Comparison of Three Intraocular Pressure Measurement Methods Including Biomechanical Properties of the Cornea

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Purpose. The aim of this study was to show the usefulness of three methods for measuring IOP: Goldmann applanation tonometry, rebound tonometry, and Ultra-High-Speed Scheimpflug technology.

Methods. The examined group consisted of 96 patients (192 eyes), including 63 women and 33 men with a mean age of 59.3 ± 19.9 years. Together, 152 healthy eyes and 40 eyes with different pathologies were examined. Intraocular pressure was measured using the Goldmann applanation tonometer (GAT), the Icare Pro rebound tonometer (RT), and Ultra-High-Speed Scheimpflug technology (UHS ST; Corvis ST with pachymetry). Additionally, corneal pachymetry was conducted with a Scheimpflug camera (Pentacam) and an Ultrasound Pachymeter (A-scan Plus) as a comparison for Corvis ST pachymetry.

Results. The mean IOPs were 15.6 ± 3.75 mm Hg, 15.6 ± 3.5 mm Hg, and 16.1 ± 4.0 mm Hg when measured with the GAT, the RT, and the UHS ST, respectively. The mean central corneal thickness (CCT) was 543.7 ± 52.7 μm, 547.9 ± 54.0 μm, and 556.25 ± 38.8 μm as measured with the UHS ST, the Pentacam, and the Ultrasound Pachymeter, respectively. In comparison between devices, there was a significant difference between IOP values measured with the GAT and the RT versus the UHS ST ($P < 0.001$), and there was no significant difference between GAT and RT ($P = 0.5$). No significant differences were observed in CCT measured with the UHS ST, Pentacam, and Ultrasound Pachymeter.

Conclusions. We showed that the RT Icare Pro ensures IOP measurements that are more comparable with the measurements obtained with the GAT than the measurements that are provided by UHS ST.

Keywords: intraocular pressure, corneal biomechanics, tonometry

Elevated IOP is the basic measurable pathogenic factor of glaucomatous optic nerve injury in primary and secondary glaucoma and also occurs as a result of other eye diseases or the consequence of many ophthalmic procedures.[1,2] Proper measurement of IOP is one of the basic tools for glaucoma patient follow-up; however, many factors can influence the measurement accuracy. The factors that influence IOP measurements are mostly central corneal thickness (CCT), biomechanical properties of the cornea (tissue elasticity derivatives), and corneal astigmatism.[3–6] A reduction in IOP by only 1 mm Hg evokes a 10% reduction in the risk for visual field deterioration and a 10% improvement in outcome for patients suffering from ocular hypertension.[7] Therefore, investigating accurate and repeatable methods for measuring IOP, which includes all factors affecting IOP values, is very important.[8]

The Goldmann applanation tonometer (GAT, Haag-Streit AG, Koeniz, Switzerland), which uses force proportional to the IOP to flatten the corneal surface, is still the reference standard for IOP measurement.[9,10] The GAT is strongly affected by the CCT and requires CCT correction to adjust IOP measurements.[11,12] The Icare Pro rebound tonometer (RT; Icare, Helsinki, Finland) and Ultra-High-Speed Scheimpflug technology (UHS ST; Corvis ST; Oculus, Wetzlar, Germany) are the new alternative techniques for IOP measurements. The Icare Pro tonometer is based on a rebound measuring principle, in which a very light probe is used and launched against the corneal surface to make fleeting contact. The resilience rebound of this probe is processed into the IOP value. The CCT also affects this method, and the Icare Pro tonometer requires its own formula for CCT correction.[13–15] The UHS ST is a noncontact air-puff–type tonometer combined with pachymetry; it automatically calculates the CCT correction and the biomechanical properties of the cornea.[16,17] In this study, we compare these new IOP measurement techniques with GAT as the reference standard.

Methods

Examined Group

The examined group consisted of 96 patients, and 192 eyes were examined. Patients were recruited from the Ophthalmol-

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Table 1. Mean IOP for Each Measurement Method

	n	Mean IOP	SD	Minimum IOP	Maximum IOP	Normal Distribution*
GAT	192	15.557	3.7454	9.0	39.0	<0.0001
GAT+CCT	192	15.708	3.6924	10.0	38.3	<0.0001
RT	192	15.564	3.5275	6.2	33.4	<0.0001
RT+CCT	192	15.715	3.3492	7.1	32.7	<0.0001
Corvis	192	16.105	4.0655	9.0	43.0	<0.0001

* Kolmogorov-Smirnov test.

ogy Clinic of Medical University of Silesia, Railway Hospital, in Katowice, Poland. The mean age of the patients was 59.3 ± 19.9 years. Among the 192 eyes, 152 presented no pathologies, and 40 eyes were diagnosed with different ocular pathologies (13 eyes with glaucoma, 12 with corneal edema less than 700 µm, and 15 with keratoconus). The study was approved by the Ethical Scientific Committee. The research followed the tenets of the Declaration of Helsinki. Before all procedures, patients were informed about the purpose of the study, and signed informed consents were obtained.

