# Evaluating Biomechanic Properties of the Cornea

The Ocular Response Analyzer has many clinical applications including a noninvasive measurement of corneal hysteresis.

BY DAMIEN GATINEL, MD, PHD

Although many available instruments are used to study the geometric and optic (eg, corneal topography, pachymetry) or histomorphologic (eg, confocal microscopy) properties of the cornea, the estimation of its biomechanic properties was, for many years, strictly the domain of scientific research. The recently introduced Ocular Response Analyzer (ORA; Reichert, Inc., Depew, New York) (Figure 1), however, now provides a noninvasive measurement of corneal hysteresis, the world's first estimate of corneal biomechanic properties. One clinical application of this new measurement is to detect corneas with biomechanic risk in the context of corneal refractive surgery. Indeed, certain LASIK-induced corneal ectasias may be caused by further degeneration of an initially precarious corneal biomechanic state like forme fruste keratoconus.

The objective measurement of these biomechanic properties may help increase the accuracy of intraocular pressure (IOP) measurements that, as we know, are affected by corneal properties. We have been using the ORA since November 2005 in a range of clinical contexts. This article highlights the definition of hysteresis, the principles of the measurement achieved by the ORA, and the clinical application of these principles.

## CORNEAL HYSTERESIS

Sir James Alfred Ewing of Scotland first described the phenomenon of hysteresis—a property of certain physical systems characterized by the nature of its response times to an applied force—in 1890. Such systems react slowly and do not instantaneously return to their original form, because they absorb part of the incident mechanical energy that dissipates as heat.

The ORA exerts a mechanical force on the cornea via a precisely metered air pulse. The manner in which the cornea responds to this mechanical stress provides information about its biomechanic properties. The mechanical behavior of corneal tissue can be described as a system with viscoelastic behavior. The cornea includes both elastic and viscous properties, both of which affect corneal behavioral characteristics. Viscous systems exhibit hysteresis, which is not present in purely elastic systems.

## PROPERTIES

**Elastic behavior.** A perfectly elastic system (eg, metal spring) stores energy and returns it completely. After compression—even prolonged—stored energy is returned almost instantly. Under certain conditions of tension, an elastic system may oscillate when the energy is returned.

**Viscous behavior.** A viscous system resists applied force proportionally to the intensity of the deformation forces exerted. The incident mechanical energy is converted into thermal energy, which explains a different return path to the original state of equilibrium.

The ORA is a noncontact device that occupies approximately the same space as a traditional air-puff tonometer. It consists of an air-jet source that is situated between an infrared transmitter and receiver, which form a 90° angle (Figure 2). Figure 3 summarizes the principal signal acquisition times and stages of corneal response to the mechanical force exerted by the air jet.

The instrument emits a rapid calibrated air jet toward the corneal dome. The jet's force causes an inward deformation of the cornea followed by a return to its normal configuration. The pressure exerted by the air jet is continuously recorded during the 20-millisecond application, and applanation is detected by measuring the intensity

Figure 1. The Ocular Response Analyzer is a noncontact device.

