Corneal Thickness Association With Ocular and Corneal High-Order Aberrations

Engy M. Mohamed, M.D., Jadwiga C. Wojtowicz, M.D., Wayne Bowman, M.D., H. Dwight Cavanagh, M.D., Ph.D., Vinod Mootha, M.D., Steven Verity, M.D., and James P. McCulley, M.D., F.R.C.Ophth.

Purpose: To investigate the association among central corneal thickness, peripheral corneal thickness (PCT), and wavefront aberrations in the anterior cornea, posterior cornea and the whole eye in myopia.
Methods: Sixty-four eyes of 64 myopic subjects were evaluated with a Pentacam rotating Scheimpflug camera (Oculus, Inc., WA) corneal topographer for: (1) wavefront aberrations from the anterior and posterior corneal surface, (2) corneal thickness (central and peripheral), and (3) with a wavefront aberration-supported cornea ablation wavefront analyzer (Wavescan, Visx, Inc., Santa Clara, CA) for wavefront aberrations generated in the whole eye. Relationships between the wavefront aberrations and corneal thickness were analyzed.
Results: The mean age of subjects was 34.75 ± 10.08 years. The central corneal thickness was 550.5 ± 28.459 μm. The mean peripheral thickness was 629.9 ± 32.1 μm. Central and PCTs were not significantly correlated with corneal or ocular high-order aberrations. Intraocular pressure was significantly correlated with ocular trefoil ($r = -0.307$, P=0.001).
Conclusions: Central and PCT were not significantly associated with either anterior or posterior corneal Zernike aberrations; in addition, no association with the whole ocular wavefront aberrations was found.

Key Words: Corneal thickness—Corneal high-order aberrations—Ocular high-order aberrations.

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The Pentacam, a rotating Scheimpflug camera, offers a noninvasive way to examine the anterior segment. Studies evaluating the reliability of Pentacam measurement of central corneal thickness (CCT), peripheral corneal thickness (PCT), and corneal aberrations have recently been published.[1–6] Preoperative assessment of central and PCT is important in various fields of ophthalmology, especially preceding keratorefractive surgery[7] to help ensure the postoperative stability and integrity of the cornea.[8] Most of the studies have reported central measurements, but only a few have reported peripheral thickness along the horizontal and vertical meridian.[9,10] It is important to note that peripheral corneal morphology plays a critical role in soft contact lens wearers and refractive surgery.

From the Ophthalmology Department, University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

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Address correspondence and reprint requests to James P. McCulley, MD, FRCOphth, UT Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd, Dallas, TX 75390-9057; e-mail: James.McCulley@utsouthwestern.edu.

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Optical aberrations are the main factors that degrade image quality in the eye. As a dominant structure in determining the refractive power of the eye, the cornea was found to be a critical contributor to wavefront aberrations in the whole eye.[11–14] However, complete knowledge of the sources of higher-order aberrations (HOAs) is far from established.

Basic data regarding the distribution of wavefront aberrations of the human eye in the normal myopic population are essential to allow us to gain a better understanding of HOAs to more fully characterize their geographical variation and optical function.

The aim of this study was to investigate the association of central and PCT (CCT) and HOAs in the anterior cornea, posterior cornea, and the whole eye in myopic eyes and to assess their contribution to the distribution of the measured aberrations.

Subjects

Following Institutional Review Board approval, 64 myopic subjects were retrospectively enrolled from patients who presented for refractive surgery evaluation at Laser Vision Center at the University of Texas, Southwestern Medical Center at Dallas from June 2008 to December 2008. All charts were reviewed, and subjects were excluded if they met one of the following criteria: previous ocular or corneal surgery or trauma; corneal scar, cataracts, or media opacities that could alter wavefront measurements; or discontinued contact lens wear <8 weeks before the WaveScan measurements for rigid gas-permeable lenses, 4 weeks for toric soft lenses, and 2 weeks for soft lenses. Wavescan measurements with 6 mm or more pupil diameter were included. Only Pentacam captures of 9 mm or higher were included. To avoid variability, only one eye of each subject was chosen as observations made on a person's two eyes are generally not independent but positive.[15] Therefore, the right eye was used in all patients. Intraocular pressure (IOP) was measured by standard pneumotonometry.

