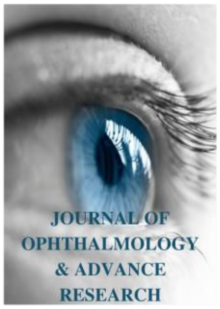

E-ISSN: 3050-9459
Journal of Ophthalmology and Advance Research

ATHENAEUM SCIENTIFIC PUBLISHERS

Research Article

Association Between Corneal Epithelial Thickness, Higher-Order Aberrations and Contrast Sensitivity in Refractive Surgery Candidates

Themistoklis K Gialelis[1*], Aikaterini E Mouzaka[1]

[1]Department of Biomedical Sciences, Sector of Optics and Optometry, University of West Attica, Greece

***Correspondence author:** Themistoklis K Gialelis, Department of Biomedical Sciences, Sector of Optics and Optometry, University of West Attica, Egaleo Park, Athens, Greece; Email: thgialelis@uniwa.gr; themisg2010@gmail.com

Citation: Gialelis TK, et al. Association Between Corneal Epithelial Thickness, Higher-Order Aberrations and Contrast Sensitivity in Refractive Surgery Candidates. J Ophthalmol Adv Res. 2025;6(2):1-6.

https://doi.org/10.46889/JOAR.2025.6206

Received Date: 27-05-2025

Accepted Date: 16-06-2025

Published Date: 23-06-2025

Abstract

Purpose: To report the relationship between changes in the thickness of the corneal epithelium at its apex (epithelial thickness peak, ET peak) and alterations in Contrast Sensitivity (CS) and Higher-Order Aberrations (HOAs) following Photorefractive Keratectomy (PRK) and Laser-Assisted In Situ Keratomileusis (LASIK).

Methods: A retrospective analysis was conducted on data from 58 eyes that underwent LASIK and 60 eyes that underwent PRK. Measurements of Corrected Distance Visual Acuity (CDVA), Weber contrast (SC WEBER), logarithm of CS (CS LOGS), ET peak, Low-Order Aberrations (LOAs) and HOAs were obtained before and after surgery (mean follow-up: 12.18 ± 1.48 months). Statistical correlations between the changes in these parameters were analyzed.

Results: Significant postoperative changes were observed in CS, ET peak and HOAs in both surgical groups. In the PRK group, a mean increase of 6.62 ± 1.31 μm in ET peak showed a significant correlation with a reduction in CS and changes in specific LOAs (Z00, Z02, Z11) and HOAs (Z31, Z42). Conversely, in the LASIK group, despite a similar average increase in ET peak (6.55 ± 1.26 μm), no significant correlation was found with CS reduction or changes in HOAs, although correlations with LOAs (Z00, Z02, Z11) were present. Changes in ET peak did not correlate with CDVA in either group.

Conclusion: While both photorefractive keratectomy and laser-assisted in situ keratomileusis resulted in comparable postoperative increases in central corneal epithelial thickness, these changes were significantly linked to decreased contrast sensitivity after photorefractive keratectomy but not after Laser-Assisted In Situ Keratomileusis. This difference might be due to variations in the ablation profile and the corneal healing process between the two techniques. The findings suggest that epithelial remodeling has a different impact on visual function depending on the type of refractive surgery performed.

Keywords: Photorefractive Keratectomy (PRK); Laser-Assisted In Situ Keratomileusis (LASIK); Contrast Sensitivity; High Order Aberrations; Low Order Aberrations; Epithelial Thickness at the Apex of the Cornea

Introduction

In the recent years, the role of the epithelium as a parameter in the outcomes of keratorefractive surgery has been investigated widely [1]. Nowadays, the Epithelium Thickness (ET) tent to be a standard preoperative examination for screening candidates at higher risk for complications (i.e. progressive ectasia and exacerbation of ocular surface disease) in refractive surgery. It also plays an important role in the decision of performing surface ablation instead of LASIK or enhancements and phototherapeutic surgery. But most importantly, the wound healing mechanisms of epithelium could help to understand and predict the refractive surgery clinical outcomes.

