The 13th meeting of the Asia-Pacific Vitreo-retina Society (APVRS) opened yesterday to a magnificent heart-thumping Chinese dance and drum performance, as some 4,000 delegates from over 40 countries gathered at the National Exhibition and Convention Center (NECC), Shanghai, China, one of the largest exhibition complexes in the world.

“The APVRS congress is an established first-rate platform in the Asia-Pacific region for scientific change, research, and discovery in the field of vitreo-retinal disease. Shanghai is an economic, financial, cultural and scientific center of China, with numerous places of interest and also Chinese cuisine waiting for you to explore it,” Congress president Professor Xiaoxin Li said in her welcome address.

“Every year we prepare the best programs and scientific sessions,” said Congress president Professor Xun Xu.

“I was also born in the year of the pig. For the Chinese, the pig symbolizes fortune and more importantly, a huge potential for growth,” he explained.

The Asia-Pacific region has become one of the most important engines for the world economy, with China and Japan coming in second and third respectively after the United States.

“The Asia-Pacific region is progressing very rapidly. Likewise, the growth of APVRS has been tremendous and amazing,” said Prof. Lam.

“Time flies. Without our noticing, it is already 12 years since we last organized the APVRS in China in 2007,” said Professor Dennis Lam, president of the APVRS, in his welcoming speech.

He said that the Chinese believed that a period of 12 years carries a special meaning as it completes a cycle in the Chinese zodiac where each year is represented by an animal such as the tiger, dog or monkey.

The year 2007 was the year of the pig and 2019 is too, he noted.
TREAT WITH FORESIGHT

Briefing Instructions

[Drug Names] Generic name: Aflibercept Intravitreal Injection Trade name: EYLEA English name: Aflibercept Intravitreal Injection [Components] Active ingredient is Aflibercept [indications] Eylea is indicated for adults for the treatment of neovascular (wet) age-related macular degeneration (nAMD), diabetic macular edema (DME). [Dosage and method of administration] Eylea is for intravitreal injection into the eye only. [Precautions] The recommended dose for Eylea is 2 mg aflibercept, equivalent to 50 micrograms. For nAMD, Eylea treatment is initiated with one injection per month for three consecutive doses. The treatment interval is then extended to two months. Based on the physician’s judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at two months or further extended, using a treat-and-extend dosing regimen. For DME, Eylea treatment is initiated with one injection per month for five consecutive doses, followed by one injection every two months. After the first 12 months of treatment with Eylea, the treatment interval may be extended. Please read details in instructions. [Adverse Reactions] Serious ocular adverse reactions in the study eye related to the injection procedure have occurred in less than 1 in 1,000 intravitreal injections with Eylea and included blindness, endophthalmitis, retinal detachment, cataract traumatic, cataract, vitreous haemorrhage, vitreous detachment, and intracocular pressure increased (see [Special warnings and precautions for use]). The most frequently observed adverse reactions (in at least 5% of patients treated with Eylea) were conjunctival haemorrhage (25%), visual acuity reduced (11%), eye pain (10%). Please read details in instructions. [Contraindications] Hypersensitivity to the active substance aflibercept or to any of the excipients listed in [Components], Active or suspected ocular or periocular infection, Active severe intraocular inflammation, [Special warnings and precautions for use] Increase in intraocular pressure increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including those with Eylea (see [Adverse Reactions]). Special precaution is needed in patients with poorly controlled glaucoma (do not inject Eylea whilst the intraocular pressure is ≥ 30 mmHg). In all cases, both the intraocular pressure and the perfusion of the optic nerve head must therefore be monitored and managed appropriately. Systemic effects: There are limited data on safety in the treatment of patients with DME with a history of stroke or transient ischaemic attack or myocardial infarction within the last 6 months. Other: Treatment should be withheld in patients with rhegmatogenous retinal detachment or stage 3 or 4 macular holes. In the event of a retinal break, the dose should be withheld. The dose should be withheld within the previous or next 28 days in the event of a performed or planned intravitreal surgery. Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the fetus (see [Pregnancy and Lactation]). Effects on ability to drive and use machines: Injection with Eylea has minor influence on the ability to drive and use machines due to possible temporary visual disturbances associated either with the injection or the eye examination. Patients should not drive or use machines until their visual function has recovered sufficiently. Special precautions for disposal and other handling: For the intravitreal injection, a 30 G x ½ inch injection needle should be used. Please read details in instructions. [Drug Classification] Prescription drug [Manufacturer] Name of the Manufacturer: Vetter Pharma-Fertigung GmbH & Co. KG [Manufacturing address: Veter Pharma-Fertigung Eisenbahnstr. 2-4 88085 Langenargen Germany] [The version of instructions] Approval date: 2nd Feb. 2019, 8th May 2018 [Revision date: 30th Nov, 2018, 12th Apr, 2019] For completed information, please read Eylea’s Instructions, Bayer.

阿柏西普眼内注射液
艾力雅
From just dozens of participants at the first APVRS in Hong Kong, and hundreds in China in 2007, today there are thousands, he said, predicting even more growth for the Congress in years to come.

“APVRS will soar to new heights in terms of training, education, services, and most importantly, preventing and treating blinding retinal and macular eye diseases in the Asia Pacific region.”

“Enjoy the congress, enjoy Shanghai. See you next year in Hong Kong,” Prof. Lam said, ending his speech.

The APVRS was created in 2006 when three visionaries Dennis Lam, Yasuo Tano, and Ian Constable wanted to create a network for Asian countries to share knowledge and promote research and education in the field.

“These three had a vision for the region,” said Associate Professor Andrew Chang, Secretary-General of the APVRS.

“Over the past decade, we have seen retina exploding, new technologies, better diagnoses, better outcomes and therapies for our patients,” he told the audience.

“We need to nurture the young because the young are the future of retina in our region,” Associate Professor Chang added.

Yesterday’s opening ceremony also saw this year’s APVRS Tano Lecture awarded to Professor Paul Mitchell, Professor of Ophthalmology, Westmead Institute for Medical Research, University of Sydney.

The APVRS Tano Lecture was established in 2009 in memory of Professor Yasuo Tano, the founding president of APVRS.

