Journal of Ophthalmology

Femtosecond Laser in Anterior Segment Surgery

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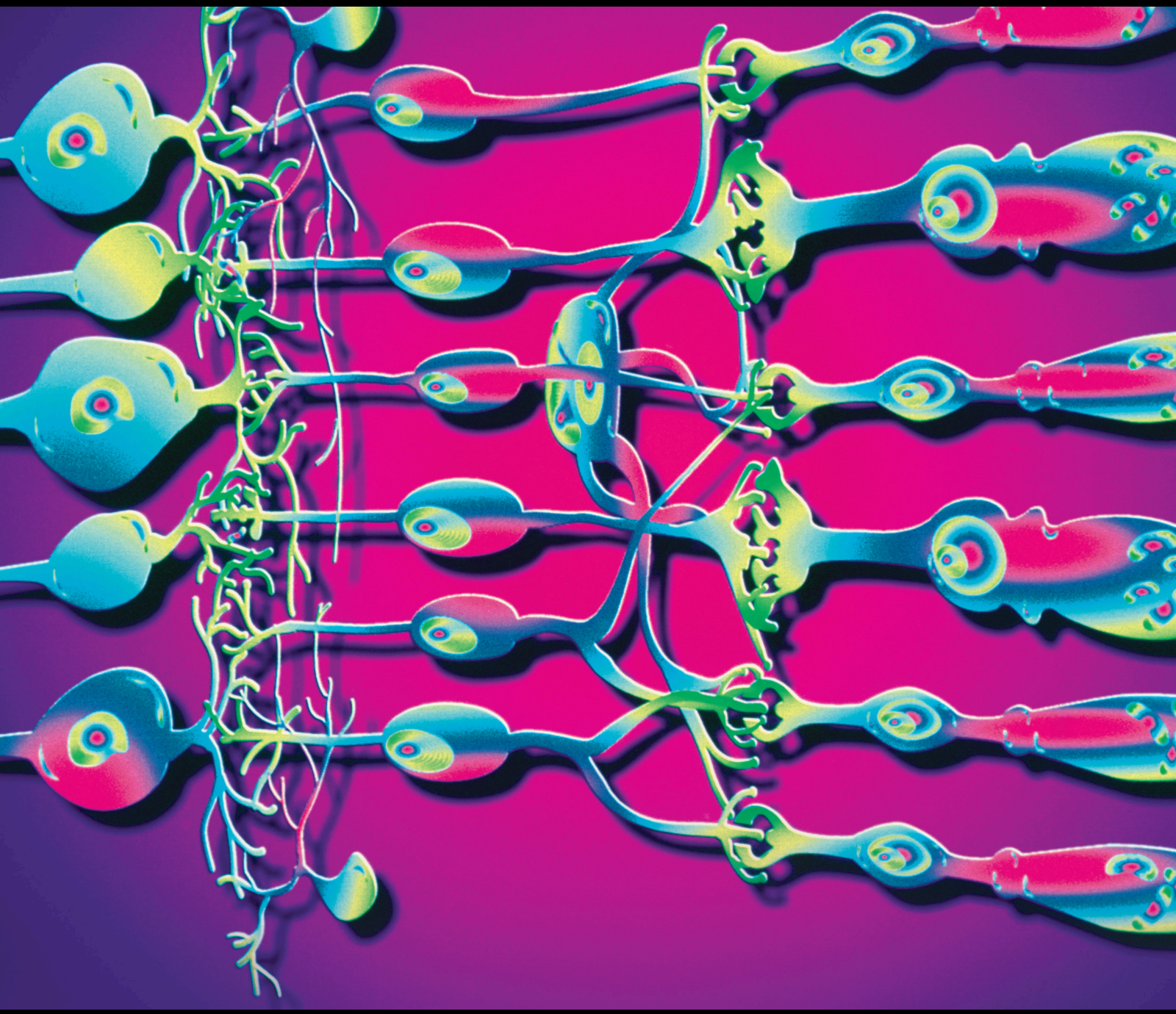

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Editorial

Femtosecond Laser in Anterior Segment Surgery

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The application of femtosecond lasers in ophthalmology has enabled precise and reproducible tissue cutting, which is expected to improve the outcomes of surgical treatment, particularly in anterior segment surgeries such as cornea, cataract, and refractive surgery.

As we have introduced in the call for papers for this Special Issue, the articles published cover topics focused on the application of femtosecond lasers in anterior segment surgery, including the development of the technologies behind femtosecond lasers and their application in ophthalmic surgery, the efficacy and safety of anterior segment surgery using femtosecond lasers, and imaging techniques associated with the application of femtosecond lasers.

Femtosecond lasers have been increasingly used in cornea and refractive surgery. The laser can be used to create customized trephination edges for deep anterior lamellar keratoplasty and penetrating keratoplasty and for allowing ultrathin cut for Descemet stripping automated anterior lamellar keratoplasty. It can also be helpful for improving the consistency and reproducibility of refractive surgery, including laser-assisted in situ keratomileusis (LASIK), small incision lenticule extraction (SMILE), intrastromal corneal ring segment implantation, and astigmatic keratotomy.

Femtosecond laser cataract surgery (FLACS), in which a femtosecond laser is employed for corneal incision, anterior capsulotomy, lens fragmentation, and liquefaction, is also expected to improve the reproducibility and safety of cataract surgery. In this Special Issue, the authors contributed 10 original papers and one review article regarding the use of femtosecond lasers in anterior segment surgery.

The authors have reported the results of their research on various topics related to femtosecond lasers in anterior segment surgery: (1) extrusion of femtosecond laser-implanted intrastromal corneal ring segments in keratoconic eyes: prevalence, risk factors, and clinical outcomes; (2) clinical observation of silicon hydrogel contact lens fitted immediately after SMILE; (3) preliminary results of a novel standardized technique of femtosecond laser-assisted deep anterior lamellar keratoplasty for keratoconus; (4) long-term evaluation of capsulotomy shape and posterior capsule opacification after low-energy bimanual femtosecond laser-assisted cataract surgery; (5) anatomical and visual outcomes after LASIK performed in myopic eyes with the WaveLight® refractive suite (Alcon® Laboratories Inc., USA); (6) correlation analysis of refractive and visual quality after wavefront-optimized laser in situ keratomileusis for 50% and 100% angle kappa compensation; (7) comparison of femtosecond laser-assisted cataract surgery and conventional phacoemulsification in shallow anterior chambers and glaucoma; (8) characteristics of facial asymmetry in congenital superior oblique palsy according to trochlear nerve absence; (9) a modified femtosecond laser technique for

anterior capsule contraction syndrome; and (10) evaluation of astigmatic correction using a vector analysis after combined femtosecond laser-assisted phacoemulsification and intrastromal arcuate keratotomy. This Special Issue also includes one review article on the application of femtosecond lasers in anterior segment surgery.

We believe these papers will provide readers with valuable information on the application of femtosecond lasers in anterior segment surgery and new ideas for research on related topics.

Conflicts of Interest

The editors declare no conflicts of interest.

Acknowledgments

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Research Article

Evaluation of Astigmatic Correction Using Vector Analysis after Combined Femtosecond Laser-Assisted Phacoemulsification and Intrastromal Arcuate Keratotomy

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The aim of this study was to evaluate astigmatic correction in patients with mild to moderate astigmatism after combined femtosecond laser-assisted cataract surgery (FLACS) and intrastromal arcuate keratotomy (ISAK), using vector analysis. This retrospective study included patients with corneal astigmatism of 0.5–3.0 diopters (D) who underwent FLACS and ISAK. Vector analyses of astigmatism were performed using the Alpins method, considering three vectors: target-induced astigmatism (TIA), surgically induced astigmatism (SIA), and difference vector (DV). Magnitude of error (ME), angle of error (AE), correction index (CI), and coefficient of adjustment (CA) were calculated. Subgroup analysis according to the axis of astigmatism, patient age, and white to white (WTW) diameter was conducted. In total, for the 79 eyes of 79 patients, the TIA was 1.21 ± 0.52 *D*, the SIA was 0.76 ± 0.53 D, and the DV was 0.86 ± 0.50 D. The ME (difference between SIA and TIA) was -0.46 ± 0.45 D, and the CI (ratio of SIA and TIA) was 0.62 ± 0.34; both these parameters demonstrated slight undercorrection. The CA (inverse of the CI) was 2.48 ± 2.61. The AE was $4.02^\circ \pm 28.7^\circ$, and the absolute AE was $21.7^\circ \pm 19.0^\circ$. In the univariate regression analyses to identify factors that affected the CI, there was a negative correlation between age and the CI ($P = 0.022$). In conclusion, vector analysis after the combined FLACS and ISAK revealed slight undercorrection, regardless of the astigmatism meridian. The precision of the nomogram should be improved through long-term vector analysis for the results of arcuate keratotomy and through further research on the relationship between patient demographics and CI. Overall, this study has shown that FLACS and ISAK could reduce postoperative corneal astigmatism effectively and safely.

1. Introduction

Although modern cataract surgery allows for rapid visual recovery, preexisting corneal astigmatism remains a common obstacle to achieving excellent uncorrected visual acuity. Uncorrected astigmatism significantly compromises a patient's vision and leads to reduced quality of life [1]. Corneal astigmatism greater than 1.0 diopter (*D*) was found in 27.95% of 23,239 eyes in a recent study [2]. A variety of treatment options exist to reduce this corneal astigmatism during surgery, including toric intraocular lens (IOL) implantation, opposite clear corneal incisions, manual arcuate keratotomy, limbal relaxing incision, or a combination of these approaches [3–6].

The advent of femtosecond laser technology allows precise control of corneal incisions, capsulorhexis (centration, size, and regularity), and nucleus fragmentation and may yield promising surgical outcomes and early recovery of visual acuity of patients, with effects on IOL centration and reduced usage of total phacoemulsification energy. Among these surgical steps and as compared to manually delivered keratotomy, arcuate keratotomy (AK) with femtosecond

laser has been known to be efficacious in reducing corneal astigmatism in mild to moderate corneal astigmatism, with high reliability and reproducibility [7–9]. According to a recent study, the outcomes of AK with femtosecond laser were comparable to those of toric IOL implantation in eyes with low to moderate astigmatism [10].

The position, length, and depth of the incisions are guided by nomograms based on the amount of astigmatism, type of astigmatism, and the patient's age. There are various types of nomograms according to the laser devices and types of AK—paired or single type and penetrating or intrastromal AK, respectively [11–14]. In intrastromal AK (ISAK), the cut is performed within the stroma and does not reach Bowman's layer. The ISAK has the advantage of theoretical elimination of the risk of infection and minimization of postoperative pain. In addition, wound gape and epithelial ingrowth could be avoided because of the absence of an open wound [15]. The mainly used nomogram for ISAK is Version 3 nomogram provided by Dr. Julian Stevens in 2015 [16]. However, studies on the evaluation of nomograms are limited.

The aim of our study was to evaluate astigmatic correction in patients with mild to moderate astigmatism using Alpins vector analysis method after combined femtosecond laser-assisted cataract surgery (FLACS) and ISAK using a nomogram provided by Dr. Julian Stevens. Additionally, we investigated an approach to increase the accuracy of ISAK and to determine the adjustments needed for the nomogram.

2. Subjects and Methods

This retrospective study included patients who underwent combined FLACS and ISAK between 2016 and 2019 at the Asan Medical Center in Seoul, Korea. All procedures adhered to the tenets of the Declaration of Helsinki, and the study was approved by the Institutional Review Board of Asan Medical Center at the University of Ulsan in Seoul, Korea.

2.1. Preoperative and Postoperative Examinations. A standard preoperative ophthalmic examination that included Autorefractive keratometer (KR-1; Topcon Corp., Japan), noncontact tonometry (CT-80; Topcon Corp., Japan), slit-lamp biomicroscopy, fundoscopy, partial coherence interferometry (IOLMaster 500; Carl Zeiss Meditec AG, Germany), specular microscopy (Cellchek SL; Konan Medical USA, Inc., CA, USA), scanning-slit topography (ORBscan; Bausch and Lomb, Inc., NY, USA), and ocular aberrometry (OPD-Scan; Nidek Co., Ltd., Japan) was performed. Preoperative ocular biometric measurements, including axial length, anterior chamber depth, and keratometric values, were performed to calculate the IOL power using partial coherence interferometry. Steep keratometry (K), flat K, and steep meridian values to be entered into the calculator were determined by the surgeon, with consideration of data obtained with the autorefractive keratometer, simulated K of scanning-slit topography, and partial coherence interferometry. Patients were evaluated at one day, one week, one month, and three months after surgery. The visual acuity, intraocular pressure, and keratometric measurements through the autokeratometer were assessed every visit. The manifest refraction and keratometric measurement obtained through scanning-slit topography were assessed at one month and three months after surgery.

2.2. Surgical Techniques. A single experienced surgeon performed FLACS using a Catalys Precision Laser System (Abbott Medical Optics, Inc., CA, USA). The central corneal thickness (CCT) and longest white-to-white (WTW) diameter were obtained during surgery on the laser platform. To avoid the effect of cyclotorsion in the supine position, the horizontal line was marked on the eye with a pen while the patient was sitting. The horizontal line was then aligned on the laser's nonapplanating liquid optics interface. A femtosecond laser was used to perform capsulorhexis capsulotomy and lens fragmentation, followed by ISAK when the corneal astigmatism exceeded 0.50 D and was not exceeding 3.0 D. The length of the arcuate keratotomy was determined using the nomogram provided by Dr. Julian Stevens [16].

All ISAKs consisted of a pair of symmetric intrastromal incisions with a depth of 20–80% of the corneal thickness and a limbus-based flap, 8.0 mm in diameter. The arc length ranged from 30° to 90°, depending on the patient's age and the magnitude and axis of astigmatism. After the laser procedure, a main limbal incision was created using a 2.2 mm keratome, and the anterior capsule button was removed using forceps.

Phacoemulsification was performed using a Whitestar Signature Phacoemulsification System (Abbott Medical Optics, Inc., CA, USA). A single-piece IOL (Tecnis ZCB00; Abbott Medical Optics, Inc., CA, USA) was implanted in all eyes. Postoperatively, all patients were administered 1% prednisolone acetate suspension (Pred Forte®; Allergan, Inc., CA, USA) and 0.5% moxifloxacin (Vigamox®; Alcon Laboratories, TX, USA) for one month.

2.3. Analysis of Astigmatic Correction. The magnitude and axis of the keratometric astigmatism were used to determine the ISAK profiles and to analyze the postoperative outcome of the astigmatic correction. Vector analysis and graphic displays were performed using the Alpins method, facilitated by the ASSORT Group Analysis Calculator [17].

In this study, target-induced astigmatism (TIA) was defined as the astigmatic change the surgeon intended to induce to correct the patient's preexisting astigmatism based on the magnitude and axis. The astigmatic correction was calculated using a nomogram calculator that incorporated the value of keratometric astigmatism (magnitude and axis) and the surgeon-specific flattening effect (−0.25 D to 0.00 D) of a 2.2 mm main incision and a 1.0 mm side port. The surgically induced astigmatism (SIA) is the amount and axis of a stigmatic change achieved by the ISAK. The difference vector (DV) is the astigmatic change that would enable the initial surgery to achieve its intended target based on the magnitude and axis. The DV is an absolute measure of success and is preferably zero.

The arithmetic difference values between the SIA and TIA magnitudes and axes were defined as the magnitude of error (ME) and angle of error (AE), respectively. The ME is positive for overcorrections and negative for undercorrection. The AE is positive if the achieved correction is on an axis counterclockwise to where it was intended and negative if the achieved correction is clockwise to its intended axis. The correction index (CI), coefficient of adjustment (CA), and flattening index (FI) were also calculated. The CI is the ratio of the SIA to the TIA, with a value greater than 1.0 indicating overcorrection and a value less than 1.0 indicating undercorrection. The CA is calculated by dividing TIA by SIA, that is, the inverse of the CI. This is the value used for the adjustment of the magnitude of future astigmatism treatments that is preferably 1. The FI is the dividing amount of astigmatism reduction achieved by the effective proportion of the SIA at the intended meridian by the TIA, which is preferably 1.0. Ocular residual astigmatism (ORA) is a dioptric measure of the noncorneal component of total refractive astigmatism, that is, the vector difference between refractive and corneal astigmatism [18].

2.4. Subgroup Analysis. Patients were categorized into three groups according to the axis of astigmatism: with-the-rule (WTR) astigmatism (steep corneal meridian from 60° to 120°); against-the-rule (ATR) astigmatism (steep corneal meridian either from 0° to 30° or from 150° to 180°); and oblique (OBL) astigmatism (all other astigmatism not belonging to WTR and ATR). Subgroup analyses were conducted to assess the magnitude of astigmatism and the change in astigmatism after surgery.

Patients were categorized into five groups according to their age: under 50 years; from 50 to 59 years; from 60 to 69 years; from 70 to 79 years; and 80 years or older. In addition, patients were categorized into three groups according to the longest WTW diameter: less than 11 mm; from 11 to 12 mm; and more than 12 mm. Subgroup analyses were also conducted to assess the correlation between the SIA and TIA magnitudes in each subgroup classified according to age and WTW.

