Intraocular Pressure: Goldmann Tonometry, Computational Model, and Calibration Equation

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Purpose: There exists a concern about the general accuracy of intraocular pressure (IOP) measurements using tonometry, and especially Goldmann applanation tonometer (GAT) because it considers the cornea as an infinite thin shell. In this study, the relationship between the true IOP and tonometric IOP, external curvature radius (ECR), and central corneal thickness (CCT) is explored.

Methods: In this study, the calibration of the IOP measurements through GAT for different values of CCT, ECR, and E (Young modulus), is done through computational simulations of the mechanical behavior of the cornea subjected to the applanation process using the finite element method (FEM). Previous to this simulations, experimentations on rabbits were performed to confirm that inaccurate readings are obtained with GAT in certain conditions. This methodology is also followed to establish the range of corneal parameters of patients for which the GAT measure of pressure is reliable. The calibration equation for GAT measurements is developed from a statistical multiple linear regression analysis.

Results: Based on a statistical variable analysis of the computational modeling results, a calibration equation is established for the GAT that relates the true IOP with the ECR, CCT, and GAT measurements.

Conclusions: Our results show that GAT measures are linearly dependent on the modulus of elasticity of the cornea; nevertheless, if we consider a healthy cornea with a specific modulus of elasticity, it is possible to correct the measure with a linear equation involving CCT and ECR.

Key Words: tonometry, intraocular pressure, Goldmann tonometer, finite element method, Imbert law, GAT

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The most commonly used tonometer to measure the intraocular pressure (IOP) is the Goldmann applanation tonometer (GAT). This device has the disadvantage of being calibrated for adult healthy eyes,[1] which is why it is not recommended for application in children[2] or for pathological corneas. Today, new devices are being developed for IOP measurement without directly considering the influence of several corneal parameters like external curvature radius (ECR), central corneal thickness (CCT), and E (Young modulus). Besides, these new devices are being validated by comparison to GAT, which is not calibrated itself for variations in corneal parameters. According to this, it is established as the main objective of this study to propose a calibration equation for the measurements obtained using the GAT, and to determine the range of parameters to obtain a true IOP (TIOP) measure. These objectives will be accomplished using computational tools by means of the finite element simulation of the mechanical behavior of the cornea, and statistical tools through multivariate analysis.

For this study, it is emphasized that the GAT is not calibrated for different corneal parameters like CCT, ECR, or corneal rigidity, a fact demonstrated through animal experiments and numerical analysis finite element method.[3–6] Therefore, the validity of IOP measurements registered through GAT is restricted to specific geometric features as the ECR and CCT.[7,8] In addition, IOP measurements are highly dependent on different values of corneal rigidity such as those reported in the literature by analytical methods,[9] or determined through experimentation.[10–14] Therefore, it is required to establish a range of values of the parameters involved in the IOP measurement (geometrical, material, and functional) and different conditions for which the GAT measurement is accurate.

The calibration dimensions are defined as the geometrical characteristics of the human cornea and applanation zone for which the GAT measurements and the TIOP are supposed to be equal. These calibration dimensions are: ECR, 7.80 mm; CCT, 0.520 mm; and applanation area, 7.35 mm^2.[15] The elasticity modulus (E) was not considered for the development of the applanation tonometry theory because it was considered that the cornea behaved as an infinite thin elastic shell following Imbert law.

This investigation presents a technical way—a multiple linear regression (MLR) equation—to estimate the IOP knowing in advance the CCT, ECR, and the IOP lecture from GAT. For this equation, it is supposed that the corneal rigidity is standard but permits to correct GAT measures with less uncertainty than using the current nomograms.

MATERIALS AND METHODS

In this study, a method that can be suitable for a better understanding of tonometry readings on clinical practice is described, and an equation to obtain the TIOP as a function of the GAT measurement and the geometrical parameters of the cornea is proposed.

