Comparison of the Ocular Response Analyzer and the Goldmann Applanation Tonometer for Measuring Intraocular Pressure after Deep Anterior Lamellar Keratoplasty

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PURPOSE. To compare intraocular pressure (IOP) measured using the Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY) with that measured using the Goldmann applanation tonometer (GAT) in keratoconic eyes after deep anterior lamellar keratoplasty (DALK) and evaluate the influence of central graft thickness (CGT), corneal astigmatism, corneal hysteresis (CH), and corneal resistance factor (CRF) on the IOP measurements.

METHODS. IOP using the GAT (IOPGAT), CH, CRF, Goldmann-correlated IOP (IOPG), cornea-compensated IOP (IOPcc), and GAT were measured in 23 keratoconic eyes undergoing DALK. Bland-Altman plots were used to evaluate agreement between the tonometers. The correlation between refraction, CH, CRF, and CGT with IOP readings was investigated using multivariate regression analysis.

RESULTS. Mean patient age was 27.2 ± 6.5 years. Mean CGT, CH, and CRF were 547.0 ± 42.6 μm, 9.6 ± 2.1 mm Hg, and 9.4 ± 2.1 mm Hg, respectively. Mean IOPGAT, IOPG, and IOPcc were 11.3 ± 2.9, 14.1 ± 2.4, and 15.6 ± 2.6 mm Hg, respectively (P < 0.001). The 95% limit of agreement for IOPG and IOPGAT was between −2.61 and 8.19 mm Hg and for IOPcc and IOPGAT it was between −0.69 and 9.21 mm Hg. CH and CRF were significantly associated with IOPGAT. No significant association was found between CGT and IOP readings obtained using either the ORA or GAT.

CONCLUSIONS. IOP readings by the ORA were significantly greater than those by the GAT, and CH and CRF play a more important role in post-DALK IOP readings by both GAT and ORA than other graft characteristics including curvature and central thickness. (Invest Ophthalmol Vis Sci. 2011;52:5887–5891) DOI:10.1167/iovs.10-6771

Deep anterior lamellar keratoplasty (DALK) is considered an alternative procedure to penetrating keratoplasty (PK) for corneal pathologies not affecting the endothelium and Descemet’s membrane (DM).1 This technique of transplantation has been found effective to restore visual acuity with refractive outcomes comparable to those of PK in keratoconic eyes, while avoiding complications such as endothelial graft rejection and preserving the eye integrity against blunt trauma.1,2

The main aim of corneal transplantation of any kind is to restore optical properties of the eye. However, it is of particular importance to understand the nature of the change in biomechanical properties of the graft when refractive surgery of the transplanted cornea is anticipated. Further, monitoring intraocular pressure (IOP) after corneal transplantation is very important, as high IOP (>21 mm Hg) is encountered in transplanted eyes at a high incidence, ranging from 10% to 42%.3–6 Although Goldmann applanation tonometry (GAT) is considered the gold standard for measuring IOP, high astigmatism and surface irregularities after corneal transplantation can decrease its accuracy, and therefore other tonometers can alternatively be used.7–9 Further, decreased rigidity of the ocular wall in some conditions such as keratoconus, that may require corneal transplantation, can result in underestimating IOP measured with GAT.

In an attempt to circumvent the aforementioned problems with GAT in grafted eyes, several tonometers have been tried and compared to find an ideal instrument.10–11 Recently, Reichert Ophthalmic Instruments (Buffalo, NY) introduced a new technology noncontact tonometer that measures IOP as well as new metrics called corneal hysteresis (CH) and corneal resistance factor (CRF).12 The Ocular Response Analyzer (ORA; Reichert Ophthalmic Instruments) uses an air puff that causes inward and then outward corneal deformation, from which two applanation pressure measurements are obtained. By taking an average from these two measurements, a Goldmann-correlated IOP (IOPG) is calculated.12 Cornea-compensated IOP (IOPcc) determines IOP values, less dependent on corneal properties such as central thickness.12,13 Hysteresis, which is said to be a measure of the viscoelastic properties of the cornea, is the difference between the inward and outward applanation pressures. Hysteresis is influenced by corneal thickness and rigidity.12

The main objective of the present study was to evaluate the agreement between IOP measurements obtained with the ORA and GAT in keratoconic patients who underwent DALK using Anwar’s big-bubble technique1 and investigate the influence of biometric characteristics of the graft, including central graft thickness, mean keratometry, astigmatism, and size, as well as CH and CRF, on these measurements.