2.5. Statistical Analyses. Data were presented as mean ± standard deviations. A Shapiro–Wilk test was used to assess the distribution of the numerical data. Wilcoxon's signed-rank test was used to compare postoperative astigmatism with preoperative astigmatism. The Kruskal–Wallis test was used to compare the magnitude of astigmatism or amount of astigmatic change after surgery between subgroups. Pearson's or Spearman's correlation analysis, depending on the distribution of data, was used to assess the relationship between the SIA and TIA magnitudes. Regression analysis was used to identify factors that affected the CI. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using SPSS version 21.0 software (IBM SPSS Inc., IL, USA).

3. Results

Data were available for 79 eyes (56 right and 23 left eyes) of 79 patients who underwent routine examinations at one week, one month, and three months postoperatively. The mean age of these 35 males and 44 females was 66.95 ± 10.75 years. Table 1 lists the preoperative patient demographics. All incisions were placed as intended, and no cases experienced inadvertent placement within the visual axis. There was no penetration of the Bowman or Descemet membranes, and all incisions were confined within the corneal stroma. No adverse events occurred during the follow-up period.

Table 1: Preoperative patient characteristics and ocular biometric parameters.

$N = 79$	
Age	66.95, 10.75
Sex (M : F)	35 : 44
Laterality (OS : OD)	23 : 56
Astigmatism axis (ATR : WTR : OBL)	35 : 29 : 15
Preop endothelial cell count (cell/mm^2)	2532.37, 424.47
Longest white-to-white (mm)	11.37, 0.50
Central corneal thickness (μm)	585.35, 32.49

ATR, against-the-rule; WTR, with-the-rule; and OBL, oblique astigmatism. Data are given as numbers or as means, SD.

As a result of classifying subgroups according to the axis of astigmatism, 35 patients were categorized into the WTR group, 29 patients were categorized into the ATR group, and 15 patients were categorized into the OBL group. As a result of classifying subgroups according to the patient age, seven patients were under 50 years, seven patients were from 50 to 59 years, 28 patients were from 60 to 69 years, 30 patients were from 70 to 79 years, and seven patients were 80 years or older. As a result of classifying subgroups according to the longest WTW diameter, 12 patients were less than 11 mm, 58 patients were from 11 to 12 mm, and nine patients were more than 12 mm.

The values of corneal astigmatism measured by the autokeratometer and topography recorded preoperatively and at one and three months postoperatively are displayed in Table 2. We evaluated the values from the autokeratometer and scanning-slit topography and recorded all the data from the devices. Preoperative astigmatism was recorded as 1.23 ± 0.52 D from the autokeratometer and 1.17 ± 0.66 D from the scanning-slit topography. The corneal astigmatism decreased significantly at one and three months after surgery compared to the preoperative measurement, based on both devices (all $P < 0.001$).

Table 3 and Figure 1 show the outcomes of vector analysis by the comparison of the preoperative with the postoperative (three months) values measured by the autokeratometer. The lower, left image in Figure 1 shows a statistically significant correlation between the overall SIA and TIA magnitudes. As a result of the linear regression, $r^2 = 0.40$, $P < 0.001$, and overall CI was 0.62 ± 0.34 D, demonstrating undercorrection. As shown in the lower, right image in Figure 1, AE was in the highest proportion between −5° and 5°, and the average AE was 4.02° ± 28.7°. However, the absolute AE, which is the mean of the magnitude of AE, was 21.7° ± 19.0°.

The detailed values of the changes in these parameters measured by the autokeratometer according to the

Table 2: Corneal astigmatism values recorded preoperatively and at 1 and 3 months postoperatively.

	Autokeratometer (KR-1®)			Topography (ORBscan®)		
	K Astig (mean, SD) range	*P*#	Δ† (mean, SD)	K Astig (mean, SD) range	*P*#	Δ† (mean, SD)
Preop	1.23, 0.52			1.17, 0.66		
Postop 1 mo	0.85, 0.42	<0.001	−0.38, 0.51	0.96, 0.45	<0.001	−0.21, 0.67
Postop 3 mo	0.80, 0.45	<0.001	−0.44, 0.55	0.94, 0.50	<0.001	−0.23, 0.73

ΔChange of corneal astigmatism compared with preoperative data. #Wilcoxon's signed-rank test (comparison with baseline time point). †Algebraic method.

Table 3: Outcomes of vector analysis via the comparison of the preoperative with the postoperative values measured by the autokeratometer.

	Mean, SD
TIA (D)	1.21, 0.52
SIA (D)	0.76, 0.53
DV (D)	0.86, 0.50
ME (D)	−0.46, 0.45
AE (degree)	4.02, 28.7
Absolute AE (degree)	21.7, 19.0
CI	0.62, 0.34
CA	2.48, 2.61
FI	0.45, 0.21
ORA (D)	0.06, 0.47

TIA, target-induced astigmatism; SIA, surgically induced astigmatism; DV, difference vector; ME, magnitude of error; AE, angle of error; Absolute AE, absolute angle of error; CI, correction index; CA, coefficient of adjustment; FI, flattening index; and ORA, ocular residual astigmatism.

astigmatism axis are displayed in Table 4. The corneal astigmatism decreased significantly in all axes of astigmatism ($P = 0.001$ or $P < 0.001$ in WTR and ATR; in OBL, $P = 0.013$ at one month after surgery and $P = 0.040$ at three months after surgery). The magnitudes of residual astigmatism were 0.89 ± 0.47 D in WTR, 0.75 ± 0.40 D in ATR, and 0.68 ± 0.46 D in OBL at three months after surgery. There was no significant difference between the subgroups in terms of either astigmatism magnitude or amount of reduction, regardless of the postoperative period (at one month after surgery, $P = 0.072$ for the astigmatism magnitude and $P = 0.230$ for the amount of reduction; at three months, $P = 0.217$ for the astigmatism magnitude and $P = 0.639$ for the amount of reduction). Figure 2 depicts the single angle polar plots displaying the distribution of the correction index according to the astigmatism axis. The CI was 0.60, 0.58, and 0.77 in the WTR, ATR, and OBL subgroups, respectively.

According to univariate regression analyses aimed at identifying factors that affected the CI at three months, there was a negative correlation between the age and the CI ($P = 0.022$). The WTW, CCT, AE, and axis of astigmatism did not show any significant correlation with the CI. ($P = 0.810$ for WTW, $P = 0.454$ for CCT, $P = 0.654$ for AE, $P = 0.182$ for axis of astigmatism). Figure 3 shows the correlation between the SIA and TIA magnitudes in the subgroups according to the age and the longest WTW. In the subgroup analysis according to age, a correlation between the TIA and SIA magnitudes was observed in all groups, except for those aged 80 years or older ($P = 0.021$ for under 50 years, $P = 0.016$ for 50 to 59 years, $P = 0.001$ for 60 to 69 years, $P < 0.001$ for 70 to 79 years, and $P = 0.816$ for 80 years or older). In correlation analysis in subgroup defined by WTW, a correlation between the TIA and SIA magnitudes was observed in all groups, except for those with the longest WTW less than 11 mm ($P = 0.473$ for WTW less than 11 mm, $P < 0.001$ for WTW from 11 to 12 mm, and $P = 0.021$ for WTW more than 12 mm).

4. Discussion

In this study, the combined FLACS and ISAK exhibited relatively satisfactory results but resulted in undercorrection of astigmatism, regardless of the meridian. In the univariate regression analysis of the factors affecting the CI, there was a significant negative correlation with age. There was no significant correlation with CI in terms of the type of astigmatism, CCT, or WTW.

In the present study, paired intrastromal keratotomy was performed, However, recently published studies have reported a lower CI in ISAK than in penetrating keratotomy. Day et al. used paired intrastromal keratotomies and reported a CI of 0.63 ± 0.32 after one month [19], while Byun et al., who used the same platform, reported a CI of 0.87 ± 0.50 after six months [20]. In contrast, Visco et al. reported a higher CI (0.94) at three months after paired penetrating keratotomy [11]. In the current study, which used paired intrastromal keratotomy, the CI was 0.62 ± 0.34 after three months, which was comparable to that reported in previous studies. Therefore, to improve the accuracy of ISAK, it is necessary to attempt to increase the lower CI, as compared to penetrating AK.

The astigmatism that could be corrected with AK varies depending on the study, but is generally limited to 3 D or less, and, in general, mild to moderate astigmatism is limited by a difficulty in the accurate measurement of the magnitude and axis of astigmatism. Thus, accurate evaluation of preoperative corneal astigmatism and consideration of various situations is essential for effective femtosecond-assisted ISAK. As the anterior corneal astigmatism shifts from WTR to ATR with aging while posterior corneal astigmatism remains as ATR, this should be considered and corrected [21]. In a penetrating AK-related study, the total corneal power and anterior astigmatism were significantly decreased after surgery, but posterior astigmatism remained unchanged [22]. Moreover, the ATR and OBL astigmatism had more marked image quality deterioration than WTR astigmatism [23]. In addition, various nomograms are currently used in femtosecond-assisted ISAK, although a perfect standard nomogram has not yet been developed, and there are many variations depending on the measurement devices of astigmatism. Thus, it is reasonable to recommend

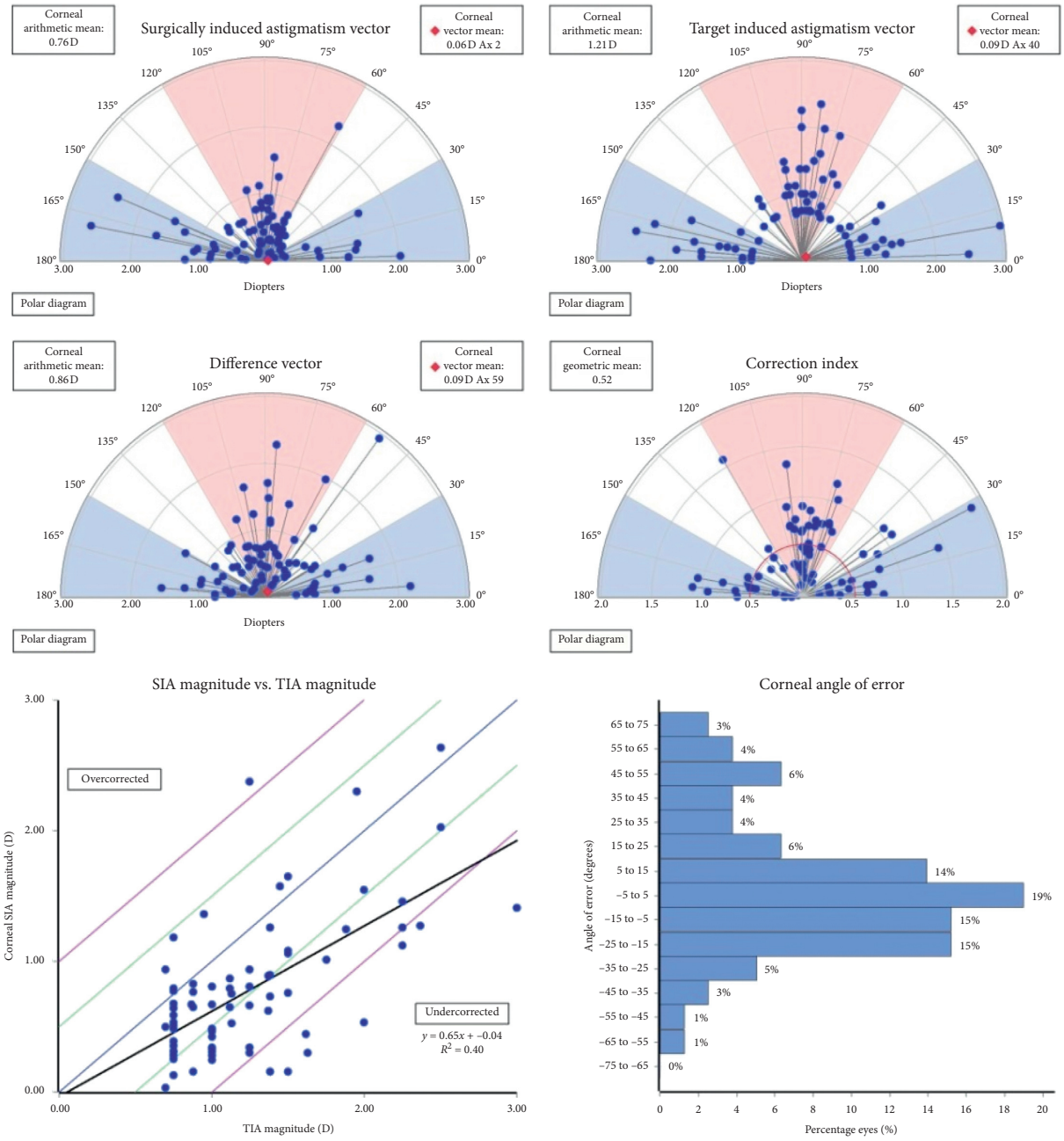

Figure 1: Outcomes of vector analysis by comparison of the preoperative with the postoperative (three months) values.

the postoperative target astigmatism as a WTR type from 0.25 to 0.5 D, rather than to strive for complete correction with 0 D [11, 24, 25].

The residual astigmatism measured by the autokeratometer at three months in this study was 0.80 ± 0.45 D. In previous studies, when ISAK was used, Day et al. reported 0.74 D at one month, Byun et al. reported 0.63 D at six months, and Chan et al. using penetrating AK reported 0.87 D at two months [19, 20, 26]. Residual astigmatism in this study was not larger than that of previous studies, and it could be expected that it would decrease slightly over the long period of time after surgery. According to a previous study using penetrating AK, the CI was 0.53, 1.01, and 0.95 in WTR, ATR, and OBL, respectively. Ideally, this value of CI is the result of undercorrection in WTR and full correction in ATR and OBL types [12]. When the nomogram of this study was applied, all groups exhibited a similar degree of undercorrection, which were appropriate for WTR, but was insufficient for ATR and OBL astigmatism as compared with the ideal amount of correction.

In the correlation analysis of factors that could affect CI, age alone showed a statistically significant negative correlation with CI. Currently used nomograms tend to decrease the arc length of ISAK in older patients. According to this result, it is necessary to increase the arc length to compensate for the lower CI in older patients, but aging-related changes

Table 4: Detailed values of changes in these parameters measured by the autokeratometer according to the astigmatism axis.

		K Astig (mean, SD)	$P^{\#}$	K Astig Δ (mean, SD)	P^{*}	$P^{\#}$
Preop	WTR	1.34, 0.61	0.128			
	ATR	1.23, 0.46				
	OBL	1.00, 0.30				
1 month postop	WTR	1.00, 0.50	0.072	−0.34, 0.57	0.001	0.230
	ATR	0.75, 0.29		−0.48, 0.47	<0.001	
	OBL	0.71, 0.33		−0.29, 0.40	0.013	
3 months postop	WTR	0.89, 0.47	0.217	−0.45, 0.60	<0.001	0.639
	ATR	0.75, 0.40		−0.48, 0.48	<0.001	
	OBL	0.68, 0.46		−0.32, 0.54	0.040	

ATR, against-the-rule; WTR, with-the-rule; OBL, oblique astigmatism. ΔChange of corneal astigmatism compared with preoperative data. *Wilcoxon signed-rank test (comparison with baseline time point). #Kruskal–Wallis test between subgroups.

