

# Study of corneal biomechanical properties and associated factors in school-age children

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## Abstract

**Purpose:** To study and analyze the correlation among corneal biomechanical properties and associated factors including central corneal thickness (CCT), corneal curvature (CT), and intraocular pressure (IOP) in school-age children.

**Methods:** A cross section investigation was conducted. An ocular response analyzer was utilized to assess the corneal biomechanical properties, such as corneal hysteresis and corneal resistance factors, in children of school age. Multivariate regression analysis was used to investigate the relationship between corneal biomechanical properties and other ocular parameters including CCT, corneal curvature (k1 and k2), and IOP. The right eyes of all subjects were selected for statistical analysis.

**Results:** A total of 571 children were enrolled; 303 male and 268 female, with an average age of  $10.47 \pm 1.0$  years. The mean value of corneal hysteresis was  $10.98 \pm 1.78$  mmHg, corneal resistance factor was  $11.46 \pm 1.69$  mmHg, and CCT was  $556.01 \pm 28.97$   $\mu\text{m}$ .

**Conclusion:** The feasibility of corneal biomechanical detection in school age children was validated and supplemented fundamental data of corneal biomechanical properties in school-age children and preliminarily addressed associated factors. (*Eye Science* 2013; 28: -)

**Keywords:** corneal biomechanical properties, central corneal thickness, school-age children

Biomechanics, as a new marginal discipline, analyzes the structure and function of biological systems such as humans, animals, plants, organs, and cells by the methods of mechanics. The human

cornea mainly consists of collagen fibers, and the toughness and elasticity of these fibers give the cornea certain biomechanical properties. Previous studies indicated that corneal biomechanical properties (corneal hysteresis [CH] and corneal resistance factor [CRF]) play a vital role in intraocular pressure (IOP) measurement, glaucomatous optic nerve damage, and refractive surgery, etc<sup>1,2</sup>. The ocular response analyzer is the only instrument in the world that is capable of measuring corneal biomechanical properties. This study was designed to assess corneal biomechanical properties in school-age children and to look for a correlation between corneal biomechanical properties and other parameters including central corneal thickness (CCT), corneal curvature, and IOP.

## Materials and methods

### Study subjects

The study subjects were grade 3 to 5 primary school students from Jinsha Primary School in Jinping District, Shantou City. The right eye data were used for subsequent statistical analysis. Jinsha Primary School is a first-class school in Shantou with over 2 000 students, most of whom are from immigrant families. Inclusion criteria: primary school students, without a history of severe systemic diseases, glaucoma, uveitis, retinal detachment, corneal illnesses, ocular trauma or eye surgery; no corneal opacity was detected. Informed consent was obtained from the guardians of the enrolled students.

### Measurement methods

CH, Goldmann-related IOP (IOPg), and CRF were measured using an ocular response analyzer. CCT was assessed by a pachymeter and corneal curvature was detected by an autorefractor.

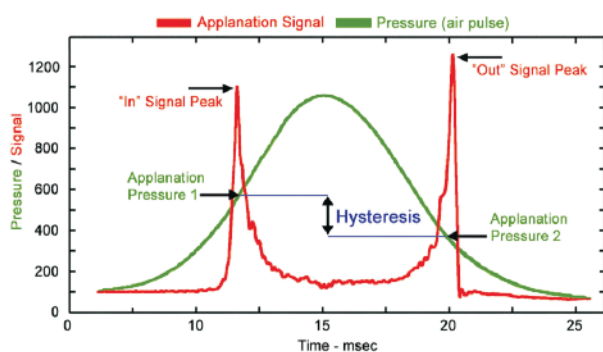
### Ocular response analyzer

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The ocular response analyzer is a revolutionary non-contact instrument designed to measure IOP and corneal biomechanical properties (software version ORA 2.02; Reichert Inc., U.S.) The instrument makes measurements by applanating the cornea with a puff of air and monitoring the shape of the cornea with an electro-optical detection system as two applanation spikes (P1 and P2) are recorded (Figure 1). In theory, two applanation pressures should be equal. Actually, varying corneal biomechanical properties cause a discrepancy in two applanation pressure values. Based upon these differences, corneal biomechanical properties such as CH and CRF can be estimated. Meanwhile, IOPg and corneal-compensated IOP can be measured.



