

Comparison of three methods of intraocular pressure measurement and their relation to central corneal thickness

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Abstract

Purpose The purpose of this study was to compare the reliability of the 'gold standard' Goldmann applanation tonometer (GAT), with that of the ocular response analyser (ORA), and the dynamic contour tonometer (DCT).

Patients and methods A total of 694 subjects were recruited to participate from the TwinsUK (UK Adult Twin Registry) at St Thomas' Hospital, London. Intraocular pressure (IOP) was measured using GAT, ORA, and the DCT. The agreement between the three methods was assessed using the Bland–Altman method. Repeatability coefficients and coefficient of variation between first and second readings of the same eye were used to assess reliability.

Results Mean age was 57.5 years (SD, 13.1; range, 16.1–88.5). The mean IOPs, calculated using the mean of two readings from the right eye were as follows: Goldmann (GAT), 14.1 ± 2.8 mm Hg; IOPg (ORA), 15.9 ± 3.2 mm Hg; IOPcc (ORA), 16.6 ± 3.2 mm Hg; and DCT, 16.9 ± 2.7 mm Hg. The 95% limits of agreement were for ORA (IOPcc): GAT, -2.07 to 7.18 mm Hg; for DCT: GAT, -0.49 to 6.21 mm Hg; and for DCT: ORA (IOPcc), -3.01 to 4.85 mm Hg. Coefficients of variation for the three tonometers were GAT, 8.3%; ORA, 8.2%; DCT, 6.3%. The repeatability coefficients were 3.4 mm Hg for GAT, 3.57 mm Hg for ORA and 3.09 mm Hg for DCT. GAT and ORA (IOPg) readings showed a positive correlation with central corneal thickness ($P < 0.005$).

Conclusions This study found similar reliability in all three tonometers. Bland–Altman plots showed the three instruments to have 95% limits of agreement

outside the generally accepted limits, which means they are not interchangeable. GAT measurements were found to be significantly lower than the two newer instruments.

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Introduction

Glaucoma is the second leading cause of blindness, affecting an estimated 70 million people worldwide.¹ Although it no longer forms part of the definition of the disease, elevated intraocular pressure (IOP) is the principal modifiable risk factor for the development and progression of open-angle glaucoma.^{2–4}

Although the Goldmann applanation tonometer (GAT) has been the 'gold standard' for measuring IOP in the clinical setting for several decades, recently there has been a growing interest in developing new technology to measure a more accurate IOP.⁵ It is well known that GAT is affected by the central corneal thickness (CCT).^{6,7} The Ocular Hypertension Treatment Study showed that CCT is an important and independent risk factor for the progression of ocular hypertension to a first diagnosis of glaucoma.⁸ It has been estimated that a measurement error of between 0.11⁹ and 0.71 mmHg⁷ occurs per 10 μ m deviation from the average CCT of 550 μ m.

We set out to compare the GAT with two relatively new instruments that are designed to produce IOP readings less dependent on CCT; the ocular response analyser (ORA; Reichert,

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Buffalo, NY—software version 1.10) and the Dynamic Contour Tonometer (DCT, Pascal; Swiss Microtechnology AG, Port, Switzerland—software version 2.2). The ORA is a non-contact air-puff tonometer that ejects an air impulse lasting 20 ms and monitors the time course changes of the cornea by an electro-optical collimation detector system. The difference between ‘inward’ and ‘outward’ applanation pressure depends on the viscoelastic properties of the corneal shell, because opposition forces absorb energy from the air impulse (corneal hysteresis).^{10,11} The ORA derives two IOPs: the Goldmann-correlated IOP (IOPg), which the manufacturers have calibrated with GAT, and the corneal-compensated IOP (IOPcc), which is designed to be independent of the CCT.

The DCT is a contact tonometer with a concave surface with radius of curvature of 10.5 mm, which creates a distribution of forces between the central contour of the tip and the cornea that equals the forces generated by the internal pressure of the eye.¹² Its measure of IOP is supposedly independent of CCT.