Equipment

Intraocular pressure was measured using a slit lamp–mounted GAT, an RT with the patient in a sitting position, and a UHS ST (Corvis ST). To adjust the IOP, the CCT was measured with two Scheimpflug technology devices, a Scheimpflug camera (Pentacam HR; Oculus, Wetzlar, Germany) and Corvis ST, and compared with ultrasound pachymetry (A-scan Plus; Accutome, Inc., Malvern, MA), which is accepted as the reference standard for CCT measurement. For measurements with the GAT and the RT, the CCT correction was calculated. For the GAT, the Ehlers formula was used. For the RT, the manufacturer's recommendation calculation was used: $PCCT = PPRO + 0.02(545 - CCT)$, where PCCT is the CCT-corrected IOP, PPRO is the IOP value measured with Icare PRO, and CCT is the measured CCT value.

Study Design

The study was designed as a prospective, comparative analysis of the IOP and CCT values obtained from both eyes of the examined patients. The exclusion criterion was the presence of a corneal wound or scarification, which could affect the measurements. Because IOP tends to fluctuate over time, patients were examined with all three methods in the shortest possible time to capture the most current IOP. The applied methods are characterized by a various invasiveness, which means that they can evoke changes in the after-measurement IOP. To avoid recording daily IOP fluctuations or after-measurement IOP fluctuations, each consecutive measurement was performed in the same sequence (i.e., right eye, left eye and again right eye, left eye). The IOP was first measured twice using the RT, and then two measurements with the GAT (after local topical anesthesia with 0.5% proxymetacaine hydrochloride, Alcaine; Alcon, Fort Worth, TX) were obtained. Finally, patients were examined twice with the Corvis ST; this measurement was saved for last because the air-puff tonometer affects the after-measurement IOP the most significantly. From all values, the mean IOP for each eye was calculated. Between each pair of measurements, a 5-minute break was taken to minimize after-measurement fluctuations in the IOP. The CCT was measured 1 hour after all IOP procedures. Each measurement method was performed by different experienced physicians, in separate rooms, and the results were cross-masked from the other measurements.

Statistical Analysis

Statistical analysis was performed with IBM SPSS Statistics 20 (IBM, Armonk, NY) and MedCalc 12.3.0: (MedCalc Software, Ostend, Belgium). Descriptive statistical results are presented as the mean ± SD. The Kolmogorov-Smirnov test was used to evaluate whether the data were normally distributed. Measurements were compared using a paired-samples Wilcoxon test. For correlation analysis between the IOP value and the CCT, the Spearman rank correlation coefficient was used due to the deviation of many parameters from linear correlation. Bland-Altman plots were created to estimate the agreement among the three tested methods, and 95% limits of agreement were also yielded as the mean ± 1.95 SD of the difference. A P value less than 0.05 was considered significant.

Results

The mean IOPs before and after CCT correction were 15.557 ± 3.740 mm Hg and 15.708 ± 3.690 mm Hg, respectively, when measured with GAT, and 15.564 ± 3.520 mm Hg and 15.715 ± 3.350 mm Hg, respectively, when measured with RT. For the Corvis ST, the mean corrected IOP was 16.105 ± 4.060 mm Hg (Table 1). The mean CCTs were 556 ± 38 µm for the ultrasound pachymetry, 543 ± 52 µm for the Corvis ST, and 547 ± 54 µm for the Pentacam, and there was no significant difference among the CCT measurements ($P > 0.05$, Wilcoxon paired test).

All values in the groups and subgroups were not normally distributed; thus, for statistical analysis, nonparametric tests were used. The exception was the linear Pearson coefficient, which was selected for cluster analysis because we built our model on linear dependency rather than on outlier values.

In a single IOP values analysis, the highest IOP was typically measured with the Corvis ST (48.5% of all measurements), and

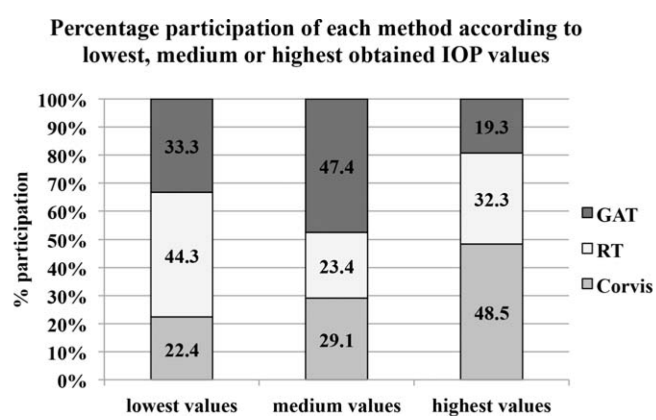

Figure 1. Percentage participation of each measurement method according to lowest, medium, or highest IOP values obtained for each eye. In most cases the highest values were measured with Corvis and the lowest with RT Icare Pro.

