Reproducibility and Clinical Relevance of the Ocular Response Analyzer in Nonoperated Eyes: Corneal Biomechanical and Tonometric Implications

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PURPOSE. To assess the reproducibility of the ocular response analyzer (ORA) in nonoperated eyes and the impact of corneal biomechanical properties on intraocular pressure (IOP) measurements in normal and glaucomatous eyes.

METHODS. In the reliability study, two independent examiners obtained repeated ORA measurements in 30 eyes. In the clinical study, the examiners analyzed ORA and IOP-Goldmann values from 220 normal and 42 glaucomatous eyes. In both studies, Goldmann-correlated IOP measurement (IOP-ORAg), corneal-compensated IOP (IOP-ORAc), corneal hysteresis (CH), and corneal resistance factor (CRF) were evaluated. IOP differences of 3 mm Hg or greater between the IOP-ORAc and IOP-ORAg were considered outcome significant.

RESULTS. Intraexaminer intraclass correlation coefficients and interexaminer concordance correlation coefficients ranged from 0.78 to 0.93 and from 0.81 to 0.93, respectively, for all parameters. CH reproducibility was highest, and the IOP-ORAg readings were lowest. The median IOP was 16 mm Hg with the Goldmann tonometer, 14.5 mm Hg with IOP-ORAg ($P < 0.001$), and 15.7 mm Hg with IOP-ORAc ($P < 0.001$). Outcome-significant results were found in 77 eyes (29.38%). The IOP-ORAc, CH, and CRF were correlated with age ($r = 0.22$, $P = 0.001$; $r = -0.23$, $P = 0.001$; $r = -0.14$, $P = 0.02$, respectively), but not the IOP-ORAg or IOP-Goldmann.

CONCLUSIONS. The ORA provides reproducible corneal biomechanical and IOP measurements in nonoperated eyes. Considering the effect of ORA, corneal biomechanical metrics produces an outcome-significant IOP adjustment in at least one quarter of glaucomatous and normal eyes undergoing noncontact tonometry. Corneal viscoelasticity (CH) and resistance (CRF) appear to decrease minimally with increasing age in healthy adults. (*Invest Ophthalmol Vis Sci.* 2008;49:968–974) DOI:10.1167/iovs.07-0280

Intraocular pressure (IOP) elevation is most commonly associated with glaucoma.[1] Although analyzing the anatomic structure and visual function are of pivotal importance,[2,3] ac-curately measuring IOP remains challenging.[4,5] The Goldmann tonometer (GT) is the gold standard. However, some corneal factors can affect the accuracy of the GT, such as corneal thickness, corneal curvature, edematous and scarred corneas, keratoconus, and corneal rigidity.[6–10]

A new noncontact tonometer (NCT; Ocular Response Analyzer [ORA]; Reichert, Delpew, NY) uses a rapid air impulse and an advanced electro-optical system to record two applanation pressures (Fig. 1) during corneal movements in and out.[11] However, the cornea resists the dynamic air puff, causing delays in the inward and outward movement, resulting in two pressure values, the average of which is the Goldmann-correlated IOP measurement (IOP-ORAg).[11] Corneal hysteresis (CH) is a new measurement of corneal tissue properties reflecting the tissue capacity to absorb and dissipate energy.[11] CH may, therefore, have a prominent role in obtaining an IOP estimate of the true IOP with fewer corneal artifacts. Furthermore, CH may provide new information about biomechanical corneal properties useful for indicating keratorefractive surgery and planning retreatment to avoid iatrogenic keratectasia.[12–15] CH also provides a basis for two new parameters, corneal-compensated IOP (IOP-ORAc), which is mathematically derived from CH and is intended to produce improved IOP estimates—an assumption that should be confirmed by manometric studies—and corneal resistance factor (CRF), which appears to indicate corneal "resistance" (Luce DA, personal communication, 2005). Although CH may reflect mostly corneal viscosity, CRF (defined as a linear function of the inward and outward applanation pressures) may predominantly relate to the elastic properties of the cornea.[16]

CH, which does not vary diurnally,[17,18] decreases in glaucomatous eyes[11,19] and may have an implication in glaucoma damage[20] that only longitudinal studies will demonstrate. However, there are possible systematic and random possible sources of error with any tonometer.[21] Whereas the former are adjustable,[22] the latter are inherent in instrument design and quality, can only be assessed by repeated measurements on the same patient, and are not adjustable.[21] The ORA has a varying systematic error compared with the GT, depending on the ORA prototype[22,23] or the production unit tested,[16,19] that can be further calibrated.[22] To our knowledge, no study has analyzed ORA repeatability for IOP estimations and biomechanical parameters, a need that other authors[22] share with us.

