

Characterization of Corneal Indentation Hysteresis*

Match W. L. Ko, Dongming Wei and Christopher K.S Leung

Abstract— The aim of this study is to design and develop a non-invasive corneal indentation method to measure the corneal hysteresis behavior under dynamic corneal indentation. Corneal indentation method is adapted for the design and development of a measurement method for the characterization of Corneal Indentation Hysteresis (CIH). Fourteen porcine eyes were tested using the corneal indentation method. The CIH measured in enucleated porcine eyes showed indentation rate and intraocular pressure dependences. The CIH increased with the indentation rate at lower IOP (< 25 mmHg) and the CIH decreased with the indentation rate at higher IOP (> 25 mmHg). The CIH was linear proportional to the IOP within an individual eye. The CIH was positively correlated with the IOP, corneal in-plane tensile stress and corneal tangent modulus (E). A new method based on corneal indentation for the measurement of Corneal Indentation Hysteresis *in vivo* is developed. To our knowledge, this is the first study to introduce the corneal indentation hysteresis and correlate the corneal indentation hysteresis and the corneal tangent modulus.

I. INTRODUCTION

The corneal biomechanical properties are of great interest due to its clinical potential application, particularly in early detection of keratoconus [1]. It has been also suggested that the corneal biomechanical properties may reflect the biomechanical behavior of the globe and give an indication of the susceptibility of glaucoma developing and progression [2, 3]. Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY, USA) is the first commercially available instrument capable to measure *in vivo* corneal biomechanical properties. The device uses a rapid jet of air to indent the cornea. The infrared reflectance profile from ORA during the bi-directional applanation process is measured and analyzed to provide two parameters of corneal biomechanics, corneal hysteresis (CH) and corneal response factor (CRF). The CH and CRF provided by ORA are non-standard biomechanical terms that are different from the classical knowledge of corneal biomechanics. The CH may be produced with different combinations of elastic modulus and the viscous damping parameters. The aim of this study is to design and develop a

non-invasive corneal indentation method to measure the corneal hysteresis behavior under dynamic corneal indentation.

II. MATERIALS AND METHODS

A. Corneal indentation

Conventional corneal indentation methods used in ophthalmology include Schiötz Tonometry and Goldmann Applanation Tonometry (GAT). Schiötz Tonometry measures a single depth produced on the corneal surface by a known weight indenter. GAT measures a single reaction load by the cornea under a predefined area of applanation. Both of the two methods measure only a single point on the corneal load-displacement relationship in a static manner, which is not enough to explore the entire behavior of the cornea under external applied load.

Corneal indentation method is adapted for the development of measurement method for the corneal hysteresis behavior [4, 5]. The corneal indentation tangent modulus (E_{IOP}) at a fixed IOP are defined as [4],

$$E_{IOP} = \frac{a(R-t/2)\sqrt{1-\nu^2}}{t^2} \frac{dF}{d\delta} \Big|_{IOP}, \quad (1)$$

where σ is the indentation stress, ε is the corresponding strain, F is the indentation load, R is the anterior radius of curvature, t is the central corneal thickness, ν is the Poisson's ratio of the cornea ($\nu \sim 0.5$ since the cornea consists principally of incompressible water [6]), a is the corneal geometry coefficient, and δ is the indentation depth (displacement).

The geometry constant a is determined from μ (Table 1) [7],

$$\mu = r_o \left[\frac{12(1-\nu^2)}{(R-t/2)t^2} \right]^{1/4}, \quad (2)$$

where r_o is the radius of the of the cylindrical flat-end indenter. The corresponding change of strain (ε) can be calculated using [8],

$$d\varepsilon = \frac{d\delta|_{IOP}}{R-t/2}. \quad (3)$$

In the current study, it is assumed that the change of stress is only contributed by the indentation. The change in IOP during the corneal indentation is little and ranged from 1-3 mmHg [5], hence the change in the stress within the indentation period can be neglected.