To our knowledge, this is the largest sample to date comparing the ORA to the GAT and the second largest sample comparing the DCT and GAT, in the same group of unselected individuals.

Materials and methods

Data were available on 694 individuals who were recruited from the TwinsUK (UK Adult Twin Registry), based at St Thomas’ Hospital, London. The subjects were twin volunteers from the general population, and were part of a twin study on glaucoma heritability.^{13,14} Subjects were recruited for studies other than eye studies, and subsequently asked to attend for an eye examination. All subjects provided informed consent, and the study was reviewed by the Local Research Ethics Committee. The methods adopted in this study adhered to the tenets of the Declaration of Helsinki Principles. All 694 subjects had two readings performed on both eyes with all three instruments, by a single investigator (FC).

A drop of proxymetacaine 0.5% with fluorescein was instilled in both eyes before testing. IOP measurement with the ORA was performed first, as it is a non-contact device—first and second readings were taken for the right eye and if the accuracy was poor a third reading was taken, and the same for the left eye. Poor accuracy was defined by abnormal symmetry between the signal peaks of the distribution graph. IOP readings above 50 or below 5 mm Hg were discarded and the measurement repeated. In the case of the DCT, two readings per eye were again taken; with this instrument, readings were alternated between eyes. For each individual reading displayed, the DCT uses the average of 5 or 6 IOP

readings. Only those measures with reliability score recommended by the manufacturer (≤ 3 on a scale 1–5) were accepted (mean reliability was 1.8 ± 0.9). For the GAT, the gauge was set at 0 mm Hg and dialled up to the subject’s IOP; this was repeated on the contralateral eye. The dial was next set at 40 mm Hg and moved down to the individual’s IOP to provide a second reading for each eye. A sample of individuals was assessed in random order to see if there was any applanation effect induced by using this order of IOP measurement; however, none was found. All measurements were taken in immediate succession to eliminate bias due to diurnal fluctuation.

Data handling and preliminary analyses were undertaken using STATA (Intercooled Stata for Windows 95, version 5.0; StataCorp, College Station, TX; 1997). Pearson correlation coefficients between right and left eyes were calculated and as right and left eyes showed significant correlation, right eye measures were arbitrarily used for further analyses, including coefficient of variation between first and second readings of the right eye, and repeatability coefficients between first and second readings of the right eye.¹⁵ The coefficient of variation between first and second readings of one eye is the standard deviation of the difference between the two readings, divided by the total mean of both readings. The lower the coefficient of variation, the less variation between readings and therefore the more reliable the instrument. The repeatability coefficient can be calculated as 1.96 times the standard deviations of the differences between the two measurements. The agreement between each instrument and GAT and between the two newer instruments was assessed using the Bland–Altman method.¹⁶ For the ORA, only IOPcc was used for the coefficient of variation, repeatability coefficient, and Bland–Altman plots, as this is the measure that is supposed to be independent of CCT. The 95% limits of agreement, estimated by mean difference ± 1.96 standard deviations of the differences, provide an interval within which 95% of differences between measurements by the two methods are expected to lie. Proportional bias was determined from the gradient of the Bland–Altman plot of the mean difference between the two instruments against the mean of the two instruments. The correlation between each instrument’s IOP readings and CCT was also compared using Pearson’s correlation coefficient. For the mean IOPs of all four measurements and for the correlations between IOP and other parameters and for the Bland–Altman plots, the mean of four readings, two from each eye, was used.

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Results

The study sample consisted of 1388 eyes, of 694 individual twin subjects. Mean age was 57.5 years (SD 13.1, range 16.1–88.5). Of these, 95% were women and all were Caucasian. A previous diagnosis of glaucoma had been made in seven subjects (1%), but exclusion of these individuals did not alter the mean values or the correlations and so they remained in further analyses. In total 13 eyes required a third measurement for the GAT, 9 for the ORA, and 24 for the DCT. Results were also unchanged if the familial relationships were taken into account, randomly selecting only one of each pair of twins. However, as this study is comparing measurement variation within individuals, all twin subjects are included in the results reported.