The aims of the present study were to evaluate the precision of the ORA IOP and biomechanical corneal measurements by assessing intraobserver and interobserver reproducibility, evaluating the effects of the ORA corneal biomechanical properties on IOP adjustment by NCT in nonoperated eyes, and assessing a possible relationship between ORA parameters (compared with GT reading) and age in a healthy population.

MATERIALS AND METHODS

A prospective, cross-sectional study was performed to evaluate IOP measurements using the ORA in nonoperated eyes. Informed consent
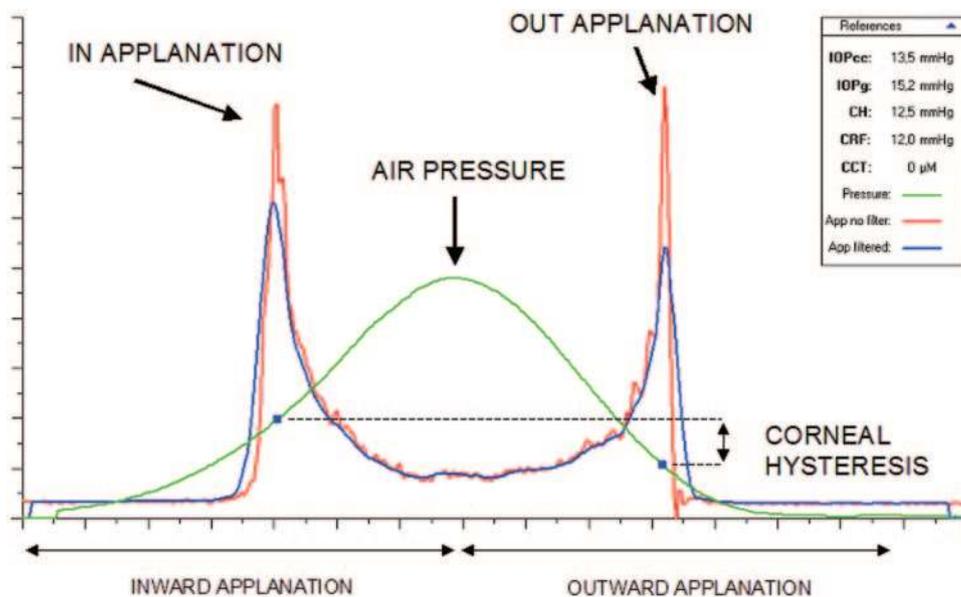
FIGURE 1. Profiles corresponding to an ORA measurement of IOP and corneal biomechanical properties.

was obtained from each patient according to the tenets of the Declaration of Helsinki.

Reproducibility Study

Three repeated measurements (each measurement was the average of three good-quality readings) by two examiners were obtained to evaluate the intraoperator and interoperator reproducibility of the same instrument. A good-quality reading was defined as one that exhibited force-in and force-out applanation signal peaks on the ORA wavefront that were fairly symmetrical in height. Interoperator repeatability was assessed by comparing the results of one examination by one examiner with one performed in the same eye in the same session by another examiner. Each eye was assigned a random order for the operators.[24] Between examinations, the device was moved away from the subject, and the operator left the room and waited 5 minutes so that the examiner repositioned the patient before performing another examination. Thirty eyes (30 healthy patients) were included. Exclusion criteria included corneal astigmatism >3 diopters and any previous ocular surgery.

Clinical Study

We obtained IOP measurements by ORA and GT in 262 consecutive eyes (262 patients), of which 42 had a diagnosis of primary open-angle glaucoma and 220 were normal. The same exclusion criteria as for the reliability study were used. One eye of each patient was selected randomly and determined to have a healthy cornea by meticulous biomicroscopic examination. Of the 42 glaucomatous eyes, 16 (38%) received a primary diagnosis; the remaining 26 (62%) were already receiving topical IOP-lowering medications. All ORA measurements were obtained using the same calibrated instrument by the same examiner. An independent examiner masked as to the ORA results obtained the GT values using a calibrated Goldmann handheld tonometer (Perkins; Columbus, OH). We evaluated the IOP-ORAg, IOP-ORAc, CH, and CRF using the ORA tonometer and the IOP obtained by the GT. The average of three readings from each tonometer was recorded. If one measurement was incorrect (not meeting the good-quality requirements in ORA measurements and distortions or excessive narrowing or widening of the normal-appearing fluorescein bands in GT measurements), the measurement was repeated. The ORA measurement was taken before Goldmann IOP to avoid the effect of topical anesthesia on NCT measures[25-27] and to prevent bias of ORA markers of corneal biomechanical properties by previous applanation tonometries or by corneal modification from corneal anesthesia.[22] Moreover,

we have previously demonstrated that after three repeated air-puffs, IOP readings do not decrease noticeably.[28]

