Challenges and Rewards from Multi-regional Ophthalmic Studies

by John Butcher

There are multiple issues conducting large population-based ophthalmic studies across different countries, but they can provide invaluable information, experts told the APAO 2018 conference delegates yesterday.

Language barriers, standardization of data and techniques, developing a study, deciding where to conduct it, and handling large amounts of information, are among the many issues multi-regional studies face, ophthalmologists said during the afternoon meeting. But lessons have been learned from previous studies and advances in knowledge and technology could make such studies easier.

Dr. Ching-yu Cheng, of the glaucoma department at the Singapore National Eye Centre (SNEC) spoke about his experiences working with the Asian Eye Epidemiology Consortium (AEEC).

Population-based glaucoma studies began growing in number in the 1990s, he said, exploding in number during the 2000s, particularly in Asia, to the point where there are around 50 today.

While they have shed light on glaucoma in Asia, showing little difference among racial groups in the region and different risk factors from Europeans, the results have been "inconsistent" and "further studies are needed," he said.

Lessons were learned about the need to harmonize epidemiological data, and ensure sufficient resources are in place, he told the audience, adding that advances in big data technology could make it easier to handle large quantities of complex data across multiple regions.

The AEEC in particular focuses on deriving conclusions about major risk factors for eye disease across Asia. Specifically, it aims to document relatively uncommon diseases, develop prediction models for eye diseases, provide a platform for international cooperation and build capacity in the number of epidemiology researchers.

Cont. on Page 16 >>
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The collection of paintings is making its very first appearance at the 33rd Asia-Pacific Academy of Ophthalmology (APAO) Congress, held in conjunction with the 29th Hong Kong Ophthalmological Symposium at the Hong Kong Convention and Exhibition Centre from 8–11 February 2018.

Each of the eye paintings features one of ten patients from across the Asia-Pacific region and tells a story of success made possible with AcrySof® IQ IOLs. As lasting patient outcomes are the driving force of what Alcon does, all pieces draw focus to the brilliance of the human eye. Meticulously crafted, each one epitomizes the great precision and expertise that goes into a successful cataract surgery. Every brush stroke was carefully applied with the intention of evoking a naturalistic interplay of texture and colour, capturing how AcrySof® IQ IOLs are catalysts for the improvement of both sight and life.

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This article has been supported by an educational grant from Alcon.
Patients in an eye surgeon’s operating theatre today may think they have ended up in a 3D cinema by mistake, as the surgeon and his assistants pop on their 3D eyewear.

Surgeries are undergoing a digital revolution as the NGENUITY 3D Visualization System (Alcon, Fort Worth, TX, USA) takes over the conventional microscope.

In vitreoretinal surgery, image depth plays a crucial role in how a surgeon views the eye.

With NGENUITY, surgeons can now benefit from the use of a precise and optimized 3D surgical display in their operating theatres which can help to reduce the margin of error with higher magnification and better control of each movement.

At the Alcon Lunch Symposium on “New Advancements in Vitreoretinal Surgery: The Importance of Improving Visualization,” several surgeons from around the region shared their experiences on using the 3D system.

Among the benefits discussed is that it will help surgeons to see anatomical structures, traction, vitreous, and tissue layers, and may enable surgeons to decrease dye concentrations when staining tissue layers.

It is also better to use NGENUITY posture-wise, as surgeries can take up to several hours and the heads-up display may help to improve fatigue.

Dr. Kazuaki Kadonosono from the Department of Ophthalmology and Microtechnology, Yokohama City University Medical School, Japan, presented on “Improving Visualization in the New Era of Digital Microscopy.

NGENUITY produces 11% to 42% finer depth resolution at high magnification than ocular microscopes, he said.

When asked during the Q&A if it was difficult to adjust to the 3D system, he said: “It is very easy to familiarize one’s self with NGENUITY. Some of my colleagues have only started using NGENUITY recently, and they found that less time is spent on surgery with this system.”

Dr. Marco Mura, Chairman of Retina Division of the King Khaled Eye Specialist Hospital Saudi Arabia and Associate Professor, Johns Hopkins University, USA, in his presentation entitled “See it better. Do it better,” said that the system provides high magnification and depth, which cannot be achieved with a normal microscope. This results in better control for surgeons.

NGENUITY provides improved visualization at high magnification compared to analog microscopy, he said, adding that it provides 26% to 48% greater magnification. It delivers up to 5 times better depth of field, produces 11% to 42% finer depth resolution, image customization, improved ergonomics and an excellent teaching environment as it facilitates training with different doctors, as everyone in the theatre gets to see what the surgeon is seeing, unlike with a conventional scope.

“The quality of the image is so great that you can see all the details. This improves the outcome for patients [hopefully]. You can use this platform to conduct surgery very safely. It is much easier to work with NGENUITY than with a normal scope as the magnification is much greater,” said Dr. Mura.

Dr. Mura also discussed “Innovations in Ophthalmology.” Talking about Alcon’s
Ultravit High Speed Vitrectomy Probes, he said they were designed to provide the surgeon with added versatility. The bevel tip design brings the cutting port into closer proximity to the retina, allowing the surgeon to access cutting planes that may not be available with a standard flat tip probe. It can achieve a cut speed of 10,000 cpm, increases capability to aspirate, and follows the angle of the retina.

Dr. Wai-Ching Lam of the University of Hong Kong, talked about “Transitioning from Optical to Digital Microscopy.” “The transition is seamless, like learning to drive on the other side of the road,” he said.

Some new users have said they felt dizzy, and the color was too “real” or “unreal.” Others said it felt “too immersive,” like they were “Alice in Wonderland.”

He explained that it is important to set it up 1.2 m from the surgeon, and to keep it at eye level for optimal performance.

“Don’t over-think about the whole process. Just do it!” he said, adding that doctors should easily transition straight away.

“The transition is very simple for most surgeons. You will very quickly forget you are using the monitor. Just sit down, relax and enjoy the show,” said Dr. Lam.

“After using it for one or two cases, you can get used to it. By the middle of the day, you will be just fine,” he concluded.

“The quality of the image is so great that you can see all the details. This improves the outcome for patients. You can use this platform to conduct surgery very safely.”

– Dr. Marco Mura
New Procedures and Technological Advances in Cornea Surgery

by John Butcher

Changes in surgical procedures and technology are improving the ease and outcomes of cornea surgery, according to ophthalmologists.