MATERIALS AND METHODS

In this cross-sectional comparative study, 23 eyes of 21 (13 male) patients who had undergone DALK using Anwar’s big-bubble technique were included. The underlying pathology was keratoconus in all
participants. The technique of DALK for keratoconus was previously described in detail, and a bared Descemet’s membrane was achieved in all cases. All sutures were removed at least 6 months before participants entered the study. The presence of any ocular diseases other than keratoconus; systemic disorders, such as diabetes mellitus; and a history of additional ocular surgeries such as a previous corneal graft, cataract extraction, and refractive surgery of any kind; and use of topical eye drops or contact lenses led to patient exclusion. This study was approved by the Institutional Ethics Committee according to the Declaration of Helsinki and a written informed consent was signed by all participants after the nature of the study was explained.

An ocular examination including uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA) using the Snellen acuity chart, slit-lamp biomicroscopy, manifest refraction, and keratometry was performed and preoperative IOPGAT was compiled from medical records. In each eye, IOP was measured twice using a Goldmann applanation tonometer (AT 020; Carl Zeiss Meditec Inc., Dublin, CA) and averaged, after anesthetizing the cornea with a drop of 0.5% tetracaine. To reduce the effect of corneal astigmatism on the measurements and measurements were performed by a single qualified ophthalmologist (SF).

The ORA was used to measure IOPa, IOPcc, CH, and CRF. Briefly stated, the patients were seated and asked to keep their eyes wide open while fixating on a green target light at the center of red lights. After an air puff was released, the measured parameters were displayed on the monitor. For each patient, four consecutive readings with good quality and two distinct peaks (Fig. 1) were obtained and averaged after the outliers were excluded. Because measuring IOP with one tonometer may influence the after measurement, the tonometers were used in a random order with a 5-minute interval between readings to minimize the effect of IOP fluctuation. To avoid the effect of sleeping and diurnal variation on the measurements of central graft thickness (CGT), CH, CRF, and IOP as well, the measurements were taken in the morning, at least 3 hours after patients awakened, when postawakening decline had already occurred.

The last examination was CGT using an ultrasonic contact probe (A/B scan; Sonomed Inc., Lake Success, NY) after instillation of topical 0.5% tetracaine. The probe was held perpendicular to the center of cornea and five measurements were obtained within a range of ±2 μm and averaged for statistical analysis. All examinations and measurements were performed by a single qualified ophthalmologist (SF).

**Statistical Analysis**

Statistical analysis was performed using commercial software (SPSS version 17; SPSS Inc., Chicago, IL). Data were presented as mean ± SD after their normal distribution was examined. Repeatability (intraobserver variability) of ORA measurements was calculated as 2.77 times the within-subject SD. Paired t-test was used to compare pre- and postoperative IOPGAT. Repeated measurement comparison analysis adjusted for multiple comparisons by the Bonferroni method was used to compare mean IOP readings by the ORA and GAT. The agreement between the two tonometers was evaluated with Bland-Altman plots. The correlation of biometric characteristics of grafts (CGT, recipient and donor trephine size, mean keratometry, and astigmatism) as well as the ORA measurements (CH and CRF) with the IOP readings by both tonometers was investigated using multivariate regression analysis. P < 0.05 was considered an indication of statistical significance.

**RESULTS**

Mean patient age was 27.2 ± 6.5 years (17–44 years) and mean follow-up period after keratoplasty was 29.2 ± 3.3 months (19–52 months). Mean recipient and donor trephine size was 7.90 ± 0.16 mm (7.50–8.00 mm) and 8.20 ± 0.18 mm (7.75–8.50 mm), respectively, with a trephine disparity of 0.25 mm in 19 and 50 mm in four eyes. Postoperative spherical equivalent refractive error, mean keratometry, and keratometric astigmatism were –4.11 ± 2.46 (–12.25 to +1.15) D, 46.28 ± 2.02 (41.5 to 49.0) D, and 4.49 ± 2.80 (0.50 to 10.0) D, respectively.

