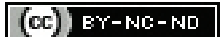


# Measurement of Corneal Biomechanical Properties using Corneal Visualisation Scheimpflug Technology and Ocular Response Analyser in Healthy Saudi Female Adults: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Corneal biomechanics is a relatively new discipline of research that focuses on the physical and biological interactions in the anterior part of the eye. Corneal biomechanics is influenced by a wide range of variables, including environmental influences, hydration, and hormone changes. Central Corneal Thickness (CCT), Intraocular Pressure (IOP), and age are other variables that might impact the corneas. The biomechanical properties of the cornea, at any level of cell to tissue to the sub-organ, might cause serious corneal diseases.

**Aim:** To measure the corneal biomechanical properties in healthy Saudi females.

**Materials and Methods:** This cross-sectional study was conducted in the Department of Optometry and Vision Science, College of Applied Medical Science, King Saud University, Riyadh, Saudi Arabia on 53 right eyes of Saudi female participants from April 2021 to April 2022. The IOP, CCT, and the corneal biomechanical properties at the first applanation (time-T1, velocity-V1, length-L1, deformation amplitude-DA1), second applanation (time-T2, velocity-V2, length-L2, deformation amplitude-DA2), highest concavity (Highest Concavity Time-HCT, Highest Concavity Radius-HCR, Highest Concavity Deformation Amplitude-HCDA), and Peak Distance (PD) were evaluated by using Corneal Visualisation Scheimpflug Technology (CST) whereas, Ocular Response Analyser (ORA) was used for

the comparison of biomechanical properties. The statistical analysis of the data was done by applying statistical package IBM Statistical Package for the Social Sciences (SPSS) (version 24) and conducting Analysis of Variance (ANOVA) tests.

**Results:** The mean age of the participants was  $20.74 \pm 1.89$  years, mean Spherical Equivalent (SE) refraction was  $-1.41 \pm 1.97$  Diopters (D), the mean IOP was  $16.82 \pm 1.96$  mmHg, and the mean CCT was  $569.43 \pm 27.22$   $\mu$ m for the right eyes. The results showed that the two most affecting factors in the biomechanical parameters were IOP and CCT. A potential association was found between first applanation time (T1) and corneal speed during the first applanation (V1) for both IOP and CCT ( $p < 0.001$ ) in the linear regression analysis, while a significant difference was observed in V1 ( $p = 0.029$ ) in SE. In the second applanation, a significant association was found in T2 with IOP ( $p < 0.001$ ) and CCT, cord length of the second applanation (L2) with CCT, and V2 with SE, IOP, and CCT was observed. A significant association between time and SE ( $p = 0.034$ ) was notice in the highest concavity parameter. However, deformation amplitude exhibited the significant association between SE and IOP, radius with IOP and CCT, and the PD with SE, IOP, and CCT ( $p < 0.001$ ).

**Conclusion:** Most of the corneal biomechanical parameters were affected with CCT and IOP. Thus, the biomechanical characteristics of the cornea can be used to compare normal eyes with pathological eyes.

**Keywords:** Central corneal thickness, Corneal hysteresis, Deformation amplitude, Intraocular pressure, Peak distance

## INTRODUCTION

Cornea is very essential for human eye vision, as 70% of the refractive power of the whole eye is provided by the cornea. Any changes in the features of cornea can lead to eye problems [1,2]. Biomechanical characteristics play a vital role in maintaining shape and transparency of the cornea and have been a subject of study since 1970 [3,4]. Biomechanical properties clinically improve various treatments and management procedures that interact mechanically with the eye [5]. A keen interest in ocular biomechanical properties has emerged among refractive and glaucoma specialists due to their utilisation in the screening, diagnosis and treatment [6]. The biomechanics of cornea are affected by several variables, including elasticity [7], moisture content [8], viscosity [9] and corneal stroma thickness [10,11]. The stroma is the principal load-bearing layer among the five layers of cornea [12]. Numerous research studies have reported that eyes with keratoconus [13], Fuchs corneal dystrophy [14], glaucoma [15] and after refractive surgery have considerably different corneal biomechanics in contrast to normal eyes [16,17].

