ORIGINAL ARTICLE

Variability of Corneal Deformation Response in Normal, Keratoconic, and Post-LASIK Cases

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ABSTRACT

Purpose: The purpose of the study was to determine the repeatability of corneal biomechanical properties obtained with Corvis-ST in normal, keratoconic, and post-LASIK eyes and compare the results between groups. **Material and Methods:** A total of 30 eyes of 15 subjects in each of the normal, keratoconus, and post-LASIK groups underwent Corvis-ST measurements. The intra-observer intraclass correlation coefficient (ICC) and precision were calculated to evaluate the repeatability of measurements for each group. One-way ANOVA and *post hoc* test were used for comparison of precision between groups. **Results:** CCT, intraocular pressure (IOP), A1-time, corrected IOP had excellent repeatability in all of the three study groups. Regarding the other parameters, A1-time, A2-time, A1-length, and A2-velocity showed excellent repeatability (ICCs >0.90), deformation amplitude demonstrated close to excellent (ICC:0.895), and the parameters of A1-velocity and radius showed good repeatability in normal corneas (ICCs>0.75). In the keratoconus group, deformation amplitude and A1-time showed excellent repeatability (ICCs>0.90), and the parameters of A2-time, A1-length, A1-velocity, A2-velocity, and radius revealed good repeatability (ICCs>0.75). In post-LASIK eyes, A1-time, A2-time, A2-velocity, deformation amplitude, and radius demonstrated good repeatability (ICCs>0.75). Comparing the groups, the precision of A1-length was better in normal and keratoconus corneas compared to the post-LASIK group (P = 0.003 and P = 0.004, respectively). A2-length had a better precision in the normal group compared to keratoconus (P = 0.025). PD showed better precision in normal corneas compared to post-LASIK eyes (P = 0.008). **Conclusions:** The results of this study demonstrated good repeatability for most of Corvis-ST measured indices in the normal and keratoconus groups and a considerable number of these variables in the post-LASIK eyes.

Key words: Corneal deformation response, keratoconus, LASIK, normal eye, scheimpflug imaging

INTRODUCTION

Corneal biomechanical properties play a fundamental role in the normal corneal function and are implicated as a critical factor in the development of different corneal pathologic states, such as keratoconus and post-LASIK ectasia that represents classical examples of corneal biomechanical failure.[1-4] In addition, they affect different aspects of clinical assessments like intraocular pressure (IOP) measurement,[5] progression of pathologies like glaucoma,[6,7] and response to different surgeries like refractive surgery.[8-10] Hence, characterization of corneal biomechanical properties could be potentially valuable and applicable from both diagnostic and therapeutic aspects.

In the past, biomechanical assessments in clinical practice were hampered by the complexity of the procedure and their limitation to *ex vivo* laboratory measurements. In recent years, there have been great advances with the introduction of non-invasive methods which allow for measurement of biomechanical parameters in a clinical setting. The ocular response analyzer (Reichert Ophthalmic Instruments, Buffalo,

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NY, USA), a dynamic bidirectional corneal applanation, was the first device introduced in 2005, which determines several parameters from inward and outward applanation in response to the pressure applied by an air-puff jet.[11]

A recent development in this field was the introduction of the Corvis-ST (Oculus Optikgeräte GmbH, Wetzlar, Germany),[12] which is based on dynamic ultrahigh speed Scheimpflug imaging technology. Corvis-ST uses a high-speed camera at a rate of 4330 frames per second to capture a series of horizontal Scheimpflug images allowing for direct observation of corneal deformation in response to an air puff jet. Observing the corneal relaxation response provides an excellent tool for evaluation of corneal biomechanics, making Corvis-ST a promising tool for *in vivo* evaluation of corneal biomechanical responses in the normal state, different corneal pathologies like keratoconus, and after different surgeries like refractive surgery. However, before the application of a device could be justified for characterizing the corneal biomechanical behavior in different states, it is necessary to ascertain it provides reliable measurements in these conditions.

The purpose of this study was to evaluate the repeatability of Corvis-ST measurements in normal, keratoconic, and post-LASIK subjects.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Review Board of Noor Ophthalmology Research Center and the study adhered to the tenets of the Declaration of Helsinki. The written informed consent was obtained from volunteers.

