**Evaluation of changes in corneal biomechanics after orthokeratology using Corvis ST**

**Highlights:**

The changes in Corvis ST parameters post orthokeratology lens wear are primarily related to alterations in corneal shape, rather than variations in corneal biomechanical properties.

**Abstract:**

**Purpose:** To investigate the alterations in corneal biomechanical metrics induced by orthokeratology (ortho-k) using Corvis ST and to determine the factors influencing these changes.

**Method:** A prospective observational study was conducted to analyze various Corvis ST parameters in 32 children with low to moderate myopia who successfully underwent ortho-k lens fitting. Corneal biomechanical measurements via Corvis ST were acquired at six distinct time points: baseline (pre) and 2 hours (pos2h), 6 hours (pos6h), and 10 hours (pos10h) following the removal of the first overnight wear ortho-k, one week (pos1w) and one month (pos1m) subsequent to the initiation of ortho-k.

**Result:** Significant differences were observed in Corvis ST Biomechanical parameters DAR2, IIR, CBI, and cCBI post ortho-k intervention. The integration of covariates (CCT, SimK, and bIOP) mitigated the differences in DAR2, IIR, and cCBI, but not in CBI. Initially, the stiffness parameter at first applanation, SP-A1, did not demonstrate significant variations, but after adjusting for covariates, noticeable differences over time were observed. The Stress-Strain Indeces, SSIv1 and SSIv2, did not manifest considerable changes over time, irrespective of the adjustment for covariates. No significant disparities were identified among different ortho-k lens brands.

**Conclusion**: Corneal biomechanics remained consistent throughout the one-month period of ortho-k lens wear. The observed changes in Corvis ST parameters subsequent ortho-k are primarily attributable to alterations in corneal pachymetry and morphology, rather than actual alterations in corneal biomechanics. The stability of corneal biomechanics post ortho-k treatment suggests the safety of this approach for adolescents from a corneal biomechanics perspective.

**Keywords:** Corneal biomechanics, Corvis ST, Overnight orthokeratology, Corneal ectasia

**Introduction**

Orthokeratology (ortho-k) is a widely practiced clinical approach that utilizes rigid contact lenses to temporarily reduce refractive error and slow down myopia progression [1, 2]. The unique reverse-geometry design of ortho-k lens allows for mechanical interaction with the cornea, triggering corneal central thinning and mid-peripheral thickening which may potentially impact the biomechanics of the cornea [3, 4]. Corneal biomechanics characterize the tissue’s response to external forces, and include stiffness, elasticity and viscosity [5].

In previous studies, the correlation between corneal biomechanics and ortho-k has been primarily investigated using the Ocular Response Analyzer (ORA), with two fundamental parameters, corneal hysteresis (CH) and corneal resistance factor (CRF) [6-9]. CH is a measure of the viscoelasticity of the cornea, while CRF relates to its mechanical resistance to applied loads. Previous studies by Lam et al. reported insignificant reductions in CH and CRF after one night of ortho-k wear [8], and in another study observed significant reductions in only CRF [10]. However, in longer observations, significant decreases in both CH and CRF were noted [7, 11]. The downward trend of CH stabilized at one month, whereas CRF continued to decrease for two more months. By the six-month mark, there was an 8.7% mean reduction in CRF and a 5.8% mean reduction in CH compared to baseline [9].

Other studies have utilized alternative instruments to assess corneal biomechanics. Lam et al. used a corneal indentation instrument and found that short-term ortho-k did not alter the tangent elastic modulus [8]. However, the tangent modulus increased, while the corneal overall stiffness remained stable after six months of ortho-k wear [9].

The scarcity of clinical technologies capable of assessing corneal biomechanics is believed to significantly contribute to the limited research conducted on corneal biomechanical modifications following ortho-k treatment. The Corneal Visualization Scheimpflug Technology (Corvis ST) is a visual measurement of the biomechanical response of the cornea which uses an ultra-high speed Scheimpflug camera that enables direct visualization of corneal movement during the measurements and provides more detailed insight on corneal biomechanics than ORA. However, only a limited number of studies have explored the changes in Corvis ST parameters subsequent to ortho-k treatment.

It has been noted that corneal biomechanics are age-related, with the cornea tending to exhibit a more rigid state in older individuals [12, 13]. Although most current studies primarily involve adult subjects, ortho-k lenses are more frequently applied on adolescents and children due to the need for myopia control. Thus, research that focuses on changes in corneal biomechanics after ortho-k in pediatric patients is of paramount importance.

The aim of this study is to scrutinize the alterations in corneal biomechanical metrics resulting from overnight ortho-k using Corvis ST. Furthermore, this study strives to identify the factors associated with these changes and shed light on the underlying causes contributing to these alterations.

**Method**

**Study subjects**

This prospective study was conducted at the Eye Hospital of Wenzhou Medical University in Wenzhou, China and included a cohort of 41 subjects (41 eyes), each successfully fitted with ortho-k lenses. To prevent inter-eye correlation that could influence the results of the analysis, only one eye (the right eye) per subject was included in the study. Candidates for the study underwent a comprehensive ophthalmic examination to screen for corneal abnormalities and to confirm eligibility for ortho-k. Eligibility criteria included age between 8 and 18 years, no prior history of wearing rigid gas permeable contact lenses, no history of corneal surgery, and no existing ocular or systemic diseases. Additionally, the refractive error in all subjects was ≥-6.00 D and the astigmatism was ≥-1.50 D. Refractive examination without cycloplegia were performed by a single experienced ophthalmologist. The purpose and details of the study were explained to the subjects and their legal guardians, and written consent forms were obtained before commencement of the study.

