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Editor's comment: Accurate measurement of intra-ocular pressure is essential in the diagnosis and management of patients with glaucoma, but the errors associated with its measurement can be significant. The contribution from the mechanical properties of the cornea, in particular, means the error is likely to be greater in patients with the condition. The study by Leung, Ko and Lam highlights the variability in such measures, and presents a new method of trans-corneal tonometry (individual-specific tonometry, or IST) to address this problem. Their findings suggest that when variation in corneal stiffness is taken into account the measurement accuracy may be improved.

Richard Black, Editor in Chief

Individual-specific tonometry on porcine eyes☆

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ABSTRACT

Intraocular pressure (IOP) monitoring is important in the diagnosis and management of glaucoma. The measurement of IOP is affected by corneal properties, but the effect of corneal stiffness on IOP measurement is unaccounted for in pressure measurement instruments such as the Goldmann Applanation Tonometer (GAT). A new instrumented non-invasive indentation tonometry that can measure IOPIST, a corneal stiffness-corrected intraocular pressure is developed. The inter-individual corneal variations of 12 porcine eyes ex vivo were independently characterized; and their true intraocular pressure, IOPT's, were set using a manometer before indentation using the new indentation tonometry. Analyses of the load–displacement data showed that porcine corneal stiffness varied more than five times from 0.045 to 0.253 N/mm. Analysis showed that, without individual stiffness correction, inter-individual variation of IOPGAT can vary up to 8 mm Hg from IOPT at 15 mm Hg; the error becomes larger at high IOPT. In comparison when corneal stiffness is accounted for, IOPIST has a significantly smaller error of 1.82 ± 1.70 mm Hg for IOPT between 12 and 40 mm Hg than IOPGAT. The results showed that the new tonometry successfully accounted for inter-individual variations in IOP measurement.

1. Introduction

Intraocular pressure (IOP) monitoring is important in the diagnosis and management of glaucoma. New trans-scleral method [1] has been developed to increase measurement convenience, but methods to improve measurement accuracy of IOP measurement have not been successfully developed [2]. The current gold standard of tonometry, the Goldmann Applanation Tonometry (GAT), is known to be affected by individual variations of the central corneal thickness, the corneal radius of curvature and the corneal elastic modulus [2–10]. While healthy eyes normally have an IOP lower than 21 mm Hg, up to 15 mm Hg in measurement error had been attributed to individual variations in the corneal biomechanical properties [3]. Amongst the property variations, study showed that the corneal tangent modulus of an individual varies with the individual's IOP (Fig. 1) [11]. This suggests that IOP measurements not only vary with individuals, but also vary with the individual's IOP at the time of the measurement. Since the corneal stiffness increases with IOP, the measurement error for glaucoma sufferers with high IOP would be higher than the measurement error at low IOP, even for the same individual.

The measurement error from ignoring individual corneal property contribution can be understood by examining the theoretical basis of conventional tonometric methods. The GAT method is derived from the modified Imbert–Fick Law, which is a force balance between the measured applied force F, surface tension force of the tear film s, pressure force $A \cdot IOP$ and corneal resistance force b [12],

$$F + s = A \cdot IOP + b \tag{1}$$

where A is the applanation contact area between the GAT probe and the cornea. GAT empirically requires the operator to applanate the cornea to an area $A_{GAT} = 7.35\ \text{mm}^2$ such that the surface tension

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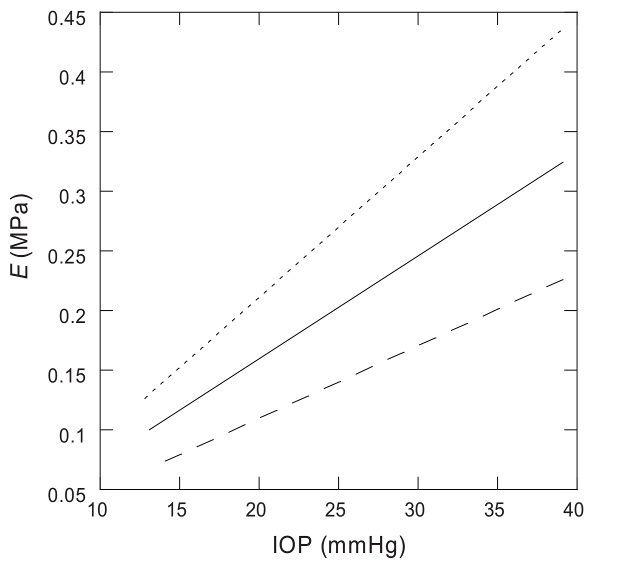

Fig. 1. Dependence of corneal tangent modulus E on IOP. Different lines represent different eyes.