Fifteen patients (30 eyes) in each group consisting of normal, keratoconus, and normal stable post refractive (PRK) surgery (LASIK) patients were included in the study.

Keratoconus was diagnosed by a corneal specialist based on the combination of signs in examination including scissor reflex, stromal thinning, conical protrusion of the cornea at the apex, vogt striae, Fleischer ring, and typical topographic findings based on the Rabinowitz definitions of the anterior topographic features related to keratoconus: An increased area of corneal power surrounded by concentric areas of decreasing corneal power; Inferior-superior corneal power asymmetry; and Skewing of the radial axes above and below the horizontal meridian, with ≤150° between arms.[13]

The normal subjects were selected from the refractive surgery clinic patients scheduled for refractive surgery. The inclusion criteria for normal subjects were the absence of the aforementioned signs of keratoconus and a maximum posterior corneal elevation <29 µm.[14]

Post-LASIK subjects were selected from the subjects with at least 1 year of uneventful follow-up, stable refraction, and no sign of keratectasia following surgery.

Patients with corneal scarring, history of hydrops, trauma, ocular surgery (other than refractive surgery in the post-LASIK group), or any ocular or systemic disease affecting the eye were excluded from the study.

Examinations

All patients underwent complete ophthalmic examination including refraction, slit lamp examination, IOP measurement, and funduscopy. Corneal topography was done with the Pentacam HR (Oculus, Wetzlar, Germany) in all patients.

Corvis-ST was used to obtain corneal biomechanical data. Measurements were taken by a single experienced technician between 9 and 12 am. For each subject two examinations were performed, with a 20 min interval between measurements.

After seating the patient and proper positioning and centering on the corneal center using the four red alignment markers on the computer screen, the device automatically emits a focused puff of air at a pressure of 60 mmHg from a nozzle, at a distance of 11 mm from the cornea. In addition to IOP, corrected IOP, and pachymetry, the following measurements are displayed: Time, velocity, and length of the first and second applanations (A1 and A2), and the characteristics of the highest point of concavity including the time, concave radius of curvature, peak distance, and deformation amplitude. The Corvis measured parameters described in detail elsewhere.[12,15] The biomechanical data captured by the device were then exported to the attached computer.

Statistical analysis

The normality of the data was tested using the Kolmogorov–Smirnov test. Intraclass correlation coefficient (ICC) and precision, defined as the mean difference ± 1.96 × Sw (standard deviation of within-subject measurements) which represents the 95% confidence interval for the difference in the measurements, were used to evaluate the intra-observer repeatability of measurements. One-way ANOVA with adjustments for the correlation between fellow eyes was used for comparison of precision among groups. Repeatability was interpreted as excellent if ICC >0.9, good if between 0.75 and 0.9, and poor to moderate if <0.75.[16] $P < 0.05$ was considered statistically significant.

RESULTS

Normal group

The mean age in the normal group was 30.01 ± 2.56 years, and 66.7% of the patients were female. The mean manifest refraction spherical equivalent (MRSE), keratometry (Kmean), and CCT were −1.03 ± 0.61D, 43.67 ± 1.76D, and

545.10 ± 46.04 μm, respectively. As shown in Table 1, ICC was best for pachymetry (0.997) and worst for A2-length (0.701) and peak distance (0.567) parameters. Except for A2-length (0.701), peak distance (0.567), HC-time (ICC not calculated due to non-normal distribution of data), and the ICCs for other parameters were >0.75 in this group.

Keratoconus group

The mean age was 34.33 ± 3.14 years in the keratoconus group, and 66.7% of the patients were male. The mean K-max and CCT were 47.59 ± 2.96D and 505.09 ± 39.13 μm, respectively. As shown in Table 2, ICC was best for pachymetry (0.992) and worst for peak distance (0.493). Except for peak distance (0.493), A2-length and HC-time variables (ICC not calculated due to non-normal distribution of data), and the ICCs for other parameters were >0.75 in this group.