The mean IOPs were calculated using the mean of four readings, two from the right eye and two from the left. The mean IOPs for all measures were as follows: Goldmann (GAT), 14.1 ± 2.8 mm Hg; IOPg (ORA), 15.9 ± 3.2 mm Hg; IOPcc (ORA), 16.6 ± 3.2 mm Hg; and for DCT, 16.9 ± 2.7 mm Hg. The mean CCT was 542 ± 34 μ m. The range of IOPs and mean differences between the instruments are shown in Table 1; both the newer instruments gave significantly higher IOP readings than GAT. Figure 1 shows the IOP frequency distribution for GAT.

Right/left eye correlations were the following: GAT, 0.83 ($P < 0.001$); IOPg, 0.79 ($P < 0.001$); IOPcc, 0.67 ($P < 0.0001$); DCT, 0.82 ($P < 0.0001$). The coefficients of variation for the three tonometers were the following: GAT, 8.3%; ORA, 8.2%; DCT, 6.3%. The mean of absolute differences between the first and second readings of the right eye were as follows: for GAT, 1.5 mm Hg (SD: 1.2); ORA (IOPg), 1.4 mm Hg (SD: 1.2); ORA (IOPcc), 1.7 mm Hg (SD: 1.5); and DCT: 1.2 mm Hg (SD: 1.2). The repeatability coefficients were calculated between readings one and two of the right eye. These were found to be, for GAT, 3.4 mm Hg; ORA, 3.57 mm Hg; and DCT,

Table 1 Mean IOPs and the difference between ORA and DCT mean IOP from GAT mean IOP, in an adult population of British twins

| Tonometers | Mean IOP (mmHg) | SD | Range (mmHg) | Difference from GAT IOP | Significance |
|-------------|-----------------|-----|--------------|-------------------------|--------------|
| GAT | 14.1 | 2.8 | 7.5–24.3 | — | — |
| IOPg (ORA) | 15.9 | 3.2 | 8.2–26.6 | +1.8 | $P < 0.001$ |
| IOPcc (ORA) | 16.6 | 3.2 | 7.3–30.6 | +2.5 | $P < 0.001$ |
| DCT | 16.9 | 2.7 | 11.3–27.2 | +2.8 | $P < 0.001$ |

DCT, dynamic contour tonometer; GAT, Goldmann applanation tonometer; IOPcc, corneal-compensated IOP of ocular response analyser; IOPg, Goldmann correlated IOP of ocular response analyser; IOP, intraocular pressure.

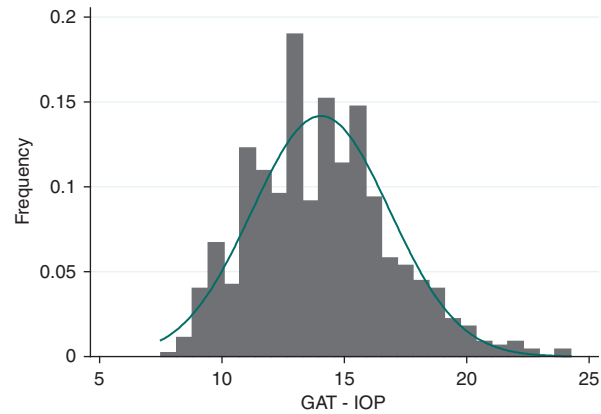


Figure 1 Frequency distribution graph for intraocular pressure in an adult population of British twins.