force s is counter-balanced by the corneal resistance b. In this condition, the IOP can be computed via,

$$IOP_{GAT} = \frac{F_{GAT}}{A_{GAT}} \tag{2}$$

where F_{GAT} is the indentation force measured by GAT. The method is accurate for a patient with a cornea resistance b equal to s. Error arises when b and s are not equal. From Young [13], the corneal resistant force b is related to the corneal radius of curvature r, the corneal thickness t, and the corneal tangent modulus E (see Eq. (7)). The relation shows that doubling of E would double b. Individual and IOP induced variations of E would result in deviation of b away from b assumed in GAT, and lead to large measurement error in GAT [3]. To account for variations in inter-individual corneal properties, a new individual-specific tonometry (IST) is developed (US Provisional Patent Application (US 61/675,361)). The validity of the method was tested on porcine eyes ex vivo. The IOP_{IST}'s measured using IST were compared with true IOP_T from the manometer to determine whether the new method can account for the corneal properties' influence.

2. Methods

2.1. Methodology of individual-specific tonometry[1]

In GAT, the eye is applanated to a constant $A_{GAT} = 7.35\ \text{mm}^2$. The surface tension force s which depends on the size of the contact area is fixed when the applanation area is fixed. Since GAT assumes that $b = s$, the corneal resistance b is also fixed. In actual eyes, E of the cornea changes from individual to individual and is dependent on the pressure in the eye at the time of the measurement. During applanation, b may become equal to s at an arbitrary A^*, which often is not A_{GAT}. The area A^* at which the individual's corneal resistance force counter-balances the surface tension force, can be computed from the corneal load–displacement curve.

[1] A table of variable definitions is provided in supplementary materials to enhance readability.

In individual-specific tonometry (IST), the corneal resistance that exactly counter-balances the surface tension force at a specific applanation area A^* is b^*, such that,

$$b^* = s^* \tag{3}$$

where s^* is the specific surface tension force at A^*. Accordingly, Eq. (1) becomes,

$$IOP_{IST} = \frac{F^*}{A^*} \tag{4}$$

where F^* is the applied force at A^* and IOP_{IST} is the individual-specific intraocular pressure. The starred quantities (F^*; A^*; b^*) are uniquely related to each other. They cannot be determined from a single load tonometry tests such as GAT. Instead, they are determined from the indentation load–displacement curve (Fig. 3).

In instrumented corneal indentation, the indenter contact with the cornea is initially a point. With indentation, the contact becomes a partial contact and then full contact where the entire flat tip is in contact with the cornea even with increasing δ. The change in contact force as a function of indent depth δ can be obtained by differentiating Eq. (1),

$$\frac{dF}{d\delta} + \frac{ds}{d\delta} = \frac{d}{d\delta}(A \cdot IOP) + \frac{db}{d\delta} \tag{5}$$

In the full contact regime where the contact area no longer changes as a function of δ, the surface tension force s and $A \cdot IOP$ are independent of δ. In the full contact regime, Eq. (5) can then be simplified to,

$$\left.\frac{dF}{d\delta}\right|_{\text{fc}} = \left.\frac{db}{d\delta}\right|_{\text{fc}} \tag{6}$$

where the term on the left is the slope of the load–displacement curve in the full contact regime (see Appendix in supplementary materials for details).

From Young [13], the corneal resistant force b is,

$$b = \frac{E \cdot t^2}{a(r - t/2)\sqrt{1 - \nu^2}}\delta \tag{7}$$

where E is the corneal tangent modulus, r is the corneal radius of curvature, t is the corneal thickness, ν (≈0.5 [14]) is the Poisson's ratio of the cornea and a is the corneal geometric coefficient. The corneal geometric constant a is determined from μ,

$$\mu = \frac{D}{2}\left[\frac{12(1 - \nu^2)}{(r - t/2)^2 t^2}\right]^{1/4} \tag{8}$$

where D is the diameter of the contact area between the indenter and the cornea. The relation between a and μ is given in Table 1 [13].

Differentiating Eq. (7) with respect to the corneal indentation depth δ at full contact gives,

$$\frac{db}{d\delta} = \frac{E \cdot t^2}{a(r - t/2)\sqrt{1 - \nu^2}} \tag{9}$$

The change in corneal resistant force at full contact can be related to the change of the corneal resistant force at an arbitrary δ via,

$$\left.\frac{db}{d\delta}\right|_{fc} a_{fc} = \left.\frac{db}{d\delta}\right|_{\delta} a_{\delta} \tag{10}$$

Mathematically, the corneal resistance force b^* can be determined from the slope via,

$$b^* = \left.\frac{db}{d\delta}\right|_{\delta^*} \delta^* \tag{11}$$