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Research Article

Contrast Sensitivity and Corneal Aberrations Analysis in Relation with Epithelial Thickness Changes at the Corneal Apex after Refractive Surgery

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Abstract

Purpose: To report the changes in Contrast Sensitivity (C.S) and corneal aberrations (HOAS and LOAS) in relation with the Epithelial Thickness (ET) changes at the corneal apex (ET peak) after PRK and LASIK.

Materials and Methods: 58 eyes underwent LASIK and 60 PRK. Corrected Distance Vision Acuity (CDVA), Weber Contrast (SC WEBER), logarithm of CS (CS LOGS), ET peak, LOAs and HOAs were measured before and after refractive surgery. Moreover, the correlation was studied among changes of all parameters. Mean follow up was 12.18 +/- 1.48.

Results: Statistically significant differences were found between preoperative and postoperative values in C.S, E.T and Higher Order Aberrations (HOAs) in both refractive surgery methods. In the PRK group, the mean increment of ET peak was 6.62±1.31 microns and it appeared to be associated with change in C.S and changes in aberrations, LOAs (Z00, Z02, Z11) and HOAs (Z31 and Z42). However, the change in the epithelium did not seem to affect the CDVA. In the LASIK group, the mean increment of E.T peak was 6.55±1.26 microns but there was not found any association with C.S reduction, changes in HOAs and CDVA. However, there was a correlation with the ET increment and the LOAs (Z00, Z02, Z11).

Conclusions: Although PRK and LASIK found to have similar ET postoperative increment, in PRK these changes seemed to strongly correlate with CS contrary to LASIK. This is probably due to differences in the ablation sublayer and healing process between two techniques.

Keywords: Contrast sensitivity; High order aberrations; Low order aberrations; PRK-LASIK

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) tend 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 [1-3]. But most importantly, the wound healing mechanisms of epithelium could help to understand and predict the refractive surgery clinical outcomes [1-3]. A total increasement of ET after both PRK and LASIK has been demonstrated in previous studies [2,3]. 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]. Within this manner, we investigated changes in epithelial thickness at the corneal apex (ETpeak) after refractive surgery. Moreover we investigated if these changes affect C.S and aberrations. To our knowledge, this is the first study to investigate changes in ET (peak) in relation to C.S and aberrations after PRK and LASIK.

Materials and Methods

Fifty-nine patients (118 eyes) with mean age 31.1 +/- 7.05 (range from 23 to 50 years), 26 male and 33 females were included in the study. Twenty-nine patients underwent LASIK and thirty patients underwent PRK. Twenty-nine patients had undewent LASIK to correct myopia of -1.25D to -8.25 D and myopic astigmatism of -0.50D to -3.50 D. Thirty patients underwent PRK to correct myopia of -1.25D to -6.75 D and myopic astigmatism of -0.25D to -1.25 D. All patients had stable refraction for at least 2 years. Patients who were pregnant or who had systemic disease or a history of previous ocular disease or surgery were excluded from the study. Examinations were performed preoperatively and postoperatively mean follow up was 12.18 +/- 1.48 (min 11 max 14) months. The study protocol adhered to the Declaration of Helsinki and was approved by the local ethics committee. Informed written consent was obtained from all patients. All patients underwent preoperative and postoperative examinations including Uncorrected Distance Visual Acuity (UDVA), Corrected Distance Visual Acuity (CDVA), manifest and cycloplegic refractions, noncontact intraocular pressure and anterior segment slit-lamp microscopy. Regarding the LASIK and PRK operation, ofloxacin drops were instilled in both eyes, while povidone iodine solution was used for the disinfection of the eyelids and surrounding tissues. Proxymetacaine hydrochloride drops provided the required local anesthesia. Emmetropia was the refractive target in all cases. For the removal of the epithelium in the PRK group, alcohol 20% for 20-30 seconds was used. For the LASIK group, Alcon/WaveLight ® FS200 femtosecond Laser was used for the creation of the flap. The hinge was created at the 12 o'clock position. The Allegretto Wave excimer laser (software version: 2.020⁄WaveLight AG, Erlangen, Germany) was used for the ablation in all groups. After LASIK, the flap was repositioned with an irrigation cannula and the interface was irrigated. Proper alignment was ensured by gentle handling with a wet microsponge. All operations were performed at the Eye Day Clinic, Athens by the same skilled surgeons.