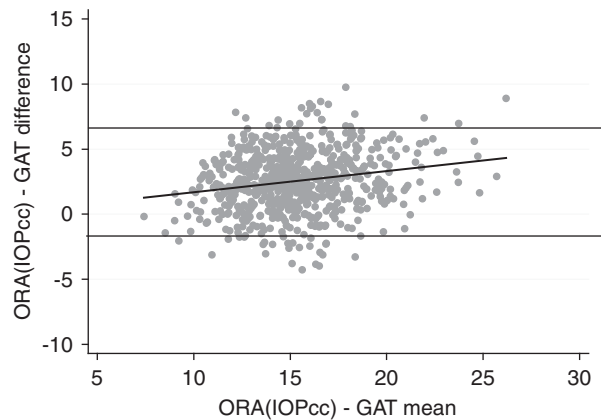


Figure 2 Bland–Altman plot between intraocular pressure using ocular response analyser (IOPcc) and Goldmann applanation tonometer. 95% limits of agreement are shown as two horizontal lines above and below the mean (–2.07 to 7.18 mmHg). Bias is shown by regression line through plot ($r = 0.19$, $P < 0.001$).

3.09 mm Hg. Bland–Altman plots were computed between ORA (IOPcc) and GAT; DCT and GAT; and DCT and ORA (IOPcc); the results are shown in Figures 2–4. The limits of agreement for ORA (IOPcc)–GAT were –2.1 to 7.2 mm Hg; for DCT–GAT were –0.5 to 6.2 mm Hg; and for DCT–ORA (IOPcc) were –3.0 to 4.9 mm Hg. We found a proportional bias between GAT readings and ORA (IOPcc). As the IOP reading increases, the difference between ORA (IOPcc) and GAT also increased, so that with higher IOPs, the GAT and ORA (IOPcc) readings were more dissimilar ($r = 0.19$, $P < 0.001$). In the case of the DCT, there did not appear to be any proportional bias ($r = 0.04$, $P = 0.26$).

Comparing correlations between IOPs generated and CCT, as expected the GAT ($r = 0.13$, $P < 0.001$) and the ORA IOPg ($r = 0.32$, $P < 0.0001$) readings were

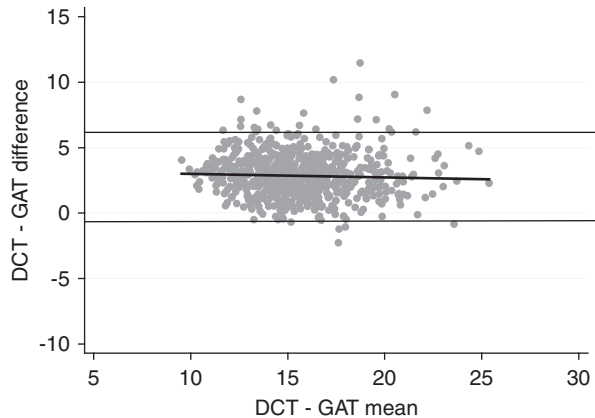


Figure 3 Bland–Altman plot between intraocular pressure using dynamic contour tonometer and Goldmann applanation tonometer. 95% limits of agreement are shown as two horizontal lines above and below the mean (−0.49 to 6.21 mmHg). Insignificant bias is shown by regression line through plot ($r = -0.04$, $P = 0.26$).

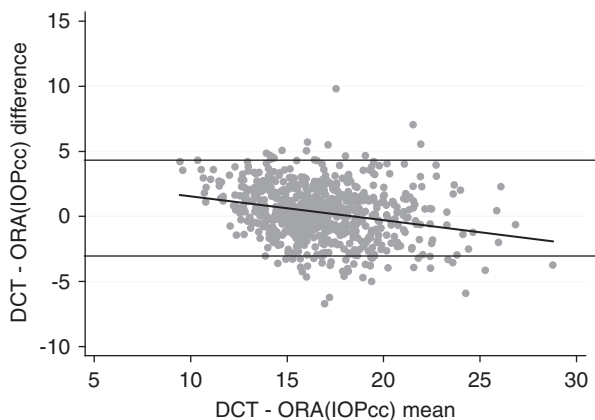


Figure 4 Bland–Altman plot between intraocular pressure using dynamic contour tonometer and ocular response analyser (IOPcc). 95% limits of agreement are shown as two horizontal lines above and below the mean (−3.01 to 4.85 mmHg). Bias is shown by line through plot ($r = -0.25$, $P < 0.001$).