**Corvis ST Examination**

The Corvis ST instrument (Oculus 72100, Wetzlar, Germany) captured Scheimpfug images of the anterior segment at a rate of 4330 frames/s, covering 8.0 mm horizontally and recorded 140 images, thus illustrating corneal deformation in response to a metered air puff. Measurements of corneal biomechanics were taken at six different time points: baseline (pre) and 2 hours (pos2h), 6 hours (pos6h), and 10 hours (pos10h) after the removal of ortho-k lens following the first overnight wear. Additionally, measurements were taken one week (pos1w) and one month (pos1m) after wearing ortho-k, approximately two hours after the lenses were removed. These time points were selected to assess the short- and mid-term changes in corneal biomechanics post-ortho-k. All participants receiving five repeated measurements, and their eligibility for inclusion was based on achieving a minimum of one measurement with good quality scores (QS). Only data from qualified scans (error state<=1) and QS showing OK were included in analysis.

The following parameters from the Corvis ST software were selected: biomechanically corrected intraocular pressure (bIOP), simulated keratometry [3mm] (SimK), central corneal thickness (CCT), deformation amplitude ratio [2mm] (DAR2, the ratio between the deformation amplitude at the apex and 2 mm), integrated inverse radius (IIR, the integrated area under the radius of the inversed curvature during the concave phase), the stiffness parameter at first applanation (SP-A1, calculated as the adjusted pressure at the first applanation minus bIOP divided by the defection amplitude at the first applanation), Corvis biomechanical index (CBI, calculated based on a logistic regression formula calculated from different Corvis ST parameters). With the updated software (software version v1.6r2187), new Corvis ST parameters were added, including Corvis biomechanical index for the Chinese population (cCBI), the updated stress-strain index (SSIv2), and the earlier stress-strain index (SSIv1). The later development of SSIv2 was based on a more comprehensive set of numerical models that incorporated changes in abnormal corneas [14].

**Ortho-k lenses and lens fitting**

For each subject, the best suitable ortho-k lenses were chosen from four brands according to the different fitting situations. Details of the four lens brands were provided by the manufacturer and are listed in *Table 1*. A trial fit was arranged: an initial diagnostic lens was inserted onto the subject’s eye to evaluate lens fitting. Corneal topography was obtained using the Medmont E300 Corneal Topographer (Medmont Pty Ltd, Victoria, Australia). The lens fitting was assessed 30 min after a subject put on the diagnostic lens. An ideal lens fitting should ensure good lens centration, allow the lens to move smoothly upon blinking, and display a bull’s eye fluorescein pattern with a central bearing zone approximately 4 to 5 mm in diameter. Based on the diagnostic lenses that gave the best fit, the parameters of ordered ortho-k lenses were determined. At each session after wearing, an experienced optometrist assessed the lens fitting again before taking it off. Subjects with optimal lens fitting stayed in the study and those without were excluded.

**Statistical analysis**

Only data from the right eyes of the subjects were included for analysis. Statistical analysis was conducted using SPSS Statistics 23.0 (IBM, Armonk, NY, USA). The Shapiro-Wilks test was applied to determine if the data were normally distributed. A two-way mixed design repeated measures analysis of variance (MANOVA) was used to analyze changes in corneal biomechanical indices at the examined time points, and also to make comparisons among different brands. Generalized estimating equation (GEE) models were employed to evaluate the association between the Corvis ST metrics and internal factors, given that it was a typical repeated measure designed study. The GEE models were adjusted for covariates, including CCT, bIOP, and SimK. An autoregressive correlation structure was assumed in these models to account for the within subject correlation. Pearson or Spearman analysis was used to explore the relationship between corneal biomechanics metrics and baseline data of subjects for normally and non-normally distributed data, respectively. A P-value of 0.05 was chosen to denote statistical significance.

**Results**

**Sample demographics**

In this prospective study, the initial participant cohort comprised 41 individuals. However, nine participants were excluded due to their Corvis ST data not meeting inclusion criteria in a timely manner (Figure 1). Consequently, the study proceeded with the inclusion of data from 32 participants. The mean age of these subjects was 12.05 ± 1.9 years with a range of 9-17 years. *Table 2* provides an overview of the baseline ocular parameters for the subjects wearing different brands of ortho-k lenses. The baseline subject parameters for each of the four ortho-k lens brands were not statistically different (p > 0.05, *Table* 2).

**Temporal evolution of corneal biomechanical parameters**

DAR2 exhibited an obvious time effect, with a significant decrease from baseline to pos2h after ortho-k wearing (p < 0.05, *Figure 2*), followed by non-significant fluctuations from pos2h to pos1m. Upon adjusting for covariates (including CCT, bIOP, and SimK), the previously significant difference between baseline and pos2h after wearing became non-significant (p > 0.05, *Figure 2*). No significant differences were also found in DAR2 changes from baseline to pos1m among different brands of ortho-k lenses (p > 0.05).

IIR demonstrated stability from baseline to pos1w, but followed by a significant increase from pos1w to pos1m after wearing ortho-k lenses (p < 0.05). After adjusting for covariates, IIR was not significantly different among different time points (p > 0.05，*Figure 2*). Furthermore, there was no significant difference in IIR changes from baseline to pos1m among the various brands of ortho-k lenses (p > 0.05).