All eyes underwent refractive surgery in a 6,5mm optical zone. ET peak measurements were obtained using epithelial map (pachymetry model) of an OCT tomography system (Avanti XR OCT, Optovue) each eye was measured three times and the average value was used for the analysis. The method has showed excellent repeatability when generated the pachymetry map [4]. C.S in means of brightness increment, between a small object and its background divided by the average background luminance (SC Weber) and its logarithm (SC Logs), preoperatively and postoperatively, were obtained by the Freiburg Vision Test ('FrACT' Vs 3.9.3 · 2015-06-01 · F16.0). "FrACT" is a widely used visual test battery in form of a free computer program with respect to objectivity and reliability [5] It uses psychometric methods combined with anti-aliasing and dithering to provide automated, self-paced assessment of visual acuity (Bach 1996), contrast sensitivity and vernier acuity [5]. An anterior segment analyzer (Pentacam HR (Oculus GmbH, Wetzlar, Oculus, Germany) was utilized. The Pentacam anterior segment analysis system provides a 360° uniform rotation scanning technique based on the Scheimpflug principle, which is a reliable technique for measuring anterior, posterior, and total corneal aberrations.. Zernike was utilized for analysing the anterior corneal surface (Z00, Z11, Z02, Z22,Z31, Z3, Z40,Z42, Z44)within the 6-mm diameter range centred on the corneal vertex. Only cases where the quality parameters of the examination were shown as "OK" were selected, which indicated the repeatability and reproducibility of the measurements that could be reproduced for a clinical diagnosis. The above mentioned inspections were performed in complete darkness by the same skilled technician.

Statistical Method

Statistical analysis was performed using SPSS Version 25. Categorical variables were compared using the Chi-Square test. For continuous variables, as they were normally distributed, the Paired Samples T-Test, one-way and two-way ANOVA was used. For non-parametric variables the Wilkoxon and Friedman test was used. Pearson and Spearman correlation was used to determine the relationship between parametric and non-parametric variable, respectively. p-value of less than 0.05 was considered to show a statistically significant result.

Results

In Table 1 demographic data are presented between the two operational methods (PRK, LASIK). Mean follow up was 12.18 +/- 1.48. Kolmogorov test for normality showed that not all parameters followed normal distribution.We presented the Table 1 the demographics distribution by age and sex in each group. No difference were found for age between female and male cases.

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 60 PRK).

Tables 2 and 3 present the analysis between the preoperative and last postoperative data in relation with the type of refractive surgery for PRK and LASIK, respectively. The mean values with standard deviation are presented, along with 95 % Confidence intervals and median, as all variables did not follow a normal distribution according to the Kolmogorov - Smirnov method. In the PRK group, the mean increment of ET peak was 6.62±1.31 95%CI [3.99-9.25] microns. Also, most HOAs increased while CS (BS weber and SC Logs) decreased. In the LASIK group, the mean increment of ET peak was 6.55±1.26 95%CI [3.97-9.14] microns. The CS decreased while the spherical aberration (Z40) increased.