The study includes 3 phases: experimentation, computational modeling and simulation, and statistical analysis. The experimentation phase involves the IOP determination

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on animals (adult leporids) to verify whether the TIOP measurements correspond to those measured with Goldmann tonometry. The computational phase involves the development of a computational model that was prepared to simulate the cornea subjected to the tonometer applanation. The finite element method software selected was COMSOL.[16] Through the postprocess of the computational analysis, the stress variations that occur in the cornea before and during tonometric measurement are determined. The finite element model is built and validated for human eyes (according to Imbert law and calibration geometry). In addition, the final geometrical dimensions of the cornea after loading, and the force on the tonometer tip and the TIOP are calculated. Finally, the results are analyzed using statistical tools.[17]

Experimentation

As mentioned before, direct measurements of IOP in adult rabbits were carried out to verify whether the TIOP measurements correspond to those obtained by means of Goldmann tonometry. The IOP measurements in rabbits were determined through 2 manometric devices: a pressure transducer and a column of water. These measurements were carried out in adult rabbits 2 years old in average. This species was selected because leporids are easily found and they have a fast healing of the anterior chamber after cannulation.

The devices for the direct measurement of the IOP were designed and calibrated through comparison with a water column (demineralized H_2O) for different heights: 10, 30, and 50 cm of H_2O.

Computational Model

A 2-dimensional axisymmetric spherical geometrical model is assumed and adopted for the human cornea (half nasal-temporal cut). The material model is linearly elastic and isotropic.[12] It is prescribed as boundary condition, a restriction of first order (roller) on the corneo-scleral limbus with an inclination of 23 degrees from a horizontal line.[10] The physiological load corresponding to the IOP is applied normal to the posterior face of the cornea. The adopted mesh consisted of 5 layers through the corneal thickness maintaining an aspect ratio >0.65 for the formation of the quadrilaterals. The quasistatic model, including the cornea and the applanation cone, simulates the tonometry process through a controlled displacement (5 μm steps) for the approximation of the tonometer onto the cornea until the desired area of applanation is achieved.[18]

The computational simulations were performed for different values of corneal mechanical, functional, and geometrical parameters: E, IOP, ECR, and CCT. These parameters range within the following values:

(a) E: 0.29,[9] 1.00, 10.0, 20.4 MPa.[12]
(b) CCT: 500 to 600 μm.
(c) ECR: 6.4 to 8.0 mm.
(d) IOP: 10 to 20 mm Hg.[2] It also includes 5 mm Hg (low IOP), 30 mm Hg (high IOP).

The criterion used for the selection of each of the parameter ranges and values is described below.

Variations of CCT

The range of variation of CCT within normal range in humans is between 537 and 567 μm.[19] Liu and Roberts,[20] in their analytical study of the tonometry, considered a range of 300 to 900 μm, which includes atypical values (but possible) of the human corneal dimensions. The range established for the Colombian population is 500 to 600 μm.

Variation of ECR

Liu and Roberts[20] in their analytical study of the tonometry considered a range for the radius of curvature between 3.00 and 11.00 mm, which includes atypical values of the human corneal dimensions. In this study, a variation range of 6.40 to 8.00 mm is considered according to data collected for a Colombian population sample of 506 patients, performed by the Barraquer Institute of America in Bogota, Colombia.

Variation of IOP and Mechanical Properties of the Cornea

In order to assess the impact of functional and material parameters in the tonometry process, several computational models of the cornea including the tonometer cone were prepared. Each model includes different ranges of IOP and E for the corneal tissue, while holding constant values for ECR = 7.8 mm, CCT = 0.520 mm, and support conditions as indicated above. These ECR and CCT values correspond to the calibration geometry of human corneas for the Goldmann tonometry.[21] The influence of these parameters on the tonometry process has been also addressed in previous works[20,22,23] concluding the relevance of mechanical properties of the cornea in the tonometry process.

As it is not yet established, a consensus on an appropriate range of values for the corneal tissue elasticity modulus, it is considered as a wide range to take into account its influence on the tonometry applanation. The range of IOP in humans as established above is defined according to the Goldmann tonometer readings reported in the literature[2] and also according to the data collected for a Colombian population sample performed in the Barraquer Institute of America in Bogota, Colombia.

