater effect on the total corneal power in keratoconus eyes than previously realised.
“This means that in keratoconus, the posterior corneal surface theoretically has a much higher effect than it does in normal eyes,” Dr Chamon said.

To determine whether their theory was correct, Dr Chamon and colleagues analysed every patient who underwent a Scheimpflug examination using the Pentacam in three Brazilian institutions from October 2012 through January 2019.

After duplicate examinations of the same eyes were excluded, ultimately 33,658 examinations were unique. Of those, the examinations that were considered unreliable, abnormal, or performed after a corneal surgery were removed. The final number of unique examinations was 24,060. Of these, 16,192 were normal, and 7,868 were keratoconic. The Pentacam provided nine classifications of the keratoconic eyes from normal to grade 4.

Dr Chamon showed that, in normal eyes, the average anterior-posterior ratio was 0.82. In those with possible keratoconus, no difference was detected between normal eyes and possible keratoconus. As the keratoconic grades increased, the ratios ranged from 0.82 down to 0.79 in grades 3–4 as expected, and 0.80 in grade 4 probably because of the small number of patients, he noted.

**Conclusion**

Dr Chamon concluded that the anterior-posterior ratio has been well determined for normal corneas. “Keratoconic corneas present a different anterior:posterior ratio, with a greater effect of the posterior interface,” he said. “The more advanced the keratoconus, the greater the influence is. Formulas that estimate the total corneal power and, therefore, astigmatism, should not be used in eyes with keratoconus.”

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This article is based on Dr Chamon’s presentation at the American Academy of Ophthalmology 2019 annual meeting. Dr Chamon disclosed holding patents related to crosslinking, wavefront systems, and biomechanics, none of which are related to the subject of this report.
Fluorometholone acetate: More than meets the eye

In ongoing battle to control inflammation, penetrating the ocular tissue is key

By Lynda Charters; Reviewed by Dr Beeran Meghpara

One issue faced by many patients is inflammation, and ophthalmologists may have an new weapon in their arsenal to combat the issue.

The ability of a drug to penetrate into the ocular tissues is key to controlling inflammation, and fluorometholone acetate may fill that role for physicians.

“All fluorometholones are not the same,” noted Beeran Meghpara, MD, and with good reason.

Fluorometholone is the active steroid in formulations used to treat ocular inflammation; however, it is what doesn’t meet the eye that makes the difference, i.e., the vehicle.

If the vehicle prevents the drug from optimally penetrating through the ocular surface into the underlying tissue, the drug will not be as effective as if the penetration was at its potential peak.

According to Dr Meghpara, fluorometholone acetate ophthalmic suspension (Flarex, Eyevance Pharmaceuticals) is proving to be a key option in his practice. He is co-director of Refractive Surgery at Wills Eye Hospital, and clinical assistant professor of ophthalmology, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, USA.

“The acetate in the formulation makes the drug more lipophilic, which facilitates better penetration into the ocular surface,” he noted. It results in a more potent treatment effect compared with a regular fluorometholone, i.e., without acetate, with the same side effect profile.

The side effects of the steroids used to treat ocular diseases have historically been the greatest concerns. These include elevated IOP leading to glaucoma, a higher incidence of cataract formation, worsening of concurrent infections, and delayed healing.

“Generally speaking, the higher the potency of the steroid, the more likely it is that side effects will develop and that they will be worse,” Dr Meghpara explained.

Fluorometholone acetate, however, is considered one of the safer steroids. When side effects do occur, it is with a lower frequency and they are less severe.

Calming ocular surface disease

Probably the most common ocular surface disease of patients presenting to a cornea practice is dry eye syndrome, which results from inflammation of the ocular surface, tears and lacrimal glands.

“The goal is to break the cycle of inflammation,” Dr Meghpara said.

When treating these patients over the long term, among some “go-to” drugs he notes as safe for chronic use are cyclosporine ophthalmic emulsion 0.05% (Restasis, Allergan), lifitegrast ophthalmic solution 5% (Xiidra, Novartis), and cyclosporine A ophthalmic solution 0.09% (Cequa, Sun Pharmaceuticals).

‘Fluorometholone acetate provides the potency of a strong steroid, but the drug has the side effect profile of a milder steroid...The drug provides the best of both worlds.’

– Dr Beeran Meghpara

“These are great drugs for treating dry eye,” Dr Meghpara said. “However, the beneficial effects of these drugs require time to build up.”

Until those beneficial effects become apparent, he uses fluorometholone acetate for the short term in combination with one of the long-term therapies to obtain more immediate relief for his patients.
“This approach calms the inflammation, and the patients feel better and often see better,” he said.

For dry eye, Dr Meghpara prescribes fluorometholone acetate twice daily for about 4–6 weeks. By that time, the benefits of the chronic-use medication are beginning to kick in.

Allergic conjunctivitis is the second most common chronic offender seen in cornea practices, especially in the spring and fall when symptoms tend to become more severe.

In these patients, a short controlled course of fluorometholone acetate can calm the ocular surface and provide relief from the characteristic symptoms of tear, itching, and discomfort.

Giant papillary conjunctivitis—also known as contact-lens-induced papillary conjunctivitis—tends to appear less often in clinical practice, but it is a common complication associated with the wearing of contact lenses.

Despite the lower incidence, these patients seek treatment and can benefit from short-term treatment with fluorometholone acetate, which allows them to resume wearing their lenses more quickly.

Steroids generally are not intended for use while wearing contact lenses. Other less common ocular surface disorders include episcleritis, generally a self-resolving condition that responds rapidly to treatment with fluorometholone acetate, and marginal ulcers. The latter, while not technically an infection, is an inflammatory response to staphylococcal antigens on the eyelid surface.

