



# Corneal biomechanical properties: Precision and influence on tonometry



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## ABSTRACT

**Purpose:** To assess the precision and reproducibility of the corneal biomechanical parameters, and their relationships with the intraocular pressure (IOP) measured with the Goldmann tonometer and a non-contact tonometer.

**Methods:** Readings for biomechanical properties and for IOP measured with the Goldmann and non-contact tonometers, were taken on one randomly selected eye of 106 normal subjects, on each one of two measurement sessions. Measurements with the ocular response analyzer (ORA) and the noncontact tonometer were randomized, followed by the measurement of central corneal thickness and with the Goldmann tonometer.

**Results:** Repeatability coefficients for CCT, corneal hysteresis (CH) and corneal resistance factor (CRF) in Session 1 were  $\pm 0.01 \mu\text{m}$ ,  $\pm 3.05 \text{ mmHg}$  and  $\pm 2.62 \text{ mmHg}$ , respectively. The mean CCT, CH, CRF, Goldmann and noncontact tonometry did not vary significantly between sessions. Reproducibility coefficients for CCT, CH and CRF were  $\pm 0.02 \mu\text{m}$ ,  $\pm 2.19 \text{ mmHg}$  and  $\pm 1.97 \text{ mmHg}$ , respectively. Univariate regression analysis showed that CCT, CH and CRF significantly ( $P < 0.0001$ ) correlated with the IOP measured with the Goldmann and noncontact tonometers (and with the differences between tonometers) in Session 1. There were no significant correlations with the differences between tonometers in Session 2. Multivariate analysis revealed a minimal effect of CCT on Goldmann measurements but a significant effect on those of the noncontact tonometer.

**Conclusions:** Measurement of the biomechanical properties of the cornea, using the ORA, are repeatable and reproducible, affect Goldmann tonometry less than noncontact tonometry, and have a minimal influence on the difference in measured intraocular pressure between tonometers.

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## 1. Introduction

Accurate measurement of intraocular pressure (IOP) is vital for the diagnosis and management of glaucoma because, as has been shown by all the major glaucoma trials, it is the only variable which can be altered to prevent or delay the onset and/or progression of glaucoma [1–7].

The Goldmann applanation tonometer (GAT) is the clinical gold standard for IOP assessment, but as with most tonometers, its measurements are influenced by the biomechanical properties of the cornea [8–12]. In contrast the true IOP, as measured intracamerally, is not subject to the biomechanical properties of the cornea [13,14].

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However, the exact relationship between the corneal biomechanical properties and the IOP measured through the cornea is still unclear. The central corneal thickness (CCT) is supposed to influence the IOP measured through the cornea with an overestimation of IOP in thicker corneas and an underestimation in thinner corneas. A number of formulae [8,11,15,16] have been computed to correct trans-corneally measured IOP for the effect of CCT but their usage has failed to gain wide acceptance to date. Some of the studies have even come to contradictory conclusions. Foster et al. [16] found no relationship between corneal thickness and the difference in the measured IOP (between applanation tonometry and intracameral cannulation), leading them to provide a correction formula for IOP measured by applanation tonometry which did not take corneal thickness into consideration. This result was in contrast to studies by Ehlers et al. [8] and Whitacre et al. [15]. Both latter studies reported significant relationships between the corneal thickness and the measurement error between the IOP measured by applanation tonometry and the true IOP (as measured by intracameral cannulation). Data from the Ehlers et al. [8] and Whitacre et al. [15] studies suggest that a 10% increase in corneal thickness would

result in a 3.5 mmHg [8] and 1.1 mmHg [15] increase in the IOP measured by applanation tonometry.

The recent introduction of the Ocular Response Analyzer® (ORA) – Reichert Ophthalmic Instruments, Depew, NY, USA – means that corneal biomechanical properties other than CCT may be measured, indirectly, *in vivo*. The ORA fires a metered air pulse at the cornea, causing it to indent and thus pass through two (inward and outward) applanation events. From the two IOP readings, the ORA computes two corneal biomechanical properties. Corneal hysteresis (CH) is supposed to represent the viscoelastic properties of the cornea. The corneal resistance factor (CRF) is thought to predominantly reflect the elastic resistance of the cornea, and could reflect the overall resistance of the eye [17,18].

Previous studies have demonstrated statistically significant reductions in CH and CRF in post-lasik eyes [19,20], pseudophakic eyes [21], keratoconus [18,19,22], in eyes with glaucoma [23–27], and in Fuchs corneal dystrophy [17]. It seems that CH and CRF are significantly lower in normal relatives of keratoconus patients [28] and in patients who showed a more rapid progression of glaucomatous visual field loss [23,29]. However, one recent study [30] reported only a weak relationship between CH and CRF on the one hand, and structural (retinal nerve fibre layer thickness) and functional (visual field) oculo-visual damage in glaucoma, on the other.