Constraints for the Cornea Model and Tonometer Model

The corneo-scleral limbus is established as the region for the boundary conditions as presented by ElSheikh et al.[24] The displacement constraint at this region is set according to a plane inclined at 23 degrees from the horizontal line that is defined by the corneo-scleral limbus ring in the axisymmetric model. Translational and rotational displacements in the plane of 23 degrees (roller) are allowed but not those perpendicular to it. In this way, it is possible to get the same behavior for the restricted cornea as that when considering the entire eye globe.

In the apical axis, a condition of symmetry given by an axisymmetric model is considered. The 2-dimensional modeling results from the analysis take into account a rotation of the plane around the symmetry axis, thus the simulations are effectively 3-dimensional. The load conditions given by the IOP are a natural boundary condition, and it is applied perpendicular to the posterior surface of the cornea.

The model includes the flattening effect of the tonometer tip over the cornea, which is induced in a controlled alignment of the tonometer over the cornea. Displacement of the tonometer tip or cone was increased to reach the desired area of applanation according to the procedure described by Goldmann (fulfilment of Imbert law). The displacement increments are made by means of a

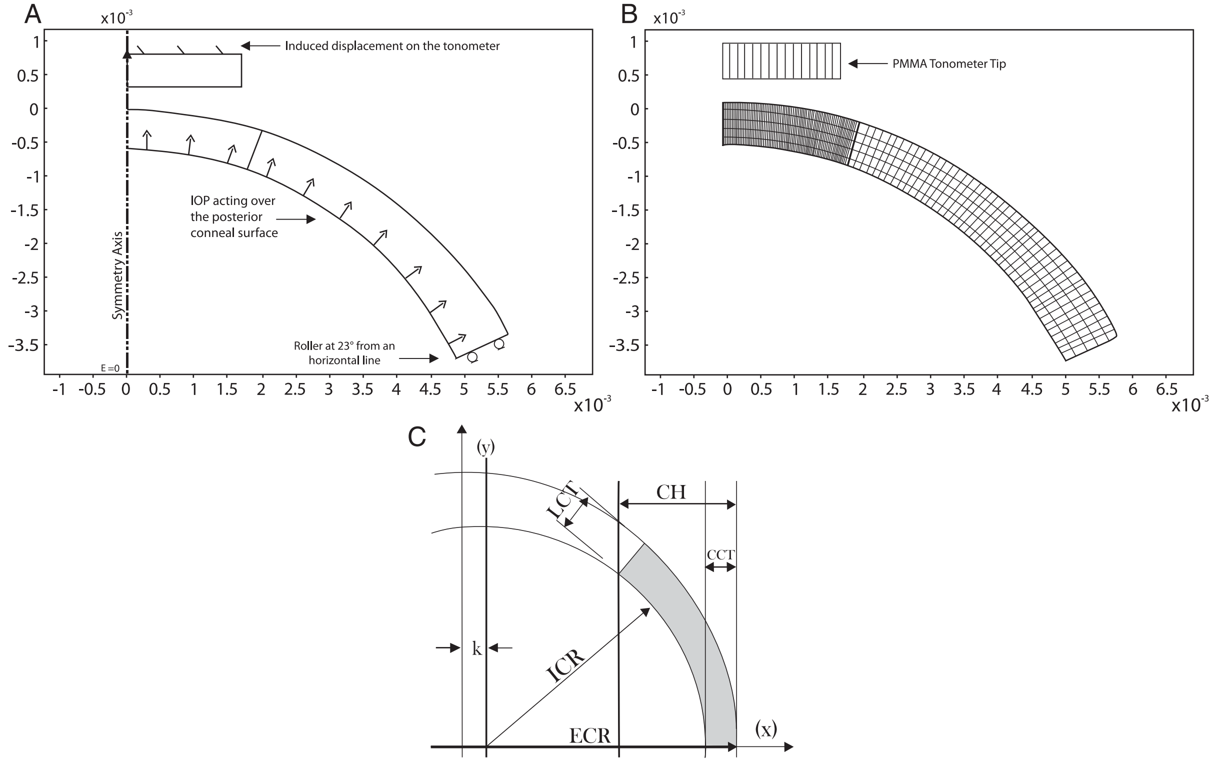

FIGURE 1. Definition of an analytical model. A, Constraints for the 2-dimensional computational model (units, m). B, Mesh for the computational model of the tonometric process (units, m). C, Geometrical parameters for the computational model of the cornea (not to scale). CCT indicates central corneal thickness; CH, corneal height; ECR, external curvature radius; ICR, interior corneal radius; IOP, intraocular pressure; LCT, limbal corneal thickness; PMMA, Poly(methyl methacrylate) or acrylic glass.

contact parameter defined in COMSOL software. The displacement increments of the cone to describe the behavior and applanation levels of the cornea were selected to be every 5 μm (Fig. 1).