Dr Meghpara noted that a steroid in addition to an antibiotic is helpful in this scenario.

In blepharitis, a related condition, the inflammation can spill over onto the ocular surface and cause blepharoconjunctivitis or blepharokeratoconjunctivitis, also responsive to a topical steroid.

“Fluorometholone acetate provides the potency of a strong steroid, but the drug has the side effect profile of a milder steroid,” he concluded. “The drug provides the best of both worlds. I am confident starting treatment with the drug and confident it is going to work. I am concerned about side effects, but not greatly.”

DR BEERAN MEGHPARA, MD
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Imaging of the macula using optical coherence tomography (OCT) has become nearly indispensable in glaucoma clinical practice.

Julia A. Rosdahl, MD, PhD, associate professor of ophthalmology, Duke University, Department of Ophthalmology, Chapel Hill, NC, USA, demonstrated the importance of the technology for her patients, describing the case of a 69-year-old Caucasian man who she last saw 5 years earlier, and who did not want treatment at that time. After another physician recommended treatment, he returned for a second opinion for his normal tension glaucoma.

The patient had visual acuities of 20/25 in both eyes and intraocular pressures of 13 mm Hg in both eyes (untreated). He had a paracentral visual field (VF) defect that had not worsened measurably over the 5 years. Progressive retinal nerve fibre layer (RNFL) thinning was seen on the optical coherence tomography (OCT) maps and corresponded to the VF defect. The glaucoma appeared to have progressed. The patient was skeptical.

Macular OCT showed inferior thinning and, as Dr Rosdahl pointed out, progression analysis showed two characteristic arcuate-shaped areas of progression. With this information, the patient was convinced of his progressive disease and agreed to treatment.

Preserving the RGCs

Most retinal ganglion cells (RGCs) are in the macula, in the inner three layers of the retina (RNFL, ganglion cell layer, inner plexiform layer). These layers are collectively termed the ganglion cell complex and account for 40% of the macular thickness. Once the RGCs are affected, blindness ensues. Measurement of the RGCs is useful to assess glaucoma because the RGC numbers in the macula are relatively consistent amongst the population, Dr Rosdahl explained.

More RGCs are present in the central retina than in the peripheral retina. Therefore, the numbers of RGCs sampled during automated VF testing varies considerably between the periphery and central tissues, with VF points in the periphery representing smaller numbers of RGCs than VF points centrally.

Commercially available OCTs have the glaucoma protocol for image acquisition and analysis, all of which show high levels of structure/function correlation in patients with glaucoma. Dr Rosdahl noted that the devices appear to be more helpful in patients with a mean deviation better than –10 decibels on automated VF testing. This is not a cut-off, though, as she showed an example where the macular OCT scans helped in a patient who could no longer perform automated VF testing.

“The main difference among the machines is based on the differences in the areas of the retina sampled and the layers that are included in the analysis,” she said.

All machines sample areas of different sizes. The Cirrus 5000 (Carl Zeiss Meditec) uses data from an elliptical annulus 4-mm high and 4.8-mm wide that is centred on the fovea, the Spectralis (Heidelberg Engineering) uses data obtained from a 10×10-mm square, the 3D OCT-2000 (Topcon Medical Systems) from a 7×7-mm square, the Avanti widefield OCT (Optovue) a 7-mm circle centered 1 mm temporal to the fovea, and the RS-3000 Advance 2 (Nidek) a 9×9-mm square.

All machines have different macular analysis protocols. The Cirrus provides a thickness map of the ganglion cell and inner plexiform layers; the machine also has a deviation map and table that compare the obtained thickness to an age-matched control. Horizontal OCT scans of the fovea in each eye is another device feature.

The Spectralis provides a total retinal thickness map and two plots that show the asymmetry between
the patient’s eyes and compare the superior and inferior hemispheres in one eye. The Spectralis offers the Glaucoma Module Premium Edition, allowing segmentation of the individual retinal layers. The 3D OCT-2000 instrument produces thickness and deviation maps of the ganglion cell layer.

The Avanti reports on the ganglion cell complex thickness as a percentage of the age-matched control. The scans of the right and left eyes are shown with summary tables. The RS-3000, similar to the Avanti, shows the thicknesses of the three layers (RNFL, ganglion cell layer and inner plexiform layer). The report includes thickness and deviation maps.

**Pearls for using OCT in glaucoma**

When using the glaucoma protocol, some noteworthy abnormalities may appear that are in fact not glaucoma. She described the case of a patient with diffuse macular thinning but an intact RNFL seen using the Cirrus. This would promote physicians to look for other non-glaucomatous disorders.

In patients with age-related macular degeneration, the maps of the macula are irregular and should be used with caution after glaucoma. In patients with retinal vein occlusions, all layers of the retina will become thinner, not just layers containing ganglion cells.

In non-arteritic ischemic optic neuropathy, thinning of the retina occurs in affected eyes.

**Conclusion**

Dr Rosdahl concluded that macular OCT is useful for examining RGCs and axons, the cells that are affected by glaucoma.

“The currently available devices differ in the areas sampled as well as the layers that they assess,” she said. “However, all of the devices perform similarly with respect to structure and function correlations.”

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Dr Rosdahl has no financial interest in any aspect of this report.
The international SPECTRUM registry recently completed enrollment of patients for the Hydrus Microstent (Ivantis Inc.), a microinvasive glaucoma surgery device used to treat patients with mild to moderate primary open-angle glaucoma. In the United States, the device is indicated for placement in combination with cataract surgery or as a stand-alone procedure.