Advances in Descemet’s membrane endothelial keratoplasty (DMEK) as an alternative to Descemet’s stripping endothelial keratoplasty (DSEK) is offering a new avenue for cornea surgeons, speakers told a morning session audience at the APAO conference in Hong Kong, yesterday. The use of surgical microscopes is also improving the ease of surgery, they added.

DSEK and DMEK are endothelial keratoplasty (EK) techniques, a cornea transplant method that is the preferred way to restore vision when the inner cell layer of the cornea stops working properly. The two techniques are very similar, except that with DMEK the donor tissue implanted does not include any stromal tissue. It is pure replacement of endothelium. Advances in DMEK are now making it a more viable option, according to ophthalmologists.

DSEK remains the most common EK technique, according to U.S.-based ophthalmologist Dr. Sanjay Patel, benefiting from the availability of precut tissue and familiarity with the technique, but there are questions about whether the newer DMEK technique is better, particularly in terms of vision.

The downsides of DMEK are that there are fewer long term outcomes to draw from, given the relative infancy of the technique, and pre-stripped tissue necessary for the surgery is not available everywhere, he said.

However, studies suggest that it may lead to better vision than DSEK, according to Dr. Patel.
Vision and graft survival are the measures of success in cornea surgery, Dr. Patel told the audience. Graft survival appears to be similar for DSEK and DMEK surgery, although there is not enough long term data on DMEK to properly judge, he said.

So, for him, the reason for using the DMEK technique as opposed to DSEK is “visual acuity.”

“Vision has made us take the leap to next level which is DMEK,” Dr. Patel told the audience.

Initial data from DMEK studies suggest better outcomes for patients in terms of improved vision over one year and no greater levels of rejection. However, DSEK patients catch up over a five-year period with their vision gradually improving, according to Dr. Patel. Vision may still be slightly better with DMEK and it may “get there faster,” he added.

These studies should not be considered concrete however, according to Dr. Patel, as there is no randomized controlled data beyond six months and because they do not take into account disease severity.

This does not mean DMEK will completely replace DSEK, noted Dr. Patel. Some patients may prefer DSEK surgery, others may have medical reasons for it being better than DMEK (such as an inability to lie flat for an extended period during surgery), and DSEK may still work better for more complex eyes, he said.

In many cases DSEK may be a first option, with DMEK a second, if DSEK and penetrating keratoplasty, a full-thickness corneal transplant, have failed, and if there is no previous vitrectomy, he added.

In short, it is best to “individualize your care,” he told the audience. “Choice depends on patient preference and medical factors.”

Professor Donald Tan, from the Singapore National Eye Centre, added that, “patient selection for conventional DMEK is critical. Many patients may not be suitable for DMEK.”

DMEK involves no touching and “works fine” on a normal iris, but there are major challenges in un-scrolling the donor without damaging it.

An alternative approach to DMEK is the hybrid DMEK (H-DMEK) technique, which involves using DSEK techniques to perform DMEK surgery.

“When we switch from DSEK to DMEK we want to keep it a simple and similar technique,” he said.

These “pull through” techniques add surgical control, he said, and overcome the “no touch technology” with DMEK which can be challenging to use.

Other speakers talked about the usefulness of surgical microscopes in cornea operations.

Taiwan-based ophthalmologist Dr. Ming Cheng Tai said he had found using a surgical microscope, in his case the Rescan 700 (Carl ZEISS Meditec, Jena, Germany), “extremely useful in all stages of DSEK and DMEK.”

Corneal specialist Dr. Anthony Kuo said surgical microscopes could provide an en face view of surgery that was helpful in doing complex tasks.

Studies had shown ophthalmologists using a surgical microscope were much closer to their target than those without, and those who had used one for a particular surgery remained more accurate afterwards even without the use of the microscope.

The tests show what optical coherence tomography (OCT), a non-invasive imaging test that uses light waves to take cross section pictures of the retina, could do for surgeons, Dr. Kuo added.

The next generation of OCT systems will typically work faster than the current spectral domain OCT systems, he said, adding, “You begin to imagine that you can operate purely on the OCT information.”

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Artificial Intelligence (AI) is now a buzzword around the world for many reasons, but in ophthalmology, it has potential to assist doctors in various ways, such as in screening patients for specific eye diseases.

Research and development is now on the rise in computer science and medicine. Deep learning can teach computers to do what human brains do naturally, so an artificial intelligence-based grading algorithm can be used to identify, with high reliability, which patients should be referred to an ophthalmologist for further evaluation and treatment.

At the APTOS Symposium on AI-based screening in ophthalmology, chaired by Dr. Mingguang He and Dr. Robert Chang, the first presentation of the day was on screening for eye diseases, such as diabetic retinopathy (DR), glaucoma, and age-related macular degeneration (AMD). Dr. Gavin Tan from the Singapore National Eye Centre (SNEC) and Duke-NUS Medical School, Singapore, said that with the wide availability of imaging devices now, AI is a cost-effective option for screening large numbers of patients. Moreover, fundus cameras and optical coherence tomography (OCT) are common at optometry practices, while the existing diabetic camera screening network can be used for the screening of non-diabetic patients. Nonetheless, there are challenges for AI screening. First of all, there are complications in defining the gold standard, and there needs to be high specificity to avoid false positives. There also needs to be higher sensitivity to sight threatening diseases. For now, AI is unable to screen for all diseases. Further validation and clinical trials are needed. Also, for implementation, where does the software fit? There is also a need for the clinician to accept the software black box. Furthermore, there are also legal and ethical issues to address.

Dr. Stuart Keel from the Center for Eye Research Australia presented on AI screening in Australia. He shared that about 1.5 million people have diabetes mellitus (DM) in Australia, and this figure is expected to increase to 2.9 million by 2025. At the moment, there is sub-optimal adherence to retinal examination guidelines and low availability of eye health services in non-metropolitan areas. Unfortunately, DR is a leading cause of vision loss among Australians. To address this problem, Australia is investing in DR screening, where non-eye care physicians are to perform DR screening using retinal photography. The total investment is $33.8 million from 2016-2017 to 2019-2020. There will be an AI-based grading and diagnosis system for referable DR, glaucoma suspects, late-wet AMD, and possible cataract.