Table 1 provides further information regarding CGT, pre- and postoperative IOPGAT, IOPa, IOPcc, CH, and CRF. The repeatability of the ORA measurements is presented in Table 2.

As demonstrated in Table 1, preoperative IOPGAT was significantly lower than the postoperative value (P = 0.02). Repeated measurement comparison analysis adjusted by the Bonferroni method demonstrated that IOPa was significantly higher than IOPGAT, with a mean difference of 2.8 mm Hg (95% confidence interval [CI], 1.3–4.3 mm Hg; P < 0.001), and IOPcc was higher than IOPGAT, with a mean difference of 4.3 mm Hg (95% CI, 2.9–5.6 mm Hg; P < 0.001). Similarly, the difference between IOPa and IOPcc reached a significant level (P = 0.02), in favor of IOPcc (mean difference, 1.5 mm Hg; 95% CI, 0.2–2.7 mm Hg).

Bland-Altman plots produced a 95% limit of agreement (LOA) for IOPa and IOPGAT between -2.61 and +8.19 mm Hg.
PK eyes, Rao et al.9 found no significant difference among the ocular blood flow (OBF) tonometry and Tonopen with GAT in ing keratoplasty (PK). Comparing IOP measurements using encountered in IOP measurement with the GAT after penetrat-

problems (graft surface irregularities and high astigmatism)

to find a reliable instrument that can circumvent the

generated by the X-Pert tonometer may change after complete

suture removal. Ceruti et al.11 compared IOP readings with

those by ORA, after DALK using the big-bubble technique.

Multiple regression analysis showed that CH and CRF, but not CGT; recipient and donor trephine size; keratometric astig-

matism; and mean keratometry were significantly associated with IOPGAT, IOPr, and IOPcc (Table 3). No significant corre-

lation was found between CGT and CH or between CGT and CRF (Table 3).

DISCUSSION

After corneal transplantation, IOP should be closely monitored to detect and treat ocular hypertension (>21 mm Hg), which reportedly occurs at a high incidence, ranging from 10% to 42%.3–6 The most accurate method for measuring IOP is to insert a manometric probe into the anterior chamber and directly measure the pressure, but this method is not feasible in the clinical setting. GAT is considered the gold standard in the clinical measurement of IOP; however, one can question its appropriateness, as its accuracy is severely affected by corneal edema and irregularity and any alteration in corneal thickness and rigidity.15–18 Further, GAT was originally designed for measuring IOP in normal corneas and any biomechanical changes within the graft or host–graft complex can negatively impact its accuracy.19

To the best of our knowledge, this is the first report to evaluate CH and CRF and compare IOP readings by GAT with those by ORA, after DALK using the big-bubble technique. However, various authors9–11 have examined different tonometers to find a reliable instrument that can circumvent the problems (graft surface irregularities and high astigmatism) encountered in IOP measurement with the GAT after penetrat-

ing keratoplasty (PK). Comparing IOP measurements using ocular blood flow (OBF) tonometry and Tonopen with GAT in PK eyes, Rao et al.9 found no significant difference among the three tonometers. The problem with their study was that they recruited patients with different corneal pathologies, such as bullous keratopathy, corneal dystrophies, herpetic keratitis, and keratoconus. Such a heterogeneous group can make it difficult to draw a rational conclusion because ocular rigidity, which can affect IOP measurements, may differ in various conditions requiring corneal transplantation. A study by Lisle and Ehlers10 demonstrated that IOP readings by the X-Pert noncontact tonometer showed considerable variation from the values obtained with GAT in PK eyes. However, their results cannot be generalized, as they conducted the study within 13 months of PK, when the sutures were still in place. It is possible that the response of a grafted cornea to the air pulse generated by the X-Pert tonometer may change after complete suture removal. Ceruti et al.11 compared IOP readings with dynamic contour tonometry (DCT) and GAT in eyes undergo-

ing either PK or DALK, and found a high correlation between DCT and GAT. However, IOP readings obtained by means of DCT were 2.5 mm Hg higher than those by GAT, and this difference decreased with an increase in IOP values.