Table 2. Spearman Rank Correlation Coefficient for GAT and RT Versus CCT

	Pachymetry Pentacam	Pachymetry Corvis
GAT		
Correlation coefficient	0.319	0.300
Significance level *P*	<0.0001	<0.0001
n	192	192
GAT with CCT		
Correlation coefficient	−0.193	−0.158
Significance level *P*	0.0034	0.0294
n	192	192
RT		
Correlation coefficient	0.349	0.330
Significance level *P*	<0.0001	<0.0001
n	192	192
RT with CCT		
Correlation coefficient	−0.186	−0.124
Significance level *P*	0.05	0.0869
n	192	192

the lowest IOP was measured with the Icare RT (44.3% of all measurements) (Fig. 1). In the Wilcoxon paired test analysis, no significant differences were observed between the IOP values measured with GAT and Icare RT ($P > 0.05$). There was a significant difference between Corvis and GAT (Wilcoxon test, $P < 0.001$) and between Corvis and RT (Wilcoxon test, $P < 0.03$). Using the Spearman correlation test, the relation between the IOP and the CCT was checked; in addition, the CCT was corrected for GAT and RT. In this analysis, the CCT significantly affected the IOP values before correction (for GAT, $r = 0.319$ and $P < 0.0001$, and for RT, $r = 0.349$ and $P < 0.0001$). After CCT correction, the values showed negative, weak, but still significant correlations (for GAT, $r = -0.193$ and $P = 0.03$, and for RT, $r = -0.186$ and $P = 0.05$) (Table 2, Fig. 2). Bland-Altman plots were constructed to show agreement between GAT and RT, GAT and Corvis, and RT and Corvis before and after CCT correction. For the GAT-RT comparison, the mean of the difference was 0.0 and the 95% limit of agreement was +4.5 mm Hg before the CCT; these values were unchanged after CCT correction. For the GAT-Corvis comparison, the mean of the difference was –0.5 before CCT with 95% limit of agreement of +4.4 mm Hg; these values were –0.5 and +5.5 mm Hg, respectively, after CCT correction. For the RT-Corvis comparison, the mean of the difference was –0.5 and the 95% limit of agreement was +5.4 mm Hg before CCT correction; and after CCT correction, –0.5 and +6.3 mm Hg, respectively (Fig. 3).

The corneal functional properties were analyzed using UHS ST. For each cornea, the following parameters were calculated: deformation maximum amplitude (Def. Amp. Max.), the maximum amplitude of deflection at the corneal apex (highest concavity) (mm); first A time, the time from the start until the first applanation (ms); first A length, the cord length of the first applanation (mm); A1 velocity, corneal speed during the first applanation moment (m/s); second A time, the time from the start until the second applanation (ms); second A length, the cord length of the second applanation (mm); A2 velocity, corneal speed during the second applanation moment (m/s); and HC time, the time from starting until the highest concavity