Measurement Technique of the Pentacam

For the examination, the seated subject was asked to keep both eyes open and fixate on a blue light source (light-emitting diode at 475 nm) in the center of the Scheimpflug camera. The examiner focused and aligned the real-time image of the subject's eye using the displayed arrows for facilitation. To reduce the risk for observer dependency, the automatic release mode was used, which means the scan commences as soon as the x-, y-, and z- plane alignment criteria are met. This reduces the confounding operator-induced unreliability that can occur with manual scanning, which depends on operator judgment of alignment. Thus, the Pentacam system started the measurement automatically whenever correct alignment with the corneal apex and focus was achieved. The noncontact measuring process with the Pentacam system takes 2 sec, performing 12 to 50 single captures (in this study, 25 captures were used) while rotating around the optical axis of the eye. As every slit image consists of 500 true elevation points, the Pentacam system detects, in total, up to 25,000 height values, which are processed to a three-dimensional model of the entire anterior eye segment. Then the internal software provides a large number of different calculations. It performs automatically the conversion of the corneal elevation profile into equivalent corneal wavefront data using the Zernike polynomials with an expansion up to the 10th order.[16] Acceptable maps had at least 10.0 mm of corneal coverage with no extrapolated data in the central 9.0 mm zone. All scans were centered on the pupil center. The HOAs of 6-mm pupils up to the 6th order were extracted. The CCT at the center of the pupil was determined and PCTs were examined 3.0 mm superiorly, inferiorly, nasally, and temporally from the pupil as defined in the Pentacam settings. Finally, the thinnest point of the cornea was evaluated.

Measurement Technique of the WaveScan

The WaveScan System (Visx, Inc., Santa Clara, CA) is a diagnostic instrument designed to measure and display refractive errors and wavefront aberrations of the whole eye using a Hartmann-Shack wavefront sensor. The measurements with this device were taken at the center of the entrance pupil and without pupil dilation. Only wavefront data across 6.0 mm pupils were analyzed.

Statistical Analysis

SigmaStat 3.5 program was used for statistical analysis. The Mann-Whitney rank sum test was used to analyze the difference in means between anterior and posterior corneal aberrations. Spearman Correlation was used to assess the correlations between anterior and posterior corneal aberrations and also between wavefront aberrations and different independent factors such as CCT, PCT, and age. We derived Zernike aberrations from the 3rd to the 6th coefficients (22 terms) for both anterior and posterior corneal surfaces in addition to the ocular aberrations. The Benferroni adjustment was applied for multiple tests to keep the overall type I error level of 0.05 ($P' < 0.001$). A P value < 0.05 was considered statistically significant.

RESULTS

The study included 64 subjects; 36 women and 28 men. The mean age of subjects was 34.7 ± 10 years (range 19–55 years). The mean spherical equivalent refractive error was −4 ± 2D (range −0.5 to −11.6D). The mean IOP was 16.2 ± 2.6 mm Hg (range 11.5–22.5). The CCT was 550.5 ± 28.459 μm. The superior cornea had the highest PCT (659.1 ± 37.7 μm) values followed by the nasal cornea (632.4 ± 35.2 μm), the temporal cornea (615.4 ± 33.7 μm), and the inferior cornea (612.9 ± 29.9 μm). The mean peripheral thickness is 629.9 ± 32.1 μm. In 58% of eyes, the thinnest point was inferiorly followed by the temporal area in 37.5% and only 4.5% had the thinnest point in the nasal quadrant.

There were statistically significant differences between almost all anterior and posterior corneal aberrations except for Z_3^{-3} (P=0.71), Z_4^{-2} (P=0.06), Z_5^{5} (P=0.45), Z_5^{3} (P=0.56). Figure 1 shows the comparison between anterior and posterior Zernike components.

There was a statistically significant positive relationship between the anterior and the posterior corneal surface aberrations only in Z_3^{1} (r = 0.352, P=0.0047) (Table 1).

Anterior and posterior corneal Z_4^{0} (spherical aberrations [SA]) were always positive with the anterior values (0.53 ± 0.15) being always lower than the posterior values (1.2 ± 0.35). In contrast,