CBI exhibited consistent and significant increases from pos6h to each of the subsequent time points (p < 0.05). On the other hand, cCBI underwent a significant increase from baseline to pos6h, followed by a stable period from pos6h to pos10h, and then showed a sustained increase from pos10h to pos1w and from pos1w to pos1m (both p < 0.05). After adjusting for covariates, the growth trend of CBI remained and was significant between each two successive time points (all p < 0.05, *Table 4*). In comparison, the changes in cCBI were more stable with no significant differences between each time point and the baseline (all p > 0.05, *Table 4*). No significant differences were observed in changes in CBI and cCBI across different brands of ortho-k lenses (p > 0.05).

In contrast to the aforementioned parameters, SP-A1, SSIv1 and SSIv2 did not exhibit any significant changes from baseline to any of the post-wearing time points, nor did they demonstrate any differences between different brands of ortho-k lenses (p > 0.05). After adjusting for covariates, significant differences over time were observed in SP-A1, but not in SSI parameters. As shown in *Figure 2* and *Table 4*, there were no significant differences over time in SSIv1 or SSIv2, regardless of whether the covariates CCT, SimK and bIOP were considered (p > 0.05).

**Relationship between Corvis ST parameters and basic characteristics**

*Table 3* shows the results of correlation analysis. The changes (∆) in corneal biomechanical parameters were calculated by subtracting the baseline values from those measured after one month of wearing ortho-k lens. The results showed that ∆CBI was significantly correlated with ∆CCT and ∆bIOP (r = 0.511, p = 0.004, and r = 0.444, p = 0.014, respectively) as illustrated in *Figure**2*. Additionally, both ∆SP-A1 and ∆DAR2 were significantly correlated with ∆bIOP, with correlation coefficients of 0.484 (p=0.007) and -0.619 (p<0.001), respectively. Moreover, ∆cCBI was significantly correlated with ∆SimK (r = 0.533, p = 0.002). Age, spherical refractive error, and spherical equivalent did not exhibit a significant correlation with changes in corneal biomechanical parameters after one month of ortho-k treatment (*Table* 3, all P > 0.05). These results suggested that for adolescents, age and ortho-k lens design had insignificant influence on the observed changes in corneal biomechanics.

**Discussion**

The current study utilized the Corvis ST to track the changes in corneal biomechanics metrics during one month of ortho-k treatment and aimed to elucidate the underlying factors that contribute to these changes. The key findings of this research indicate that corneal biomechanics remained stable over this period. The observed alterations in Corvis ST parameters following ortho-k were primarily attributed to variations in corneal pachymetry and morphology rather than genuine alterations in corneal biomechanics.

Previous studies that required *in vivo* measurement of corneal biomechanics relied on the ORA and Corvis ST and noted the dependence of their parameters on IOP and/or CCT [15, 16]. However, the utilization of a single parameter cannot adequately describe all biomechanical properties of the cornea, including its overall and material mechanical stiffness and viscoelasticity. Thus, to construct a comprehensive understanding of corneal biomechanics, the analysis encompassed various measurement metrics, each providing useful specific insight.

DAR2 is the ratio between the amplitude of the deformation at the apex and at the 2 mm from the apex, with lower values reflecting an increase in corneal stiffness. Another parameter, IIR, the integrated area under the radius of the inversed curvature during the concave phase, and has demonstrated robust correlation with the overall stiffness of the cornea, with higher values indicating softer corneas [17]. In this study, and after accounting for covariates (CCT, SimK, and bIOP), DAR2 and IIR did not exhibit significant changes following ortho-k. This suggests that the observed alterations in these two parameters were not indicative of biomechanical weakening but rather the result of changes in corneal morphology and thickness.

The study also considered the changes in CBI and cCBI, which were obtained using logistic regression that involved several dynamic Scheimpflug analyzer parameters (including pachymetric features and corneal deformation parameters). The results demonstrated that ortho-k treatment had led to significant increases in CBI and cCBI (*Figure 2*). After adjusting for covariates, the changes in cCBI were no longer significant, while those in CBI remained significant. The mismatch between the change trends in CBI and cCBI may be due to their use of data from different ethnic groups, potentially leading to higher false positives for CBI in Chinese subjects. As the CBI was derived using data from a mixed South American and White population [18], this parameter may not accurately represent the biomechanical characteristics of Chinese individuals. This observation is in line with previous research that has shown that Chinese individuals tended to have lower values of SSIv1 and SPA1 (developed using data from non-Chinese participants) compared to a White population, possibly falsely indicating softer corneas [19]. These ethnic differences in metrics of corneal biomechanics suggest that the CBI may be unreliable if used to assess corneal biomechanical changes in Chinese subjects [20]. On the other hand, the cCBI, which has been specifically optimized for Chinese patients, has, in earlier studies, demonstrated superior performance in detecting keratoconus in this population [21], and therefore the cCBI may be a more reliable metric than the CBI.

As mentioned previously, DAR2, IIR, CBI, and cCBI all attempted to reveal the corresponding changes in corneal biomechanics, but studies proved that none of them was independent of CCT and IOP [22, 23] – this is consistent with the results of the correlation analysis in this study. The presence of this correlation poses a challenge in determining whether the observed changes in these parameters were solely due to alterations in corneal thickness and IOP, or if they truly reflect changes in the underlying corneal biomechanics. To address the potential impact of these confounding factors, indirect methods were employed, such as a covariate correction method based on the generalized estimation equation provided by the SPSS.

