Clinical research symposium highlights multiple factors and challenges involved in measuring quality of vision

Cheryl Gutman in London

All ophthalmologists are familiar with patients who complain about unclear vision despite having 20/20 uncorrected visual acuity. That situation underlines the need for continued research to identify, understand, and quantify the multiple factors influencing vision as well as for developing better vocabulary to describe the visual experience in order to facilitate more meaningful communication between patients, physicians, and investigators, said Marie-Jose Tassignon MD, PhD, University of Antwerp, Belgium.

During the XXIV Congress of the ESCRS, Dr Tassignon and Jose Cunha-Vaz, MD, University of Coimbra, Portugal, served as co-chairpersons for a clinical research symposium dedicated to examining the question “Can we measure quality of vision?” At the session, an international faculty discussed how wavefront aberrations, corneal transparency, corneal hysteresis, tear film, contrast sensitivity, glare, and photoreceptor alignment influence vision. The speakers also presented methods for assessing those parameters and their impact on the visual experience.

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Discussing wavefront aberrations, Jos Rozema MD, University Hospital, Antwerp, Belgium, said it is important to distinguish the good, the bad, and the ugly. Contrary to common belief, a flat wavefront is not the only good wavefront, he stated.

“A flat wavefront generally gives a better monochromatic point spread function (PSF) and modulation transfer function (MTF) along with sharper, less distorted vision. However, results from published studies, such as those investigating the wavefront profiles of US Navy pilots, suggest that small amounts of certain higher order aberration geometries may be useful. In addition, we know eyes can suffer from having a wavefront that is too well corrected, as that situation can be associated with reduced depth of focus,” Dr Rozema said.

“While a smooth wavefront is generally preferred, further study is required to determine which aberration geometries are acceptable and beneficial. For that, however, we need benchmarks that are not now available,” he added.

Dr Rozema characterised a good wavefront as one with any regular aberrations that are easily corrected with spectacles or lenses. That category includes eyes with regular ametropia or astigmatism as well as those that are emmetropic and have only minor higher order aberrations. A bad wavefront is one in which there is a dominant higher order aberration geometry, such as coma or trefoil, leading to a distorted PSF and that cannot be easily corrected. Examples of eyes with a bad wavefront are those with keratoconus or a corneal scar. The ugly wavefront contains large amounts of microaberrations that cannot be measured because their spatial frequency is below the spatial resolution of available aberrometers. Such a wavefront cannot be corrected with spectacles or lenses and is particularly found in eyes that suffer an unintended postoperative result, said Dr Rozema.

Assessing corneal ultrastructure

Oliver Stachs PhD, University Augenklinik, Rostock, Germany, discussed corneal transparency and assessment of corneal ultrastructure with confocal microscopy. Prof Stachs pointed out that a material may achieve transparency if it has a homogeneous refractive index. However, in the case of the mammalian cornea, the collagen fibrils are embedded within a ground substance that has a lower refractive index. Various theories have been introduced to explain its transparency. According to Maurice, uniformity of collagen size and organisation gives rise to destructive interference of scattered light, whereas Goldman proposed a theory of diffraction wherein light scattering is not produced because of periodic fluctuations in the index of refraction over distances small compared with the light wavelength.

To enable rapid, non-invasive, high-resolution imaging of the cornea ultrastructure with 3-D reconstruction, Prof Stachs and colleagues have modified the commercially available confocal scanning laser microscope (Heidelberg Retina Tomograph II, Heidelberg Engineering) by attaching an anterior segment adapter (Rostock Cornea Module). Using that technology, they determined that the nuclei of the keratocytes are the principle light-scattering structures in the corneal stroma and that the migrating cells in a wounded cornea were much more reflective than their stationary counterparts in a normal transparent cornea. In addition to its use for evaluating the basis for corneal haze, this imaging technology has multiple other applications for improving understanding of the normal and pathological cornea, said Prof Stachs.

“This diagnostic technology allows in vivo visualisation and analysis of the arrangement of the epithelium, nerves, keratocytes, microorganisms, and infiltrating inflammatory cells in the living cornea, and it also can measure cell layer thickness. With those capabilities, confocal microscopy may help to clarify morphological variation of all corneal cell layers under various clinical and experimental conditions,” he stated.

Coming to terms with corneal hysteresis

David Luce PhD, Reichert, New York, told attendees that improved understanding of corneal biomechanics will provide greater insight into factors influencing quality of vision. He discussed corneal hysteresis (CH) and the related parameter, the corneal resistance factor (CRF).

Dr Luce characterised CH as “the judge, jury, and executioner of corneal shape.” He explained that it is a measure of the dynamic resistance or viscoelastic properties of the cornea and is defined by the measurement process employed in the Ocular Response Analyzer (ORA, Reichert). That process involves monitoring of corneal curvature in response to an air jet and allows separation of the corneal properties from the pressure function.

Dr Luce pointed out that CH is not Young’s modulus and that corneal biomechanics cannot be well described by a single modulus.

“That is because the cornea is a system in the mechanical sense and is not a material like a pure piece of plastic,” he explained.

