“Recent developments in imaging, optics, and vision require special attention and time to make research comprehensible and useful for all ophthalmologists.”

Philippe Sourdille MD

“Recent developments in imaging, optics, and vision require special attention and time to make research comprehensible and useful for all ophthalmologists. The aggressive marketing of ophthalmic firms is another reason to scientifically and clinically analyse the rationale – if there is one – of new commercial products,” he said.

In his introductory lecture, Dr Sourdille underscored the importance of appreciating the truly dynamic nature of the anterior segment.

“Everything in the anterior segment is dynamic and every component in the anterior segment moves and changes dimensions. We know that corneal curvature and anterior chamber depth changes, the iris and the pupil move, as do the ciliary processes, the zonular system, and obviously the crystalline lens. Even the anterior chamber angle, traditionally thought to be stable has, in fact, only one really immobile component - the scleral spur. The interesting thing is that most of these movements are interactive and interdependent and a comprehensive approach to all is mandatory,” he said.

Unravelling the mysteries of accommodation

The role of biometry in helping to shed light on the complex anatomical forces at work in the process of accommodation were discussed at length by D. Jackson Coleman MD FACS, in his keynote address to the clinical research symposium.

Dr Coleman reiterated Dr Sourdille’s insistence on the essentially dynamic nature of accommodation.

“The eye and the process of accommodation really is a totally global response even though most of us have been concentrating on the lens. But it really has to do with all the structures in the eye and when we try to measure what is happening, one of the problems we have is determining what is the fiducial surface – in other words, what is the structure from which we measure all other changes?” he asked.

Dr Coleman noted that there are four primary areas where accurate biometry is required in developing areas of refractive surgery: intraocular lens placement; accommodating lenses; surgery for presbyopia; and post-LASIK enhancement.

“Very high frequency (VHF) ultrasound can provide unique and accurate measurement of the critical dimensions of the angle and sulcus, as well as the anatomic movement caused by physiologic stimuli of the ciliary body in order to optimise lens and haptic sizing and position,” said Dr Coleman.

He further observed that understanding the mechanics of the accommodative process may facilitate accommodating lens design, and that presbyopia surgery can also benefit from measurement of the proper position of scleral expansion, with surgical implants or laser-induced relaxation.

Focusing on the virtues of the Artemis eye scanner developed at the Weill Medical College of Cornell University by a team including Dr Coleman, Dan Reinstein MD and Ron Silverman PhD, Dr Coleman said that the original goal of the technology was to be able to image the entire anterior segment “in one sweep”, and see the changes in real-time rather than fitting together composite images. The VHF ultrasound system is able to image not only the cornea and iris, but ciliary body and ciliary processes for uniquely optimal lens sizing. Certainly, diagnostic evaluation of cysts and tumours is easily performed.

“We developed it for biometry but also to detect abnormalities and anatomic changes, including tumours. And we can measure a wide range of anatomical changes very accurately with this system, as well as demonstrating ciliary body responses to accommodation and pharmacologic agents. We can measure angle-to-angle, sulcus-to-sulcus, anterior chamber depth and examine the anatomy of iris and angle,” he said.

Turning to discussion of current theories relating to accommodation, Dr Coleman said that there is still a huge amount of debate surrounding issues such as capsular contraction, reproducible curvature and the role of the vitreous in the accommodative process.

However, while there are many different schools of thought on particular aspects of accommodation, Dr Coleman said that there is now broad consensus on a number of issues.
“I think we all agree on the paraboloid shape of the anterior lens and that the lens translates anteriorly. I think we also agree that the posterior lens does not change its shape or vary its position much. We all know that the presbyopic lens increases in volume and has a flatter anterior curvature. There are changes in the ciliary body and we know that the Muller’s muscle portion moves in during accommodation. The sulcus tends to remain stable; the sulcus ring is commonly ellipsoidal not circular and the zonule separates through ciliary processes and there are accessory zonules that form in the anterior vitreous that are a very integral part of the accommodative process,” he said.

In addition, in contrast to the capsular mechanism of lens shape change, the presence of vitreous support of the lens indicates that a cataract surgery would explain the paraboloid anterior lens shape and the other features of accommodation, he added.

In terms of the positioning of IOLs and ICLs, Dr Coleman said that VHF ultrasound provides an extremely valuable tool for reducing the “fudge factor” and provides more accurate lens power.

He noted that the use of intraocular lenses in the phakic eye might offer certain advantages over corneal surgery and contact lenses for certain patients. Precise lens sizing is critically important to minimise tissue damage, and maximise optical performance, added Dr Coleman.