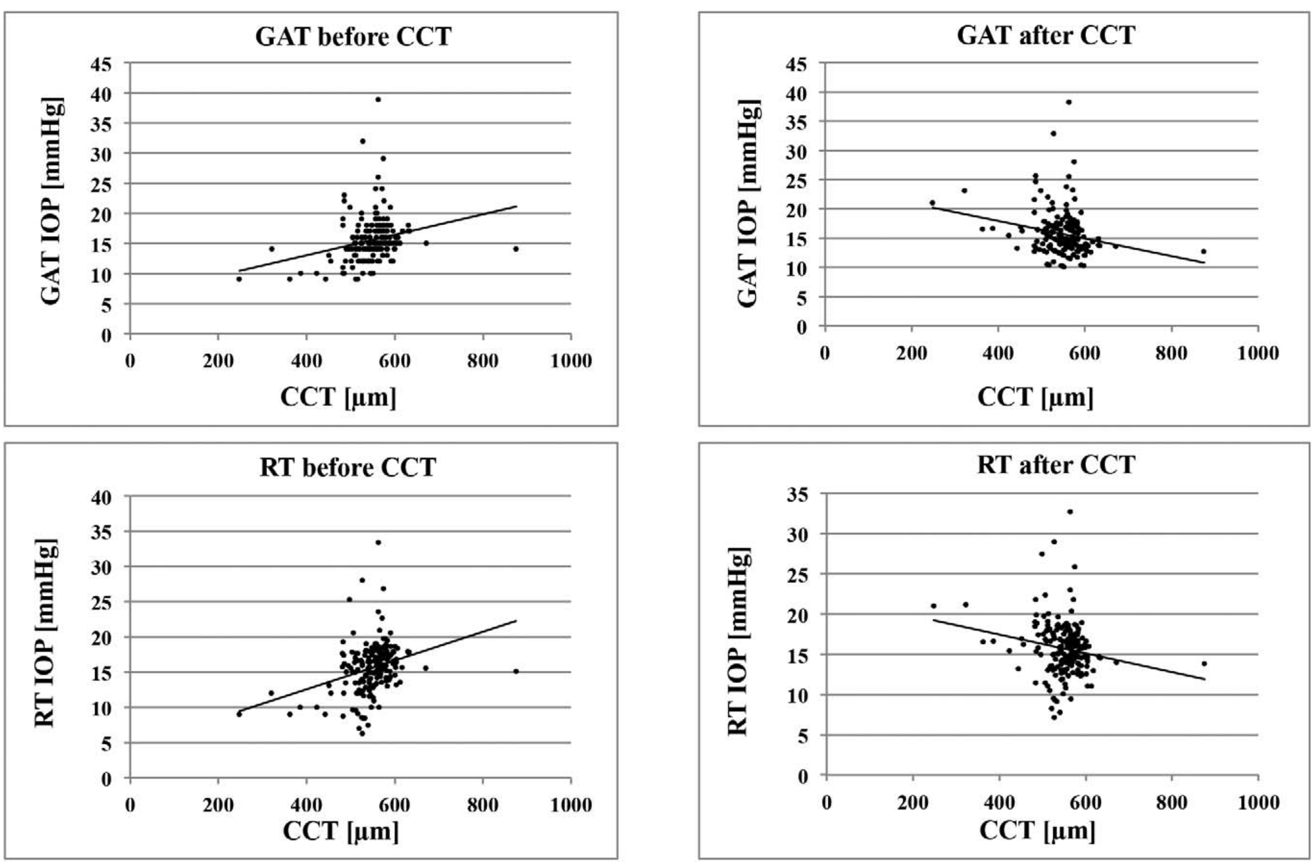

Figure 2. Correlation plots for the GAT and RT before and after CCT correction (*x*-axis, IOP values [mm Hg], *y*-axis, CCT values [µm]).

