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# Five year changes in central and peripheral corneal thickness: The Shahroud Eye Cohort Study

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ABSTRACT

*Purpose:* To determine five year changes in corneal thickness from the apex to the 8 mm periphery and related factors through a longitudinal population-based study of middle-aged Iranians.
*Methods:* In the first phase, 4670 of the 5190 participants, and in the second phase, 4666 of the 4737 participants were examined with the Pentacam. In this report, analysis was done on right eye data of 2509 people who had no diabetes, pterygium, or history of eye surgery, and their image quality was displayed as “ok”. Thickness changes in different parts of the cornea and their relation with age, gender, refractive error, and intraocular pressure (IOP) were assessed using repeated measures analysis of covariance.
*Results:* Corneal thickness reduced by $1.5 \pm 11.7$ μm in the apex, $2.6 \pm 11.7$ μm in the thinnest point, and $5.3 \pm 12.2$, $7.7 \pm 14.3$, and $11.4 \pm 18.6$ μm in peripheral rings of 2, 3, and 4 mm radius, respectively (all $p < 0.001$ with and without adjusting for baseline thickness). Of the studied thickness variables, only changes in the 4 mm ring significantly related with age ($p < 0.001$) and gender ($p < 0.001$); there was less change in older age and in men. Thickness changes were not related to refractive error or IOP (all $p > 0.05$).
*Conclusion:* Corneal thickness decreased with age in this sample of 40–64 year olds. There was significantly greater thinning in the periphery compared to the corneal center even after controlling for baseline thickness. Results of this longitudinal study can be helpful in understanding age-related changes in the cornea and the eye.


## 1. Introduction

Corneal thickness is a sensitive indicator of corneal health, and its changes reflect alteration in its physiological function. Aging is a factor that can affect different layers of the cornea including the epithelium [1] and endothelium [2]. Such changes can affect the prognosis of ocular surgeries, such as cataract, in the middle-aged and the elderly [3]. Corneal thickness also has a known relationship with intraocular pressure (IOP) measurement, such that a thin cornea is associated with falsely low IOP readings which can lead to misdiagnosis of ocular hypertension and glaucoma [4,5]. Understanding age-related physiological changes in the human cornea enables a better prediction of the prognosis of disease and outcome of surgical procedures.

The normal range and age-related decline in the central and pericentral corneal thickness was described in a 40–64 year old Iranian population in the first phase of the Shahroud Eye Cohort Study [6]. While the central cornea is important in vision assessments, the corneal periphery can have an important role in penetrating keratoplasty, matching donor and host corneas, lens fitting, as well as in refractive surgery due associations with aberrations and refraction [7,8]. Nonetheless, peripheral changes have been studied less. In the present report, we review longitudinal thickness changes over five years in the 8.0 mm zone of the cornea through a population-based study, and relationships between these changes and other factors such as age, gender, refraction, IOP.

## 2. Materials and methods

This report is based on data from the Shahroud Eye Cohort Study which has been conducted in two phases, 5 years apart, in

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2009 and 2014. The protocol of the study has been published elsewhere [9].

One of the examinations performed for all participants was imaging with the Pentacam HR (Oculus Inc., software version 1.17r72, data management version 6.03r11). Measurement repeatability of this device has already been described through previous studies [10]. IOP was measured using a Goldmann applanation tonometer (AT900, Haag-Streit), and manifest refraction was determined using a Heine Beta 200 ophthalmoscope with ParaStop (HEINE Optotechnik). Any ocular condition including the diagnosis of corneal disorders and pterygium was established by an ophthalmologist.

Cases with any history of refractive surgery, cataract surgery, ocular trauma or surgery which can impact corneal thickness and those whose Pentacam image quality was not displayed as “ok” were excluded from the database. Since preliminary analyses pointed to different trends in cases with pterygium or diabetes, the presence of either condition was added to the exclusion criteria. Corneal thickness values were examined in the apex, thinnest point, at 2–4 mm from the center in the superior, inferior, temporal, and nasal orientations, and corneal rings of 2 (average of 12 points at 30° intervals), 3 (average of 4 points at 90° intervals), and 4 mm (average of 20 points at 18° intervals) radius. Considering the high correlation of studied variables in fellow eyes (all $r > 0.76$), only right eye data were used in the analyses. We used repeated measures analysis of covariance (within and between subjects) to examine 5-year thickness changes and the impact of age, gender, refractive error, and IOP with these changes, and compare central changes with peripheral changes. In the analysis of 5 year intra-individual changes, multiple models were used to control for independent variables influencing corneal thickness. To assess the effect of refractive status, cases were categorized as emmetrope, myope ($\leq -0.5$ D) and hyperope ($\geq +0.5$ D) based on their spherical equivalent refraction.

## 3. Results

Of the 5190 participants of Phase I, 4737 participated in the second phase (Phase II response rate: 91.3%). Of these, 4670 and 4666 had Pentacam imaging in Phase I and II, respectively, and cases who had Pentacam data from both phases were considered for inclusion in this analysis. After applying the exclusion criteria for this report, data from 2509 right eyes were analyzed. The mean age of these participants was 49.9 ± 6.0 years, and 59.8% were female.

