A LOOK AT MYOPIA RESEARCH IN CHINA

Wenzhou Medical University (WMU) is one of the leading educational and research medical universities in China. Beyond its academic excellence and high-end medical services, WMU is a leader in advanced research in ophthalmology and optometry. Against the backdrop of an unprecedented rise in myopia in East Asia, several research programs at WMU have been vigorously dedicated to furthering understanding of the condition and developing new treatments for it. This interview with Professor Lu Fan, the president of Wenzhou Medical University, explores in depth the scope of the latest scientific and clinical efforts to slow down the myopia pandemic.

Prof. Fan Lu
MD, MS/OD, President of Wenzhou Medical University, China

Prof. Lu Fan graduated from WMU in 1986, majoring in general medicine. Following graduation, she completed a residency in ophthalmology at the affiliated hospital. In 1991, Prof. Lu Fan completed a master's degree in Optics and Ophthalmology. She later attended the New England of College of Optometry (NECO), becoming the first graduate of the joint MS/OD program offered by NECO and WMU. After her doctor of optometry (OD) degree in 2002, Prof. Lu Fan returned to China to help pioneer the establishment of optometry as a medical discipline in the country. She was the recipient of the 2002 China National Award for Outstanding Women.
Prof. Lu Fan has been involved extensively with the advancement of eye care and optometric education in China, training leaders in medical education and the health care system. In May 2010, she was given an honorary doctor of science degree from the New England College of Optometry in recognition of her contribution and advancement of the profession of optometry in China. In October 2015, she was appointed president of WMU. Her research focuses on vision functions, refractive surgery, contact lenses and refractive techniques in myopic children. Prof. Lu Fan has authored several publications in relation to these research fields.

KEYWORDS
Myopia, high myopia, myopia control, myopia management, dopamine (DA), peripheral refraction errors, orthokeratology (Ortho-K), atropine, outdoor activities, eyeglasses, contact lenses, myopia prevention, genetic therapy, refractive surgery, keratoconus, posterior scleral reinforcement (PSR), etiology, ocular bio-imaging.

Points de Vue: Professor Lu Fan, what are **the key challenges regarding myopia in China?** What have been the most significant achievements in scientific and clinical practice over the past ten years?

Prof. Fan LU: Myopia control and management still face significant challenges. First, an increasing number of patients with progressing myopia tend to be younger than in the past. Second, the overuse of smartphones has dramatically changed people's behavior. Children, for example, tend to spend a lot of time reading at a very short distance. The prevalence of myopia among both urban and rural children has gone up as a result. Third, the impact of high myopia on an individual's eyesight is unpredictable and uncontrollable.

We have done a lot of scientific and clinical research work focusing on myopia in the past decade. As to the basic research, we have found that the level of dopamine (DA) and its receptors affect the occurrence of myopia. Interventions regarding myopia have made large steps forward. Many new concepts and techniques appear to help control myopia, such as the correction of peripheral refraction errors, the usage of orthokeratology and atropine eye drops. In addition, adequate outdoor activities are critical for myopia prevention.

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How would you define **the current scope of myopia research at Wenzhou Medical University (WMU)?**
What are the **top three research areas**?

The entire project of myopia research at WMU combines resources from the eye hospital with those of the school of optometry and ophthalmology. The research fields cover clinical practices, genetic studies, biology, innovation in medicine, ocular imaging developments, etc. The top three research areas are: 1) fundamental research, including establishing animal models, dopamine effects and genetic therapy, which are supported by the National Basic Research Program of China (973 Program); 2) clinical studies on the correlation of child behavior and myopia, epidemiological investigations, myopic function changes and visual acuity after refractive surgery; 3) optometric interventions, such as optical corrections, rigid gas permeable (RGP) lenses and orthokeratology, which are always the areas most beneficial to the public.

What can be learned from **research on biochemical mechanisms** regarding myopia onset and its progression?
What are the perspectives for eye care professionals for a potential pharmacological approach in myopia treatment?

Although myopia is the most common human eye disorder in the world, the exact cause is still unclear. Myopia usually results from inherited genes interacting with environmental factors. Multiple genetic myopic loci and pathways have been identified. The onset of myopia and its progression interact as an entity and a complex disorder.