significantly correlated with CCT. Neither the IOPcc (ORA) ($r = 0.02$, $P = 0.67$) nor DCT ($r = 0.06$, $P = 0.14$) readings were significantly correlated with CCT. All four instruments gave IOP readings that showed a highly significant (all with $P < 0.0001$) positive correlation with age (GAT, 0.2; IOPg, 0.14; IOPcc, 0.29; DCT, 0.21). All four IOP readings also showed strongly significant positive correlations with both systolic [GAT, 0.14 ($P < 0.0001$); IOPg, 0.12 ($P < 0.01$); IOPcc, 0.21 ($P < 0.0001$); and DCT, 0.13 ($P < 0.002$)] and diastolic blood pressures (GAT, 0.14 ($P < 0.0001$); IOPg, 0.11 ($P < 0.01$); IOPcc, 0.16 ($P < 0.0001$); and DCT, 0.17 ($P < 0.001$)). When CCT, systolic blood pressure, and diastolic blood pressure were included in

the regression analysis, age was no longer found to be significantly correlated with GAT ($P = 0.19$) or IOPg ($P = 0.06$); however, it was still significantly correlated with IOPcc ($P < 0.001$) and DCT ($P = 0.01$). CCT was also found to have a significant negative correlation with age of -0.12 ($P < 0.005$).

Discussion

Comparison of the reliability of these two newer tonometers with the ‘gold standard’ GAT has shown that the DCT had a marginally greater reliability, with a coefficient of variation (6.3%) less than that of the GAT and ORA (8.3 and 8.2%, respectively). We ascribe this lower coefficient of variation in the DCT to the fact that each individual IOP reading is an average taken over approximately 5 s. In the case of the GAT and ORA, each IOP point estimate is taken at a single, static point in time, although in reality the GAT IOP is taken as the average within the ocular pulse cycle.

It is usually considered that a tonometer with limits of agreement within ± 3 mmHg compared to GAT is clinically acceptable and therefore interchangeable; the two newer tonometers had limits of agreement outside this range, and there was proportional bias, suggesting they are not interchangeable with GAT.¹⁷ In a study by Pepose *et al*,¹⁸ comparing the same three instruments, the DCT was the only tonometer that did not show a significant change in IOP measurement pre- and post-LASIK. The wide limits of agreement found in this study are similar to the literature for both ORA^{17,19} and DCT.^{20,21}

There are conflicting findings in the literature regarding the difference in IOP measurement between GAT and ORA; our ORA IOPg measures were on average 1.8 mmHg higher than the GAT pressures, similar to another study that found IOPcc to overestimate GAT by 1.7 mmHg.²² In contrast, a study by Medeiros and Weinreb²³ found very similar mean IOP between GAT and IOPcc, with the difference being almost zero, similar to a Chinese cohort study.¹⁷ Yet another study looking at 48 eyes of 48 patients found mean IOPg to be 7.2 mmHg higher than GAT and IOPcc 8.3 mmHg higher.¹⁹ This study found a proportional bias between GAT and ORA; that is, as the IOP increased, the difference between ORA and GAT increased proportionately, with the ORA measures being even higher. There is conflicting evidence in the literature regarding proportional bias between these two instruments; two studies have reported a proportional bias,^{17,19} with the difference between ORA and GAT increasing with higher IOP. Another study has found no proportional bias.²³

The mean IOP of 14.1 mmHg was comparable to large population-based studies (the Los Angeles Latino Eye