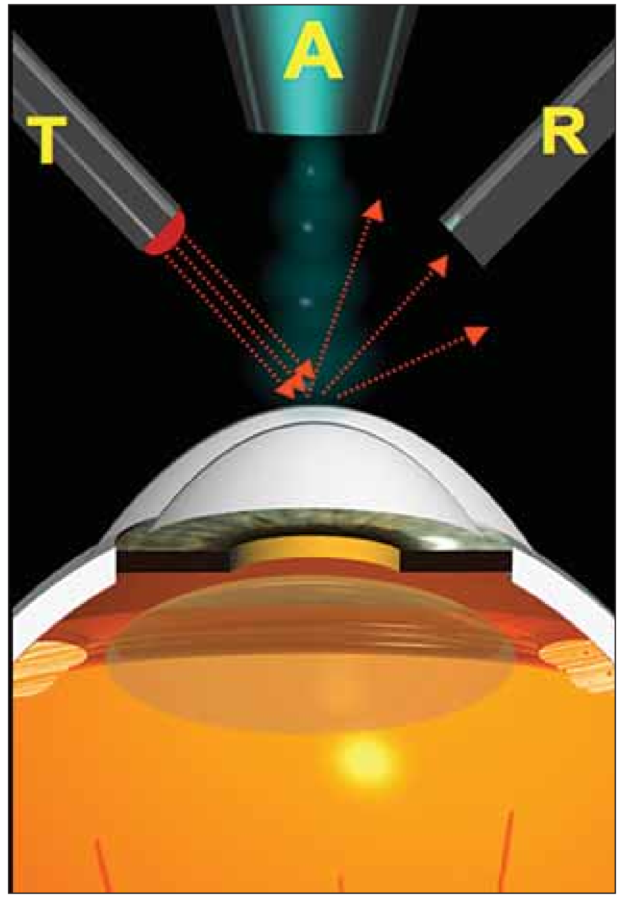



Figure 2. Illustration of the measurement principles, including the calibered air jet (A), infrared transmitter (T), and the infrared receiver (R).

of an infrared light beam reflected by the cornea. Lower corneal curvature caused by the deformation under the force of the air pulse results in a higher intensity of light reflection, which is detected by a photosensitive sensor. Applanation corresponds to the maximum amount of reflected light intensity, because at this moment the corneal surface acts somewhat like a flat mirror. The applanation pressure is recorded by measuring the air-pulse pressure at the time of the infrared peak.

The originality of the ORA lies in its capacity to make two consecutive applanation measurements. The first is made at the moment of flattening during the inward corneal deformation, and the second is made as the cornea returns to its initial state. Milliseconds after the first applanation is detected, the air jet is interrupted. Due to pump inertia, the air pressure exerted on the cornea continues to increase for a few milliseconds before reaching a maximum, after which it gradually decreases back to the initial state of equilibrium. The roughly bell-shaped pressure curve obtained throughout the examination is Gaussian in form. For a few moments after the first applanation, the corneal dome is subject to a pressure higher than the IOP, and the central corneal profile becomes slightly concave at the front. The intensity of reflected infrared light decreases during this portion of the measurement process. As the air-jet pressure declines toward zero, the cornea begins to return to its normal configuration. In the process, the cornea passes through a second applanation, also indicated by a peak of reflected infrared light. The corneal dome then returns to its initial state.

## PRESENTATION OF SIGNALS

For each measurement, three curves are displayed on one graph. The x-axis represents time (milliseconds). The green Gaussian curve represents the pressure exerted against the corneal dome, and the red curve represents the intensity of infrared light detected during the measurement. The blue curve is obtained by mathematical smoothing of the red curve, and its function is to reduce undesirable noise in the red signal. The time intersection of the peaks of the smoothed curve (blue) with the pressure curve (green) defines the two successive applanation pressures.

## CALCULATION OF QUANTITATIVE INDICES

The ORA apparatus measures two consecutive applanation pressures (ie, P1 and P2), expressed in millimeters of mercury. It is important to note that P1 is measured as the cornea is subjected to, and resists, an increasing positive pressure of the calibrated air jet; P2 is measured while the cornea is returning to its state of equilibrium, during the decrease of positive air jet pressure.

Because the second applanation occurs with reduced air jet pressure, the cornea responds differently than during the first (inward) applanation. Statistical analysis of various populations enabled the developers to characterize the manner in which the cornea responds at P1 and P2. This understanding has permitted the derivation of a number of ocular parameters based on P1 and P2 values.

## PARAMETERS

**Corneal hysteresis (CH).** This parameter is equal to the difference between P1 and P2 (P1-P2). This difference in the measured applanation pressures is a result of viscous damping in the corneal tissue.

**Corneal resistance factor (CRF).** This formula (P1-K X P2, where K=0.7) gives more weight to P1 compared with P2. The K-value was determined on the basis of clinical studies and statistical correlation models. CRF is thought to be a better indicator of the cornea's total viscoelastic response to the air pulse.

**Goldmann correlated IOP (IOPg).** Basically, this formula is an estimate of IOP correlated to Goldmann tonometry. IOPg is equal to the arithmetic average of P1 and P2 ([P1+P2]/2).

**Corneal compensated IOP (IOPcc).** Again, the K-value in this formula was determined on the basis of clinical studies and statistical regression models. IOPcc compensates for the viscoelastic properties of the cornea and is calculated using a specific ratio of P1 and P2, where P2 is weighted more (IOPcc=P2-0.KxP1).