Progress is made step by step in the field of biochemical mechanisms for human myopia. However, there is much still to be done. For example, the results of the animal model need to be studied further when applied to human beings. Myopia is not the outcome of a single gene and pathway, and the potential target of pharmacological approach may need more detection. Therefore, a lot of work still has to be done to develop an effective treatment for myopia.

What are WMU's key areas of research on **refractive surgery** in myopia treatment?
How would you define the key clinical challenges and post-operative concerns in patients, especially those with high myopia?

The refractive surgery center at WMU's eye hospital is one of the biggest and most important refractive surgery affiliations in China today. About five thousand patients undergo refractive surgery annually in our center. A full 98% are myopia patients. Among the myopia patients, 88% are aged 20 to 30.

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As to the key clinical challenges and post-operative concerns when it comes to refractive surgery, safety is the most important and persistent issue. Although the techniques and surgical skills at the facility are mature and advanced, there is still a small group of patients that suffer from severe complications. One of the worst complications is keratoconus. The most possible reason is that these patients are not suitable candidates and they might already have sub-clinical keratoconus before the refractive surgery. Therefore, strict candidate screening is critical. Given this, we did research focusing on sub-clinical keratoconus filtering. Using the study results, we built the diagnostic indices for sub-clinical keratoconus detection. In addition, longitudinal parts are still ongoing to prove our custom-designed indices can discriminate effectively. We do hope the results will be helpful when selecting candidates and improving safety.

In terms of the patients with high myopia, intraocular refractive surgery is preferable to surgery on the cornea. The anterior/posterior chamber implantation of intraocular lenses (IOLs) might cause severe endothelial cell loss. As a consequence, cataract surgery is more recommended for the older patients with high myopia. Moreover, monitoring the fundus changes is quite important as well. Currently, we also try surgery of posterior scleral reinforcement (PSR) for very high myopia control. The PSR aims to reduce the posterior segment structure changes induced by high myopia. We do find the PSR is helpful for delaying axial length elongation and improving visual acuity after surgery. Above all, high myopia and its complications are more likely to cause blindness. More efforts are being made with respect to refractive surgery to ensure visual health.

There are many **optical methods** to correct and control myopia progression in clinical settings. What is the **current research focus with regard to optical solutions** at WMU? How will the latest findings in this area influence future clinical practice?

At WMU's eye hospital, eyeglasses, soft contact lenses, daytime RGP lenses and orthokeratology (Ortho-K) are all used for the correction of myopia in patients. One of the influential research areas is orthokeratology. The mechanism of how orthokeratology slows myopia progression is a hot topic. According to our studies, wearing Ortho-K lenses over the long term can improve accommodation amplitude, change wavefront aberration and correct peripheral refractive errors. All factors combined together slow the axial length elongation, which delays myopia progression.

What can we learn from **etiology findings**?
What are **the most myopigenic conditions for myopia onset and its progression in children**?
What factors can/can't be modified?

In terms of the etiology, it is very complicated. Myopia is not only caused by a hereditary factor, but it is also affected by environment factors. A lot of different theories, such as genetic loci changes, RNA alterations during the process of transcription and translation and various pathways, have been constructed to interpret the occurrence of myopia. The most myopigenic condition is always the hereditary one. A child with two myopic parents has a greater likelihood of being myopic than a child with only one myopic parent. However, at present this cannot be controlled when the baby is born. Luckily, there are some environmental factors that can be modified to postpone the onset of myopia and its progression, such as good reading habits, enough outdoor activities and a healthy diet.

What are the **key vision functions** that have been studied in myopic children, and what specificities have already been uncovered through WMU's research? What do we know about the relationship between **visual and behavioral functions** – **such as posture** – in children with regard to myopia progression?