In the present study, all patients had the same underlying pathology (keratoconus), and the results should be interpreted in this context because the response of the cornea to the air pressure by the ORA is not only dependent on the grafts, but also the abnormal recipient cornea left after trephination, as well as the sclera rigidity and wound healing process, may all influence CH, CRF, and IOP readings.

We found ORA to be completely safe for such eyes, as wound dehiscence did not develop in any cases. This observation implies that after complete suture removal, the surgical wound is strong enough to sustain inward deformation of the graft caused by a rapid air puff. In addition, we investigated the repeatability of the ORA measurements after DALK, which was found to be moderate. This measure reflects the greatest difference one would expect between any pair of measurements using that method.14 Because ORA measurements are obtained in a small fraction of 1 second (approximately 20 ms), each IOP measurement by ORA occurs within a very brief segment of the ocular pulse that can be as high as 7.2 mm Hg.20 This explains why the repeatability has been reported to be moderate.21–24 Compared to previous studies, we observed better repeatability than did Moreno-Montanes et al.21 but our results were similar to those of other studies.22–24 Variation observed in different studies can be attributed to taking samples from patients with different underlying diseases, ranging from nor-

mal subjects21 to glaucoma patients22–24 to keratoconus pa-

tients undergoing DALK (this study).

In this study, the order of using the tonometers was random-

ized because measurements of one tonometer can poten-
tially interfere with subsequent measurements of another.25 It also means the ORA was measured after the topical anesthesia used for GAT in some cases; it has been suggested, but not proven, that the accuracy of parameters measured by ORA can be modified by prior use of topical anesthesia.26

In the present study, no correlation was found between mean keratometry or astigmatism and IOP readings obtained using the two tonometers, indicating that the readings are not affected by graft steepness and astigmatism. To reduce the effect of corneal astigmatism on readings by GAT, the tonometer tip was rotated 45° to the least-curved meridian. There are other ways to compensate for under- or overestimation of IOP resulting from high astigmatism, which include taking an average of values measured at two axes 90° apart or reducing or adding 1 mm Hg for every 4 D against-the-rule or with-the-rule astigmatism, respectively.27 Further, the ORA presented IOP measurements independent of keratometry readings, without any compensation, indicating the measurements of this noncontact tonometer are not affected by graft astigmatism, which is usually high after complete suture removal (up to 10.0 D in this study).

Table 1. Study Characteristics and Their Statistical Distribution

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean ± 1 SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>CGT, μm</td>
<td>547.0 ± 42.6</td>
<td>442.0–625.0</td>
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<tr>
<td>Preoperative IOPGAT, mm Hg</td>
<td>9.4 ± 1.8</td>
<td>6.0–14.0</td>
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<tr>
<td>Postoperative IOPGAT, mm Hg</td>
<td>11.3 ± 2.9</td>
<td>5.0–17.0</td>
</tr>
<tr>
<td>IOPr, mm Hg</td>
<td>14.1 ± 2.4</td>
<td>8.7–18.0</td>
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<tr>
<td>IOPcc, mm Hg</td>
<td>15.6 ± 2.6</td>
<td>11.7–21.4</td>
</tr>
<tr>
<td>CH, mm Hg</td>
<td>9.6 ± 2.1</td>
<td>5.7–12.9</td>
</tr>
<tr>
<td>CRF, mm Hg</td>
<td>9.4 ± 2.1</td>
<td>4.7–15.3</td>
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CGT, central graft thickness; IOPGAT, intraocular pressure measured by Goldmann applanation tonometer; CH, corneal hysteresis; CRF, corneal resistance factor; IOPr, Goldmann-correlated IOP; IOPcc, cornea-compensated IOP.

