

Assessment of intraocular pressure measured by Reichert Ocular Response Analyzer, Goldmann Applanation Tonometry, and Dynamic Contour Tonometry in healthy individuals

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Abstract

• **AIM:** To investigate the accuracy of intraocular pressure (IOP) as measured by a Reichert Ocular Response Analyzer (ORA), as well as the relationship between central corneal thickness (CCT) and IOP as measured by ORA, Goldmann applanation tonometry (GAT), and dynamic contour tonometry (DCT).

• **METHODS:** A total of 158 healthy individuals (296 eyes) were chosen randomly for measurement of IOP. After CCT was measured using A-ultrasound (A-US), IOP was measured by ORA, GAT, and DCT devices in a randomized order. The IOP values acquired using each of the three tonometries were compared, and the relationship between CCT and IOP values were analyzed separately. Two IOP values, Goldmann-correlated IOP value (IOPg) and corneal-compensated intraocular pressure (IOPcc), were got using ORA. Three groups were defined according to CCT: 1) thin cornea (CCT<520 μ m); 2) normal-thickness cornea (CCT: 520-580 μ m); and 3) thick cornea (CCT>580 μ m) groups.

• **RESULTS:** In normal subjects, IOP measurements were 14.95 \pm 2.99mmHg with ORA (IOPg), 15.21 \pm 2.77mmHg with ORA(IOPcc), 15.22 \pm 2.77mmHg with GAT, and 15.49 \pm 2.56mmHg with DCT. Mean differences were 0.01 \pm 2.29mmHg between IOPcc and GAT (P >0.05) and 0.28 \pm 2.20mmHg between IOPcc and DC (P >0.05). There was a greater correlation between IOPcc and DCT (r =0.946, P =0.000) than that between IOPcc and GAT (r =0.845, P =0.000). DCT had a significant correlation with GAT (r =0.854, P =0.000). GAT was moderately correlated with CCT (r =0.296, P <0.001), while IOPcc showed a weak but significant correlation with

CCT (r =0.155, P =0.007). There was a strong negative correlation between CCT and the difference between IOPcc and GAT (r =-0.803, P =0.000), with every 10 μ m increase in CCT resulting in an increase in this difference of 0.35mmHg. The thick cornea group (CCT>580 μ m) showed the least significant correlation between IOPcc and GAT (r =0.859, P =0.000); while the thin cornea group (CCT<520 μ m) had the most significant correlation between IOPcc and GAT (r =0.926, P =0.000). The correlated differences between IOPcc and DCT were not significant in any of the three groups (P >0.05).

• **CONCLUSION:** Measurement of IOP by ORA has high repeatability and is largely consistent with GAT measurements. Moreover, the ORA measurements are affected only to a small extent by CCT, and are likely to be much closer to the real IOP value than GAT.

• **KEYWORDS:** intraocular pressure; tonometry; central corneal thickness

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INTRODUCTION

Intraocular pressure (IOP) is not only an important parameter in the diagnosis of glaucoma, but is also the key indicator for monitoring glaucoma progression and evaluating the effects of treatment. As a key value for diagnosis, IOP must be measured using a reliable technique. The "gold standard" for measuring IOP is the Goldmann applanation tonometer (GAT), which is currently the most widely used tonometer. However, Goldmann and Schmidt^[1] themselves emphasize the limitations of this instrument, and observe that the greatest precision is achieved when the central corneal thickness (CCT) is 520 μ m. When corneal thickness deviates from this size, the accuracy of the device gradually deteriorates. Therefore, IOP would be underestimated in thin corneas and overestimated in thick

corneas. This observation has been confirmed by many studies over recent years [2-5], which indicating that the accuracy of IOP measurement by GAT is closely associated with corneal thickness.

To minimize the impact of corneal thickness on GAT measurement, ophthalmologists typically measure CCT using a variety of techniques and calculate the true value using a correction formula. The appropriate formula was published by Wu *et al* [6]: Corrected IOP=GAT IOP measurements- (CCT-555)×(1/24). However, measurement of corneal thickness and the use of correction formula are not completely accurate or reliable, and are still not widely accepted [2,7,8].

In order to measure IOP more accurately, the third-generation tonometers have been in use since 2004. The most representative example of this updated technique is known as dynamic contour tonometry (DCT). The measuring head curvature of this device is similar to the curvature of the corneal surface, and does not cause corneal flattening or indentation when brought into contact with the corneal surface [9]. Thus, this instrument eliminates the impact of the tangent and any elastic deformation on the measured value. However, DCT is no longer accurate when IOP is greater than 40mmHg or less than 5mmHg. Furthermore, the technique relies on high patient cooperation, and can cause corneal instability in the early stages after laser in situ keratomileusis (LASIK).

