SCIENTIFIC REPORT

The relative effects of corneal thickness and age on Goldmann applanation tonometry and dynamic contour tonometry

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Aims: To establish the effects of central corneal thickness (CCT) on intraocular pressure (IOP) measured with a prototype Pascal dynamic contour tonometer (DCT), to evaluate the effect of CCT and age on the agreement between IOP measured with the Pascal DCT and Goldmann applanation tonometer (GAT), and to compare the interobserver and intraobserver variation of the DCT with the GAT.

Methods: GAT and DCT IOP measurements were made on 130 eyes of 130 patients and agreement was assessed by means of Bland-Altman plots. The effect of CCT and age on GAT/DCT IOP differences was assessed by linear regression analysis. Interobserver and intraobserver variations for GAT and DCT were assessed in 100 eyes of 100 patients.

Results: The mean difference (95% limits of agreement) between GAT and DCT was -0.7 (-6.3 to 4.9) mm Hg. GAT/DCT IOP differences increased with thicker CCT (slope 0.017 mm Hg/ μ m, 95% CI 0.004 to 0.03 , $r^2=0.05$, $p=0.01$), and with greater age, slope 0.05 mm Hg/year (95% CI 0.012 to 0.084 , $r^2=0.05$, $p=0.01$). The intraobserver variability of GAT and DCT was 1.7 mm Hg and 3.2 mm Hg, respectively. The interobserver variability was (mean difference (95% limits of agreement)) 0.4 (-3.5 to 4.2) mm Hg for GAT and 0.2 (-4.9 to 5.3) mm Hg for DCT.

Conclusions: GAT is significantly more affected than DCT by both CCT and subject age. The effect of age suggests an age related corneal biomechanical change that may induce measurement error additional to that of CCT. The prototype DCT has greater measurement variability than the GAT.

The current “gold standard” for intraocular pressure (IOP) measurement is the Goldmann applanation tonometer (GAT), which makes a static measurement of the force required to flatten a fixed area of the cornea. In designing the tonometer, Goldmann recognised that corneal effects, such as central corneal thickness (CCT) and the precorneal tear film, would influence the pressure measurements, and this has been shown in various studies.^{1–6}

A new slit lamp mounted tonometer, the Pascal dynamic contour tonometer (DCT; Swiss Microtechnology AG, Port, Switzerland) has been developed to remove the corneal biomechanical effects from IOP measurement by using a direct transcorneal method. When the Pascal DCT is placed on the eye, the cornea takes the contour of the tip so that its biomechanical effects on IOP measurement are reduced. The DCT gathers 100 IOP readings per second. Recent studies have indicated that its IOP measurements are independent of CCT⁷ and are unchanged following thinning of the CCT with laser in situ keratomileusis (LASIK).^{8,9}

The primary purpose of this study was to assess the agreement between the GAT and Pascal DCT, and to establish the effects of CCT on IOP measurements made with these two devices. A secondary aim was to evaluate the intraobserver and interobserver variability of the Pascal DCT.

METHODS

Patients attending their routine appointment in the ocular hypertension or pigment dispersion clinics at the Glaucoma Research Unit (Moorfields Eye Hospital, London, UK) between February and May 2004 were invited to take part in the study (see table 1 for demographic data). Informed consent, according to the tenets of the Declaration of Helsinki, was obtained before examination. The study had local ethics committee approval.

For the tonometer comparison study, 130 eyes of 130 patients were examined; 71 patients (55%) were on topical ocular hypotensive therapy (table 2). Two GAT and three DCT (prototype version 1.2) readings were obtained in a randomised order. Measurements were performed by either one of two technicians (ETW or JMS) and by a clinician (AK) also in a randomised order. With GAT measurements, the tonometer was set at 10 mm Hg before each reading. For DCT, three readings of “good” quality were saved (score ≤ 3 on a scale up to 5, as recommended by the manufacturer). The observers were masked to each other’s results. Keratometry was performed with the IOLMaster (Carl Zeiss Meditec, AG, Germany) before tonometry, and CCT was measured with the Altair ultrasonic pachymeter (20 MHz solid tip probe; Optikron 2000, Rome, Italy) after tonometry. The sample size chosen allows a study power of 90% ($p<0.05$) to detect a correlation of $r=0.3$ between CCT and IOP.

For the intraobserver and interobserver variability study, 100 eyes (49 left eyes) of 100 (45 female) patients were examined. The mean patient age was 60 years (range 26–83; SD 13.2 years). This group was a subset of that used in the previous study. The order of GAT/DCT and technician/clinician was randomised with a 5 minute break between GAT and DCT measurements. Measurements were obtained as already described, and the agreement between technicians and clinician was assessed.