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The corresponding change of in-plane tensile stress induced by the indentation can be calculated using [7],

$$\sigma = \frac{a\sqrt{1-\nu^2}}{2t^2} F|_{IOP}. \quad (4)$$

A typical load-displacement curve obtained from the corneal indentation on the porcine cornea was shown in Figure 1. The area bounded by the loading- and unloading-displacement curve is the work done by the corneal indentation. The corneal indentation loading ($W_{loading}$) and unloading ($W_{unloading}$) work done are defined as,

$$W_{loading} = \int_0^{\delta_{max}} F_{loading} d\delta, \quad (5)$$

$$W_{unloading} = \int_0^{\delta_{max}} F_{unloading} d\delta. \quad (6)$$

The area bounded by the loading and unloading-displacement displacement is the corneal indentation net work done (W_{net}) during the corneal indentation and is mathematically defined as,

$$W_{net} = \oint F d\delta. \quad (7)$$

The corneal indentation hysteresis (CIH) is defined as the area bounded by the loading and unloading stress-strain curve,

$$CIH = \oint \sigma d\varepsilon. \quad (8)$$

Substituting equation (3) and (4) in equation (8) and simplifying gives,

$$\begin{aligned} CIH &= \frac{a\sqrt{1-\nu^2}}{2t^2(R-t/2)} \cdot \oint F d\delta \\ &= \frac{a\sqrt{1-\nu^2}}{2t^2(R-t/2)} \cdot W_{net}. \end{aligned} \quad (9)$$

The corneal indentation hysteresis and corneal tangent modulus were examined as a function of the in-plane tensile stress in the cornea. The bi-axial in-plane tensile stress (σ_t) induced by the intraocular pressure in a membrane can be calculated using Laplace's Law [7],

$$\sigma_t = \frac{R-t/2}{2t} IOP \quad (10)$$

Table 1 Relationship between a and μ . [7]

μ	0	0.1	0.2	0.4	0.6	0.8	1.0	1.2	1.4
a	0.433	0.431	0.425	0.408	0.386	0.362	0.337	0.311	0.286

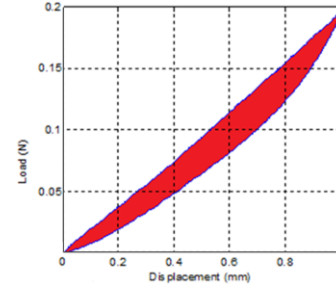


Figure 1 Typical load-displacement data acquired during the indentation on the porcine cornea

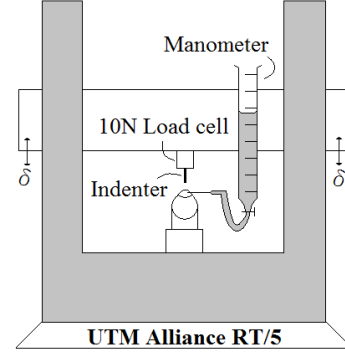


Figure 2 Schematic setup of the corneal indentation experiment.

B. Ex vivo experiments on porcine eyes

Fourteen porcine eyes were obtained from a local abattoir and tested using the corneal indentation method for the characterization of the corneal indentation hysteresis. Experiments were conducted within 12 hours of the animals being killed. The porcine eyes were kept moist and cold inside an insulated bucket with refrigerants at 4°C. The extraocular muscles and the extraneous fat were removed carefully before the indentation measurement. The corneal radius of curvature of the porcine eyes was taken using a DSLR camera (Canon 50D with EF 100mm f/2.8L Macro IS USM Lens, Canon, Inc., Tokyo, Japan) and analyzed using a customized Matlab program (Matlab 2013b, The MathWorks, Natick, MA). The central corneal thickness was measured by a camera-mounted Leica M205C stereomicroscope (Leica Microsystems, Wetzlar, Germany).

The experimental setup for corneal indentation is shown in Figure 2. The porcine eye was held on a test jig and placed under the indenter for indentation. The anterior chamber was cannulated and filled with saline via a needle connected to a manometer for the control of the intraocular pressure as shown in Figure 2. The IOPs for experiment were set between 12 mmHg and 40 mmHg. Three cycles of loading and unloading between 5 to 50 mmHg were applied to condition the tissue and ocular structure in order to stabilize its behavior before indentation test. A 10 N load cell (MTS 100-090-795, S-Beam type, load resolution 0.0001 N) was screw-mounted onto the crosshead of a material test frame (universal testing machine UTM (Alliance RT/5, MTS Corporation, Eden Prairie,

Minnesota, USA)) (Figure 2). A 5 mm cylindrical flat-end indenter was screw-mounted onto the bottom of the load cell. The porcine eye was placed underneath the indenter and the cornea apex was then aligned with the indenter. The porcine corneas were indented to a depth of 1 mm at indentation rates between 5 - 50 mm/min after a minimum stabilization period of 10 minutes. The indentation loading and unloading load (F)-displacement (δ) data were recorded.