“In order to place the lens in the most suitable anatomic axis, whether the angle to angle or sulcus to sulcus meridian, measurements can be made ensuring that the lens is placed in the correct meridian to prevent ‘propeller ing’ and providing optimal fixation,” he concluded.

Benefits of UBM scan

The refractive surgery applications of one of the oldest available anterior segment imaging instruments – analogue very high frequency ultrasound biomicroscopy, UBM – was then discussed by Italian ophthalmologists Giorgio Marchini MD and Marina Modesti MD.

UBM is a B-scan ultrasonic immersion procedure with a linear scanning mode providing quantitative and qualitative information about structures of the anterior segment.

“Ultrasound biomicroscopy is a technique that gives us valuable information. The principal advantage is that the axial resolution is very high, but we have less penetration in the tissue,” said Prof Marchini. Prof Marchini noted its specifications can be summarised with the “rule of 5s” – it operates at a 50 MHz frequency, has a 5.0 mm beam focus, 50 microns of axial and lateral resolution, a 50-micron focal distance, and a 5.0 mm exploration depth.

“This gives us high quality images of the anterior segment and we can study different situations and different problems – for example behind the iris, the rotation, the position and thickness of ciliary processes, the relationship between the lens and the iris and the zonular apparatus. For cataract surgery we can obtain a lot of information about the relationship between ciliary processes, zonule, capsular bag and so forth,” he said.

Prof Marchini noted that one of the principal difficulties with using imaging devices of this type is obtaining objectively reliable and reproducible measurements.

“Our studies have shown that when we have the same observer who analyses and measures the same image, the agreement is very good. But different observers of the same images might have less agreement mainly because of the subjective nature of the placement of the landmarks in order to obtain the measurements. However, if we measure different images by different operators the agreement is unacceptable,” he said.

While UBM has some valuable biometry functions and other applications, Prof Marchini pointed out its limitations: it cannot, for example, be used to measure the angle-to-angle or sulcus-to-sulcus distances and it cannot image the nuclear and posterior portions of the crystalline lens or provide corneal pachymetric topography maps.

Marina Modesti MD reported data from a study conducted at the University of Verona, Italy, using two different ultrasound biomicroscopy systems to analyse the anterior segment structures modification in pseudophakic monofocal eyes during accommodation.

The study included 26 eyes of 23 patients (mean age 75 years) implanted with four different monofocal IOLs. After a mean postoperative period of 7.05 months, a high frequency ultrasound biomicroscopy study using the HiScan System (Optikon 2000) with 35 MHz probe and UBM System 840 (Carl Zeiss Meditec) was performed in all eyes.

The results for both systems showed a statistically significant difference before and after accommodative stimuli for anterior chamber angle, scleral ciliary process angle and iris-ciliary process angle. The HiScan System and UBM System analysis demonstrated an accommodative movement of the anterior segment structures in eyes implanted with standard monofocal IOLs, noted Dr Modesti.

Dr Modesti concluded that cataract surgery induces an increase in posterior chamber depth and in iris ciliary process distance (sulcus).

“Our studies have shown that when we have the same observer who analyses and measures the same image, the agreement is very good. But different observers of the same images might have less agreement mainly because of the subjective nature of the placement of the landmarks in order to obtain the measurements. However, if we measure different images by different operators the agreement is unacceptable,” he said.
A helping hand

A new generation of 20-30 MHz handheld analogue ultrasound scanners for anterior segment analysis offers a wealth of valuable information to clinicians, according to French ophthalmologist Michel Puech MD.

"Handheld high frequency systems are simple to use, provide easy means of focusing and offer many applications from anterior segment to posterior segment. They are also comparatively inexpensive. The downside of such devices are that the measurements are less accurate compared to Artemis, for example," he said.

Dr Puech reported that Aviso (Quantel Medical), a new linear scan probe in the 20-50 MHz range gives excellent image clarity. "The new system using the linear probe with the 50 MHz movement of the transducer gives very clear high resolution images. While sector scan devices such as Ultrascan (Alcon) and Isoscan (Cornea) give information on the centre of the cornea, they do not have the same ability for dealing with the periphery of the cornea. With the linear scan we can observe the angle-to-angle distance, obtain measurements of the sulcus-to-sulcus distance and the variation of the angle precomesas and the ciliary bodies," he said.

Dr Puech noted the utility of such devices for detecting pathologies of the anterior and posterior segment.

"For instance, in cases of malignant melanoma of the ciliary body we have a problem with very high frequency ultrasound as the tissue of the melanoma absorbs the signal and we are not always able to observe the posterior limit of the malignancy. When we use just a smaller frequency we are able to observe the posterior limit of the melanoma," he said.