Data analysis

Bland-Altman plots¹⁰ were used to assess the agreement in IOP measurements between techniques (DCT measurements by the clinician versus GAT measurements by the technicians), and between observers for each of the two techniques. Mean difference and 95% limits of agreement were calculated. Linear regression analysis was used to

Abbreviations: CCT, central corneal thickness; DCT, dynamic contour tonometer; GAT, Goldmann applanation tonometer; IOP, intraocular pressure; LASIK, laser in situ keratomileusis

Table 1 Demographic data of comparison group (n = 130)			
	Mean	SD	Range
Eye (left/number)	60		
Sex (female/number)	52		
Age (years)	61	13.3	22–83
CCT (μm)	556	36.9	468–642
Keratometry (mm)	7.74	0.21	7.10–8.44
Corneal astigmatism (mm)	0.17	0.13	0–0.88
GAT (mm Hg)	19	4.6	9–33
DCT (mm Hg)	19	4.0	11–29

determine the associations between GAT/DCT differences, and CCT and age.

Repeatability (intraobserver variability) of IOP measurements with GAT and DCT was calculated as 2.77 times the within subject standard deviation (*wsSD*)¹¹:

$$wsSD = SD(observation\ 1 - observation\ 2)\sqrt{2}$$

where *SD* is the standard deviation, and *observations 1* and *2* are the recorded IOP measurements. The *wsSD* was only calculated if the magnitude of *SD* was unrelated to that of mean IOP readings.

To establish the effect of the choice of reading, repeatability was calculated for DCT readings 1 and 2, and 2 and 3. The repeatability of GAT and DCT measurements was calculated for the clinician and technicians.

To assess the effect of DCT reading quality on repeatability, the association between the *SD* of DCT IOP measurements and average reading quality was determined.

All statistical analyses were performed using Medcalc Version 7.4.2.0 (Medcalc Software, Mariakerke, Belgium).

RESULTS

IOP measurements satisfying the quality criteria were obtained for all patients. Tables 1 and 2 summarise the demographic data of the study group.

Agreement between GAT and DCT measurements

The average of two GAT readings was compared with that of DCT readings 2 and 3 (see “Intraobserver and interobserver variability,” below). The mean difference (95% limits of agreement) between GAT and DCT was −0.7 (−6.3 to 4.9) mm Hg, and no relation between GAT/DCT differences and average was found (fig 1).

Effect of CCT on GAT and DCT IOP measurements

There was a relation between GAT/DCT IOP differences and CCT (slope 0.017, 95% CI 0.004 to 0.03, *r*² = 0.05, *p* = 0.01) (fig 2). Analysing treated and untreated eyes separately showed no relation between GAT/DCT IOP differences and

Figure 1 Bland-Altman plot of GAT/DCT IOP differences against GAT/DCT mean.

Figure 2 Relation between CCT and GAT/DCT IOP differences.

Figure 3 Relation between age and GAT/DCT IOP differences.

Table 2 Status and treatment of “comparison” group (total n = 130, treated eyes n = 71)					
Diagnosis	No of eyes (number treated)	Prostaglandin analogue (number)	β blocker (number)	α agonist (number)	CAI (number)
OHT	29/58	15	12	0	2
POAG	21/21	17	2	1	1
PDS	14/30	7	6	1	0
Glaucoma suspect	7/21	3	3	1	0

OHT, ocular hypertension; POAG, primary open angle glaucoma; PDS, pigment dispersion syndrome.

CCT in treated eyes ($n = 71$, CCT slope 0.004, 95% CI 0.012 to 0.020, $r^2 = 0.003$, $p = 0.65$), but an association in untreated eyes ($n = 59$, CCT slope 0.025; 95% CI 0.003 to 0.046, $r^2 = 0.083$, $p = 0.03$). Analysis of variance (ANOVA) performed to test whether treatment status had an effect on either CCT or GAT/DCT differences for the whole dataset showed no significant effect (F ratio 0.23, $p = 0.6$ for CCT and F ratio 1.7, $p = 0.2$ for GAT/DCT difference).

Effect of age on GAT and DCT IOP measurements

GAT/DCT differences were associated with age (GAT/DCT difference = $0.05 \times \text{age} - 3.6$, slope 95% CI 0.012 to 0.084, $r^2 = 0.05$, $p = 0.01$) (fig 3). There was no relation between GAT/DCT IOP differences and age in treated eyes ($n = 71$, age slope -0.031 , 95% CI -0.086 to 0.024 , $r^2 = 0.018$; $p = 0.27$), whereas an association was found in untreated eyes ($n = 59$, age slope 0.079, 95% CI 0.029 to 0.130, $r^2 = 0.14$, $p = 0.003$). Linear regression analysis showed no significant association between CCT and age (slope 0.174, 95% CI 0.65 to -0.31 , $r^2 = 0.004$, $p = 0.48$). Multiple regression analysis demonstrated an association between GAT/DCT differences, and both CCT and age (GAT/DCT difference = $0.045 \times \text{age} + 0.016 \times \text{CCT} - 12.5$, $r^2 = 0.09$, $p = 0.01$ for both age and CCT).