The SPECTRUM registry currently includes almost 3,000 eyes enrolled; of these, 700 surgeries in which the Hydrus Microstent was implanted were stand-alone glaucoma procedures. Seventy percent of the patients have completed the 3-year follow-up examination.

At the 3-year time point, probably the most important findings are not only the marked stability of the intraocular pressure (IOP) over the long-term following placement in the eye but also the improvement following the wearing off of the effect of phacoemulsification in the patients who underwent the combination procedure, said Prof. Gus Gazzard, FRCophth MA, MBBChir, MD.

Prof. Gazzard, professor of ophthalmology University College and consultant ophthalamic surgeon, Moorfields Eye Hospital, London, said patients seem to have stable pressures out that far and beyond that point.

“I have been implanting the microstent for several years and, thus far, have implanted between 250 and 300 of the devices,” he said. “The device provides great pressure control and it may even be greater than we are seeing with alternative devices.”

He emphasised that the microinvasive glaucoma surgery (MIGS) effect in patients implanted with the microstent in combination with cataract surgery seems to be increasing with time as the phaco effect wears off.

“The data are both reassuring and powerful because they show that the Hydrus effects are increasing, which is both surprising and gratifying,” he explained.

The key to this control may be the manner in which the implantation process modifies Schlemm’s canal.

This microstent, which lives up to its name in that it is the size of an eyelash, focuses on the natural outflow system of the eye with a trimodal mechanism of action. A large opening is created in the trabecular meshwork, the canal is dilated and scaffolded, which increases the cross-sectional area of the outflow system, and about 90° of the outflow system is covered.

“What is exciting for me is that the microstent keeps the canal open, it does not simply obtain access to the physiologic Schlemm’s canal,” Prof. Gazzard said. “The fact that there is scaffolding dilatation of the drainage duct provides more robust long-term pressure lowering.”

Practically speaking, he continued, surgeons can be certain that they have achieved access to the canal and that there is viable communication between the anterior chamber and the natural outflow channels. Other mechanisms and devices may not access the natural drainage channels and there is no real certainty of the correct placement of the devices.

Recent reported results
Results achieved with the microstent were presented at the 2019 meeting of the American Academy of Ophthalmology.

In the Horizon trial, which compared pure phacoemulsification with phacoemulsification and Hydrus Microstent placement and cataract extraction, found that at 3 years, which is the longest outcome reported with a MIGS device, the microstent enhanced the IOP lowering achieved by cataract surgery alone.

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A microstent provides stable intraocular pressure lowering in patients with primary open-angle glaucoma who underwent cataract surgery with stent placement or a stand-alone procedure.
“There was persistent, maintained, greater pressure lowering with the Hydrus device compared with only cataract extraction,” Prof. Gazzard said. “Fewer drops were used and the procedure was seen to be very safe.”

Another noteworthy finding was that the rate of trabeculectomy decreased with the use of the microstent. In the control arm of the trial, 3.9% of patients went on to trabeculectomy because of glaucoma progression compared with 0.6% in the treatment arm, which Prof. Gazzard described as a robust clinical outcome. The endothelial cell count showed a positive result in patients who had completed 4 years of follow-up.

The full results of the Horizon trial will be released in the spring of 2020, with more to follow in 2021.

**Other considerations**

Placing the Hydrus is a safe procedure with low risk of adverse events. Prof. Gazzard reported no problems with chronic inflammation, allergy, obstruction, and uveitis in his patients.

Outside of the US, the microstent can be placed in patients with angle closure glaucoma, uveitis, trauma, congenital anomalies and neovascular glaucoma. In the US, the stent is limited to patients with mild to moderate primary open-angle glaucoma in conjunction with cataract surgery.

“The results provide a glimpse into what the future of MIGS in the US might look like once the indications are expanded. It also speaks to how important following patients is over the long term,” said Dave Van Meter, president and chief executive officer of Ivantis.

**SPECTRUM registry results**

The 3-year results reflect the findings of the microstent in more than 900 eyes, in more than 200 of which the microstent was implanted during a stand-alone procedure. These results are likely indicative of what to expect in 2020 from the US results.

The patients in the Australia registry had the full spectrum of glaucoma, ranging from very mild disease that was addressed with the microstent in conjunction with cataract surgery to patients with moderate disease that was refractory to medical therapy who received the microstent as a stand-alone procedure and finally to severe cases for which conventional surgery was unsuccessful and required placement of the microstent during a stand-alone procedure. More than 70% of the eyes completed the 3-year follow-up evaluation.

When placed in the eye in conjunction with cataract surgery, the microstent achieved an IOP decrease in excess of 20% with discontinuation of all anti-glaucoma medications.

When positioned during a stand-alone procedure, the microstent achieved in a mean IOP decrease of approximately 30% and all anti-glaucoma medications were discontinued.

The average IOP achieved in all patients was 15 mm Hg or less in both the combination cataract surgery and standalone treatment groups.

**Aerie provides marketing authorisation updates**

Aerie Pharmaceuticals has announced that the European Commission (EC) granted a marketing authorisation for netarsudil ophthalmic solution 0.02% (Rhokiinsa) for the reduction of elevated IOP in adult patients with primary open-angle glaucoma or ocular hypertension.

“The receipt of an EC marketing authorisation . . . is an important milestone for Aerie as it once again demonstrates the potential value of Aerie’s netarsudil franchise at an international level,” said Vicente Anido Jr., PhD, chairman and chief executive officer at Aerie Pharmaceuticals, in a prepared statement.