Variable	Period	Number	Mean	StDev	Lower 95%	Upper 95%	Score Mean	Z	prob>ChiSq
B SC (WEBER)	LastPostOp	42	0.25	0.01	0.25	0.26	37.02	0.27	0.7834
	pre-op	30	0.25	0.01	0.25	0.26	35.77	-0.27	
B CS (LOGCS)	LastPostOp	42	2.60	0.01	2.60	2.61	38.83	1.23	0.2179
	pre-op	30	2.60	0.02	2.59	2.61	33.23	-1.23	
CDVA (Snellen)	LastPostOp	42	-0.15	0.03	-0.16	-0.14	30.99	-3.24	0.0012*
	pre-op	30	-0.08	0.11	-0.12	-0.04	44.22	3.24	
SC (WEBER)	LastPostOp	42	0.37	0.20	0.30	0.43	32.07	-2.13	0.0326*
	pre-op	30	0.60	0.56	0.39	0.81	42.70	2.13	
CS (LOGCS)	LastPostOp	42	2.48	0.18	2.42	2.54	41.05	2.18	0.0286*
	pre-op	30	2.35	0.31	2.23	2.46	30.13	-2.18	
ET PEAK (μm)	LastPostOp	34	58.59	6.76	56.23	60.95	41.32	4.04	<.0001*
	pre-op	30	51.97	3.33	50.72	53.21	22.50	-4.04	
Z00	LastPostOp	34	127.69	6.84	125.31	130.08	22.71	-4.48	<.0001*
	pre-op	30	137.57	7.26	134.86	140.28	43.60	4.48	
Z11	LastPostOp	34	2.19	0.97	1.85	2.53	39.12	3.02	0.0025*
	pre-op	30	1.54	1.07	1.14	1.94	25.00	-3.02	
Z02	LastPostOp	34	75.91	4.07	74.49	77.33	23.09	-4.30	<.0001*
	pre-op	30	81.06	4.38	79.42	82.70	43.17	4.30	

Z22	LastPostOp	34	0.76	0.28	0.66	0.85	25.53	-3.18	0.0014*
	pre-op	30	1.13	0.54	0.93	1.33	40.40	3.18	
Z31	LastPostOp	34	0.46	0.23	0.38	0.54	34.12	0.73	<0.05*
	pre-op	30	0.40	0.25	0.31	0.50	30.67	-0.73	
Z3	LastPostOp	34	0.13	0.06	0.11	0.15	25.71	-3.10	0.0019*
	pre-op	30	0.21	0.12	0.16	0.25	40.20	3.10	
Z40	LastPostOp	34	1.92	0.27	1.83	2.02	46.50	6.40	<.0001*
	pre-op	30	1.27	0.21	1.19	1.34	16.63	-6.40	
Z42	LastPostOp	34	0.13	0.07	0.10	0.16	33.74	0.56	<0.01*
	pre-op	30	0.12	0.06	0.10	0.14	31.10	-0.56	
Z44	LastPostOp	34	0.12	0.07	0.09	0.14	32.82	0.14	0.8823
		30	0.11	0.05	0.09	0.13	32.13	-0.14	

*Statistically significant (p<0,05). B CS LOGS: logarithm of contrast sensitivity of the both eyes, B SC WEBER: Weber contrast sensitivity of the both eyes, CDVA: Corrected Distance Vision Acuity, CS LOGS:, logarithm of contrast sensitivity ET PEAK: Epithelial thickness at the apex of the cornea, SC WEBER: Weber contrast sensitivity

Table 2: Data analysis with Wilcoxon Signed-Ranks test in PRK group.

Variable	Period	Number	Mean	StDev	Lower 95%	Upper 95%	Score Mean	Z	prob>ChiSq
B SC (WEBER)	LastPostOp	19	0.28	0.02	0.26	0.29	26.08	0.02	0.9756
	pre-op	32	0.27	0.03	0.26	0.28	25.95	-0.02	
B CS (LOGCS)	LastPostOp	19	2.56	0.04	2.54	2.59	24.58	-0.53	0.5901
	pre-op	32	2.58	0.04	2.56	2.59	26.84	0.53	
CDVA (Snellen)	LastPostOp	19	-0.15	0.02	-0.16	-0.14	18.13	-3.15	0.0016*
	pre-op	32	-0.10	0.07	-0.12	-0.08	30.67	3.15	
SC (WEBER)	LastPostOp	19	0.40	0.27	0.27	0.52	15.00	-4.07	<.0001*
	pre-op	32	0.98	0.58	0.77	1.19	32.53	4.07	
CS (LOGCS)	LastPostOp	19	2.47	0.23	2.36	2.58	36.89	4.03	<.0001*
	pre-op	32	2.11	0.33	2.00	2.23	19.53	-4.03	
ET PEAK Mm	LastPostOp	18	58.78	4.57	56.50	61.05	36.67	4.07	<.0001*
	pre-op	32	52.22	3.77	50.86	53.58	19.22	-4.07	
Z00	LastPostOp	19	125.48	6.64	122.28	128.68	14.47	-4.26	<.0001*
	pre-op	32	135.27	4.16	133.77	136.77	32.84	4.26	
Z11	LastPostOp	19	2.68	0.91	2.24	3.12	37.32	4.18	<.0001*
	pre-op	32	1.36	0.76	1.09	1.64	19.28	-4.18	
Z02	LastPostOp	19	74.65	3.69	72.87	76.43	14.74	-4.16	<.0001*