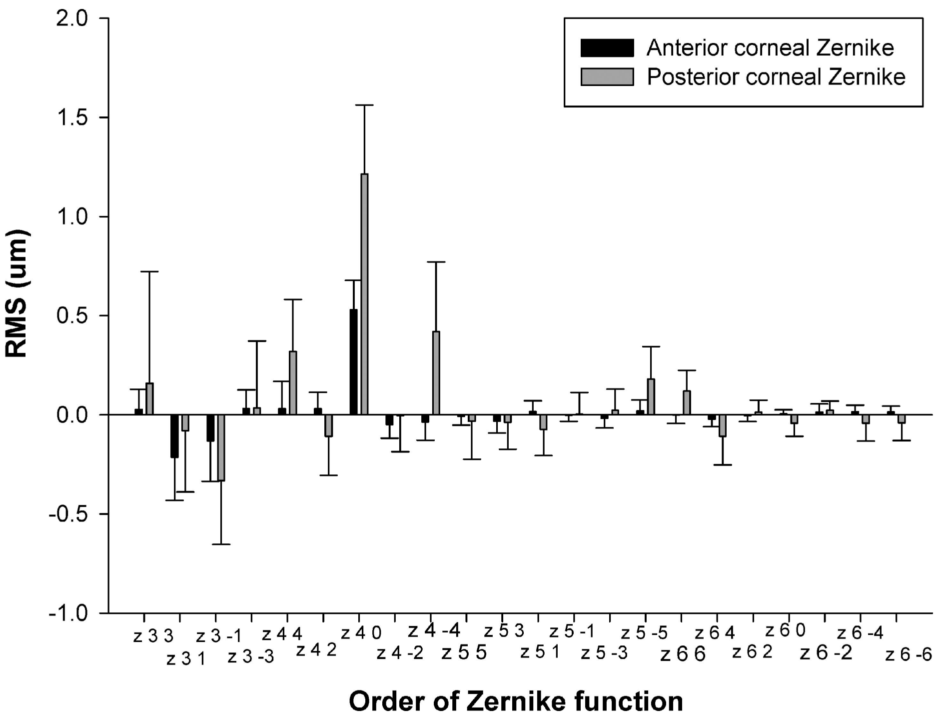

FIG. 1. Comparison of Zernike aberrations between anterior and posterior corneal surfaces.

TABLE 1. *Zernike Aberrations Up to 6th Order of Anterior and Posterior Corneal Surface in 64 Eyes*

	Anterior corneal (mean ± SD)	Posterior corneal (mean ± SD)	Mann-Whitney test (*P*)	Correlation coefficient	*P*
Z_3^{3}	0.061 ± 0.29	0.159 ± 0.564	0.021	0.0423	0.739
Z_3^{1}	−0.215 ± 0.216	−0.08 ± 0.31	0.004[a]	0.352	0.00447[b]
Z_3^{-1}	−0.131 ± 0.205	−0.337 ± 0.32	0.001[a]	−0.0824	0.516
Z_3^{-3}	0.032 ± 0.09	0.034 ± 0.338	0.712	−0.187	0.138
Z_4^{4}	0.0313 ± 0.138	0.324 ± 0.27	0.001[a]	−0.0721	0.57
Z_4^{2}	0.0313 ± 0.0826	−0.108 ± 0.197	0.001[a]	0.0357	0.779
Z_4^{0}	0.53 ± 0.148	1.215 ± 0.37	0.001[a]	0.192	0.129
Z_4^{-2}	−0.05 ± 0.0679	−0.0045 ± 0.181	0.056	0.137	0.278
Z_4^{-4}	−0.036 ± 0.0924	0.42 ± 0.351	0.001[a]	−0.0563	0.658
Z_5^{5}	−0.0069 ± 0.045	−0.0328 ± 0.191	0.454	0.166	0.19
Z_5^{3}	−0.0313 ± 0.0605	−0.038 ± 0.135	0.564	0.0822	0.517
Z_5^{1}	0.0165 ± 0.0539	−0.073 ± 0.132	0.001[a]	0.217	0.08
Z_5^{-1}	−0.0034 ± 0.0302	0.00303 ± 0.109	0.262	0.0959	0.453
Z_5^{-3}	−0.0177 ± 0.0491	0.0228 ± 0.107	0.009	0.0590	0.642
Z_5^{-5}	0.0198 ± 0.0555	0.18 ± 0.164	0.001[a]	0.0851	0.502
Z_6^{6}	−0.0015 ± 0.0421	0.12 ± 0.104	0.001[a]	0.206	0.102
Z_6^{4}	−0.0228 ± 0.0373	−0.108 ± 0.145	0.001[a]	0.0781	0.538
Z_6^{2}	−0.0042 ± 0.03	1.028 ± .16	0.012	0.0414	0.744
Z_6^{0}	0.00359 ± 0.0215	−0.0421 ± 0.066	0.001[a]	0.125	0.324
Z_6^{-2}	0.013 ± 0.042	0.0225 ± 0.0464	0.039	0.153	0.227
Z_6^{-4}	0.0149 ± 0.033	−0.0423 ± 0.0905	0.001[a]	0.153	0.228
Z_6^{-6}	0.015 ± 0.03	−0.041 ± 0.09	0.001[a]	0.14	0.2

[a] $P' < 0.001$ statistically significant after Bonferroni Adjustment.