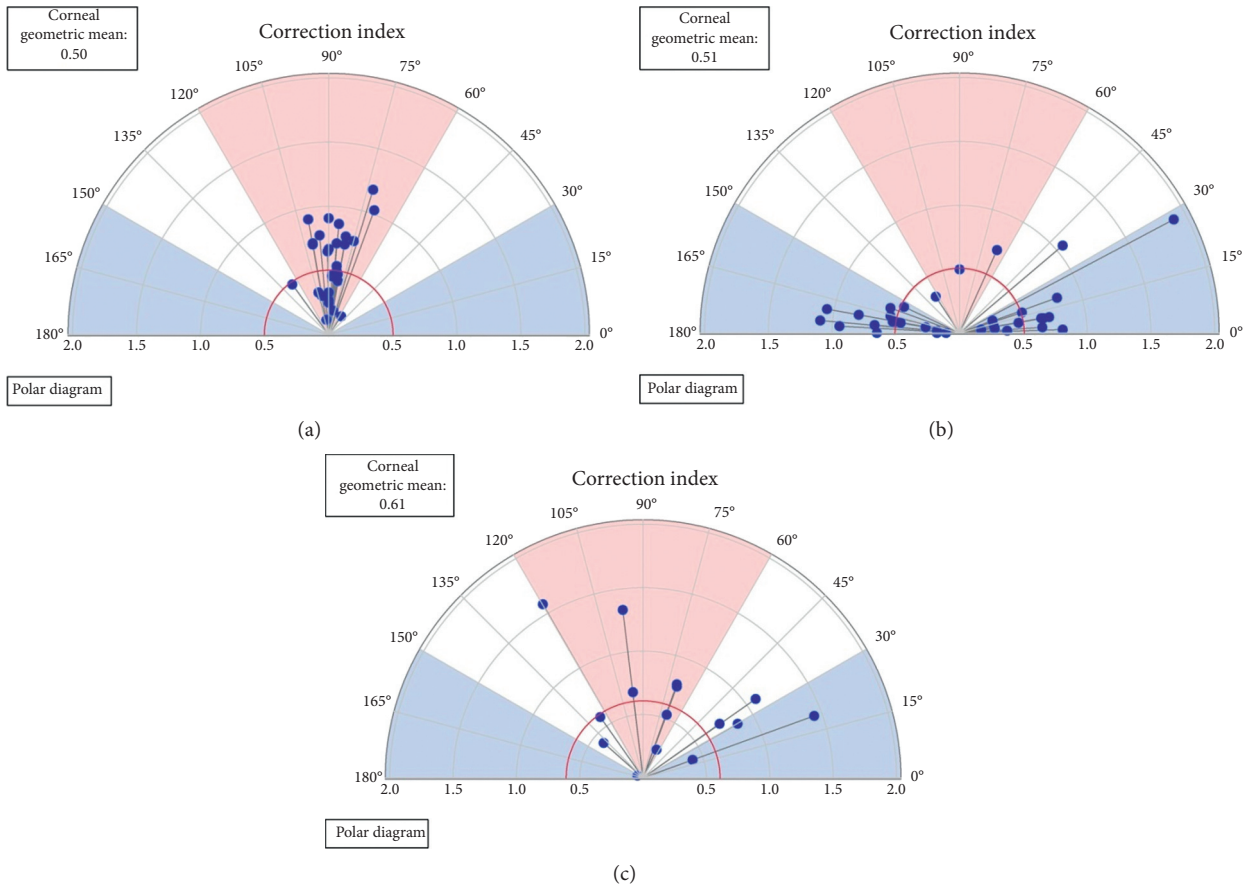

Figure 2: The single angle polar plots displaying the distribution of the correction index according to the astigmatism axis. (a) WTR, with-the-rule astigmatism; (b) ATR, against-the-rule astigmatism; and (c) OBL, oblique astigmatism.

in the cornea described above should be considered. Further research is needed on factors that can affect CI.

Based on the results of astigmatism correction in the nomogram we used in this study, the accuracy of our results could potentially be improved, and high CI could be achieved by the adjustment of the nomogram. For example, the arc length and axis of the nomogram could be adjusted using long-term CA or AE data or in consideration of the age-related change in astigmatism and CI as mentioned above. In a recently published study, a numeric planning tool using an optimization algorithm was used to reduce postoperative astigmatism with higher accuracy, which could be combined with our approach [27].

The current study was limited by its retrospective design, small sample size, and short follow-up period. In addition, among the preoperative corneal astigmatism values measured

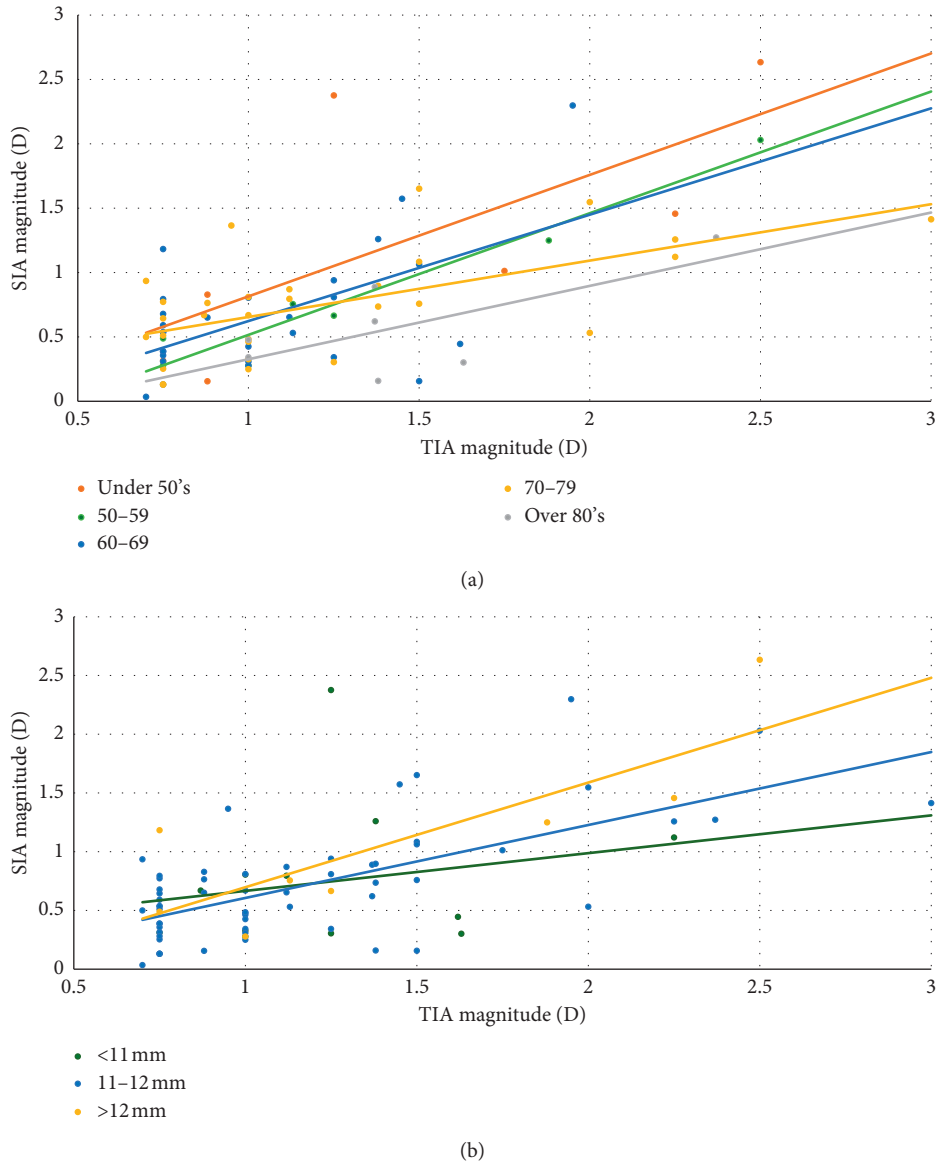

Figure 3: Correlation analysis between the surgically induced astigmatism and target-induced astigmatism in subgroups according to the patient age (a) and the longest white-to-white corneal diameter (b).

using various equipment, the inconsistent selection was used as the reference value for ISAK. In other words, in the auto-keratometry, topography, partial coherence interferometry, and ocular aberrometry, slightly different astigmatism magnitudes and axes were measured. Among these, the surgeon determined the reference value of TIA as the most appropriate measurement value or an arbitrary value after considering several measurements. More reliable results could be expected in future studies that consistently apply one of the various measuring devices.

5. Conclusions

In conclusion, our study showed that FLACS and ISAK reduced postoperative corneal astigmatism effectively and safely. However, the precision of the nomogram should be improved through a long-term vector analysis on the results of AK and further research on the relationship between patient demographics and CI.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflicts of interest presented herein.

Authors' Contributions

Su Young Moon and Ho Seok Chung contributed equally to this study.

Acknowledgments

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Research Article

A Modified Femtosecond Laser Technique for Anterior Capsule Contraction Syndrome

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Anterior capsule contraction syndrome (ACCS) is a rare, late complication of cataract surgery, associated with impairment of visual function. In this paper, we describe a new surgical technique to treat ACCS by femtosecond laser procedure. The femtosecond laser was used to perform an anterior capsulotomy with a customized size, in order to avoid IOL damage. After ophthalmic viscosurgical device injection in the anterior chamber, the anterior capsule flap was separated from the IOL surface by gentle hydrodissection. This manoeuvre enabled an easy and safe removal of the fibrotic material by vitreal microscissors. Our technique allowed a complete removal of the fibrotic material and opening of the capsule, with immediate complete visual acuity recovery without IOL damage. In conclusion, femtosecond laser appears to be safe and effective for treatment of ACCS with long-lasting efficacy.

1. Introduction

Anterior capsular phimosis or anterior capsule contraction syndrome (ACCS) is one of the late complications following cataract surgery [1–3].

ACCS is characterized by an excessive fibrosis response after capsulorhexis, which causes reduction in the size of the anterior capsulotomy and capsular bag diameter. It is often associated with impairment of visual function [3–8]. Rarely, this zonular traction may lead to IOL dislocation and retinal detachment [1, 9].

Once ACCS occurs, removal of fibrous membrane may be required to improve visual function. Currently, the most common technique for treating ACCS is Nd:YAG laser anterior capsulotomy [10]. However, most severe cases often require surgical removal of the fibrous membrane [11–13]. Recently, the use of femtosecond laser technology to treat ACCS has been proposed with different techniques [10, 11, 14].

We describe a novel technique which consists of femtosecond laser capsulotomy followed by surgical removal of the fibrotic material, in a patient with severe ACCS, performed one year after cataract surgery.

2. Materials and Methods

2.1. Surgical Procedure. After corneal topical anesthesia, lid speculum is applied, and the patient is placed under the femtosecond laser system LenSX® (Alcon, Fort Worth, TX, USA) in order to maximize suction applanation. The procedure starts with eye docking and centering. Once the operator acquires all information from LenSX® anterior OCT and establishes cutting parameters, capsulotomy may be performed. Specifically, live OCT imaging is used to establish the depth of capsulotomy by taking into consideration the shape and thickness of the anterior phimosis. The diameter was set in correspondence with the higher gap between the posterior surface of the capsule and the anterior surface of the IOL (see video in Supplementary Materials). The capsulotomy width performed was based on the patient's maximal mydriasis.

At the end of the femtosecond laser procedure, the surgical bed is rotated under the operating microscope, the previous paracenteses of cataract surgery are manually reopened, and the ophthalmic viscosurgical device (OVD) is inserted into the anterior chamber. Gentle hydrodissection is performed to release the adherences between the anterior capsule and the anterior surface of the IOL. The removal of the anterior capsule, previously incised with the femtosecond laser, is easily performed with rhexis forceps with a continuous curvilinear capsulorhexis-like movement.

Residual fibrotic tissue bridges are cut by 23-gauge vitreal microscissors through the femtosecond laser previous incision. OVD is then removed from the anterior chamber, and the procedure is completed with stromal hydration of the surgical wounds.

3. Results

LenSx® femtosecond laser system was used to treat ACCS in a 74-year-old woman who came to our observation complaining diminished visual acuity in her left eye. She reported a clinical history of myopia and referred phacoemulsification cataract surgery with implantation of ARTIS PL E (Cristalens, France) in her left eye (LE) 11 months before. She denied any known medical condition and history of ocular inflammation or trauma. Ophthalmological examination revealed a best-corrected visual acuity of (BCVA) of 20/40 in the LE and 20/20 in the fellow eye. Slit lamp examination showed the presence of anterior capsule fibrosis involving the visual axis in the LE (Figure 1).

Intraocular pressure was 13 mmHg in both eyes, and ophthalmoscopic fundus examination was normal. LenSX optical coherence tomography (OCT) of the anterior segment showed a complete adherence of the anterior capsule to the anterior surface of the IOL, with different phimosis thickness ranging from 50 to 531 μm (Figure 2).

Given the thickness and irregularity of the anterior capsule fibrosis and the adherence between the anterior capsule and the IOL, the LenSx® femtosecond laser system was used to treat ACCS with the procedure described. In this patient, the incision depth for the capsulotomy was set at 600 μm (manually selecting a capsule delta up of 280 μm and capsule delta down of 320 μm), in order to include the entire fibrotic capsule thickness; given the highly fibrotic material, the laser pulse energy was increased to 6 μJ (from the standard 4 μJ used in cataract surgery), and the spacing was decreased to 5 μm horizontally and 3 μm vertically. The capsulotomy width (5 mm) was based on the patient's maximal mydriasis. Residual fibrotic tissue bridges after the femtosecond incision were cut by 23-gauge vitreal microscissors (Alcon-Grieshaber, Fribourg, Switzerland) (Figure 3).

The day after the procedure, the patient's BCVA recovered to 20/20 in her LE; slit lamp examination showed no inflammation in the anterior chamber, complete removal of capsular fibrosis, and IOL stability. Intraocular pressure was 12 mmHg (Figure 4(a)). The patient was treated with betamethasone 0.2% and chloramphenicol 0.5% (Betabioptal® eye drops, Thea Farma, France) 1 drop 4 times a day for 7 days. After one year of uneventful follow-up, the patient had a BCVA of 20/20; slit-lamp examination showed no recurrence of anterior capsule fibrosis and IOL stability (Figure 4(b)).

4. Discussion

ACCS is a rare late complication of cataract surgery, with onset during the first week following surgery and progressing for several months [15]. Small diameter capsulorhexis, pseudoexfoliation syndrome, chronic ocular inflammation, high myopia, and advanced age have been associated with ACCS. Nd:YAG laser anterior capsulotomy is the most commonly used technique for ACCS treatment [10]. Despite the high success rate, this technique has unpredictable efficacy in restoring visual acuity in patients with thick fibrosis. Moreover, several complications have been described such as IOL pitting, cystoid macular edema, or residual fibrotic material in the anterior chamber that may cause inflammation and secondary glaucoma [1, 11, 16–19].

Alternatively, surgical removal of the fibrous membrane may be performed by capsulorhexis to peel the fibrotic capsule, using microincisional scissors or vitrector-cut capsulotomy [16, 20, 21]. This procedure allows a better centration of the IOL, but may be complicated by lens dislocation in case of zonular weakness. Zinkernagel et al. described a minimally invasive surgical technique using standard 23-gauge vitreoretinal forceps and horizontal scissors to bimanually remove the fibrotic anterior capsule and to perform haptic amputation [16]. However, a potential risk of IOL or iris damage may be associated with the use of vitrector scissors.

Recently, the use of femtosecond laser technology has been proposed to treat severe ACCS [10]. In fact, femtosecond laser allows to extend the capsulorhexis more precisely and less traumatically than cutting by Nd:YAG laser, ensuring a 360 degree overlap of the IOL optic. In addition, the incision depth of capsulotomy may be located between the IOL and the anterior capsule surface, allowing a complete removal of the fibrotic tissue with low risk of IOL damage [11].

Specifically, femtosecond laser can cut hard tissues such as highly fibrotic and adherent anterior capsules, allowing treatment of severe ACCS cases [10]. Ibarz et al. described a case of bilateral simultaneous femtosecond laser-assisted capsulotomy for the treatment of severe anterior capsule contraction that had caused complete occlusion of the anterior capsule in one eye and partial occlusion in the fellow eye one month after cataract surgery. The authors favored the femtosecond laser in order to minimize the risk of IOL folding, inflammation, and intraocular pressure peaks, and the procedure resulted safe and easy to perform despite the extreme case of anterior capsule contraction. The femtosecond laser capsulotomy parameters were similar to the ones set in our technique. Capsulotomy was completed with forceps and scissors in one eye and a Sinskey hook in the fellow eye. After one-month follow-up, the patient presented 20/20 best-corrected visual acuity, and the IOL showed no signs of damage [22].

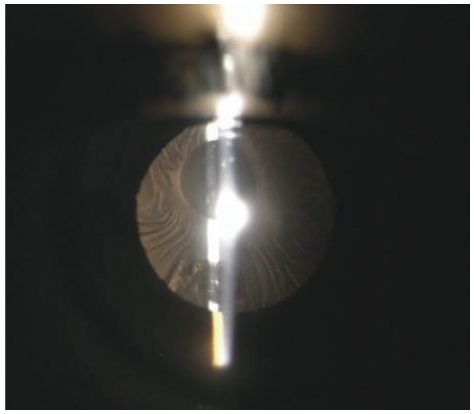
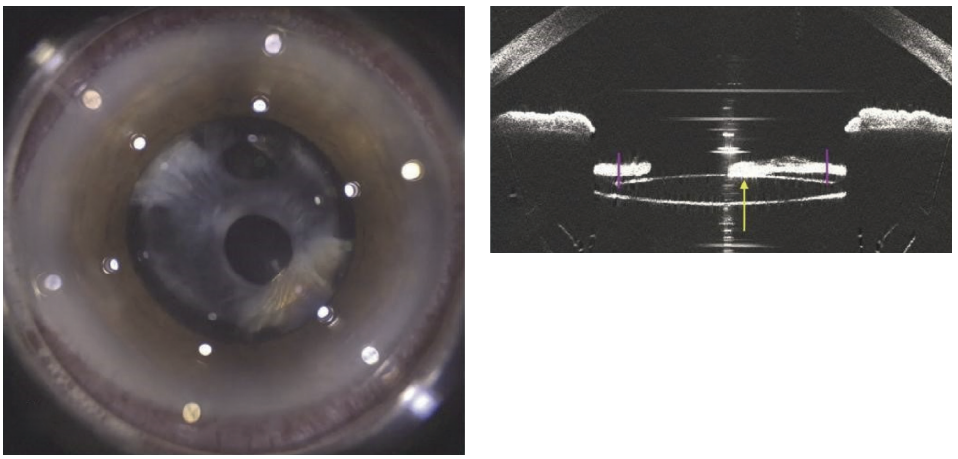


Figure 1: Slit lamp exam showing the presence of thick anterior capsule phimosis, involving visual axis.