III. RESULTS

The mean corneal radius of curvature and central corneal thickness ($n = 14$) were 7.98 ± 0.87 mm and 1.06 ± 0.11 mm, respectively. A typical load-displacement curve obtained from the corneal indentation on the porcine cornea was shown in Figure 1. The plot showed distinct loading and unloading behavior of the cornea under indentation. The area bounded by the loading and unloading load-displacement curve are defined as the corneal indentation work done (W_{net}) and the corneal indentation hysteresis (CIH) can be determined using equation (9) and W_{net} . The load-displacement curves ascertained at different indentation rates and different set intraocular pressures were showed in Figure 3. The measured $W_{loading}$, $W_{unloading}$ and CIH using different indentation rates and different intraocular pressures were shown in Figure 4. The CIH as a function of intraocular pressure, in-plane tensile stress and corneal tangent modulus were shown in Figure 5.

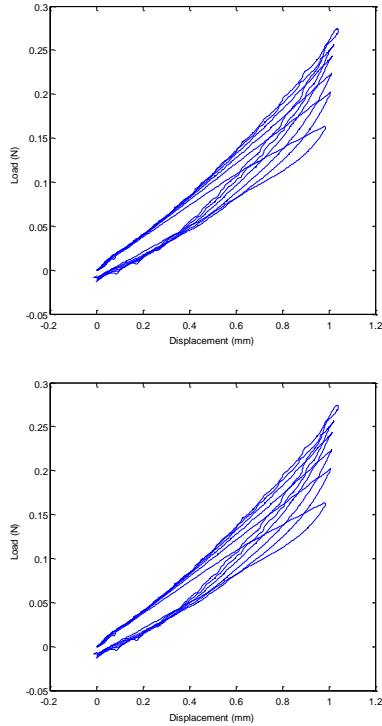


Figure 3 (a) Indentation rate dependence of the load-displacement curve under fixed IOP. (b) Intraocular pressure dependence of the load-displacement curve measured under the same indentation rate.

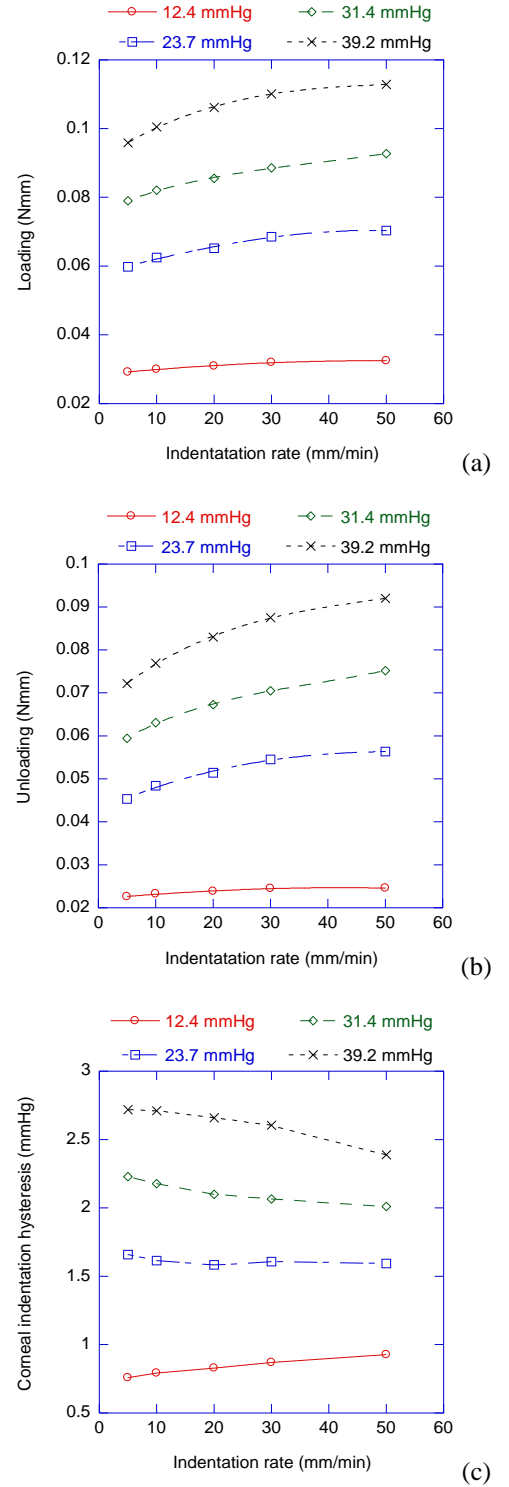


Figure 4 Corneal indentation (a) loading work done ($W_{loading}$), (b) unloading ($W_{unloading}$) work done and (c) indentation hysteresis (CIH), as a function of indentation rates for porcine eye at different set intraocular pressure (IOP).