Post-LASIK group

The mean age of the patients in the post-LASIK group was 30.67 ± 5.22 years, and 73.3% of the patients were female. The mean MRSE, Kmean, and CCT were −0.04 ± 0.36D, 43.34 ± 1.32D, and 499.979 ± 38.56 μm, respectively. As shown in Table 3, ICC was best for pachymetry (0.995) and

Table 1: Repeatability of indices measured with Corvis-ST in the normal group of the study (*n*=30)

Parameters	Take 1	Take 2	ICC (95% CI)	Precision
IOP (mmHg)	18.48±5.31	18.32±5.10	0.983 (0.965–0.992)*	8.45
Corrected IOP (mmHg)	18.68±4.88	18.37±4.64	0.981 (0.960–0.991)*	8.55
Pachymetry(μm)	545.10±46.04	548.77±46.90	0.997 (0.994–0.999)*	35.83
Time to A1 (ms)	7.68±0.79	7.66±0.78	0.982 (0.962–0.991)*	1.30
Time to A2 (ms)	20.89±0.56	20.91±0.60	0.954 (0.901–0.978)*	1.49
A1 length (mm)	1.74±0.07	1.74±0.09	0.940 (0.874–0.972)*	0.22
A2 length (mm)	1.77±0.23	1.69±0.26	0.701 (0.372–0.858)*	1.35
A1 velocity (ms)	0.12±0.03	0.12±0.02	0.764 (0.459–0.886)*	0.13
A2 velocity (ms)	−0.31±0.08	−0.32±0.08	0.912 (0.814–0.958)*	0.30
Time of highest concavity (ms)	16.17±0.41	16.15±0.33	NC	3.41
Deformation amplitude (mm)	0.87±0.17	0.88±0.13	0.895 (0.780–0.950)*	0.39
Peak distance (mm)	4.26±0.86	4.35±0.84	0.567 (0.090–0.794)**	3.58
Radius (mm)	7.62±0.81	7.62±0.94	0.772 (0.509–0.889)*	4.83

*P<0.001, **P<0.05, IOP: Intraocular pressure, NC: Not calculated because of non-normal distribution. ICC: Intraclass correlation coefficient, CI: Confidence interval

Table 2: Repeatability of indices measured with Corvis-ST in the keratoconus group of the study (*n*=30)

Parameters	Take 1	Take 2	ICC (95% CI)	Precision
IOP (mmHg)	13.58±2.56	13.33±2.54	0.905 (0.805–0.953)*	3.46
Corrected IOP (mmHg)	15.37±2.54	15.14±2.64	0.909 (0.813–0.955)*	9.64
Pachymetry (μm)	505.09±39.13	504.62±38.43	0.992 (0.984–0.996)*	35.75
Time to A1 (ms)	6.90±0.39	6.87±0.38	0.907 (0.810–0.955)*	1.47
Time to A2 (ms)	21.41±0.44	21.46±0.47	0.865 (0.720–0.935)*	1.84
A1 length (mm)	1.74±0.05	1.74±0.06	0.772 (0.532–0.889)*	0.21
A2 length (mm)	1.59±0.33	1.65±0.27	NC	2.76
A1 velocity (ms)	0.13±0.02	0.13±0.02	0.781 (0.551–0.893)*	0.12
A2 velocity (ms)	−0.36±0.06	−0.37±0.08	0.782 (0.541–0.893)*	0.42
Time of highest concavity (ms)	16.13±0.53	16.10±0.41	NC	3.98
Deformation amplitude (mm)	1.02±0.13	1.03±0.13	0.938 (0.871–0.969)*	0.41
Peak distance (mm)	4.06±1.17	4.31±1.01	0.493 (−0.035–0.753)	5.87
Radius (mm)	6.21±0.96	6.19±0.78	0.856 (0.704–0.929)*	3.80

*P<0.001, **P<0.05, IOP: Intraocular pressure, NC: Not calculated because of non-normal distribution. ICC: Intraclass correlation coefficient, CI: Confidence interval

worst for A1-velocity (0.660), HC-time (0.629), A1-length (0.553), and A2-length (0.354). Except for A1-velocity (0.660), HC-time (0.629), A1-length (0.553), and A2-length (0.354), and PD (ICC not calculated due to non-normal distribution of data), and the ICCs for other parameters were >0.75.

Intergroup comparison of measurements

The comparison of Corvis-ST parameters showed significant differences in terms of measurement precision for A1-length ($P = 0.001$), A2-length ($P = 0.019$), A2-velocity ($P = 0.041$), PD ($P = 0.007$), and HC-radius ($P = 0.079$, borderline) among groups. The precison of A1-length was better in the normal and keratoconus compared to post-LASIK group ($P = 0.003$ and $P = 0.004$, respectively). A2-length had better precision in the normal group compared to keratoconus ($P = 0.025$) and a trend toward better precision of A2-velocity measurements in the normal compared to the keratoconus group was noted ($P = 0.057$). PD showed better precision in the normal group compared to post-LASIK ($P = 0.008$). The differences in the precision of other parameters were not statistically significant (all $P > 0.050$).