To further mitigate the impact of confounding factors and derive accurate corneal material properties, the SSI algorithm was developed as a means of generating a material stiffness parameter that represented the stress-strain behavior of corneal tissue [24]. In this study, both SSIv1 and SSIv2 remained unchanged after ortho-k regardless of whether the covariates CCT, SimK and bIOP were adjusted or not, suggesting that there were no significant alterations in the corneal material properties. Nieto-Bona et al. [25] also reported no significant differences in SSIv1 after ortho-k. Similar to the target of SSI, the tangent modulus of corneal tissue was derived in another earlier study [26]. Lam et al. [8] used that method – a corneal indentation device – and the results indicated short-term ortho-k had no significant effect on corneal tangent modulus.These findings seem to indicate no significant change in corneal material properties took place due to ortho-k wear.

Previous reports on the SSIv1 indicated its dependence on IOP but not CCT [24, 27]. In other studies, SSIv1 was independent of both parameters [28, 29]. Both sets of studies were cross-sectional, which may have influenced the correlation results. In this longitudinal self-matched study, there was no significant correlation between the two versions of SSI (SSIv1 and SSIv2) on one hand, and CCT, SimK, and bIOP on the other, suggesting that these novel parameters may provide independent information on corneal material biomechanics.

To better understand the change in corneal biomechanics after ortho-k, it is important to analyze corneal morphological and cellular changes that take place due to treatment. Different corneal layers contribute to overall corneal biomechanics to varying degrees, with the stroma being the thickest layer and the largest contributor to corneal stiffness – in contrast, the much thinner and softer epithelium contributes very little [7, 30, 31]. Several studies have confirmed that the corneal thickness changes noted after ortho-k wear were primarily due to epithelial remodelling rather than stromal changes [32-34]. For these reasons, it is reasonable to expect that the cornea would experience little biomechanical changes following ortho-k treatment as observed in this study. Further, different ortho-k lens designs induce varied optical changes mainly due to corneal epithelium distribution [35], instead of modifications in collagen fiber within the stroma [36]. Consequently, these findings suggest minimal impact of ortho-k lens design on corneal biomechanics.

This study has several limitations. Firstly, the sample size was small, even though it was large enough for the statistical analysis carried out. This diminutive sample size has the potential to diminish the statistical analysis's power. In future studies, efforts will be made to address this limitation by expanding the sample size to enhance the robustness of analyses. Secondly, different types of reverse geometry contact lenses were used, but again the effect of this point on the study results was likely low as the lenses had similar diameters and optical zone designs, and led to comparable central flattening. Moreover, using different lens designs did not lead to significant changes in corneal biomechanical parameters in the study.

In conclusion, the current study revealed that the changes in Corvis ST biomechanical parameters observed after ortho-k wear were primarily due to alterations in corneal pachymetry and morphology rather than variations in corneal biomechanics including its material stiffness. Corneal biomechanics remained stable throughout one-month of ortho-k lens wear, which suggests the safety of this approach for adolescents.**Contributors** PPZ, FJ, AE and FJB drafted the conception of the work together. JJ and FJ conducted the clinical examination of the patients and assessed the fitting of orthokeratology lenses. The Corvis ST data were obtained by XBZ and JJW. JFW, JJ and ZYR performed the data analysis. PPZ, JFW and ZYR wrote the first manuscript. JFW, JJW, XBZ, AE and FJB review and revised the manuscript thoroughly. All authors approved the submitted version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

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**Competing Interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by Institutional Review Board (IRB) of the Eye Hospital of Wenzhou Medical University (number KYK-2015-29). Participants gave informed consent to participate in the study before taking part.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

**References:**

[1] VanderVeen DK, Kraker RT, Pineles SL, Hutchinson AK, Wilson LB, Galvin JA, et al. Use of Orthokeratology for the Prevention of Myopic Progression in Children: A Report by the American Academy of Ophthalmology. Ophthalmology 2019;126(4):623-36. https://doi.org/10.1016/j.ophtha.2018.11.026.

[2] Modjtahedi BS, Abbott RL, Fong DS, Lum F, Tan D. Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children: The Academy's Task Force on Myopia. Ophthalmology 2021;128(6):816-26. https://doi.org/10.1016/j.ophtha.2020.10.040.

[3] Maseedupally V, Gifford P, Lum E, Swarbrick H. Central and paracentral corneal curvature changes during orthokeratology. Optom Vis Sci 2013;90(11):1249-58. https://doi.org/10.1097/opx.0000000000000039.

[4] Li F, Jiang ZX, Hao P, Li X. A Meta-analysis of Central Corneal Thickness Changes With Overnight Orthokeratology. Eye Contact Lens 2016;42(2):141-6. https://doi.org/10.1097/icl.0000000000000132.

[5] Vincent SJ, Cho P, Chan KY, Fadel D, Ghorbani-Mojarrad N, Gonzalez-Meijome JM, et al. CLEAR - Orthokeratology. Cont Lens Anterior Eye 2021;44(2):240-69. https://doi.org/10.1016/j.clae.2021.02.003.

[6] González-Méijome JM, Villa-Collar C, Queirós A, Jorge J, Parafita MA. Pilot study on the influence of corneal biomechanical properties over the short term in response to corneal refractive therapy for myopia. Cornea 2008;27(4):421-6. https://doi.org/10.1097/ICO.0b013e318164e49d.