[b] $P < 0.05$ statistically significant.

ocular SA (0.116 ± 0.172) were found to have some negative values.

No correlation was found between Zernike aberrations and CCT or the mean PCT. In addition, no correlation was found between central or PCT and ocular aberrations such as coma, trefoil, and SA (Table 2).

Age correlated positively with anterior SA, anterior y-axis pentafoil, posterior y-axis coma (Table 3). Although age showed negative correlation values approaching significance with 6th order anterior astigmatism and posterior SA (P'=0.003, P'=0.004), respectively. Ocular aberrations did not correlate with age. Also, age was not correlated with either CCT or PCT.

There was no significant correlation between manifest spherical equivalent and the Zernike aberrations. Mean keratometric power showed significant positive correlation with anterior and posterior SA (r = 0.5, P'<0.001; r = 0.5, P'<0.001, respectively), whereas it showed negative correlation with anterior secondary astigmatism (Z_6^{2}) (r = −0.4, P'<0.001). The 5th order trefoil showed correlation values approaching significance with keratometric power (r = −035, P'=0.007).

IOP was significantly correlated with ocular trefoil (r = −0.307, P'=0.0014). Additionally, IOP was found to have positive correlation with posterior 2^{ry} astigmatism at 135 (Z_4^{-2}) which approached significance (P'=0.007).

TABLE 2. *Correlation Between Ocular Wavefront Aberrations and Other Parameters*

	Total RMS	HOA RMS	Ocualr coma	Ocular trefoil	Ocular SA
CCT					
r	−0.0629	0.0248	0.0354	−0.177	−0.0828
P	0.62	0.845	0.781	0.162	0.514
PCT					
r	−0.0108	0.0477	0.0157	−0.102	−0.0503
P	0.932	0.707	0.902	0.42	0.692
IOP					
r	−0.0645	−0.197	−0.053	−0.307	0.0963
P	0.612	0.118	0.677	0.001[a]	0.448
Age					
r	−0.109	−0.101	−0.138	−0.167	0.175
P	0.391	0.427	0.276	0.185	0.167

[a] Statistically significant.

SA indicates spherical aberration; CCT, central corneal thickness; PCT, peripheral corneal thickness; IOP, intraocular pressure; RMS, root mean square; HOA, higher-order aberrations.

DISCUSSION

Anterior and Posterior Corneal Aberrations

Our results showed that the anterior and posterior corneal aberrations and ocular aberrations varied widely from subject to subject, which is consistent with previous studies.[17–20] The study also showed absence of correlation between ocular HOA root mean square and spherical equivalence (r = −0.174, P'=0.168), which is also consistent with findings in the studies of Zadok et al.,[20] Cheng et al.,[21] and Carkeet et al.[22]

In a population study,[23] all higher-order Zernike aberrations except SA in the whole eye were found to be near zero on average; however, our current study found significantly positive or negative Zernike aberrations for several terms. This could be due to a difference in subject selection between the two studies. The previous study included emmetropic subjects, and our study was of myopic subjects only. Subjects with myopia manifest more wavefront aberrations than those who are emmetropic.[24] In addition, myopic eyes after 2 hr of near work manifest show higher levels of HOAs.[25]

Corneal Thickness and Wavefront Aberrations

Our study revealed no correlation between central and PCT on one hand and ocular and corneal abbrations on the other hand. In

TABLE 3. *Correlation of Age With Zernike Aberrations*

Ant Z_4^{0}	Spherical aberration	(*P*<0.001)	Positive
Ant Z_5^{-5}	y-axis Pentafoil	(*P*<0.001)	Positive
Post Z_3^{-1}	y-axis Coma	(*P*<0.001)	Positive

Ant indicates anterior; Post, posterior.

a study by Qu et al.,[26] only one Zernike aberration, Z_4^2 (2^{ry} astigmatism) for the anterior corneal surface was significantly correlated with CCT. The SA Z_4^0 was positively correlated with CCT, with coefficients approaching significance for the anterior cornea.