(a) (b)

Figure 2: Femtosecond laser system (a) and LenSX® anterior optical coherence tomography (OCT) (b) allow the visualization of fibrotic adherence between anterior capsule and the anterior surface of the IOL .

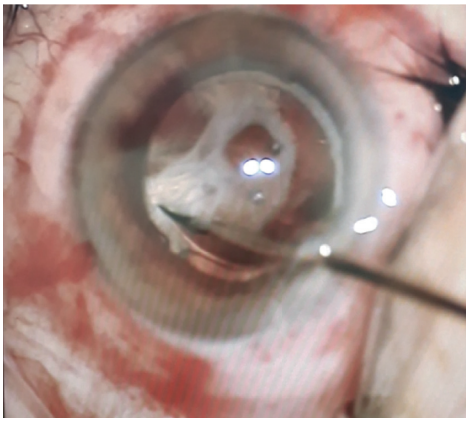
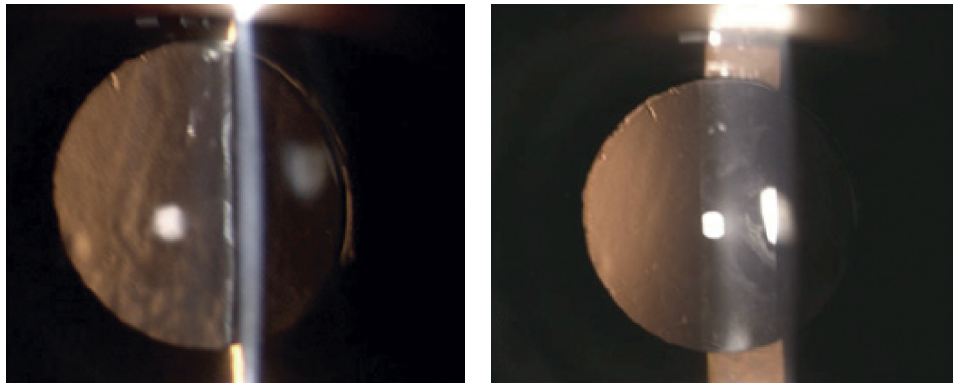


Figure 3: Intraoperative image of residual fibrotic tissue removal using 23-gauge vitreal microscissors following femtosecond laser capsulotomy.

In this report, we describe the use of femtosecond laser to treat ACCS in the presence of a very thick and irregular capsule fibrosis and its efficacy after one year of follow-up. We propose the use of femtosecond laser capsulotomy followed by OVD injection in the anterior chamber and surgical removal of the cut fibrotic capsule using rhexis



(a) (b)

Figure 4: The day after the procedure, slit lamp examination shows complete removal of the fibrotic phimosis and absence of intraocular inflammation (a). After one-year follow-up, anterior capsule opening was unchanged (b).

forceps and vitreal microscissors. Unlike previously reported techniques, we did not use OVD before femtosecond laser treatment because OCT images clearly showed the presence of a gap between the capsule and the IOL.

In conclusion, we describe an innovative and safe treatment for ACCS using femtosecond laser technology combined with bimanual surgical procedure to remove very thick and extended ACCS, allowing a prompt and long-lasting visual acuity recovery that remained stable after one year of follow-up. The high costs of femtosecond laser and the lack of standardized protocols due to anecdotal reports represent the main limitation to a routinely use of this technique. In addition, the high costs of the technique represent an issue in developing countries. Hopefully, femtosecond laser-assisted procedures can become more accessible in the short term, especially for patients who present with extensive capsular fibrosis and adherences. Further studies with large number of patients will help in the future to establish standardized laser settings and procedures.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Consent

Written informed consent was obtained from the patient to publish medical data and figures described in this article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Supplementary Materials

Video: video shows the femtosecond laser capsulotomy of anterior capsule phimosis. The procedure starts with eye docking and centering with LenSX®. The operator establishes cutting parameters by LenSX® optical coherence tomography. After establishing a pupil diameter of 5.4 mm, the operator sets the femtosecond laser capsulotomy depth and performs femtosecond laser anterior capsulotomy. (*Supplementary Materials*)

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Research Article

Characteristics of Facial Asymmetry in Congenital Superior Oblique Palsy according to Trochlear Nerve Absence

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Background/Aims. Facial asymmetry is affected by various developmental factors, and congenital superior oblique palsy (SOP) is one of the most common causes of asymmetric development of the face. The presence of facial symmetry is usually assessed subjectively, which varies with the examiner. We aimed to objectively assess facial asymmetry in patients with unilateral congenital SOP according to the presence or absence of the trochlear nerve on high-resolution magnetic resonance imaging (MRI). *Methods*. A total of 287 consecutive patients diagnosed with congenital SOP and 82 control subjects were included. Congenital SOP patients were grouped according to the presence (present group) or absence (absent group) of the trochlear nerve using thin-section high-resolution MRI of cranial nerves. We developed a computer-aided detection (CAD) system that could automatically analyze objective indices of facial asymmetry using frontal face photographs. *Results*. Of the 287 patients with congenital SOP, 60% of patients had ipsilateral trochlear nerve absence and superior oblique muscle (SO) hypoplasia (absent group), while the remaining 40% had a normal SO and trochlear nerve (present group). All but one objective indices related to facial asymmetry were significantly different between congenital SOP patients and controls (all $P < 0.05$). Among these features, the angle of nose deviation was significantly larger in the absent group compared to the present group ($P < 0.001$). *Conclusion*. Objective analysis of facial asymmetry using our novel CAD system was useful for identifying distinct features of congenital SOP. Deviation of the nose was more prominent in congenital SOP patients with trochlear nerve absence.

1. Introduction

Congenital superior oblique palsy (SOP) is one of the most common causes of ocular torticollis in children, of which the patient tilts his or her head to use both eyes together [1–3]. In children with torticollis, asymmetric development of the face is an irreversible but under-recognized complication of long-standing head tilt, especially if the head tilt is intermittent or mild [3–6]. Facial asymmetry is progressive if the head tilt persists in young children, and early strabismus surgery to correct the head tilt may help prevent facial asymmetry in congenital SOP [7]. Meanwhile, regarding the etiologic classification of congenital SOP, patients with an absent trochlear nerve may show more prominent head tilt and facial asymmetry compared to those with the presence of a trochlear nerve [8]. Therefore, successful treatment and prevention of facial asymmetry depend on an accurate diagnosis of the cause and careful monitoring of the degree of facial asymmetry, which may help determine the timing of intervention in patients with congenital SOP [9].

Facial asymmetry is usually assessed qualitatively by the subjective judgement of the observer. A few attempts have been made to quantify the degree of facial asymmetry objectively using several landmarks of anthropometric measurements on photographs, cephalometric assessment, and with the help of 3-dimensional analysis [2, 4, 9, 10]. However, there is a risk of radiation using cephalometric radiographs, and optical 3-dimensional surface analysis

using a 3-camera fringe projection system is not easily accessible, time-consuming, and expensive [2, 4, 9, 10]. Besides, most of the studies are not validated in a large number of subjects and we do not know which asymmetry index is significantly related to perceived symmetry in various congenital and developmental situations related to facial growth. Therefore, a simple and reliable method to detect facial asymmetry using two-dimensional face photographs could be cost-effective and useful.

In this study, we developed an objective method to quantify the amount of facial asymmetry assisted by computer-aided automated feature extraction. Using this novel software, we aimed to determine if the asymmetry of facial characteristics differed among various etiologies of congenital SOP.

2. Materials and Methods

2.1. Subjects. A retrospective review of medical records was performed on 287 consecutive patients diagnosed with congenital SOP who underwent high-resolution thin-section magnetic resonance (MR) imaging at Seoul National University Bundang Hospital between November 2003 and October 2019. The subjects were divided into two groups according to MR image findings of the ipsilateral trochlear nerve; congenital SOP without a trochlear nerve (absent group) and congenital SOP with symmetric trochlear nerves on both sides (present group). Subjects with orthotropic or horizontal strabismus with no apparent head tilt, oblique muscle dysfunction nor any vertical strabismus were included as the control group.

Congenital SOP patients were included if they showed the typical signs of apparent underdepression and overelevation in adduction on the affected side, positive head-tilt test, large fusional amplitudes of vertical deviation, and/or a history or photographic evidence of long-standing strabismus or anomalous head posture dating back to infancy. Patients who had primary overaction of the inferior oblique muscle (IO) on the affected side, any evidence of acquired disease, a history of head or ocular trauma, or other potential causes such as plagiocephaly, skew deviation, or the ocular tilt reaction were excluded. All patients underwent a thin-section MRI at the brainstem level to clarify the presence of the trochlear nerve following the protocols introduced in our previous study [8, 11]. Approval to conduct this study was obtained from the Institutional Review Board of Seoul National University Bundang Hospital.

We noted patient characteristics, including gender, birth history, family history, initial signs/symptoms at presentation (chief complaint) such as head tilt, ocular deviation, or diplopia, age at onset, best-corrected visual acuity, cycloplegic refractive errors, and presence of amblyopia defined as a difference of two or more lines between monocular visual acuities and anisometropia >1.50 diopters. Extraocular movements and any incomitance were documented at the time of initial presentation and during follow-up examinations, including Bielschowsky's head-tilt test and ocular alignment with a prism cover test in six cardinal positions of gaze at distance in cooperative patients.

2.2. Computer-Aided Detection of Facial Asymmetry. We proposed a computer-aided detection (CAD) system that could automatically analyze objective indices of facial asymmetry. The proposed system consists of two steps: (i) image preprocessing with facial feature extraction and (ii) measurement of each facial asymmetry feature.

2.3. Extraction of Facial Indices. First of all, the system automatically detects facial features such as the eyes, nose, mouth, and facial outlines from the frontal facial photograph of a patient and uses them as the basis for calculating facial asymmetry indices (Figure 1). Facial features of the eyes, nose, mouth, and facial outlines are defined by 68 landmark points using the active appearance model (AAM) [12]. The AAM is a vector-based algorithm that extracts facial features using a statistical model regarding the shape and texture information of an object based on principal component analysis [12]. It has been widely used in various applications such as face recognition, face modeling, and facial expression recognition [13].

2.4. Objective Measurement of Facial Asymmetry. Seven indices of facial asymmetry were automatically extracted from frontal face photographs as follows: the degree of face tilt, slope of eyebrows, difference in slopes of eyes, difference in hemifacial area, nasal deviation, slope of lips, and difference in the slopes of eyes and mouth (Figure 2). Each feature is used as a variable for geometric calculation to estimate the degree of facial asymmetry.

The slope, width, and height of all facial asymmetry indices are calculated using two or more facial landmarks geometrically. To calculate the degree of face tilt, the system uses landmark points of four facial features, the eyebrows, eyes, mouth, and jaw, from previously extracted data. The facial midline is determined by these features using an algorithm of line fitting [14]. The angle between the facial midline and the vertical line is defined as the degree of face tilt.

Facial asymmetry indices are measured on the assumption that a patient's face is aligned without tilting. This is not true, particularly in patients with torticollis. Therefore, the system adjusts the value of all slopes based on the previously obtained degree of face tilt. Slope correction allows the system to calculate the value of each facial asymmetry feature, even when the patient's face is tilted in the image.

2.5. Statistical Analysis. Clinical characteristics and facial asymmetry indices were compared between patients with congenital superior oblique palsy with and without a trochlear nerve and controls using one-way ANOVA. All tests were performed using the SPSS version 25.0 software package (SPSS Inc., Chicago, IL, USA). A post hoc analysis was used to determine significant differences between two

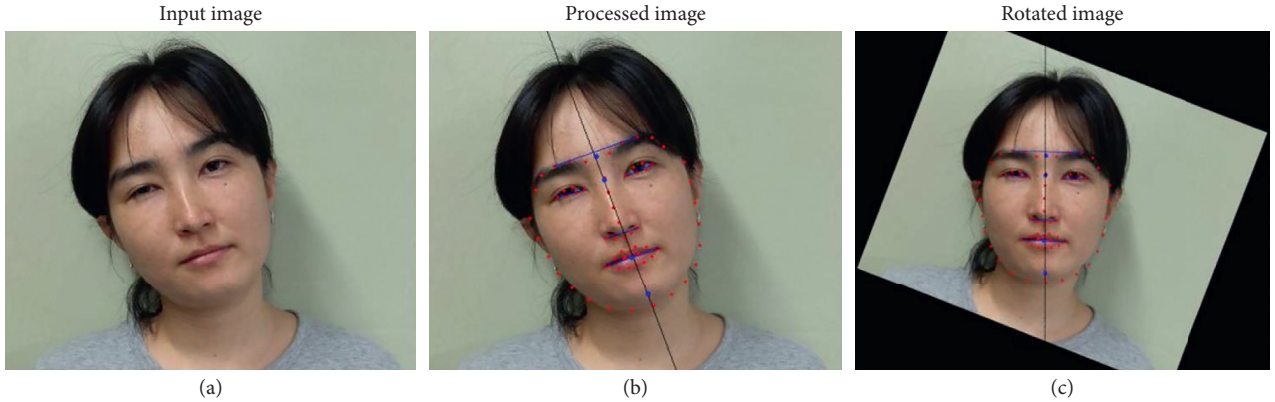

Figure 1: Automated analysis of facial asymmetry indices using computer-aided detection. (a) The original frontal face photograph is uploaded in the software. (b) The system automatically detects facial features of the eyes, nose, mouth, and facial outlines defined by 68 landmark points using the active appearance model (AAM). The degree of face tilt (°) is calculated by the angle of the line that passes between the landmark points of the facial midline (black line) in reference to the vertical line (angle of inclination 90°). (c) Rotation of the image is automatically processed according to the degree of face tilt.

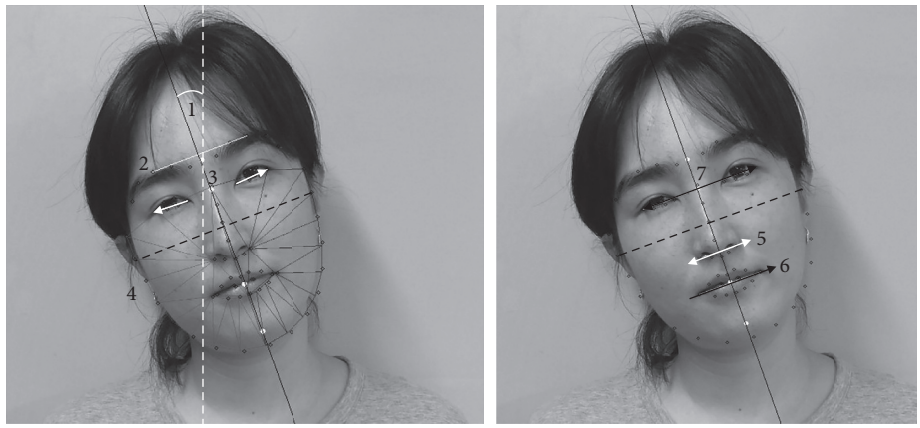

Figure 2: Seven indices of facial asymmetry automatically measured by the software. (1) Face tilt (°) is the angle between the vertical line (white dotted line) and the line that passes between the landmark points of the facial midline (black line). (2) Slope of eyebrows (°) is the angle between the line connecting both eyebrows (white line) and the perpendicular line to the facial midline (black dotted line). (3) Difference in slopes of eyes (°) is calculated by the difference in slopes of the lines passing through the eye corner points of each eye (white arrows). (4) Difference in hemifacial area (%) was calculated by the proportion of "absolute difference of left and right hemifacial area" to "total face area." (5) Nose deviation (°) is the angle between the line connecting the corners of the nasal base (white double headed arrow) and the perpendicular line to the facial midline (black dotted line). (6) Slope of lips (°) is the angle between the line that passes through the corners of both lips (black arrow) and the perpendicular line to the facial midline (black dotted line). (7) Difference in slopes of eye and mouth (°) was calculated by the angle between the line connecting the center of each eye (black double-headed arrow) and the line that passes through the corners of both lips (black arrow). The center of each eye was calculated as the average coordinate of six landmark points on the upper and lower eyelids.

specific groups. Scheffe post hoc analysis was used when the groups met equal variance assumptions, while Dunnett T3 post hoc analysis was used when the equal variance was not assumed.

3. Results

3.1. Subjects' Characteristics. Finally, 287 patients with congenital SOP and 82 control subjects were included. Among the patients with congenital SOP, 173 (60%) showed ipsilateral absence of the trochlear nerve and SO hypoplasia (absent group), while the remainder (40%) showed symmetric trochlear nerves on both sides (present group). The clinical characteristics of congenital SOP patients and controls are summarized in Table 1. The mean age at examination, gender, cycloplegic refractive error, presence of anisometropia, and amblyopia were not significantly different between the three groups. In the control group, horizontal strabismus was found in 84% of subjects of which the majority was exotropia.