**Figure 1** Corneal hysteresis

CH and CRF are regarded as two new parameters describing corneal biomechanical properties. CH represents the corneal viscoelastic property and its capacity for adsorbing and damping the energy of the air pulse. The value was equal to the difference between two applanation IOP (P1-P2). The CRF reflects the total corneal resistance, including viscosity and elasticity, which is equal to  $P1 - (0.7 * P2)$ . The IOPg had a relatively strong correlation with Goldmann applanation IOP<sup>3</sup>. Compared with applanation IOP, the corneal-compensated IOP measurement is subject to less influence from corneal factors such as CCT and corneal astigmatism, etc., making it one of the favorable methods for IOP measurement<sup>4,5</sup>.

The study subjects sit in front of the instrument, fixating on the green target and feeling a very gentle puff of air from the air tube. Two operators were assigned for each subject because children had difficul-

ties in cooperation with the test. One operator was responsible for operating the computer and instrument and the other one instructed and assisted the children to fixate their head position. The measurement results were strictly selected according to the criteria proposed by Reichert Inc. Ideally, the peak-amplitude of the applanation signals will be symmetrical and above the green pressure curve. The raw applanation signal curve will be smooth and its peak amplitude will be above that of filtered signal curve (Figure 1). The measurement was performed three times and the signal with the highest waveform score (WS) was selected. The results of CH, CRF, and IOPg were obtained.

### Central corneal thickness

After ocular response analyzer measurement, the patients were administered one droplet of alcaïn in the test eyes for surface anesthesia. CCT was measured by an A-ultrasound pachymeter (Reichert Inc., New York, USA) for eight times. The average value was obtained after eliminating the maximal and minimal measurement values.

### Corneal curvature

Corneal curvature was measured by an autorefractor three times and the mean value was calculated (k1 and k2).

### Statistical analysis

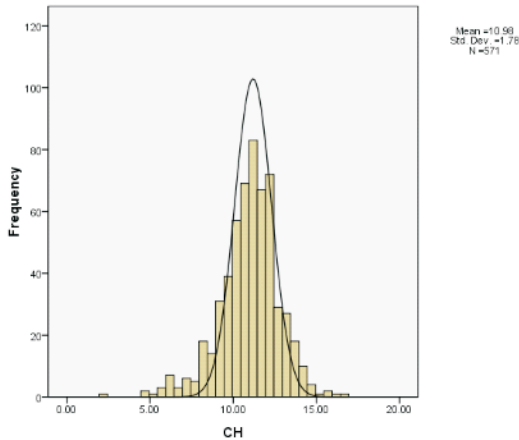
SPSS17.0 statistical software was utilized for statistical analysis (SPSS Inc, Chicago, Illinois, USA). The correlation between corneal biomechanical properties (CH and CRF) and other ocular parameters such as age, gender, CCT, corneal curvature (k1 and k2), and IOP was investigated by multivariate regression analysis. IOPg-related factor analysis was performed by bivariate single factor and multivariate analysis.  $P < 0.05$  was considered as statistically significant.

## Results

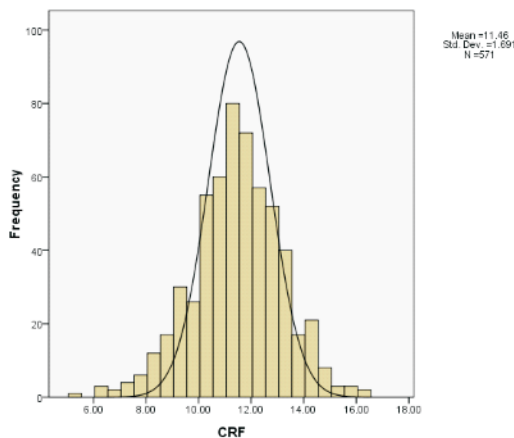
### Age, gender, CCT, and corneal biomechanical properties of study subjects

A total of 571 subjects, 303 males and 268 females, aged  $10.47 \pm 1.0$  years on average, were enrolled in this study. As shown in Table 1, the mean CH, CRF, CCT, IOPg, k1, and k2 were  $10.98 \pm 1.78$  mmHg,  $11.46 \pm 1.69$  mmHg,  $556.01 \pm 28.97$   $\mu$ m,

17.36±3.06 mmHg, 42.62±1.41 and 43.88±1.53, respectively. Both CH and CRF showed normal distribution (Figures 2 and 3). Mean waveform score was 7.05±1.44 according to the ocular response analyzer.