Meshing

The implemented mesh used quadrilateral elements (structured) to get a better visualization of the stress distribution and deformation of the flattening the cornea.

The mesh refinement is performed to understand the discontinuities that may arise in determining the stresses in the areas of study. The refinement was complemented by a mesh convergence analysis. These 2 analyses were performed to determine the optimal mesh for the computational simulation of the applanation of the cornea.

The mesh consisted of 5 layers through the corneal thickness maintaining an aspect ratio >0.65 for the formation of the quadrilaterals elements (Fig. 1). Each model consisted an average of 15 quadrilaterals elements for the rigid tonometer tip, 250 elements for the area of study on the cornea, and 220 for the cornea not in contact with the tonometer tip.

Geometry Construction

It should be noted that for the construction of the corneal geometrical model, it is necessary to know some information that it is not collected on a regular basis by the ophthalmologist in the clinical practice. Geometry information such as interior corneal radius (ICR), limbal corneal thickness (LCT), and corneal height (CH) (Fig. 1) should be obtained through 4 equations developed from analytical relationships for the Gullstrand schematic eye geometries (Equations 2.1 to 2.4).

$$\mathrm{LCT} = \frac{0.75}{0.52}\mathrm{CCT} = 1.44\mathrm{CCT} \tag{2.1}$$

$$\mathrm{CH} = \frac{3.8}{6.66}\mathrm{ECR} = 0.57\mathrm{ECR} \tag{2.2}$$

$$k = \frac{\mathrm{CCT}^2 - \mathrm{LCT}^2 + 2\mathrm{ECR}(\mathrm{LCT} - \mathrm{CCT})}{2(\mathrm{CH} - \mathrm{CCT})} \tag{2.3}$$

$$\mathrm{ICR} = \mathrm{ECR} - \mathrm{CCT} - k \tag{2.4}$$

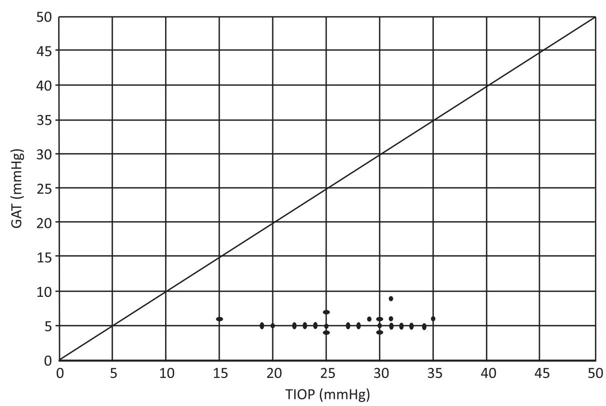

FIGURE 2. Goldmann applanation tonometer (GAT) measures compared with true intraocular pressure (TIOP) in rabbits (mm Hg). Continuous line: expected behavior.

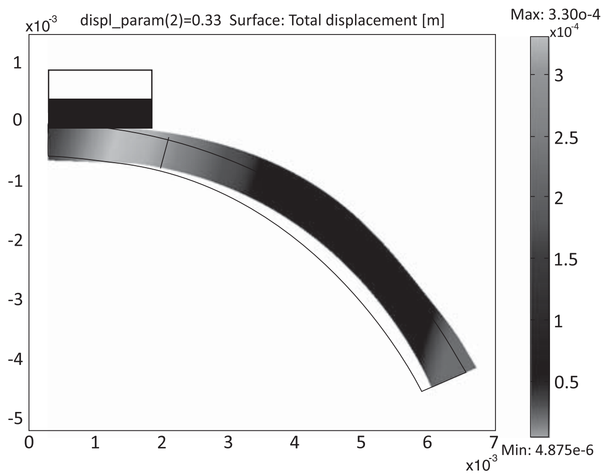

FIGURE 3. Corneal displacement due to tonometer applanation. Displacement parameter of the tonometer tip: 330 μm.

where k is the distance along the x axis determining the ICR origin (distance between centers of interior and exterior radii).