Early onset of head tilt before 1 year of age was significantly more frequent in the absent group compared to the present group in congenital SOP patients ($P = 0.005$). The angle of hypertropia in primary gaze was larger in the absent group compared to the present group ($P < 0.001$).

Table 1: Clinical characteristics of congenital superior oblique palsy patients with the absence of a trochlear nerve (absent group) and the presence of a trochlear nerve (present group) compared with controls.

	Absent group ($n = 173$)	Present group ($n = 114$)	Control ($n = 82$)	P value
Age at examination	21.7 ± 22.8	22.8 ± 20.1	16.9 ± 17.3	0.122[a]
Male gender	101 (58%)	68 (60%)	45 (55%)	0.792[c]
Cycloplegic refractive errors (D)	−0.23 ± 2.03	−0.57 ± 2.52	−0.37 ± 2.67	0.488[a]
Anisometropia >1.50 (D)	9 (5%)	10 (9%)	11(13%)	0.080[c]
Amblyopia	15 (9%)	2 (2%)	6 (7%)	0.054[c]
Horizontal strabismus	**86 (50%)**	**67 (59%)**	**69 (84%)**	<0.001[a]
Exotropia	80/86 (93%)	57/67 (85%)	52/69 (75%)	—
Esotropia	6/86 (7%)	10/67 (15%)	17/69 (25%)	—
Unilateral SOP	171 (99%)	114 (100%)	—	0.255[c]
Right	91 (53%)	52 (46%)	—	0.235[c]
Early onset of head tilt[d]	**70 (41%)**	**28 (25%)**	—	0.005[b]
Hypertropia (PD)	**14.2 ± 8.6**	**10.3 ± 6.8**	—	<0.001[c]

y = years; D = diopters; SOP = superior oblique palsy; PD = prism diopters; significant factors are expressed in bold characters; [a]P value by one-way ANOVA; [b]P value by the independent t-test; [c]P value by the Pearson chi-square test; [d]patients who had reliable data at the time of onset of definite head tilt before 1 year of age.

Table 2: Objective measurement of facial asymmetry features in congenital superior oblique palsy patients with the absence of a trochlear nerve (absent group) or presence of a trochlear nerve (present group) compared with controls.

	Absent group (1) ($n = 173$)	Present group (2) ($n = 114$)	Control (3) ($n = 82$)	P value[a]	Post hoc
Face tilt (°)	5.36 ± 5.00 (0–26.30)	4.23 ± 3.69 (0–20.50)	2.17 ± 1.99 (0–12.65)	<0.001	1, 2 > 3
Slope of eyebrows (°)	3.92 ± 2.68 (0–11.81)	3.34 ± 2.50 (0–10.59)	1.87 ± 1.50 (0–8.08)	<0.001	1, 2 > 3
Difference in slopes of eyes (°)	9.51 ± 5.51 (0–22.62)	7.64 ± 5.58 (0–24.45)	11.07 ± 5.05 (0–26.73)	<0.001	1, 3 > 2
Difference in hemifacial area[b] (%)	3.73 ± 3.58 (0.03–21.52)	3.28 ± 3.49 (0–17.84)	2.58 ± 2.09 (0.05–10.57)	0.034	1, 2 > 3
Nose deviation (°)	3.91 ± 2.91 (0–12.34)	2.87 ± 2.39 (0–11.28)	2.02 ± 1.53 (0–7.80)	<0.001	1 > 2 > 3
Slope of lips (°)	4.04 ± 3.61 (0–17.99)	3.63 ± 3.01 (0–14.15)	2.10 ± 1.99 (0–12.22)	<0.001	1, 2 > 3
Difference in slopes of eye and mouth (°)	0.04 ± 0.03 (0–0.22)	0.03 ± 0.02 (0–0.13)	0.02 ± 0.02 (0–0.08)	<0.001	1, 2 > 3

Values are presented as mean ± standard deviation. [a]P value by one-way ANOVA. Post hoc test was performed by Dunnett T3. [b]Proportion of "absolute difference of left and right hemifacial area" to "total face area."

3.2. Facial Asymmetry in Congenital Superior Oblique Palsy. Objective analysis of the seven indices of facial asymmetry was performed using frontal face photographs of congenital superior oblique palsy patients with and without a trochlear nerve and control subjects (Table 2).

All indices of facial asymmetry except the difference in the slopes of eyes were significantly different between congenital SOP patients and controls (all $P < 0.05$). Among the six indices that were significantly different between congenital SOP and controls, only the angle of nose deviation was significantly larger in the absent group compared to the present group ($P < 0.001$). No other feature, including the degree of face tilt, showed a significant difference between both groups of congenital SOP.

4. Discussion

In this study, we developed a novel automated CAD software to objectively assess the characteristics of facial asymmetry. Facial asymmetry features were significantly different in congenital SOP compared to controls. While most of the asymmetry indices were not significantly different according to the specific etiology of congenital SOP, the angle of nose deviation was larger in the absent group, which could be the most sensitive index of progressive facial asymmetry related to persistent head tilt.

Yi and Jang [15] found that facial asymmetry occurs more commonly with a deviated nose and suggested that a deviated nose might be a developmental defect caused by a discrepancy in the 2-side facial bone growth. In this study, nose deviation was the most obvious differentiating point between congenital SOP patients with versus without the trochlear nerve, which suggests a more prominent developmental defect of facial bone growth in congenital SOP patients without a trochlear nerve. This may probably be related to an earlier onset of head tilt, and early surgery could be helpful for congenital SOP patients with an absent trochlear nerve.

In spite of the rapid development in imaging technology, verification of the trochlear nerve is challenging because of its small diameter as well as its oblique course in the cisternal area [16]. A high-resolution and thin-section sequence using a 3 Tesla (T) MRI could classify the etiology of SOP according to the presence or absence of the trochlear nerve, and we have found some clinical differences between the two groups [8, 11, 17]. However, a 3T MRI may not always be available, and thin-section sequence imaging with 0.25 mm thickness requires a long scanning time. Therefore, any clues

to predict the absence or presence of the trochlear nerve would be very useful, and the results of our study could add more to the existing clues [18, 19].

Head tilt in old photographs and facial asymmetry could be strong evidence of congenital SOP. However, there are some debate about the relationship between facial asymmetry and torticollis. Wilson and Hoxie [5] found contralesional hemifacial microsomia in most of the patients with congenital SOP. Paysee et al. [20] reported head tilt in 86% and facial asymmetry in 76% of patients with unilateral congenital SOP, while patients with acquired SOP showed head tilt in only 33% and none of them had facial asymmetry. In contrast, Velez et al. [21] evaluated three facial morphometric features in frontal photographs: the angle of inclination of each orbit, relative facial size, and facial angle. They concluded that facial asymmetry was not useful for distinguishing congenital SOP from acquired SOP or heterotopic rectus muscles.

Many algorithms have been proposed for automatic face recognition, most of which use Haar-like features that were introduced in the first real-time face detector, boosting the digital image features used in object recognition [22]. However, the detection capability of these algorithms is weakened when the image is rotated or the contrast has changed. In this study, we set facial landmark points that were initially detected in frontal face photographs using the AAM [12]. This method is based on shape and texture information of each landmark that is trained in advance with a large amount of face image data. A part having a texture most similar to each landmark can be searched to find the location of the landmark point more robustly than the existing algorithms [12]. In future work, higher performance can be expected by using machine learning for disease classification based on the results of asymmetric facial features.

There are some limitations in this study. First, we only obtained facial images of Asians. Obamiyi et al. [23] found radiographic differences such as the smallest mean cranial base and significantly larger Y-axis in the Chinese patients with temporomandibular joint disorders. Cheong and Lo [24] assumed that facial asymmetry might be more common in the normal Asian population than those in the Western countries. Further studies are necessary to reveal the differences in facial asymmetry according to different races. Second, all patients in this study had congenital SOP. Therefore, we could not be sure about the usefulness of this CAD software in other causes of facial asymmetry. Lastly, our software is based on 2-dimensional analysis. A 3-dimensional facial analysis may provide more precise information on developmental defects. Nevertheless, we could find some useful indices to differentiate congenital SOP patients with the absence of a trochlear nerve. In addition, our novel automated CAD software could avoid exposure to radiation hazard and save the time and cost for optical 3-dimensional surface analysis.

5. Conclusions

In conclusion, objective analysis of facial asymmetry using our novel CAD system was useful for identifying distinct features of congenital SOP. Deviation of the nose was more prominent in congenital SOP patients with the absence of a trochlear nerve.

Data Availability

Data supporting the findings of the current study are available from the corresponding author upon reasonable request.

Ethical Approval

Ethical approval was provided by the Institutional Review Board of Seoul National University Bundang Hospital. All aspects of the research protocol were in compliance with the Declarations of Helsinki.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

H.K.Y. and S.J. are co-first authors. H.K.Y. and S.J. contributed substantially to the conception or design of the work and the acquisition, analysis, or interpretation of the data and also drafted the manuscript. T.K.W.B. and J.-M.H. revised the manuscript. H.K.Y., S.J., T.K.W.B., and J.-M.H. approved the final version of the article.

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Research Article

Comparison of Femtosecond Laser-Assisted Cataract Surgery and Conventional Phacoemulsification in Shallow Anterior Chambers and Glaucoma

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Purpose. To compare femtosecond laser-assisted cataract surgery (FLACS) versus conventional phacoemulsification in shallow anterior chamber cataract patients with glaucoma or zonulysis. *Methods*. This was a single-center retrospective review of cataract surgeries in shallow anterior chamber and glaucoma patients between January 2016 and December 2018 in which a LenSx femtosecond laser was used. The outcome measures included pre- and postoperative uncorrected and corrected distance visual acuity (UDVA and CDVA), intraocular pressure (IOP), endothelial cell density (ECD), endothelial cell loss (ECL), and object scatter index (OSI). *Results*. One hundred and six eyes of 106 patients with a mean anterior chamber depth of 1.54 ± 0.51 mm were included in this study. Among them, 26 (23.2%) had zonulysis and 18 eyes had capsular tension ring implantation in general. The percentage of capsular tension ring implantation was statistically significantly lower in the FLACS group ($P = 0.027$). The UDVA, CDVA, ECD, and IOP were not statistically significant between the two groups at all time points. The postoperative ECL and OSI of the FLACS group was better than those of the conventional group ($P < 0.01$). *Conclusions*. FLACS can reduce ECL and improve visual quality compared to the conventional phacoemulsification in shallow anterior chamber patients. Also, it has the trend of reducing the use of capsular tension rings in subluxated cataracts. It is an ideal choice for patients with complicated cataract such as with shallow anterior chambers, glaucoma, and zonulysis.

1. Introduction

Femtosecond laser-assisted cataract surgery (FLACS) has become increasingly common since its introduction in 2009. Randomized controlled trials (RCTs) [1] and meta-analyses [2] have shown that it is not superior to manual phacoemulsification in terms of primary visual and refractive outcomes or overall complications. However, the benefits of FLACS, such as consistent and reproducible capsulotomy and nucleus fragmentation which result in less ultrasound energy required during phacoemulsification, may be especially advantageous in complex situations including shallow anterior chambers (ACs) and subluxated or white cataracts [3]. With growing experience in the use of femtosecond lasers, patients with heterogenous clinical features are being increasingly reported. Most of these are case reports or short case series. Recently, an RCT in India compared intraoperative performance and postoperative outcomes between FLACS and conventional phacoemulsification in eyes with a shallow AC and found that FLACS maintained clearer corneas, showed less increase in CCT, lower AC inflammation, and better UDVA in the early postoperative period [4]. However, the ACD average and range in that study were 2.33 mm and 2.1–2.5 mm. ACD is shallower in the Chinese population. The average ACD of Chinese healthy people was 2.89 ± 0.32 mm (range: 1.56–3.81 mm), [5] and that of angle-closure glaucoma patients was 1.86 ± 0.45 mm (range: 0.68–3.98 mm) [6]. Therefore, it is more meaningful to compare FLACS and conventional phacoemulsification in Chinese patients with shallow AC and angle-closure glaucoma. To explore the performance of femtosecond laser in patients with shallow anterior chamber, this study was

conducted. The aim of the study is to evaluate the clinical outcomes of FLACS versus conventional phacoemulsification in eyes with shallow anterior chambers, glaucoma, or zonulysis and to compare their visual acuity and quality, IOP, and endothelial cell loss.

2. Methods

2.1. Design. This observational retrospective study was performed on patients who underwent cataract surgery at the Department of Ophthalmology of People's Hospital of Guangxi Zhuang Autonomous Region from January 2016 to December 2018. Informed consent was obtained from all subjects. This study was approved by the Institutional Review Board of People's Hospital of Guangxi Zhuang Autonomous Region and was conducted in accordance with contents of the Declaration of Helsinki.

2.2. Patients. After explaining the advantages and disadvantages of femtosecond laser-assisted surgery by the doctor, the patients chose the type of surgery by themselves. The patients were classified into two groups according to their operation methods. Inclusion criteria were symptomatic cataract for which the patient desires surgery and anterior chamber depth (ACD) less than 2.4 mm, with an elevated intraocular pressure of >21 mmHg. Exclusion criteria were <18 years of age, unable to give consent for surgery and research, and any other ocular diseases but glaucoma. Only one eye of each patient was included in the study, and in cases of bilateral cataracts, the eye undergoing surgery first was included.

2.3. Surgical Procedure. The surgical technique has been standardized for both groups. All surgeries were performed by the same experienced ophthalmologist. In the FLACS group, a 2.2 mm three-plane main incision, a 1.0 mm side-port corneal incision, a femtosecond laser-assisted capsulotomy (5.0 mm), and a six-piece lens division in a crisscross pattern were performed with a femtosecond laser (LenSx Lasers, Alcon Laboratories, Inc.). A 2.2 mm two-plane main incision and a 1.0 mm side-port corneal incision were made with a keratome in the conventional group, and capsule forceps were used to complete a 5.0 mm continuous curvilinear capsulorhexis in these patients. Both groups adopted phacoemulsification using the phaco-chop technique with the Centurion Vision Phacoemulsification System (Alcon Laboratories, Inc.). Intraoperatively, DisCoVisc (Alcon Laboratories, Inc.) was used to maintain the anterior chamber in all patients. All eyes in both groups accepted the single-piece, hydrophobic acrylic, aspheric intraocular lens (AcrySof SN60WF, Alcon Laboratories, Inc.).When finishing the phaco part and before implanting the IOL, if the dislocation of capsule is greater than one quadrant and less than two quadrants, we implanted a capsular tension ring.

2.4. Evaluation. Preoperatively, the medical histories of all patients were recorded. The uncorrected and corrected distance visual acuity (UDVA and CDVA) were evaluated by Snellen chart and documented in logarithm of the minimum angle of resolution (logMAR) units. Anterior chamber depth (ACD) measurement was performed using Scheimpflug imaging (Pentacam, Oculus Optikgerate GmbH) from the endothelial layer to the anterior lens surface. Postoperative visits occurred at day 1, week 2, and months 1, 3, and 6 and included a routine examination including UDVA, CDVA, and intraocular pressure (IOP) assessment and notation of any complications. Endothelial cell density (ECD) and object scatter index (OSI) were measured preoperatively and at 3 and 6 months postoperatively. A noncontact autofocus EM-3000 specular microscope (Tomey Corp.) was used to take endothelial photographs and to automatically count ECD values, and OSI was measured by using the Optical Quality Analysis System (OQAS, Visiometrics SL, Terrassa, Spain).

2.5. Statistical Analysis. Continuous data were conveyed by mean ± standard deviation and categorical data by number (percentage). Comparisons among the FLACS and conventional groups were analyzed using *t*-test for continuous variables and using a two-sided confidence interval of 95%. The chi-square test or Fisher's exact test was used for an association in four-fold table. Statistical analyses were performed with *R* project (version 3.4.2). The level of significance was set at a P value of less than 0.05 for all parameters.

3. Results

A total of 106 eyes with 106 cataracts and shallow AC were included in this study, specifically 52 eyes in the FLACS group and 54 in the conventional group. Among all patients, 26 (24.5%) eyes had subluxated crystalline lenses, including 10 eyes in the FLACS group and 16 eyes in the conventional group. The range of lens dislocation was from 2 to 6 clock hours. Table 1 shows the demographic data. Preoperatively, there was no statistically significant difference in age, gender composition, and ACD. The capsular tension rings (CTRs) were implanted in 18 (69.2%) eyes, including 4 eyes in the FLACS group and 14 eyes in the conventional group. The percentage of CTR implantation was statistically significantly lower in the FLACS group ($P = 0.027$). There were no intraoperative complications such as posterior capsule tear, vitreous loss, or Descemet's membrane detachment in either group. Table 2 presents the pre- and postoperative UDVA, CDVA, and IOP values across the two groups at different time points. The postoperative UDVA and CDVA were better than preoperation in both groups ($P < 0.01$) (Figure 1). However, there was no statistically significant difference between the two groups. The groups' pre- and postoperative ECD and endothelial cell loss (ECL) values are shown in Table 3, and a statistically significant difference in ECL is evident ($P < 0.001$). As illustrated in Table 4, the OSI of the FLACS group at 3 and 6 months after surgery was statistically significantly better than that of the conventional group ($P = 0.003$).