[7] Chen R, Mao X, Jiang J, Shen M, Lian Y, Zhang B, et al. The relationship between corneal biomechanics and anterior segment parameters in the early stage of orthokeratology: A pilot study. Medicine (Baltimore) 2017;96(19):e6907. https://doi.org/10.1097/md.0000000000006907.

[8] Lam AK, Leung SY, Hon Y, Shu-Ho L, Wong KY, Tiu PK, et al. Influence of Short-Term Orthokeratology to Corneal Tangent Modulus: A Randomized Study. Curr Eye Res 2018;43(4):474-81. https://doi.org/10.1080/02713683.2017.1418895.

[9] Lam AKC, Hon Y, Leung SYY, Shu-Ho L, Chong J, Lam DCC. Association between long-term orthokeratology responses and corneal biomechanics. Sci Rep 2019;9(1):12566. https://doi.org/10.1038/s41598-019-49041-z.

[10] Chen D, Lam AK, Cho P. A pilot study on the corneal biomechanical changes in short-term orthokeratology. Ophthalmic Physiol Opt 2009;29(4):464-71. https://doi.org/10.1111/j.1475-1313.2008.00625.x.

[11] Yeh TN, Green HM, Zhou Y, Pitts J, Kitamata-Wong B, Lee S, et al. Short-term effects of overnight orthokeratology on corneal epithelial permeability and biomechanical properties. Invest Ophthalmol Vis Sci 2013;54(6):3902-11. https://doi.org/10.1167/iovs.13-11874.

[12] Elsheikh A, Geraghty B, Rama P, Campanelli M, Meek KM. Characterization of age-related variation in corneal biomechanical properties. J R Soc Interface 2010;7(51):1475-85. https://doi.org/10.1098/rsif.2010.0108.

[13] Knox Cartwright NE, Tyrer JR, Marshall J. Age-related differences in the elasticity of the human cornea. Invest Ophthalmol Vis Sci 2011;52(7):4324-9. https://doi.org/10.1167/iovs.09-4798.

[14] Eliasy A. In vivo measurement of corneal stiffness and intraocular pressure to enable personalised disease management and treatment*.* The University of Liverpool (United Kingdom); 2020.

[15] Vinciguerra R, Elsheikh A, Roberts CJ, Ambrósio R, Jr., Kang DS, Lopes BT, et al. Influence of Pachymetry and Intraocular Pressure on Dynamic Corneal Response Parameters in Healthy Patients. J Refract Surg 2016;32(8):550-61. https://doi.org/10.3928/1081597x-20160524-01.

[16] Huseynova T, Waring GOt, Roberts C, Krueger RR, Tomita M. Corneal biomechanics as a function of intraocular pressure and pachymetry by dynamic infrared signal and Scheimpflug imaging analysis in normal eyes. Am J Ophthalmol 2014;157(4):885-93. https://doi.org/10.1016/j.ajo.2013.12.024.

[17] Fernández J, Rodríguez-Vallejo M, Martínez J, Tauste A, Salvestrini P, Piñero DP. New parameters for evaluating corneal biomechanics and intraocular pressure after small-incision lenticule extraction by Scheimpflug-based dynamic tonometry. J Cataract Refract Surg 2017;43(6):803-11. https://doi.org/10.1016/j.jcrs.2017.03.035.

[18] Vinciguerra R, Ambrósio R, Elsheikh A, Roberts CJ, Lopes B, Morenghi E, et al. Detection of Keratoconus With a New Biomechanical Index. Journal of Refractive Surgery (Thorofare, NJ : 1995) 2016;32(12):803-10. https://doi.org/10.3928/1081597X-20160629-01.

[19] Vinciguerra R, Herber R, Wang Y, Zhang F, Zhou X, Bai J, et al. Corneal Biomechanics Differences Between Chinese and Caucasian Healthy Subjects. Frontiers In Medicine 2022;9:834663. https://doi.org/10.3389/fmed.2022.834663.

[20] Liu Y, Zhang Y, Chen Y. Application of a scheimpflug-based biomechanical analyser and tomography in the early detection of subclinical keratoconus in chinese patients. BMC Ophthalmol 2021;21(1):339. https://doi.org/10.1186/s12886-021-02102-2.

[21] Vinciguerra R, Ambrosio R, Wang Y, Zhang F, Zhou X, Bai J, et al. Detection of Keratoconus With a New Corvis Biomechanical Index Optimized for Chinese Populations. American Journal of Ophthalmology 2023;252:182-7. https://doi.org/10.1016/j.ajo.2023.04.002.

[22] Sedaghat MR, Momeni-Moghaddam H, Azimi A, Fakhimi Z, Ziaei M, Danesh Z, et al. Corneal Biomechanical Properties in Varying Severities of Myopia. Front Bioeng Biotechnol 2020;8:595330. https://doi.org/10.3389/fbioe.2020.595330.

[23] Bao F, Deng M, Wang Q, Huang J, Yang J, Whitford C, et al. Evaluation of the relationship of corneal biomechanical metrics with physical intraocular pressure and central corneal thickness in ex vivo rabbit eye globes. Exp Eye Res 2015;137:11-7. https://doi.org/10.1016/j.exer.2015.05.018.

[24] Eliasy A, Chen KJ, Vinciguerra R, Lopes BT, Abass A, Vinciguerra P, et al. Determination of Corneal Biomechanical Behavior in-vivo for Healthy Eyes Using CorVis ST Tonometry: Stress-Strain Index. Front Bioeng Biotechnol 2019;7:105. https://doi.org/10.3389/fbioe.2019.00105.

