Clinical Evaluation of Methods to Correct Intraocular Pressure Measurements by the Goldmann Applanation Tonometer, Ocular Response Analyzer and Corvis ST Tonometer for the Effects of Corneal Stiffness Parameters

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Conflict of Interest

The authors indicate no financial conflict of interest.

Abbreviated title

Effectiveness of Corneal stiffness Correction in Intraocular Pressure Measurements

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Abstract

Purpose: To evaluate the effectiveness of methods to correct intraocular pressure (IOP) measurements obtained using the Goldmann Applanation Tonometer (GAT), the Ocular Response Analyzer (ORA) and the Corvis ST Tonometer (CVS) for the effects of corneal stiffness parameters; central corneal thickness (CCT), corneal curvature (R) and age in a Chinese population.

Patients and Methods: Data were collected for 99 eyes of 99 participants. While cornea corrected IOP was obtained directly from ORA (ORA-IOPcc), cornea correction in GAT and CVS was implemented using multi-parameter equations developed earlier. The study also included IOP measurements by the Dynamic Contour Tonometer (DCT), which is thought to be less affected by corneal stiffness parameters than other tonometers. Statistical analyses were performed to determine the association of both uncorrected and corrected IOP with the main stiffness parameters; CCT, R, and age.

Results: After correction, a significantly decreased association between the GAT (from r = 0.15 to r = -0.02), ORA (from r = 0.24 to r = -0.19) and CVS (from r = 0.47 to r = 0.004) IOP measurements and the CCT was found, to levels below that with the DCT-IOP (r = 0.11). The IOP measurements made by the four tonometers, both uncorrected and corrected, did not correlate with age. The same was true for R except with ORA-IOPcc (r = 0.23).

Conclusions: CCT accounted for the majority of variance in IOP, while age and R had a much smaller effect. The IOP correction processes studied were successful in reducing reliance of IOP measurements, especially those by GAT and CVS, on CCT in a healthy Chinese population.

Keywords: corneal stiffness; correction, intraocular pressure

Introduction

Intraocular pressure (IOP) represents a fundamental factor of ocular health, and is critically important in the diagnosis and management of ocular hypertension, various forms of glaucoma and other ocular diseases. In the Early Manifest Glaucoma Trial, a reduction in IOP by 1 mmHg from baseline in glaucoma patients was reported to lead to a reduction of approximately 10% in progression risk [1]. It is therefore imperative that IOP measurement by tonometry be as accurate as possible.

The accuracy of IOP measurement, whether using contact or non-contact tonometers, is potentially affected by a number of error sources including variations in biomechanical parameters such as corneal thickness, curvature and age [2-6]. This applies to the Goldmann Applanation Tonometer (GAT), which has maintained its status as the reference standard for the measurement of IOP despite reports on its dependence on the cornea's stiffness parameters. Several studies assessed the effect of the central corneal thickness (CCT) on GAT measurement of intraocular pressure (GAT-IOP), providing a wide range of estimations between 0.7 and 7.1 mmHg for every 100 μm change in CCT [3, 7-11]. The complexity of the problem increased when subsequent studies suggested that it was the overall corneal stiffness, or resistance to deformation under tonometry loading, rather than CCT, which was responsible for errors in GAT-IOP [12]. This observation drew attention to other stiffness-related factors, besides CCT, including the cornea's curvature and material properties, which vary with both age and medical history [6, 13]. In response, a number of multi-parameter correction equations [10] were developed to mitigate errors induced by CCT, central corneal radius of curvature (R) and age on GAT-IOP, and these equations were successful to different extents in reducing the association of IOP measurements with the cornea's stiffness parameters [14-16].

As a further response to the problems reported in GAT with the stiffness-related inaccuracies, the Dynamic Contour Tonometer (DCT) was developed by SMT Swiss Microtechonology AG, Switzerland, based on the principle of contour matching, Figure 1A [17, 18]. Since its development, the DCT has been presented as a digital tonometer that was much less affected by the corneal stiffness parameters than GAT; a claim that has been validated in a number of clinical studies

[17, 19].

Similar efforts had been made with non-contact tonometers that use an air impulse and correlate corneal deformation to the value of IOP. These efforts started with the introduction of the Ocular Response Analyzer (ORA) in 2005 by Reichert Ophthalmic Instruments, Depew, NY, which produces the cornea-compensated IOP (or IOPcc) that is claimed to be less dependent on corneal thickness than applanation tonometers [20]. The device uses a fast air impulse with a gradually increasing pressure up to a level beyond what is necessary to applanate the central cornea, Figure 1B. During this stage, the concave cornea applanates at a pressure known as P_1, then takes a convex shape as the pressure increases to its highest level, P_{max}. The pressure then gradually decreases going through another applanation phase at a pressure known as P_2. The device uses pressures P_1 and P_2 to provide two estimates of IOP; IOPcc and the Goldmann-correlated IOP (IOPg) [21]. The validity of the claim of superior accuracy of IOPcc was assessed in a number of clinical studies, which found that IOPcc measurements were not associated with corneal thickness [22], but reported a significant statistical association with increasing age [23, 24], which is known to lead to corneal stiffening [25]. To the best of the authors' knowledge, no attempt had been made to assess the effect of R on ORA-IOP measurements.