To evaluate the effect of the ORA corneal biomechanical metrics on NCT values (IOP-ORAc), *measurement-significant adjustments* (IOP-ORAc minus IOP-ORAg) were defined as IOP corrections of ±1.5 mm Hg or greater.[29] Similarly, any ORA biomechanically derived IOP adjustments of ±3.0 mm Hg were designated as *outcomes-significant*.[29]

All analyses were performed using the SPSS program (version 13.0 for Windows; SPSS Inc., Chicago, IL) and the Stata program (version 9.0 for Windows; Statcorp LP, College Station, TX). Significance was determined by the Mann-Whitney *U* nonparametric test, and data were expressed as medians and 25% and 75% interquartile ranges (IRs) because the values were found to be nonnormally distributed. The association between two variables was tested using the Spearman correlation coefficient given the nonnormal distribution of at least one variable. The significance level was set at $P < 0.05$, by a two-tailed test. Agreement between IOP measurements was evaluated as described by Bland and Altman.[21]

To assess intraoperator repeatability, we calculated the within-subject SD (s_w) of two consecutive measurements in each eye by one examiner.[30] Precision (repeatability coefficient) was defined as ±1.96 s_w.[30] The difference between a subject's measurement and the true value from a statistical standpoint was expected to be ≤1.96 s_w for 95% of the observations.[12] We computed the "repeatability" (2.77. s_w), which is another useful way of presenting measurement error[30] and which represents the value below which we expected 95% of the absolute differences between two measurements to lie.[30,31] We also calculated the intrasession reliability of the measurement method with the intraclass correlation coefficient (ICC).[21]

To assess interoperator reproducibility, a Bland-Altman plot showed the difference between both examiners' readings against the average of the two.[21] Provided that the differences were normally distributed and no association between the measurement and the difference was shown, each 95% limit of agreement (LoA) was calculated as the average difference in measurements from the two examiners ±1.96 SD (SD); lower values indicated higher interoperator repeatability.[31] The paired *t*-test also established whether there was a significant systematic bias between measurements from different examiners. The interoperator reliability of the measurement method was calculated with the concordance correlation coefficient (CCC).[32]

TABLE 1. ORA Intraexaminer Repeatability: Within-Subject Standard Deviation (s_w), Precision (1.96 s_w), Repeatability (2.77 s_w) Scores, and Reliability (ICC)

ORA Parameter	s_w (mm Hg)	Precision (mm Hg)	Repeatability (mm Hg)	Reliability (95% CI)
Goldmann-correlated IOP	3.333	6.53	9.23	0.93 (0.87–0.95)
Corneal-compensated IOP	2.384	4.67	6.60	0.78 (0.48–0.89)
Corneal resistance factor	1.946	3.81	5.39	0.93 (0.84–0.96)
Corneal hysteresis	1.454	2.85	4.03	0.84 (0.67–0.92)

RESULTS

Reproducibility Study

The intraexaminer within-subject SDs ranged from 1.45 mm Hg for CH to 3.33 mm Hg for IOP-ORAg (Table 1). Precision ranged from 2.85 mm Hg for CH to 6.53 mm Hg for IOP-ORAg. Repeatability, which ranged from 4.03 to 9.23 mm Hg, was better for CH than for CRF and for IOP-ORAc than for IOP-ORAg. Intraexaminer reliability (ICC) ranged from 0.78 to 0.93 (good to excellent) for the ORA parameters and tended to be slightly better for ORA biomechanical metrics than for ORA IOP readings, though the difference was not significant because all 95% confidence intervals (CIs) overlapped.