Another presentation was on AI screening in the United States by Dr. Robert Chang from the Stanford University School of Medicine. He spoke about a multicenter study to evaluate performance of an automated device for the detection of DR. The US is currently waiting for the US Food and Drug Administration’s approval.

Dr. Mingguang He from the Center for Eye Research Australia and Zhongshan Ophthalmic Center, Sun Yat-sen University talked about AI screening in China. He said that deep learning addresses the problem of learning hierarchical representations with a single algorithm. Currently, various types of AI screenings are being developed, such as for chest X-rays (lung nodules), hand X-rays (skeletal age), mammography (breast cancer), chest CT (lung cancer), brain CT (Alzheimer’s disease, stroke), and fundus photography (DR). AI-based screening for DR is being done in collaboration with several partner organizations, with accuracy of 90% or more.

The last presentation was by Dr. Kim Ramasamy from the Aravind Eye Hospital and Postgraduate Institute of Ophthalmology, Madurai, India. He shared his knowledge about AI screening in India. It is unfortunate that by the time patients with DR visit eye units, 45% of them had already lost vision before the condition was diagnosed. He believed that screening for DR should not be limited to only ophthalmologists. Current ongoing projects include those with Google Deep Learning and Microsoft Intelligent Network for Eyecare (MINE). He hopes that further research will be able to determine whether use of the algorithm could lead to improved care and outcomes compared with current ophthalmologic assessment.

If properly implemented on a worldwide basis, this algorithm has the potential to reduce the workload on doctors and increase the efficiency of limited healthcare resources. We hope that this technology will have the greatest impact in parts of the world where ophthalmologists are in short supply.

Another advantage is that the algorithm does not require any specialized, inaccessible, or costly computer equipment to grade images. It can be run on a common personal computer or smartphone with average processors.
Top 5 Pearls

The Do’s and Don’ts of Refractive Surgery with IOLs

by Hazlin Hassan

Some of the region’s experienced surgeons were on hand yesterday to share their top 5 pearls on how to perform the most advanced and popular refractive intraocular lens (IOL) surgeries. There was a lively discussion on how to achieve the most accurate refractive results and which IOL was the best and in the end everyone agreed to disagree, based on their patients’ individual preferences, geographical location and need.

IOLs are artificial lenses that are implanted inside the eye to replace the eye’s natural lens when it is removed during cataract surgery. The lenses are also used for vision correction surgery. IOLs have come a long way from when they were first introduced in the 1980s. Today there is a wide variety of IOLs to choose from, which may prove mind-boggling to the patient. The best IOL for the patient depends on many factors, including their lifestyle and visual needs, such as whether they do a lot of work on digital devices, or frequently drive at night.

Types of IOLs include monofocal, multifocal, accommodative and toric lenses.

Dr. David Smadja of the refractive surgery department at the Bordeaux Hospital University, France, strongly recommends profiling patients by using a preoperative questionnaire and matching each patient’s profile including hobbies and activities with the appropriate surgical strategy. He gave three examples of patients: a night driver, a chemistry professor where most of his work would be at intermediate range, and a fashion designer who would want better near vision glasses-free.

All three have different specific visual needs and therefore would require different lenses based on those needs. If a surgeon decided to randomly implant different types of IOLs into each patient, then chances are that none of them would be happy with the outcome.

Dr. Jorge Alio at the Miguel Hernandez University, Spain, shared with the audience his top 5 pearls on refractive lensectomy, which is a routine procedure for cataract surgeons. Now, IOLs may even restore near vision with the use of multifocality, pseudacommodation or partial accommodation, and therefore, is becoming more and more popular, he noted.

He urged surgeons to be aware of the pros and cons of the procedure. Some of the advantages of the procedure which he highlighted include the availability of very good surgical technology for lens removal as well as the availability of the procedure for every anterior segment surgeon. But there are disadvantages such as intraoperative complications, postoperative endophthalmitis, loss of accommodation, posterior vitreous detachment, retinal detachment, incomplete refractive outcomes, and macular disease, among others.

Advising surgeons to make adequate indications for myopic, hyperopic, astigmatic and presbyopic RLE, and to use adequate biometric tools and IOL calculation formulas, he added that surgeons should also consult independent evidenced based information about multifocal IOLs, and manage complications adequately. He concluded by saying that RLE is a safe procedure if used for properly selected patients but can cause complications and more severe than in corneal refractive surgery. In addition, RLE should not be undertaken in patients below the age of 50-55 years.

Dr. Robert Ang from the Asian Eye Institute of the Philippines, shared his top tips on “Managing Unhappy Post-Cataract Patients.” Common reasons for unhappiness include complications such as infections, capsule rupture, inflammation, poor quality of vision and photic phenomena, he noted. Some patients will also still need glasses despite premium IOLs, he said. His advice was to allow the patient to vent, do not get defensive, acknowledge that there is a problem, diffuse the situation, empathize and sympathize and try to switch hats from being an ophthalmologist to a psychologist or psychiatrist. However he cautioned against overpromising a solution.

What needs to be done is to institute a treatment plan and to discuss the possibility of a referral to a colleague or subspecialist, he said. Patients must also be informed that there may be a scenario where the unhappiness may not be solved. One way of minimizing unhappy patients before they happen would be to provide preoperative counseling and information sheets as well as consent forms and waivers.
Children must be Focus of Myopia Treatment, Say Experts

by John Butcher

Children are the priority of myopia treatment, ophthalmologists told the APAO conference yesterday, but it must be approached correctly.

Risks of developing high level myopia when the condition starts young are more serious than in adults, experts said at a morning symposium. This makes them the focus of myopia treatment, but there are special factors that should be taken into account when dealing with children and their families.

Dr. Audrey Chia, of Singapore National Eye Centre, highlighted the myopia epidemic in Singapore, where 80% of children born after the 1980s have myopia to some degree, compared to 3% of people born in the 1960s.

This shows the risk of large numbers developing high level myopia over time as "children who get myopia younger are at more risk of becoming highly myopic," and the importance of tackling childhood myopia, Dr. Chia said. However, there are particular protocols an ophthalmologist should observe when dealing with children who have myopia and their families.

Dr. Chia said she splits her first consultation into three parts: questions, discussion and assessment.