DISCUSSION

Our study results showed good repeatability for most Corvis-ST parameters in the normal (10 of 13 parameters), keratoconus (10 of 13 parameters), and post-LASIK eyes (8 of 13 parameters). However, differences in the repeatability of different parameters in each group and among groups were observed, which could be specifically relevant for the reliability of the comparisons of Corvis-ST biomechanical parameters among these groups.

The repeatability for pachymetry was excellent in all study groups which is in agreement with the results of previous studies in normal[15,17-20] keratoconus[21] and PRK eyes.[22] This finding is quite expected, considering this parameter is a static state measurement and the technology of Scheimpflug imaging used in the Corvis-ST has been shown to have good correlation with the other well-established methods like Pentacam which uses a similar technology for pachymetry measurements.[23]

Regarding the IOP and corrected IOP, excellent repeatability in the normal and keratoconus groups (ICC >90) and good and close to excellent repeatability in the post-LASIK group were observed. In previous studies, Corvis-ST measured IOP showed good repeatability in normal corneas and keratoconic patients.[15,17,18,20,21] Chen *et al*. also reported good repeatability (ICC: 0.99) in post-PRK eyes.[22]

With respect to the close association of IOP with A1-time (the current Corvis software uses this index for estimation of IOP measurement) and the corrected IOP with IOP and CCT (a correction applied to IOP based on a correction table such as Dresden and Ehlers according to central corneal thickness),[24] the good repeatability observed for all of these variables in our study is in agreement with the close relation of these parameters.

Regarding the other parameters, A1-time, A2-time, A2-velocity, DA, and HC-radius showed good repeatability in all study groups. A1-length and A1-velocity showed good repeatability in the normal and keratoconus eyes and poor to moderate repeatability in the post-LASIK group. The parameters of A-2 length, HC-time, and PD (provided normal distribution and ICC caluclation) showed poor to moderate repeatability in all three groups.

Table 3: Repeatability of indices measured with Corvis-ST in the post-LASIK group of the study (*n*=30)

Parameters	Take 1	Take 2	ICC (95% CI)	Precision
IOP (mmHg)	14.07±1.86	14.02±2.27	0.855 (0.696–0.931)*	3.00
Corrected IOP (mmHg)	16.07±2.10	15.93±2.32	0.868 (0.723–0.937)*	8.75
Pachymetry (μm)	499.97±38.56	502.03±37.47	0.995 (0.990–0.998)*	32.25
Time to A1 (ms)	6.99±0.30	6.99±0.36	0.874 (0.736–0.940)*	1.29
Time to A2 (ms)	21.34±0.34	21.35±0.38	0.895 (0.779–0.950)*	1.35
A1 length (mm)	1.78±0.11	1.74±0.14	0.553 (0.061–0.787)**	0.70
A2 length (mm)	1.57±0.36	1.62±0.32	0.354 (−0.357–0.693)***	2.43
A1 velocity (ms)	0.13±0.02	0.13±0.02	0.660 (0.286–0.838)*	0.11
A2 velocity (ms)	−0.37±0.06	−0.37±0.08	0.848 (0.680–0.928)*	0.31
Time of highest concavity (ms)	16.24±0.49	16.22±0.39	0.629 (0.220–0.823)**	3.06
Deformation amplitude (mm)	0.97±0.07	0.98±0.09	0.864 (0.715–0.936)*	0.37
Peak distance (mm)	4.05±1.20	4.35±1.18	NC	10.10
Radius (mm)	6.64±0.88	6.45±0.72	0.885 (0.758–0.945)*	3.10

*$P<0.001$, **$P<0.05$, ***Non-significant, IOP: Intraocular pressure, NC: Not calculated because of non-normal distribution. ICC: Intraclass correlation coefficient, CI: Confidence interval

Comparing our findings in normal eyes with previous studies, similar to our results, Nemet *et al*.[19] and Hon and Lam[17] found good repeatability for CCT, IOP, A1-time, and DA in normal eyes. In addition to these variables, Chen *et al*. reported good repeatability for A2-time[22] and Wu *et al*.[20] reported good repeatability for A2-time and A1-length variables in a study of a Chinese population. In addition to parameters reported by these studies, our study also showed excellent repeatability for A2-velocity and good repeatability for HC-radius in normal eyes.