Interexaminer reproducibility average differences and their corresponding 95% LoA illustrated the closeness between examiners (Table 2, Figs. 2, 3). No significant difference in the mean value of each parameter was found between examiners; the narrow 95% LoA indicated that measurements obtained by both examiners were interchangeable. CCC values and 95% CIs confirmed this. For all ORA parameters, the CCCs were very high, ranging from 0.81 to 0.93. All CIs excluded the null value of 0, indicating their significance. The markers of corneal biomechanical properties showed a trend toward better CCC values than the ORA IOP measurements, but the difference did not reach statistical significance.

Clinical Study

Of the 262 eyes (median age, 69 years; IR, 55–75 years; range, 19–88 years) included in this segment, 42 had a diagnosis of primary open-angle glaucoma (median age, 63 years; IR, 50–72 years); 220 were normal (median age, 69 years; IR, 55–76 years).

The median IOP in all eyes was 16 mm Hg (IR, 14–18) using GT, 14.5 mm Hg (IR, 12.7–17.3) with IOP-ORAg, and 15.7 mm Hg (IR, 13.22–18.7) with IOP-ORAc. The differences were significant between GT and IOP-ORAg ($P < 0.001$) and between GT and IOP-ORAc ($P < 0.001$).

The median difference in all eyes between IOP-ORAc and IOP-ORAg was 1.5 mm Hg (IR, 0.7–3.0; $P = 0.001$). This median difference did not differ significantly between normal and glaucomatous eyes (1.5 mm Hg [IR, 0.7–3.0] and 1.7 mm Hg [IR, 0.92–3.7], respectively; $P = 0.34$). Figure 4 shows the corresponding scatter and Bland-Altman plots between IOP-ORAc and IOP-ORAg; each 95% LoA was wide (-3.32–5.57 mm Hg), indicating these ORA parameters are not interchangeable.

In this series, 135 eyes (51.5%) had at least a measurement-significant adjustment in the NCT examination after the ORA markers of corneal biomechanical properties were considered. IOP-ORAg was lower than IOP-ORAc by ≥1.5 mm Hg in 26 eyes (9.9%) and higher than IOP-ORAc by ≥1.5 mm Hg in 109 eyes (41.6%). IOP-ORAg was lower than IOP-ORAc by ≥3 mm Hg in 9 eyes (3.4%) and higher than IOP-ORAc by ≥3 mm Hg in 68 eyes (25.9%).

Twenty-two glaucomatous eyes (52.3%) had at least a measurement-significant adjustment in their NCT examination after ORA corneal biomechanical metrics were considered. IOP-ORAg was lower than IOP-ORAc by ≥1.5 mm Hg in 5 eyes (11.9%) and higher than IOP-ORAc by ≥1.5 mm Hg in 17 eyes (40.4%). Outcomes-significant IOP changes were detected in 13 eyes (30.9%). IOP-ORAg was lower than IOP-ORAc by ≥3 mm Hg in 2 eyes (4.76%) and higher than IOP-ORAc by ≥3 mm Hg in 11 eyes (26.2%).

One hundred thirteen normal eyes (51.3%) had at least a measurement-significant adjustment in their NCT examination after ORA markers of corneal biomechanical properties were considered. IOP-ORAg was lower than IOP-ORAc by ≥1.5 mm Hg in 21 eyes (9.5%) and higher than IOP-ORAc by ≥1.5 mm Hg in 92 eyes (41.8%). Outcomes-significant IOP changes were detected in 64 eyes (29.1%). IOP-ORAg was lower than IOP-ORAc by ≥3 mm Hg in 7 eyes (3.2%) and higher than IOP-ORAc by ≥3 mm Hg in 57 eyes (25.9%).

Table 3 shows a comparison of the IOP values, CRF, and CH in normal and glaucomatous eyes. Only CH was not significantly different between the groups.

In the entire series, IOP-ORAc was weakly positively correlated with age ($r_s = 0.18$, $P = 0.005$), whereas IOP-ORAg and GT were not ($r_s = 0.03$, $P = 0.59$; $r_s = -0.03$, $P = 0.67$, respectively). CH and CRF were inversely correlated with age ($r_s = -0.26$, $P < 0.001$; $r_s = -0.19$, $P = 0.002$, respectively).

In glaucomatous eyes, IOP-ORAc was positively correlated with age ($r_s = 0.34$, $P = 0.02$), whereas IOP-ORAg and GT were not ($r_s = 0.22$, $P = 0.16$; $r_s = 0.13$, $P = 0.42$, respectively). CH but not CRF was inversely correlated with age ($r_s = -0.33$, $P = 0.03$; $r_s = -0.12$, $P = 0.44$, respectively).