Every year, the APVRS honors an individual of over 45 years of age for exemplary leadership and significant contributions in advancing the understanding, diagnosis and treatment of vitreoretinal diseases with the APVRS Tano Lecture.

Before delivering his lecture titled The Growing Contribution of Wide Field OCT Angiography to the Current Understanding and Management of Diabetic Retinopathy, Prof. Mitchell paid tribute to Professor Tano.

“He was larger than life in so many ways. He was an extraordinary surgeon and left an incredible legacy. He was the founding president of this society and he really was a giant,” shared Prof. Mitchell.

During his lecture, Prof. Mitchell highlighted that there is great potential for WF OCT in managing diabetic retinopathy (DR).

“It will progressively replace the traditional fluorescein, which is a relatively invasive test. You can do this (use the WF OCTA) every week, you can do this every day if you want and you can see acute and long-term chronic changes,” he explained.

“Wide-field OCTA imaging now provides unrivalled resolution of the macular and peripheral retinal vascular bed, including superficial and deep layers,” Prof. Mitchell said, adding that deep layers are not visualized on fluorescein angiography (FA).

OCTA imaging promises better understanding of early changes in the retinal capillary bed in diabetes. Capillary non-perfusion is the principal biomarker for diabetic retinopathy.

“The over-riding advantage is that OCTA can be repeated regularly, as it avoids the need for dye injections with attendant potential side effects,” noted Prof. Mitchell.

WF OCTA can show temporal changes in the peripheral capillary bed, allowing it to have an incremental role in DR monitoring. He added several studies would evaluate the role of WF OCTA in contributing towards the management of diabetic macular edema (DME) with anti-VEGF. It is also useful in managing proliferative diabetic retinopathy (PDR), detecting retinal neovascularization (RNV), and may also help in evaluating the need for panretinal photocoagulation (PRP).

The likely future directions of WF OCTA include software to quantify foveal avascular zone measures, distribution and area of capillary non-perfusion, capillary bed dilatation, and superficial versus deep capillary bed analyses. It could also be used in fractal analysis of the retinal capillary bed, retinal vascular caliber measures for arterioles and venules, and new vessel characteristics including the number of discrete fronds.

“The sky is the limit. These are very exciting times,” Prof. Mitchell said, concluding his lecture.

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The sky is the limit.
These are very exciting times.

– Prof. Paul Mitchell
In a session focused on geographic atrophy (GA), an advanced form of dry age-related macular degeneration (AMD), some noteworthy advancements and discoveries were shared among an early audience on Day 1 of the 13th Asia-Pacific Vitreo-retina Society (APVRS) Congress in Shanghai, China.

Dr. Kourous Rezaei from the Illinois Retina Associates (United States) shared details of the results of the recently concluded study in his presentation entitled Zimura Pivotal Trial in Geographic Atrophy Secondary to AMD.

The overall data showed that the primary efficacy endpoint was achieved for both Zimura 2mg and Zimura 4mg dose which led to a reduction of 27% in GA growth over 12 months, compared to their respective sham groups. The drug was well tolerated by a generally balanced cohort across baselines. He highlighted that the majority of the patients tested on were extrafoveal and he believes that because these lesions were shown to grow faster, therefore, it validates the potential of Zimura (Iveric Bio, NY, USA) as blocking the fast-growing lesions. The results were robust, he said, as he pointed out that the overall data suggested a dose response relationship. It was also revealed that they are at a stage of initiating the second pivotal trial with plans to begin enrolling in the first quarter of 2020.

The next speaker, Prof. Yasuo Yanagi from Ashikawa Medical University (Japan), who is also based in the Singapore National Eye Centre (SNEC) and Singapore Eye Research Institute (SERI) unveiled a fascinating look at Longitudinal Changes of Pachydrusen. His study highlighted a new type of drusen – pachydrusen, which can look very similar to drusen-like deposits (DLDs). It is about 125 microns, with irregular outer contour, and better-defined outer borders, distributed over the posterior pole, with scattered distribution over the posterior pole, numbered in isolation or in groups of only a few yellow-white deposits.

Finally, they are typically related with thick chorioids. He took the audience through a quick study of the characteristics of the various types of extracellular deposits such as drusen, reticular pseudodrusen, pachydrusen and DLDs, drawn from a five-year study in a rural population of Hokkaido, Japan. He said the higher the age, and the more they smoked, the more prevalent pachydrusen is. They found that the prevalence of pachydrusen and DLDs may be higher than previously thought. He demonstrated the dynamic changes of the pachydrusen within the space of five years with a spontaneous regression in these pachydrusens and DLDs. These eyes, also, typically did not develop atrophy.

Artificial intelligence (AI) peeks into Predicting AMD Progression and manages to diagnose eye disease such as diabetic retinopathy, AMD and glaucoma from fundus photos, as shown by Google Health Research Director, Dr. Dale Webster. He gave an example of AI predicting the risk of heart attacks from fundus photographs through the deep learning of characteristics of patients, creating predictive features from these categorized characteristics. The implications are useful for better patient care as a result of AI being able to measure the severity of a disease, to show any new signals and to predict progressions of a disease.

Prof. Paul Mitchell, who was also one of the chairpersons for this session together with Dr. Yushen Wang then presented on the Role of OCT Angiography in Assessing Atrophic Changes in Treated Neovascular AMD. He discussed several vital questions when it comes to GA changes in patients with neovascular AMD (nAMD) who are being treated with anti-VEGF agents, going over the frequency of atrophy development in these patients, the risk factors, the time course of atrophy in treated patients, frequency of seeing CNV membranes in OCTA and their appearance as GA progresses. As he reminded the audience that CNV (choroidal neovascularization) is a biomarker for AMD, the main question he brought up was this: “Once OCTA-defined CNV disappears in these treated cases, should we stop therapy?”

Prof. Mitchell emphasized that “a randomized clinical trial (RCT) is needed in cases when CNV is absent on OCTA”. He went on to say that non-invasive OCTA can form the kernel of trials of stopping or suspending therapy in patients with atrophy while those with no signs of residual CNV could continue on or suspend injections, with potentials for rescue. “OCTA will be of great assistance in assessing treatment futility,” he said. Future studies are needed in this topic for better segmentation of OCTA images, he further concluded.