Table 1: Baseline demographics between the two groups.

	FLACS group	Conventional group	P value
Age (year)	67.19 ± 10.37	67.33 ± 8.84	0.958
Gender (female/male)	40 (76.92%)/12 (23.08%)	40 (74.07%)/14 (25.93%)	1
ACD (mm)	1.43 ± 0.62	1.64 ± 0.40	0.146
(i) Range	0.53 mm–2.38 mm	0.89 mm–2.36 mm	
With zonulysis	10 (19.2%)	16 (29.6%)	0.353
(ii) Preop subluxation range (o'clock)	3.20 ± 0.92	3.12 ± 0.96	0.845
(iii) CTR implantation	4 (40%)	14 (87.5%)	0.027*

The values are represented as mean ± SD in age and ACD; number (percentage) in gender, with glaucoma, with subluxated lens, and CTR implantation. ACD, anterior chamber depth; CTR, capsular tension ring; FLACS, femtosecond laser-assisted cataract surgery. *Statistically significant.

Table 2: Pre- and postoperative UDVA, CDVA, and IOP between the two groups at different time points.

		Preop	Day 1	Week 2	Month 1	Month 3	Month 6
UDVA	FLACS group	1.06 ± 0.97	0.48 ± 0.54	0.49 ± 0.54	0.49 ± 0.54	0.46 ± 0.55	0.41 ± 0.48
	Conventional group	1.05 ± 0.93	0.47 ± 0.40	0.44 ± 0.33	0.44 ± 0.34	0.41 ± 0.32	0.41 ± 0.32
	P value	0.989	0.959	0.72	0.668	0.64	0.988
CDVA	FLACS group	0.94 ± 1.00	0.44 ± 0.57	0.44 ± 0.57	0.42 ± 0.58	0.40 ± 0.59	0.36 ± 0.51
	Conventional group	0.99 ± 0.95	0.40 ± 0.43	0.36 ± 0.35	0.35 ± 0.37	0.31 ± 0.35	0.31 ± 0.35
	P value	0.847	0.795	0.539	0.564	0.468	0.666
IOP	FLACS group	20.76 ± 4.15	12.87 ± 2.63	13.91 ± 3.10	13.98 ± 2.38	14.45 ± 2.21	14.84 ± 2.87
	Conventional group	21.16 ± 5.76	13.55 ± 2.90	13.79 ± 3.13	14.25 ± 2.88	13.88 ± 2.92	14.51 ± 2.27
	P value	0.767	0.364	0.882	0.714	0.422	0.627

The values are represented as mean ± SD. UDVA, uncorrected distance visual acuity; CDVA, corrected distance visual acuity; IOP, intraocular pressure; FLACS, femtosecond laser-assisted cataract surgery.

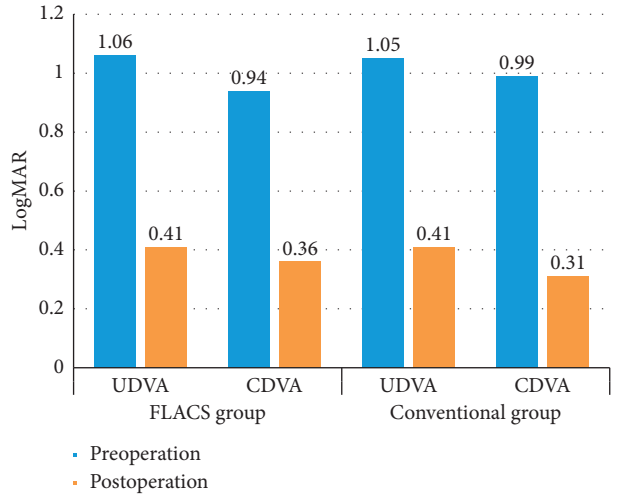

Figure 1: Pre- and postoperative UDVA and CDVA in the two groups. The postoperative LogMAR UDVA and CDVA were better than preoperation in both groups ($P < 0.01$).

4. Discussion

At present, femtosecond laser-assisted cataract surgery (FLACS) is being applied more and more in eyes with challenging cataracts or those with associated comorbidities, for example, dense or subluxated cataracts or Fuchs endothelial dystrophy, and this has revealed patients who are likely to benefit from the procedure. A shallow anterior chamber (AC) is a certain challenge for cataract surgeons worldwide, and extreme caution is needed when operating on such eyes because phacoemulsification will occur much closer to the endothelium, which increases the risk of endothelial cell loss.

One previous study has defined a shallow AC as an ACD less than 2.7 mm [7], and two others defined it as less than 2.5 mm [4, 8]. In order to include more patients, we defined a shallow AC as an ACD less than 2.5 mm. An RCT in India has previously compared FLACS with conventional phacoemulsification in eyes with shallow ACs [4]. The ACD average and range were 2.33 mm and 2.1–2.5 mm, respectively, in that study and 1.55 mm and 0.53–2.38 mm in ours. As such, ACD in the present study was shallower which

Table 3: Pre- and postoperative operative ECD between the two groups at different time points.

	Preoperation	Month 3	Month 6	ECL at month 6	ECL%
FLACS group	2185.51 ± 666.55	2022.07 ± 622.69	2001.85 ± 616.47	183.66 ± 70.83	8.40%
Conventional group	2473.25 ± 679.83	2176.85 ± 570.98	2155.09 ± 565.27	318.16 ± 130.07	12.86%
P value	0.117	0.336	0.336	<0.001*	<0.001*

The values are represented as mean ± SD. ECD, endothelial cell density; ECL, endothelial cell loss; FLACS, femtosecond laser-assisted cataract surgery. *Statistically significant.

Table 4: Pre- and postoperative OSI between the two groups at different time points.

	Preop	Month 3	Month 6
FLACS group	3.51 ± 1.64	1.95 ± 0.57	1.88 ± 0.54
Conventional group	4.30 ± 1.97	2.41 ± 0.53	2.34 ± 0.54
P value	0.111	0.003*	0.003*

The values are represented as mean ± SD. OSI, object scatter index; FLACS, femtosecond laser-assisted cataract surgery. *Statistically significant.

makes our findings more representative of shallow AC patients.

Excessive ultrasound energy can lead to endothelial cell injury and cause early postoperative corneal edema which has itself been identified as the main cause of delayed visual rehabilitation and decreased satisfaction [9, 10]. Patients with shallow ACs are at higher risk of corneal endothelial cell injury [8, 11]. Previous studies have reported ECL from 4% to 12% after uneventful conventional phacoemulsification [12, 13]. The benefit of femtosecond laser in ordinary cataract patients is still unclear. An RCT found that the endothelial cell loss was 10.2% ± 13.7 in the FLACS group and 9.7 ± 13.7% in the conventional group ($P = 0.76$) [1]. However, two other RCTs, in Denmark [14] and Poland [15], showed that the ECL% was statistically significantly lower in the FLACS group postoperatively. FLACS had a statistically significant difference over conventional phacoemulsification for corneal endothelial cell reduction ($P = 0.006$) in a meta-analysis of 14, 567 eyes [2]. However, femtosecond laser may offer more help in high-risk cases. For example, FLACS has been found to be superior to phacoemulsification in reducing postoperative ECL in patients with Fuchs endothelial dystrophy, leading to a lower risk of corneal decompensation, particularly in patients with moderate or hard nucleus [16]. In our study, we observed no corneal endothelial decompensation and the mean ECL at 6 months was 8.40% and 12.86% in the FLACS group and conventional group, respectively. There was statistically significantly less ECL in the FLACS group ($P < 0.001$). Using a femtosecond laser can therefore be said to reduce intraoperative endothelial cell injury as compared to conventional phacoemulsification in angle-closure glaucoma and shallow AC patients.

In patients with glaucoma, it is common to see weak zonules, and in these cases, it is difficult to keep the capsule centered and to achieve precise sizing; the use of femtosecond lasers can solve these problems effectively. More precise capsulotomy sizing can be achieved with a femtosecond laser than in manual capsulorhexis, and femtosecond laser capsulotomies suffer less modification over time [17]. Using a femtosecond laser can ensure the centration and size of the capsulorhexis so that postoperative capsule contraction will not cause significant intraocular lens displacement. Fujikado and Saika found the increase in coma with decentration of aspheric IOLs suggesting an impact upon visual quality [18]. Mihältz et al. previously described a significant difference in IOL tilt between FLACS and conventional cohorts. Although there was no refractive difference, the authors note that coma was significantly less in the FLACS group, which implied the contribution of FLACS capsulorhexis in visual quality [19]. In our study, there was no statistical difference in postoperative visual acuity between the two groups. However, the OSI of the FLACS group at 3 and 6 months was statistically significantly better than that of the conventional group. Therefore, a FLACS approach can achieve better postoperative visual quality for angle-closure glaucoma and shallow AC patients.

For patients with zonulysis, femtosecond laser capsulorhexis can reduce the pulling of suspensory ligament during capsulorhexis, thus avoiding the expansion of dislocation range and reducing CTR implantation and even IOL suspension. Chee et al. treated patients with severely subluxated cataracts using femtosecond laser to perform the capsulotomy and nuclear fragmentation, preserving 90% capsular bags in eligible cases [20]. Ju et al. used femtosecond laser in the management of zonulysis, and 89.66% eyes showed stably centered IOLs [21]. Grewal et al. reported that FLACS helped a patient with traumatic subluxated cataract achieve a CDVA of 20/20 and a well-centered IOL [22]. Schultz et al. [23] and Crema et al. [24] reported that femtosecond laser-assisted cataract surgery helped Marfan syndrome patients gain a CDVA of 20/25~20/20. In our study, the postoperative UDVA and CDVA were better than preoperation in both groups. The percentage of capsular tension ring implantation was statistically significantly lower in the FLACS group ($P = 0.027$). Our study showed the application of femtosecond laser technology increases the surgical safety and efficacy for zonulysis and helps to restore patients' visual function to the maximum extent.

The limitation of this study was that it was a retrospective study but not a randomized controlled trial. In order to fully respect the patient's right of choice, the type of surgery was chosen by the patients but not randomly assigned. However, after comparing the baseline of the two groups, we think the two groups are still comparable. Another limitation was that we did not measure the capsulorhexis or the position of IOL for it was a retrospective study. The next step should be comparing the quality of the capsulorhexis and the position of IOL between the two groups.

5. Conclusion

Femtosecond laser-assisted cataract surgery can help patients to get a better visual quality and reduce endothelial cell injury compared to the conventional phacoemulsification in shallow anterior chamber patients. It is an ideal choice for patients with complicated cataracts such as with shallow anterior chambers, angle-closure glaucoma, and zonulysis. It has significance for improving postoperative visual quality of these patients. Also, it has the trend of reducing the use of capsular tension rings in zonulysis cataracts.

Abbreviations

AC: Anterior chamber
ACD: Anterior chamber depth
CDVA: Corrected distance visual acuity
CTR: Capsular tension ring
ECD: Endothelial cell density
FLACS: Femtosecond laser-assisted cataract surgery
IOL: Intraocular lens
IOP: Intraocular pressure
logMAR: Logarithm of the minimum angle of resolution
OSI: Object scatter index.
Phaco: Phacoemulsification
SD: Standard deviation
UDVA: Uncorrected distance visual acuity.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors have no conflicts of interest in any concept or product described in this article.

Acknowledgments

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Research Article

Correlation Analysis of Refractive and Visual Quality after Wavefront-Optimized Laser In Situ Keratomileusis for 50% and 100% Angle Kappa Compensation

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Purpose. To analyze the distribution of the offset between the pupil center and the coaxially sighted corneal light reflex (*P-Dist*), the effects of 50% and 100% angle kappa adjustments on refractive and visual quality in patients with moderate myopia were investigated. *Methods*. A randomly selected 254 patients (254 eyes) with moderate myopia who underwent femtosecond laser-combined LASIK were examined. During the operation, the *P-Dist* of the patients was recorded by the *x*- and y-axis eyeball-tracking adjustment program of the WaveLight Eagle Vision EX500 excimer laser system. Preoperatively and 3 months postoperatively, the WaveLight® ALLEGRO Topolyzer was used to measure the pupil size and center position, and the wavefront sensor was used to measure the wavefront aberrations. The visual function tester (OPTEC 6500) measured contrast sensitivity. *Results*. The average *P-Dist* was 0.220 ± 0.102 mm. When the *P-Dist* >0.220 mm, the postoperative residual cylinder was 0.29 ± 0.34 D in the group with the 50% adjustment and 0.40 ± 0.32 D in the 100% group, which was significantly higher than the 50% group ($P = 0.036$). The coma was 0.21 ± 0.17 μm in the 50% adjusted group and 0.34 ± 0.25 μm in the 100% group, which was significantly higher than that in the 50% group ($P = 0.021$). At the 1.5 c/d spatial frequency, contrast sensitivity in the adjusted 100% group was significantly lower than that in the 50% group under visual glare conditions ($P = 0.039$). *Conclusion*. The postoperative visual acuity and spherical equivalent were not affected in the two groups. However, when *P-Dist* >0.220 mm, the residual astigmatism and coma were lower in the 50% group. Individualized operations for those with moderate myopia and large-angle kappa in which 100% adjustment is chosen may not result in a better visual quality effect than 50%.

1. Introduction

The human eye is a complex optical system with multiple axes (visual axis, optical axis, pupillary axis, etc.) and multiple angles (angle kappa, angle alpha, etc.) [1]. The angle kappa is defined as the angle between the visual axis and pupillary axis. In the individualization of corneal refractive surgery, the ideal excimer laser cutting center should completely overlap with the visual axis because the visual axis is difficult to determine during the operation. The eye-tracking system usually locates and tracks the pupil (pupil center), but the pupil center is different from the visual axis [1]. If angle kappa adjustment is not considered during the pupil positioning and tracking scan, it will lead to surgically induced decentration [2], resulting in an increase in higher-order aberrations (HOAs) after surgery [3]. Therefore, adjusting the excimer laser cutting center from the pupil center to the visual axis to compensate for the offset effect of angle kappa has become the consensus among corneal refractive surgeons [4, 5].

The current individualized laser cutting technology for angle kappa adjustments corrects only the offset between the static pupillary axis and visual axis but does not take factors such as dynamic changes in the pupil, cornea, and lens into account. However, angle kappa is not a fixed value, and it will change under different conditions. It can be affected by

factors such as light during surgery, surgical stimulation, emotional tension, and convergence adjustment caused by watching the indicator at close range [6–8]. According to the data regarding changes in angle kappa, can we obtain individual kappa angle adjustment vector percentages, find the cutting center point closest to the visual axis, and ensure that each excimer laser spot is in the exact position?

In this study, by analyzing the distribution rule of the vector between the pupil center and the coaxially sighted corneal light reflex, it is intended to analyze the effect of individualized excimer laser in situ keratomileusis with different angle kappa compensation, through the percentages of 50% and 100% angle kappa compensation, on diopter and visual quality in eyes with moderate myopia. The study provides a reliable theoretical and experimental basis for the design of an optimized femtosecond laser combined with excimer laser in situ keratomileusis that meets the optical characteristics of individual human eyes.

2. Materials and Methods

2.1. Patient Selection. Two hundred and fifty four patients (254 eyes; the right eyes) with moderate myopia who underwent femtosecond laser-assisted in situ keratomileusis (FS-LASIK) at the Department of Ophthalmology in Affiliated Hospital of YanBian University from January to May 2019 were randomly selected for preoperative and postoperative follow-ups at 3 months. The range of preoperative spheres was −3.00 to −6.00 D. The cylinder was 0 to 1.50 D, and the refractive state was stable in the last 2 years (the annual change was less than 0.5 D) (Table 1). Before the operation, the subjects were randomly assigned to 50% (127 patients, 127 eyes) and 100% (127 patients, 127 eyes) angle kappa adjustment groups. The use of soft contact lens was stopped for more than 2 weeks, and the use of rigid permeable contact lens was stopped for more than 1 month. The corneal thickness was ≥480 μm before surgery and postoperative residual stromal bed thickness was >300 μm. The exclusion criteria included subjects with ocular pathology, ophthalmic disorders, amblyopia, strabismus, previous intraocular surgery, laser treatment, or retinal complications. Informed consent was obtained from all subjects using a consent form approved by the Institutional Review Board of the Affiliated Hospital of Yanbian University.

2.2. Surgical Techniques. All patients underwent slit-lamp examination. Computer optometry and retinoscopy were used for objective optometry and cycloplegic refraction, comprehensive optometry, intraocular pressure (IOP), corneal thickness, eye axis, and fundus examination. At the preoperative and postoperative l-week, 1-month, and 3-month examinations, a WaveLight® ALLEGRO Topolyzer (WaveLight Laser Technologies, AG, Erlangen, Germany) was used to measure the pupil size and center position, and a wavefront sensor (VISX WaveScan) was used to measure HOAs of the eyeball (including 3–6 total higher-order aberrations, spherical aberrations, coma, and trefoil) under the condition of a normal pupil diameter of 5 mm in the darkroom. The Optec 6500 Vision Tester (Stereo Optical Co., Chicago, IL, USA) was used to measure the contrast sensitivity at 5 spatial frequencies (1.5, 3.0, 6.0, 12.0, and 18.0 c/d). The preoperative examination, operation, and postoperative observations were made by the same physician.