	pre-op	32	79.62	2.51	78.72	80.53	32.69	4.16	
Z22	LastPostOp	19	1.11	0.51	0.86	1.36	24.37	-0.59	0.5458
	pre-op	32	1.18	0.57	0.97	1.38	26.97	0.59	
Z31	LastPostOp	19	0.47	0.27	0.34	0.60	30.82	1.77	0.0746
	pre-op	32	0.33	0.18	0.26	0.39	23.14	-1.77	
Z3	LastPostOp	19	0.17	0.11	0.12	0.23	22.53	-1.28	0.1984
	pre-op	32	0.20	0.10	0.16	0.24	28.06	1.28	
Z40	LastPostOp	19	2.05	0.45	1.83	2.27	42.00	5.91	<.0001*
	pre-op	32	1.16	0.16	1.11	1.22	16.50	-5.91	
Z42	LastPostOp	19	0.13	0.10	0.08	0.18	28.45	0.90	0.3649
	pre-op	32	0.09	0.05	0.08	0.11	24.55	-0.90	
Z44	LastPostOp	19	0.09	0.07	0.06	0.13	24.58	-0.52	0.5987
		32	0.09	0.04	0.07	0.11	26.84	0.52	
*Statistically significant (p<0,05), B CS LOGS: logarithm of contrast sensitivity of the both eyes, B SC WEBER: Weber contrast sensitivity of the both eyes, CDVA: Corrected Distance Vision Acuity, CS LOGS:, logarithm of contrast sensitivity ET PEAK: Epithelial thickness at the apex of the cornea, SC WEBER: Weber contrast sensitivity									

Table 3. Data analysis with Wilcoxon Signed-Ranks test in LASIK group.

According to the Spearman analysis regarding the group participated in a PRK procedure (Table 4), the alteration of the ET peak appeared to be related to the change of C.S. (p<0,01) (correlation coefficient CC=-0,36). Also, the change of ET peak seemed to affect changes in the deflection of the LOAs closing-opening of the pupil (Z00), vertical deflection myopia or hypermetropia (Z02), a secondary horizontal astigmatism (Z11) and changes in the HOAs such as coma -fourth-level horizontal astigmatism (Z31) and high-level five-digit vertical astigmatism (Z42). However, the change in ET during healing did not appear to affect the subjective vision of the participants in this group.

PRK	ET_peak	
	Correlation Coefficient	p
BCS(LOGCS)	0,42	<0.01
BCS(Weber)	-0,37	<0.01
CS(LOGCS)	0,44	<0.01
SC(WEBER)	-0,36	<0.01
Z00	-0,43	<0.01
Z02	-0,44	<0.01
Z11	0,41	<0.01
Z31	0,33	<0.05
Z42	-0,37	<0.01
B CS LOGS: logarithm of contrast sensitivity of the both eyes, B SC WEBER: Weber contrast sensitivity of the both eyes, CS LOGS:, logarithm of contrast sensitivity, SC WEBER: Weber contrast sensitivity		

Table 4. Spearman analysis in PRK group.

As for the group underwent LASIK surgery (Table 5), it was observed that the change in ET was not corelated with changes in C.S and HOAs. Conversely shown correlation with changes of LOAs (Z00, Z02, Z11) which did not affect the change of subjective vision of participants in this group.

