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Editorial

Corneal biomechanics: Where are we?

Corneal biomechanics emerged as a very hot topic for research in Ophthalmology.[1,2] In this issue, Sharifipour and coworkers[3] present an observational cross-sectional study in healthy individuals that evaluated the correlations of corneal viscoelastic properties measured by the Ocular Response Analyzer (ORA, Reichert, Buffalo, NY) with central corneal thickness (CCT) in different age groups. In this study, corneal hysteresis (CH) and corneal resistance factor (CRF) had a significant negative correlation with age ($P < 0.001$). Other studies had already demonstrated that CH and CRF have a negative correlation with age and a positive correlation with CCT.[4] While statistical methodology was done properly in these studies, it is very important to note that CH and CRF do not express stiffness or the stress–strain behavior of corneal tissue. It is well recognized that corneal stiffness increases with age due to enzymatic pathways such as transglutaminase and lysyl oxidase, generating natural collagen crosslinking.[5] In agreement with such concept, Elsheikh and coworkers analyzed human corneal specimens ranging in age between 50 and 95 years with an inflation test, finding a significant increase in stiffness associated with age and also with the load rate.[6]

The ORA was introduced in 2005 as the first instrument for assessing corneal biomechanics *in vivo*.[7] The ORA is a non-contact tonometer (NCT) that monitors corneal deformation using the infrared reflex of the corneal apex. The applanation is detected as a peak on this reflex and is correlated with the pressure of the air puff. The inward phase (P1) and in the outward phase (P2) applanations are registered. The air puff maximal pressure is related to P1 as the system has an integrated loop to control the pump, which generates a collimated air pulse or puff with a symmetrical configuration. P1 and P2 pressure measurements are the basis for the first generation variables as reported by the original ORA software. The difference between the two pressures is called CH. *Hysteresis* is derived from the Greek, meaning ''lagging behind''.[8] Corneal resistance factor is also derived from the inward and outward pressure values, based on a formula ($P1 - kP2$), where k is a constant that was empirically developed to augment the correlation with CCT. The concept was to develop a parameter (CRF) that reflects the resistance to deformation, but this is still related to IOP.[7] Shah and coworkers first reported that hysteresis was significantly lower in keratoconic eyes compared to normal eyes.[9] However, accuracy of CH and CRF is not good enough for using these values as single parameters for ectasia diagnosis.[10] Even though pressure-dependent variables are relatively limited for detecting ectatic corneal disease, low CH is very relevant in glaucoma. CH is associated with optic nerve neuropathy in glaucoma. Interestingly, CH is more strongly associated with glaucoma presence, risk of progression, and effectiveness of glaucoma treatments than CCT.[11]

Beyond pressure-dependent parameters, different waveform-derived parameters were introduced for characterizing corneal deformation.[8,12,13] Dupps and coworkers developed parameters related to the intensity of deformation in accordance to the pressure applied, along with other aspects of response and combinations of these variables.[14] These parameters were found as better representatives of corneal structure in studies related to the diagnosis of ectatic disease.[14,15] Interestingly, integration of biomechanical data with corneal tomography has been demonstrated to augment accuracy for the identification of milder forms of ectasia.[16,17]

The Corvis ST (Oculus, Wetzlar, Germany) was introduced as the second instrument for "*in vivo*" biomechanical assessment of the cornea. This is also a NCT system with a collimated symmetrical air puff pressure profile. However, unlike the ORA, the Corvis ST produces a consistent air puff maximal pressure for every examination. In addition, it has an ultra-fast Scheimpflug camera that takes 140 frames during the 33 ms of the measurement, which allows for a more detailed evaluation of corneal deformation.[18] The Corvis ST provides a set of corneal deformation parameters based on the dynamic inspection of the corneal response.[19] Deformation amplitude refers to the movement of the corneal apex in the anterior-posterior direction and is determined as the highest displacement of the apex at the highest concavity moment. Studies involving contact lenses with different material properties mounted on an anterior chamber model with adjusted pressures have demonstrated the impact of the chamber pressure on the deformation response.[20] Novel corneal deformation parameters (CDP) were developed to improve ectasia detection.[21] The Vinciguerra Screening Report provides these data along with correlations of normality values and biomechanically adjusted intraocular pressure. In addition, the horizontal Scheimpflug image of the undisturbed cornea provides data for calculating the profile or the rate of increase of

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corneal thickness from the apex towards nasal and temporal sides. In addition, the characterization of the thickness data on the horizontal Scheimpflug image enables the calculation of the Ambrósio Relational Thickness through the horizontal meridian (ARTh).[22] ARTh has been combined with the CDP to generate the Corvis Biomechanical Index (CBI) that optimizes accuracy for detecting keratoconus. Vinciguerra and coworkers[23] demonstrated that with a cut off of 0.5, CBI was able to correctly identify 98.2% of the keratoconic cases with 100% specificity. Further integration of the Corvis ST and Pentacam has already been tested and also provides the most accurate platform for early ectasia diagnosis. (Integration of corneal tomography and biomechanical parameters for diagnosis of ectatic disease. Ambrósio and coworkers, Poster ESCRS 2015).

Other approaches that combine deformation of the cornea with analysis of high-speed imaging, such as swept-source OCT or supersonic shear-wave imaging technology, have been proposed.[8] The Brillouin optical microscopy is another technology that has been proposed to measure *in vivo* corneal biomechanics through the analysis of light scatter. This technology led to new insights regarding corneal biomechanics in ectatic diseases. Brillouin imaging showed differences between healthy and keratoconic corneas. Interestingly, it revealed that the mechanical weakening is primarily concentrated within the area of the corneal protrusion. Brillouin shift measures outside the protruded or conic area were comparable with that of healthy corneas.[24] These findings are in agreement with the concept of focal weakening, starting a biomechanical decompensation cycle as proposed by Roberts.[2] We predict fast developments and a bright future for corneal biomechanical assessments for ectasia detection, refining refractive surgery, glaucoma, and other applications for Ophthalmology.

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