The key vision function that we have studied is lag of accommodation. Near vision posture is indirectly linked to myopia through lag of accommodation, peripheral defocus, light and contrast. Based on our previous studies, tasks done at short distances significantly influence posture. Video games produce the shortest working distance and the highest head tilt. Illuminance and contrast significantly influence near posture. The worst posture comes when there is low illumination and contrast. Thus, recommendations for parents should be: 1) work in a bright environment (≥ 300lux); 2) ensure a high contrast for the text when reading; 3) make sure there is an adequate working distance, especially for video games. In addition, the lens type, such as single vision lenses or progressive addition lenses (PALs), and the near-phoria status affected near vision posture. During reading, myopic esophoric children used a lower portion of their PALs compared with exophoric children, resulting in greater addition power, which might partially explain why myopic children with near esophoria exhibited superior treatment effects in myopia control clinical trials using PALs. Therefore, I think the near-work posture plays an important role in the development of myopia progression in children.

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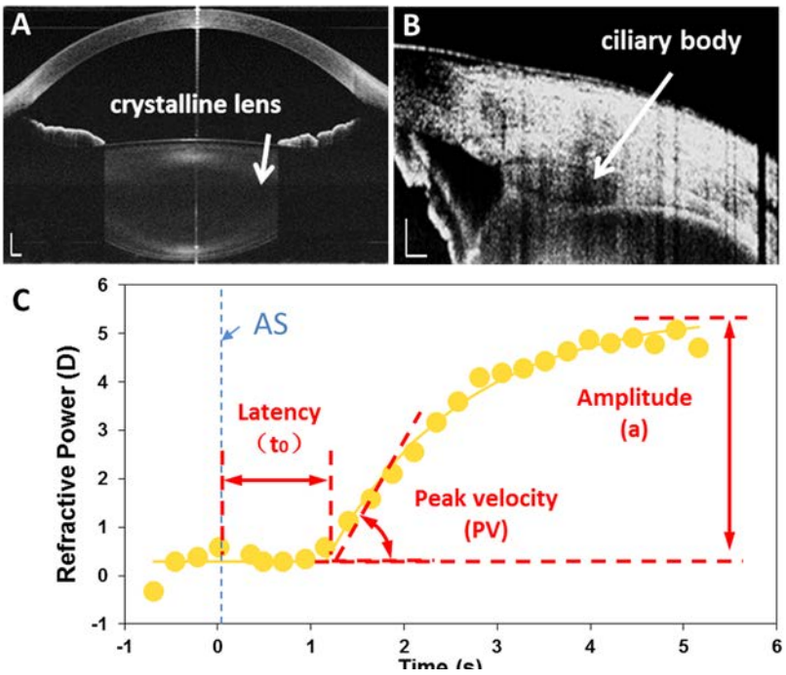

FIG.1| The ocular OCT images and accommodation response curve. A represents the OCT image of the anterior segment and lens; B is the OCT image of the ciliary body; and C is the accommodation stimulus response curve. AS: accommodation stimulus; Latency: the time accommodation starts from the point ACC (accommodation) stimulus is given; Peak velocity: the speed required to reach the peak; Amplitude: the maximum amount of accommodation; Bars = 500μm.

How can the **research in ocular bio-imaging** help better understand accommodation mechanisms in myopia onset, its progression and its control in human eyes? What are the latest findings in this area?

Ocular bio-imaging is helpful evidence in researching accommodation mechanisms for myopia. Using the custom-built optical coherence tomography (OCT) system, the lens, ciliary body and anterior segment can be imaged (Fig. 1-A, B). Combined with the open-filed autorefractor and wavefront aberration system, the accommodation function parameters and all the ocular aberration variations can be captured simultaneously. With this system, we keep records of the accommodation response curves for Ortho-K lens wearers (Fig 1-C). As a result, the accommodation response speed and amplitude improves after three and five months. The long-term effects need to be studied further.

What are the key collaborative projects and partnerships that WMU has initiated to accelerate research on myopia?

Myopia research is a big project, including the mechanism, image recording, visual functions and corrections. We collaborate with Prof. Xiongli Yang from the Chinese Academy of Sciences on the myopic mechanism and pathway study and Zeng Changqin from the Chinese Science Academy for studying the genetics of high myopia. Also, we work together with ESSILOR to study the visual function in myopic students.

Beyond research, how would you define the **key educational challenges** in optometry and ophthalmology with regard to myopia? How can education be helpful in growing eye care services and preventing the pandemic of myopia?