Thus, a greater understanding of corneal biomechanics is crucial for the diagnosis and treatment of the aforementioned disorders [18]. Also, the refractive surgery for the prediction of the development of ectasia requires detailed information about corneal biomechanics [19]. Various studies have addressed a strong correlation between Corneal Hysteresis (CH) and Corneal Resistance Factor (CRF) with Central Corneal Thickness (CCT) [20-22]. A study conducted by Hwang HS et al., reported that Corneal Volume (CV) was positively correlated with CH but not with CRF [23]. However, Çevik SG et al., illustrated a positive correlation between CH, CRF and CV and a negative correlation between CH, CRF and both of posterior steep and average posterior values [24]. Meanwhile, Montard R et al., reported significant association between CH and CRF with corneal pachymetry, but not with corneal compensated IOP (IOPcc) [25]. Hence, more studies are required to observe the trend of corneal biomechanics and anterior segment parameters. Recently, ORA and CST have been the two main tools available for the study of corneal biomechanical properties [26]. The ORA, a bidirectional applanation

tonometry, is used to measure CH, CRF and IOP [27-29]. The ORA has many shortcomings, such as poor repeatability and it is easily influenced by morphological features of cornea [27]. Therefore, CST was designed based on Scheimpflug imaging technology, which can capture more than 10 biomechanical characteristics of corneal deformation after an air puff [30]. These biomechanical values and associated factors in the healthy cornea should be known to verify the changes in these parameters. Therefore, the present study aimed to evaluate the corneal biomechanical metrics in healthy Saudi females by CST and ORA.

## MATERIALS AND METHODS

The present cross-sectional, time-bound study was performed on the healthy eyes of 53 healthy Saudi females in Department of Optometry and Vision Science, College of Applied Medical Science, King Saud University, Riyadh, Saudi Arabia, from April 2021 to April 2022. Ethical approval (IRB Approval ID E-20-5624) was obtained from the Office of Human Research Protection (OHRP) at the College of Medicine, KSU, Riyadh, Saudi Arabia.

**Inclusion and Exclusion criteria:** The present study included the healthy right eyes of young females in the 18-24 years of age range who had never had any eye surgery, were free from ocular or systemic diseases and had refractive error of less than -6.00 D. Participants who were unable to complete all the examinations, as well as pregnant and lactating females, were excluded.

### Study Procedure

All the participants were subjected to an extensive eye examination to detect any eye problem. A Snellen chart was applied for slit-lamp microscopy and visual acuity tests to examine the Best Corrected Visual Acuity (BCVA). An auto kerato-refractometer (TRK-1P Topcon, Tokyo, Japan) was used to determine refractive power and a fundus examination was conducted to assess the fundus. After all these investigations, biomechanical properties were measured using ORA and CST.

All the subjects signed the consent form after knowing the procedure and objectives of the study. The examinations were conducted by a qualified optometrist using the same devices between 10:00 and 13:00 hours and recorded the average of each parameter was recorded. The CST measurements were recorded thrice per participant, with a time interval of one minute between each measurement and data storage as well as processing operations was noted on the CST instrument. The parameters measured with CST were considered reliable according to the "OK" quality index displayed on the device monitor.

The ORA measurement was also performed three times on each participant with a time interval of 5-min between each measurement. The high-quality index (It is the waveform score measured with the ORA) greater than seven was employed and the average value was selected for the analysis. ORA (ORA; Reichert Ophthalmics, Depew, NY) is a dynamic bidirectional applanation device used to analyse corneal biomechanics in a simpler, non invasive way. It has ability to calculate the CH and CRF to improve the accuracy of IOP measurement by using corneal biomechanical data. It provides two distinct IOP parameters: IOPg and the IOPcc. It functions by sending an air pulse that moves the cornea inward and slightly convex before it comes back to its natural form. This response is used to detect corneal biomechanical properties in a very short span of time—about 20 milliseconds—and after this process cornea regains to its normal shape [31].