Such scanning systems are also useful in detecting problems such as ciliary body detachment, retinal detachment, macular oedema or other macular diseases in the posterior segment, noted Dr Puech. They are also extremely beneficial in cases of phakic IOL implantation, to ensure correct anatomical positioning of the IOL and avoiding problems such as endothelial cell loss or pupil ovalisation.

"We can also observe other complications with the new intermediate systems — for example, the positioning of the footplates of the implant directly in the ciliary body. In eyes with posterior phakic IOLs, high frequency ultrasound is a better system to observe behind the iris and determine the position of the IOL," he said.

Dr Puech said the new generation of handheld probes are easy to use, have many applications for anterior segment to posterior pole, and show increased resolution with increased frequency. The linear scan device also allows better visualisation of the anterior segment.

"In terms of refractive surgery we know the complications, so we need a very high level of patient selection and we need to observe carefully the dynamic nature of the anterior segment anatomy, in particular the high variation of angle and iris shape," he advised.

Artemis applications

The Artemis II VHF digital ultrasound arc-scanning technology offers clinicians a wide range of potential applications not only in the practice of corneal and intraocular refractive surgery but also in all other anterior segment surgery, according to one of its creators, Dan Z. Reinstein MD.

Looking back over the progress in imaging technologies over the past decade, Dr Reinstein noted that the ophthalmic community has overcome its initial scepticism as to whether high-precision internal structural biometry was actually necessary or desirable in routine phakic IOL implantation and corneal refractive surgery.

"As Schepens made me with Artemis II system, Dr Reinstein said that the FDA and CE approved device uses 50MHz scanning with digital signal processing to deliver very high resolution imaging and high precision biometry of the anterior segment and the entire cornea. Examination time per eye with the Artemis is about three minutes, and is very easy to perform both for the trained technician and the patient.

Dr Reinstein said that the system’s ability to measure all the vital internal measurements of the eye could help to make a valuable contribution to cataract surgery by predicting the final location of an IOL rather than using fudge constants. He added that he uses the Artemis on a daily basis in his practice for a wide range of applications.

"I use the Artemis for corneal refractive surgery, for example, to determine true corneal thickness, which is essential in the prevention of ectasia. I use it for screening for keratoconus through examination of epithelial thickness profiles, and to analyse any flap complications. I also use it to analyse irregular astigmatism because all corneas with irregular astigmatism demonstrate tissue-healing effects in the epithelium and therefore wavefront and topography measurements are not sufficient to make diagnoses.

"I also use the Artemis internal corneal data as well to guide phototherapeutic keratectomy. And finally I use it to get me out of trouble when the cornea has a thinner than predicted residual stromal thickness — I have no cases of ectasia in my experience of over 9,000 LASIK procedures, and I attribute this to a great extent to my use of the Artemis, which has prevented me on a number of occasions from performing what may have seemed like a routine enhancement without Artemis data," he said.

Dr Reinstein commented that the Artemis will probably enable phakic IOL technology to reach similar safety levels as LASIK, given that it can provide both anterior chamber and posterior chamber dimensions as well as iris configuration to ensure that phakic lenses are properly sized and appropriately chosen for a given eye’s anterior segment anatomy.

"It can also provide external landmarks for internal structures such as the lens equator plane, thus probably eventually playing an important role in improving the efficacy of scleral surgery to reverse presbyopia," he said.

Describing the accuracy and reproducibility of the system in the cornea, Dr Reinstein said that the Artemis does not have to average multiple measurements to arrive at a highly accurate mean value — the surface localisation precision has been published at 0.87 microns.

"The Artemis can map the thickness of individual layers of the cornea, providing 3D maps of epithelial, flap and residual stromal thickness. The precision of measurement in two-dimensions shows that throughout the entire cornea we can measure the epithelium with a better precision than 1.2 microns throughout a 10.0 mm radius," he said.

Similar pinpoint accuracy can be achieved for the anterior segment, with a reproducibility of angle-to-angle measurements of ±0.12 mm and that of sulcus to sulcus of ±0.152 mm.
To underscore the versatility of the system, Dr Reinstein demonstrated how Artemis could be used for a broad array of diagnostic purposes such as screening for keratoconus, flap complications, microfolds, irregular astigmatism, mechanical complications, presbyopia surgery and phakic IOL applications.

“All in all, anatomical and structural input clearly will provide improved diagnosis and emphasises the values of the mechanistic and cognitive approach we have taken which is really about controlled ocular engineering,” he said.