Table 2. Repeatability of Ocular Response Analyzer (ORA) Measurements

<table>
<thead>
<tr>
<th>ORA Characteristics</th>
<th>Mean (mm Hg)</th>
<th>95% Confidence Interval (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td>IOPg</td>
<td>4.41</td>
<td>3.44–5.20</td>
</tr>
<tr>
<td>IOPcc</td>
<td>5.53</td>
<td>4.62–6.50</td>
</tr>
<tr>
<td>CH</td>
<td>4.56</td>
<td>2.88–5.77</td>
</tr>
<tr>
<td>CRF</td>
<td>4.10</td>
<td>2.66–5.11</td>
</tr>
</tbody>
</table>

CH, corneal hysteresis; CRF, corneal resistance factor; IOPg, Goldmann-correlated IOP; IOPcc, cornea-compensated IOP.
Among different graft parameters, CH and CRF showed significant positive correlations with IOP$_{GAT}$ whereas other anatomic parameters, including graft thickness and size, were not associated. It is well documented that central thickness of a virgin cornea has an effect on IOP readings by GAT; it is overestimated in eyes with thick corneas and underestimated in those with thin corneas. However, this study failed to show any association between central graft thickness after DALK and IOP readings by either the ORA or GAT. This observation is in line with other studies evaluating the correlation between central graft thickness and IOP$_{GAT}$. It was previously observed that the influence of corneal thickness on IOP measurement is reduced in soft corneas. Therefore, the thin recipient rims retained after corneal transplantation can be one explanation for the lack of correlation. In addition, it is possible that corneal transplantation alters the normal relationship between central thickness and IOP readings observed in nongrafted eyes. For example, the wound healing in the area between recipient and donor corneas may influence the biomechanical properties of a recipient–donor cornea as a whole, exceeding the effect of CGT. As a result, CH and CRF are likely to measure cumulative effects of corneal stiffness, viscosity, elasticity, and that contributed by wound scarring in transplanted eyes, and hence demonstrate better correlation with IOP than with CGT.

In nongrafted eyes, IOP$_{c}$ has been reported to be equal to IOP$_{GAT}$. In the present study, however, it was significantly higher than IOP$_{GAT}$. Considering GAT as the gold standard and comparing other tonometers to it, some studies found a variation of $\pm 3$ mm Hg in the readings between these tonometers acceptable. Using the same criterion for our study, only 44.1% of IOP$_{c}$ readings lie within this range, while the 95% LOA is between $-2.61$ and $+8.19$ mm Hg. The observed discrepancy can be attributed to the change in tissue stiffness associated with wound healing.

IOP readings by the ORA demonstrated a stronger association with CH and CRF than those by the GAT (Table 3). From the clinical aspect, however, this significant association should be interpreted with caution. All the parameters measured by ORA are based on the first (P1) and second (P2) applanation pressures, and the instrument uses some mathematical equations to translate these pressures into CH, CRF, IOP$_{c}$, and IOP$_{g}$. For example, CH is the difference between P1 and P2 and IOP$_{c}$ is the average of the two. That is why a strong association was found between these two mathematically related parameters. However, the significant correlation of CH and CRF with IOP$_{GAT}$ is meaningful, especially in the absence of a correlation with thickness, because these parameters were measured independently.

In the present study, IOP$_{c}$ yielded the highest values. This measurement is intended to compensate for biomechanical properties, which may be affected by graft and retained recipient rim influences. Based on the results of the present study, however, it is not possible to know how closely IOP$_{c}$ estimates the true pressure. To decide which among the IOP$_{GAT}$, IOP$_{c}$, and IOP$_{g}$ can provide the most accurate reading, it is required to measure IOP simultaneously through inserting a manometric probe into the anterior chamber.

There are some limitations in the present study. First, the sample size was small. With a larger sample, the correlation as
well as the difference between the readings by ORA and GAT could be estimated with higher precision. Second, CH and CRF were not measured before keratoplasty. Therefore, it is not possible to determine to what extent these parameters were changed by DALK. In observing the significant increase in IOPGAT postoperatively, however, it is inferred that DALK can at least partially increase CH and CRF in keratoconic eyes.

To summarize, the ORA is a safe noncontact method for measuring IOP after DALK with moderate reproducibility. In addition, CH and CRF play a more important role in post-DALK IOP readings than graft curvature and central thickness. A study with a larger sample size is advocated to investigate the role of the ORA after DALK, and comparing IOP and corneal biomechanical properties before and after surgery will help determine the extent to which corneal transplantation can alter these parameters.

References