[25] Nieto-Bona A, Porras-Ángel P, Ayllón-Gordillo AE, Carracedo G, Piñero DP. Short and long term corneal biomechanical analysis after overnight orthokeratology. Int J Ophthalmol 2022;15(7):1128-34. https://doi.org/10.18240/ijo.2022.07.13.

[26] Ko MW, Leung LK, Lam DC, Leung CK. Characterization of corneal tangent modulus in vivo. Acta Ophthalmol 2013;91(4):e263-9. https://doi.org/10.1111/aos.12066.

[27] Liu G, Rong H, Pei R, Du B, Jin N, Wang D, et al. Age distribution and associated factors of cornea biomechanical parameter stress-strain index in Chinese healthy population. BMC Ophthalmol 2020;20(1):436. https://doi.org/10.1186/s12886-020-01704-6.

[28] Padmanabhan P, Lopes BT, Eliasy A, Abass A, Vinciguerra R, Vinciguerra P, et al. Evaluation of Corneal Biomechanical Behavior in-vivo for Healthy and Keratoconic Eyes Using the Stress-Strain Index. J Cataract Refract Surg 2022. https://doi.org/10.1097/j.jcrs.0000000000000945.

[29] Gao R, Ren Y, Li S, Xu H, Lin X, McAlinden C, et al. Assessment of corneal biomechanics in anisometropia using Scheimpflug technology. Frontiers In Bioengineering and Biotechnology 2022;10:994353. https://doi.org/10.3389/fbioe.2022.994353.

[30] Ma J, Wang Y, Wei P, Jhanji V. Biomechanics and structure of the cornea: implications and association with corneal disorders. Surv Ophthalmol 2018;63(6):851-61. https://doi.org/10.1016/j.survophthal.2018.05.004.

[31] Elsheikh A, Alhasso D, Rama P. Assessment of the epithelium's contribution to corneal biomechanics. Exp Eye Res 2008;86(2):445-51. https://doi.org/10.1016/j.exer.2007.12.002.

[32] Zhang J, Li J, Li X, Li F, Wang T. Redistribution of the corneal epithelium after overnight wear of orthokeratology contact lenses for myopia reduction. Cont Lens Anterior Eye 2020;43(3):232-7. https://doi.org/10.1016/j.clae.2020.02.015.

[33] Ran Z, Moore J, Jiang F, Guo H, Eliasy A, Lopes BT, et al. A new approach for quantifying epithelial and stromal thickness changes after orthokeratology contact lens wear. R Soc Open Sci 2021;8(12):211108. https://doi.org/10.1098/rsos.211108.

[34] Wan K, Yau HT, Cheung SW, Cho P. Corneal thickness changes in myopic children during and after short-term orthokeratology lens wear. Ophthalmic Physiol Opt 2021;41(4):757-67. https://doi.org/10.1111/opo.12824.

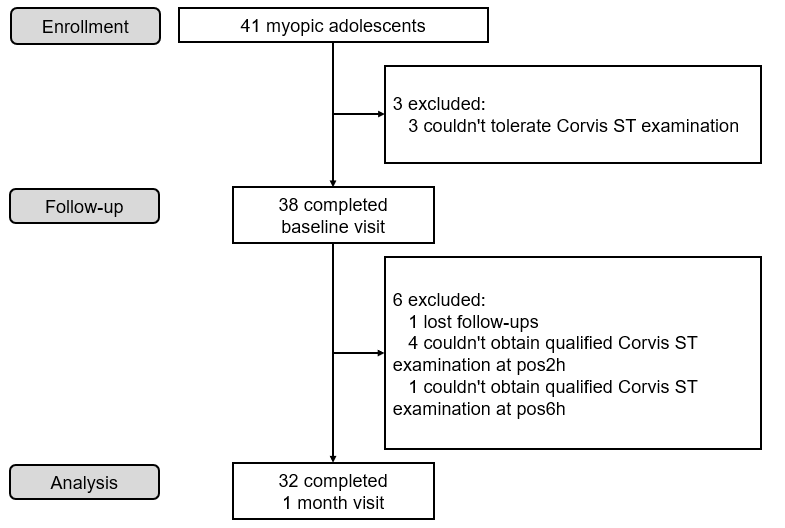
[35] Meng Z, Chen S, Zhe N, Cao T, Li Z, Zhang Y, et al. Short-term Changes in Epithelial and Optical Redistribution Induced by Different Orthokeratology Designs. Eye Contact Lens 2023;49(12):528-34. https://doi.org/10.1097/icl.0000000000001045.

[36] Cheah PS, Norhani M, Bariah MA, Myint M, Lye MS, Azian AL. Histomorphometric profile of the corneal response to short-term reverse-geometry orthokeratology lens wear in primate corneas: a pilot study. Cornea 2008;27(4):461-70. https://doi.org/10.1097/ICO.0b013e318165642c.