Intraobserver and interobserver variability

With both techniques, IOP reading SDs were independent of the mean IOP. The repeatability of IOP measurements for each observer are summarised in table 3. The difference between two measurements on the same subject would be less than the value for repeatability in 95% of pairs of observations.

The repeatability of DCT measurements improved when the first reading was discarded. For this reason, the average of readings 2 and 3 was used for the interobserver variability study. The mean difference (95% limits of agreement) in average GAT readings between clinician and technician was 0.4 (-3.5 to 4.2) mm Hg. The mean difference (95% limits of agreement) in average DCT measurements between clinician and technician was 0.2 (-4.9 to 5.3) mm Hg. The association between DCT recording quality and DCT measured IOP variability approached, but did not reach, significance (Pearson $r = 0.18$; 95% CI -0.02 to 0.37 ; $p = 0.08$).

DISCUSSION

In this study, a significant positive association between GAT/DCT IOP differences and CCT was found. The association of CCT with GAT/DCT IOP differences was studied as 55% of our subject population were on topical hypotensive therapy, which may confound the effect of CCT on IOP measurements. The association was shown not to be affected by treatment status, although a separate analysis indicated that GAT/DCT differences in untreated eyes were more affected by CCT compared with treated eyes. This finding, however, was not significant, perhaps because of the small subject numbers.

DCT IOP measurements have been reported to be independent of CCT,^{8,9} while studies have shown an increase in GAT IOP measurements with CCT, with slopes of 0.23 mm Hg¹² and 0.27 mm Hg¹³ increase per 10 μm increase

in CCT reported in UK populations. Our findings indicate a slope of 0.17 mm Hg per 10 μm increase in CCT. A steeper slope would be expected if the DCT was not affected by CCT, and a study with greater power is required to test the hypothesis that CCT has a weak effect on DCT measured IOP. It is also possible that the association between IOP measurement and CCT is affected by a change in corneal biomechanics through the use of topical hypotensive therapy, especially prostaglandin analogues. Prostaglandin analogues are known to alter the extracellular matrix of the ciliary muscle,¹⁴ and they may also affect the extracellular matrix of the cornea, altering its rigidity. Approximately 32% of patients in our study were on prostaglandin therapy, and it is possible that this may have affected IOP measurement.

Overall, GAT/DCT differences were positively associated with age (slope 0.05, $r^2 = 0.05$, $p = 0.01$) and this relation increased when untreated eyes alone were assessed (slope 0.08, $r^2 = 0.14$, $p = 0.003$). In younger eyes, DCT readings were greater than GAT readings, and this difference reversed in older eyes. It has been suggested that age related increase in corneal "stiffness" may induce a further measurement error with GAT,¹⁵ and studies have shown age related changes that may contribute to this increase.¹⁶⁻¹⁸ DCT measurements may be less affected as the effect of corneal biomechanics on IOP measurement is reduced with this technique. However, the association found here requires to be validated in further studies powered to detect this effect.

In this study, the intraobserver variability of IOP readings was greater with the DCT compared with the GAT, although opposite findings were reported in a recent paper by Kauffmann *et al.*⁷ Possible explanations for the difference include differences in study subjects (patients versus hospital staff volunteers), order of testing (randomised order versus GAT followed by DCT), instrument model, and DCT reading quality. The association of reading quality and measurement variability approached significance ($p = 0.08$) in this study, therefore tighter quality control may result in improved repeatability. The better repeatability of GAT in this study may have been because the observers were not masked to their own results. Although the GAT drum was rotated to 10 mm Hg between readings, an element of digit preference may have remained. The DCT, on the other hand, provides objective IOP measurements and the operator cannot directly manipulate the readings.

The interobserver variability was relatively low for GAT and DCT measurements, with mean difference (95% confidence intervals) being 0.4 (-3.5 to 4.2) mm Hg for GAT and 0.2 (-4.9 to 5.3) mm Hg for DCT. This value is in concordance with most reports of GAT reproducibility.¹⁹

This study shows that the DCT is less affected by CCT than the GAT. Age accounted for as much intersubject variation in GAT/DCT differences as did CCT, suggesting a significant effect of age related corneal stiffening on IOP measurement with GAT. However, measurement variability was higher with the prototype DCT compared with the GAT. A non-significant trend relating reading quality and measurement variation suggests that tonometry technique may be a source of variation.

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Table 3 Repeatability of measurement technique (mm Hg)

Method	Technician	Clinician
GAT 1 and 2	1.6	1.7
DCT 1 and 2	4.2	3.3
DCT 2 and 3	3.2	2.6

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