At the consultation stage she asks a series of questions to create a picture of the child. They include age, questions about environmental factors that could affect myopia progression, allergies, family history of myopia, questions about general health and about past myopia treatments. She also requests if possible for them to bring past glasses prescriptions to the meeting.

She follows that up with a discussion of the options. That could be some form of treatment, or simply monitoring the condition to see how it progresses. This stage should take into account the parental views, and specific issues and desires from the treatment that the child has, she said.

The final part of the first meeting ends with an assessment of the condition, Dr. Chia added, culminating in the creation of a chart plotting the progression of myopia in the patient.

From the meeting the ophthalmologist "needs to know what the treatment effects are going to be," and the parents need to be aware of any issues pertaining to the treatment that involve them, according to Dr. Chia.

For example, they should know that if their child is treated with atropine, it should not be stopped abruptly, she said, but rather use should be tapered down gradually.

In younger children stopping the use of atropine can cause a rebound in myopia, while in older children it is safer to do so, she added.

Ultimately, the treatment should be tailored to the needs of the child and the consultation should allow the ophthalmologist to do that, she told the audience.

"You may have to think about unpredictability," she said.

Professor Pauline Cho talked about the use of orthokeratology, gas permeable contact lenses that temporarily reshape the cornea to reduce refractive errors such as myopia, hyperopia and astigmatism, to treat children with myopia.

"Parents must be willing to take responsibility, sign a consent form and ensure proper use of the lenses," she told the audience, including cleaning, and insertion and removal for younger children.

The child must also learn how to insert and remove them before she would prescribe the lenses, in case an eventuality arises where that is necessary, she added.

Aftercare is important, she said, and a compliant child.

"It is our responsibility that children have access to our service," she said.

"Parents may hesitate or delay consultations if they have to pay every time they come back. So, it is best to build in aftercare when charging for the lenses and service at the beginning. The costs should include scheduled aftercare."

Cho also said she recommended annual replacement of lenses, due to deposits and scratches, and case replacement every month, for reasons of hygiene.

She also cautioned against using a suction holder to remove lenses, as they are the most often contaminated item and if a patient becomes dependent on one and loses it they could face problems removing the lenses.
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Proper patient monitoring and follow-up of retinal diseases used to require a highly specialized and expensive fundus camera. That is no longer the case with the new DIYretCAM, a smartphone adapter for fundus imaging created by Dr. Biju Raju and colleagues from the Department of Vitreoretinal Diseases, Vasan Eye Care Hospital in Association with Ranjini Eye Hospital, Kochi, India. Made using a smartphone and materials easily and cheaply available anywhere in the world, this new device is giving doctors and patients access to good quality images that will improve patient outcomes.

As the name suggests you can make this optical tube device yourself using simple PVC, sandpaper, Super Glue, cardboard and a few other materials. The cost is less than $1 (USD), and is designed to be easier to construct than your typical purchase from IKEA. According to Dr. Raju, most people can complete the build in around 30 minutes, plus he has a video available online to guide you on the step-by-step procedure. Then just pop in a 20D lens, attach to your smartphone and you’re ready to go.

So what can the DIYretCAM image? You can see the central retina and the peripheral retina up to the pars plana. The device can be mounted on a slit lamp to give more control, providing better focus of the retina while imaging the disc and posterior pole. Additionally when using matched filters, fluorescein angiography of the central and peripheral retina can be performed.

“Besides the routine ophthalmic imaging, the DIYretCAM becomes extremely useful in documenting the retinal changes in a bedridden patient or while screening neonates for retinopathy of prematurity (ROP), for which currently there are no cost-effective techniques,” explained Dr. Raju.

Once the images are obtained, Dr. Raju recommends using Adobe PhotoShop Express (a free tool) to edit the image for brightness and contrast. He even learned that central reflection can be removed using the app's blemish removal tool. Also, with the PicsArt app (also a free tool), a montage of multiple fundus images can be created, keeping the entire process simple and able to be completed solely with a smartphone. No computer needed! Once the images are ready, they can be shared securely to professional peers easily using instant messaging apps like WhatsApp.

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Maria Cecilia Aquino, MD, Glaucoma Specialist, National University Hospital Singapore

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to a conventional fundus imaging system, particularly those who are serving the peripheral or rural centers. And because of the DIYretCAM’s simple construction and ability to be adapted to any smartphone, patients all around the world can benefit from it. It is the epitome of teleophthalmology, allowing images to be shared quickly and easily from remote areas to retinal specialists.

That is precisely one the factors which motivated Dr. Raju to invent this device.

“I believe that teleophthalmology, in its true sense, should be a smartphone based imaging technology, because of the wide range of connectivity options that smartphones offer and because almost everyone has a good smartphone nowadays,” he said. More importantly, because Dr. Raju is a passionate advocate for better access to care for all, he has kept his design open source instead of going the commercial route so that it can equally reach everyone around the world.

With the DIYretCAM, patient monitoring and follow-up of retinal diseases are no longer reliant on an expensive and specialized fundus camera. Using just a smartphone and some other basic materials, you can have your own DIYretCAM in about 30 minutes for the amazing price of $1. DIYretCAMs for all are finally here!

References:

*http://www.ijo.in/text.asp?2016/64/9/663/194325

Editor’s Note: A version of this article first appeared in issue 01 of PIE Magazine, Asia-Pacific’s first and only magazine dedicated to the posterior segment, published by Media MICE Pte Ltd. It was one of PIE’s most popular articles of 2017.
Effects of Green Tea Extract in Experimental Autoimmune Uveoretinitis

Green tea extract (GTE) has been studied extensively for its antagonistic effects on oxidation and inflammation. So, could this herbal remedy reduce inflammation associated with uveitis? The current standard therapy for uveitis – a group of blinding diseases of intraocular inflammation – is corticosteroid. This treatment has many potential side effects, and a considerable portion of patients fail to respond to the steroid. Thus, seeking an effective alternative treatment, Dr. Jian Li and colleagues investigated the anti-inflammatory effects of GTE on experimental autoimmune uveoretinitis (EAU).

In this study, EAU was induced in C57BL/6J mice, while controls were mock induced with PBS. Long-term effects of GTE on EAU were monitored in real time by noninvasive technologies including optical coherence tomography, fundus fluorescein angiography, and electroretinography (ERG). Histological changes and proinflammatory gene expression were assessed after killing the animals.