In the CATT study, wet AMD is treated with anti-VEGF is the gold standard, but Dr. Lee-Jen Chen from Mackay Memorial Hospital in Taipei, Taiwan, brought up an interesting phenomenon in the CATT study where more and more patients (12% in the first year and 38% in the fifth year) develop GA in the course of anti-VEGF injections, leading to the question: “Do anti-VEGF injections really increase the chances of GA?”

After explaining the risks factors of GA associated with older age, VA of less than 20/200, large CNV and foveal intraretinal fluid, Dr. Chen said: “Patient factor is more important than the drop factor.” He reckoned that it is retinal angiomatous proliferation (RAP) that contributes to the development of GA very often through anti-VEGF injection. However, this is not necessarily a bad thing especially for RAP because when comparing the RAP and non-RAP, VA actually improves in the RAP group. In RAP cases after anti-VEGF injections compared with natural occurrence of RAP, the VA is much better, he said. Also, CNV is shown to decline from 32% in the fovea in year 1 and decreases to 10% in year 5. The lesions keep growing but disappears later. He concluded that perhaps the treat-and-extend regimen can improve overall groups’ VAs.

Overall, the various aspects of discoveries and AMD was eye opening with Prof. Mitchell’s call for more studies in this topic impressed upon the audience at the end of the session.
APVRS 2020
Hong Kong, China
18-20 DEC, 2020
The 14th Asia-Pacific Vitreo-retina Society Congress
Conbercept and ranibizumab go head-to-head in ME treatment

Anti-VEGF remains a mainstay of treating conditions like macular edema (ME). As such, agents are often compared in trials of safety and efficacy, as in a poster titled The Efficacy of Conbercept or Ranibizumab Intravitreal Injection for ME by Dr. Wang You.

The study included 360 eyes of 264 ME patients, split into three equal groups of 120. Patients in Group A received intravitreal ranibizumab 0.5mg (IVR), while Group B received intravitreal conbercept 0.5mg (IVC). Group C patients did not receive IVC or IVR.

It was found that patients in Groups A and B had better postoperative best corrected visual acuity (BCVA) and differences in thickness in macular fovea changes, over the untreated Group C. Between Groups A and B, there was a difference in medication frequency, at 2.48 and 3.75, respectively.

These results led Dr. You to conclude that “intravitreal injection of ranibizumab or conbercept is an effective therapeutic option in ME. However, the IVC group was more economical than the IVR group”.

Assessing an intraoperative helper: iOCT

Intraoperative OCT or iOCT is a newer addition to ophthalmic prop box. In a poster titled Efficacy of Intraoperative Optical Coherence Tomography in Various...
Vitreo-retinal Indications, Dr. Sabia Handa and co-authors evaluate the efficacy of iOCT in diagnostic and surgical decision-making for various vitreoretinal indications.

The authors collected surgical data of patients who underwent surgery for a vitreoretinal indication, using microscope-integrated iOCT assisted procedures. From there, they were split into 4 groups depending on the usefulness of iOCT: a) as an alternative to surgical adjuvant (like dyes); b) as a surgical step endpoint guide; c) as an informative tool necessitating an additional surgical maneuver; or d) as a diagnostic tool for pediatric patients.

In the end, 67 eyes were enrolled, and successful image acquisition was possible for 65. They found the efficacy of iOCT in the various groups were: a) 27 of 31 eyes (87.1%); b) 6 of 6 eyes (100%); c) 6 of 21 eyes (28.57%); and d) 8 of 9 eyes (88%).

This led the authors to conclude that “in our experience, iOCT has come up as an effective tool in diagnostic and surgical decision-making”.

Heads-up: Looking at digitally assisted surgery

Heads-up surgery promises better technology and ergonomics for physicians... but how does digitally assisted vitreoretinal surgery (DAVS) compare with conventional microscopes? In a poster titled Evaluating the Use and Outcomes of Digitally Assisted Vitreo-retinal Surgery: A Systematic Literature Review, author Leighton Morris takes a look at all available evidence.

The investigator found that “most studies on DAVS support the clinical benefit and physician preference of the technology compared to conventional microscopes. However, some studies show a steeper learning curve evidenced by lengthened surgical and set-up”. Data for this conclusion was collected through a systematic literature review on PubMed, with additional targeted searches in EMBASE. In all 302 abstracts and 16 full text papers were included for analysis.

Results showed that four studies suggest that heads-up displays provide improved surgical ergonomics and comfort for the primary surgeon; while another four suggest a reduced need for endo-illumination with DAVS compared to conventional microscopes. There were also a few studies which noted that DAVS lengthened surgical and set-up time compared to conventional microscopes.

Using AI to detect PCV

Artificial intelligence (AI) is gaining support and traction in the ophthalmic industry for its potential benefits in patient diagnosis and management. In a poster titled Utility of a Public-available Artificial Intelligence in Diagnosis of Polypoidal Choroidal Vasculopathy, Dr. Youxin Chen and co-authors investigate the feasibility of training AI to diagnose PCV using indocyanine green angiography (ICGA).

In the study, the AI model was trained by a data set of 430 ICGA images of normal, neovascular age-related macular degeneration (nAMD) and PCV eyes on a publicly available AI platform. The authors used two methods to test the model: The 1-step method distinguished normal, nAMD, and PCV images simultaneously; the 2-step method identified normal and abnormal ICGA images at the first step and diagnosed PCV from the abnormal ICGA images at the second step. From here, the method with the higher performance was compared to retinal specialists and ophthalmic residents in diagnosis of PCV.

It was found that the 2-step method performed better, distinguishing normal and abnormal images with an accuracy of 1 and diagnosing PCV with an accuracy of 0.83 – which was comparable to retinal specialists and superior to ophthalmologic residents.

This led the authors to conclude that “in this evaluation of ICGA images from normal, nAMD, and PCV eyes, the models trained on a publicly available AI platform had comparable performance to retinal specialists for diagnosing PCV”.