More recently, a non-contact tonometer was developed by OCULUS Optikgeräte, Inc. (Wetzlar, Germany) under the name Corvis ST (Corneal Visualization Scheimpflug Technology, CVS) [26]. The particular promise of the CVS is due to the high precision of its ultra-high-speed Scheimpflug technology used to monitor the dynamic reaction of the cornea to air pressure and the wide range of tomography and deformation parameters quantified by the device, which have the potential to enable accurate estimates of corneal stiffness, Figure 1C. In recent clinical studies, the device was shown to have good repeatability [26, 27], but its IOP measurements were clearly influenced by variations in corneal stiffness parameters [26].

In order to address the effect of corneal stiffness on the IOP measurements CVS-IOP, a recent study developed a correction equation based on numerical simulation of the CVS procedure. The equation was subsequently validated using a clinical dataset involving 632 patients and shown success in significantly reducing the association of CVS-IOP with both CCT and age [28]. No significant effect of R on CVS-IOP was found, both numerically and clinically, and therefore R was excluded from the correction equation.

The current study has two major objectives. First, it presents an assessment of the association between IOP measurements made by each of the four tonometry devices; GAT, DCT, ORA and CVS, and the dominant corneal stiffness parameters, namely CCT, age and R. Since these parameters are expected to lead to changes in overall corneal stiffness, a weak association between the IOP measurements and the parameters would be evidence that the tonometer was strongly independent of corneal stiffness. The second objective is to assess the effectiveness of IOP corrections produced earlier for GAT, ORA and CVS. Although these correction methods have found success in earlier studies in reducing the dependence of IOP measurements on corneal stiffness parameters, this paper concentrates on their performance in a healthy Chinese population. Finally, the range of IOP measurements made in this study enabled consideration of the inter-correlation between the IOP readings taken by the four tonometers, both before and after correction for the effects of corneal stiffness.

METHODS

Clinical data

99 healthy subjects (46 male and 53 female) aged between 19 and 49 years (mean 29.2±7.1 years) were recruited from patients who planned to undergo corneal refractive surgery, and from medical interns of the Eye Hospital, Wenzhou Medical University, China. The exclusion criteria included a history of trauma and ocular surgery, ocular disease, Snellen best spectacle corrected distance acuity less than 20/25, intraocular pressure by GAT over 21 mmHg and cylindrical refractive error or corneal astigmatism of more than 3.00D. Patients who continued to wear contact lenses until less than two weeks before the date of the data collection were also excluded. The study followed the tenets of the Declaration of Helsinki and was approved by the Ethic Committee of the Eye Hospital. Signed informed consent that allowed use of the data for research was obtained from each participant.

All participants underwent the following tests in a single session and in the same order: measurement of topography, CCT and R, all with the Pentacam, and IOP using ORA (ORA-IOPg, ORA-IOPcc), CVS (CVS-IOP), GAT (GAT-IOP) and DCT (DCT-IOP). R was taken as the average of Rh and Rv, where Rh and Rv were the curvature in horizontal and vertical direction, respectively. The measurements by the four tonometers were repeated 3, 5, 3 and 3 times, respectively, allowing 3 minutes between each two subsequent readings. Further, contact measurements by GAT and DCT were taken 20 minutes after conduct of all non-contact measurements, and a drop of topical Alcaine 0.5% (Alcon, Missisauga, Canada) was applied before the measurements. This scheme was thought, based on earlier evidence, to be sufficient to avoid reductions in IOP while minimizing diurnal effects [29] All measurements were taken with participants being in the sitting position and with undilated pupils, during regular office hours (8 am to 6 pm). They were taken by the same clinician (ZXH) and using the same instruments to minimize potential for variability associated with either the instrument or the operator, and in line with procedures adopted in earlier studies [30-32].

GAT-IOP correction

An earlier study compared all multi-parameter GAT-IOP correction equations available in the literature at the time and found the equation developed by Elsheikh et al to be most successful in reducing the association between GAT-IOP and corneal stiffness parameters [14]. The equation was developed in a parametric study based on simulations of the GAT procedure in numerical models of human eyes with wide ranges of CCT, R, age and true IOP, and was assessed both experimentally (on 19 human donor corneas) and clinically [10, 33]. This equation, which is further assessed as part of this study, provided a corrected value of GAT-IOP in the form:

$$\text{GAT-IOP}_c = \frac{\text{GAT-IOP}}{A_{CCT} \times A_R \times A_{Age} \times A_{GAT\text{-}IOP}} \quad (1)$$

where

A_{CCT} = effect of variation in CCT (mm) = $0.68 \times (CCT - 0.520)^2 + 1.12 \times (CCT - 0.520) + 1.0$

A_R = effect of variation in R (mm) = $1 - 0.06 \times (R - 7.8)$

A_{Age} = effect of variation in age (years) = $0.3\times10^{-6}\times Age^3 - 88\times10^{-6}\times Age^2 + 0.0085\times Age + 0.815$

$A_{GAT-IOP}$ = effect of variation in measured GAT-IOP (mmHg) = $1.427\times(GAT-IOP+3.373)^{-0.119}$. Earlier assessment of the equation found CCT and GAT-IOP to have the largest effects on the correction results, while age and R had the lowest effects [10].