The marketing authorisation is valid in all 28 countries of the European Union, plus Iceland, Norway, and Liechtenstein, according to the company.

The company also announced that the European Medicines Agency (EMA) has accepted for review the marketing authorisation application (MAA) for netarsudil and latanoprost ophthalmic solution 0.02%/0.005%. (Roclanda.)

The product is currently marketed as Rock-latan in the United States, where it is indicated for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension.

An opinion from the EMA’s Committee for Medicinal Products for Human Use on the MAA for Roclanda is expected in late 2020, according to the company in a prepared statement.

“As EMA review continues of the Roclanda MAA, we expect to complete and analyze our Mercury 3 study in the second half of 2020,” Dr Anido added.
Efficacy of atropine for controlling myopia progression in children

Range of unanswered questions may be addressed by ongoing research

By Cheryl Guttman Krader; Reviewed by Dr Donald Tan

A n abundance of evidence from randomised, controlled clinical trials supports the use of topical atropine to prevent myopia progression. Study results also show that using a low dose of atropine minimises adverse effects and myopic rebound after treatment discontinuation. In addition, the findings indicate that the pharmaceutical formulation affects efficacy, said Donald Tan, MD.

Now, research in this area is continuing and is investigating not only the use of atropine for preventing myopia progression, but also whether it can prevent or delay the onset of myopia.

Dr Tan is adjunct professor in ophthalmology, Duke - National University of Singapore Medical School, and Visiting Senior Consultant, Singapore National Eye Centre, Singapore. He previously served as Director of the Singapore Eye Research Institute (SERI) and the Singapore National Eye Centre.

Over a period of two decades, the SERI completed five randomised controlled trials on myopia progression involving approximately 1,900 children, including two studies investigating atropine [ATOM1 (Atropine for the Treatment of Myopia) and ATOM2]. Now, SERI is conducting ATOM3 that is testing atropine as intervention to prevent or delay myopia onset in children.

Discussing atropine treatment as a pharmaceutical strategy for myopia control to address the global myopia burden, Dr Tan said, “A Cochrane systematic review published in 2011 identified over 180 published interventional studies for approaches to reduce myopia progression. Since then, more than 30 clinical trials on the use of atropine eye drops for myopia control were registered on the clinicaltrials.gov website.”

“These studies tested or are testing atropine in concentrations ranging from 1% to 0.005% in eyedrop, gel and ointment formulations and as standalone treatment or with adjunctive therapies that include orthokeratology, soft bifocal contact lenses, ketorolac, acemanisodiamine and acupuncture. Clearly, this is a fervent area of interest.”

Brief history

Studies investigating topical atropine began in Asia in the 1970s. Despite the long-term history of use and evidence of its efficacy, the mechanism of action by which atropine may control myopia is unknown, Dr Tan said.

‘Initially it was thought that atropine might block accommodation, but that is now known not to be true.’

— Dr Donald Tan

“Initially it was thought that atropine might block accommodation, but that is now known not to be true. The current concept is that it works either through a neurochemical cascade that begins with muscarinic receptors at the retina or via a non-muscarinic mechanism involving a direct effect on scleral fibroblasts mediated by inhibition of glycosaminoglycan synthesis,” he said.

Dr Tan is chair of the previous ATOM studies. ATOM1 was a 2-year interventional trial launched in 1999 that compared atropine 1% with placebo in children ages 6 to 12 years old with –1 to –6 D myopia. The results showed that atropine significantly reduced myopia progression and its effect on refraction strongly correlated with a reduction in increase of axial length. However, the treatment

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- Results from many rigorous clinical trials demonstrate the efficacy of topical atropine for reducing myopia progression in children.
- Many more studies in populations around the world are ongoing.
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was associated with significant side effects, and 1 year after it was stopped, significant rebound of both axial length and spherical equivalent were observed.

To try to minimise treatment-related side effects, ATOM2 tested lower doses of atropine: 0.5%, 0.1% and 0.01%. It enrolled children aged 6–12 years with ≥–2 D of myopia. The trial had a 1-year washout period following 2 years of treatment, and atropine 0.01% was restarted for 2 years in any child whose myopia rebounded during the washout.

Results from ATOM2 demonstrated that both atropine-related ocular adverse events and myopic rebound decreased with decreasing dose. The study also found that restarting atropine treatment the 0.01% formulation was able to reverse myopia progression that occurred during the washout year.

“At the end of 5 years, treatment with atropine 0.01% was associated with a 50% reduction in myopia progression,” Dr Tan said.

Based on epidemiological evidence that a younger age of onset is associated with higher degrees of myopia measured both by higher SE and longer axial lengths, ATOM3 is designed to test whether intervention with atropine can prevent or delay the onset of myopia.

Synthesising the contemporary literature
A network meta-analysis of randomised controlled studies investigating interventions for myopia control in children published in 2016 by Huang et al. found that moderate and high dose atropine markedly slowed myopia progression. In 2017, Gong et al. published a meta-analysis that included 19 studies of atropine involving more than 3100 children.

The investigators concluded that the data showed the efficacy of atropine was dose-independent within the dose range studied, whereas the adverse effects were dose dependent, increasing with increasing dose.

Dr Tan said that the authors stated that low-dose atropine seems to herald a new therapeutic scenario that decreases the adverse effects and seems to decrease the rebound effects.

“They even went on to suggest that pharmaceutical companies could produce 0.01% atropine commercially to aid further global research.”

In 2017, the American Academy of Ophthalmology Technology Assessment Committee issued a report on atropine for preventing myopia progression in children. The group reviewed 17 studies, of which eight were level I or II, and concluded that lower doses of atropine were slightly less effective than higher doses but were associated with less myopic rebound and fewer side effects.