Another non contact device, named as Corneal visualisation Scheimpflug Technology (CST), were also used for the measurement of corneal biomechanical parameters. It captures cross-sectional images of the cornea after the application of an air puff for 30 milliseconds, using a high-speed Scheimpflug camera which takes over 4,300 images per second [32]. The cornea underwent

from natural to three distinct conditions due to the air puff, which includes, the first applanation (A1), second applanation (A2) and the highest concavity. As the cornea deforms in response to the air puff, the Intraocular Pressure (IOP) can be determined at the point of first applanation. All the corneal deformation responses to the air puff are captured by the CST in around 100 milliseconds. A study reported in 2016 stated that CST was able to give one important parameter known as biomechanically corrected IOP (bIOP-CorVis), which is obtained in terms of corneal dynamic reactions and physical corneal structures [33]. This IOP is impacted by biomechanical properties, including maximum concavity radius, age and Central Corneal Thickness (CCT). The formula for bIOP-CorVis is given below [34,35]:

$$\text{bIOP} = C_{\text{CCT1}} \times C_{\text{AP1}} \times C_{\text{age1}} + C_{\text{CCT2}} \times C_{\text{age2}} + C_{\text{DCR}} + a_{19}$$

$$C_{\text{CCT1}} = (a_1 \times \text{CCT}^3 + a_2 \times \text{CCT}^2 + a_3 \times \text{CCT} + a_4)$$

$$C_{\text{AP1}} = (a_5 \times \text{AP1} + a_6)$$

$$C_{\text{age1}} = (a_7 \times \{\text{Ln}(\text{Beta})\}^2 + a_8 \times \{\text{Ln}(\text{Beta})\} + a_9)$$

$$C_{\text{CCT2}} = (a_{10} \times \text{CCT}^3 + a_{11} \times \text{CCT}^2 + a_{12} \times \text{CCT} + a_{13})$$

$$C_{\text{age2}} = (a_{14} \times \{\text{Ln}(\text{Beta})\}^2 + a_{15} \times \{\text{Ln}(\text{Beta})\} + a_{16})$$

$$\text{Beta} = 0.5852 \times \exp(0.0111 \times \text{age}[\text{year}])$$

$$C_{\text{DCR}} = a_{17} \times \text{HCR} + a_{18}$$

Where  $C_{\text{CCT1}}$ ,  $C_{\text{AP1}}$  and  $C_{\text{age1}}$  denoted CCT, air pulse and age at applanation 1, whereas,  $C_{\text{CCT2}}$  and  $C_{\text{age2}}$  represent the CCT, age at applanation 2 and  $C_{\text{DCR}}$  represents the correction based on biomechanical response (HCR). The constants are denoted as  $a_1$  to  $a_{19}$ . The achieved adjustment of biomechanical parameter is therefore found more accurate. The current study is a part of ongoing project and there is no overlap among the results of the study.

## STATISTICAL ANALYSIS

The statistical analysis of the data was done by using the IBM SPSS statistical package (version 24.0). The normality of the data was checked using the Shapiro-Wilk normality test. An Analysis of Variance (ANOVA) was carried out for all the dependent variables according to the different diagnostic categories, with multiple comparisons made to distinguish the diagnostic differences, taking p-value <0.05 as statistically significant. Dependent variables analysed were time, velocity and length for the investigated studies (IOP, CCT, SE).

## RESULTS

The right eyes of 53 healthy Saudi female adults with a mean age of  $20.74 \pm 1.89$  years (range: 18-26 years) and a mean Spherical Equivalent (SE) of  $-1.41 \pm 1.97$  D were included in the study. The average value of Central Corneal Thickness (CCT) in all the subjects was found  $569.43 \pm 27.22$   $\mu\text{m}$  [Table/Fig-1]. The mean values for the first applanation, second applanation and highest concavity parameters are presented in [Table/Fig-2]. The present study demonstrated a substantial correlation between T1 and V1 regarding IOP and CCT in the first applanation; but only a significant difference in V1 was found for SE. On the other hand, the second applanation demonstrated a substantial correlation in T2 with IOP and CCT, L2 with CCT and V2 with SE, IOP and CCT [Table/Fig-3-5]. However, the highest concavity parameters showed a significant association of time with SE, deformation amplitude with SE and IOP; the radius with IOP and CCT and the PD with SE, IOP and CCT [Table/Fig-6a,b,7].