CVS-IOP correction

Similar to the GAT equation, a correction equation was developed in an earlier study to reduce the effect of variations in corneal stiffness parameters on CVS-IOP [28]. The study was based on numerical simulations of the air impulse experienced in CVS and the resulting correction equation was assessed clinically. R and, to a smaller extent, age were found to have a considerably lower effect on the correction result than CCT and CVS-IOP, leading to the exclusion of R from the correction equation:

$$CVS-IOP_c = (C_{CCT1}\times C_{CVS-IOP} + C_{CCT2})\times C_{Age} + C \qquad (2)$$

Where $CVS\text{-}IOP_c$ = corrected value of CVS IOP, C_{CCT1}, C_{CCT2} = parameters representing the effect of variation in CCT (mm):

$$C_{CCT1} = 4.67\times10^{-7}\times CCT^2 - 7.8\times10^{-4}\times CCT + 0.63$$

$$C_{CCT2} = -1.73\times10^{-5}\times CCT^2 + 2.02\times10^{-3}\times CCT - 0.97$$

$C_{CVS-IOP}$ = effect of variation in measured CVS-IOP (mmHg) $= 10 + (CVS-IOP+1.1611)/0.38911$

C_{Age} = effect of variation in age (years) = $-2.01\times10^{-5}\times Age^2 + 1.3\times10^{-3}\times Age + 1.00$

C=1.5mmHg

Statistical analysis

Comparisons of IOP values from different tonometers were performed using MANOVA of repeated measuring. The correlations of IOP with CCT and age were assessed by the Pearson's or Spearman linear correlation factor according to the normal distribution test. Only the data from the right eye were taken and included for analysis. Commercial software SPSS 20.0 (Chicago, USA) was utilized in all statistical analyses and a two-tailed probability of P < 0.05 was considered statistically significant.

RESULTS

Patient Demographics

The mean central corneal radius was 7.78±0.27 mm (7.24-8.98 mm) and mean CCT 533.6±30.4 µm (440.7-603.7µm). IOP was successfully measured using the GAT, ORA, CVS and DCT in all eyes. Table 1 shows the mean and range of measured and corrected IOP values obtained using the four tonometers.

Agreement between IOP measurements of the four tonometers

There was a lack of agreement between the four tonometers; DCT-IOP was higher (F(2.61, 140.86)= 38.36, p=0.00) than GAT-IOP, ORA-IOPg and CVS-IOP in 91%, 87% and 91% of the cases, respectively (Figure 2). On average, DCT-IOP was approximately 3.5±2.2, 2.5±2.5 and 3.5±2.3 mmHg higher than GAT-IOP, ORA-IOPg and CVS-IOP, respectively, or in terms of trend, DCT-IOP was 20.5±12.9%, 14.7±14.7% and 20.1±13.7% higher than the other three tonometers. After correction of IOP measurements by GAT, ORA and CVS, DCT was still higher on average by 3.8±2.5, 2.4±2.5 and 3.6±1.9 mmHg, respectively, or by 22.5±14.4%, 13.5±14.5% and 20.2±0.10%.

On the other hand, compared with GAT, the reference standard in tonometry, ORA-IOPg and CVS-IOP, were respectively higher on average by 1.0±3.2 mmHg and lower by 0.1±2.7 mmHg. Figure 3A depicts a comparison between GAT-IOP and ORA-IOPg results. The small average difference between the measurements is compatible with the fact that ORA-IOPg is intended to estimate GAT-IOP, and that the correlation between the two measurements is statistically significant (r = 0.51). Another comparison between CVS-IOP and GAT-IOP (Figure 3B) reveals an interesting trend in which CVS-IOP appears to underestimate GAT-IOP for GAT-IOP above 13 mmHg, and overestimate GAT-IOP below this level. A similar trend has been observed between CVS-IOP and ORA-IOPg but with a turning point at ORA-IOPg = 12 mmHg (Figure

3C). Introducing IOP corrections caused only minor changes in these trends with ORA-IOPcc and CVS-IOPc becoming respectively higher than GAT-IOPc by 1.4±3.6 mmHg and 0.3±2.9 mmHg on average.

Correlation of IOP measurement with corneal stiffness parameters

Results of the main correlation studies are presented in Table 2. While uncorrected non-contact measurements ORA-IOPg and CVS-IOP positively correlated with CCT, the contact measurements GAT-IOP and DCT-IOP showed no correlation, Figure 4. However, following correction for corneal parameters, the correlation became insignificant between ORA-IOPcc and CCT, and between CVS-IOPc and CCT. Further, the correlation between GAT-IOPc and CCT significantly reduced with correction. On the other hand, The IOP measurements made by the four tonometers, both uncorrected and corrected, did not correlate with age, possibly due to the narrow age range of the participants, Figure 5. Further, all uncorrected and corrected IOP measurements by the four tonometers, except ORA-IOPcc, did not correlate with R, Figure 6.

DISCUSSION

Glaucoma is a progressive irreversible optic neuropathy that affects 2.4% of those aged over 49 [34], rising to 4% in white, and 13% in some black, subjects by the age of 80 [35]. Worldwide, glaucoma is responsible for more blindness than any other eye condition except cataract, but unlike cataract, the blindness is irreversible. With IOP being the main modifiable risk factor for glaucoma, an accurate assessment of IOP is of great importance for diagnosis and decision making regarding treatment modalities in patients with glaucoma [36]. Clinical evidence has shown reduction of IOP as being critical for glaucoma management, and that delays in detection and management of elevated IOP may cause visual impairment.

Errors in IOP measurement could be caused by a number of technical and clinical factors. In addition to possible reading errors, calibration issues, misalignment of the tonometric mires, valsalva maneuver, nervousness or forced eyelid closure, the effect of variations in corneal stiffness could be significant. The effects of these factors in reducing the accuracy of IOP measurement could be one of the reasons behind the rates of glaucoma-related blindness, whilst under care, being unacceptably high; at 6%, 9% and 15% at 5, 10 and 15 years, respectively [37]. With this management outcome and the subsequent increasing burden of the disease, there is a need to improve the accuracy of IOP measurement.