Table 1: Patient demographics and characteristics.

	50% group	100% group	P value
Age (years)	23.51 ± 6.82	24.68 ± 4.51	0.954
Spherical equivalent (D)	−5.05 ± 1.35	−5.21 ± 1.56	0.292
Sphere (D)	−4.62 ± 1.05	−4.85 ± 1.26	0.685
Cylinder (D)	−0.87 ± 0.61	−0.72 ± 0.59	0.198
Corneal K-value (D)	42.61 ± 1.23	43.56 ± 1.54	0.294
Corneal thickness (μm)	529.72 ± 32.26	535.24 ± 41.23	0.586
Intraocular pressure (mmHg)	13.42 ± 1.37	12.08 ± 2.04	0.319
Pupil diameter (mm)			
Photopic	3.25 ± 0.49	3.52 ± 0.37	0.216
Mesopic	6.24 ± 0.71	6.38 ± 0.56	0.659
Axial length (mm)	26.71 ± 1.59	26.95 ± 1.82	0.482

2.3. Evaluation Index. The WaveLight FS200 femtosecond laser (Alcon Laboratories, Inc., Fort Worth, TX) was used to produce 110 μm corneal flaps with a diameter of 8.5 mm. The WaveLight EX500 excimer laser (Alcon Laboratories, Inc.) was used for excimer laser cutting with a wavefront aberration optimized cutting program. The same surgeon performed all surgeries, and the targeted refraction was +0.50 diopter (D).

The following procedures were used. The eye was conventionally disinfected, and the eyelid was opened with a blepharostat. After making a flap with the femtosecond laser, the patients were asked to lie flat and to watch the upper green indicator light. The examiner could see the reflective point of the corneal vertex (coaxial corneal reflection point) and the red reflection in the center of the pupil (optical axis center; origin of Cartesian coordinate system) under the microscope, while adjusting the illumination of the operating microscope and indoor lighting to keep the pupil size consistent with the preoperative examination; if the actual pupil in the treatment image differed in diameter by more than 20% from the diagnostic image, it was possible to modify the actual pupil size and diameter by changing the lighting conditions using the "microscope/op field illumination brightness knob." The x- and y-axis eye-tracking adjustment program of the EX500 excimer laser system was used to record the *P-Dist* (the offset between the pupil center and the coaxially sighted corneal light reflex) while the patient was supine. The 50% and 100% *P-Dist* adjustment was manually entered into the excimer laser device. The excimer laser cutting center was moved from the pupil center to the direction of the visual axis (coaxially sighted corneal light reflex).

The diameter of the optical cutting was 6.5 mm, and laser cutting was performed according to a predesigned

procedure. After completion, the flap was reset, the residue under the flap was washed, and the eyelid opener was removed.

2.4. Statistical Methods. All statistical analyses were performed using SPSS 21 for Windows (SPSS Inc., Chicago, IL, USA). Independent sample t-tests were used to compare the *P-Dist* indexes in the 50% and 100% groups. Paired t-tests were used to compare the preoperative and postoperative values, and a P value of <0.05 was considered to indicate a significant difference.

3. Results

3.1. The Distribution of Decentration between the Pupil Center and the Coaxially Sighted Corneal Light Reflex. The distribution of decentration between the pupil center and the coaxially sighted corneal light reflex was 0.220 ± 0.102 mm (range: 0.010 to 0.580 mm) with 32% of eyes ≤0.15 mm, 88% of eyes ≤0.30 mm, and 98% of eyes ≤0.45 mm (Figure 1); there were 130 eyes (50%: 62 eyes, 100%: 68 eyes) in the *P-Dist* < 0.220 mm (small-angle kappa) and 124 eyes (50%: 65 eyes, 100%: 59 eyes) in the *P-Dist* > 0.220 mm (large-angle kappa), with the 50% group at 0.215 ± 0.125 mm and the 100% group at 0.226 ± 0.97 mm. There was no significant difference between the two groups ($P = 0.641$). The distribution of decentration between the corneal center and the pupil center under photopic and scotopic conditions showed that under photopic conditions, the superior temporal region accounted for 35%, the inferior temporal region accounted for 28%, the superior nasal region accounted for 20%, and the inferior nasal region accounted for 17%; under scotopic conditions, the superior temporal region accounted for 26%, the inferior temporal region accounted for 32%, the superior nasal region accounted for 23%, and the inferior nasal region accounted for 19% (eye ratio) (Figure 2).

3.2. Comparison of Postoperative Visual Acuity and Diopter. There was no significant difference between the 50% (0.02 ± 0.01) and 100% (0.03 ± 0.02) groups in postoperative distance-corrected visual acuity (logMAR acuity) ($t = 0.009$, $P = 0.954$). Postoperatively, the two groups showed slight hyperopia drift that accounted for more than 91% within ± 0.50 D. When the *P-Dist* < 0.220 mm, the residual postoperative cylinder was 0.31 ± 0.28 D in the 50% group and 0.34 ± 0.41 D in the 100% group. There was no significant difference between the two groups ($t = -0.339$, $P = 0.412$). When P-*Dist* > 0.220 mm, the residual postoperative cylinder was 0.29 ± 0.34 D in the 50% group and 0.40 ± 0.32 D in the 100% group, which was significantly higher than that in the 50% group ($t = -2.047$, $P = 0.036$) (Table 2).

More eyes achieved zero astigmatism in the 50% group (53 eyes, 41.7%) than in the 100% group (40 eyes, 31.5%). More eyes had astigmatism greater than 0.75 D in the 100% group (9 eyes, 7.1%) than in the 50% group (2 eyes, 1.6%). There was a significant difference in the distribution of the postoperative cylinder between the 50% and 100% groups ($\chi^2 = 5.64$, $P = 0.042$).

3.3. Higher-Order Aberration Analysis. There were no significant differences in preoperative HOA, RAS, spherical aberrations, coma, and trefoil at different *P-Dist* values between the 50% and 100% groups ($P > 0.05$) (Table 3). When the *P-Dist* < 0.220 mm, the coma in the 50% group was 0.17 ± 0.12 μm, and the coma in the 100% group was 0.22 ± 0.19 μm. There were no significant differences between the two groups ($t = -1.424$, $P = 0.256$). However, when *P-Dist* > 0.220 mm, the coma was 0.21 ± 0.17 μm in the 50% group and 0.34 ± 0.25 μm in the 100% group, which was significantly greater than that in the 50% group ($t = -2.322$, $P = 0.021$); in the 100% group, the coma was 0.22 ± 0.19 μm in those with *P-Dist* < 0.220 mm and was 0.34 ± 0.25 μm in those with *P-Dist* > 0.220 mm, which was significantly different ($t = -2.017$, $P = 0.045$).

3.4. Contrast Sensitivity Comparison. When the *P-Dist* < 0.220 mm, there was no significant difference in the contrast sensitivity between the 50% and 100% groups under conditions of photopic vision and photopic glare when adjusted across 5 spatial frequencies ($P > 0.05$). However, when the *P-Dist* > 0.220 mm, contrast sensitivity in the 100% group was significantly lower than that in the 50% group under the condition of a 1.5 c/d spatial frequency and postoperative photopic glare ($t = 3.673$, $P = 0.039$) (Figure 3).

4. Discussion

Although compensation for angle kappa combined with various modes of personalized LASIK has a good theoretical basis, there is still a significant gap between the actual and ideal visual quality [9, 10]. The currently available [11] angle kappa adjustment is compensated according to the vector percentage between the pupil center and the corneal coaxial reflection point, but the input value is a fixed decentration.

Pande and Hillman [12] showed that the corneal coaxial reflective point was the ideal excimer laser cutting center because the corneal coaxial reflective point is the closest point to the visual axis and is not affected by changes in the pupil size and center position, with an average of 0.02 mm. Therefore, the angle kappa can be understood as the distance between the pupil center and the corneal coaxial reflective point. The corneal reflection point will be more accurate and stable [13] if the errors in the patient's eyeball swing and excimer laser tracking system can be supplemented with limbal vascular network tracking during the operation. In this study, we measured the distance between the pupil center and the corneal coaxial reflection point, showing that the average *P-Dist* was 0.220 mm, the minimum was 0.010 mm, and the maximum was 0.580 mm. Accordingly, based on the above average value, we divided individuals into *P-Dist* groups with >0.220 mm (large-angle kappa) and <0.220 mm (small-angle kappa), and we tried to verify which

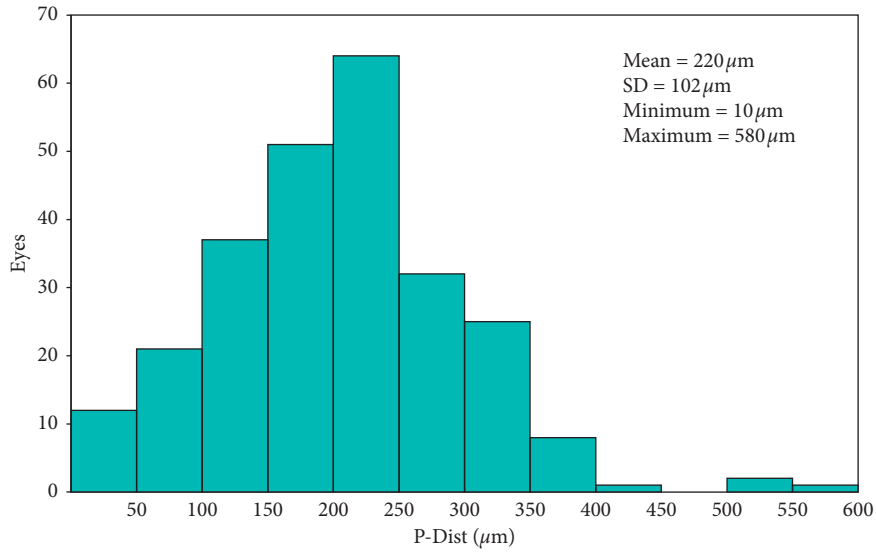

Figure 1: Decentration of the *P-Dist* (distance between the pupil center and the coaxially sighted corneal light reflex).

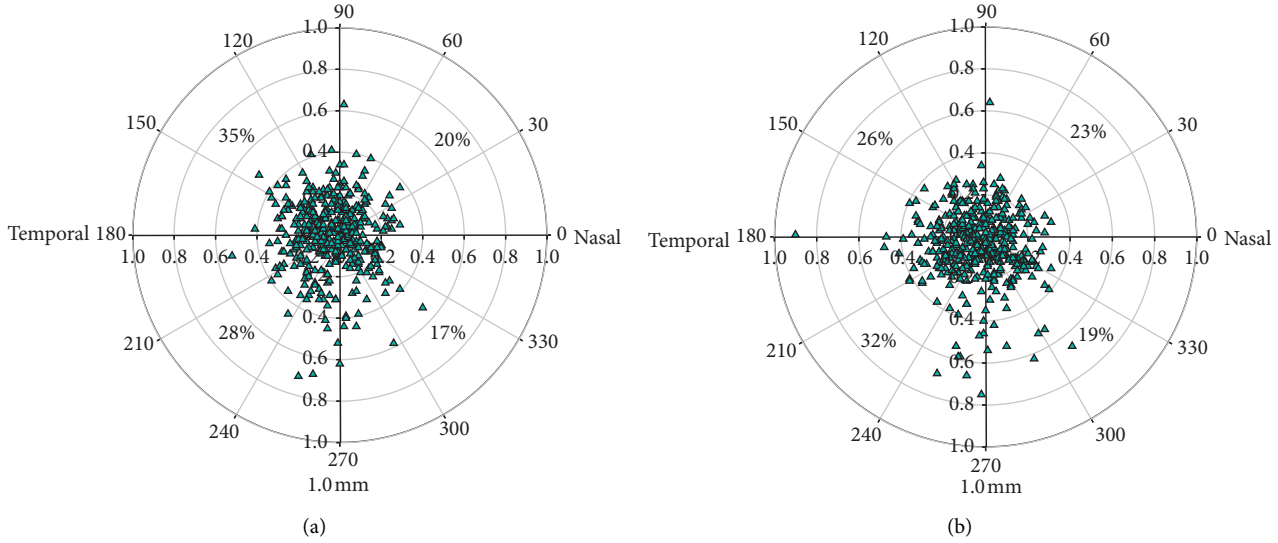

Figure 2: Decentration of the pupil center under (a) photopic and (b) mesopic conditions (the center of the coordinate is the geometric center of the cornea, and the cyan points are pupil centers).

compensation proportion, either 50% or 100% ablation centration, was closer to the visual axis based on an exploration of the effects of personalized excimer laser in situ keratomileusis with different angle kappa compensation levels on the diopter and visual quality in those with moderate myopia.

This study showed that there was no significant difference in postoperative uncorrected visual acuity and spherical equivalent between the 50% and 100% groups. The residual diopters in the 50% and 100% groups were very small, and the equivalent spherical mirrors presented slight hyperopia drift that accounted for more than 91% of those within +0.50 D. The 50% and 100% groups had overcorrection after cutting by a WaveLight EX500 excimer laser, which is consistent with the results of an evaluation of that excimer laser in treating myopia [10]. When the *P-Dist* > 0.220 mm, the postoperative residual cylinder power was 0.29 ± 0.34 D in the 50% group and 0.40 ± 0.32 D in the 100% group. The 50% group had less residual astigmatism than the 100% group. In addition, we found, regarding the astigmatism data, that more eyes achieved zero residual astigmatism, but fewer eyes had astigmatism greater than 0.75 D in the 50% group than in the 100% group.

When *P-Dist* > 0.220 mm, the coma in the 100% group was significantly higher than that in the 50% group, and contrast sensitivity in postoperative visual glare conditions at low spatial frequency was also lower than that in the 50% group. The increase in spherical aberration and trefoil was attributed to the ablation profile; however, the induced coma could have been caused by the position of the ablation centration points [14] and astigmatism [4]. Mrochen et al. [15] also reported that subclinical decentered ablation

Table 2: Comparison of diopters between different *P-Dist* groups at 3 months.

Category	*P-Dist* < 0.220 mm	*P-Dist* > 0.220 mm	*t* value	*P* value
Spherical (D)				
50% group	0.24 ± 0.35	0.28 ± 0.41	−0.072	0.241
100% group	0.15 ± 0.32	0.19 ± 0.38	−0.470	0.394
t value	1.213	0.774		
P value	0.097	0.324		
Cylinder (D)				
50% group	0.31 ± 0.28	0.29 ± 0.34	0.308	0.145
100% group	0.34 ± 0.41	0.40 ± 0.32	−1.096	0.265
t value	−0.339	−2.047		
P value	0.412	0.036*		
Spherical equivalent (D)				
50% group	0.27 ± 0.31	0.26 ± 0.38	0.052	0.892
100% group	0.25 ± 0.34	0.30 ± 0.33	−0.685	0.787
t value	0.674	−0.857		
P value	0.251	0.136		
LogMAR				
50% group	0.01 ± 0.03	0.02 ± 0.02	0.042	0.652
100% group	0.01 ± 0.02	0.02 ± 0.03	0.054	0.765
t value	0.009	0.012		
P value	0.924	0.714		

Note. *P-Dist*: distance between the pupil center and the coaxially sighted corneal light reflex. *$P < 0.05$ (the paired *t*-tests were used to detect differences between the 50% group and the 100% group; correlations with different *P-Dist* were determined using the unpaired *t*-test). There were 130 eyes in small-angle *k* group (62 eyes in the 50% group and 68 eyes in the 100% group) and 124 eyes in large-angle k group (65 eyes in the 50% group and 59 eyes in the 100% group).

Table 3: Comparison of higher-order aberrations between different *P-Dist* groups at 3 months (the pupil diameter is 5.0 mm).

Category	*P-Dist* < 0.220 mm	*P-Dist* > 0.220 mm	*t* value	*P* value
HOA RMS				
50% group	0.35 ± 0.19	0.29 ± 0.15	0.202	0.514
100% group	0.41 ± 0.23	0.32 ± 0.17	0.944	0.354
t value	−1.529	−0.569		
P value	0.124	0.253		
Coma				
50% group	0.17 ± 0.12	0.21 ± 0.17	−1.323	0.391
100% group	0.22 ± 0.19	0.34 ± 0.25	−2.017	0.045*
t value	−1.424	−2.322		
P value	0.256	0.021*		
Spherical aberration				
50% group	0.09 ± 0.07	0.12 ± 0.09	−1.261	0.354
100% group	0.13 ± 0.12	0.14 ± 0.10	−0.085	0.102
t value	−1.525	−0.194		
P value	0.247	0.136		
Trefoil				
50% group	0.21 ± 0.12	0.24 ± 0.15	−0.825	0.265
100% group	0.24 ± 0.15	0.30 ± 0.17	−1.434	0.142
t value	−0.516	−0.186		
P value	0.234	0.258		

Note. *$P < 0.05$ (the paired *t*-tests were used to detect differences between the 50% group and the 100% group; correlations with different *P-Dist* were determined using the unpaired *t*-test). There were 130 eyes in small-angle *k* group (62 eyes in the 50% group and 68 eyes in the 100% group) and 124 eyes in the large-angle *k* group (65 eyes in the 50% group and 59 eyes in the 100% group).