An increase in Epithelial Thickness (ET) after both PRK and LASIK has been demonstrated in previous studies. The increment persists during the postoperative visits and seems to play a role in the possible regression of the refractive result occurring mostly after PRK [2,3]. The interaction between changes in the corneal epithelium, the development of HOAs and alterations in CS after refractive surgery is still an active area of research. Previous studies have demonstrated that the corneal epithelial thickness distribution is not uniform and may vary with refractive error and after procedures like LASIK and PRK [2,4]. Such changes may influence the Higher-Order Aberrations (HOAs) and, subsequently, contrast sensitivity [3,5]. Notably, the role of changes in epithelial thickness at the very center of the cornea, the most important area for central vision, in influencing CS and HOAs after surgery has not been fully understood. In our study we investigated the changes in CS and corneal aberrations in correlation with ET peak changes after refractive surgery.

Materials and Methods

Study Design and Participants

This retrospective study analyzed data collected from 118 eyes of 59 patients who had refractive surgery for nearsightedness or nearsightedness with astigmatism. The study included 58 eyes that had LASIK and 60 eyes that had PRK. The average age of the patients was 31.1 ± 7.05 years (ranging from 23 to 50 years), with 26 males and 33 females participating. The LASIK group included eyes with myopia ranging from -1.25 D to -8.25 D and myopic astigmatism from -0.50 D to -3.50 D. The PRK group included eyes with myopia from -1.25 D to -6.75 D and myopic astigmatism from -0.25 D to -1.25 D. All patients had stable vision correction needs for at least 2 years before surgery. Patients who were pregnant, had systemic diseases or a history of previous eye diseases or surgeries were not included in the study. The study plan followed the Declaration of Helsinki and was approved by the local ethics committee. All patients gave their written consent after being fully informed about the study.

Surgical Procedures

All surgeries were performed by the same experienced surgeons at the Eye Day Clinic in Athens. In both groups, ofloxacin eye drops were administered and a povidone-iodine solution was used to disinfect the eyelids and surrounding tissue. Proxymetacaine hydrochloride eye drops were used for local anesthesia. The intended refractive outcome in all cases was to achieve emmetropia (perfect focus).

For the PRK group, the epithelium was removed using 20% alcohol for 20-30 seconds. For the LASIK group, a femtosecond laser (Alcon/WaveLight® FS200) was used to create the corneal flap, with the hinge positioned at the 12 o'clock mark. In both the PRK and LASIK groups, the Allegretto Wave excimer laser (software version: 2.020/WaveLight AG, Erlangen, Germany) was used to ablate the stromal tissue within a 6.5 mm optical zone. Following LASIK, the flap was repositioned and the area underneath it (the interface) was irrigated. Proper alignment was ensured using a wet microsponge.

Ophthalmic Examinations

All patients underwent thorough examinations before and after surgery, including Uncorrected Distance Visual Acuity (UDVA), Corrected Distance Visual Acuity (CDVA), manifest and cycloplegic refractions, non-contact measurement of intraocular pressure and slit-lamp microscopy of the anterior segment of the eye. The average follow-up period was 12.18 ± 1.48 months (ranging from 11 to 14 months).

Corneal Epithelial Thickness Measurement

The thickness of the ET peak was measured using the epithelial map (pachymetry model) of an OCT tomography system (Avanti XR OCT, Optovue). Three measurements were taken for each eye and the average value was used for the analysis. The reliability of this method for pachymetry mapping has been previously reported [6].

Contrast Sensitivity Assessment

Contrast sensitivity was evaluated before and after surgery using the Freiburg Vision Test ('FrACT' Vs 3.9.3 • 2015-06-01 • F16.0) under completely dark conditions. The test provided measurements of Weber contrast (SC WEBER) and the logarithm of Contrast Sensitivity (CS LOGS). 'FrACT' is a validated and reliable psychometric test for assessing visual acuity, contrast sensitivity and visual acuity [6].

