Techniques for anterior segment imaging advancing on multiple fronts

Cheryl Guttman in Fort Lauderdale

ADVANCED imaging modalities provide valuable new tools in a range of applications that include diagnosis and tracking of pathology, planning and monitoring of refractive surgery, and studies of accommodation, reported researchers at a mini-symposium held during the annual meeting of ARVO.

A series of speakers reviewed current applications of optical-, ultrasound-, magnetic resonance-, and Scheimpflug photography-based anterior segment imaging devices and provided a look at new technological developments that will further enhance the capabilities of these modalities.

W. Matthew Petroll PhD, University of Texas Southwestern Medical Center, Dallas, discussed in vivo confocal microscopy, noting that it is ideally suited for in vivo evaluation of the cornea because of its non-invasive optical sectioning capability.

Currently, two systems are commercially available—the Confoscan IV (Nidek) and the Heidelberg Retina Tomograph (HRT) II with Rostock Cornea Module (Heidelberg Engineering).

The Confoscan IV is a scanning slit confocal microscope that has a favourable signal to noise ratio due to its light transmission capabilities, and is also very easy to operate as it incorporates such features as automated alignment.

The HRT II with Rostock Cornea Module is a true laser scanning confocal microscope that cuts thinner optical sections to provide higher resolution. As a trade-off, however, it can only scan 80 microns at a time and so cannot be used to image through the entire cornea in a single-automated scan. Rather, the operator has to manually adjust the instrument in order to change the depth of focus.

"Any system has advantages and trade-offs, and it is up to the user to consider the pros and cons in terms of the intended applications when selecting an instrument," Dr. Petroll said.

In addition to generating a 3D image of the entire cornea, the technique produces a curve of image intensity versus depth that allows unbiased, quantitative measurement of epithelial, stromal, and endothelial thickness. As a result, this technology has several potential applications in refractive surgery. They include the measurement of flap and bed thickness and the amount of tissue removed and assessing corneal wound healing response (changes in epithelial and stromal thickness). It can also be used to characterise keratoocyte activation, quantify haze, and identify interface particles.

Multiphoton confocal microscopy using femtosecond pulsed lasers to generate second harmonic signals is now being developed as a new technology for studying the cornea.

"However, the real power of this technology is the ability to create a 3D reconstruction of the cornea," Dr. Petroll said.

That capability is possible thanks to the technique of confocal microscopy through-focusing. Developed by Dr. Petroll and co-workers about a decade ago, it involves stacking of 2D images spanning the full thickness of the cornea.

"Currently, this modality can only be used for ex vivo examination. However, if it can be developed for in vivo use, it has the potential to provide a very powerful technique for non-invasive investigation of corneal microstructure," Dr. Petroll said.

Ultrasound

Ronald H. Silverman PhD, Weill Medical College of Cornell University, New York, discussed the use of high-frequency ultrasound imaging as a method for precise biometry of the cornea and anterior segment. He explained this technology became available in the early 1990s when usable high-frequency (35 to 50 MHz) transducers and electronics optimised for those frequencies were introduced.

"Prior to this time, transducers were operating at a frequency of 10 MHz and provided low resolution. A 50 MHz transducer provides spatial resolution of about 30 microns, but attenuation becomes a factor that limits use of this technology to the anterior segment," Dr. Silverman said.

Ultrasound biomicroscopy (UBM) was introduced in the mid 1990s and was the only commercially available high-frequency ultrasound ophthalmic imaging system until quite recently. Its major uses have been for imaging of anterior segment pathology, pseudophakic implants, and phakic IOIs, as well as for biometry. However, it has several limitations, including the fact that it is an immersion procedure and uses a linear scanning technique that is not well adapted to the curvature of the cornea.

Those drawbacks are overcome in the Artemis 2 system (Ultralink, LLC). The Artemis 2 uses a reverse water bath setup that allows the transducer to be coupled to the eye with the patient in a sitting position. In addition, it features arc-scan geometry that maintains normality and constant range to the surface of the eye. The Artemis 2 also allows the operator to see the eye during the imaging procedure and provides a fixation target for the patient that is advantageous for achieving reproducible results.

Using digital signal processing to convert the data to high-resolution images, the Artemis 2 can be used to obtain precise and reproducible measurements of corneal layer thicknesses, anterior chamber depth, and angle-to-angle and sulcus-to-sulcus dimensions. In addition, combination of scanned pachymetry with optical surface topography allows topographic description of the posterior corneal surface.

Currently there are also multiple handheld high-frequency ultrasound systems with 35 to 50 MHz transducers. While they provide good-quality images, they lack optical centration mechanisms that are present on the Artemis 2 and also use sector versus arc geometry scanning, noted Dr. Silverman.

Dr. Silverman and colleagues at Ultralink are now working to develop a system using a higher frequency 70 MHz transducer. They have also developed annular array technology using a multi-element transducer that produces much greater depth of field.

"These methodologies may offer even greater diagnostic capabilities," Dr. Silverman said.

Magnetic resonance imaging

Susan Strenk PhD, UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey, discussed high-resolution magnetic resonance imaging (MRI). She pointed out the advantages of this technology are that it allows full visualisation in vivo of the iris, ciliary muscle, ciliary processes, and lens as well as the geometric relationships between those structures without being hampered by pigmentation in the iris. Another benefit of MRI is that it offers unsurpassed soft tissue contrast that can...
be used to improve visualisation of various tissues.

Dr Strenk presented data from in vivo and in vitro studies in phakic and pseudophakic eyes to demonstrate how high resolution MRI of the anterior segment can be used to acquire information about IOL position and behaviour and to study the mechanisms of accommodation and presbyopia development.