Our initial experience with the ORA allowed us to identify the average values and typical range of hysteresis and corneal resistance in various clinical contexts such as chronic glaucoma, keratoconus, and postoperative complications of corneal refractive surgery. In our preliminary statistical study, we determined that the average CH value among normal patients is approximately 11 ±1.25 mm Hg. The definition of normality is, in this case, conservative. Although no patients with ocular hypertension or suspected keratoconus were included in the analysis, slightly ametropic patients were largely represented. CH appeared to be weakly correlated with central corneal thickness in our study ($R^2$=0.3).

The value of CH was significantly lower for eyes with keratoconus (approximately 8.5 mm Hg), but there is a significant dispersion around this average. A cornea affected by keratoconus is softer than a normal cornea, and therefore, its capacity to absorb incidental energy is less. The value of the CRF (average, 8.5 mm Hg) is also reduced in the case of keratoconus.

The ORA developers calibrated CH and CRF to match on average, however, values for the same cornea are sometimes quite different, as they describe various properties of that cornea. We believe that when a patient presents with a lower CRF value compared with the CH (eg, 7 mm Hg vs 8 mm Hg), they have a fragile cornea with biomechanic instability. Lower reproducibility of CH and CRF indices between successive measurements on the same eye is also an indicator of an underlying biomechanic irregularity, and it certainly indicates a less homogeneous response of the corneal wall to the air-jet stimulus.

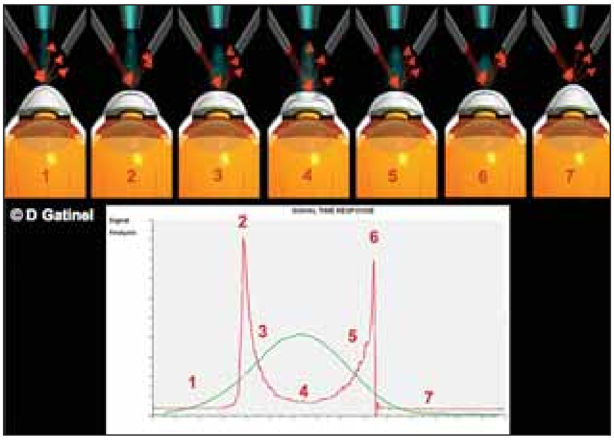



**Figure 3. Here, the ORA measurement storyboard is represented. First is the emission of the calibered air jet (1), followed by the first applanation, where the air-jet emission is stopped (2). Due to inertia, the air pressure exerted against the corneal dome continues to increase (3). This causes the corneal dome to become slightly concave and less reflective in the direction of the infrared receiver. The air pressure reaches its maximum (4), and the decay in air pressure allows the cornea to deform back to its equilibrium state (5). The undertaking of a second applanation on its way (6) is followed by the cornea returning to its equilibrium state (7).**

We observed a universal reduction of the CH value in all patients following refractive LASIK surgery. Although the amount of CH reduction can be higher in some patients, the average drop is approximately 2 mm Hg. This reduction appears to be permanent and without clinical consequences. We observed stable post-LASIK CH in patients past 1 year. Although CH values after LASIK are lower than before LASIK, they remain statistically higher than in patients with keratoconus.

We recently reported the effect of an isolated LASIK flap incision (ie, a photoablation-free bioptic procedure associating LASIK and the insertion of a phakic IOL) into an eye with a thin cornea and low hysteresis (8.5 mm Hg). This isolated and uncomplicated incision induced an approximate 1 mm Hg reduction of the CH value.

Several preliminary studies suggest that in the event of prolonged ocular hypertension, the CH value becomes reduced. In some cases, the CH value seems to return to normal after the pressure is brought under control via medication or surgery. In other cases, the CH seems to remain low despite the lower IOP. The reduced CH could indicate the alteration of corneal tissue properties, which are due to prolonged hypertension. In this context, CH could be regarded as a prognostic marker of a glaucomatous condition. It is also reasonable to postulate that a reduction of corneal hysteresis could indicate a general biomechanic