Most tonometry techniques, whether contact or non-contact, are based on monitoring corneal response to an applied mechanical force, and hence are all affected, to different extents, by corneal resistance to deformation (or mechanical stiffness) [38]. Clinical studies to quantify the effects of corneal stiffness (which varies with corneal thickness, curvature, age and medical history) started more than 50 years ago, and concentrated on the thickness for being the most prominent stiffness parameter [39]. Using both clinical data and mathematical modelling, the studies estimated errors in GAT-IOP within the wide range of 0.7-7.1 mmHg for a change in CCT of 100 microns[3, 7-11]. Similar work has shown a similar effect of CCT on IOP readings by ORA and CVS, with IOP being underestimated in thin corneas and overestimated in thick corneas [32, 40, 41]. In the present study, only ORA-IOPg and CVS-IOP measurements were significantly influenced by CCT (p=0.03 for ORA-IOPg and p=0.00 for CVS-IOP) with the relationships being similar to those reported by others [32, 41]. No statistically significant relationship was found between GAT-IOP and CCT (p=0.18), although there was an overall trend of GAT-IOP increase of 1.5 mmHg for a 100 μm increase in CCT [40]. Similarly, DCT measurements were not significantly correlated with CCT (p=0.36) with an average increase in IOP by 0.8mmHg for a 100 μm increase in CCT, which is compatible with earlier studies reporting low effect of CCT on DCT-IOP measurements [31, 42].

Following a period in which attention has been limited to CCT, there is now growing appreciation that it is corneal stiffness, more than the parameters affecting it such as CCT, that should be considered when improving accuracy of IOP measurement [6, 13]. Corneal stiffness is influenced by both geometric parameters (e.g. thickness, curvature, diameter and astigmatism) and material parameters (which vary with age and medical history). However, while earlier studies have confirmed the importance of CCT, they disagreed on the significance of curvature, leading to it being considered in studies on GAT and ignored in a recent study on CVS [28]. On the other hand, the effect of corneal diameter and astigmatism, although recognized, has not been quantified yet [43]. Further, since no solution has been developed to date to directly measure the biomechanical properties of corneal tissue in vivo (mainly the tangent modulus), attention has to be given instead to the parameters that are related to the properties and can be measured such as age, topography deterioration in keratoconus and tissue changes due to refractive surgeries. Earlier studies have quantified the change in tissue stiffness associated with aging [25, 44, 45], but the effect of other parameters on stiffness has not been quantified yet.

In this study, both CCT and age (and curvature in the case of GAT) have been considered in correcting IOP measurements for the effects of variations in corneal stiffness. After correction, a significantly decreased association for the GAT-IOP (from $r = 0.15$ to $r = -0.02$), ORA-IOPg (from $r = 0.24$ to $r = -0.19$) and CVS-IOP (from $r = 0.47$ to $r = 0.004$) with the CCT was found, demonstrating the effectiveness of the stiffness-related, correction processes used, especially in CVS and to a lower extent in GAT. On the other hand, the IOP measurements made by the four tonometers, both uncorrected and corrected, did not correlate with age, possibly due to the narrow age range (19-49 years) of the study participants. Further, only ORA-IOPcc correlated with R while other IOP measurements did not show significant correlation with the corneal curvature.

The study also showed that measurements by different tonometers for the same participants differed significantly. Relative to measurements by GAT, the reference standard in tonometry, ORA-IOPg, CVS-IOP and DCT-IOP were different by 1.0±3.2, -0.1±2.7, 3.5±2.2 mmHg, respectively. The results were similar to previous studies where GAT was lower by 0.6±2.2 and higher by 0.5±2.2 mmHg than ORA-IOPg[46] and CVS-IOP [47], respectively. On the other hand, the difference between GAT and DCT appears to be higher than the values reported earlier, which varied between -1.0 to -2.8 mmHg [30, 31, 48], although a clear positive correlation between DCT and GAT was still evident in this study ($r = 0.65$; $P = 0.00$). The tendency of DCT to give higher IOP measurements compared with GAT agreed with the results of clinical studies, and an ex vivo test program showing GAT values to be consistently lower than true IOP by an average of 4.0 mmHg in human cadaver eyes, whereas the DCT values were closer to the true

IOP[19] (lower by 0.58±0.70 mmHg).

Further, while IOP measurements by the two non-contact tonometers, ORA-IOPg and CVS-IOP, were similar (mean difference 1.1±2.1 mmHg), they were lower than, and statistically different from, DCT-IOP; by 2.5±2.5 mmHg (14.7±14.7%, p=0.00) and 3.5±2.3 mmHg (20.1±13.7%, p=0.00), respectively. However, there was still a statistically significant correlation between ORA-IOPg and DCT-IOP (r=0.62, p=0.00) and between CVS-IOP and DCT-IOP (r=0.51, p=0.00). The first of these findings is consistent with results of earlier studies [46, 49], although these studies reported a lower difference between ORA-IOPg and DCT-IOP (mean values 1.8 and 2.29 mmHg) than observed herein. No earlier study considered the correlation between IOP measurements by the CVS and DCT.

In conclusion, the study provides an assessment of four commonly-used tonometers and the effectiveness of methods to reduce dependence of their IOP measurement. on corneal stiffness parameters. The results clearly demonstrated the success of corrections, especially in CVS and GAT, in reducing dependence on CCT, the main corneal stiffness parameter. The corrections, which have been assessed before in European populations, have been found in this study to be effective in a healthy Chinese population with young age (<49 years).