These issues were partially addressed in the development of a new IOP measuring instrument known as the Ocular Response Analyzer (ORA), developed in the US by Reichert (Reichert Inc., Depew, NY). ORA is a non-contact tonometer benefiting from bilateral applanation by use of a single-pulse air stream and software to remove the impact of the corneal factors described above. As well as offering the features of traditional non-contact tonometers, the additional advantages of ORA include the fact that superficial anesthesia is not required, cross-contamination does not occur, and the cornea is not touched directly. Furthermore, the technique is speedy and offers high accuracy and repeatability [10].

The basic principles of ORA IOP measurement are similar to those of the traditional non-contact tonometer, except for using a dynamic bi-directional applanation process for the measurement of IOP and corneal biomechanical properties. In other words, the technique applies a rapid pulse of air to the cornea and uses an advanced electro-optical analysis system to monitor the deformation of the cornea, accurately measuring the inward movement of the cornea and the slight depression through flattening due to the parallel pulse air. After cessation of the pulse flow, the pressure reduces and the cornea begins to return to its normal shape. During this process, the cornea goes through its flattened conformation

again, giving two applanation values throughout the process. The two values are not consistent due to the dynamic nature of the pulse flow and the attenuation of corneal viscosity. The difference between the two values is known as the corneal hysteresis (CH), which is the result of corneal viscoelastic attenuation. The mean value of two provides the repeatable simulation of Goldmann-corrected IOP value (IOPg). CH measurement reflects the characteristics of the cornea and enables evaluation of two other parameters: corneal compensation intraocular pressure (IOPcc) and corneal resistance factor (CRF). IOPcc is less affected by corneal characteristics than measurement using an applanation tonometer. CRF, the overall hardness of the cornea, is associated with CCT.

This study takes GAT, the most commonly used technique, as the standard and compares the measurement of IOP values in normal individuals with those derived using ORA and DCT. In addition, the correlation of the three IOP readings with CCT is assessed, and the accuracy and superiority of ORA in measuring IOP is determined.

MATERIALS AND METHODS

Patients Between April and September 2008, we invited patients and their families attending the out-patient department or medical examination center at our hospital to enter our study by having their CCT and IOP measured. All individuals recruited had IOP ≤ 21mmHg, no family history of glaucoma, C/D ≤ 0.3, peripheral anterior chamber depth ≥ 1/3CT, and were aged 11 to 80 years. Volunteers were required to have no eye disease except mild age-related cataract and/or refractive errors.

Methods Corneal thickness was measured using a hand-held ultrasonic corneal pachymeter (SP-100, Tomey, Japan). A drop of oxybuprocaine (0.4%) was instilled before the corneal thickness was measured. The individual was asked to fix on a target to minimize eye movement. The measurement was taken five times within the pupil margin. Care was taken not to dent the cornea with the pachymetry tip. Values were accepted if the standard deviation (SD) of each measurement was within 5.0µm. An average of five measurements was obtained for data analysis.

IOP was recorded using GAT (Haag-Streit, Bern, Switzerland), DCT (PASCAL[®], Ziemer Ophthalmic System, Port, Switzerland), and ORA (Reichert Inc., Depew, USA) in randomized order for each participant. Each measurement was made two or three times, with an interval between each measurement of 15 minutes.

The measurement of IOP with the GAT or DCT performed after a drop of oxybuprocaine (0.4%) and a drop of fluorescein sodium (0.25%) was instilled. GAT values at each time point were taken as the mean of two measurements if within 3mmHg, or the mean of three measurements if the first two differed by 4mmHg or more.

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DCT measures pressure continuously as long as it is in adequate contact to the eye. The tonometer gives out a whistling sound, the rhythm of which coincides with the ocular pulse and the cardiac cycle. The IOP be measured for a period of 6-8 cardiac cycles. The instrument gives a quality score that ranges from 1 to 5 (lower scores indicate better quality). All measurements performed in the study had a quality reading of 1-3.

The procedure for performing ORA measurement is similar to that for a traditional non-contact tonometer. The patient is asked to fix on the target (red blinking light) in the ORA, and the ORA is activated by pressing a button attached to the computer. The instrument puffs an air jet onto the center of the cornea similar to that used in traditional air-puff tonometers. The resulting applanations allow corneal biomechanical parameters such as CH and CRF to be recorded. In addition, the device provides a value of IOPcc and IOPg. Four measurements were recorded by a trained technician in every volunteer, and the mean of the readings was used^[11].