A Peculiar Case: Overlapping White Dot Syndrome

In this poster by Dr. Sushma Jayanna, titled Overlapping White Dot Syndrome, the author presents a case of a 42-year-old female, with a history of diminished vision in the left eye for two weeks.

At presentation, the patient’s BCVA was 20/20 in the right eye and 20/60 in the left, and the anterior segment of both eyes was unremarkable. Mild vitritis was found in the left eye, with multiple round placoid chorioretinitis lesions at the posterior pole. The patient’s history and clinical picture were suggestive of inflammatory pathology.

On fundus autofluorescence, there was a hypoauteofluorescent center and hyperautofluorescent margins, suggesting activity. Meanwhile, using fluorescein angiography, initial hypo and late hyperfluorescence of the lesion was noted, which was suggestive of acute posterior multifocal placoid pigmentary epitheliopathy. It was found that a few lesions also showed an initial wreathlike hyperfluorescent pattern, which is characteristic of multiple evanescent white dot syndrome.

The investigator concluded that “systematic evaluation including multimodal imaging of white dot syndromes can help in diagnosing rare associations and overlaps”. Dr. Jayanna also noted that “the possibility of other differentials like multifocal choroiditis (MFC) and punctate inner choroidopathy (PIC) should also be kept in mind to be ruled out”. 🎯
**Future Considerations in RVO and Patient Management**

*by Joanna Lee*

"Retinal vein occlusion (RVO) is the second most common visually disabling disease affecting the retina, affecting 16 million people worldwide," said Dr. Sherman Valero from the Philippines, as he introduced the reasons steroids are used in the treatment of RVO.

The current indication for Ozurdex (Dexamethasone 0.7 mg implant, Allergan, Dublin, Ireland) in China is RVO. The use of corticosteroids, as Dr. Valero pointed out in his session, has potential effects on macular edema, in particular being anti-inflammatory, anti-edematous, being potent vasoconstrictors and blocking VEGF-induced vasodilation. Specifically, dexamethasone, fluocinolone and triamcinolone have distinct pharmacologic and clinical profiles that are relevant to the individualized management of patients with retinal disease. What was interesting was that dexamethasone has the lowest incidence of patients developing ocular hypertension at 10-15% as opposed to 30% and up to 65% incidences with other types of corticosteroids.

Leading into dexamethasone’s efficacy and safety for vitrectomized patients was Dr. Sun Xiaodong from China. He began with a look at Novadur (Allergan, Dublin, Ireland), a new drug delivery technology which uses a biodegradable PLA/PLGA polymer implant containing 0.7mg dexamethasone. Dr. Sun pointed to a multi-centered retrospective study of 72 RVO-macular edema patients with 13 vitrectomized and 59 non-vitrectomized eyes.

The study showed no significantly statistical difference in CMT nor BCVA change between the two groups within 8 weeks after the injection of Ozurdex, with improvements in both groups of eyes in terms of CMT and BCVA. Thus, he concluded that Ozurdex is the first choice for RVO-ME recommended by authoritative guidelines.

As Dr. Marc De Smet from Lausanne, Switzerland, said that real world data could present a better picture of dexamethasone’s usage for patients, he highlighted a few pivotal studies, both registration studies and randomized independent clinical studies that showed improvements in visual acuity. In particular, a Chinese registration study in BRVO even showed sustained improvements than the pivotal GENEVA study (conducted by Allergan).

The 12-month Korean COBALT study showed 18 letters of improvement within 6 months and 15 letters by the end of the year, with a treatment frequency of every four months.

Regarding safety, especially in the risk of elevated intraocular pressure, the Safodex study showed 40% of patients with RVO not needing any IOP lowering medication, with another 30% needing one drop, but very few that require two or three.

Referring to the CONSTANCE study, Dr. De Smet warned that cardiovascular events are not uncommon and that is something that needs consideration if treating these patients. Overall, he concluded that anti-VEGF response is limited in many patients, with 40% having less than 15 letters at 1 year. Ozurdex works best if introduced early and used to prevent edema occurrence and it is to be considered as a first line of treatment.

Furthermore, Dr. Michael Singer provided a practical, yet invigorating insight, into how he approaches the treatment of RVO patients with his eye on both ischemic and inflammatory components. He uses a patient’s fluorescein angiography (FA) and OCT baseline as a guide to follow-up and to monitor the treatment effect. For patients under 45-years-old, he would usually start anti-VEGF therapy, twice for a loading dose and follow-up monthly to see the effect. If the OCT shows as dry, he would extend by two weeks up to four months (as the longest interval). If there’s swelling captured on the OCT, then he would contract the injections by 2 weeks.

If there has been insufficient treatment, or if the patient is unable or unwilling to come for monthly therapy, or if patient has recently suffered from a heart attack or stroke, then consider a dexamethasone implant and follow-up with patients at 6-8 weeks for any rise in IOP. He advised to follow-up 2 months later to check for any occurrence of swelling again. "If that occurs, treat it again with a dexamethasone implant,” he said. In an interview, Dr. Singer revealed he has been doing this for the last five years. “The results have been good as patients’ OCT have been drier and the injection interval has increased,” he shared.

Overall, the session was a deep insight into considerations of dexamethasone, its safety and efficacy as seen in various types of studies.
Advances in technology and techniques are revolutionizing the field of ophthalmology, attendees on the opening day of the 13th Asia-Pacific Vitreo-retina Society (APVRS) Congress in Shanghai, China, were told.

In an early morning symposium, speakers introduced a range of the latest developments on swept-source optical coherence tomography (SS-OCT), ultra-wide field imaging, doppler optical coherence tomography, fluorescence lifetime imaging ophthalmoscopy, adaptive optics and the use of artificial intelligence in retinal imaging.

Professor Gemmy Cheung, a senior consultant at Singapore National Eye Centre (SNEC), introduced SS-OCT, a relatively new form of imaging that is capable of capturing structures and details invisible to previous generations of OCT machines. Swept-source penetrates deeper, wider and in higher resolution than spectral-domain technology is capable of, Dr. Cheung told conference delegates.

The hope is that SS-OCT will be able to better discern the details of deeper tissues, therefore helping clinicians to better detect and treat problems. “The future is really swept-source,” said Dr. Cheung, adding that advances and improvements in the technology are still being made.