“One caveat about the studies, however, is that the most robust research was carried out in Asian populations,” Dr Tan said.

Among currently ongoing studies, three are being conducted in the United States.

The formulation effect
More recently, the Low-concentration Atropine for Myopia Progression (LAMP) study compared atropine 0.01%, 0.025% and 0.05% versus placebo in children with myopia.

Results collected after 2 years indicated that the highest concentration studied was most effective.

Dr Tan observed that the efficacy of the 0.01% concentration in ATOM2 for reducing refractive change was more similar to that seen in the LAMP group treated with atropine 0.025% while the effect of the 0.01% concentration on axial length in ATOM2 almost equaled that achieved using the 0.05% concentration in LAMP. Pupil dilatation was also almost twofold greater in the ATOM2 atropine 0.01% group than in the atropine 0.01% group in LAMP.

“It appears the effect of atropine differs in different formulation. The formulation used in LAMP was different than the ATOM formulation. Yet in ATOM-J, a study done in Japan, benefit was observed using the ATOM formulation of atropine 0.01%, but it was not as effective as the same formulation in ATOM2,” Dr Tan concluded.

“We do not know yet what the best formulation will be. More studies are needed, and certainly there are a lot ongoing.”

‘We do not know yet what the best formulation will be. More studies are needed, and certainly there are a lot ongoing.’

– Dr Donald Tan

“We are doing this study in Singapore where we can confidently predict that 5-year-old children whose refraction is between +1 and –0.49 D will become myopic later in life. We call these children pre-myopes,” said Dr Tan.

ATOM3 is enrolling children aged 5–9 years whose refractive error (by cycloplegic refraction) is between +1 and –0.49 D and who have at least one parent with myopia. They are being randomised to receive 0.01% atropine or placebo. Treatment will be continued for 2.5 years and then children will be followed during a 1-year washout period.

Synthesising the contemporary literature
A network meta-analysis of randomised controlled studies investigating interventions for myopia control in children published in 2017 by Huang et al. found that moderate and high dose atropine markedly slowed myopia progression. In 2017, Gong et al. published a meta-analysis that included 19 studies of atropine involving more than 3100 children.

The investigators concluded that the data showed the efficacy of atropine was dose-independent within the dose range studied, whereas the adverse effects were dose dependent, increasing with increasing dose.

Dr Tan said that the authors stated that low-dose atropine seems to herald a new therapeutic scenario that decreases the adverse effects and seems to decrease the rebound effects.

“They even went on to suggest that pharmaceutical companies could produce 0.01% atropine commercially to aid further global research.”

In 2017, the American Academy of Ophthalmology Technology Assessment Committee issued a report on atropine for preventing myopia progression in children. The group reviewed 17 studies, of which eight were level I or II, and concluded that lower doses of atropine were slightly less effective than higher doses but were associated with less myopic rebound and fewer side effects.

“One caveat about the studies, however, is that the most robust research was carried out in Asian populations,” Dr Tan said.

Among currently ongoing studies, three are being conducted in the United States.

The formulation effect
More recently, the Low-concentration Atropine for Myopia Progression (LAMP) study compared atropine 0.01%, 0.025% and 0.05% versus placebo in children with myopia.

Results collected after 2 years indicated that the highest concentration studied was most effective.

Dr Tan observed that the efficacy of the 0.01% concentration in ATOM2 for reducing refractive change was more similar to that seen in the LAMP group treated with atropine 0.025% while the effect of the 0.01% concentration on axial length in ATOM2 almost equaled that achieved using the 0.05% concentration in LAMP. Pupil dilatation was also almost twofold greater in the ATOM2 atropine 0.01% group than in the atropine 0.01% group in LAMP.

“It appears the effect of atropine differs in different formulation. The formulation used in LAMP was different than the ATOM formulation. Yet in ATOM-J, a study done in Japan, benefit was observed using the ATOM formulation of atropine 0.01%, but it was not as effective as the same formulation in ATOM2,” Dr Tan concluded.

“We do not know yet what the best formulation will be. More studies are needed, and certainly there are a lot ongoing.”
Corneal collagen crosslinking imperative in paediatric keratoconus

Performing in certain cases at presentation better than waiting for progression

**By Cheryl Guttman Krader**

Findings from studies investigating the efficacy and safety of corneal collagen crosslinking (CXL) for keratoconus in paediatric-age patients and developmentally delayed adults and the consequences of leaving their ocular disease untreated provide a solid evidence base for offering CXL to these populations, said Ken K. Nischal, MD.

“In the United States, CXL is only approved for the treatment of progressive keratoconus in patients aged 14–65 years, and so it may not be offered to younger children even if indicated,” said Dr Nischal, professor of ophthalmology and Chief, Division of Pediatric Ophthalmology and Strabismus, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

“My take on this issue is that technology should be for those who cannot advocate for themselves or who are the most vulnerable. Those individuals are the children and developmentally delayed adults. In fact, there is mounting evidence that CXL should be offered to children at presentation rather than waiting for progression.”

**Addressing the aggressive natural history**

Multiple published studies demonstrate that keratoconus progresses at a rate that is much faster in children than in adults and that CXL arrests disease progression in paediatric patients, said Dr Nischal.