Corneal Aberration Analysis

Corneal aberrations were analyzed using an anterior segment analyzer (Pentacam HR, Oculus GmbH, Wetzlar, Germany). This system uses a 360° uniform rotation scanning technique based on the Scheimpflug principle to measure aberrations of the front, back and total cornea. Zernike polynomials were used to analyze the aberrations of the anterior corneal surface (including Z00, Z11, Z02, Z22, Z31, Z3, Z40, Z42, Z44) within a 6 mm diameter area centered on the corneal vertex. Only examinations with "OK" quality parameters, indicating reliable and reproducible measurements, were included in the analysis.

Statistical Analysis

Statistical analysis was performed using SPSS Version 25. Categorical variables were compared using the Chi-Square test. For continuous variables, normality was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous variables were compared using the Paired Samples T-Test, one-way and two-way ANOVA. Non-normally distributed variables were analyzed using the Wilcoxon Signed-Ranks test and Friedman test. Pearson and Spearman correlation coefficients were used to determine the relationship between parametric and non-parametric variables, respectively. A p-value of less than 0.05 was considered statistically significant.

Results

Patient Demographics

Table 1 presented the demographic data of the patients in the LASIK and PRK groups. No statistically significant difference was found in age distribution between the two groups or between male and female patients within each group. The mean follow-up time was 12.18 ± 1.48 months.

Variables	LASIK		PRK			Total	
	N	Years mean±sd (min-max)	N	Years mean±sd (min-max)	p	N	Years mean±sd (min-max)
Age (years)[a]		33.9±8.3 (22-50)		27.8±3.8 (23-36)	P>0.05		30.7±6.8 (22-50)
Female Patients	19	34.4±7.9 (24-50)	8	29.8±4.11 (23-36)	P>0.05	27	33.3±7.3 (23-50)
Male Patients	10	33.1±8.6 (22-49)	22	27.2±3.6 (23-35)	p>0.05	32	29.3±6.4 (22-49)

Table 1: Patient demographics (n = 118) (58 LASIK and 60PRK).

Preoperative and Postoperative Changes

As the Kolmogorov-Smirnov test indicated that not all parameters followed a normal distribution, mean values with standard deviation, 95% confidence intervals and medians were reported.

In the PRK group, the mean increase in ET peak was 6.62 ± 1.31 μm (95% CI [3.99-9.25]). Statistically significant increases were observed in most HOAs (specifically Z31 and Z42, p<0.05 and p<0.01, respectively), while both Weber contrast (SC WEBER, p<0.05) and the logarithm of contrast sensitivity (CS LOGS, p<0.05) showed statistically significant decreases postoperatively. Significant changes were also noted in LOAs (Z00, Z11, Z02, all p<0.0001) and CDVA (p<0.001).

In the LASIK group, the mean increase in ET peak was 6.55 ± 1.26 μm (95% CI [3.97-9.14]), which was not statistically different from the PRK group. Contrast sensitivity (SC WEBER and CS LOGS) significantly decreased (both p<0.0001) and spherical aberration (Z40) significantly increased (p<0.0001). Similar to the PRK group, significant changes were observed in LOAs (Z00, Z11, Z02, all p<0.0001) and CDVA (p<0.002). However, unlike the PRK group, most other HOAs (Z22, Z31, Z3, Z42, Z44) did not show statistically significant changes.

Correlations Between Parameter Changes

Spearman correlation analysis in the PRK group revealed a statistically significant correlation between the change in ET peak and the change in both Weber contrast (ϱ = -0.36, p<0.01) and the logarithm of contrast sensitivity (ϱ = 0.42, p<0.01). Furthermore, changes in ET peak were significantly correlated with changes in LOAs (Z00: ϱ = -0.43, p<0.01; Z02: ϱ = -0.44, p<0.01; Z11: ϱ = 0.41, p<0.01) and specific HOAs (Z31: ϱ = 0.33, p<0.05; Z42: ϱ = -0.37, p<0.01). Notably, no significant correlation was found between the change in ET peak and the change in CDVA.