LASIK	ET_peak	
	Correlation Coefficient	p
Z00	-0,3	<0.05
Z02	-0,31	<0.05
Z11	-0,31	<0.05
ET PEAK: Epithelial thickness at the apex of the cornea		

Table 5. Spearman analysis in LASIK group.

Discussion

In this study we investigated whether there is a correlation between changes of the ET peak with changes of the CS and the aberrations before and after refractive surgery (PRK and LASIK), on the corneal apex. We found that the ET peak increased 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 [1-3,6-8]. Moreover no difference between groups suggests that the epithelial changes occur as a function of changes in the anterior corneal curvature and not necessarily related to tissue removal. The corneal flattening in myopic eyes may contribute to the postoperative epithelial thickening due to the lack of mechanical influences of the upper eyelid that polishes the corneal surface with blinking [9]. Nevertheless our results are in accordance with previous studies published in the literature. Sedaghat et all, proposed that a significant decrease in thickness was seen 1 month after PRK in all zones. Afterward, epithelial thickening continued in all zones and reached the preoperative thickness in the midperipheral and peripheral zones 6 months later, whereas the thickness in the central 5-mm zone was significantly thicker than before surgery [10]. XiangJun also found that the corneal epithelial thickness increased after PRK up to 3 months postoperatively and it was affected by the amount of myopia treated, treatment zone, and preoperative epithelial thickness [3].

In PRK surgery, changes in ET peak seem to correlate with changes of C.S. This correlation was studied for the first time. The ET peak 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 and dry eyes as well. 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 [8]. Moreover the new subepithelial interface after PRK also accumulates water that colocalizes with the hyaluronan [12]. The sharp demarcations of these zones create sharp shifts in a refractive index in these areas, could probably cause light scattering which may affect the CS. Furthermore, changes in ET peak seemed 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 [13,14]. 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 [12,15]. 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. also report an increase in HOAs caused by PRK surgery during epithelial remodeling [13].

In LASIK there was statistically increased in ET peak. This is in accordance to previous studies which indicated that LASIK induced increment in epithelial thickness of approximately 20% that persisted after surgery [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 [8]. However, in Lasik there was no correlation among ET peak increasement and C.S 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 C.S. while in PRK there was complex interaction of epithelial cells and activated keratocytes [9]. A total 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 [16]. 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 [17].

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 deeper 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, and this maybe affect the correlation among CS and ET peak in LASIK and PRK group. In LASIK group, changes in ET peak was found to correlate with changes in LOAs (Z00, Z02, Z11), which did not affect changes in subjective vision. This 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. Larger optical zone reduced overall HOAs as well as spherical aberrations, after LASIK. The effects were more significant in high myopia than in low [18]. Also, the high refractive corrections both myopic and hyperopic can result in very high levels of HOAs [19] after LASIK surgery. However, this is the first study which show that there was no correlation among HOAS increment and postoperative epithelial thickness. As it was mentioned above, postoperative corneal ET peak 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 the application of statistical analysis in both eyes of some cases. The inclusion of bilateral cases was performed in order to increase the power of the study and to reduce the number of subjects that had to be recruited. The optimal way to address this issue is to use only one eye from each patient or to use advanced statistical analysis. However, this has not always been the case in all publications. Nevertheless previous studies published in the literature of PRK or LASIK patients, it was found that correlations were low in eyes having undergone refractive surgery, and that results were similar when using one or both eyes of the patients [20,21]

Conclusion

In conclusion, the epithelium thickness increased after refractive surgery. In PRK group, changes in ET peak seemed to correlate with C.S which is decreased. In LASIK group changes in ET peak did not corelate with C.S which seemed to be more stable. The difference between the two types of surgery can be related to the change in the shape of the cornea, the conversion of biomechanics, the healing of the corneal flap, and the reconstructed of corneal epithelium and layer. Moreover, changes of ET peak affected the aberrations in both techniques, but not in the same manner. In terms of CS, LASIK seems to offer better results and for this reason could be advised, when there are no other parameters to influence our decision what type of refractive technique should be selected.

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