Discussing some of these papers, he cited a study by Chatzis and Hafezi that reported a progression rate of 88% after 1 year of follow-up in a series of 59 eyes of 42 children awaiting CXL for keratoconus.1 Another study by Leon-Mesplie et al. showed that children who did not have CXL for keratoconus had a sevenfold increased risk of requiring a keratoplasty compared to adults.2

“If you don’t want to do CXL in a child, you certainly do not want to have to perform penetrating keratoplasty considering the extra problems that it brings in terms of operative and postoperative issues,” Dr Nischal said.

Other papers in the peer-reviewed literature show the safety and benefit of CXL for keratoconus in paediatric patients. In what is the largest published study to date, Padmanabhan et al. analyzed data from 194 eyes of 153 children aged 8–18 years that underwent CXL for documented progressive keratoconus.3 Of the 194 eyes, 142 had CXL using the standard Dresden protocol and 52 were treated using hypoosmolar riboflavin.

The CXL was associated with keratometric flattening and stabilisation of pachymetry during follow-up extending to 6.7 years. Of the total cohort, 59 eyes were followed for longer than 4 years, and reversal of keratometric flattening occurred in 14 (24%) of those eyes.

“Interestingly, however, the flattening did not correlate with significant changes in vision or corneal pachymetry,” Dr Nischal said.

Findings from a study by Mazzotta et al. suggest that regression after CXL may be more likely in patients with severe allergy who are eye rubbers.4

‘In the United States, CXL is only approved for the treatment of progressive keratoconus in patients aged 14–65 years, and so it may not be offered to younger children even if indicated.’

– Dr Ken K. Nischal

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Corneal collagen crosslinking should be offered to paediatric patients and developmentally delayed adults, and can be performed safely and with good outcomes using strategies for overcoming the intraoperative and postoperative issues that are unique to these populations.
There is mounting evidence that CXL should be offered to children at presentation rather than waiting for progression.’

– Dr Ken K. Nischal

These investigators reported outcomes for 62 eyes of 47 patients aged 8–18 years who underwent CXL and represents the report with the longest post CXL follow-up for a paediatric population. The outcomes were stable at 10 years in 80% of eyes. A 2 D increase in mean keratometry occurred in four eyes of two patients who had severe ocular allergy and were eye rubbers, but stability was achieved after repeat CXL. No other patients in the series needed a repeat treatment because of CXL failure.

Two papers have reported on performing CXL for keratoconus in developmentally delayed patients.5,6 “These individuals, who often have Down syndrome, already have challenges. Not performing CXL and therefore leaving them to possibly develop hydrops from progressive corneal thinning and lose vision makes their lives and the lives of their families much worse,” Dr Nischal said.

The barriers and the solutions

Reluctance to perform CXL in children and developmentally delayed adults may be partly due to concern that they will not remain still during a procedure performed using local anaesthesia. In addition, children and developmentally delayed adults may not comply with instructions to avoid eye rubbing that not only increases the risk of regression over time but also the chance for infection following the procedure.

To overcome these potential problems, Dr Nischal said that he performs CXL in most paediatric patients and developmentally delayed adults under general anaesthesia with a regimen that will result in complete paralysis. “If there is not complete paralysis, the eye may roll up during the UV light application, leaving me grabbing for forceps to try to hold the eye in place,” he explained.

Dr Nischal said he uses integrated intraoperative OCT (Carl Zeiss Meditec) to assess adequacy of the riboflavin soak. An OCT scan prior to the soak allows for baseline evaluation and after the soak there is a visible change in reflectivity on the OCT. The OCT is also used after UV exposure: “If I see a clear interface after the UV light application, I know I am going to get a good result, but I do not yet have enough follow-up to know what the outcome is in cases where I cannot see the interface,” Dr Nischal stated.

To protect the eye in the early post-treatment period while the epithelial defect is healing, he usually places a temporary central tarsorrhaphy for 2 days and prescribes topical moxifloxacin six times daily to be applied at the medial canthus. “So far, we have not had any cases of infection, and the children seem comfortable with the tarsorrhaphy in place,” Dr Nischal said.

“Interestingly, patients who had CXL elsewhere with placement of a bandage contact lens reported much less pain and discomfort with their second eye procedure using tarsorrhaphy. One case involved a developmentally delayed patient whose parents were very frightened about the child tolerating the second eye procedure. The parents reported that, with the lids sutured shut, the child did not touch the eye and was very relaxed.” In addition, Dr Nischal is aggressive with treatment for allergic conjunctivitis-related inflammation both pre- and post-CXL as a strategy to mitigate eye rubbing. Patients are also referred for behavioural therapy to reduce eye rubbing.

Positive experience

Between July 2018 and September 2019, Dr Nischal performed CXL in 18 eyes of paediatric patients. All cases were done using the standard Dresden protocol. Sixteen cases were done using general anaesthesia, of which 14 had a temporary tarsorrhaphy placed and two had a bandage contact lens. Eight of the cases involving temporary tarsorrhaphy were in developmentally delayed or non-verbal children. Topical anaesthesia with post-CXL placement of a bandage contact lens was used in two eyes of healthy teenagers aged 15 years.

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Study targets gene therapy for exudative AMD patients

Trial results show promise of transfection with genes for anti-VEGF proteins

By Cheryl Guttman Krader; Reviewed by Dr Szilárd Kiss

Anti-VEGF gene therapy for exudative age-related macular degeneration (AMD) has transformative potential for reducing treatment burden and improving patient outcomes, according to Szilárd Kiss, MD.

Two investigational anti-VEGF gene therapies are currently being investigated in clinical trials: RGX-314 (Regenxbio) and ADVM-022 (Adverum). Dr Kiss described the two technologies and reviewed some preliminary clinical trial results that support their promise for providing sustained benefit with a single injection.