Dr. Li and colleagues found that GTE effectively alleviated ocular inflammation in EAU by improving the clinical signs of ocular inflammation, reducing the fold change of retinal choroidal thickness and the major retinal vessel diameter, reserving the ERG scotopic and photopic amplitudes during EAU, and suppressing the expression of proinflammatory genes (P < 0.05). These results lead them to conclude that GTE is a potent anti-inflammatory agent and could be used to treat inflammation associated with autoimmune uveitis.

Long-Term Visual and Functional Outcomes of Diode Laser-Treated Retinopathy of Prematurity in Hong Kong Kowloon West Cluster

Dr. Lok Yoong Mak and colleagues evaluated the long-term visual outcome, refractive status and structural outcome in patients with retinopathy of prematurity (ROP) treated with diode laser, in this retrospective study. A total of 48 eyes of 24 patients with ROP who received laser therapy from 2004-2013 at Princess Margaret Hospital in Hong Kong were included, with a mean follow-up of 8.42 years. For the most part, Snellen visual acuity (VA) improved: 29 eyes (60.4%) achieved a VA of 0.7 or better, and 34 eyes (70.8%) achieved a VA of 0.5 or more. Three eyes (6.3%) had an unfavorable visual outcome of VA < 0.1, including 1 eye which progressed to vision with no light perception. For refractive outcome, 34 eyes (72.3%) were myopic, among which 31.9% progressed to high myopia of ≥ -6.0 diopters (D). Overall mean spherical equivalent was -4.85 D. Anisometropia of > 1.50 D between both eyes was present in 43.5% of patients. Seven patients (29.2%) developed manifest squint with 3 patients (12.5%) requiring squint surgery.

According to these results, Dr. Mak and colleagues suggested that while favorable visual and anatomical outcomes were achieved in the majority of the ROP cases treated with diode laser photocoagulation, the development of refractive error including myopia and astigmatism is common. Additionally, anisometropia, ambyopia, and strabismus are common sequelae of laser-treated ROP and should be actively managed in long-term follow-up.
To investigate the causes of macular serous retinal detachment (without hemorrhage at the macula) in patients 40 years and older, Dr. Kunho Bae and colleagues examined 394 eyes of 363 Korean patients with serous retinal detachment. Patients were examined using spectral domain optical coherence tomography, fluorescein and indocyanine green angiographies. Of 394 eyes, 178 eyes (45.2%) had central serous chorioretinopathy (CSC), 171 eyes (43.4%) had polypoidal choroidal vasculopathy (PCV), 32 eyes (8.1%) had occult choroidal neovascularization (CNV) secondary to age-related macular degeneration, 8 eyes (2.0%) had pure retinal pigment epithelial detachment, 1 eye had macular telangiectasia, and another had retinal macroaneurysm. A total of 162 of 237 (68.4%) eyes of patients over 60 years old had PCV. This led the investigators to conclude that PCV is a primary cause of macular serous retinal detachment without hemorrhage in Korean patients over 50 years of age. Since clinical and fluorescein angiographic findings are indistinguishable among CSC, PCV, and occult CNV, indocyanine green angiography might help to establish a more definitive diagnosis.

Dr. Chang Rae Rho studied the visual outcomes after micromonovision small incision lenticule extraction (SMILE) in patients with presbyopia and myopia. In total 144 eyes of 72 patients were included in the study, where the dominant eye was treated for distance vision, and the nondominant eye was treated for near vision by targeting between -0.50 and -1.75 diopters (D). In total, 72 patients (144 eyes) with a mean age of 46.0 ± 4.9 years were included in this study. The dominant eye was treated for distance vision and the nondominant eye for near vision by targeting between -0.90 ± 0.44 and -0.99 ± 0.54 D, respectively. In total, 79% of eyes were within ± 0.50 D, and 98% within ± 1.00 D, of the intended refraction. A UDVA of 0.0 logarithm of the minimum angle of resolution (logMAR) (20/20) or better, and an uncorrected near visual acuity of Jaeger (J) of 3 (20/32) or better, were observed in 84% of patients.

Patient compliance is an obstacle often met by ophthalmologists. Dr. Pascale Shen and colleagues explored this issue to see if compliance in treatment for age-related macular degeneration (AMD) could be enhanced through one-on-one counseling. Forty-one (41) Chinese subjects aged 50-80 with history of AMD were recruited for the study. Each subject was given a structured questionnaire to evaluate their baseline compliance toward management, as well as factors that may have influenced their compliance. Following the questionnaire interview, the subjects were counseled regarding treatment compliance, and a second questionnaire was given four weeks later to assess the efficacy of the counseling. The study found that prior to counselling, only 9 (22.0%) felt they understood their illness, with only 8 (19.5%) scoring more than 70% in a short quiz about awareness of AMD. This led Dr. Shen and colleagues to conclude that the subjects’ knowledge on AMD is insufficient. A total of 73.2% reported that they have been fully compliant to the prescribed management by their ophthalmologist. Of the remaining 11 (26.8%) subjects, 7 (63.6%) and 4 (36.4%) reported noncompliance for diet modifications and self-monitoring by Amsler grid, respectively. Reasons for noncompliance included forgetfulness (45.5%) and a perceived lack of effectiveness of the prescribed management (27.3%). Twenty-two subjects (53.7%) were satisfied with the doctor’s explanation of their illness, with only 8 (19.5%) scoring more than 70% in a short quiz about awareness of AMD. This led Dr. Shen and colleagues to conclude that the subjects’ knowledge on AMD is insufficient. A total of 73.2% reported that they have been fully compliant to the prescribed management by their ophthalmologist. Of the remaining 11 (26.8%) subjects, 7 (63.6%) and 4 (36.4%) reported noncompliance for diet modifications and self-monitoring by Amsler grid, respectively. Reasons for noncompliance included forgetfulness (45.5%) and a perceived lack of effectiveness of the prescribed management (27.3%).

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It does this by breaking the organization into tiers, with a steering committee at the helm, followed by a coordinating center in Singapore, and multiple projects across different regions below that. The coordination center is the heart of the organization, which compiles information and supports each of the individual projects, he said.

The AEEC has faced multiple challenges, despite learning from previous studies. They include data sharing between regions which may have different policies on what and how information can be shared, as well as the scale of the data collected and language barriers.