**Figure 2** Distribution of corneal hysteresis of 571 school age children



**Figure 3** Distribution of corneal resistance factor of 571 school age children

### Analysis of related factors of CH and CRF

Multivariate regression analysis showed no correlation between CH/CRF and gender, age, and k1 ( $P>0.05$ ), while CH/CRF was correlated with k2, CCT, and IOP ( $P<0.01$ ), and especially CCT (standard regression coefficient=0.500 and 0.447).

### Analysis of related factors of IOP

Bivariate single factor analysis of IOPg and CCT showed that IOPg was positively correlated with CCT ( $r=0.315, P<0.01$ ). Multivariate analysis revealed that IOPg was correlated with CH and CRF, rather than with CCT ( $P>0.05$ , Table 3).

**Table 1** Corneal biomechanical properties, central corneal thickness, corneal curvature, intraocular pressure and Waveform Score of 571 eyes( $\bar{x}\pm sD$ )

Parameters	Mean( $\bar{X}\pm SD$ )	95% Confidence Interval
CH (mmHg)	10.98±1.78	10.84–11.13
CRF (mmHg)	11.46±1.69	11.32–11.60
CCT ( $\mu m$ )	556.01±28.97	553.63–558.39
IOPg (mmHg)	17.36±3.06	17.11–17.61
K1	42.62±1.41	42.50–42.74
K2	43.88±1.53	43.76–44.01
WS	7.05±1.44	6.93–7.17

### Discussion

A substantial number of studies have suggested that corneal thickness partially affects the accuracy of IOP measurement and increased corneal thickness probably overestimates IOP<sup>6,7</sup>. Corneal thickness is a vital index of corneal rigidity and it is one of the biological properties that influences IOP. Minimization of the effect of corneal thickness on IOP measurement to the greatest extent possible requires that ophthalmologists utilize a correction formula to calculate the actual IOP. Nevertheless, the results were

**Table 2** Multivariate regression analysis of corneal biomechanical properties

Parameters	CH		P	CRF		P
	Regression coefficient (SE)	Standardized regression coefficient		Regression coefficient (SE)	Standardized regression coefficient	
Gender	0.083(0.135)	0.023	0.540	0.072(0.115)	0.021	0.533
Age	0.027(0.064)	0.015	0.678	0.022(0.054)	0.013	0.688
k1	-0.095(0.094)	-0.075	0.315	-0.081(0.080)	-0.067	0.312
k2	0.325(0.086)	0.279	<0.01	0.277(0.073)	0.251	<0.01
CCT	0.031(0.002)	0.500	<0.01	0.026(0.002)	0.447	<0.01
IOPg	-0.138(0.022)	-0.237	<0.01	0.182(0.019)	0.330	<0.01

not sufficiently stable or reliable and are not widely accepted. In addition, corneal thickness is one of corneal biological properties affecting IOP. Thus, correction of IOP based only on corneal thickness is both theoretically and practically unfeasible. Clinically, some cases that presented with corneal edema after cataract surgery had decreased IOP measurements, suggesting that corneal thickening underestimated rather than overestimated the IOP measurement. This evidence indicated that depending on corneal thickness alone to reflecting corneal rigidity or the correct IOP measurement is far from sufficient and that additional parameters are urgently required that can reflect corneal biological properties in a comprehensive manner.

Fung<sup>9</sup> stated that biological parenchyma, such as the cornea, had viscoelastic properties, including laxity, creep, and hysteresis. Compared with corneal thickness and curvature and other static parameters, corneal biomechanical properties under external force might reflect the overall properties of the cornea in a more comprehensive pattern. Additional information may provide more references for the incidence and progress of corneal diseases and preoperative and postoperative corneal pathological changes. Previously, corneal biomechanical properties were measured *in vitro*. The ocular response analyzer has enabled ophthalmologists to measure corneal biomechanical properties *in vivo*. CH and CRF, as novel parameters of corneal biomechanical properties, have verifiable significance in IOP measurement, estimates of glaucomatous optic nerve damage, and refractive surgery outcomes, etc.<sup>1,2</sup>

Corneal biomechanical properties, especially when CH was lower than the normal value, probably act as risk indicators for the progression of certain diseases. Previous studies indicated that the CH was lower in patients with glaucoma than in healthy subjects<sup>3</sup>. Congdon et al found that low CH was correlated with visual field progression of glaucoma<sup>10</sup>. Luce<sup>11</sup> et al noted that the patients with keratoconus and corneal dystrophy and those who had undergone LASIK had decreased CH. Pepose<sup>12</sup> et al suggested that corneal viscosity and elasticity were reshaped by refractive surgery, leading to a reduction in CH. The CH measurement played an extremely vital role in

preoperative corneal evaluation and postoperative follow up. Recent findings indicated that CH was negatively correlated with axial length, hinting that CH possibly acts as an influential factor or early diagnosis index of myopia progression<sup>13,14</sup>.