Statistical Analysis Statistical analysis was performed using SPSS 14.0 software for Windows. The average comparison of two samples was performed using *t*-tests, and the relationship between two variables was assessed using linear correlation regression analysis. A value of $P < 0.05$ indicates a statistically significant difference between two parameters, while $P < 0.01$ indicates a highly statistically significant difference. $r > \pm 0.65$ and $P < 0.001$ indicates a high-level correlation; $\pm 0.2 \leq r \leq \pm 0.65$ indicates a moderate-level correlation; and $r < \pm 0.2$ and $P < 0.05$ indicates a low-level correlation.

RESULTS

A total of 158 healthy individuals with 296 eyes in total completed this study, 90 of whom were male (164 eyes). None of the subjects had eye disease except for mild age-related cataracts and/or refractive errors. The average age of participants was 33.56 ± 16.62 years (30.62 ± 15.77 years for men and 37.22 ± 16.99 years for women). Table 1 summarizes the principal characteristics of all subjects.

Using the formula for coefficient of variation (CV), $CV = S/\bar{X} \times 100\%$, we obtained CV of IOPcc, GAT, and DCT measurements of 5.39%, 5.36%, and 5.01%, respectively. All CV values were considerably less than 20%, indicating good reproducibility in repeated measurements of IOP of using ORA, GAT, or DCT.

The differences between the measurements of the three different tonometers are shown in Table 2. Good bilateral correlations were observed between IOPcc and GAT ($r = 0.845$, $P = 0.000$), IOPcc and DCT IOP ($r = 0.949$, $P = 0.000$), IOPcc and IOPg ($r = 0.871$, $P = 0.000$), IOPg and GAT IOP ($r = 0.956$, $P = 0.000$), IOPg and DCT IOP ($r = 0.809$, $P = 0.000$), and DCT and GAT IOP ($r = 0.854$, $P = 0.000$).

Table 1 Characteristics of normal individuals

Parameters	Minimum	Maximum	Mean	SD
Age (yr)	11	80	33.56	16.62
DCT (mmHg)	9.60	24.50	15.49	2.56
GAT (mmHg)	9.00	24.00	15.22	2.77
IOPcc (mmHg)	9.5	24.9	15.21	2.77
IOPg (mmHg)	7.5	22.8	14.95	2.99
CH (mmHg)	6.80	14.70	10.15	1.31
CRF (mmHg)	1.00	15.40	9.78	1.75
CCT (μm)	445	625	524.32	34.79

DCT: Dynamic Contour Tonometry; GAT: Goldmann Applanation Tonometer; IOPcc: corneal-compensated intraocular pressure; IOPg: Goldmann-correlated IOP value; CH: Corneal hysteresis; CRF: Corneal resistance factor; CCT: Central corneal thickness; SD: Standard deviation.

Table 2 Average differences between the three tonometers

Difference	(mean \pm Sd) (mmHg)	<i>t</i>	<i>P</i>
DCT vs GAT	0.27 \pm 2.01	1.30	0.20 ^a
DCT vs IOPcc	0.28 \pm 2.20	1.28	0.21 ^a
GAT vs IOPcc	0.01 \pm 2.29	0.84	0.42 ^a
GAT vs IOPg	0.27 \pm 2.21	1.12	0.20 ^a
IOPcc vs IOPg	0.26 \pm 2.11	1.10	0.26 ^a

^a $P > 0.05$

Table 3 IOP Measurement differences between groups of different corneal thickness

Group	Mean Difference (mean \pm Sd) (mmHg)		
	GAT	IOPcc	DCT
1 2	-1.45 \pm 0.71 ^a	0.29 \pm 0.63	-0.71 \pm 0.67
2 3	-1.64 \pm 0.81 ^a	0.25 \pm 0.52	-1.23 \pm 0.76 ^a
1 3	-3.09 \pm 0.97 ^a	0.54 \pm 0.66	-1.94 \pm 0.90 ^a

Group 1: Thin cornea group; Group 2: Normal-thickness cornea group; Group 3: Thick corneal group ^a $P < 0.05$.