Characteristics	Mean±Standard deviation	Range
Age (Years)	20.74±1.89	18 to 26
Spherical Equivalent (SE) (Diopter)	-1.41±1.97	-5.50 to 3.25
Intraocular Pressure (IOP), mmHg	16.82±1.96	13.50 to 21.90
Central Corneal Thickness (CCT) in $\mu\text{m}$	569.43±27.22	528 to 658

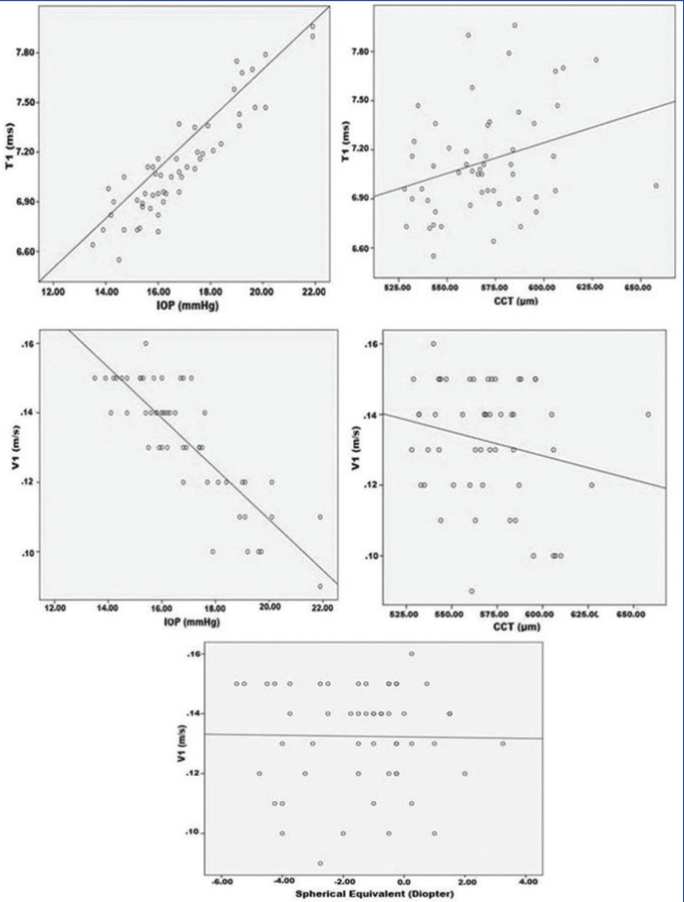
[Table/Fig-1]: Demographic and ocular features of participants.

Characteristics		Mean±Standard deviation	Range
First Applanation (A1)	T1 (ms)	7.13±0.33	6.55 to 7.96
	L1 (mm)	2.39±0.31	1.79 to 3.04
	V1 (m/s)	0.13±0.02	0.09 to 0.16
Second Applanation (A2)	T2 (ms)	21.77±0.37	20.92 to 22.36
	L2 (mm)	2.25±0.51	1.40 to 4.72
	V2 (m/s)	-0.26±0.03	-0.33 to -0.18
Highest concavity	Time (ms)	17.07±0.50	15.02 to 17.79
	DA (mm)	1.04±0.09	0.84 to 1.27
	Radius (mm)	8.1004±0.87	6.43 to 11.34
	Peak Distance (PD) (mm)	4.9183±0.25	4.25 to 5.47

[Table/Fig-2]: CST parameters.

First Applanation (A1), p-value (Standardised Coefficient (SC))				Second Applanation (A2), p-value (Standardised Coefficient (SC))		
Parameters	T1	L1	V1	T2	L2	V2
Age (years)	0.671 (-0.018)	0.575 (-0.081)	0.360 (0.065)	0.513 (0.049)	0.756 (-0.042)	0.360 (-0.076)
SE (D)	0.856 (0.007)	0.640 (-0.066)	0.029 (-0.155)	0.812 (-0.018)	0.243 (0.157)	0.002 (0.272)
IOP (mmHg)	<0.001 (0.907)	0.268 (0.160)	<0.001 (-0.850)	<0.001 (-0.838)	0.051 (0.270)	<0.001 (0.790)
CCT (μm)	<0.001 (0.294)	0.254 (0.161)	0.004 (-0.205)	0.038 (-0.155)	0.029 (0.295)	0.047 (0.164)