“Considering the treatment burden of anti-VEGF therapy for other ocular diseases, we can imagine that exudative AMD is just the first indication that will be targeted for anti-VEGF gene therapy,” said Dr Kiss, chief, Retina Service, associate professor of ophthalmology, and associate dean at Weill Cornell Medical College, New York, NY, USA.

RGX-314 delivers a gene for an anti-VEGF antigen-binding fragment (Fab) protein that is similar to ranibizumab. It uses adeno-associated virus-8 (AAV8) as a vector and is administered in the operating room as a subretinal injection.

“AAV is the most common viral vector carrier used for gene therapy. Different AAV serotypes have different tissue selectivity,” Dr Kiss explained. “AAV8 is a wild-type AAV that has the propensity for greater transfection of retinal cells compared with AAV2 following subretinal gene therapy delivery.”

Dose-exalating design

The Phase I study of RGX-314 has a dose-exalating design and is enrolling previously treated patients requiring frequent injections for exudative AMD.

Results have been reported for 42 subjects enrolled across five cohorts who completed at least 6 months of follow-up, which is the primary endpoint.

On average, the patients had been diagnosed 56 months previously and had received an average of 33 anti-VEGF injections (9.6/year). Mean baseline BCVA was 55.7 ETDRS letters and mean OCT-measured central retinal thickness (CRT) was 399 μm.

The treatment has been well-tolerated in all dose cohorts. Most adverse events have been rated mild in severity, and there have been no serious drug-related adverse events.

“Fifteen serious adverse events were recorded in nine subjects and there were two deaths, but none were related to the treatment,” Dr Kiss said. There has been no observed clinically determined immune responses, drug-related ocular inflammation, or post-surgical inflammation exceeding that expected following routine vitrectomy.

Two ocular procedure-related serious adverse events occurred, including a peripheral retinal detachment that was repaired and a case of endophthalmitis following collection of an aqueous humor sample.

‘Standardisation, automation and surgeon skill are critical for the success and safety of subretinal gene therapy.’

– Dr Szilárd Kiss

In the fourth dose cohort, which included 12 patients, BCVA remained stable through 6 months and mean CRT improved. Five (42%) patients were injection-free through the 6 months, requiring no rescue anti-VEGF therapy.

The fifth dose cohort includes 12 patients who have

IN SHORT

Two anti-VEGF gene therapies are being investigated in clinical trials of patients with exudative age-related macular degeneration. Initial efficacy and safety results are encouraging.
5–6 months of available follow-up. This group also had stable BCVA and improved CRT, and nine of the patients (75%) remained injection-free.

“Standardisation, automation and surgeon skill are critical for the success and safety of subretinal gene therapy,” Dr Kiss noted. “Surgeons need extensive training that begins in the wet lab and then moves into a virtual reality environment.”

ADVM-022 is an AAV vector encoding aflibercept. It uses a novel AAV.7m8 capsid for gene delivery, which is an engineered vector optimised for strong retinal transfection following in-office intravitreal injection.

Optic trial

OPTIC, the Phase I clinical trial investigating ADVM-022 in exudative AMD, is evaluating two dose levels of the gene therapy. Eligible subjects must demonstrate a meaningful response to anti-VEGF therapy and are receiving an injection of aflibercept (Eylea, Regeneron) 7–14 days prior to ADVM-022 injection.

Data from median follow-up of 8 months was available for six patients enrolled in OPTIC.

This first cohort had received an average of 6.2 anti-VEGF injections in the 8 months prior to study screening and a mean of 35.3 injections since being diagnosed with exudative AMD.

There were some other interesting findings, and patients were requiring few, if any, injections.

Dr Kiss pointed out that one patient had received 109 previous injections.

“Of the 52 rescue injection opportunities during the 8-month follow-up period, zero rescue injections were needed in any of the first six subjects,” he said.

In this small group there have been no serious adverse events nor any adverse events meeting criteria for dose-limiting toxicity.

According to the research, there were 19 ocular adverse events potentially related to the investigational agent, of which 14 were mild and five rated as moderate in severity.

Mild anterior inflammation and vitreous cells were the most common adverse events, and all were well controlled with topical corticosteroids.

The research team reported that there were no cases of vasculitis, retinitis, or choroiditis.

Evaluations for efficacy showed BCVA remained stable and CRT improved while all patients remained injection-free.

Retinal gene therapy

Gene therapy approaches represent three basic categories, the choice of which depends on the underlying pathology. Both RGX-314 and ADVM-022 are gene augmentation approaches as they are designed to deliver a gene for a functioning protein that is not naturally produced.

Gene augmentation can also be utilised to replace a non-functioning gene, as represented by voretigene neparvovec-rzyl (Luxturna, Spark Therapeutics) the FDA-approved gene therapy that replaces the non-functioning RPE65 gene in those patients with biallelic RPE65 mutation-associated retinal dystrophy.

As another approach, gene therapy can aim to edit existing genes. This approach is applicable to diseases caused by a single-nucleotide, gain-of-function/dominant-negative mutation. Or, in the case of pathologies caused by a dominant mutation, gene therapy can be designed to inactivate the causative gene.
Gene therapy zeroes in as promising treatment for LHON

Gene therapy for Leber’s hereditary optic neuropathy (LHON) seems to be the first promising treatment for the disease. LHON, a maternally inherited disease, causes optic nerve atrophy that in most cases results in simultaneous or sequential bilateral visual loss. Disease onset typically happens in patients between 14 and 21 years of age.