In normal eyes, IOP-ORAc was weakly positively correlated with age ($r_s = 0.22$, $P = 0.001$), whereas IOP-ORAg and GT were not ($r_s = 0.07$, $P = 0.29$; $r_s = 0.07$, $P = 0.92$, respectively). CH and CRF were inversely correlated with age ($r_s = -0.26$, $P < 0.001$; $r_s = -0.18$, $P = 0.006$, respectively).

TABLE 2. ORA Interexaminer Reproducibility: Mean Difference between Examiners, 95% LoA, and CCC

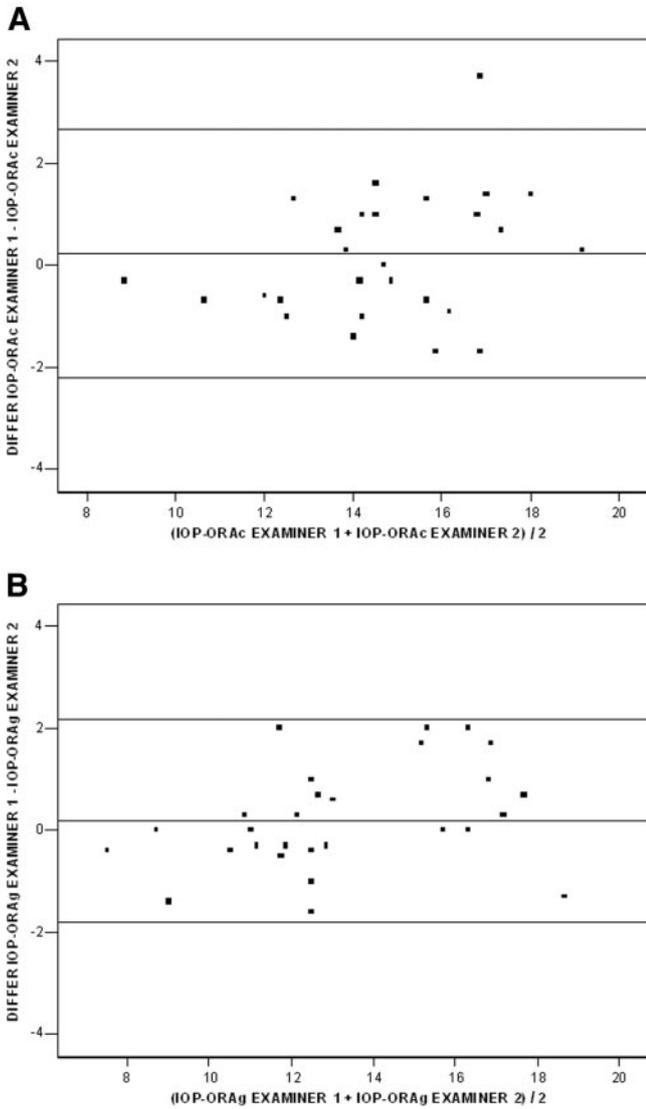| ORA Parameter	Average Difference (mm Hg)	95% LoA (mm Hg)	CCC (95% CI)
Goldmann-correlated IOP	0.05	−2.87, 2.97	0.89 (0.82–0.97)
Corneal-compensated IOP	0.05	−2.68, 2.79	0.81 (0.68–0.94)
Corneal resistance factor	−0.023	−1.38, 1.34	0.93 (0.89–0.98)
Corneal hysteresis	0.06	−1.07, 1.19	0.92 (0.87–0.98)

FIGURE 2. Bland-Altman plot showing the agreement between examiners 1 and 2 in measuring (**A**) IOP-ORAc in mm Hg and (**B**) IOP-ORAg in mm Hg (30 healthy eyes; median age, 29 years; 25% and 75% interquartile ranges, 23.75–33 years).

Discussion

We obtained excellent intraexaminer reliability scores (>0.9) for Goldmann-correlated IOP and CRF (Table 1) and found clinically useful reliability estimates (>0.7)[33] in the IOP-ORAc and CH. These values are similar to those for other tonometers and are considered by previous authors as clinically adequate.[33] The ICCs for rebound tonometry[34] were 0.82, 0.73, and 0.87, respectively, for the first, second, and third examiners, and the ICCs for the GT and tonometer (Tono-Pen; Reichert) were 0.97 and 0.95, respectively.[35] Although no significant difference was found, ORA corneal biomechanical metrics showed a trend toward slightly better than ORA IOP readings, perhaps because corneal tissue biomechanical properties are fairly constant, whereas the IOP changes with the cardiac cycle, and NCT measures the IOP within 1 to 3 ms, making the ocular pulse a crucial source of variability.[36] Kotecha et al.[22] found that the coefficient of variation of ORA IOP measurements was four to five times greater than that of GT IOP measurements. However, they calculated coefficients of variation for CH and CRF nearly twice as high as those for