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Figure Legends

Fig. 1 Operation principle of the dynamic contour tonometer (DCT), Ocular Response Analyzer (ORA) and Corvis ST (CVS); A: In the DCT, a tonometer tip is pushed against corneal apex until contour matching is achieved, at which point the reading of the pressure sensor is assumed to equal the IOP; B: In ORA, external air pressure increases until the cornea applanates at pressure P_1, The air pressure continues to increase to a peak, Pmax, then decreases gradually, going through a second applanation event at air pressure, P_2. Pressures P_1 and P_2 are used to estimate IOP using an equation of the form $IOP_{cc}=K_1P_1+K_2P_2$, where K_1 and K_2 are constants; C: In CVS, external air pressure increases until the cornea applanates at pressure AP_1. This pressure is used to estimate IOP in an equation of the form $IOP_{cc}=C_1*AP_1+C_2$, where C1 and C2 are constants.

Fig. 2 Measurement comparison between DCT-IOP and readings by the other three tonometers (A) GAT, (B) ORA and (C) CVS

Fig. 3 Comparisons between GAT-IOP, ORA-IOPg and *uncorrected* CVS-IOP measurements

Fig. 4 Relationship between CCT and both uncorrected and corrected IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT

Fig. 5 Relationship between age and both uncorrected and corrected IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT

Fig. 6 Relationship between R and both uncorrected and corrected IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT

Table 1 Mean, standard deviation and range of IOP measurements by the four tonometers. Both corrected and uncorrected values are presented for GAT, ORA and CVS. The differences in IOP measurements by GAT, ORA and CVS relative to DCT are provided.

Tonometer reading	Mean ± SD (mmHg)	Range (mmHg)	Mean Difference with DCT (mmHg)
GAT-IOP	13.5±2.9	7.5-21.0	-3.5±2.2
GAT-IOP$_c$	13.1±3.1	6.8-21.6	-3.8±2.5
ORA-IOPg	14.4±3.0	8.5-23.9	-2.5±2.5
ORA-IOPcc	14.4±3.0	7.3-25.9	-2.4±2.5
CVS-IOP	13.3±2.1	7.5-18.1	-3.5±2.3
CVS-IOP$_c$	13.4±1.7	9.5-18.0	-3.6±1.9
DCT-IOP	16.8±2.5	9.6-21.6	-

IOP = intraocular pressure; GAT = Goldmann applanation tonometer; GAT-IOPc =Corrected GAT-IOP measurements; ORA-IOPg = Goldmann-correlated IOP by the Ocular Response Analyzer; ORA-IOPcc = cornea-compensated IOP by ORA; CVS = Corvis ST; CVS-IOP$_c$ = Corrected IOP by Corvis ST; DCT = Pascal Dynamic Contour tonometer

Table 2 Association of IOP measurements made by the four tonometers with the main cornea stiffness parameters; CCT, age and R

	CCT (mm)	Age (years)	R (mm)
DCT-IOP	r = 0.11, p = 0.36 0.8 mmHg/100 µm	r= -0.17, p=0.13 -0.054 mmHg/year	r=0.15, p=0.22 1.16 mmHg/mm
GAT-IOP	r = 0.15, p = 0.18 1.5 mmHg/100 µm	r= -0.18, p=0.10 -0.081 mmHg/year	r=0.12, p=0.28 1.18 mmHg/mm
GAT-IOPc	r = -0.02, p = 0.87 -0.2 mmHg/100µm	r= -0.24, p=0.06 -0.117 mmHg/year	r=0.17, p= 0.16 2.19 mmHg/mm
ORA-IOPg	r = 0.24, p= 0.03 2.4 mmHg/100 µm	r= -0.09, p=0.40 -0.031 mmHg/year	r= 0.13, p=0.24 1.55 mmHg/mm
ORA-IOPcc	r = -0.19, p = 0.09 -1.9 mmHg/100 µm	r= -0.10, p=0.35 -0.060 mmHg/year	r=0.23, p=0.04 1.92 mmHg/mm
CVS-IOP	r = 0.47, p = 0.00 3.3 mmHg/100 µm	r= -0.20, p=0.07 -0.053 mmHg/year	r=0.11, p=0.32 0.41 mmHg/mm
CVS-IOPc	r = 0.004, p = 0.97 0.02 mmHg/100 µm	, r= -0.22, p= 0.06 -0.051 mmHg/year	r= 0.06, p=0.58 0.48 mmHg/mm

Results include r, p and gradient of association between IOP measurements with CCT, age and R. GAT = Goldmann applanation tonometer; GAT-IOPc =Corrected GAT-IOP measurements; ORA-IOPg = Goldmann-correlated IOP by the Ocular Response Analyzer; ORA-IOPcc = cornea-compensated IOP by ORA; CVS = Corvis ST; CVS-IOPc = Corrected IOP by Corvis ST; DCT = Pascal Dynamic Contour tonometer