Corneal Thickness and IOP

In contrast to the past studies of Qu et al.,[26] our study found no significant correlation between IOP and CCT or PCT. In addition, our results in myopic patients could not confirm a showed no correlation of defocus with IOP contrary to the previously mentioned study, which showed positive increase with anterior corneal and whole eye aberrations. A significant relationship between myopic refractive error and IOP in older subjects has been documented in the literature.[27,28] We found no significant association between astigmatism in the anterior cornea and IOP whereas there was an association that approached significance with posterior 2^{ry} astigmatism. In contrast, Qu et al.[26] found significant negative correlations between secondary astigmatism (Z_4^{-2}) and IOP for the anterior cornea and whole eye. This could be due to the subjects' age, which were much lower than the ages of subjects in a study by Ninn-Pedersen.[15] Our subjects' ages ranged from 19 to 55 years; Ninn-Pedersen's subjects included subjects as old as or close to 100 years (mean ~70–80 years). The comparison might imply a difference in the association of IOP with wavefront aberrations between young people and older people however further study of this issue is needed.

Mierdel et al.[29] examined the diurnal fluctuations in HOAs in the whole eye and tested the correlations between the changes in the aberrations and the diurnal changes in IOP and CCT. These investigators found that only one term of ocular Zernike aberrations (Z_4^2, 2^{ry} astigmatism) significantly changed with the diurnal change in IOP while in the present study, IOP only correlated significantly with ocular trefoil. How ocular trefoil could be linked to IOP is a puzzle to us because trefoil is asymmetric with the optical axis of the cornea and further study is warranted.

Also, in the Mierdel et al.[29] study, three ocular Zernike aberrations changed significantly with CCT which are anterior Z_3^3, Z_4^{-2}, Z_4^4, whereas our results did not show any association. However, the repeatability of their data was statistically challenged by Cheng and Lam[30] because the data were based on a single measurement selected from five repeats with the smallest root mean square value.

Corneal Aberrations and Age

Contrary to Oshika et al.,[31] our myopic patient study group demonstrated a positive correlation between age and anterior SA Z_4^0, y-axis pentafoil and posterior y-axis coma, and a negative correlation which approached significance with posterior SA Z_4^0 and y-axis astigmatism. These observations might imply that the central to peripheral balance of the corneal curvature is affected by age.[31] Our study found no correlation with ocular SA, which is contrary to Wang et al.[32] results who reported no correlation between age and corneal SA, however, found correlation with ocular SA.[19] This discrepancy may be explained by our smaller sample size.

We found no correlation between age and CCT and PCT. Thus, it can be concluded that corneal thickness is independent of age in myopic eyes between 19 and 55 years. According to Ehlers and Hjortdal,[33] corneal thickness seems to reach normal adult values during the first or second year of life and the decrease with age is rather small.

Although we may not be able to apply the current results to subjects of all races, ages and refractive status, it is suggested that comalike aberrations of the cornea tend to show age-related changes. Because comalike aberrations consist of tilt and/or asymmetry, these results imply that the corneas become less symmetric along with aging.

The absence of correlation between HOAs and refractive error is not surprising and is consistent with findings in the studies of Cheng et al.[21] and Carkeet et al.[22] In these two studies of a population of normal eyes, the wavefront aberrations were not correlated with refractive error.

Potential limitations of our study include the following: (1) Pentacam describes the corneal elevations and then corneal aberrations are reconstructed by internal software. However, this approach has been used by multiple authors.[5,34] (2) Only one WaveScan and Pentacam measurement per eye were used; because previous studies showed that single Pentacam[5,35] and wavescan[36] reading was sufficient to reliably determine wavefront error.(3) Zernike terms up to the 6th order might provide an incomplete characterization of ocular aberrations; however, the contribution of each order to the overall HOA decreased with increasing order, suggesting that higher orders contribute even less to the aberrations in these eyes.

In conclusion, this study found that anterior and posterior corneal wavefront aberrations varied greatly from subject to subject in myopic individual. The association between anterior and posterior corneal aberrations was greater with asymmetric HOAs, such as y-axis coma and astigmatism. There was no correlation between CCT and PCT and corneal or ocular aberrations. To the best of our knowledge, no other studies published to date have evaluated the posterior corneal aberrations and their association especially with central and PCT as well as other ocular parameters. This is potentially important for laser-assisted in situ keratomileusis and photo refractive keratectomy where the corneal thickness is often surgically diminished by much more than a few micrometers. How will the change of corneal thickness change the aberrations? Does the change in thickness affect the posterior corneal aberrations? We are also unaware of other studies that attempt to evaluate a correlation between PCT and corneal aberrations. These questions are worthy of additional research.

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