Inconsistency in measurements between regional projects is also an issue as well as differing technology that can be hard to combine, he said.

Getting information on a wide range of demographics has also proved difficult, he added, which has resulted in holes in data for West Asia and older people.

The AEEC’s approach to dealing with these challenges has been coordination via its Singapore base, according to Dr. Cheng. It harmonizes data, provides regular updates on projects and organizes meetings.

The organization has realized the need to incentivize individual projects, he added, for example through author credits.

It has also come to understand the importance of continued funding to support manpower and infrastructure development.

Dr. Jonas Jost, professor of ophthalmology of the Medical Faculty Mannheim of Ruprecht-Karls-University Heidelberg, Germany, who works with Dr. Cheng at the AEEC, said that before beginning any multi-regional study, organizers need to assess where are the most representative area to conduct it. They also need to know where people reside in order to find study participants, he added, and the interview should be as large and all-encompassing as possible.

Professor Paul Baird, a molecular geneticist who heads ocular genetics at the Centre for Eye Research Australia and is involved with the Asian Eye Genetics Consortium (AEGC) which was launched in 2004, also shared his experiences of multi-regional research.

Asia is one of the most diverse regions of the world, he told the audience, in terms of wealth, social factors and ethnicity.

Part of its importance to global studies lies in this mix, from the slums of Mumbai to the tribes of Papua New Guinea and the wealthy developed centers of Hong Kong and Japan, he added.

Despite this, and the region containing around a third of the world’s population, “we know little about it in terms of genetics,” he said.

“Eye studies have concentrated on Europe and North America, which reflects the ability to bring together infrastructure.”

Asia has been catching up in terms of genetic research, but still lags behind, he said, and there remains much “valuable information about risk factors and potential genes that could be involved with disease.”

Twenty-six centers around the world were involved in the International AMD Gene Consortium, launched in 2010, he said, but they were mostly focused on Europe and North America with less than ten percent of collected samples coming from Asia.

Those samples did show dramatic genetic differences between Europeans and Asians, he added, as well as differences within Asia.

The aim of the AEGC is to focus on Mendelian retinal diseases, such as sickle-cell anemia, Tay-Sachs disease and cystic fibrosis, in Asia, he told the audience.

“We want to bring out all aspects of mutations that may not have been uncovered," he said. "We are trying to broaden the scope of sampling across Asia."

Dr. Takeshi Iwata, division director at the National Institute of Sensory Organs, National Hospital Organization, at Tokyo Medical Center, who also works at AEGC, said the project had begun in four countries and expanded to twenty. The focus on Mendelian diseases came after a meeting in 2014, where members talked about what the organization should doing, he said. It now focuses on 37 diseases, most of them Mendelian.

Face-to-face meetings have played an important role in the AEGC’s expansion, he told the audience.

However, the organization still faces challenges, he added, particularly in getting whole families to provide DNA for genetic testing.
EIDON WideField TrueColor Confocal Scanner

A Breakthrough in Fundus Imaging

Retinal Imaging is playing an increasingly important role in ophthalmology. Technical advances in this field are leading to radical changes in the diagnosis and monitoring of several retinal pathologies, and in the objective assessment of responses to treatments and surgery.

The introduction of EIDON Wide Field TrueColor Confocal Scanner (by CenterVue; Padova, Italy) to the market has set a new standard in retinal imaging. The device uses confocal technology and white LED light illumination, a unique combination that offers details-rich images and high-fidelity to actual retinal colors. This provides eye care practitioners with an authentic perception of the retinal anatomy, giving all those details which can aid in the detection, diagnosis and follow-up of pathologies.

Yoshitaka Oka, M.D, from the Oka Eye Institute, Fukuoka, Japan, emphasized that a high-quality imaging system such as this is a very valuable tool to educate patients about the need to better manage their condition through treatment or surgery, and to better explain to them the need for further examinations. “EIDON arrived to my clinic in September 2016, and immediately became an indispensable device in my clinical practice,” shared Dr. Oka.

“In fact, EIDON has allowed me to obtain a completely new and different concept of a wide-field, high-resolution retinal image – one that represents a real breakthrough compared to any other fundus camera or scanning laser ophthalmoscope (SLO) system available in the market today,” he added.

Superior Image Quality

The primary benefit of EIDON confocal technology is the superior and unique-in-its-kind image quality that facilitates and improves the detection of changes in the retina. It is known that early signs of retinal diseases may be missed with a direct examination or with low resolution fundus imaging systems. However, EIDON’s detail-rich images, even through cataracts or other media opacities, aid in detecting the slightest morphologic abnormalities.

According to Dr. Oka, EIDON’s technology makes it the perfect tool to image and document pathologies, like in the screening of diabetic retinopathy. The high-resolution images generated by EIDON enable surgeons to conduct an examination over time of the smallest symptoms of diabetic retinopathy (DR) – symptoms like microaneurysms, dot hemorrhages and retinal neovascularization – that are otherwise hard to detect in standard fundus camera and direct ophthalmoscopy examination.

“This is why I think EIDON is also the perfect tool for DR screening and DR stage evaluation,” he said.

Also, the sharpness of the images in EIDON, due to its confocal optical engine, is able to clearly show the wrinkling of the retinal surface and the thinnest superficial retinal folds typical of the epiretinal membrane (ERM). “All these details are generally not distinguishable or completely lost in a typical fundus camera image. This is why I can certainly state that capturing the ERM is one of the most valuable capabilities of EIDON,” said Dr. Oka.

Imaging in Difficult Visualization Conditions

Even in difficult imaging conditions, such as in cases of cataract and small pupils, EIDON’s confocal technology still allows the instrument to take an image of the retina, where traditional fundus cameras cannot (a crucial limitation in several cases). “More importantly, EIDON is able to take an image of the fundus through a poorly dilated or non-dilated pupil (down to 2.0 mm), allowing for improved patient flow, facilitating operator activities and reducing patients’ waiting times,” explained Dr. Oka.

Wide-Field View

EIDON provides an 89-degree image of the retina with a single exposure. In addition, multi-field imaging allows for the automatic creation of a 163-degree montage: an essential tool in managing and follow-up peripheral lesions.