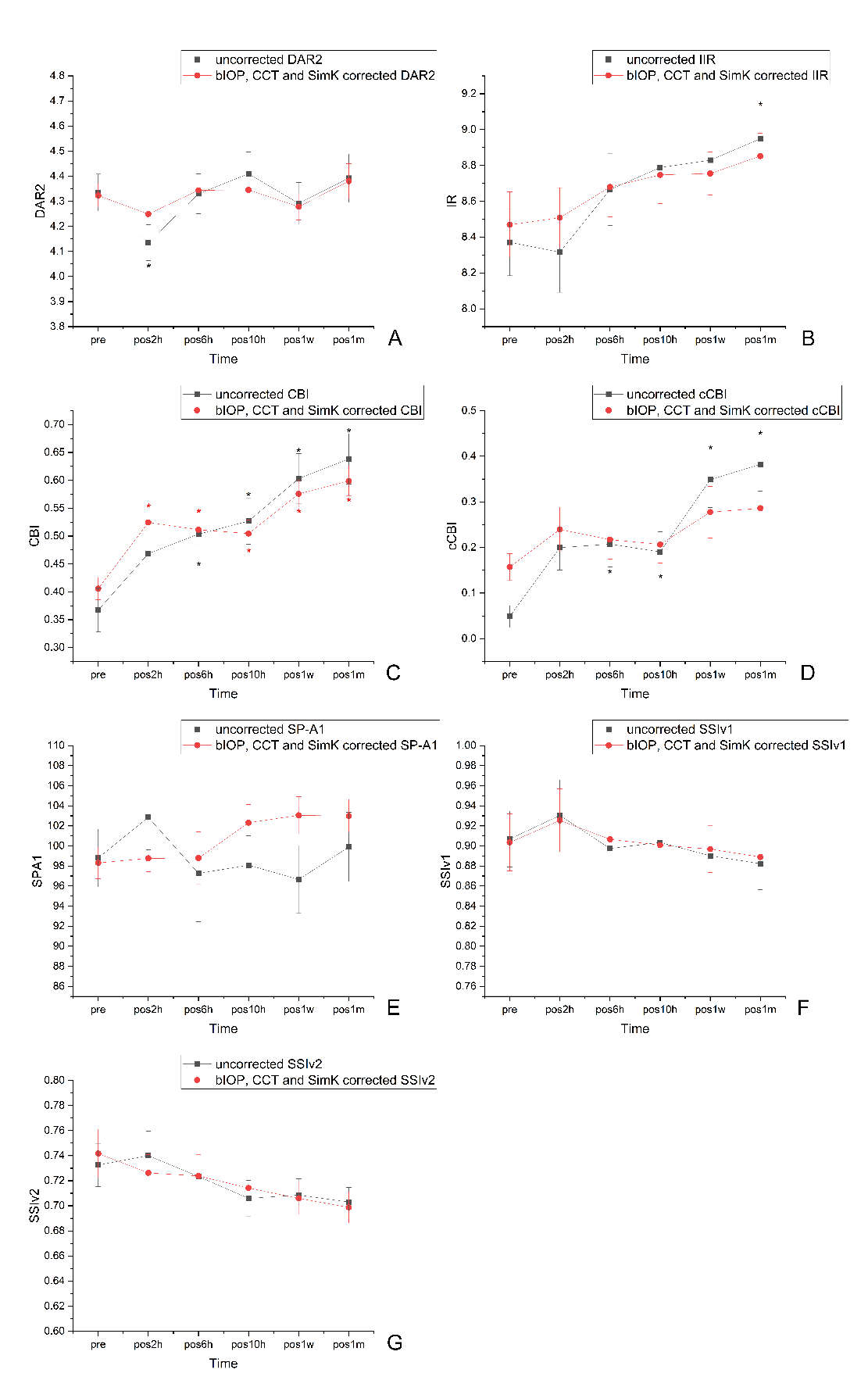
**Figure Captions:**

**Figure 1** Flowchart of the study

**Figure 2** Temporal progression of the Corvis ST parameters measured at baseline and in follow-up clinic visits over a month after starting to wear ortho-k lenses



**Figure 1** Flowchart of the study



**Figure 2** Temporal progression of the Corvis ST parameters measured at baseline and in follow-up clinic visits over a month after starting to wear ortho-k lenses

**Table Captions:**

**Table 1** The nominal ortho-k lens parameters in this study

**Table 2** Ocular parameters in subjects at baseline

**Table 3** Results of linear correlation analyses for Corvis ST parameters change for the Entire Study Cohort

**Table 4** Generalised estimating equations of Corvis ST parameters variables

**Table 1** The nominal ortho-k lens parameters in this study

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Brand | Euclid | Lucid | Dreamlite | CRT |
| Origin | USA | Korea | Holland | USA |
| Material | Boston equalens II | Boston X0 | Boston X0 | HDS 100 |
| Dk | 90 | 140 | 140 | 100 |
| OD | 10.6 | 10.6 | 10.5 | 10.5 |
| CT | 0.22 | 0.23 | 0.18 | 0.16 |
| OZD | 6.2 | 6.2 | 6.0 | 6.0 |
| RCW | 0.5 | 0.9 | 0.5 | 1.0 |

Dk, oxygen permeability (10−11 cm2×mLO2)/(s×mL×mmHg); OD, overall diameter (mm); CT, central thickness (mm); OZD, optic zone diameter (mm); RCW, reverse curve width (mm);