"Accommodation and presbyopia have generally been studied using either cadaver eyes or the rhesus monkey, but our findings from studies using MRI highlight the limitations of that information relating to post-mortem tissue changes as well as interspecies differences in presbyopia development," said Dr Strenk.

Comparative images showed the development of corneal oedema in post-mortem globes. While that phenomenon can be controlled by tissue handling techniques, lenticular changes were also noted that cannot be circumvented. The latter alterations included an increase in anterior capsular thickness and a change in lens shape.

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Comparisons between humans and rhesus monkeys showed some striking similarities with both species demonstrating Helmholtzian accommodation and the development of presbyopia at a similar rate. However, differences were noted in the geometric relationships between accommodative structures that suggest there are also differences in force vectors, which has implications for the modelling of accommodative mechanics.

The human in vivo studies investigating accommodation were performed in volunteers from 22 to 91 years of age. Since MRI allows binocular fixation, the studies were performed using physiological versus pharmacological accommodation by having the subjects gaze at near and far targets.

"Studying pharmacologically-induced accommodation may be suboptimal since the drugs can affect the iris as well as the ciliary muscle to result in "super accommodation," Dr Strenk said.

The results of the in vivo human studies showed a number of age-related changes in anterior segment structures associated with accommodation but demonstrated that ciliary muscle contractile activity persists throughout life. Collectively, the findings from those imaging studies support the Helmholtz theory of accommodation and implicate age-related increase in lens thickness in the mechanism of presbyopia development and show that the human uveal tract reacts as a unit in response to increasing lens thickness, Dr Strenk said.

Optical coherence tomography

Georges Baikoff MD presented studies he performed using high-speed optical coherence tomography (Visante™, Carl Zeiss Meditec) for in vivo investigation of accommodation in the human eye. However, he pointed out that this device is also used routinely in clinical practice for a variety of applications in evaluating the anterior segment.

Dr Baikoff noted that the data from the accommodation studies were consistent with the information gathered using MRI. Data collected from more than one hundred eyes of subjects ranging in age from seven to 82 years old showed a number of age-related changes in accommodation, including a decrease in maximum accommodative amplitude, forward movement of the crystalline lens anterior pole during accommodation, and a decrease in radius of curvature.

While iris pigmentation prevents imaging behind that tissue using the infrared light of the AC-OCT instrument, a 19-year-old albino patient provided the opportunity to observe the entire crystalline lens and ciliary body during accommodation. That study showed deformation of the crystalline lens at the time of accommodation accompanied by an increase in thickness as well as inward movement of the ciliary processes.

“These studies provide additional proof that the ciliary sulcus and ciliary processes are very malleable and indicate why it is difficult to optimally size phakic IOLs,” Dr Baikoff said.

Dr Baikoff and colleagues have also used anterior segment OCT to investigate the forward displacement of various accommodative pseudophakic IOLs in vivo. Those studies identified minimal movement at best that would translate into a maximum add of 0.25 D, he reported.

“We were somewhat amazed to observe how little these lenses moved, but our results confirm the findings in European studies that have not been in favour of the ability of these lenses to provide sustained improvements in near vision,” Dr Baikoff said.

Studies in eyes implanted with posterior chamber phakic IOLs demonstrated that during accommodation there was forward shift of the implant toward the crystalline lens that in some eyes resulted in contact and may explain the association between these refractive lenses and the development of cataract.

Dr Baikoff is collaborating with engineers at Carl Zeiss Meditec to develop 3D reconstruction capabilities for anterior segment OCT. He presented images created through software reconstruction and demonstrated how the technology allows image magnification, 360-degree visualisation from varying angles, colour scale adjustment to characterise differences in optical density of anterior segment structures, and biometric measurements using automated callipers.

“This technique will have important advantages for eliminating human error in obtaining measurements,” Dr Baikoff said.

Scheimpflug photography

Martin Baumeister MD, Frankfurt University, Frankfurt, Germany, discussed the use of Scheimpflug photography to evaluate cataract development and IOLs. He described it as an established and highly standardised method offering high penetration depth, high structural resolution, and good, operator-independent reproducibility.

This technology has been used in ophthalmology since the 1960s and is superior to conventional slit-lamp photography both in its ability to image...
over a wide focal range and for its reproducibility. Therefore, Scheimpflug photography is suitable for use in longitudinal studies.

"Using Scheimpflug photography, it is possible to document age-related cataractous changes of the lens but also to test the effects of anti-cataract drugs and monitor for possible drug-induced lens opacification"

Martin Baumeister MD

Recently, Dr Baumeister and colleagues have used Scheimpflug photography for assessing the position of phakic and pseudophakic IOLs. He presented images from one study comparing the position of three different foldable three-piece IOLs at 12 months post surgery. The implants varied with respect to material and optic edge configuration, but all demonstrated favourable performance with respect to decentration and tilt.

"We concluded from this study that differences in material, optic edge, and haptic design between these foldable IOLs resulted in no detectable influence on optic tilt and decentration. The findings also indicate optic tilt and decentration are negligible with modern IOL design and contemporary operating techniques, and that has important relevance for achieving continued optimal visual function with the new multifocal or aberration-corrected IOLs," Dr Baumeister said.

He also presented another study using serial Scheimpflug photography studies to evaluate positional stability of two anterior chamber phakic IOLs, one angle-supported model and the iris-fixated lens, and a posterior chamber device.

Dr Baumeister noted that for accurate biometric measurements with Scheimpflug photography, the image must be corrected for distortion by the optics of the camera, corneal refraction, and, when visualising the posterior portion of the lens, refraction by the anterior lens surface.