As displayed in Table 1, all studied thickness variables showed a significant decrease over these five years ($P < 0.001$) except the 3 mm nasal ($p = 0.062$). The thickness in the apex decreased in 56.6%, increased in 41.4%, and showed no change in 2.0%. The 95% limits of agreement (LoA) between corneal thickness measures of the apex and 4 mm ring were −24.43–21.43 μm (LoA width of 45.86 μm) and −47.86 - 25.06 μm (LoA width of 72.92 μm), respectively (Fig. 1). Thickness changes in the thinnest point and in the 2, 3, and 4 mm rings were significantly different from the apex, and the amount of decline increased from the apex to the periphery (all $P < 0.001$).

Thickness changes in the thinnest point and the 3 rings were then explored after grouping cases by change in apex thickness (i.e. no change, decreased apical thickness, and increased apical thickness). Results indicated that changes in the thinnest point and the 2 and 3 mm rings were parallel to apical changes, but the 4 mm ring showed thinning with age in all three groups (Fig. 2).

The effects of age, gender, spherical equivalent refraction, and IOP were examined in a multiple model. Corneal changes in different refractive groups are illustrated in Fig. 3. Thickness changes in the center, thinnest point, and 2 and 3 mm rings were not related to baseline age, and only changes in the 4 mm ring differed among age groups ($P < 0.001$); compared to the 40–45 year age group who showed the most thickness change (−13.7 ± 16.9 μm), less changes were seen in the 55–59 year (−8.4 ± 19.4, $P < 0.001$) and 60–64 year (−5.7 ± 22.2, $P < 0.001$) age groups. Corneal changes in different age groups are presented in Table 2 and Fig. 4.

Gender showed no significant relationship with thickness changes, and changes were similar in both genders. The exception was the 4 mm ring where there was significantly more thinning in women (−13.1 ± 17.6 μm) compared to men (−9.0 ± 19.7 μm). Also, unlike other studied thickness variables, baseline thickness in the 4 mm ring was significantly higher in women compared to men (677.1 ± 39.6 vs. 671.0 ± 40.3 μm, $P < 0.001$). Spherical equivalent

**Table 1**
Five-year changes in corneal thickness (microns) in the corneal apex, thinnest point, corneal points 2, 3, and 4 mm away from the center in the superior, inferior, temporal, and nasal quadrants, and 2, 3, and 4 mm radius rings, and their comparison versus the apical thickness in the Shahroud Eye Cohort Study (n = 2509).

| Corneal thickness | Phase I | Phase II | *mean change (%) | *difference with mean apical change |
|---|---|---|---|---|
| Apex | 529.3 ± 31.7 | 527.8 ± 30.2 | −1.5 ± 11.7 (−0.28) | – |
| Thinnest point | 524.9 ± 32.0 | 522.4 ± 30.5 | −2.6 ± 11.7 (−0.48) | 1.0 ± 2.9 |
| Superior | | | | |
| 2 mm | 583.3 ± 33.6 | 574.7 ± 32.7 | −8.6 ± 14.1 (−1.50) | 7.1 ± 8.8 |
| 3 mm | 635.5 ± 38.4 | 623.8 ± 36.4 | −11.7 ± 18.1 (−1.87) | 10.2 ± 14.6 |
| 4 mm | 693.8 ± 53.2 | 678.8 ± 44.6 | −15.0 ± 33.7 (−2.21) | 13.5 ± 31.7 |
| Inferior | | | | |
| 2 mm | 561.4 ± 32.4 | 555.3 ± 31.4 | −6.1 ± 14.8 (−1.10) | 4.6 ± 8.9 |
| 3 mm | 608.0 ± 34.2 | 598.1 ± 32.9 | −9.9 ± 17.1 (−1.65) | 8.3 ± 12.0 |
| 4 mm | 678.1 ± 41.6 | 659.8 ± 38.4 | −18.4 ± 24.3 (−2.77) | 16.9 ± 21.5 |
| Temporal | | | | |
| 2 mm | 549.4 ± 32.4 | 543.5 ± 30.9 | −5.9 ± 13.7 (−1.08) | 4.3 ± 6.4 |
| 3 mm | 600.3 ± 34.5 | 590.3 ± 32.6 | −10.0 ± 16.7 (−1.69) | 8.5 ± 12.1 |
| 4 mm | 648.6 ± 38.5 | 631.7 ± 35.7 | −16.9 ± 20.1 (−2.67) | 15.3 ± 16.2 |
| Nasal | | | | |
| 2 mm | 572.0 ± 32.1 | 571.3 ± 31.2 | −0.8 ± 13.4 (−0.12) | 0.8 ± 7.4 |
| 3 mm | 611.0 ± 34.8 | 611.6 ± 33.7 | 0.6 ± 16.3 (0.10)[¥] | 2.1 ± 11.6 |
| 4 mm | 687.7 ± 45.0 | 685.1 ± 42.9 | −2.6 ± 26.9 (−0.38) | 1.0 ± 24.7 |
| Average on rings | | | | |
| 2 mm | 565.6 ± 31.6 | 560.2 ± 30.8 | −5.3 ± 12.2 (−0.96) | 3.8 ± 4.2 |
| 3 mm | 613.7 ± 33.7 | 606.0 ± 32.4 | −7.7 ± 14.3 (−1.27) | 6.2 ± 8.6 |
| 4 mm | 674.6 ± 40.0 | 663.2 ± 36.9 | −11.4 ± 18.6 (−1.72) | 9.9 ± 15.1 |

All p-values based on repeated measures analysis of covariance and <0.001 unless otherwise indicated [¥] $p = 0.062$.