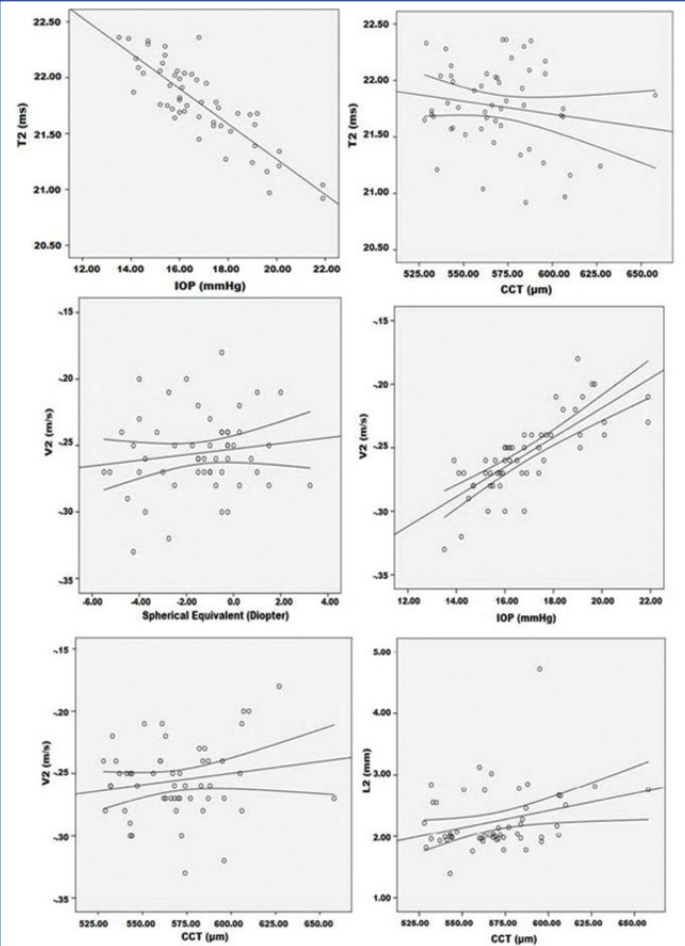
[Table/Fig-3]: Association between different ocular factors with each parameter taken by CST during first and second applanation. ANOVA was used.



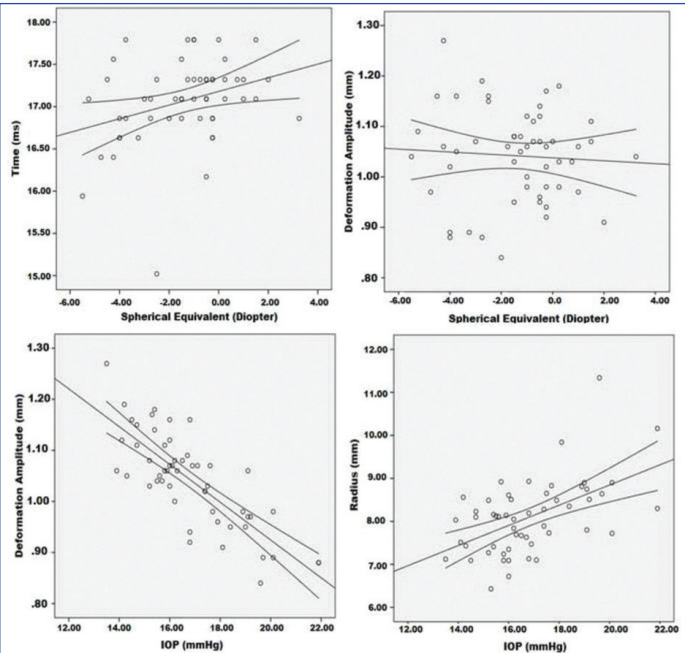
[Table/Fig-4]: Significant CST parameters at the first Applanation (A1) moment.

ORA Results

To ensure the accuracy, only 40 females were available at the same time to record the corneal biomechanical features. An insignificant association was observed between the parameters and refractive errors (emmetropia, hyperopia and low to moderate myopia) [Table/Fig-8,9].



[Table/Fig-5]: Significant CST parameters at the second Applanation (A2) moment.



[Table/Fig-6a]: Significant CST parameters at the highest concavity moment.