While CH and CRF are related to central corneal thickness, pachymetry is not the entire story. Therefore, CH and CRF cannot be predicted by corneal thickness. “CH is not low in all thin corneas and high in all thick corneas. Corneas with Fuchs’ dystrophy that are thicker due to oedema have a dramatically reduced CH because the cornea is sluggish. Even among normal corneas, there can be significant differences in CH values between eyes with the same CCT,” Dr Luce said.

Based on population studies, “eight” appears to be the CH cut-off value between normal eyes and those with Fuchs dystrophy or keratoconus. An even higher degree of separation between normal and pathologic eyes can be seen in the distribution of CRF values.
“It appears the O RA may be a tool for diagnosing corneal pathologies and perhaps for predicting eyes at risk for corneal ectasia,” he said.

Precorneal tear film also important

Discussing the precorneal tear film, Robert Iskander PhD, Queensland University of Technology, noted that although it is a thin layer, it may have an important effect on vision. Its influence is often overlooked by clinicians, but at the same time, better understanding of its role has been hampered by the absence of a reliable method for characterising tear film quality. Dr Iskander told attendees that in 1985, Mengher et al suggested that techniques similar to videokeratoscopy could have been used to measure tear film quality and its effect on vision. That concept has been recently applied by several groups of investigators who have attempted to estimate surface parameters from the corneal topography and from the quality of the tear film from those data.

However, using Placido-disk systems (most popular videokeratoscope instruments) in that approach suffers from a fundamental limitation, because measurement of corneal topography or corneal wavefront aberrations with that diagnostic technology is inseparably connected with the quality of the precorneal tear film. In other words, image acquisition with Placido-disk topography is dependent on a good quality of tear film.

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To achieve that goal, he and his colleagues engineered a high-speed videokeratoscope that can acquire data at a rate of up to 50 Hz. Such a system enables assessment of dynamic changes of corneal topography with evaluation of tear film build-up and break-up times. Once the topography is derived, ray tracing can be used to determine the corneal wavefront and from that the aberration terms can be deduced.

Improving contrast sensitivity measurements

Joaquim N Murta MD and colleagues at University Hospital Coimbra, Portugal, have been focusing their research efforts toward developing better methods for evaluating contrast sensitivity. He explained the basis for that interest.

“The ideal refractive surgery would allow patients to detect and recognise large and small objects of high and low contrast at all distances and under all lighting conditions. Wavefront-guided refractive surgery was developed to objectively diagnose and treat higher order aberrations that are thought to be responsible for scotopic and mesopic visual symptoms and to contribute to decreased contrast sensitivity. However, the presence of a low amount of wavefront aberrations postoperatively does not always correlate with contrast sensitivity measurements and there are conflicting data from published studies as to whether there are differences in contrast sensitivity outcomes between custom and conventional LASIK,” he noted.

He reported results using different techniques in a study of 40 myopic eyes of which half were treated with conventional LASIK (Planoscan, Bausch & Lomb) and the other half with a wavefront-guided technique (Zyoptix, Bausch & Lomb). The two groups were similar with respect to pre-operative refraction, age, and mesopic pupil size, and they were evaluated at three months and one year after surgery.

The results showed neither type of refractive surgery had a significant effect on contrast sensitivity. However, compared with a population of normal controls, the refractive surgery patients had reduced contrast sensitivity pre-operatively and at both follow-up visits. O ptical quality of the eye was also lower in the two refractive surgery groups than in the normal controls pre-operatively, and neither procedure showed any benefit for improving the O ptical Q uality A nalysys System (O Q A S) measures. Consistent with those findings, there was no statistically significant difference at 12 months after surgery in total higher order aberration RMS or in analyses of 3rd, 4th, and 5th order aberrations.

“These diagnostic techniques are promising for evaluating quality of vision under mesopic conditions, but they showed in this study that visual performance was not improved after LASIK, regardless of the ablation technique. Methods that objectively measure quality of vision, and particularly night vision, are mandatory to create better surgical strategies in the future that will minimise post-refractive vision disturbances,” Dr Murta said.

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“Stray light can be a problem even in eyes with good visual acuity and so perhaps stray light should be considered in the assessment of quality of vision and the decision of when to perform cataract surgery,” Dr Van Den Berg said.

Aristophanos Pallikaris, PhD, biomedical engineer, University of Crete, Heraklion, Greece, has been studying photoreceptor alignment and its role in quality of vision. He explained that the individual cones act as a classic fiberoptic element, capturing incident light and channelling the electromagnetic energy to sites of visual absorption. Resultant image quality depends on the incident angle at which the incoming rays strike the photoreceptors as the amount of light reflected and lost to the surroundings increases as the incident angle increases.