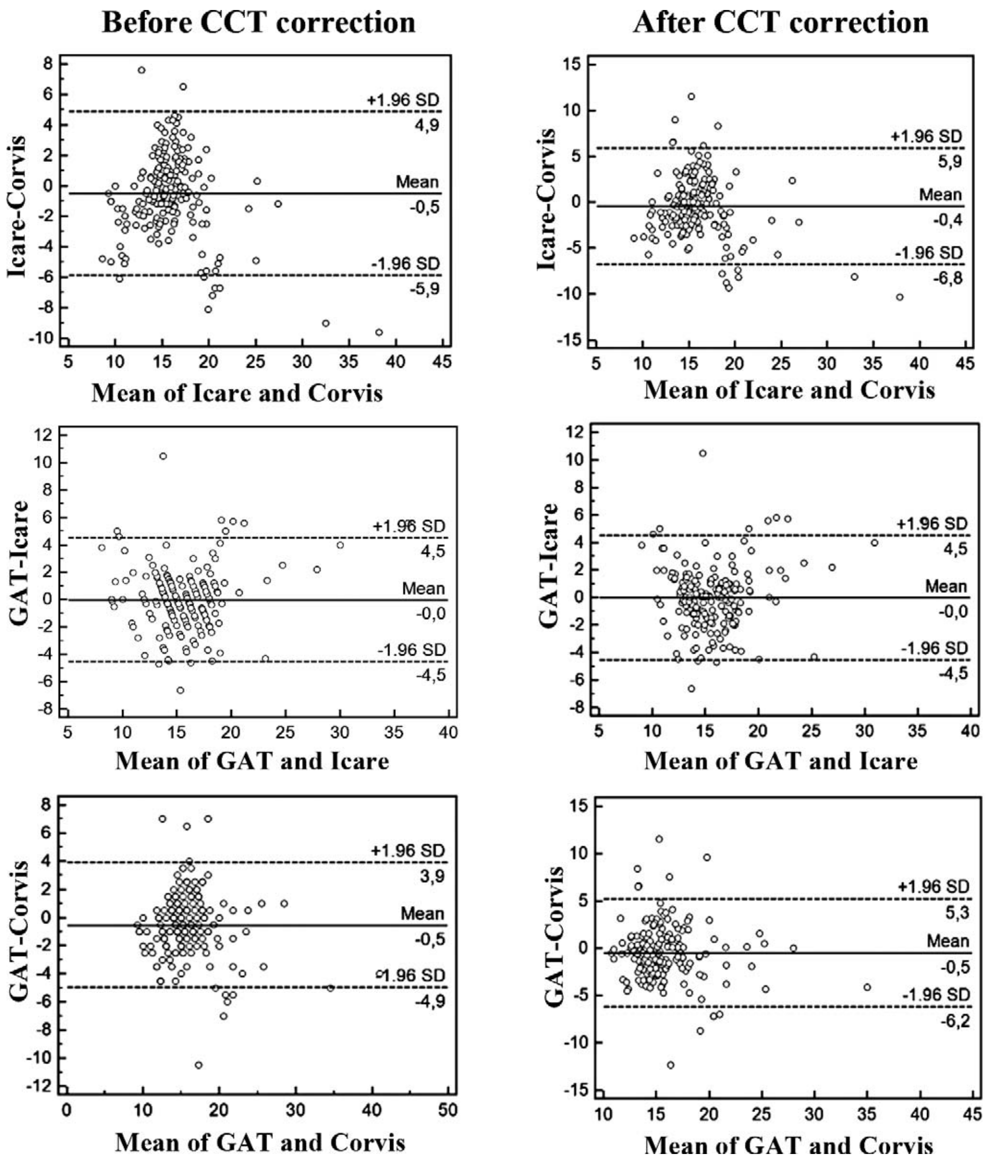

Figure 3. Bland-Altman plot of the agreement between the applied IOP measurement methods (before and after CCT correction). *Bold line*, the mean of the difference between these two methods; *dashed line*, 95% limits of agreement.

is reached (ms) (Fig. 4). These parameters were compared among normal, keratoconic, glaucomatous, and swollen corneas (CCT between 570 and 700 µm). There was a significant difference among the A1 and A2 times and velocities and the Def. Amp. Max. when comparing glaucomatous versus bullous corneas, keratoconic versus glaucomatous corneas, healthy versus glaucomatous corneas, keratoconic versus bullous corneas, and keratoconic versus healthy corneas (Table 3).

An analysis of the correlations showed strong, significant dependence among the GAT, RT, and Corvis IOP values before the CCT correction and the corneal properties expressed as the A1 and A2 times, A1 and A2 velocities, and Def. Amp. Max. After CCT correction, there was medium or weak dependence between these values. The correlation coefficients are presented in Table 4. In the cluster analysis using the Pearson correlation coefficient, the variables measured with Corvis were grouped in four supraclusters, where A1 time and A2 velocity were in one supracluster together with IOP (the strongest relation). The shortest distance from the IOP cluster was observed in the case of A1 time, A2 velocity, peak distance, and radius (Fig. 5).

Finally, to evaluate the agreement between the two new IOP measurement methods (Corvis and RT), the three sites' difference was compared between each value. The mean difference in the IOP values was 0.01 mm Hg between the RT and the GAT and 0.44 mm Hg between the Corvis and the Icare. When analyzing individual patients' measurements, the difference was more than 3 mm Hg in 33 cases (17.1%) when comparing the GAT and the Icare, and in 45 cases (23.4%) when comparing the GAT and the Corvis (Fig. 6).

Discussion

The present study compared new IOP measurement technologies; specifically, the new Icare Pro RT and UHS ST, with the GAT in healthy eyes and in eyes with glaucoma, keratoconus, and corneal edema. Because IOP may depend on mechanical properties more than just on CCT, the IOP values were analyzed regarding the mechanical properties of the cor-