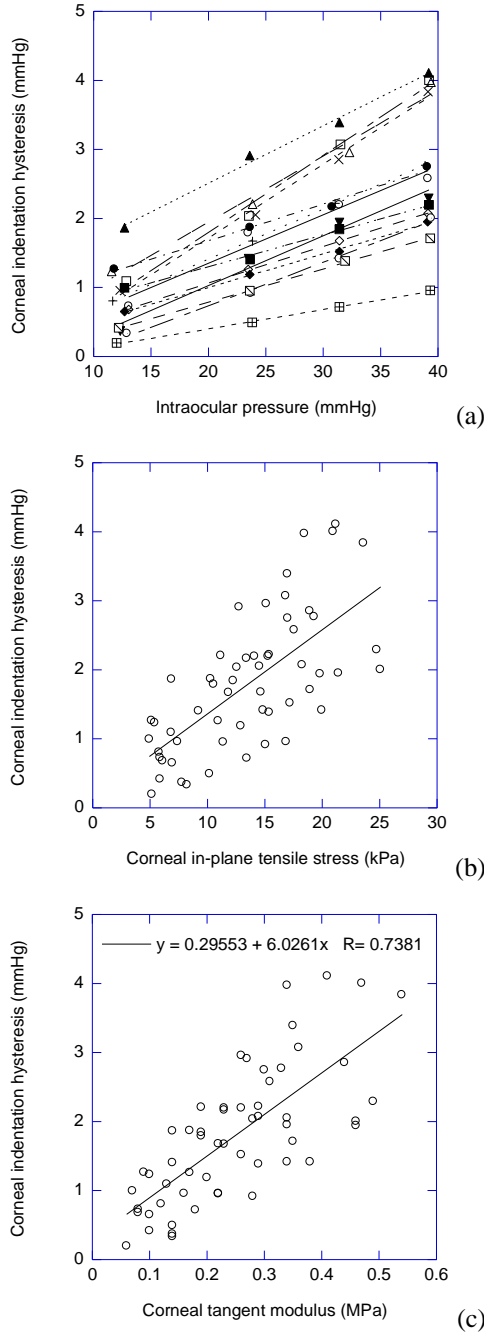


Figure 5 (a) Corneal indentation hysteresis (CIH) as a function of intraocular pressure (IOP), (b) CIH as function of corneal in-plane tensile stress, and (c) CIH as a function of corneal tangent modulus. ($n = 14$; all the above data are measured at indentation rate of 20mm/min.)

IV. DISCUSSIONS

In this study, we adapted corneal indentation method for the characterization of the corneal hysteresis behavior. The load-displacement showed that the cornea exhibit hysteresis behavior as shown in Figure 1. It is showed in Figure 3 that the net work

done (W_{net}) is indentation rate dependent and intraocular pressure dependent. The higher the indentation rate and/or intraocular pressure, the larger the area bounded by the loading and unloading load-displacement curve. The rate dependent corneal indentation loading work done, unloading work done and hysteresis were shown in Figure 4. Both of the loading and unloading work done were increased with the indentation rates. The CIH increased with the indentation rate at lower IOP (< 25 mmHg) and the CIH decreased with the indentation rate at higher IOP (> 25 mmHg).

The corneal indentation hysteresis was linear proportional to the IOP within an individual eye ($n = 14$, $r = 0.998 \pm 0.003$). The CIH measured using indentation rate of 20 mm/min at 15 mmHg ($n = 14$) was 1.00 ± 0.48 mmHg and was positively correlated with the IOP (Figure 5a, $r = 0.692$, slope = 0.068 mmHg/mmHg, $p < 0.001$), corneal in-plane tensile stress (Figure 5b, $r = 0.683$, slope = 0.1219 mmHg/kPa, $p < 0.001$), and corneal tangent modulus (E) (Figure 5c, $r = 0.738$, slope = 6.013 mmHg/MPa, $p < 0.001$), respectively.

V. CONCLUSION

In this study, a corneal indentation method was adapted to characterize the corneal hysteresis behavior under dynamic corneal indentation. To our knowledge, this is the first study to characterize the corneal hysteresis behavior using corneal indentation and correlate the corneal indentation hysteresis and the corneal tangent modulus. This method provides a new non-invasive means to measure the corneal indentation hysteresis of individuals and the development of the method is the first step towards the investigation of the relationship between corneal biomechanical properties and ocular diseases like glaucoma and keratoconus.

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