**Table 2** Ocular parameters in subjects at baseline

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameters | Euclid (n=5) | Lucid (n=10) | Dreamlite (n=9) | CRT (n=8) | ANOVA  P |
| Age(y) | 12.70±2.07 | 11.59±1.43 | 11.57±1.47 | 12.75±2.48 | 0.408 |
| Sphere (D) | -3.15±1.51 | -3.68±1.29 | -2.83±1.10 | -3.81±0.84 | 0.301 |
| SE(D) | -3.38±1.54 | -3.81±1.43 | -3.04±1.08 | -3.91±0.89 | 0.450 |
| CCT(μm) | 580.65±32.93 | 565.73±18.86 | 570.57±21.66 | 566.53±34.02 | 0.741 |
| simK(mm) | 7.68±0.31 | 7.69±0.14 | 7.84±0.22 | 7.72±0.21 | 0.415 |
| bIOP  (mm Hg) | 14.31±1.93 | 14.32±1.62 | 13.90±1.47 | 14.96±1.64 | 0.679 |

Mean±standard deviation of ocular parameters in subjects at baseline. Sphere: spherical refractve error, SE: Spherical equivalent; CCT: central corneal thickness; bIOP: biomechanically corrected intraocular pressure; SimK: simulated keratometry;

**Table 3**Results of linear correlation analyses for Corvis ST parameters change for the Entire Study Cohort

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **∆DAR2** | **∆SP-A1** | **∆IIR** | **∆CBI** | **∆cCBI** | **∆SSIv1** | **∆SSIv2** |
| **Sphere** | r=0.283,p=0.130 | r=-0.052,p=0.786 | r=-0.014,p=0.943 | r=-0.157,p=0.407 | r=-0.310,p=0.096 | r=-0.098,p=0.607 | r=-0.016,p=0.931 |
| **SE** | r=0.258,p=0.169 | r=-0.067,p=0.725 | r=-0.035,p=0.854 | r=-0.185,p=0.328 | r=-0.299,p=0.109 | r=-0.080,p=0.676 | r=-0.001,p=0.997 |
| **AGE** | r=-0.162,p=0.394 | r=0.340,p=0.066 | r=-0.165,p=0.383 | r=-0.124,p=0.515 | r=-0.222,p=0.238 | r=0.080,p=0.674 | r=-0.020,p=0.914 |
| **∆CCT** | r=-0.051,p=0.788 | r=0.277,p=0.139 | r=0.037,p=0.847 | **r=-0.511,p=0.004\*** | r=-0.087,p=0.649 | r=-0.128,p=0.500 | r=-0.331,p=0.074 |
| **∆SimK** | r=-0.143,p=0.452 | r=-0.086,p=0.650 | r=0.049,p=0.797 | r=0.301,p=0.106 | **r=0.533,p=0.002\*** | r=-0.088,p=0.645 | r=0.172,p=0.363 |
| **∆bIOP** | **r=-0.634,p<0.001\*** | **r=0.484,p=0.007\*** | r=-0.258,p=0.168 | **r=-0.444,p=0.014\*** | r=-0.123,p=0.516 | r=-0.111,p=0.559 | r=-0.107,p=0.572 |

∆: the difference before and after one month of orthokeratology; SE: Spherical equivalent; CCT: central corneal thickness; DAR2: Deformation amplitude ratio [2mm]; SP-A1: Stiffness parameter at first applanation; IIR: Integrated inverse radius; CBI: Corvis biomechanical index; cCBI: Corvis biomechanical index for Chinese population; SSIv1: Earlier stress-strain index; SSIv2: Updated stress-strain index. \* means p<0.05. The significant correlation was bold.

**Table 4**Generalised estimating equations of Corvis ST parameters variables

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Corvis ST**  **Parameters** | **Variables in generalized estimating equation** | | | | |
| **Time** | **Time** | **CCT (mm)** | **SimK (mm)** | **bIOP (mmHg)** |
| **Before** **covariates correction** | **After CCT, SimK, and bIOP correction** | | | |
| **DAR2** | **χ2=28.966, P<0.001** | χ2=5.695, P=0.337 | **χ2=40.264, P<0.001** | **χ2=15.440, P<0.001** | **χ2=56.264, P<0.001** |
| **SP-A1** | χ2=7.732, P=0.172 | **χ2=15.653, P=0.008** | **χ2=29.832, P<0.001** | χ2=0.260, P=0.610 | **χ2=50.686, P<0.001** |
| **IIR** | **χ2=50.123, P<0.001** | χ2=7.702, P=0.173 | **χ2=8.984, P=0.003** | χ2=0.38, P=0.845 | **χ2=18.840, P<0.001** |
| **CBI** | **χ2=61.456, P<0.001** | **χ2=44.868, P<0.001** | **χ2=73.156, P<0.001** | χ2=0.211, P=0.646 | **χ2=26.907, P<0.001** |
| **cCBI** | **χ2=38.462, P<0.001** | χ2=7.855, P=0.164 | χ2=3.778, P=0.052 | **χ2=22.241, P<0.001** | **χ2=5.762, P=0.016** |
| **SSIv1** | χ2=9.934, P=0.077 | χ2=3.314, P=0.652 | χ2=0.235, P=0.628 | χ2=0.033, P=0.857 | **χ2=4.543, P=0.033** |
| **SSIv2** | χ2=7.167, P=0.208 | χ2=4.898, P=0.428 | χ2=0.992, P=0.319 | **χ2=4.227, P=0.040** | **χ2=9.866, P=0.002** |

DAR2: Deformation amplitude ratio [2mm]; SP-A1: Stiffness parameter at first applanation; IIR: Integrated inverse radius; CBI: Corvis biomechanical index; cCBI: Corvis biomechanical index for Chinese population; SSIv1: Earlier stress-strain index; SSIv2: Updated stress-strain index; χ2: wald’s chi square. Time was dependent variable. CCT, SimK and bIOP were covariates. The significant difference was bold;