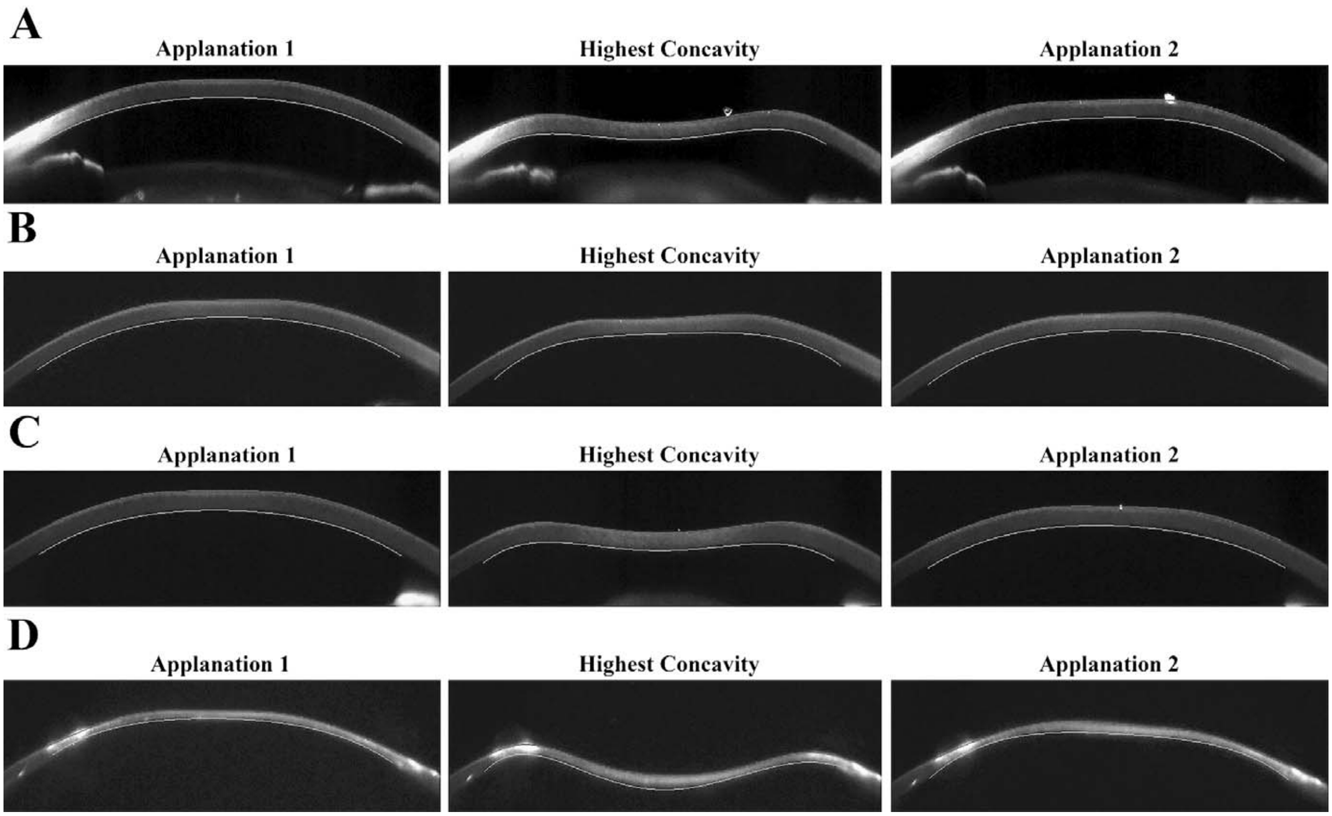

FIGURE 4. Scheimpflug images of corneas during air deflection. (A) Normal eye. (B) Glaucomatous eye. (C) Swollen cornea. (D) Keratoconic cornea.

nea.[18,19] These mechanical property coefficients were obtained using the UHS ST device.

In most reports, a tonometer with limits of agreement within ±3 mm Hg compared with the GAT is clinically acceptable and therefore interchangeable.[20,21] In our report, the mean difference between the analyzed tonometers was lower than the agreed limit; however, in single measurements, 17.1% of values from the RT and 23.4% from the Corvis showed a difference of more than 3 mm Hg compared with the GAT. Although the mean values for both Corvis and RT did not cross

TABLE 3. Comparison of Corneal Properties of Normal, Glaucomatous, Keratoconic, and Swollen Corneas

	Def. Amp. Max., mm	A1 Time, ms	A1 Length, mm	A1 Velocity, m/s	A2 Time, ms	A2 Length, mm	A2 Velocity, m/s	HC Time, ms
Normal								
Mean	1.06	7.71	1.74	0.15	21.22	1.74	−0.29	17.53
SD	0.13	0.73	0.25	0.04	5.12	0.43	0.10	0.89
Glaucoma								
Mean	0.80	8.60	1.81	0.10	19.63	1.85	−0.17	17.74
SD	0.12	2.72	0.19	0.05	5.93	0.65	0.08	0.45
Edema								
Mean	1.02	7.95	1.69	0.14	22.5	2.03	−0.29	17.67
SD	0.06	0.38	0.18	0.03	0.45	0.31	0.05	0.51
Keratoconus								
Mean	1.17	7.46	1.71	0.17	23.01	1.76	−0.41	17.98
SD	0.18	0.84	0.20	0.05	0.93	0.50	0.12	0.43
Relation, *P* values								
Keratoconus vs. bullosa	0.04	0.05	NS	0.05	0.05	NS	0.05	NS
Glaucoma vs. bullosa	0.0003	0.004	NS	0.03	0.001	NS	0.003	NS
Keratoconus vs. glaucoma	0.0001	0.003	NS	0.004	0.0001	NS	0.0001	NS
Normal vs. bullosa	NS	NS	NS	NS	NS	0.01	NS	NS
Normal vs. glaucoma	0.0001	0.0001	NS	0.001	0.0001	NS	0.00002	NS
Normal vs. keratoconus	0.01	0.02	NS	NS	0.01	NS	0.0008	0.02

TABLE 4. Correlation Among the IOP Measurements, CCT Correction, and Mechanical Properties of the Cornea