Suqin Yu, an associate professor of ophthalmology at Shanghai Jiaotong University, spoke on ultra-wide field imaging, a method of imaging the peripheral retina that makes photography more clinically practical.

The peripheral retina is the site of pathology in the majority of ocular diseases, including Coats’ disease, vasculitis, uveitis, choroidal dystrophies, retinal tears and detachments, diabetic retinopathy, retinal vein occlusions and choroidal masses, among others.

It can be used to detect a wide range of conditions, she said, many of which could be missed without this technology. Ultra-wide field imaging allows for examination of the retinal periphery in a less intrusive manner.

“I think in the future it will be used in more of our clinics,” said Dr. Yu.

Doppler OCT displays tissue images by using a backscattered light, Youngseok Song, of Asahikawa Medical University in Japan, told delegates during the symposium.

Earlier Doppler OCT technology was limited in use because it was slow and required significant training, Dr. Song emphasized to the delegates, but advances now mean it can provide real time visualization of retinal blood flow in three seconds and be operated by someone without any specific skills.

Professor Srinivas Sadda, president and chief scientific officer of the Doheny Eye Institute (Los Angeles, CA, USA) introduced the benefits of fluorescence lifetime imaging ophthalmoscopy (FLIO), an imaging system that reveals specific patterns in fundus disorders.

FLIO is an extremely fast technique, making it clinically possible, with many potential applications, Prof. Sadda told delegates.

Similar to conventional fundus autofluorescence (FAF), FLIO is mainly a qualitative imaging procedure, relying on a modified Heidelberg Spectralis platform (Heidelberg Engineering, Germany). However, in an advanced FAF, FLIO can also provide quantitative analysis by measuring the fluorescence lifetime of fluorophores.

“We are certainly excited about FLIO,” said Prof. Sadda, although the technology is still in its early stages.

Dr. Amani Fawzi, a professor of ophthalmology at Northwestern University (Chicago, Illinois, USA) spoke to the audience about adaptive optics (AO), an important advancement in technology that allows clinicians to monitor the progression of retinal disease cell by cell.

AO compensates for optical aberrations, thereby enabling any ophthalmoscope modality, including flood-illuminated fundus cameras, scanning laser ophthalmoscopes, and OCT, to produce sharper images. By doing this it can provide new insights into retinal diseases and could be used to evaluate the effectiveness of treatment.

The technology can provide “a really clear imagine of what is going on down to photo-receptor level,” Dr. Fawzi told delegates.

Adaptive optics was originally developed by astronomers as a means to compensate for the aberrations caused by turbulence in the earth’s atmosphere, before its potential in the field of ophthalmology was discovered.

It works by using a sensor that measures the aberrations introduced into light exiting the eye using a series of lenses, each of which samples a local portion of the incidence wave-front and focuses light on a charge-coupled device.

Then, based on software algorithms, a series of actuators deflect the surface of a deformable mirror to compensate for these aberrations so that light exits the surface of the mirror in parallel planes.

Earlier versions of the tech for ophthalmology were room-sized and required PhD-level staff to operate, but advances have created much smaller systems that are more simple to use, according to Dr. Fawzi.

Dr. Daniel Ting, a consultant at Singapore National Eye Centre (SNEC), talked about the revolutionary impact artificial intelligence (AI) will have on the field of ophthalmology. The subject matter has sparked enormous global interest in recent years, he told the audience, with thousands of papers published on its applications in the past few years.

While deep learning AI has been widely adopted in other areas, such as facial recognition technology, it remains on the fringes of ophthalmology, said Dr. Ting.

It has been applied to fundus photographs, OCT and visual fields, among other areas, with robust results, but there remain challenges to adopting it, both clinical and technical, including the explainability of the algorithm results, medicolegal issues, and physician and patient acceptance of the AI ‘black-box’ algorithms, he concluded.
The Challenges in Surgical Retina Symposium on the opening day of the 13th Asia-Pacific Vitreo-retina Society Congress (APVRS 2019) in Shanghai, China, was chaired by Dr. Carl Claes (director and head of ophthalmology at Antwerpen), Dr. Masahito Ohji (professor and chairman of the Department of Ophthalmology at the Shiga University of Medical Science in Shiga, Japan) and Dr. Meixia Zhang (Department of Ophthalmology, West China Hospital, Sichuan University, Chengdu, China).

Dr. Karl Bartz-Schmidt, director of the University Eye Hospital Tübingen in Germany, spoke on the repair of rhegmatogenous retinal detachment (RRD), and how to avoid complications by subretinal perfluorocarbon (PFC) in primary vitrectomy. According to Dr. Bartz-Schmidt, re-attachment of the retina by Fluid-Fluid-Air Exchange is possible.

“Under air, we achieve a better view to the anterior retina. Laser treatment becomes easier, and PFC remnants are excluded. This ultimately saves time and brings the cost down. Although there is definitely a learning curve, TGV is the preferred surgical technique,” said Dr. Bartz-Schmidt.

RRD repair is one of the most common vitreoretinal surgeries performed by a surgeon, according to recently published paper by Nagpal et al.1 In a best-case scenario, RRD can be repaired with a single surgical intervention. However, up to 10% of cases require additional interventions to ultimately repair recurrent detachments.

Further in the session, Prof. Dr. Young Hee Yoon (professor of ophthalmology at the Asian Medical Center, Korea), spoke on 27-gauge (27g+) vitrectomy for complex diabetic retinal detachment. The 27g+ is a smaller probe with increased stiffness. It has a short attraction distance and a small sphere of influence (SOI). The smaller the SOI, the more precise the surgery will be, and there is minimal risk of collateral damage. Besides that, it has a high cut rate (7500cpm-10,000 cpm). It offers flexible duty cycle control, a bevelled tip and a port closer to the end. It comes with a full range of accessories.

“The 27g+ is designed to offer surgeons exceptional access to small tissue planes, with efficiency and precision. The 27g+ high-speed bevelled microincision vitrectomy surgery (MIVS) is my first choice for treating complex diabetic retinal detachment,” said Prof. Dr. Yoon.