In the LASIK group, Spearman correlation analysis showed no statistically significant correlation between the change in ET peak and the change in either Weber contrast or the logarithm of contrast sensitivity. Similarly, no significant correlations were found between the change in ET peak and changes in HOAs. However, significant correlations were observed between the change in ET peak and changes in LOAs (Z00: $\varrho = -0.30$, $p<0.05$; Z02: $\varrho = -0.31$, $p<0.05$; Z11: $\varrho = -0.31$, $p<0.05$). Again, no significant correlation was found between the change in ET peak and the change in CDVA.

Discussion

In this study we investigated whether there is a correlation between the change of the ET with changes of the CS and the aberrations before and after PRK and LASIK surgery, on the corneal apex. We found that the ET increase after refractive surgery and the increment was found to have no statistical difference among PRK and LASIK. The corneal epithelium hyperplasia it is well established from previous studies. It is known that affected by the amount of myopia treated, treatment zone and preoperative epithelial thickness but not by stromal ingrowth which is more pronounced in PRK [1-4,7,8]. Moreover, no difference between groups suggests that the epithelial changes occur as function of changes in the anterior corneal curvature and not necessarily related to tissue removal. The corneal flattening in myopic eyes may resulted in postoperative epithelial thickening due to the lack of mechanical influences of the upper eyelid that polishes the corneal surface with blinking [9].

In PRK surgery changes in ET seemed to be correlated with changes of CS. This correlation is being studied for the first time. The ET increased after PRK in accordance to CS reduction and this was probably due to the fact that in PRK there is epithelial removal and regeneration. Corneal epithelial cells are the first cells involved in the corneal regeneration process after PRK [11]. During the reconstruction of the epithelium is likely to have a different quality of epithelial cells with differences in their shape, size and clarity. We may have alterations in corneal biomechanics as well as possible dry eye. Histological studies conducted in animals and in humans, have found that thicker epithelium after PRK caused by an elongation of the basal epithelial cells and an increased number of superficial cell layers [4]. Moreover, the new subepithelial interface after PRK also accumulates water that colocalizes with the hyaluronan [11]. The sharp demarcations of these zones create sharp shifts in refractive index in these areas, causing light scattering which may affect the CS.

Furthermore, changes in ET appeared to correlate with both low (Z00, Z02, Z11) and high-class corneal aberration such as coma (Z31) and high-class astigmatism (Z42).

Previous studies have shown that the PRK increased the ocular aberrations, reducing the optical performance of the eye undergoing treatment [12,13]. However, only recently, several concerns regarding the correction of refractive errors have been raised because of the inter-individual epithelial thickness profile variability and the associated potential refractive effect [14,15]. Ivarsen, et al., proposed that during the first year after PRK, the rather large increase in spherical aberration may be related to the changes in epithelial thickness that have been previously demonstrated to occur within the first year after surgery [2]. Seiler T, et al., 2000 also report an increase in HOAs caused by PRK surgery during epithelial remodeling [12].

In LASIK there was statistically increased in ET. This is in accordance to previous studies which indicated that LASIK induced increment in epithelial thickness of approximately 20% that persisted after surger [2,9]. According to Patel, et al., central corneal epithelium in LASIK increased 24% during the first year after surgery and remained stable during the next 7 years [4]. However, in Lasik there was no correlation among ET increasement and CS changes, contrary to PRK. In LASIK there is a creation of the lateral cut of the cornea which does not seem to affect the changes of CS. while in PRK there was complex interaction of epithelial cells and activated keratocytes [9]. A totally regeneration-remodeling of the cornea, changes the corneal structure as the cells change in shape, composition and size. Case report has demonstrated epithelial hyperplasia with an increased number of cell layers after PRK, whereas the nature of the epithelial changes after LASIK are less clear. Moreover, Hyaluronan that is reactively formed in the corneal wound after PRK colocalized to the hydrated area of the corresponding location as revealed by quantitative microradiography. The findings suggest that hyaluronan causes local shifts in water content in the corneal wound and thereby also local shifts in transparency that may affect the CS [11].