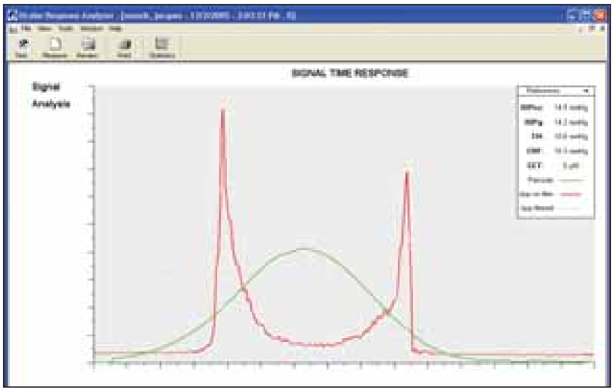



**Figure 4. The window on the right recapitulates the values of the quantitative indexes (IOPcc, IOPg, CH, CRF).**

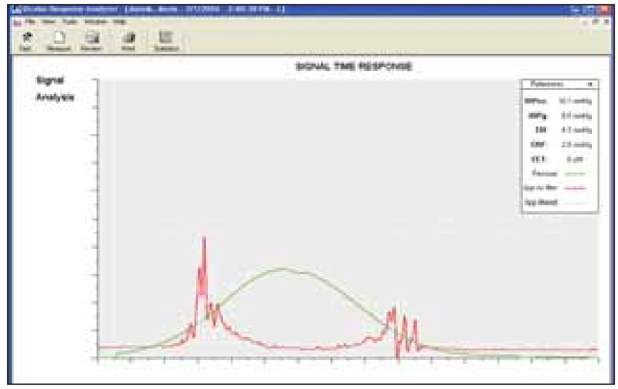



**Figure 5. The signal obtained in an eye with keratoconus. The signal shape is ragged, and the peaks are of low amplitude. The hysteresis and corneal resistance factor are low (4.3 mm Hg and 2.9 mm Hg, respectively).**

fragility of tissues in the ocular wall, including the sclera and the lamina cribrosa. This would mean that an eye with low CH would be more susceptible to glaucomatous damage—regardless of IOP—making detection of low corneal hysteresis valuable for the early detection of glaucoma.

Additionally, the ORA's measurement of IOPcc takes better account of the corneal biomechanic state, enabling IOP measurements that are less affected by corneal properties. An accurate measurement is particularly important when the biomechanic state of the cornea differs from average, such as in cases of keratoconus, normal tension glaucoma, nonglaucomatous ocular hypertension, corneal edema, and following corneal refractive surgery.

Analyzing morphologic characteristics of the intensity of the raw (ie, unsmoothed) infrared signal makes way for entirely new diagnostic prospects. These characteristics include the height and the width of the peaks and the smoothness of the infrared signal (ie, high-frequency content) (Figures 4 through 6). Currently, our institution is also conducting studies to compare the ORA measurement signals. As an example, patients affected by early keratoconus often present noisy peaks with reduced height and increased width.

The ORA is an innovative and practical clinical instrument for which the principal areas of application include the management of glaucoma and corneal refractive surgery. As well as contributing to the understanding of the physiopathogenic mechanisms of glaucoma or of the corneal response to photoablative surgery, the assessment of the biomechanic state of the cornea should make it possible to achieve important diagnostic and therapeutic progress in ophthalmology. ■

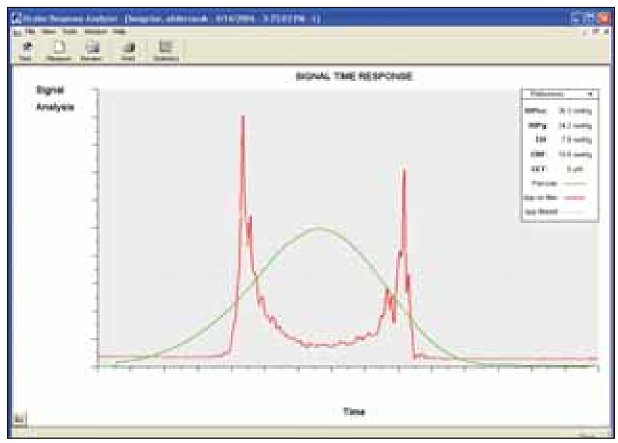
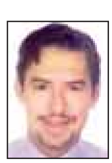



**Figure 6. The signal obtained in an eye with chronic open-angle glaucoma. The peaks usually show normal to high amplitude and are slightly deformed by high frequency oscillations. The hysteresis is low (7.8 mm Hg), but the CRF value is within the normal range (10.8 mm Hg).**



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