Using the classification of Doyle *et al*^[12], three groups were defined according to CCT thickness: 1) thin cornea (CCT $< 520 \mu\text{m}$); 2) normal-thickness cornea (CCT: $520-580 \mu\text{m}$); and 3) thick cornea (CCT $> 580 \mu\text{m}$) groups. Differences in IOP measurement between groups of different corneal thickness are presented in Table 3. IOPcc vs GAT correlation and differences between the results in the different corneal thickness groups are shown in Table 4. IOPcc vs DCT correlation and differences between the results among different corneal thickness groups are shown in Table 5. The correlated differences between IOPcc and DCT were not significant in any of the three groups ($P > 0.05$). After linear correlation analysis of the IOP values of DCT, GAT, IOPg, and IOPcc, respectively with CCT, we found a weak correlation between DCT and CCT ($r = 1.50$, $P = 0.010$). There was a moderate positive correlation between GAT and CCT ($r = 0.296$, $P < 0.001$). A positive straight-line correlation was found between IOPg and CCT ($r = 0.271$, $P < 0.001$ [double sided]), while the correlation between IOPcc and CCT was weak ($r = -0.155$, $P = 0.007$).

Table 4 IOPcc vs GAT correlation and affect of corneal thickness

	<i>n</i>	IOPcc and GAT Correlation coefficient	IOP Average of IOPcc (mean±Sd)(mmHg)	IOP Average of GAT (mean±Sd)(mmHg)	Differences between IOPcc and GAT(mean±Sd)(mmHg)
Group 1	145	0.926 ^b	15.38±2.83	14.38±2.65	1.00±1.07
Group 2	132	0.915 ^b	15.09±2.77	15.83±2.64	?0.73±1.11
Group 3	19	0.859 ^b	14.84±2.23	17.47±2.27	?2.58±1.20

Group 1: Thin cornea group; Group 2: Normal-thickness cornea group; Group 3: Thick corneal group ^b*P*<0.01.

Table 5 IOPcc vs DCT correlation and affect of corneal thickness

	<i>n</i>	IOPcc and DCT Correlation coefficient	IOP Average of IOPcc (mean±Sd)(mmHg)	IOP Average of DCT (mean±Sd)(mmHg)	Differences between IOPcc and DCT(mean±Sd)(mmHg)
Group 1	145	0.943 ^b	15.38±2.83	15.75±2.56	0.37±1.01
Group 2	132	0.957 ^b	15.09±2.77	15.56±2.60	0.47±1.16
Group 3	19	0.945 ^b	14.84±2.23	15.24±2.09	0.40±0.85

Group 1: Thin cornea group; Group 2: Normal-thickness cornea group; Group 3: Thick corneal group ^b*P*<0.01.

The difference between IOPcc and GAT with a Pearson correlation coefficient among CCT was $r=-0.803$ ($P=0.000$) with a regression coefficient, $b=-0.035$ and an intercept of 18.60. By variance analysis, $F=534.30$, and $P=0.000$. Therefore, it can be considered that the difference between IOPcc and GAT has negative linear relationship with CCT. In other words, the thicker the cornea, the greater the difference between IOPcc and GAT. For each additional 10 μ m of CCT, the difference between IOPcc and GAT increases by 0.35mmHg.

The correlation coefficient between the difference between IOPcc and GAT and the ages of the examiners was $r=0.119$, $P=0.04$, showing a weak correlation.

In normal, healthy individuals, the average CH was found to be 10.15 \pm 0.31mmHg, while the average CRF was 9.78 \pm 1.75mmHg, with a good correlation ($r=0.766$, $P<0.0001$). CH and IOPcc also had a strong correlation ($r=-0.233$, $P<0.001$), as did CH and CCT ($r=0.612$, $P<0.001$), although there was no correlation between CH and GAT ($r=0.110$, $P=0.06$). A strong correlation was also found between CRF and GAT ($r=0.591$, $P<0.001$) and between CCT and CRF ($r=0.541$, $P<0.001$).

DISCUSSION

The reliability and stability of IOP measurements is very important. Normal IOP is important to maintain the shape of the eye and normal visual function. Long-term high IOP can cause irreversible damage to the retinal ganglion cells and postganglionic nerve fibers. Studies have shown that for every 1mmHg reduction in IOP, visual field damage can be reduced by 10%^[13].

The impact of CCT on IOP must be compensated for, that is because of the current gold standard for IOP measurement, GAT, is also affected by CCT. However, although various methods are used to compensate for CCT, no method is completely satisfactory^[7]. Over the past few years, several new devices have been developed trying to resolve the known limitations of the traditional applanation tonometer.

Recent studies show that using DCT ensures that the measured IOP is affected by CCT to a lesser extent than by a conventional applanation tonometer^[14]. The ORA technique was developed for a similar purpose. This instrument is able to measure several biomechanical properties of the cornea and can correct the IOP based on these characteristics.