Moreover, the interface between epithelium and corneal stroma is different among two techniques. Injury after PRK is in the surface stroma and exposed, whereas injury after LASIK is inner stromatic and not exposed. Both epithelium and stroma are injured after PRK, but only stroma is injured after LASIK. In other words, the loss of cell-cell contact between keratocytes contributes to myodifferentiation of stromal cells and intact epithelium is the key to the prevention of stromal cell myodifferentiation after photoablation [16].

In LASIK surgery, the change in ET was found to correlate with changes in LOAs (Z00, Z02, Z11), which did not affect the change in subjective vision. These means that the intended ablation affects the thickness of corneal epithelium postoperatively. Previously there where a number of studies show that HOAS increase after LASIK. Cheng, et al., refer that LASIK-related aberrations were affected by the width-diameter of the removed visual belt and have an effect on HOAs [17]. Larger optical zone reduced overall HOAs as well as spherical aberrations, after LASIK. The effects were more significant in high myopia than in low [16]. Also, the high refractive corrections both myopic and hyperopic can result in very high levels of HOAs after LASIK surgery [18]. However, this is the first study which show that there was no correlation among HOAS increment and postoperative epithelial thickness. LASIK does not significantly affect high-order aberrations, which may be due to the individualized design (wavefront-guided / topography-guided LASIK).

More specifically, modern LASIK techniques based on wavefront or topography try to correct existing high-order aberrations or not worsen them. It may also be due to the smooth restoration of the anterior corneal profile: Modern excimer lasers have extremely precise eye trackers and smoothing software that allow for very uniform tissue removal. This limits the induction of HOAs, especially when the flap is created with a femtosecond laser. Finally, another factor is the preservation of normal corneal geometry: The LASIK method, unlike PRK, largely preserves the natural state of the surface layer of the cornea (epithelium and Bowman's membrane), which can lead to a more stable visual result [19].

As it was mentioned above, postoperative corneal ET did not affect postoperative subjective vison in both techniques. This is in accordance to previous studies which mentioned that postoperative refractive changes correlate with changes in stroma (PRK) and corneal thickness (PRK and LASIK) but not with changes in ET [2].

A limitation of this study was applying statistical analysis to both eyes in some cases. The inclusion of bilateral cases was performed in order to increase the power of the study and reduce the number of subjects to be recruited. The optimal way to deal with this issue is to use only one eye from each patient or to use advanced statistical analysis. However, this was not always the case in all publications. However, in previous studies published in the literature in PRK or LASIK patients, it was found that correlations were low in eyes that had undergone refractive surgery and that results were similar when one or both eyes of the patients were used [5].

Conclusion

In conclusion, the change of the epithelium thickness in both techniques had presented no statistically significant difference. However, the change in ET seemed to correlate with CS solely in PRK group. The difference between the two types of surgery can be related to the change in the shape of the cornea, the conversion of biodynamics, the healing of the corneal flap and the reconstructed of corneal epithelium and the layer. Moreover, the change of ET affected the aberrations in both techniques, but not in the same manner.

Value Statement

What Was Known

- Refractive surgery changes the shape of the cornea
- Changing the shape of the cornea affects vision, contrast sensitivity, epithelium and Zernike
- Changing all this affect the final vision

What This Paper Adds

- There postoperative epithelial of the cornea association with the contrast sensitivity
- There is no association of the corneal epithelium with the visual outcome
- The two techniques behave differently in terms of how they affect the thickness of the epithelium and the contrast sensitivity

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding Details

No author has a financial or proprietary interest in any material or method mentioned.