	Correlation Coefficient						
	Def. Amp. Max., mm	**A1 Time, ms**	**A1 Length, mm**	**A1 Velocity, m/s**	**A2 Time, ms**	**A2 Length, mm**	**A2 Velocity, m/s**
GAT IOP	**−0.6**	**0.7**	0.005	**−0.5**	**−0.6**	0.08	**0.5**
GAT IOP with CCT	**−0.4**	**0.4**	0.01	**−0.3**	**−0.5**	−0.001	**0.3**
RT IOP	**−0.6**	**0.65**	0.05	**−0.41**	**−0.6**	0.04	**0.5**
RT IOP with CCT	**−0.4**	**0.4**	0.05	**−0.2**	**−0.5**	−0.01	**0.3**
Corvis IOP	**−0.7**	**0.9**	0.03	**−0.5**	**−0.8**	0.06	**0.6**

Correlation coefficients marked with bold letters are significant ($P < 0.05$). The strength of dependence is described using correlation coefficient values, with $0.2 < r < 0.4$ denoting poor correlations; $0.4 < r < 0.6$ denoting medium correlations, and $r > 0.6$ denoting quite strong and strong correlations; r "+" means a positive correlation, and r "−" means a negative correlation.

the limit difference in comparison with GAT, there was additionally no significant difference between single values measured with RT in comparison with the GAT, which shows that this tonometer could be used interchangeably with the GAT and is in agreement with a previous report.[22] The IOP measured with the Corvis (an air-puff tonometer) showed the highest values of all methods, which is comparable with many previous reports that have shown that noncontact tonometers tend to overestimate IOP values.[20,23–25] Additionally, if we consider that there was a higher percentage of unacceptable measurements with this tonometer, this tonometer is not completely reliable. As proof, Bland-Altman plots can be used, where the 95% limits of agreement presented for Corvis-GAT are wider than for RT-GAT. In contrast to our findings, Hong et al.[26] reported an underestimation of IOP values measured with Corvis in comparison with GAT; however, this underestimation is described as an unknown discrepancy. As opposed to the IOP measurements, Corvis can be used interchangeably with ultrasound pachymetry (the reference standard for CCT) or the Pentacam (another device for CCT measurements based on Scheimpflug technology), which was already reported as a reliable method for measuring corneal thickness.[27]

The GAT and RT showed a medium-strength correlation between IOP and CCT. After recalculating the IOP using the CCT correction formulas (Ehlers formula for GAT and the manufacturer's formula for RT), we observed a reduction of correlation strength. For GAT, the correlation remained significant with signs of overestimation, similar to previous studies.[28,29] For RT, significance was marginal. This observation shows that although the applied correction formula modulated the IOP according to CCT (i.e., it lowered the correlation strength), this modulation was not sufficient to obtain IOP values that were totally independent of the CCT. Output IOP values for RT seemed to be less affected by the residual CCT effect than the GAT IOP, which is a promising observation in the search for the "true" IOP. There are numerous CCT correction methods to adjust the GAT IOP; however, they remain in agreement with Ehlers formula, which was selected in our study following previously described tonometer comparisons.[30] All known formulas yield different levels of error, but IOPs that have been adjusted with different methods are strongly correlated with each other.[28–31] Although using CCT correction in clinical practice for individual patients is not currently advised because adjusting the IOP does not