On the other hand, Dr. Fumio Shiraga (professor and chairman of the Department of Ophthalmology at the Okayama University Graduate School, Japan) presented on autologous transplantation of the internal limiting membrane (ILM) for refractory macular holes (MH).

According to recently published studies, treatment with autologous ILM fragment transplantation seems to be an efficient alternative for large, chronic and refractory MH.

“In my opinion, in the beginning, inverted ILM flap technique should not be considered in large MH,” said Dr. Shiraga. “Instead, the regular MH surgery should be considered for large holes. When regular surgeries fail in hole occlusion, ILM transplantation should be considered. Our study suggests that autologous transplantation of the ILM may contribute to the improvement of anatomical and visual outcomes in the treatment of refractory MH,” explained Dr. Shiraga.

Speaking about traumatic endophthalmitis, Dr. S. Natarajan, head and consultant of Vitreo-Retinal Surgery at Aditya Jyot Eye Hospital in Mumbai, India, proposed strategic thinking in ocular trauma, where an individualized approach is afforded to each patient. The priority is to determine the most suitable line of management for the patient, noted Dr. Natarajan. The advantages of pars plana vitrectomy (PPV) for these cases include increased retinal oxygenation, and reduced load of inflammation debris (hence decreasing its harmful effects on the retina). It also allows direct visualization of the retina for assessing status to aid further management and reduces severity of any retinal complications.

Dr. Dawei Sun from Harbin Medical University, China, presented on the application of foldable capsular vitreous body (FCVB) in silicone oil dependency. According to Dr. Sun, the most common FCVB cases are silicone oil dependence and prevention of complications after silicone oil tamponade.

“For early cases, it is best to select patients with no light sensation and propose the implantation of the artificial eye afterenucleation,” suggested Dr. Sun. With the familiarity of FCVB and the proficiency of surgical operation, visual oculi will gradually transit to it, he noted. “Patients with early ocular trauma or intraocular or vitreous hemorrhage should be given expectant treatment first, such as hemostatis and anti-inflammation. It is recommended to perform surgery two weeks later after the surgery is stable, and emergency surgery is not possible,” he shared.

“Physicians should evaluate the benefits and risks of surgery, and patients should fully understand the prognosis of the affected eye before surgery,” concluded Dr. Sun.

References:
Inherited Retinal Degenerative Diseases and the Way Forward

by Tan Sher Lynn

Inherited retinal degenerative diseases (IRDD) include various retinal pathologies with heterogeneous mutations which lead to progressive deterioration of photoreceptor cells accompanied by severe vision impairment. These diseases include age-related macular degeneration (AMD), retinitis pigmentosa (RP), Leber congenital amaurosis (LCA), choroideremia, Stargardt disease, Usher syndrome and achromatopsia. Among them, AMD remains one of the main causes of visual dysfunction.1 It is characterized by the severe vision failure in the central part of the retina.

At the 13th Asia-Pacific Vitreo-retina Society (APVRS) Congress in Shanghai, China, in his presentation entitled Approach to Management Of Inherited Retinal Disease (IRD) And Setting Up An IRD Clinic, Assoc. Prof. Adrian Koh said that IRDs are genetically heterogeneous, with over 260 disease genes to identify to date. Therefore, there is a need to set up an IRD Clinic as a one-stop service for patients and physicians, and as a regional referral center of expertise with the most efficient use of specialized resources and to facilitate database or registry of phenotyped cases for research and clinical trials.

Dr. Ruifang Sui, in her presentation entitled Genotype-phenotype Correlations: Pearls and Pitfalls, noted that there’s a wide clinical spectrum for IRD, whether it is early- or late-onset, rod or cone cell type, progressive or stationary, macular or retina, syndromic or non-syndromic and dysfunction or degeneration. “Genotype-phenotype correlations are observed, and big genotyping data and detailed clinical features are needed. Genome and environmental factors contribute to disease phenotype,” she said.

The subretinal approach was a method employed to treat IRD. The subretinal approach projects started in 1995 in Cologne and Tübingen in Germany, where the initial idea was to deploy a passive microphotodiode array for subretinal stimulation, according to Dr. Karl Bartz-Schmidt, in his presentation entitled The Subretinal Implant, What We Achieved and Why It Ended. However, the energy of the incoming light was not sufficient enough to produce electrical stimulation of the retina. With this knowledge, the decision has been made to develop an external powered chip, which is the active implant. In the subretinal approach, photodiodes and electrodes correspond to the retinotopic correct localization and the remaining retinal network can be utilized. “Fixation of the chip is easier and eye movements help to localize objects. There are also no visible parts of the implant outside the body,” said Dr. Bartz-Schmidt.

Nevertheless, the clinical reliability of the first generation Alpha IMS Retina Implant has a median lifetime of only 7 months.2 The Alpha IMS design was subsequently changed and renamed as Alpha AMS in order to prolong the median lifetime of the implant and improve usability and benefit for patients. The CMOS Chip is changed from 800nm to 350nm. Other changes include the foil substrate and silicone cable. “With this, a more reliable product with a clinical durability of around 5 years and visual acuity of up to 4% (20/546) is achieved,” he shared.

Nevertheless, in March 2019, Retina Implant AG in Germany discontinued its business activities, mainly due to rigid European approval and healthcare systems as well as the results, which ultimately fell short of expectations for many patients, as only half of the patients were able to recognize shapes.

Another promising treatment modality for IRD is stem cell therapy. In her presentation entitled Stem Cell Therapy in IRD, Dr. Zheng Qin Yin noted that China has the largest number of blind patients in the world, which is more than 8 million, among which 1/3 is caused by retinal degenerative (RD) diseases, including AMD, RP, diabetic retinopathy (DR) and glaucoma. Retinal degeneration is caused by specific degeneration of retinal cells that lead to irreversible blindness.

“Nevertheless, there remain challenges in stem cell transplantation. The pros of using adult stem cells (ASCs) and mesenchymal stem cells (MSCs) are increased safety, low risk of tumorigenicity and immune rejection, while the cons are limited cell sources, lower pluripotency, and more difficulty to standardize and industrialize. Meanwhile, embryonic stem cells (ESCs) are pluripotent, stable, able to proliferate in vitro and easy to industrialize; however, they carry a higher risk of tumorigenicity and gene mutation. The ideal cell source is hEROS derived C:Kitt+/SSEA-RPC as it combines the pros of ASCs and ESCs by being low in tumorigenicity, which provides pluripotent differentiation and has a long-lasting effect,” she said.