The way optometry and ophthalmology for myopia correction and treatment are studied needs to be rethought. Talented individuals with a medical background are the optimal backups for specialized training. Both the clinical skills and human concerns are required for professional proficiency.

" A COMMITMENT TO PUBLIC HEALTH BY ALL OF SOCIETY WILL POSITIVELY PROMOTE HIGH MYOPIA MANAGEMENT. ENHANCING THE LEVEL OF PUBLIC EDUCATION IS AN ESSENTIAL STEP, AND THE PARTICIPATION OF DIFFERENT MEDIA SHOULD BE ENCOURAGED. "

However, with the increasing demand of public eye care, system training at present is still insufficient. Training for optometrists and ophthalmologists is desperately needed at different angles and levels. The standardized clinical flow, including the doctors, sales assistants, dispensers and after-service staff, should be established as a team work. A personalized and accurate prescription is the basic guarantee of the entire process. Therefore, only when prevention, control and treatment are based on high qualifications will myopia management reach a high standard.

What other initiatives do you believe are required to improve the level of public awareness and that of the public health services to reduce the rates of high myopia?

A commitment to public health by all of society will positively promote high myopia management. Enhancing the level of public education is an essential step, and the participation of different media should be encouraged. Combining the basic awareness of myopia with the elementary education of children is a critical step. Next, a basic medical insurance system will bring the public a brand-new concept. The most significant way is to ensure primary eye care is covered by the basic medical insurance system. Once there is awareness of myopia, the appropriate medical advice and diagnosis can be provided. Lastly, establishing a triple-level patient transferring system will support prompt treatment for high myopic patients when complications and emergencies occur.

What, in your opinion, is the key role ophthalmic clinicians (i.e. ophthalmologists, optometrists and optical dispensers) should be playing in preventing the complications of high myopia?

Ophthalmic clinicians working as a team is key to ensuring a high medical quality. Medical consultation and specialized guidance at the hospital are the basis for managing high myopia. Patients will then learn to step up their vigilance for the complications of high myopia. It is a beneficial way to guarantee timely awareness and treatment for high myopia complications.

Where to next?
What are the key areas in scientific research, clinical practice and medical education with regard to myopia in next decade?

We have already made big steps forward in myopic research and clinical work in the past decade. In the coming future, medical education for ophthalmic clinicians must be a priority. China's rapid economic development means the need for the primary eye care is growing fast. Strict and standard training of myopia management is critical. On the other hand, biochemical research for the myopia pathogenic mechanism will continue to be a hot topic. Transforming achievements in the lab into clinical practice is the ultimate goal of all researchers and physicians. •

Interview by Eva Lazuka-Nicoulaud

“ WE HAVE ALREADY MADE BIG STEPS FORWARD IN MYOPIC RESEARCH AND CLINICAL WORK IN THE PAST DECADE. IN THE COMING FUTURE, MEDICAL EDUCATION FOR OPHTHALMIC CLINICIANS MUST BE A PRIORITY. ”

温州醫科大學
WENZHOU MEDICAL UNIVERSITY

Wenzhou Medical University is a well-known medical science university under the joint governance of the Zhejiang Provincial Government, the National Health and Family Planning Commission and the Chinese Ministry of Education. Its origins extend back to the establishment of Zhejiang Medical School in 1912. In 1958, part of this school moved from Hangzhou to Wenzhou in southeastern China, becoming Zhejiang Second Medical College and later Wenzhou Medical University. Covering 1.27 km^2, the four-campus university is a key higher-education institution in Zhejiang province.

WMU has medical doctoral degree programs in ophthalmology and the visual sciences, surgery, obstetrics & gynecology, laboratory medicine, internal medicine, pediatrics, gerontology, neurology, psychiatry & mental health, dermatovenerology, imaging & nuclear medicine, otorhinolaryngology, oncology, rehabilitation medicine, sports medicine, anaesthesiology, emergency medicine, biological therapy & reproductive medicine. WMU also has eight primary-discipline master’s degree programs. Its five affiliated hospitals offer high-quality medical service to some 20 million people.