The most frequently occurring offending mutation is ND4, appearing in ~90% of Chinese patients and in ~50–60% of US patients, according to Jiajia Yuan, PhD, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

**LHON treatment**

Dr Yuan and colleagues initially treated nine patients with LHON with gene therapy in 2011. With this first attempt, she reported seven of the nine patients had a significant improvement of 0.3 logarithm of the minimum angle of resolution (logMAR) VA at 36 months in the best-corrected visual acuity (BCVA).

“We saw a durable response in six of these patients out to 75–90 months after treatment,” she said. “In addition, a bilateral improvement was achieved, as also was observed by other groups investigating gene therapy.”

These promising results prompted a second multicentre gene therapy trial that began in 2017 that include 149 Chinese patients and ten Argentinian patients. According to Dr Yuan, the patients, who ranged in age from 7 to 45 years, received a fixed dose of $1 \times 10^{10}$ mg/eye for all patients, regardless of age.

“The treatment was found to be well tolerated and no severe adverse effects occurred,” Dr Yuan said.

Keratitis developed in one eye at 1 month and anterior inflammation in one eye at 3 months that were both considered to be unrelated to the treatment.

Ocular hypertension was the most common adverse event that developed in 27.04% of eyes that decreased slowly over time after cessation of the steroid.

A significant improvement in the BCVA occurred in 63.21% (67/106 patients) at 12 months. The rest of the patients had not reached the 12-month time point at the time of this report. Similar to the initial study, the patients showed bilateral improvement.

“This is a real-world study, in that there was no specific patient selection,” Dr Yuan explained. “The patients’ ages spanned a wide range as did the time of disease onset and the pretreatment BCVA.”

An evaluation of only the Argentinian patients showed that all had improvement in the BCVA. “These patients fared better overall than the other patients in the group, with the average improvement in the treated eye was 0.6 logMAR and the average improvement in the untreated eye was 0.9 logMAR,” Dr Yuan stated.

Importantly, this improvement in the BCVA is highly relevant for the ability of patients to function well during everyday tasks, which was seen in treated patients. Dr Yuan related that, 3 months after treatment, a patient was able to cook and watch sporting events on the computer.

Dr Yuan noted that gene therapy is a promising approach for patients with LHON. “Nine patients were treated in 2011–2012 and we continue to follow them,” she concluded. “This is the longest-term data from human gene therapy to date.”

According to Dr Yuan, nearly two-thirds of 106 patients who reached the 12-month follow-up point achieved a clinically significant improvement in the BCVA.

“Importantly, no serious adverse events occurred in the real-world studies,” she said. “We are very excited about the potential impact of gene therapy on this disease.”
Sensimed announces acquisition of majority interest by SEED

Sensimed announced the closure of a transaction whereby the Japanese public company SEED Co. Ltd has acquired a majority stake in Sensimed, with SEED now owning more than 90% of outstanding shares. The two companies have a collaborative history as they worked closely together to obtain Pharmaceuticals and Medical Devices Agency, Japan approval for SENSIMED Triggerfish in September 2018. In November of the same year, the two companies signed a memorandum of understanding concerning further collaboration. Terms of the deal were not disclosed.

“This transaction secures the Sensimed Contact Lens sensing technology going forward and ensures it will continue to play an important role in the clinical assessment and management of glaucoma patients,” said David Bailey, chief executive officer of Sensimed.

For more information, go to www.sensimed.ch

BVI expands vitreoretinal surgery presence

BVI announced it has acquired Arcadophtha SARL (Arcad), a France-based ophthalmic company specialising in silicon oils, gases and perfluorocarbons used in vitreoretinal surgery. Growth of the Arcad products will be accelerated through BVI’s broad-reaching commercial infrastructure established with the Vitreq line of vitreoretinal surgical products, according to a prepared statement.

The transaction closed during the fourth quarter of 2019. Financial terms of the transaction were not disclosed. Arcad was acquired from its founders, who will continue to support the business.

“We are pleased to welcome the Arcad team to our organisation. The products fit extremely well alongside our current vitreoretinal product offering. Arcad’s unmatched focus on product quality and vertically integrated business model aligns well with BVI’s business philosophy,” said Shervin Korangy, president and chief executive officer of BVI.

For further information, go to www.bvimedical.com

Quantel Medical, Ellex report merger agreement

Quantel Medical announced a major step forward for the company and the Lumibird group as merger discussions have been initiated with Ellex, Adelaide, Australia. In a joint statement, the companies said that a scaling of R&D capability as well as offering healthcare a greater range of solutions is needed. They added: There is a growing market need in existing territories as well as in developing countries.

Jean-Marc Gendre, Quantel Medical’s CEO added: “The future success of both companies depends on sharing R&D capability and manufacturing structures, on strengthening our approach to clinical research in order to meet the current and future needs of the ophthalmologists”.

For further information, go to www.quantel-medical.com or www.ellex.com

Aerie Pharmaceuticals reveals FDA approval of Ireland facility for netarsudil/latanoprost production

Aerie Pharmaceuticals announced that its sterile fill production facility in Athlone, Ireland has received FDA approval to produce netarsudil/latanoprost ophthalmic solution 0.02%/0.005% (Rocklatan) for the US market. The regulatory clearance follows a successful preapproval inspection of the plant and FDA review of the New Drug Application Prior Approval Supplement, which added the facility as a product manufacturer for the drug.

“We aim to have [netarsudil ophthalmic solution (Rhopressa)] produced in Athlone later in 2020, and eventually, we anticipate that Athlone will supply our ophthalmic products for all the markets in which we will operate,” said Vicente Anido Jr., PhD, Aerie chairman and chief executive officer.

For more information, go to www.aeriepharma.com
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