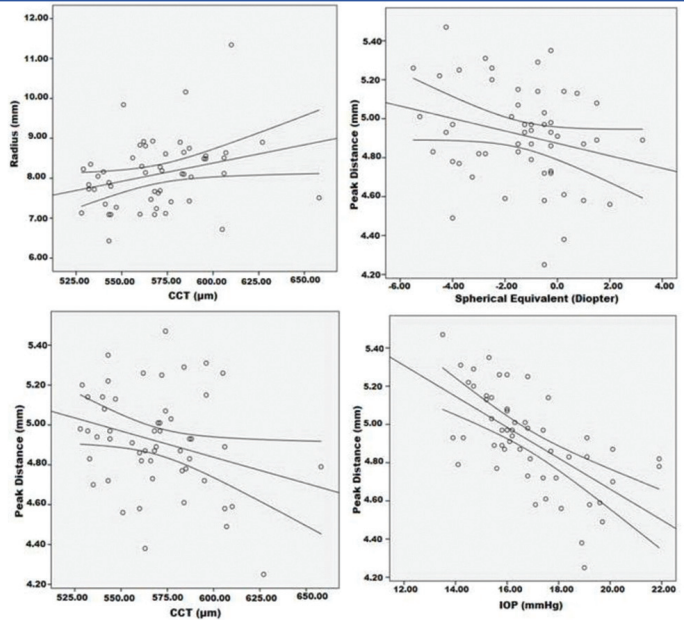
Comparison between IOPcc and bIOP

Using the paired samples t-test, the analysis revealed a significant difference (p-value <0.001) between the IOP measurements produced by ORA and CST. A weak positive correlation was observed between the CST and ORA readings for IOP (r=0.463, p=0.003). As shown in [Table/Fig-10], CST had a higher mean, with a mean difference of 3.59 (95% confidence interval: 3.17-4.02).

DISCUSSION

The accurate knowledge of corneal biomechanical parameters is important for achieving precise IOP measurement and





[Table/Fig-6b]: Significant CST parameters at the highest concavity moment.

Parameters	Highest concavity, p-value (Standardised Coefficient (SC))			
	Time	Deformation amplitude	Radius	Peak Distance (PD)
Age (years)	0.940 (0.010)	0.369 (0.078)	0.261 (0.134)	0.414 (0.078)
SE (D)	0.034 (0.298)	0.028 (-0.192)	0.837 (0.024)	<0.001 (-0.365)
IOP (mmHg)	0.580 (-0.077)	<0.001 (-0.802)	<0.001 (0.559)	<0.001 (-0.659)
CCT (μm)	0.192 (-0.178)	0.447 (-0.064)	0.014 (0.290)	0.004 (-0.279)

[Table/Fig-7]: Correlation analysis of highest concavity parameters.

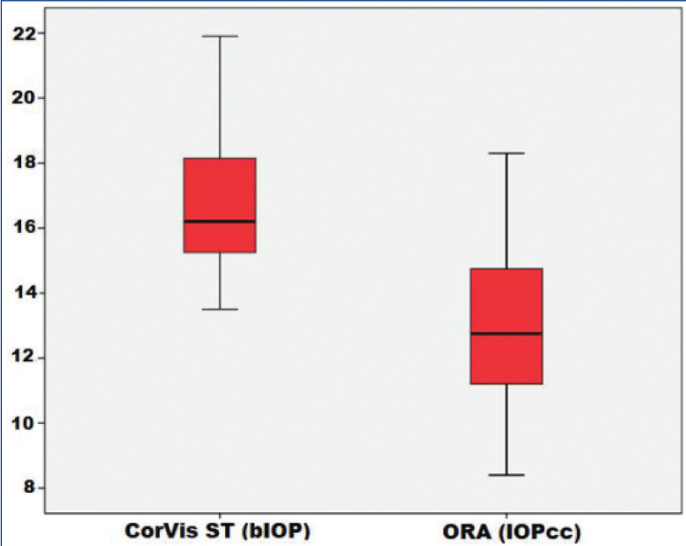
Parameters	Mean±Standard deviation	Range
Age (years)	20.45±1.87	18 to 24
Spherical Equivalent (SE) (D)	-1.38±1.86	-4.75 to 3.25
IOPcc (mmHg)	13.10±2.50	8.40 to 18.30
IOPg (mmHg)	14.36±3.15	8.70 to 20.40
CH (mmHg)	12.15±1.62	9.20 to 15.10
CRF (mmHg)	11.55±1.97	7.60 to 15.10

[Table/Fig-8]: Demographic data and ORA parameters (sample size: 40).