In this study, ORA measurement showed that mean waveform score of 571 primary school children was  $7.05 \pm 1.44$ , indicating the feasibility of accurate measurement of corneal biomechanical properties in primary school children<sup>15</sup>. The mean CH and CRF were  $10.98 \pm 1.78$  mmHg (95% CI: 10.84–11.13) and  $11.46 \pm 1.69$  mmHg (95% CI: 11.32–11.60), respectively. Rui Liu et al<sup>16</sup> found that the mean CH was  $(9.9 \pm 1.6)$  mmHg and the mean CRF was  $(10.1 \pm 1.8)$  mmHg in 205 healthy subjects, in contrast to the findings of the present study. The discrepancy might have resulted from different ages of subjects or from sampling errors. Lim<sup>17</sup> reported right eye data of 271 adolescents (approximately 68.6% of subjects were of Chinese origin,  $13.97 \pm 0.89$  years of age, on average), and the mean CH and CRF were  $11.78 \pm 1.55$  mmHg and  $11.81 \pm 1.71$  mmHg, respectively, which were slightly higher than the values in the present study.

Multivariate analysis revealed that CH and CRF were positively correlated with k2, CCT, and IOPg, but had no correlation with age, gender, and k1. Corneal surgery or corneal diseases caused changes in corneal curvature and corneal thickness, both probably leading to alterations in corneal biomechanical properties, especially corneal thickness changes (Table 2). The results in this investigation showed that CH and CRF were not correlated with age, possibly because the participants were mainly third to fifth grade pupils. Previous studies revealed that CH and CRF declined as age increased<sup>18</sup>, which may be associated with changes in corneal biological properties such as elasticity and rigidity, etc. A number of research studies reported that corneal structure changed with age, including enlargement of the space between corneal collagen fibers and increasing corneal crossing, which probably changed corneal biomechanical properties. Kamiya et al<sup>20</sup> assessed the corneal biomechanical properties of 204 subjects, aged from 19 to 89 years and the outcomes indicated that CH decreased as age increased. However, Kir-

wan et al<sup>3</sup> found no correlation between CH and age in children aged between 4 and 18 years. These findings indicate that corneal biomechanical properties rarely change in the young population while CH probably declines with age progression. Thus, the correlation between corneal biomechanical properties and age remains to be elucidated.

**Table 3** Analysis of regression of IOP-related factors

Parameters	IOPg		P
	Regression coefficient (SE)	Standardized regression coefficient	
Gender	-0.003 (0.011)	0.000	0.747
Age	0.003(0.005)	0.001	0.611
k1	0.002(0.007)	0.001	0.827
k2	-0.004(0.007)	-0.342	0.733
CCT	0.000(0.000)	0.002	0.380
CH	-2,832(0.005)	-1.647	<0.01
CRF	3.329(0.006)	1.839	<0.01

Most previous studies noted that CCT affects the accuracy of IOP measurement. In the current study, a positive correlation was noted between IOP and CCT by univariate analysis. Based on the correlation between CCT and corneal biomechanical properties, we predicted a correlation between IOP and corneal biomechanical properties as well as CCT, and examined this using multivariate regression analysis. The results revealed that IOP had no correlation with CCT while it was significantly correlated with corneal biomechanical properties. This hints that the influence of the cornea on the IOP results primarily from the corneal biomechanical properties rather than corneal thickness alone. Corneal thickness alone cannot reflect the true degree of corneal rigidity and elasticity, so it should not be the sole measurement for assessing the influence of corneal thickness while measuring IOP. Therefore, the IOP measurement instruments and correction formula are still inaccurate or unreliable for correcting CCT discrepancies.

In the present study, the selected school was dominated by immigrant children, which was fairly representative. However, this is only a school-based rather than a population-based study so the conclusion remains limited. The findings demonstrated the feasibility of assessing corneal biomechanical properties in school children, providing fundamental evi-

dence for further analyzing human corneal biomechanical properties. The significance of corneal biomechanical properties in the progression and diagnosis of corneal diseases remains to be elucidated.

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