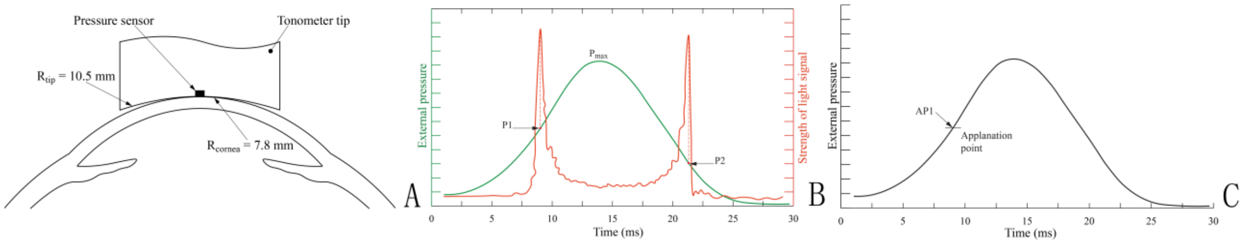

Fig. 1 Operation principle of the dynamic contour tonometer (DCT), Ocular Response Analyzer (ORA) and Corvis ST (CVS); A: tonometer tip is pushed agaist corneal apex until contour matching is achieved, at which point the reading of the pressure sensor is assumed to equal the IOP; B: external air pressure increases until the cornea applanatation at the pressure P_1, The air pressure continues to increase to a peak, Pmax, then decreases gradually, going through a second applanation event at air pressure, P_2. Pressures P_1 and P_2 are used to estimate IOP an equation of the form $IOP_{cc}=K_1P_1+K_2P_2$, where K_1 and K_2 are constants; C: external air pressure increases until cornea applanatation at pressure AP_1. This pressure is used to estimate IOP in an equation of the form $IOP_{cc}=C_1*AP_1+C_2$, where C1 and C2 are constants.

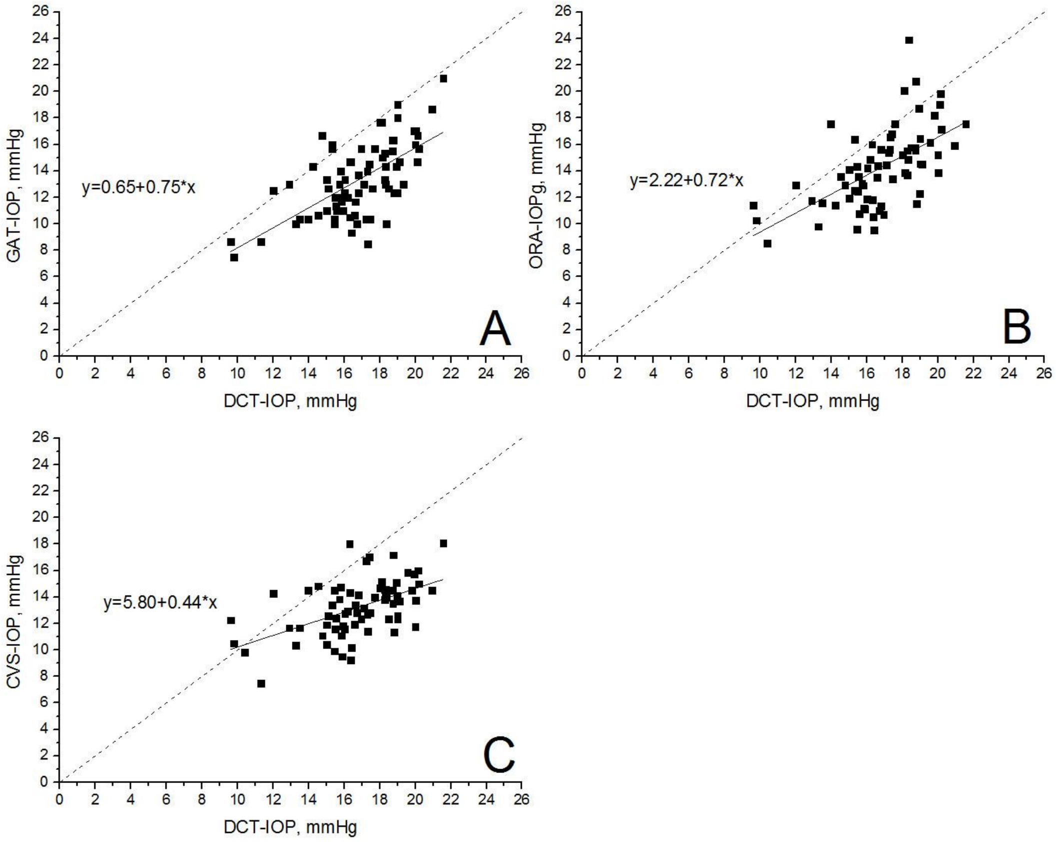

Fig.2 Measurement comparison between DCT-IOP and readings by the other three tonometers (A) GAT, (B) ORA and (C) CVS