While in graduate school at the University of Rochester, New York, Dr Pallikaris in collaboration with David R W Illiams, PhD, used an adaptive optics system to acquire high-resolution images of the cones. Their
studies showed that while there is high inter-individual variability in the directionality of the cones with respect to pupil position, most photoreceptors tend to point toward the centre of the pupil. The impact of photoreceptor alignment on the visual system relates to the Stiles-Crawford effect, which states that eyes are less sensitive to rays of light entering from the peripheral pupil compared with those entering through the centre. “The rays coming in from the periphery strike the photoreceptors at an increased incident angle. As a result, there is a greater loss of light to the surroundings with less light channelled to the site of visual absorption on the outer segment of the cones, and so there is a decrease in sensitivity. Of course, description of the Stiles-Crawford effect is the result of psychophysical experimentation that also incorporates neural factors. However, research from He and colleagues showed that there is a close relationship between the Stiles-Crawford effect and cone directionality albeit with small differences with respect to the width and peak of their Gaussian curves,” Dr Pallikaris observed.

Optical modelling research from various investigators comparing outcomes with and without incorporation of the Stiles-Crawford effect indicate that cone alignment has a minimal effect on vision when the pupil size is small whereas it has a small impact when the pupil is large, affecting depth of focus and moderating the impact of retinal image defocus.

“It might be argued that it is not important to measure the Stiles-Crawford effect because of its modest impact. However, I believe if it is measurable, it should be taken into account to construct a more complete optical model,” Dr Pallikaris said.

How to quantify visual quality

In addressing the essence of the question “Can we quantify quality of vision”, Raymond Applegate, O.D, PhD, professor and Borish Chair of Optometry, College of Optometry, University of Houston, Texas, pointed out that while measurement of optical properties (e.g., aberrations, light scattering) is one necessary component in quantifying the quality of retinal image, formation of the visual perception resulting in vision requires neural processing. Consequently, evaluating the quality of vision requires examination of the entire visual system, not just one sub-component (optical or neural).

It is equally important to choose an appropriate test by which to judge visual performance. In the age of wavefront-guided corrections, benefits and losses in visual quality can only be assessed with visual performance tests sensitive enough to reveal variations in vision. Photopic high-contrast acuity by its very design is not a sensitive enough measure of visual quality to detect subtle (less than 0.25 equivalent diopsters) as opposed to large changes (greater than 0.25 equivalent diopsters) in retinal image quality. In this simulation, subtle changes in higher order aberrations not correctable with traditional corrections, affect retinal image quality and the resulting visual quality without necessarily affecting photopic high contrast acuity.

With the entire visual system in mind, Dr Applegate noted that mesopic low-contrast acuity is a particularly good measure of visual performance capable of quantifying quality of vision, in the clinical environment in the age of wavefront-guided corrections. He noted that mesopic low-contrast acuity testing has several advantages over traditional photopic high-contrast acuity as well as contrast sensitivity testing using sinusoidal gratings. First, mesopic light levels allow evaluation with a large, physiologic pupil. Second, measuring mesopic logMAR acuity is a recognition task rather than a detection task (contrast sensitivity). Third, mesopic logMAR acuity is sensitive to both phase shifts and contrast loss in the retinal image. From a practical perspective, mesopic low-contrast logMAR acuity is also well understood by clinicians and patients as well as easy, efficient, and cost effective to administer.

To demonstrate the utility of mesopic low-contrast logMAR acuity testing as a metric for predicting visual performance and the quality of vision, Dr Applegate reported results from a study comparing mesopic low-contrast logMAR acuity with photopic high- and low-contrast logMAR acuity in a population of 49 adult volunteers with 20/17 or better visual acuity (Applegate, RA, Marsack, JD, Thibos, LN, Metrics of retinal image quality predict visual performance in eyes with 20/17 or better visual acuity, Opt Vis Sci, 83:635-40, 2006).

For each eye, 31 different single-value retinal image quality metrics were calculated from the measured wavefront error of 49 eyes of 49 subjects. Regression analysis was used to determine the ability of each metric to predict each of the four types of logMAR acuity. For better metrics of retinal image quality, mesopic low-contrast logMAR acuity testing was found to be the most sensitive to variations in retinal image quality.

“The age of refractive surgery has introduced new aberrations to the human eye. As we try to minimise these, design new corrections to optimise visual function, and understand how the aberrations affect visual quality, we need sensitive tests of visual performance capable of quantifying the quality of vision as generated by the entire visual system.

Mesopic low-contrast logMAR acuity is a clinically viable test that can quantify visual quality that meets these requirements in an efficient cost-effective manner,” Dr Applegate said.

“Both patients have better than 6/6 acuity.”

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<th>Simulated retinal image 3mm Patient without complaints</th>
<th>Simulated retinal image 3mm Patient with complaints</th>
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Left: A simulated view of a best-corrected high-contrast log MAR acuity chart of a patient without complaints (3mm pupil).

Right: A simulated view of a best-corrected high-contrast log MAR acuity chart of a patient with complaints (3mm pupil).

Both had the same acuity.

The patient of the right panel’s simulation states “I may have better than 6/6 acuity, but I DO NOT SEE AS WELL AS I USED TO.” The loss in fidelity is due to phase shifts resulting from increased high order optical aberrations

(Simulations generated using Visual Optics Laboratory (v 6.89) Server and Associates, Inc. [http://www.sarverassociates.com])