References:

Correctly diagnosing polypoidal choroidal vasculopathy (PCV) is key, in order to formulate the best possible treatment strategy in PCV management for patients, delegates at the 13th Asia-Pacific Vitreo-retina Society Congress (APVRS 2019) heard yesterday.

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in elderly people globally. It is estimated that there will be more Asians with AMD than the rest of the world combined by 2050.

In Asian populations, polypoidal choroidal vasculopathy (PCV) is a common subtype of exudative AMD, while choroidal neovascularization secondary to AMD (CNV-AMD) is the typical subtype in Western populations.

Evidence supports that symptomatic patients with PCV can have complete regression without severe vision loss with photodynamic therapy (PDT) and anti-VEGF treatment.

Recent research in the field of imaging has provided further clarification of differences between PCV and CNV-AMD. The two respond differently to intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) treatment, highlighting the need for accurate diagnoses.

Dr. K. Bailey Freund from the Vitreous Retina Macula Consultants of New York, and clinical professor of ophthalmology, NYU School of Medicine, noted that American retinal specialist Lawrence Yannuzzi used the term “IPCV” to describe an exudative maculopathy occurring mostly in middle-aged black women. These patients typically had peripapillary type 1MNV with “polyps” which are dilated neovessels originating from type 1 MNV (aneurysmal type 1 MNV).

But nowadays, the incidence of PCV is also high among Asians as well as blacks.

Aneurysmal pachychoroid neovascularopathy is a common presentation of neovascular AMD in Asian patients who often lack soft drusen.

“What is often called PCV now is not the PCV that was once described. Really what is being described is a neovascular growth pattern that can occur in multiple different disease entities. The term has changed over the years,” Dr. Freund told delegates.

Dr. Keiko Kataoka, from Nagoya University, Japan, explained that the EVEREST trial diagnosed PCV based on the following criteria: focal hyperfluorescent lesions appearing within the first 5 minutes on indocyanine green angiography (ICGA) and including at least one of the following diagnostic criteria: pulsatility on dynamic ICGA, nodular appearance when ICGA viewed stereoscopically, hypofluorescent halo on ICGA, orange subretinal nodule on color photograph and associated massive submacular hemorrhage.

Optical coherence tomographic (OCT) features of polypoidal lesions were sharply peaked pigment epithelial detachment (PED), notched or multilobulated PED, hyperreflective ring under PED while B-scan optical coherence tomographic angiography (OCTA) features of polypoidal lesions were round-ring-like flow signals inside PEDs, incomplete round-ring-like flow signals overlaid with round-ring-like OCT structures inside PEDs, and flow signals adjacent to a PED notch.

“In short, a B-scan OCTA can substitute ICGA for the diagnosis of PCV,” highlighted Dr. Kataoka.

In discussing the Appearance of Polypoidal Lesions Using Swept-source OCTA, Xiaodong Sun, MD, PhD, Shanghai General Hospital, Shanghai Jiao Tong University, explained that PCV is characterized as reddish-orange subretinal nodules in ophthalmoscopy, and polypoidal lesions with or without BVN on ICGA.

Sharing the results of a study, he said that swept-source optical coherence tomographic angiography (SS-OCTA) showed that “polyps are a form of tangled new vessels rather than aneurysmal structures” in the Asian patients involved in the study.

The identification of polypoidal lesions in patients with PCV as neovascular tangles rather than actual polypoidal lesions or aneurysmal dilatations may help facilitate better understanding of their pathogenesis and response to treatment.

Dr. Gregg Kokame from the University of Hawaii School of Medicine, Hawaii, talked about Anti-VEGF Resistance in Exudative Macular Degeneration, A Subtype of PCV.

The standard of care for exudative macular degeneration involves antiangiogenic injections with anti-VEGF, which should lead to marked resolution of leakage and bleeding, with improved visual results.

However, some cases may show anti-VEGF resistance, with persistent leakage or bleeding despite treatment.

In a retrospective study of 216 eyes with exudative AMD and ICGA using the scanning laser ophthalmoscope to evaluate for PVC, the definition of anti-VEGF resistance was persistent subretinal or intraretinal fluid after 4 intravitreal injections.

In the anti-VEGF resistant group comprising 120 eyes, 82 eyes (68.3%) received bevacizumab, 22 eyes (18.3%) received aflibercept, and 16 eyes (13.3%) received ranibizumab.

Anti-VEGF therapy has become the standard treatment for exudative AMD but continued leaking and bleeding despite initial treatment occurs in a significant number of eyes.

These patients with continued leakage and bleeding also tend to show a worse visual prognosis.

The PCV subtype of exudative AMD is more prevalent than previously thought, at 20-31% among Caucasians, and up to 50% or more among Asians. There is now a higher rate of anti-VEGF resistance regardless of ethnicity with polypoidal aneurysmal dilation of subretinal neovascular complex.

“This is important because alternative therapy can be considered, such as combination PDT or other research treatment alternatives,” concluded Dr. Kokame.
Diabetic retinopathy (DR) is a complication caused by diabetes mellitus that affects the retina. It is a leading cause of blindness in the world and screening plays a key role in the prevention and management of DR.

Dr. Tyler Hyung Taek Rim from the Singapore National Eye Centre (SNEC) presented on the topic of national healthcare records and insights into risk factors for DR.

“It is possible to predict an event of laser treatment. However, there are several discriminative factors for prediction, such as history of retinal vein occlusion (RVO), gangrene and diabetic polyneuropathy, were identified. However, this innovative and clinically relevant prediction model, as a proof of concept at this stage, still requires further validation efforts,” said Dr. Rim.

Meanwhile, Dr. Gavin Tan, a senior consultant at the Retina Centre in Singapore National Eye Centre, spoke on AI enhancement of National DR Screening Program in Singapore.