Parameters	Hyperopia (n=5)	Emmetropia (n=8)	Myopia (n=27)	Mean difference	p- value
	Mean±Standard deviation				
Age (years)	21.80±2.12	20.13±1	21±2.05	0.80	0.660
IOPcc (mmHg)	13.28±1.99	13.2±2.56	13.06±2.64	0.22	0.830
IOPg (mmHg)	14.11±3.05	14.21±3.52	14.42±3.22	0.30	0.811
CH (mmHg)	11.80±1.98	11.94±1.41	12.23±1.55	0.43	0.508
CRF (mmHg)	11.19±2.40	11.33±1.97	11.64±1.90	0.45	0.568

[Table/Fig-9]: ORA parameters with refractive errors. ANOVA was used.

correction, especially in subjects with corneal disorders. These parameters are also important after refractive surgery and for understanding the pathogenesis of corneal degenerative diseases such as keratoconus and glaucoma [36]. In the present study, various corneal biomechanical parameters of adult females were evaluated. The results revealed that CCT and IOP were the two main factors affecting the corneal biomechanical parameters. Out of 53 participants, the results of 40 healthy participants (mean age: 20.45±1.87 years, mean SE: -1.38±1.86 diopter) also were measured using ORA and this data was compared with the results of CST to validate the accuracy. All these parameters were noticed statistically insignificant with the refractive error groups. The IOP measured with CST and ORA were found weak and positively correlated (r=0.463, p-value=0.003). A study done by Wang W et



[Table/Fig-10]: Box plot for CST and ORA mean difference comparison of IOP (CST mean: 16.6950 mmHg, ORA mean: 13.1025 mmHg).

al., reported that the most notable specifications CCT, IOP, HCDA and V1 for the comparison of L1, L2 and PD [36]. While as the prominent noteworthy specifications according to Sashia BN et al.'s study were IOP, followed by T1, T2, CCT, HCR and HCDA [37].

Various studies have reported that biomechanical parameters determined by CST are independent of gender [38-40]. However, a research study conducted by Salouti R et al., found the different values of V1 and HCT for males and females [41]. Another study performed in Brazil reported a significantly low effect of CCT on corneal biomechanical parameters on Brazilian participants' eyes, with a mean patient age of 35.80±12.83 years and a range of 21.07 to 78.84 years [42]. An earlier study on 89 healthy Brazilian participants' eyes (mean age: 27.50±6.30, range: 12.54 to 39.70 years) was performed using CST to find any relationship between age and corneal biomechanical parameters. The results showed that only HCT was affected by age, because with age the cornea becomes stiffer and less viscoelastic as a result of an increase in the cross-linkage of collagen fibrils [43]. However, a similar study conducted on 108 healthy Chinese children (32 girls and 76 boys, mean age: 10.80±4.13 years, range: 4 to 18 years) reported no statistically significant relation of age with CST parameters, but CST parameters were found highly influenced by CCT and IOP [44]. The children and young adults may not have any significant effect, but the potent effect might be in old generation. A previous study reported an assessment of corneal biomechanical properties on 177 Spanish healthy populations (mean age: 33.27±7.65, range: 20-56 years) and results revealed weak association between CH and refractive error; these changes may affect IOP and hence increasing the risk of glaucoma with the age [45]. Another research carried on 215 healthy Saudi individuals (mean age: 33.6±11.75 years) for the corneal biomechanics using ORA reported a statistical difference between males and females in CH (p-value: 0.020) and CRF (p-value: 0.047) [46]. Moreover, a study carried out on the healthy black and white US participants revealed that healthy black subjects had even lower CH and CRF in comparison to white subjects, but the differences were insignificant [47]. However, the results obtained in the present study showed that the values of CH and CRF were close to each other irrespective of the age, in contrast to earlier reported studies [43,44]. This study has provided a reference database for corneal biomechanical properties in Saudi adult females, but more studies in this area are needed with ORA and CST in different age groups.

Limitation(s)

The present study was performed on young females and small sample size is also considered a limiting factor. No significant difference between the biomechanical parameters were found

because of young age range. The results presented in the present study need to be further confirmed by longitudinal cohort studies with larger sample size of different age groups of males and females with different ethnicities. For the comparison between the ORA and CST, more studies must be done after including the CCT in the comparison with IOP to give a better idea on the different results taken with the two devices.

## CONCLUSION(S)

The present study provides information that the CCT and IOP are the main factors affecting the biomechanical parameters. The parameters taken with CST and ORA instruments were compared and only a weak, positively linked significant difference was found between the IOP generated with CST and ORA.

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