Since both parameters decrease along with CCT in post-LASIK corneas, and have also been shown to be higher in thicker corneas [31], it would appear that CH and CRF are functional surrogates for CCT, which itself has been shown to be a risk factor for the onset and/or progression of primary open-angle glaucoma (POAG) and normal tension glaucoma (NTG) [5,7,32–34]. Corneal hysteresis and CRF tend to be positively correlated with CCT in a number of anterior segment diseases notably keratoconus and glaucoma. In some of these cases, CH and CRF appear to be risk factors for the development and/or progression of the disease process independent of CCT [23,35,36].

The increasing relevance of the corneal biomechanical properties makes it important to thoroughly assess repeatability, as well as long- and short-term reproducibility, for each of these biomechanical properties. Also, since most forms of glaucoma are chronic disease processes, multiple, longitudinal comparisons of IOP measurements are a necessary and crucial element of patient care [37]. A number of studies have reported on the repeatability and reproducibility of CH and CRF [22,25,38] and on the influence of these parameters on the IOP measured by indentation and applanation methods [14,24,36,39,40] but none has compared the consistency of the effect (on the measured IOP) of CH and CRF (measured on separate days), on the one hand, with that of CCT on the other. Also there are no reports in the literature of the comparative influence of these properties on the IOP measured with the GAT and that measured with a non-ORA noncontact tonometer (NCT). Only one study to date has reported on the influence of CH and CRF on the difference in measured IOP between an NCT and the GAT [41].

The goals of this study were to assess the repeatability and reproducibility of the biomechanical properties (CH and CRF) measured by the ORA, determine their effects on the IOP measured with the GAT and a NCT in comparison to the effect of CCT on those same parameters, and to study the influence of CCT, CH and CRF on the difference between the IOPs measured by the GAT and a NCT. With specific regard to the effect on the measured IOP in two separate sessions, we sought to test the null hypotheses of:

- (1) No significant difference between sessions for IOP readings with the GAT and noncontact tonometer, and for CH, CRF and CCT.
- (2) No difference in the effect of CCT or CH or CRF, between sessions, on the GAT-measured IOP and on the noncontact IOP.
- (3) No difference in session 1 and in session 2 between the effects on measured IOP, of: CCT versus CH; CCT versus CRF; and CH versus CRF.

## 2. Methods

The study cohort included one randomly selected eye of 106 routine Optometry patients, who met the criteria for participation. Randomization was carried out by a designated researcher, using a sequence of random numbers generated on a Microsoft Excel spreadsheet. The purpose of the investigation, and the rights of the participants (before, during and after the study) was explained to each subject before his/her participation, and each subject gave informed consent to participate in the study, in accordance with the 1975 Helsinki Declaration, as modified in Edinburgh 2000. The study protocol received local ethical committee approval.

Prior to inclusion in the study, each subject underwent a comprehensive ophthalmic examination which included slit-lamp biomicroscopy of the external eye and anterior segment, monocular direct ophthalmoscopy, central visual field assessment with automated static perimetry, objective & subjective refraction and pupil evaluation. Subjects with a positive history for one of the following were excluded: participation in one of the previous studies by our research group; a positive history for (or objective evidence of) anterior segment disease or surgery; a history of contact lens wear; a history of ocular hypertension or glaucoma. Therefore all subjects were oculo-visual normals in good general health. The advantage of selecting a young sample of oculo-visual normals is that the parameters measured in this study would be expected to vary within narrow limits compared with those in patients with anterior segment disease, for example. Therefore, any significant variation from one week to the next would suggest a poor reproducibility of the technique in question, within this time period.

Of the one hundred and ten subjects recruited for this study, four (three men) were lost to follow up.

Each subject was required to visit the clinic for two separate measurement sessions separated by approximately one week. In both sessions, IOP measurements were made between 14:00 h and 16:00 h to ensure that the IOP was assessed at the period of the day when it is known to be most stable [42].

The measurements made in the second session were to confirm the results of the first session, to establish reproducibility indices for the biomechanical properties measured with the ORA, and to judge the consistency of the effects of CH and CRF (on the IOP measured with the GAT and a NCT) compared with that of CCT.

In each session, the order of IOP measurements with the Ocular Response Analyzer (Reichert Ophthalmic Instruments, Depew, New York, USA) and Topcon CT80 noncontact tonometer (Topcon Medical Systems Inc., Oakland, New Jersey) was randomized by a designated researcher, using a sequence of random numbers generated on a Microsoft Excel spreadsheet. Following the measurements with the noncontact tonometers, the cornea was anaesthetized with one drop of 0.4% oxybuprocaine for assessment of the corneal thickness with the ultrasound pachymeter attached to the ORA followed by Goldmann applanation tonometry.

As there are no studies in the published literature showing that ultrasound pachymetry causes an ocular massage effect, we deemed that the potential effect of performing pachymetry before Goldmann tonometry would be less than that if the order of measurements were reversed (i.e. if Goldmann tonometry was performed before pachymetry, we believed that the effect on the corneal thickness measured would have been greater). Our reasoning is supported by the conclusion, by AlMubrad and Ogbuehi

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