This study showed that differences in IOPcc measured using GAT and DCT were small, and that there was a statistical significant correlation between the two techniques which is consistent with the results from Medeiros *et al*^[15], though their study reported a larger difference between IOPcc and GAT compared with ours. The following reasons for this discrepancy are suggested: 1) in the study from Medeiros *et al* the selected CCT range was from 439 to 642 μ m. Both the highest and lowest values are therefore high compared with this study; 2) The smaller sample size of the Medeiros' study (78 volunteers with a total of 153 eyes).

Furthermore, our results also showed that the difference between DCT and GAT measurements is relatively small. Although this finding is in contrast with results of an earlier study by Cheng *et al*^[16], there are important differences between the two studies: 1) Cheng *et al* used a non-contact lens corneal endothelium to measure CCT, unlike our study in which corneal thickness was measured by A-US. The average value of CCT was higher in the study of Cheng *et al* 2) Cheng's study used a smaller sample size, and only one eye per case; 3) The average age of patients in the Cheng's study (41.2 years) was older than in the present study.

After alternately measuring ORA, GAT, and DCT in 296 eyes using the same observer, we find that DCT, ORA, and GAT measurements show some variability, but there are no statistically significant differences. A statistical significant correlation is also found between ORA and GAT. This shows that the stability of repeated measuring using ORA is equivalent to that with GAT^[17], and that ORA IOP measurements are valid and reliable.

In this study, we found that there is weak correlation between the differences in ORA and GAT measurements and the patient age. This is consistent with the findings of White *et al* [18]. White found that ORA readings of young people are higher than their GAT readings, and vice versa in the elderly. We speculate that higher GAT measurements among the elderly may be due to changing biological characteristics of the cornea, such as increasing cornea hardness and reduced elasticity with age.

Increasing numbers of studies have confirmed that the differences in corneal thickness among the population that are responsible for deviations in IOP as measured by GAT from true values [19]. Mehdizadeh and colleagues [20] reported a mild and positive correlation between CCT and sclera thickness. The present study demonstrated that IOP values measured by GAT have a positive linear correlation with CCT. The further CCT deviates from the average, the further the IOP value as measured by GAT deviates from the true value. This accounts for a large proportion of individuals with a thin cornea following excimer laser surgery in whom it is not possible to obtain accurate GAT IOP measurements [21].

Our data also demonstrate that among individuals with a corneal thickness greater than 580µm, IOP values as measured by GAT were higher (2.58mmHg) than in the normal population. Although the difference in IOPcc measurements between thin cornea group and thick corneal group (0.54mmHg) was not significantly different, there was a significant difference between the two groups in GAT measurements (3.09mmHg). Furthermore, while there was poor correlation between IOPcc and GAT measurements in the thick cornea group, there was a good correlation between IOPcc and GAT in groups with normal and thin corneas. These observations indicate that GAT is greatly influenced by corneal thickness, and also confirm the findings of Doyle and others [21]. In their view, IOPcc can provide a more realistic IOP measurement compared with GAT in thick corneas with a normal structure, while in thin corneas, this IOPcc advantage does not seem so obvious. In this study, the differences between IOPcc and GAT were found to have a significant negative correlation with corneal thickness; i.e., there is small difference between IOPcc and GAT in thin corneas, but a large difference among thick corneas. This is because GAT measurements are greatly influenced by CCT [22].

We conclude from this study that IOPcc and DCT have a weak negative correlation with CCT. This may be because the IOP of IOPcc and DCT is derived according to the correction of corneal biomechanical properties while it is not sufficient to correct the pressure by corneal thickness alone.

Theoretically, ORA correct IOPg based on two corneal biomechanical properties (CH and CRF) to give IOPcc. The data from this study are contradictory in this regard. In support of this correction is the fact that the IOP values measured by ORA (IOPcc and IOPg) correlated well with CCT and that IOPcc and IOPg also had a very good correlation ($r=0.871$, $P=0.000$). This seems to prove that corneal thickness alone is not sufficient to correct IOP. As further support, there is a significant correlation between CH and IOPcc but no correlation between CH and GAT, which indicates that CH provides accurate IOP correction to a certain extent. We can find that IOPcc is an effective correction of CH, but this correction function is not fully explained by the CCT.

In summary, the average IOPcc ORA measured in normal people is 15.21 ± 2.77 mmHg with high repeatability and good agreement with GAT and DCT. IOPcc measured by ORA has a weak correlation with CCT but a good correlation with CH.

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