Sensibility Analysis

In order to study the effect of the geometry and the mechanical properties (ie, E) of the cornea on the tonometric IOP, the variables used in the computational model were reduced to 4: ECR, CCT, E, and TIOP, whereas the tonometric pressure (IOP_m) is given by the computational simulations and corresponds to the pressure in the tonometer cone after applanation.

First, the geometric variables were set as constant values, whereas the mechanical parameters for each model of the cornea were changed to detect their influence upon constant geometry values. From this, we selected a linear model for the general corneal behavior for compressive and tensile loads with a constant stiffness (E) for the following models.

Then, in determining the influence of the geometrical parameters of the cornea, these parameters will be varied and then their influence will be determined within the same tonometry process.

RESULTS

According to the experimentation in rabbits, a linear regression curve (r^2 = 0.99) was found for the relationship between the electronic pressure sensor and the water column, indicating that the electronic sensor works according to manometric laws. The results obtained from direct measurements of IOP show higher average values compared with GAT of around 5.6 times, indicating the need for the calibration of the tonometer for certain geometrical parameters of the cornea (Fig. 2).

Based on the computational simulations, it was possible to describe the rheological behavior of the cornea upon applanation. In addition, it was possible to determine the tonometry parameter given by the displacement necessary to applanate the cornea to the area required for the measure and contact pressure readings (Fig. 3).

The equation for the TIOP is established using an MLR based on a statistical study, a sensitivity analysis, and a correlation of variables (Fig. 4); the computational simulations provided the required data. The MLR includes variables such