Confocal microscopy

Confocal laser scanning microscopy is another valuable diagnostic tool that allows clinicians to expand their knowledge of corneal disease and the modifications that occur after corneal surgery, according to Maria João Quadrado MD, Coimbra University, Portugal.

Confocal microscopy is an optical sectioning technique producing images free from out-of-focus blur, said Dr Quadrado. It is a light microscopy technique and commonly employs visible wavelength lasers as light sources and confocal apertures or ‘pinholes’ in the detection path. She noted that advantages of this approach include an ability to discern 3-D positions of features which enable co-localisation to be determined, excellent spatial resolution compared to non-confocal light microscopy and the generation of completely in-focus 3-D images of microscope samples.

Dr Quadrado said that Coimbra University currently uses two confocal microscopy devices for clinical use: the Confoscan P4 (Tomey, Fortune Technologies) and more recently the Heidelberg Retina Tomograph/Rostock module HRT II + RCM.

The HRT II + RCM allows high contrast imaging of tear film, limbus, conjunctiva, kerocytes, nerves, endothelium, the lens (epithelium and fibres) and to evaluate capsular opacification in pseudophakic eyes, said Dr Quadrado.

“It also delivers high-quality images at cellular level in all corneal layers. Even in eyes with significant corneal opacities resulting from corneal oedema, the endothelial pathology can be observed. It is non-invasive, very fast, has a high resolution, works in real time and allows image storage for exam comparison,” she said.

The device can also be used to analyse cystic diseases of the cornea such as dystrophies, microorganisms such as Acanthamoeba, corneal deposits (Amiodarone, iron, Cipro), graft rejection and wound healing.

She noted that in vivo confocal microscopy is also useful to study the postoperative aspects of corneal procedures such as LASIK, PRK, INTACS insertion, penetrating keratoplasty or deep lamellar procedures.

“Confocal microscopy is a useful technique for in vivo evaluation after LASIK because it is able to show cellular modifications inside the corneal layers. It allows us to study the stromal keratocyte density and activity, haze, flap thickness, microfolds at Bowman’s layer and the particles at the interface level. It also gives us a better understanding of interface problems, wound healing, flap morphology and to obtain biometric measurements,” she said.

Other applications include detection of reflective particles after corneal surgery, diffuse lamellar keratitis, flap thickness and ablation depth and analysis of microfolds. In cases of corneal transplantation, confocal microscopy can help to detect signs of rejection, decompensation and endothelial status.

**Double Pass technique and quality of vision**

Pablo Artal MD discussed the importance of the optical quality of the retinal image to a patient’s overall quality of vision.

“The optical quality of the retinal image is really the initial physical limit to vision and imposes the major limitation to spatial vision and quality of vision. The retinal image is affected by three physical factors: diffraction, that is related to pupil size, aberrations and scatter,” he said.

He noted that aberrations mainly affect the distribution of light over a small angular distance (point spread function), while scatter causes symmetric and wide-angle distribution of light.

The double-pass technique, which is based on recording images of a point source after reflection in the retina and double-pass through the ocular media, evolved from pioneering work by researchers such as Francois Flamant in the 1950s and Dr Javier Santamaria in the 1980s, noted Dr Artal.

Dr Artal then described how the OQAS™ device (Visiometrics) uses the double-pass approach to give an objective evaluation of the optical quality of the eye in clinical environments. The main advantage of this instrument compared with aberrometers is that it permits clinicians to obtain directly the actual retinal images including higher order aberrations and intraocular scattering.

While wavefront sensors such as Hartmann-Shack measure low to mid order aberrations, they do not measure scattered light. The double pass technique records directly all the retinal image information including both aberrations and scatter, said Dr Artal.

He noted that previous studies demonstrated that measurements performed in patients following conventional refractive surgery showed a reduction of image quality when compared with normal eyes. This is in good agreement with the reported increase of aberrations, said Dr Artal.

The dimution of the retinal image quality shows a clear dependence on the pupil diameter and the refractive technique used.

Comparing the modulation transfer functions obtained from double-pass and Hartmann-Shack techniques, in eyes with low level of intraocular scattering, the estimates were quite similar. However, in eyes where scatter was more predominant, as in early cataract eyes or patients after IOL implantation with posterior capsular opacification, the MTF provided by the Hartmann-Shack sensor was always higher than that obtained from double-pass.

“We should therefore be aware in eyes with more scattering, wavefront sensors might overestimate retinal image quality. Scatter may be the crucial missing component to better understand different clinical conditions,” he warned.