References

1. Salomão MQ, Ambrósio R, Wilson SE, Belin MW. Corneal epithelial remodeling after LASIK and PRK: A review. J Refract Surg. 2017;33(4):282-9.
2. Ivarsen A, Laurberg T, Hjortdal J. Central corneal epithelial thickness changes after LASIK for myopia: A histological study. Acta Ophthalmol. 2009;87(1):68-73.
3. Chen S, Feng Y, Stojanovic A, Jankov MR, Wang Q. Changes in corneal epithelial thickness profile after transepithelial photorefractive keratectomy for myopia. J Refract Surg. 2015;31(2):104-10.
4. Patel S, Marshall J, Fitzke FW. Refractive effects of corneal epithelial remodeling following photorefractive keratectomy. J Refract Surg. 2007;23(6):565-71.
5. Gialelis TK, Tsiklis NS, Georgiou E, Vogiatzakis E, Gkika MG, Georgopoulos G. Contrast sensitivity and corneal aberrations analysis in relation with epithelial thickness changes at the corneal apex after refractive surgery. J Surg. 2021;13(6).
6. Bach M. The Freiburg visual acuity test—automatic measurement of visual acuity. Optom Vis Sci. 2006;83(8):545-50.
7. Kanellopoulos AJ, Asimellis G. Epithelial remodeling after partial topography-guided normalization and high-fluence short-duration crosslinking (Athens protocol): Results up to 1 year. Clin Ophthalmol. 2012;6:97-101.
8. Lohmann CP, Guell JL, Marshall J, Mrochen M. Corneal epithelial thickness changes after myopic photorefractive keratectomy. J Cataract Refract Surg. 1999;25(8):1057-60.
9. Erie JC. Corneal wound healing after photorefractive keratectomy: A 3-year confocal microscopy study. Trans Am Ophthalmol Soc. 2003;101:293-333.
10. Gan L, Fagerholm P, Palmblad J. Human corneal wound healing after excimer laser keratectomy: A 3-year *in-vivo* confocal microscopy study. Invest Ophthalmol Vis Sci. 2001;41(2):410-8.
11. Weber B, Fagerholm P, Johansson. Colocalization of hyaluron and water in rabbit corneas after photorefractive keratectomy by specific staining for hyaluronan and by quantitative microradiography. Cornea. 1997;16:560-3.
12. Seiler T, Kaemmerer M, Mierdel P, Krinke HE. Ocular optical aberrations after photorefractive keratectomy for myopia and myopic astigmatism. Arch Ophthalmol. 2000;118(1):17-21.
13. Verdon W, Bullimore M, Maloney RK. Near vision contrast sensitivity after photorefractive keratectomy. Arch Ophthalmol. 1996;114(12):1465-72.
14. Salah-Mabed I, Saad A, Gatinel D. Topography of the corneal epithelium and Bowman layer in low to moderately myopic eyes. J Cataract Refract Surg. 2016;42:1190-7.
15. Arba-Mosquera S, Awwad ST. Theoretical analyses of the refractive implications of transepithelial PRK ablations. Br J Ophthalmol. 2013;97:905-11.
16. Nakamura K. Interaction between injured corneal epithelial cells and stromal cells. Cornea. 2003;22(7 Suppl):S35-47.
17. Cheng ZY, Chu RY, Zhou XT. Influence of diameter of optical zone ablation on LASIK-induced higher order optical aberrations in myopia. Zhonghua Yan Ke Za Zhi. 2006;42(9):772-6.
18. Pesudovs K. Wavefront aberration outcomes of LASIK for high myopia and high hyperopia. J Refract Surg. 2005;21(5):S508-12.
19. Amin MH, Kamal MA, Sherif AM, Abdel Hafez MA, Abdallah KK. Changes of higher order aberrations after using wavefront guided LASIK and topography guided LASIK for correction of refractive errors: A comparative study. J Clin Exp Ophthalmol. 2022;13(6).