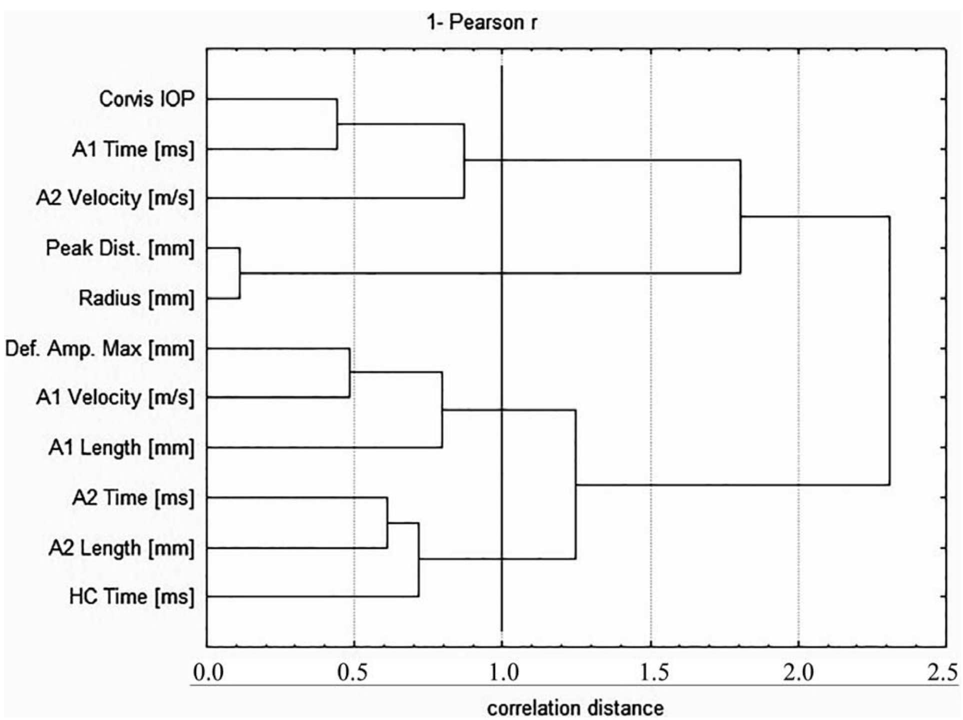

FIGURE 5. Cluster analysis for variables measured with the Corvis ST, based on the Pearson correlation coefficient.

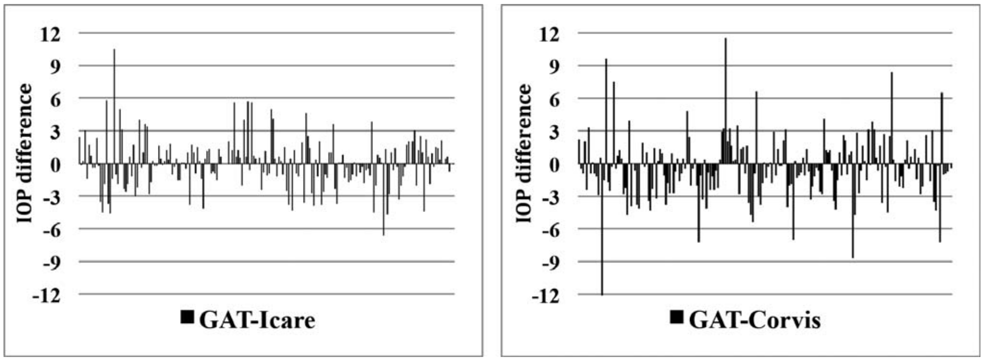

FIGURE 6. Single measurement differences between IOP values measured with GAT and the Icare (RT) and measured with the GAT and Corvis.

improve glaucoma prediction, the application of CCT correction in experimental studies, especially those performed with large groups, allows for the additional evaluation of new methods.[28,31]

For all methods, there was a strong correlation observed between the cornea's mechanical properties (mostly the time and velocity of each period of cornea deflection) and the IOP values, which is presented in Table 4. This correlation was not reduced after standard CCT correction; therefore, we expect that the IOP values, based on the cornea properties, were not accurate because they were still affected by these factors (even for Corvis, which should automatically correct the IOP values according to the mechanical attributes). Drawing conclusions about the value of each coefficient for biomechanical measurements is difficult because of the very limited available technical description of the Corvis device. However, deflection amplitude (Def. Amp. Max.) and first applanation time (first A time) have been reported as the best repeatable and reproducible indicators and should be considered as the most valuable for describing corneal biomechanics.[16,17,32] Additionally, in the Pearson correlation analysis, which is shown in Figure 5, first A time had the strongest correlation with Corvis IOP, which means that this coefficient could be especially considered in further studies on the relationship between IOP and corneal biomechanics.

There were differences in the subgroups, which shows that more factors influence the accuracy of the IOP measurements, including CCT, corneal mechanical properties, and other associated pathologies. The results presented in Table 3 show that the mechanical properties of the cornea cannot be understood in relation to corneal thickness alone. For example, the biomechanical coefficients within a group with an increased mean CCT (bullosa, mean CCT 634 μm) compared with the healthy group (mean CCT 551 μm) showed no significant difference, whereas the glaucoma group, which had a mean CCT (558 μm) that was similar to the healthy group, showed a significant difference in comparison with swollen corneas. This phenomenon can be explained by considering the mechanism of corneal changes in glaucoma and corneal edema; glaucoma is affiliated with IOP-associated increases in corneal diameter, which can cause corneal radius variation and redistribute the mechanical forces within the corneal tissue.[33]

A limitation of our study was the small size within the groups representing eye pathologies, which prevented reliable comparative statistical analyses within these groups. Another limitation was IOP measurements with constant order of applied devices, which once could cause repeatable bias (however minimized by introducing independent persons for each performed method), but on the other hand reduced the influence of after-measurement IOP fluctuations. Application of the Ehlers CCT correction formula for IOP adjustment can be considered controversial; however, it was applied not to obtain the "true" IOP but rather as an additional tool to better evaluate the devices. Although there are divergent opinions about the usefulness of this formula, it remains in clinical use.

CONCLUSIONS

We showed that rebound tonometer Icare Pro ensures IOP measurements that are more comparable with the measurements obtained with a GAT than those provided by UHS ST.

The latter device gives significantly higher IOP values than the two former techniques but can be used interchangeably with Pentacam and ultrasound pachymetry for CCT measurement.

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