EIDON TrueColor confocal technology applied to wide-field imaging improves the detection, analysis, and monitoring of pathologies affecting the peripheral retina, preserving the sharpness and details of the pictures even in the periphery accurately documenting the extent and location of these diseases.

Ease of Use

The device is very easy-to-use and requires minimal operator involvement: in full automatic it aligns the patient’s pupil, focuses on the retina, and captures a single 89-degree image of each eye, taking less than one minute.

“At the same time, the device is also very comfortable for the patient, since it uses a non-intense light source that softly flashes the patient’s eye,” explained Dr. Oka.

Multiple Imaging Modalities

EIDON technology supports different imaging modalities. In addition to the unique TrueColor imaging option, the device also allows the acquisition of infrared, red-free and autofluorescence (optional) photographs of the retina.

“Autofluorescence imaging in particular provides interesting support in the diagnosis of several diseases, since it overcomes the evaluation of the simple retinal anatomy, opening a window in the evaluation of retinal metabolism (without the risk of allergic reactions due to fluorescent dye, as in fluorangiography),” Dr. Oka concluded.

This article has been supported by an educational grant from CenterVue.
Seeing a Wider Horizon is The Future of Glaucoma Management

by Joanna Lee

Glaucoma is one of the top causes of blindness in the world with half of glaucoma patients unaware that they have the disease. The challenges in detection, fortunately, has been mediated gradually with the advent of nascent and creative technologies in detecting signs of damage to the optic nerve. Enter the swept source optical coherence tomography (SS-OCT) technology, with swept source referring to the type of short cavity laser used in the device instead of the conventional spectral domain optical coherence tomography (SD-OCT) which uses a superluminescent diode laser. This spells a step up in the world of imaging for the purpose of glaucoma detection.

At the glaucoma symposium yesterday, Professor Kazuhisa Sugiyama presented on the role of DRI OCT Triton (Topcon, Tokyo, Japan) in the detection and management of glaucoma using a swept source OCT and OCT-Angiography. He brought the audience through the advantages of the Triton which he had experienced in his practice as well as evidence from other studies. He pointed to Triton’s wide field scanning that includes optic nerve macula assessment in one simultaneous scan. The vitreous optic nerve and the lamina cribosa as well as the choroid could be seen clearly through the scans.

It even offers a better visualisation of eyes with cataract. Even at a 29 mm myopia or even 30.5 or -18 diopter (very high myopia), the optic nerve could still be seen clearly on the scan. Ridges on highly myopic eyes could also be seen, a feat that gives the SS-OCT another advantageous point over the SD-OCT.

Dr. Sugiyama also showed that even the entire structure of the posterior and anterior segment could be seen along with angles of the Schlemm’s canal being visible. The RNFL’s thickness could also be mapped out on the wide field scanner, providing better visualisation of the relationship between RNFL (retinal nerve fiber layer) thinning and visual defects.

Dr. Tae-Woo Kim pointed out that there hasn’t been much consensus over the use of the new SS-OCT and OCT-Angiography technologies. However, he explored how ophthalmologists could utilize these technologies in their clinical practice. Looking at the intricacies of evaluating deep optic nerve head (ONH), he pointed that the principle pathology of the damage occurs in the deeper portions of the eye. So, beyond looking at the RNFL, a glaucoma eye actually has deformed and compressed lamina cribosa.

Most recently, in animal models, the lamina becomes deformed when IOP was elevated. Axonal flow is hampered the lamina has been compressed. With this understanding, Dr. Kim believes there are three potential applications for deep ONH imaging – for diagnosis, seeing a wider horizon is the future of glaucoma management.
for predicting glaucoma development in glaucoma suspects as well as tracing its pathogenesis.

It has been found that posterior displacement of the lamina cribosa is shown in glaucoma eyes. Dr. Kim said that from the data, ophthalmologists could use lamina deformation as the basis to diagnose glaucoma. Using lamina cribosa imaging to diagnose is useful, he said, but it may be difficult if doctors do not know the patient’s history, for instance in the case of an ischemic optic neuropathy event.

In this case, Dr. Kim said doing a deep ONH imaging would be more informative. He provided a few references so the audience could learn to recognize the difference in a damaged lamina in a glaucomatous eye. To predict RNFL loss in eyes with suspected glaucoma, Dr. Kim and his team did a study on the morphology of the lamina cribosa. The study concluded that when IOP-related stress plays a major role, glaucoma appears with the deformation of the lamina cribosa. During his presentation, he had included the same image of the lamina cribosa taken with the SD-OCT and the SS-OCT, with less noise noted in the SS-OCT images.

Furthermore, OCT angiography is able to capture the decreased vasculature in glaucoma patients, so it has the potential to reveal the blood flow of the ONH related to glaucoma.

Some studies have suggested the decrease of parapapillary retinal blood flow indicates the development of glaucoma. Dr. Kim also presented his study which looked at how parapapillary choroidal microvasculature dropout (MvD) in primary open angle glaucoma which concluded that the presence of MvD in the parapapillary choroid was a strong predictor for initial parafoveal scotoma (IFS).

Dr. Christopher Leung who had earlier demonstrated that damage to the lamina cribosa preceeds optic nerve thinning, also shared his findings on the advances in the detection and monitoring of glaucoma with SS-OCT. He highlighted that RNFL defects can be missed by the circle scan because numerous evidence especially from Korean and Japanese studies have shown that if we only look at the clock hour neuroretinal rim, we might miss out on the glaucoma and even on glaucoma progression. Thus, using a wider field imaging and image mapping, in particular with Triton’s OCT features would provide a more sensitive and specific platform to detect RNFL abnormalities compared with only using circle scans.

He also said it would be beneficial to study the macular ganglion cell, inner plexiform layer. After following over 500 glaucoma patients over 5 years, he and his team took images of both the macular and parapapillary area of the patients every 4 months, and they found that there were changes in the macular in the GCLPI layer before seeing changes in the parapapillary area. His take home message was that doctors should pay attention to the two areas in the diagnosis of glaucoma. Dr. Leung also highlighted the Trend-based Progression Analysis (TPA) as the future of managing glaucoma. Furthermore, this detailed monitoring made possible by wider (12mm x 9mm) field scans and ultrasensitive imaging technology may prevent the loss of visual field, as concluded in his study.