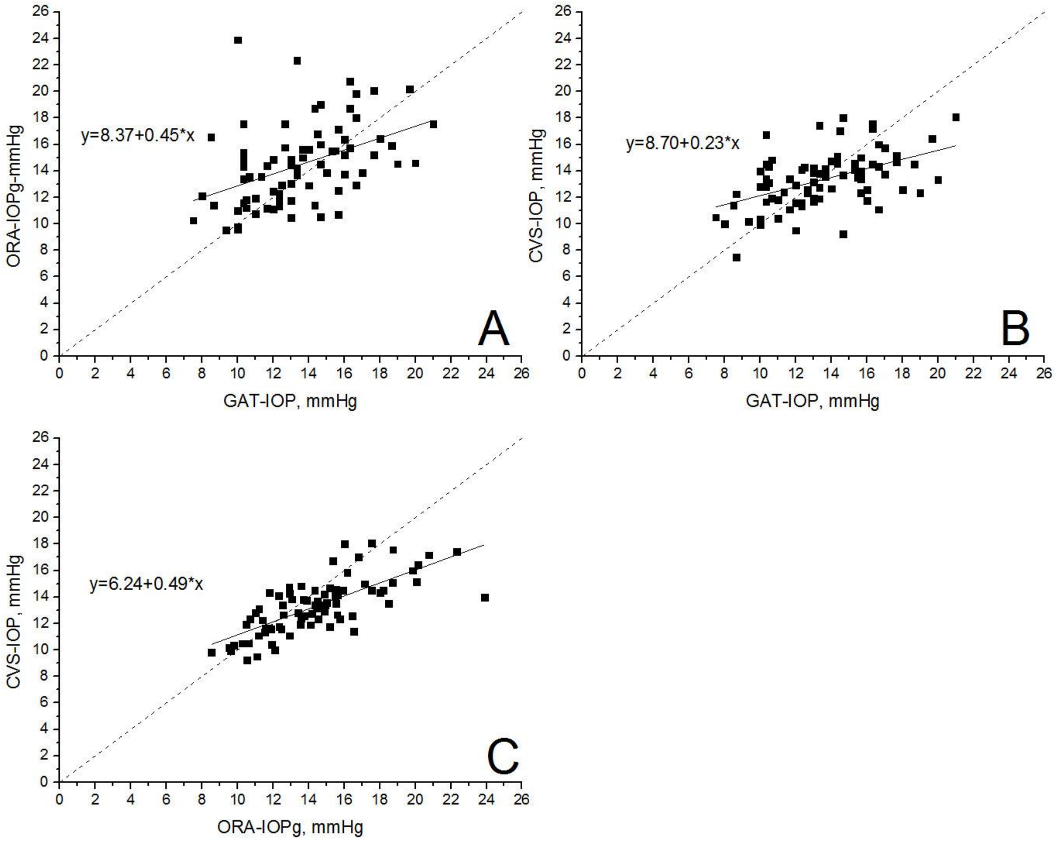

Fig.3 Comparisons between GAT-IOP, ORA-IOPg and *uncorrected* CVS-IOP measurements

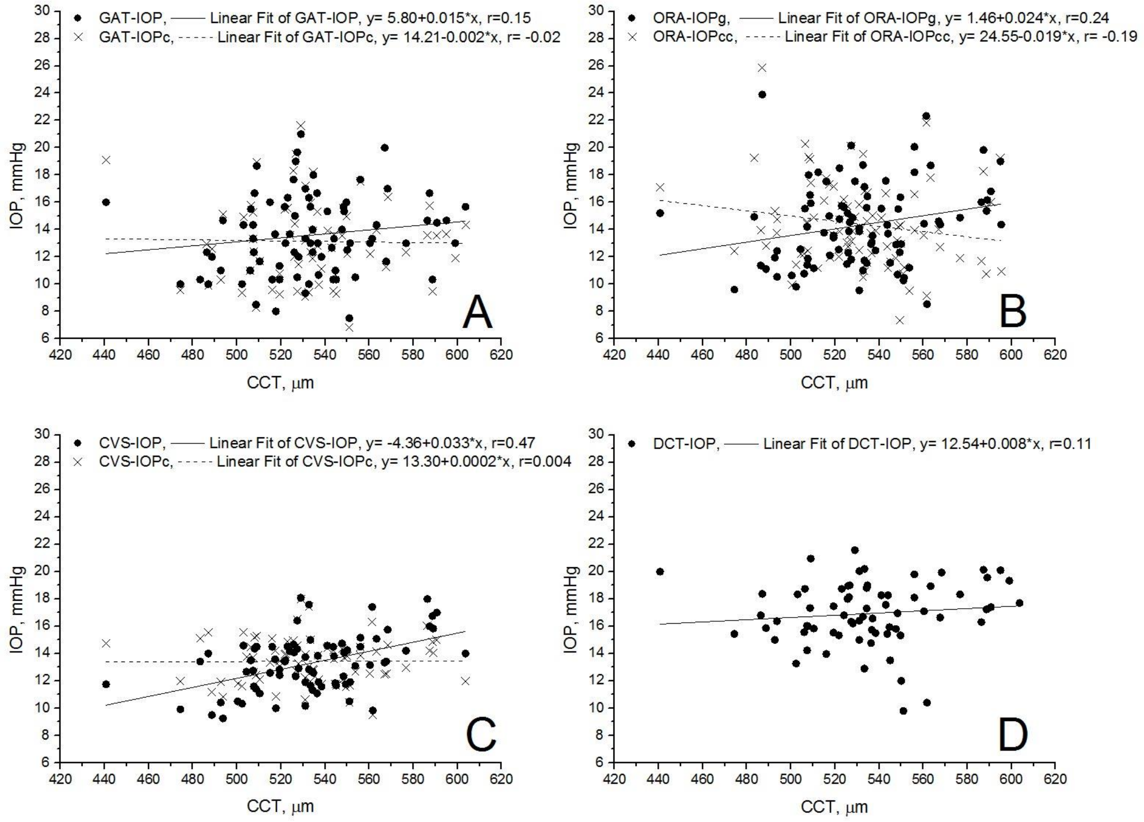

Fig.4 Relationship between CCT and both *uncorrected* and *corrected* IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT

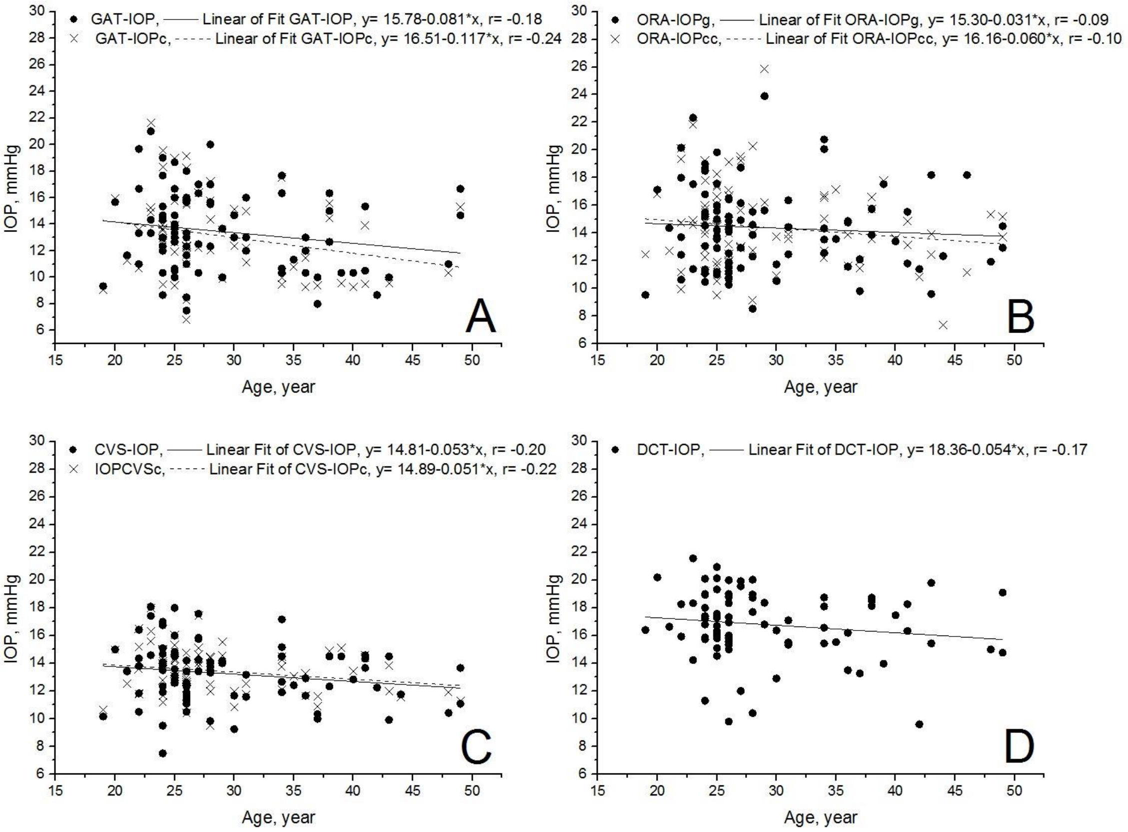

Fig.5 Relationship between age and both *uncorrected* and *corrected* IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT

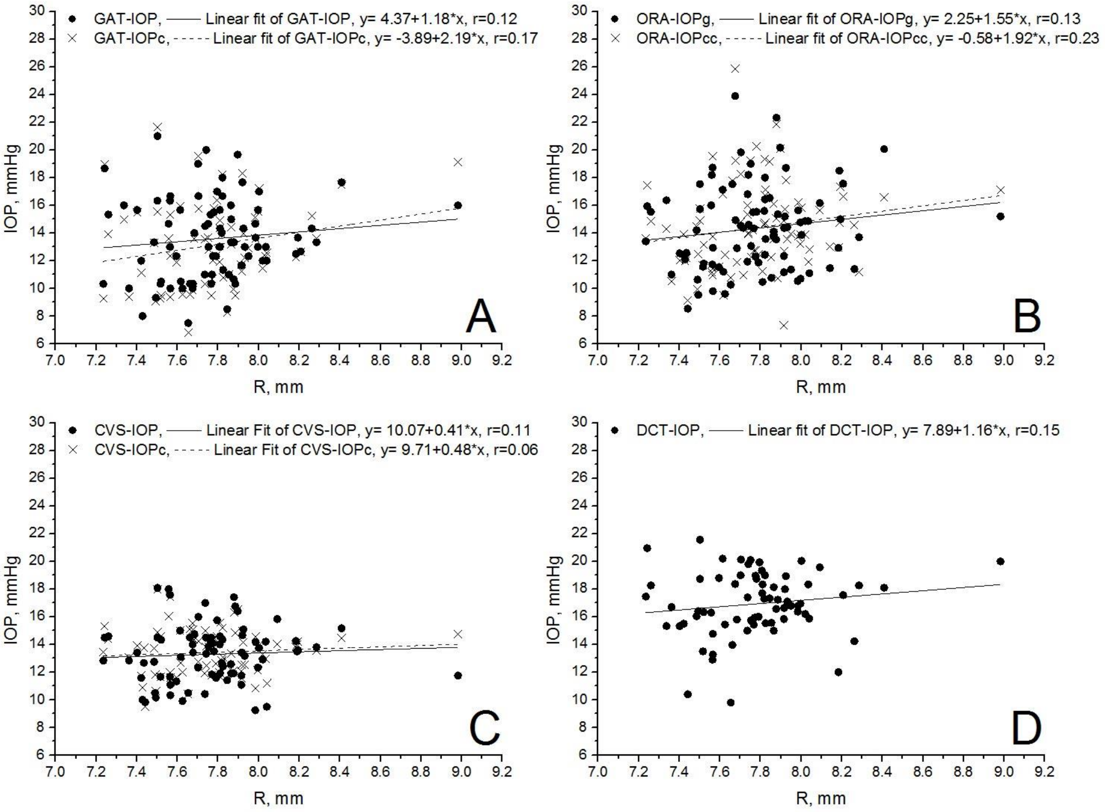

Fig.6 Relationship between R and both *uncorrected* and *corrected* IOP measurements made by the four tonometers considered, GAT, ORA, CVS and DCT