IOP-ORAc. Differences between the studies might have occurred because our ORA was a commercially available unit, whereas theirs was a prototype,[22] and because we averaged three repeated ORA readings and they did not, with averaging favoring more corneal biomechanical metrics than ORA IOP readings. The ability to yield reliable corneal biomechanical metrics is an outstanding feature of the ORA when determining candidates for keratorefractive surgery or for retreatments.[13-16] Given the growing concern about iatrogenic keratectasia,[12-15] ORA biomechanical parameters may contribute significantly to preoperative screening of patients who are not candidates for keratorefractive surgery or who seek surgical alternatives because of a biomechanically compromised cornea.[12,16]

Table 1 also shows the s_w for each ORA parameter. The precision results corroborated our ICC findings. These three estimates differentiate between statistically and clinically significant changes when different datasets obtained with the same ORA unit are compared.

When the ORA measurements recorded by two examiners were compared, the mean differences were not significantly
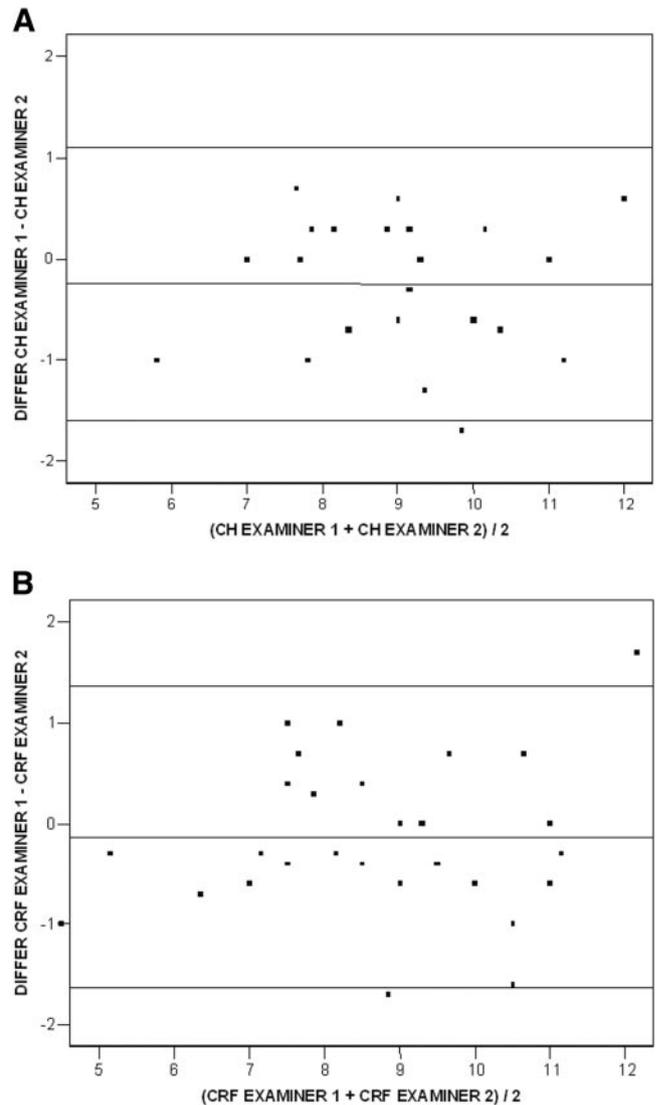