Comparing our findings in keratoconic eyes with previous reports, our observations agree with the findings of Ye *et al*. who reported good repeatability for the parameters of CCT, IOP, A1-velocity, and deformation amplitude in both normal and keratoconic patients.[21] In addition to these parameters, in our study, good repeatability for the parameters of A1-time, A2-time, and A-2 velocity, and HC-radius were also noted.

Comparing the normal and keratoconus groups, all Corvis-ST parameters showed better ICC values for repeatability except for the pachymetry, deformation amplitude, and HC-radius. The comparison of precision between these two groups also showed a significantly better precision for A2-length and a trend toward better precision of A2-velocity measurements in normal eyes. In another study, Ye *et al*. found significantly lower repeatability coefficients for the parameters of A1 and A2-length, A1-velocity, and peak distance in normal eyes compared to the keratoconic eyes; however, the inter-group difference in the ICCs was not significant.[21]

Such differences measurement repeatability, especially for the second applanation might be attributed to variations in the corneal thickness, curvature, and displacement of corneal apex which could contribute to more variability of the corneal deformation response in keratoconic eyes. In the post-LASIK eyes, excellent repeatability was demonstrated for CCT, corrected IOP, IOP, and A1-time, and good repeatability was observed for A2-time, HC-radius, DA, and A2-velocity. Similar to our findings, Chen *et al*.[22] in their study on the repeatability of Corvis-ST parameters in virgin and post-PRK eyes, reported good intra-observer repeatability for IOP, CCT, A-1 time and a good or close to good repeatability for A2-time and HC-radius in the post-PRK group.

In a comparison of the repeatability of different parameters between post-LASIK, normal, and keratoconic eyes, the parameters of A1-length in the normal and keratoconic eyes and PD in the normal group showed better precision compared to post-LASIK eyes. The alterations of corneal biomechanical properties and more variable corneal deformation response might result from the procedure effect on cornea. Changes in corneal shape (central flattening) lead to an error in the borders of applanation zone compared to virgin and keratoconic eyes. The procedure also causes changes in the peripheral corneal zone and errors in the outline of bending area and peak distance. In addition, these might be due to some unknown factors.

Regarding the parameters of highest concavity, except for the DA and HC-radius which showed good repeatability, the parameters of HC-time and PD (when measurable) showed poor to moderate repeatability in all three groups. Similar to our results, poor repeatability for the parameters of HC-time and PD have been reported in normal,[18,22] keratoconus,[18,21] and PRK[22] subjects by other authors. Among the possible explanations, limitations of the software and motion artifacts related to corneal vibrations which become more prominent when the cornea reaches its maximal deformation[25] could be factors contributing to this relatively poor performance.

Different parameters could contribute to the variability of Corvis parameters. Physiologic factors like the effect of ocular pulse amplitude and their relation the cycle of the cardiopulmonary system as addressed by Kasprzak and Iskander could affect the corneal deformation response.[26] Other factors such as the sclera rigidity and retro-orbital fat also influence the corneal deformation pattern. Other factors such as differences in the software used (better repeatability reported with updated versions in recent studies), the protocol, and the population included in different studies could affect the inter-study differences in the repeatability for Corvis-ST parameters.

The repeatability for Corvis-ST parameters was generally higher in our study compared to previous studies, which could be attributed to the more uniform age group of the participants consisting of young populations of normal, keratoconic, and post-LASIK subjects.

One of the limitations of this study is its relatively small sample size. In addition the software version used in our study did not include the newer parameters like biomechanical corrected IOP, Corvis-ST biomechanical index integrated into the later updates of the software. Larger sample studies including different keratoconus severity stages and degrees of refractive correction in post-LASIK cases are needed to further characterize the repeatability of Corvis-ST parameters in these conditions.

CONCLUSION

The results of this study showed acceptable repeatability for most Corvis-ST biomechanical properties in normal, keratoconus, and post-LASIK eyes. Corvis-ST could be a promising tool for *in vivo* evaluation of corneal biomechanical responses in these conditions.

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