Recently there is a lot of interest and research into the practical usage of AI for screening in DR.

“AI can provide similar accuracy and cost savings over a human grader driven screening model. It can also be more sensitive for vision threatening retinopathy. In a system with an existing trained human grader infrastructure, a model with secondary grader adjudication may also improve specificity. This can provide greater cost savings from reduced referrals,” explained Dr. Tan.

According to a paper published by Jianxing He, et al. in 2019, the development of artificial intelligence (AI)-based technologies in medicine is advancing rapidly, but real-world clinical implementation has not yet become a reality. In a study on Artificial Intelligence Screening for Diabetic Retinopathy, the authors suggest that the implementation of deep learning systems into routinely practiced DR screening could represent a cost-effective alternative to help reduce the incidence of preventable blindness around the world.

Prof. Paisan Ruamviboonsuk from Rajavithi Hospital, Bangkok, presented on his experience of real-life implementation of AI in diabetic retinopathy screening in Thailand. According to Prof. Ruamviboonsuk, there are 4.5 million diabetic patients in Thailand and the government specified that 60% of diabetic patients should be screened for DR, but this target has not been reached for various reasons, i.e., no full-time screeners for DR, the screenings are not in diabetic clinics, the patients are not aware of the importance of screening, among others. This is where AI will come in useful.

In fact, 32 authors (including Prof. Ruamviboonsuk) conducted a study involving a total of 25,326 gradable retinal images of patients with diabetes from the community-based, nationwide screening program of DR in Thailand. Results from the said study, published this year, is promising for AI screening in DR.

On the other hand, Dr. Sang Jun Park from the Seoul National University College of Medicine, advocates for a general-purpose algorithm for fundus images, rather than an AI-based algorithm only for DR screening.

“Currently, I am collaborating with VUNO Inc., an AI company in Korea to produce VUNO Med Fundus AI based on my algorithm. We have completed all required clinical trial studies and we are waiting for regulatory approval (Jan. 2020),” said Dr. Park.

Dr. Peiquan Zhao from the Eye & ENT Hospital, Shanghai Medical University, China, spoke on how to conduct screening for DR in China. “It is imperative for primary care physicians and endocrinologists, as well as ophthalmologists, to understand the pathophysiology and clinical course of DR and recommend timely intervention to prevent visual loss,” said Dr. Zhao.

Prof. Dr. Antonia Joussen from Charité - University Medicine Berlin in Germany, discussed the challenges in prevention of DR.

“Recent findings demonstrate a need for prompt referral and screening for DR and other complications of diabetes and highlighted the need for a coordinated approach to diabetes management,” explained Prof. Dr. Joussen.

Dr. Lu Yang, a software engineer for Google Health, talked about identifying other referable diseases during DR screening with the assistance of AI. Dr. Yang stated that 10-20% of patients presenting for DR screening do not meet the minimum DR requirements but have other referable anatomical abnormalities, the most common of which are associated with age-related macular degeneration (AMD) and glaucoma. Given the low prevalence of AMD and glaucoma, yield would be low for standalone screening programs and cost per QALY would be high. Including them as part of an establish DR program may be more cost effective.

“High quality label is the key to robust machine learning models. Collecting consistency, accurate labels is challenging. Guideline iterations and asynchronous adjudication can improve the labelling quality,” said Dr. Yang.

References:

Alcon (Geneva, Switzerland) continues to improve its 3D imaging tool called NGENUITY that provides surgeons with what it says is unprecedented visualization of the back of the eye, in greater depth and detail than traditional microscopes, and integrated it with the company’s novel CONSTELLATION Vision System, a leading technology platform for vitreoretinal surgery, to enhance it further.

The union of the two technologies has created a “multipurpose instrument” with improved control, light toxicity, precision and visualization that allows surgeons to see on one screen both high quality 3D images and the key parameters to monitor patients during surgery, said Belgian ophthalmologist, Dr. Carl Claes.

The integrated system allows surgeons to track key data parameters in real time, such as intraocular pressure, flow rates, infusion pressure and laser power, on one screen. Additional functions allow surgeons to customize the system to their own preferences, including the introduction of four preset imaging modes, two footswitch control options, advanced 2D or 3D video capture, and graphic enhancement of the user interface and procedure flow to provide an improved white balance process.

NGENUITY was a major breakthrough in improving vitreoretinal surgery when it was first launched, delivering up to a 48% increase in magnification to amplify the view of intricate tasks, as well as up to five times better depth-of-field, which helps surgeons maintain focus across an expanded surgical space. The technology also provided up to a 42% increase in depth resolution, crucial to detailed surgical work when managing challenging pathologies.

The flexibility of the system simplifies procedures and enables surgeons to introduce new techniques, said Dr. Claes. He demonstrated the efficiency of NGENUITY cutters, which he said could also be used as scissors, in a series of slides. They are small yet strong and have a high cutting rate, he told delegates, meaning there is less risk of damage to the retina during surgery.

“The performance is excellent,” he added. They can be used “almost like a vacuum cleaner” on the surface of the retina.

There are many benefits to having 3D visualization, added Japanese vitreoretinal surgeon Dr. Motohiro Kamei. This includes high magnification and depth-of-field, lower illumination, the possibility of using multiple display systems and a range of potential digital filters. NGENUITY’s potential as an educational tool is also important, he added, because it allows others to easily watch surgery as it happens.

The system also allows the clinician to sit in a more ergonomic position, he said, which aids protracted periods of surgery.

Furthermore, Dr. Harvey Uy, medical director at Peregrine Eye and Laser Institute in the Philippines, heaped praise on the NGENUITY cutting tool, which he said was smaller, faster, and more efficient than others he had used.

There is a “short learning curve” to using it, he added, and it reduces the complexity of surgery by reducing the number of instruments that need to be brought into the eye.

On the other hand, Indian ophthalmologist Dr. Srinivas Joshi rounded off the session with a series of slides demonstrating his use of the NGENUITY system in his clinical practice. He described it as a “wonderful teaching tool,” as he ran through cases that demonstrated NGENUITY’s functionality, which he said included strong periphery vision.
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RVO, retinal vein occlusion. Licenses may vary by country, please consult your local SPC.


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