FIGURE 3. Bland-Altman plot showing agreement between examiners 1 and 2 in measuring (**A**) ORA CH (mm Hg) and (**B**) ORA CRF in mm Hg (30 normal eyes; median age, 29 years; 25% and 75% interquartile ranges, 23.75-33 years).
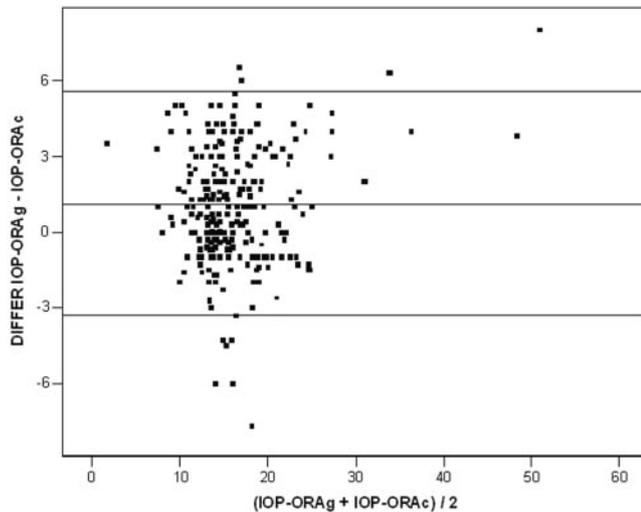
Figure 4. Corresponding scatter and Bland-Altman plots between IOP-ORAc (mm Hg) and IOP-ORAg in mm Hg (220 normal and 42 glaucomatous eyes; median age, 69 years; 25% and 75% interquartile ranges, 55–75 years).

different from 0 (Table 2). Not surprisingly, no difference in ORA measures was found, indicating that whatever the source of the variability, the interobserver variability was random. The 95% LoA (Table 2) provided useful guidelines for the variability expected using the ORA by two examiners. In fact, the amplitude of the 95% LoA was narrow, indicating that ORA readings obtained by both examiners were interchangeable. These data and the CCCs indicated that the reliability of ORA IOP and corneal biomechanical parameters obtained by different examiners were good to excellent: CCCs >0.81 indicated almost perfect agreement,[32,37] as with the four ORA parameters. These findings also indicated that no examiner bias affected the results. These reproducibility data were similar to those of other tonometers: the ICC of the rebound tonometer was 0.82,[34] with similar figures reported for other tonometers.[38–40] Overall, our results suggested that ORA reproducibility was similar to or better than that of other tonometers.[34,35,38–41]

Although it was not a primary aim of the present study to establish a correlation between GT to IOP-ORA measurements, we also studied the GT to determine whether IOP-ORAg was similar to GT and whether ORA parameters and GT are influenced by age to the same extent in the same group of patients. We found significant systematic differences between the IOP-ORAc and IOP-ORAg provided by the ORA and the IOP-GT readings; the latter provided higher readings. Such differences cannot be attributed to bias related to the order of IOP measurements because repeated measures lead to a tonometric effect that reduces[24,42] the IOP and because topical anesthetics may cause corneal drying and an associated drop in IOP,[26,27] in contrast to the current results. The systematic difference be-

tween our IOP-ORAg and GT, which was not as large as reported after an ORA prototype was analyzed,[23] agrees with the findings of others[16,19] and probably represents a modest calibration error that can be further adjusted.[22] Nevertheless, NCTs are useful for population surveys; no corneal contact or topical anesthesia are needed, which eliminates corneal disturbance,[43] and the instruments lower the risk for transmitting communicable diseases.[44] However, great variations occur with NCTs,[45] partially because of the cardiac pulse.[25,36,46–49] When comparing three NCTs with the GT, we found better sensitivity and positive predictive values for detecting IOP >20 mm Hg than in the present study using IOP-ORAc and IOP-ORAg.[50]

The median IOP difference between IOP-ORAc and IOP-ORAg was 1.5 mm Hg, which was not significantly different from that comparing normal with glaucomatous eyes and was similar to that of other studies.[23] Bland-Altman analysis confirmed that the parameters are not interchangeable and that they represent two different estimations. We found that considering the biomechanical properties measured by the ORA resulted in a considerable modification (≥3 mm Hg) in 29% of the IOP measurements, a higher percentage than the 20% of the IOP measurements Shih et al. found considering the effect of central corneal thickness (CCT),[29] which suggests that the ORA integrates more complex and complete biomechanical properties than CCT does on its own. This 29% was essentially uniform across normal and glaucomatous eyes, and 25% to 26% corresponded to higher IOP-ORAg readings than IOP-ORAc readings. Thus, in nonoperated eyes, IOP-ORAc measurements showed that nearly 25% of persons had a notably lower reading than that obtained with a conventional NCT and that another 3% to 4% had markedly higher IOP measurements than those obtained with a conventional NCT. These adjustments may lead to, respectively, elimination of unneeded diagnostic and therapeutic actions and early diagnosis and timely treatment of truly glaucomatous eyes.[29,51–53]