Not only that, but by looking at RNFL optical texture analysis (ROTA), it is possible to see retinal fiber defects.
With the advent of regenerative medicine especially in the area of eye treatments using stem cell, would ophthalmologists still have a job? This question was posed today even as rapid developments in this field, evident from the works of distinguished speakers at today’s session, has propelled eye treatments further with significant implications and vast possibilities for the future.

Dr. Masayo Takahashi spoke on her landmark study of the iPSC (induced pluripotent stem cells) trial where iPSC-RPE cells were injected into an AMD patient in an autologous mode of stem cell treatment. Even though the study stopped before the second patient was tested on, the first patient has so far not reported any signs of rejection or tumor formation with the retina remaining intact in the originally transplanted area.

Dr. Kohji Nishida, in his talk on iPS cell therapy for the cornea elaborated on the development of SEAM (self-formed ectodermal autonomous multi-zone) method where corneal epithelial progenitor cells (iCEP) are induced from human iPS (induced pluripotent stem cells) in order to generate functional corneal epithelial cell sheets. The SEAM method is promising as it mimics the whole development of the eye, including the posterior parts (e.g. neuro-retina and retinal pigment epithelium (RPE)) to the anterior parts of the eye such as the ocular surface ectoderm, lens and so on.

Dr. Nishida and his team managed to grow the corneal epithelium sheets and had successfully transplanted the human iPS cells-derived corneal epithelial cell sheets in rabbit models. The most amazing aspect of this study was the ability to isolate and produce different types of eye cells from the various zones within the same experiment. Human clinical trials of these hiPS cell-derived corneal epithelial cell sheets are in the planning stage.

Dr. De-Kuang Hwang spoke on the implications of using stem cells for treating retinal and choroidal diseases. They’ve done work where laminin modification of the subretinal bio-scaffold remodels retinal pigment epithelium-driven microenvironment in vitro and in vivo. He said that tissue reprogramming is the most important application of stem cell therapy in the future even as patient specific cell models (iPSC) in the understanding of pathophysiology and drug screening are already being applied today.

While the technology of stem-cell based products is already fast moving ahead in the field of regenerative medicine, regulation may be slower in catching up. Dr. Mandeep S. Singh shared that so far, the U.S. Food and Drug Administration (FDA) has not approved any stem cell based products. He also shared an overview of current stem cell trials being conducted. There are 25 stem cell trial sites in the US with 29 ongoing trials outside of the US and 9 trial sites across the Asia-Pacific region.

Dr. Mandeep also brought up the ethical issues arising in retinal stem cell therapy namely with patients being asked to pay doctors for experimental procedures. He also touched on strategies for stem cell treatments (for instance, deciding if the treatment should be allogeneic or autologous, if the source of stem cells should be from the lab or other humans, etc.) based on the questions that his patients had asked.

Fresh from being presented with the De Ocampo Lecture award by Asia-Pacific Academy of Ophthalmology (APAO), Dr. Yizhi Liu shared on his research on lens regeneration using endogenous stem cells for the treatment of congenital cataract. In his landmark research, he and his team had looked at how the lens can regrow itself. The functional lens regeneration was seen in human infants with cataracts within 6 months. This method is unique as it preserves endogenous lens epithelial stem/progenitor cells (LECs) while regrowing the lens. The study was hailed as one of the most notable advances of 2016, according to Nature Medicine. Dr. Liu also jokingly compared the relief of finishing his 18-year research leading to success with Leonardo DiCaprio’s long wait ever since “Titanic” to his first Oscar more than a decade later.

Nanomedicine is not to be missed out as well when Dr. Samuel Yiu presented on the new frontiers of cornea transplantation using nanomedicine for the prevention of corneal allograft rejection. His project is also groundbreaking in the use of nanofiber composite membranes to support human limbal stem cell transplantation.
APAO’s ophthalmic industry partners keep expanding every year...
Phase IIIb/IV clinical trial conducted across 62 sites. The study concluded that aflibercept monotherapy leads to favorable vision gains and high rates of polyp inactivity. Two-year data from the study demonstrated that aflibercept monotherapy is non-inferior to aflibercept + active rescue PDT.

Then Dr. Masahito Ohji from Shiga University of Medical Science, Japan, spoke on treatment approach in nAMD, with a special emphasis on the ALTAIR Study. He elaborated on the anti-VEGF therapy for nAMD, including fixed injections (monthly or bimonthly), pro re nata (PRN) (as needed), and treat and extend (T&E). The ALTAIR Study is a randomized, open-label Phase IV study evaluating the efficacy and safety of repeated doses of aflibercept with variable treatment intervals in patients with nAMD, performed at 40 sites in Japan. The primary objective of the study was to assess the efficacy of aflibercept with two different T&E dosing regimens for nAMD in Japan. Meanwhile, the secondary objective was to assess the safety of aflibercept with two different T&E dosing regimens for nAMD in Japan for up to two years.

Dr. Won Li Kee from Seoul St. Mary’s Hospital, the Catholic University of Korea, presented on the management of PCV – a clinician’s perspective. He found that aflibercept monotherapy results in good outcomes across multiple PCV studies. Anti-VEGF monotherapy avoids potential side effects associated with long-term PDT treatment. Over two years in the PLANET study, patients achieved vision gains of approximately 10 letters, despite 83% not requiring PDT. Moreover, drug-induced complete polyp regression and polyp inactivation is achievable.

The objective of the PLANET study was to determine the efficacy and safety of aflibercept monotherapy vs. aflibercept with rescue photodynamic therapy (PDT) in subjects diagnosed with PCV, and also to determine whether aflibercept monotherapy is non-inferior to aflibercept with rescue PDT based on best corrected visual acuity (BCVA) in subjects diagnosed with PCV. It was a randomized, double-masked, sham-controlled, multicenter side effects associated with long-term PDT treatment. Over two years in the PLANET study, patients achieved vision gains of approximately 10 letters, despite 83% not requiring PDT. Moreover, drug-induced complete polyp regression and polyp inactivation is achievable.

In his summary, the chairperson of the symposium, Dr. Chan Wai Man, discussed two recent reviews on the treatment of PCV and nAMD relevant to the Asia-Pacific region. He also spoke about extending the horizons in the management of nAMD and PCV.
APAO 2019

THE SCIENCES AND ARTS OF OPHTHALMOLOGY

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