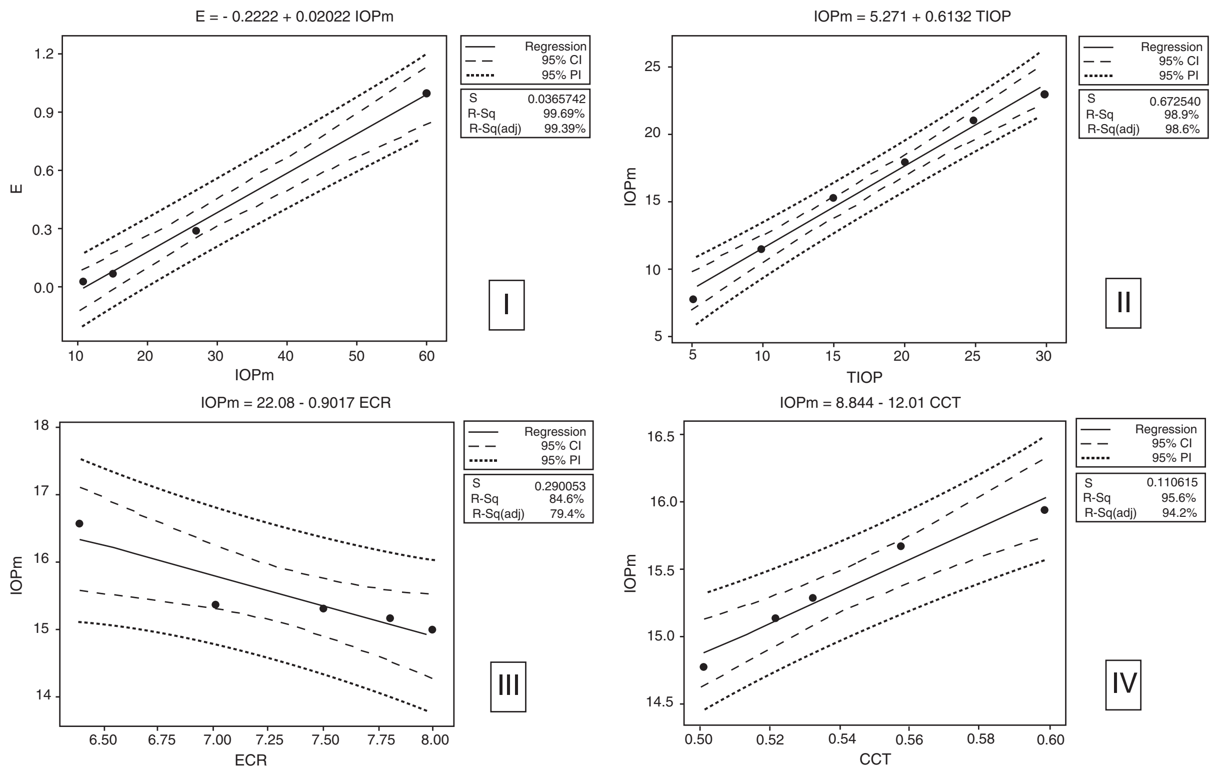

FIGURE 4. Regression curves and confidence intervals for parameters involved in IOP measurement: I, E versus IOP_m; II, IOP_m versus TIOP; III, IOP_m versus ECR; IV, IOP_m versus CCT. CCT indicates central corneal thickness; E, Young modulus; ECR, external curvature radius; IOP, intraocular pressure; TIOP, true intraocular pressure.

TABLE 1. Statistical Analysis for the MLR Equation Parameters

Term	Estimate	Standard Error	*t* Ratio	$P > \|t\|$
Parameter Estimates				
ECR	0.9310956	0.199658	4.66	0.0004
CCT	− 30.42312	2.573122	− 11.82	< 0.0001
IOP_m	1.5940297	0.068584	23.24	< 0.0001

CCT indicates central corneal thickness; ECR, external curvature radius; MLR, multiple linear regression.

as the IOP determined by means of the GAT (IOP_m), the ECR, and the CCT, for a constant elasticity modulus of 0.07 MPa. The elasticity modulus, E, is considered as the value that satisfies the Imbert law for Goldmann calibration geometry. The correlation of GAT readings is only made considering the normal CCT and ECR values in clinical practice, so that the equation of 3 variables proposed here offers a tool to determine the IOP with less uncertainty for the diagnosis of diseases affecting the optic nerve due to IOP.

The MLR obtained for the parameters considered is given by Equation 3.1 and Table 1. This equation is only valid for the range of values for each parameter considered for the cornea and a Young modulus of 0.07 MPa.

$$TIOP = (0.931 \times ECR) - (30.4 \times CCT) + (1.59 \times IOP_m) \quad (3.1)$$

where TIOP and IOP_m are given in mm Hg and ECR and CCT in mm.

DISCUSSION

According to the present computational modeling and statistical processing, it can be established that the measures obtained by the GAT are valid only when certain conditions are fulfilled. These conditions involve corneal geometries close to the calibration geometry (ECR: 7.60 to 7.90 mm, CCT: 0.510 to 0.550 mm), age of patients between 3 and 40 years (according to the variation of E with age[1]), and applanation diameter of 3.06 mm. All parameters listed above are required for Goldmann assumptions to be consistent with the Imbert law.

There is not a direct relationship between the values of IOP obtained by means of the applanation tonometry and the values obtained manometrically (experimentation setups). A possible explanation for this is that IOP is not only being affected by geometrical variations of the cornea but also is strongly influenced by the value of the material properties of the subject under consideration.

The influence of CCT and ECR measurements in applanation tonometry readings is confirmed through a correlation analysis of variables. Based on the results, it was possible to obtain an MLR to estimate the value of TIOP for the parameters obtained from clinical practice (IOP_m, ECR, and CCT) (Equation 3.1).

According to this study, it is only recommended to use the Goldmann tonometer as a reference point for calibration of new equipment, whereas the study cases corresponding to the ranges of validity of their use within a confidence interval of 95% should be performed. It is also recommended to be cautious with the use of applanation tonometry for the determination of IOP in children and elders, because it is a population where more variation of the corneal parameters (both geometric and mechanical) is present. It is important to emphasize the tonometer dependence on geometrical and mechanical parameters because this is the support of its validity.

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