In our study, ORA corneal biomechanical parameters showed that the median CH was 9.3 mm Hg in glaucomatous and normal eyes compared with 9.6 mm Hg reported previously in normal eyes.[11] Herndon[4] and Luce[11] reported that CH is independent of IOP. Laiquzzaman et al.[17] found no significant relationship between CH and IOP. Interestingly, Congdon et al.[20] found that lower CH is associated with visual field damage in glaucomatous eyes. CCT and CH may constitute pressure-independent risk factors for glaucoma, perhaps related to eye wall composition.[20] Furthermore, CH does not vary diurnally,[17,18] in contrast to IOP[17,18] and corneal thickness.[18]

There is a likely effect of age on physical corneal properties.[22,54,55] We analyzed 220 healthy adults at an interquartile age range of 55 to 76 years, when most glaucoma diagnoses are made.[56,57] In contrast to that observed for a comparably narrower age range in a pediatric population,[19] CH and CRF decreased in normal eyes with increasing age, which corroborates analyses from a mixed population of normal and glaucomatous eyes.[22] Such results can be explained because the

TABLE 3. Comparison of Evaluated Data between Normal and Glaucomatous Eyes

Values	Number	IOP Goldmann	Goldmann-Correlated IOP in ORA	Corneal-Compensated IOP in ORA	Corneal Resistance	Corneal Hysteresis
Normal	220	15 (13–17)	14 (12.3–16.7)	15 (13–18)	9.3 (8–10.5)	9.3 (8–10.65)
Glaucoma	42	18 (14.25–20)	17.3 (14.45–22.07)	18.3 (15.45–21.4)	10.3 (8.9–12)	9.3 (7.22–10.77)
*P**		<0.001	<0.001	<0.001	0.006	0.83

Data are expressed as median values in mm Hg (75% interquartile range).
* Mann-Whitney nonparametric test.

aging cornea increases in rigidity and decreases in viscoelasticity with time,[22,54,55] which is consistent with the inverse correlation we found between CH and age but not with the weak negative correlation between CRF and age. However, in glaucomatous eyes, the CRF did not correlate with age compared with CH, possibly because although corneal rigidity should be expected to increase with age, likely because of additional cross-linking, the impact of increasing IOP on CRF is unknown.

Interestingly, in normal and glaucomatous eyes, IOP-ORAc but not IOP-ORAg or GT, readings correlated significantly with increasing age. Further longitudinal studies may confirm this preliminary association.

This study had limitations. The number of patients with glaucoma was relatively small, but statistical differences in GT, IOP-ORAc, and IOP-ORAg were found between eyes with and without glaucoma. Nevertheless, the present study was the largest independent clinical study evaluating ORA to date. In addition, no measurements of corneal thickness were considered; however, the effect of corneal thickness was included in other corneal parameters, such as CRF, and the relationship between CCT and ORA parameters has been studied extensively.[22,23,58,59] Finally, it is difficult to know whether the definition of measurement-significant ($\geq$1.5 mm Hg) and outcomes-significant ($\geq$3.0 mm Hg) are useful in IOP adjustments, but these cutoff values were defined previously.[29] Despite limitations, this study was the first to evaluate the reproducibility of a production ORA unit and the practical effect of corneal biomechanical parameters on IOP measurements in nonoperated eyes. We believe the current report is a valuable contribution to the assessment of IOP measurements with a new NCT and noninvasive markers of corneal biomechanical properties.

Our results showed overall good intraexaminer and interexaminer reproducibility for ORA measurements in nonoperated eyes, with the corneal biomechanical metrics showing a trend toward the performance of slightly better than the IOP estimates. Consequently, the ability to provide reliable readings heralds a relevant role for the ORA in diagnosing glaucoma[4,22] and in assessing cornea patients or candidates for corneal-weakening surgeries.[12–16] This study also showed that accounting for the ORA corneal biomechanical metrics in the IOP measurement would associate an outcomes-significant adjustment of the NCT reading in 29% of the tested eyes, which has overt screening and cost-related implications.[52,60] Finally, patients with both normal and glaucomatous eyes have significant associations between increasing age and decreasing CH and CRF and increasing IOP-ORAc but no association with other IOP estimates. Future studies should address whether IOP-ORAc is a better estimate of the true IOP than other existing tonometry alternatives in nonoperated eyes. The risk for glaucoma increases with age,[56,57] and elevated IOP is a risk factor for glaucoma[56,57] and the one that constitutes the main therapeutic target in this prevalent eye disease.[4,56,57]

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