Study²¹ of 14.4 mm Hg and similarly aged females (55–59 years) from the Beaver Dam Eye Study²⁴ of 15.1 ± 3 mm Hg). We feel, therefore, that significant ascertainment or other biases in this twin cohort is unlikely. The mean DCT IOP was significantly higher than GAT. The manufacturer recommends discarding the first reading with the DCT, because it is usually higher than the subsequent readings. We did not do this because we did not find a significant difference in the mean IOP between first and subsequent readings. Most studies have found DCT readings to be higher than GAT.^{25,26} In contrast, a recent study on African-American subjects did not find a significant difference in mean IOPs between GAT and DCT; with mean DCT IOP only 0.4 mm Hg higher than GAT.²⁷

This study found no proportional bias between the GAT and DCT readings. There are varied results in the literature for proportional bias; some studies have, like us, found no bias between DCT and GAT measurement,^{25,28} others have found increasing differences between DCT and GAT as IOP increased,^{29,30} or decreasing differences in another.³¹ DCT values for IOP are similar to intracameral manometric IOP *in vivo*³² and are more similar than GAT (which are significantly lower) in cadaveric eyes.^{33,34} This may mean that the higher IOP readings obtained with DCT are in fact the ‘true’ IOP.

As expected in our study, the GAT measurements are positively correlated with CCT. The IOPg reading of the ORA was also positively correlated with CCT. As proposed by the manufacturers, we have found that IOPcc is an IOP reading that is independent of CCT.^{22,23} There is conflicting evidence on the relation of ORA readings with CCT; two studies have shown that it is able to provide IOP readings that are independent of CCT. Kotecha *et al*²² found that IOPcc showed a positive, albeit not significant, trend with CCT. They proceeded to refine the calculation for IOPcc, calling this new value IOPccf (corneal constant factor) and this was found to have no association with CCT.²² Another study, performed on patients undergoing glaucoma treatment showed that ORA readings were not independent of CCT,¹⁹ although GAT was not correlated with CCT in this study, in contrast to most published studies. In the case of the DCT, the literature has consistently showed that IOP readings are less dependent on CCT than GAT,^{21,25} and our study has re-confirmed the finding.

Our findings that IOP readings from all the instruments are positively correlated with systolic and diastolic blood pressures are similar to other studies.^{35,36} Most, but not all, studies find IOP rises with age as we did.^{2,37–39} Both age and blood pressure are positively correlated with IOP, but are also correlated with each other (systolic blood pressure rises with increasing age); when both are included in regression analyses, the effect

of age on IOP is diminished. Interestingly, when systolic and diastolic blood pressures were included in the regression analysis, it was found that age was no longer significantly correlated with GAT and IOPg, but still significantly positively correlated with IOPcc and DCT readings. Although the reasons are unclear as to the mechanism of this difference, we have observed that corneal hysteresis, a measure of corneal viscoelasticity, is significantly related to age, and both DCT and IOPcc are significantly correlated with hysteresis, whereas IOPg and GAT are not.¹³ Further research is needed to examine these differences.

In conclusion, we have found that the ORA and DCT generate IOP measurements that are significantly higher than those of GAT, but which are independent of CCT. All instruments had a significant but similar inter-measurement variation, although the coefficient of variation of DCT was lowest. It is worth pointing out that the ‘gold standard’ GAT has similar variation to the other machines, and as repeat measures are standard for non-contact tonometry, so clinicians should consider taking more than one reading for GAT to reduce measurement error. This study has added to the growing body of work on the ORA and DCT, which produce less corneal-dependent IOPs than GAT. We feel that, although not interchangeable with GAT, both these newer instruments have a place in the clinical setting, where it is clear that GAT readings are influenced by corneal factors.

Summary

What was known before:

- DCT and ORA give IOP readings independent of CCT.
- Both the DCT and ORA tend to give higher readings than GAT.

What this study adds:

- Knowledge on the reliability of DCT and ORA.
- Adds data on a large sample size, comparing the three tonometers.
- Shows that the three tonometers are not interchangeable.

Conflict of interest

The authors declare no conflict of interest.

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