**Editorial**

**Ocular Biomechanics – A Bright Future**

In a memorable keynote lecture at ARVO 2002, it was remarked that ocular biomechanics remained in “the dark ages” when compared to our understanding of biomechanics of other organs. This lecture came a couple of years after a seminal publication by Cynthia Roberts titled “The cornea is not a piece of plastic”, in which she attempted to explain the complex cellular and bio-composition of the tissue and the necessity of quantifying its biomechanic properties for several clinical applications.1 Since then, the field has progressed beyond recognition. This special issue features a series of state-of-the-art reviews by leaders in the ocular biomechanics field. The reviews span the latest biomechanics research in cornea, sclera, lens, vitreous and retina and all offer important perspective on future directions.

With a specific focus on corneal biomechanics, the first few years in this 20-year marathon saw initial emphasis on *ex-vivo* corneal analysis with gradual improvement in test methods and results’ reliability. At the beginning, strip testing was common. The cornea and sclera were dissected, and strips of tissue were cut out and subjected to uniaxial tension. Needless to say, the method involved several drawbacks including damage to the specimen edges, flattening a tissue that is naturally curved, using load that did not represent natural conditions, etc. However, the simple analysis method and the wide availability of material testing equipment in research labs continued to justify using this test method. Nevertheless, its results were considered adequate, but only for comparative studies, and certainly not for obtaining the actual stress-strain behaviour of the tissue.

Inflation testing then followed in which the cornea or the sclera were separated from ocular globes and subjected to internal pressure simulating the intraocular pressure (IOP). This was certainly a step forward although the clamps positioned along specimen edge did not truly represent real-life conditions. Furthermore, the analysis was initially based on shell theory, which wrongly assumed the tissue to be spherical and with uniform thickness. Over time, this analysis method was replaced with inverse modelling allowing more reliable behaviour determination. And further improvements arrived soon afterwards with testing whole eye globes allowing much better representation of boundary conditions and relating the behaviour of the cornea to that of the sclera. This development, while carrying significant technical advantages, made the testing and analysis of results much more challenging, and confined to a small number of research labs worldwide.

This work, which occupied most of the 2000s, led to huge developments in our understanding of ocular biomechanics, quantifying the tissue’s hyperelasticity, viscoelasticity, hysteresis and the effect of ageing and disease. The proven links between biomechanics and the tissue’s microstructure further enabled detailed determination of anisotropy and regional variation in material properties. However, while these advances made a step change in our understanding of behaviour “trends”, it remained impossible to apply these trends to individual eyes for purposes including treatment optimisation.

For this reason, it has been the holy grail of ocular biomechanics at the end of the 2000s to develop methods for the in-vivo determination of biomechanics aspects of pathophysiology in all the tissues of the eye. This huge need was met for the first time with the ocular response analyzer (ORA), and the provision of its corneal hysteresis (CH) and corneal resistance factor (CRF) parameters, which relate, respectively, to the tissue’s viscoelasticity and mechanical stiffness. There was suddenly a plethora of research studies attempting to quantify the effect of various parameters, such as ageing, diabetes and keratoconus, on the CH and CRF, and hence the tissue’s behaviour. This was followed in 2012 with the emergence of the Corvis® ST with a promise for more detailed monitoring of corneal deformation under an external air puff, and using this information to develop several biomechanical metrics called the dynamic corneal response parameters (DCRs). Dominant among the DCRs are the stiffness parameter (SP), the integrated inverse radius (IIR), the deformation amplitude (DA), and most recently the Stress-Strain Index (SSI). While the first three parameters showed strong correlations with the cornea’s overall stiffness (resistance to deformation), the fourth offered a method to determine the stress-strain behaviour of corneal tissue and hence the tangent modulus at any IOP.

Another significant step has been methods to map corneal stiffness – such as those to map the SSI, and others such as Brillouin microscopy, optical coherence tomography (OCT) elastography and ultrasound elastography. These methods, some of which are already available, provide unprecedented, detailed insight into tissue behaviour – something that was completely out of reach only a decade ago.

With these exciting developments, we are about to witness a revolution in eye care. The ability to quantify tissue biomechanics in vivo, in great detail and with high repeatability will now make it possible to accurately customise treatments. Example applications include the cross-linking treatment of keratoconus, intracorneal ring segment surgeries, refractive surgeries, relaxing limbal incisions and cataract surgeries. In all these applications, we can expect, in the near future, customisation tools based on in-vivo mapping of corneal biomechanics, numerical modelling of the effect of treatment on corneal tomography and artificial intelligence (AI) tools to determine the surgery parameters that are likely to lead to the best possible visual acuity outcomes.

In the posterior segment, the biomechanical properties of the vitreous humour have also received significant attention. For example, we now have a strong appreciation of the precise molecular composition of the vitreous as a unique viscoelastic tissue. In this issue, there is expert perspective provided on the vitreous and its role in biotransport, especially at the vitreoretinal interface and how this becomes altered during aging and disease. With the reliance on intravitreal drug delivery as a route for treating posterior segment diseases there is increasing need to take into account key biomechanical changes. For example, the liquefaction and solidification of the vitreous and detachment of the limiting membrane due to gel shrinkage are critical factors, not just for ocular homeostasis but also for their influence on the properties of injected drugs and efficacy.

Taken together, there has been significant progress on ocular biomechanics on a number of fronts. However, we firmly believe that a strong platform of knowledge exists in ocular biomechanics and in the coming years the multidisciplinary approaches and technological advances will see major advances made, not least as they are translated into real patient benefits.

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Reference

1. Roberts C. The cornea is not a piece of plastic. J Refract Surg. 2000;16(4):407-413.