(<1.0 mm) was the main reason for the increase in postoperative coma. We speculate that although the adjustment in the 100% group did not affect the postoperative visual acuity, when the large kappa angle (*P-Dist* > 0.220 mm) was adjusted to 100%, the offset between the cutting center and the visual axis was larger than that in the 50% group, which may be because the laser cutting center exceeded the visual axis center [16]; the increase in the incident oblique beam led to an increase in astigmatism and an increase in postoperative coma, which led to a decrease in visual quality, such as glare, and a decrease in contrast sensitivity.

In this study, eye-tracking technology based on image processing with the noninterference pupillary-corneal reflex method was used to track the pupil center of the operative

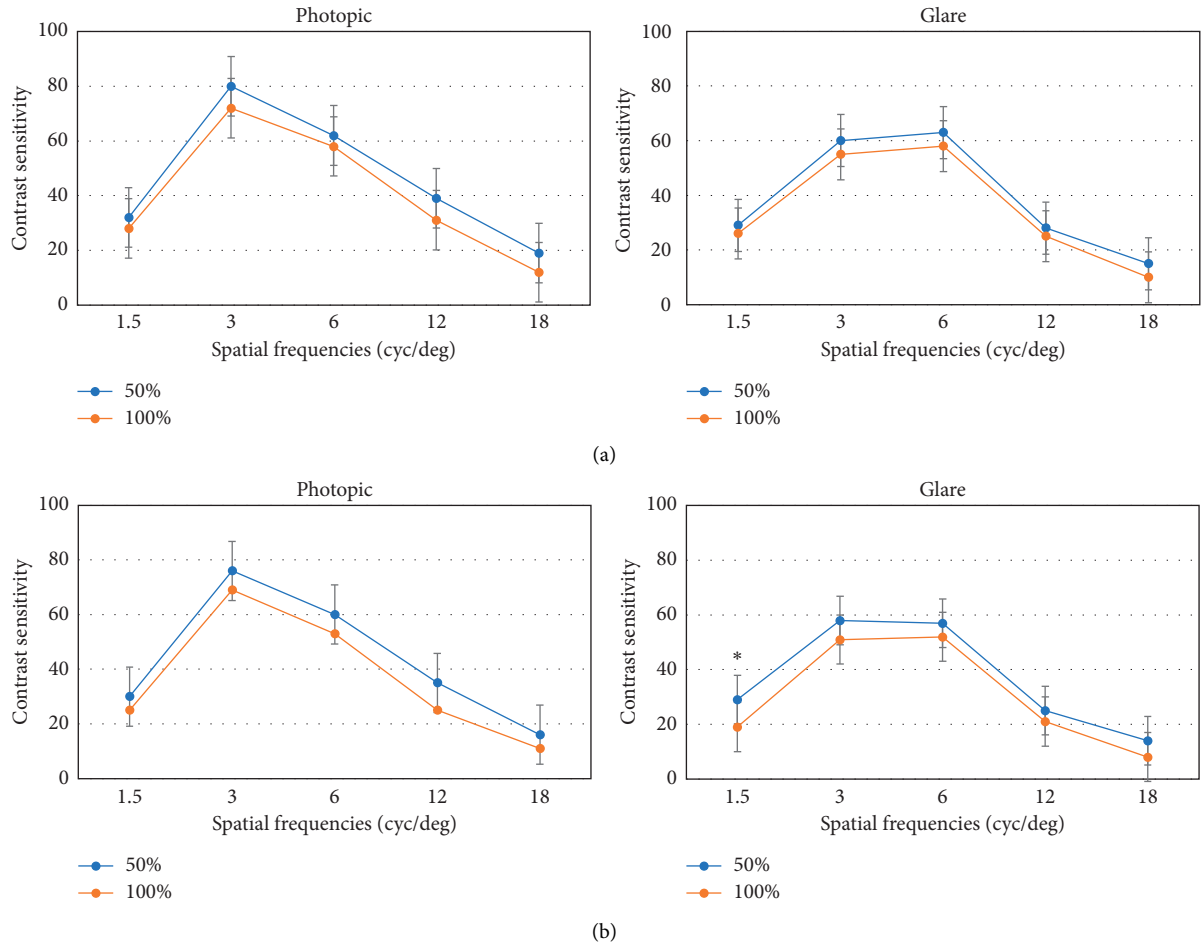

FIGURE 3: Comparison of postoperative contrast sensitivity between groups under photopic and glare conditions ((a) *P-Dist* < 0.220 mm; (b) *P-Dist* > 0.220 mm). $^{*}P < 0.05$.

eye, and the direction of the visual axis could be estimated by calculating the vector between the pupil center and the coaxially sighted corneal light reflex [17]. With the locked pupil center as the reference of the Cartesian coordinate system, the adjusted vector ratio of 50% and 100% was a fixed value, rather than a value that changed with the dynamic pupil. This study also showed that the size and position of the pupil center under photopic and scotopic conditions were dynamic changes. For the center position of the pupil, the superior temporal region accounted for 35% under photopic conditions, and the inferior temporal region accounted for 32% under scotopic conditions. The ideal decentration should refer to the pupil size and center position and the dynamic changes in angle kappa to obtain the individual curve-shifted pupil centers [18]. During the operation, the patient's pupil dynamics were monitored, and the angle kappa was adjusted to calibrate the cutting center in real time.

The larger the angle kappa is, the greater the distance between the pupil center and the coaxially sighted corneal light reflex will be. Theoretically, when 100% angle kappa is compensated, the ablation centration is closer to the visual axis, but we found that there was still a gap between the actual and expected visual quality. It is speculated that factors such as dynamic changes in the pupil center position caused by lighting, emotional tension, surgical stimulation, and adjustment of radial convergence during the operation were involved, which further confirm the importance of the accurate positioning of the ablation centration point [19] and the necessity of reasonable compensating for the percentage under different angle kappa states [20].

This study is the first to investigate the distribution of decentration between different pupil centers and the coaxially sighted corneal light reflex. The refraction, HOAs, and contrast sensitivity results were compared by adjusting the vector ratio of 50% and 100% *P-Dist*. It was shown that neither group had central vision affected, and there was no difference in equivalent spherical lens. However, in the 50% group, there was less residual astigmatism and coma. Therefore, both 50% and 100% *P-Dist* adjustments were effective in achieving good postoperative visual acuity. However, in moderate myopia patients with large-angle kappa, choosing 100% adjustment may not result in better visual quality than 50% adjustment. In the individualized operation of moderate myopia with a large kappa angle, choosing 100% adjustment may not result in a better visual quality effect than 50% adjustment. In addition, the percentage comparison with other angle kappa results, the

correspondence between angle kappa compensation and wavefront optimization, and the correspondence with visual quality need to be further explored.

Data Availability

The clinical research data used to support the findings of this study have been deposited in the Dryad repository (doi:10.5061/dryad.hhmgqnkf8). The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

XYR wrote the report. YJL was responsible for the study design. WQD, YJJ, and SHL collected the data. ZRL and CLL contributed to analysis and interpretation of the data YJL and CH contributed to the revision of the draft.

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Research Article

Anatomical and Visual Outcomes after LASIK Performed in Myopic Eyes with the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA)

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Purpose. To evaluate changes in corneal anatomy and quality of vision following LASIK refractive surgery for mild to high myopia using the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA). *Setting*. Rothschild Foundation, Paris, France. *Design*. Prospective interventional case series. *Methods*. We examined 60 myopic eyes (average SE −4.5 D, from −9.3 to −0.75 D) of 30 patients from 21.3 to 38.7 years old. Pachymetry, keratometry, *Q* factor, corneal aberrations, visual acuity (VA), contrast sensitivity, dry eye assessment, and quality of vision were measured preoperatively, one day (D1), and 1, 3, and 6 months postoperatively. *Results*. 6 months postoperatively, keratometry became flatter, and the *Q* factor became more oblate (from -0.18 ± 0.08 to $+0.19 \pm 0.06$). Pachymetry decreased by $117.9 \pm 62.2\,\mu$m at D1 and increased by $37.87 \pm 32.6\,\mu$m between D1 and M6. Refraction was emmetropic at D1 and remained stable thereafter. Six months after surgery, VA was slightly but nonsignificantly improved (<0.05 log MAR), whereas contrast sensitivity remained unchanged. Quality of vision was not affected by surgery and was more related to dry eye symptoms than to corneal HOAs ($r^2 = 0.49$; $p < 0.001$ vs. $r^2 = 0.03$; $p < 0.001$). *Conclusions*. LASIK surgery for moderate to high myopia, performed with the WaveLight® Refractive Suite, showed good postoperative outcomes, with demonstrated safety, predictability, efficiency, and stability. This is probably due to well-controlled spherical aberration and the use of large optical zones. Besides, we can assume that the patients' quality of vision depends more on the postoperative dry eye disease generated by the laser than on the induced HOAs.

1. Introduction

LASIK [1, 2] is an increasingly popular surgical option for the correction of myopia as demonstrated by the rising numbers of these procedures being performed worldwide. The technique involves use of a femtosecond laser to create a hinged flap, which is then folded back to allow photoablation of the exposed stroma using an excimer laser. In myopic LASIK, stromal tissue is removed, resulting in flattening of the central corneal curvature, which in turn decreases the excessive refractive power of the eye.

In recent years, an increasing amount of research has been focused on the assessment of quality of vision after LASIK refractive surgery [3–7].

The aim of refractive surgery is to improve visual outcomes and to reduce dependence on spectacles or contact lenses. In the 1990s, many studies were published on the correction of myopia with LASIK [8, 9] reporting low predictability, significant regression, and induced night vision disturbances [10, 11]. These issues were due in large part to the use of small optical zones [12, 13] and nonaspheric Munnerlyn ablation profiles leading to significant induced spherical aberrations [14]. In the 2000s, other studies

reported that LASIK was a safe and predictable method to correct moderate to high myopia [15, 16]. Indeed, these studies show a high success rate, reflected by favourable functional outcomes [17–20], and high physician and patient satisfaction [21].

Several studies report satisfaction rates of *c.* 90% after LASIK [15, 22, 23]; however, others report dissatisfaction, suggesting room for future improvement [24].

Most published studies evaluate the visual outcomes of LASIK in terms of visual performance (visual acuity, contrast sensitivity, and depth of focus) [25, 26]. Other studies describe the microstructural changes induced in the stroma and Bowman's layer in vivo using confocal microscopy [27]. However, many questions remain regarding the biological response of the cornea to the ablation process [28]. These microstructural disturbances of the corneal stroma may result in wavefront aberrations [29]. Recently, with the development of newer techniques, we can measure the optical wavefront after refractive surgery. Studies have revealed that although refractive errors are reduced, higher-order aberrations are generally induced [30, 31]. Along with other technical advances (eye trackers, small-spot lasers, etc.), the accurate measurement of ocular wave aberrations has opened doors for potential improvements of LASIK, in particular through customized treatments for each patient eliminating low- and high-order aberrations in the eye [32, 33].

It has been shown that analysis of the total wavefront error of the eye reflects the most complete measurement of retinal image quality, which is directly related to the visual performance [34, 35]. Although the impact on the visual performance is not fully understood, wavefront-error data have been extensively used as an objective parameter for the quality of vision in theoretical models and in clinical trials [17, 18, 36, 37]. That said, it is desirable to establish robust and clinically meaningful correlations between the results of wavefront analysis and subjective quality of vision.

This study describes the anatomical and visual outcomes of myopic LASIK performed with the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA) which includes a FS200 femtosecond laser and an EX500 excimer laser. We present anatomical changes, biomechanical corneal response (both anterior and posterior surfaces), visual performance (visual acuity, contrast sensitivity, and depth of focus), total and corneal aberrations, and patient satisfaction before and after LASIK. We also aimed to correlate all these parameters to obtain a more complete view of the present outcomes of LASIK surgery in moderate to high myopia with the aforementioned devices.

2. Patients and Methods

2.1. Patients. This study included 60 eyes of 30 patients undergoing LASIK surgery for myopia at the Rothschild Foundation from May 2015 until June 2016. All patients underwent complete ocular assessment prior to surgery, including cycloplegic refraction, slit lamp, and fundus examination. Preoperative corneal topography was performed with OPD-Scan® III (Nidek®, Japan) and the Orbscan IIz® (Bausch & Lomb®, USA).

Patients presenting with corneal disease or other ocular pathologies (amblyopia, glaucoma, cataract, retinopathy, and strabismus), those with evidence of subclinical keratoconus, or those with a history of ocular surgery were excluded from the study. We also excluded patients whose eyes tested positive for keratoconus (KC) or keratoconus suspect (KCS) diagnosed by the corneal navigator neural network, which uses Klyce and Maeda indices on OPD-Scan® III (Nidek®, Japan). Patients who had worn rigid gas-permeable lenses in the 12 months prior to examination and those who had worn soft contact lenses in the 3 weeks prior to surgery were also excluded.

We included myopic patients older than 18 years with otherwise unremarkable ophthalmic histories. The choice of the LASIK technique was justified by the presence of a thick cornea (defined as a residual stromal bed higher than 300 μm after subtracting the sum of the planned LASIK flap and laser ablation thickness) and the presence of a regular corneal surface diagnosed with an objective method based on Placido disk-derived data for the detection of eyes at the risk of ectasia [38].

All patients provided written informed consent. The study and data acquisition were achieved with the approval from the Rothschild Foundation's institutional review board. Informed consent was obtained from each patient after he/she voiced understanding about the purpose and the procedures in the study in accordance with the Declaration of Helsinki.

2.2. Surgical Procedure and Treatment Planning. The 60 eyes enrolled in this prospective study underwent uncomplicated primary LASIK performed by the same experienced surgeon (DG) using the same refractive surgery platform (FS200 femtosecond laser and EX500 excimer laser). WaveLight FS200 femtosecond laser system is a low-energy and high pulse frequency laser that emits laser pulses with the duration of 350 fs at a wavelength of 1,050 nm and a pulse repetition rate of 200 kHz.

Flap creation was performed with the FS200 femtosecond laser, using standard treatment settings (9.2 mm flap diameter and 110 μm flap thickness).

A Munnerlyn algorithm-based photoablation [39] was performed with the EX500 excimer. A standard aspheric ablation profile was planned with a plano target (at the corneal plane) refraction. The average optical zone was 6.5 mm with a transition zone of 1.25 mm. For some subjects, because of a greater deviation between the pupillary axis and the visual axis (kappa angle) [40], preoperative corneal vertex and pupillary axis were measured by WaveLight® Topolyzer^{TM} VARIO (Alcon® Laboratories Inc., USA) linked with the EX500 excimer laser. A valid assumption is to consider that the optimal centration for corneal refractive surgical procedures may be located close to or midway between the corneal vertex (first Purkinje image) and the pupil centre [41, 42]. However, in some eyes, the distance between these points can be as high as 400 μm.

This reflects the presence of a large kappa angle. Defining the proper axis for centration may be of critical importance in eyes with a large distance between the pupil centre and the corneal vertex. EX500 excimer laser software enables centration of the excimer profile of ablation from the pupil centre (0%) to the corneal reflex (100%), or in between, by a 10% step distance along the line joining the pupil centre to the corneal reflex. For this reason, all treatments were centred equidistant between the pupil centre and the corneal vertex (50%) in each patient.

2.3. Preoperative and Postoperative Evaluation. Ophthalmologic examination performed on all patients preoperatively included manifest refraction, cycloplegic refraction, noncontact intraocular pressure evaluation, slit-lamp microscopic evaluation of the anterior segment, and dilated fundoscopy. Preoperative examination included evaluation of pachymetry, keratometry, elevation and curvature topography analysis with Orbscan IIz® (Bausch & Lomb®, USA), wavefront aberrometry (root mean square on the 5.5 mm pupil), and corneal asphericity (at 6 mm diameter) analysis with the OPD-Scan® III (Nidek®, Japan) topographer (Nidek, Inc., Fremont, CA). Corneal asphericity and corneal and total ocular aberrations were analysed according to the Optical Society of America (OSA) recommendations [43]. Dry eye assessments were evaluated using the corneal tear film break up time (BUT) index.

Ten percent and 90% contrast uncorrected distance visual acuity (UDVA) and best corrected distance visual acuity (CDVA) were assessed using FrACT (Freiburg Visual Acuity and Contrast Test) 139 software at 4 meters monocularly and binocularly. This corresponds to the presentation of Landolt rings at 8 positions (Figures 1(a) and 1(b)).

Because the patients would experience a minimizing effect from myopic correction of the trial lenses, magnification adjustment was made to the corneal plane so as to properly compare preoperative and postoperative vision. Visual acuities were adjusted according to the patient's refractive correction. The trial lens vertex distance of 17 mm was used to calculate relative magnification (RM):

$$\mathrm{RM} = 1 - \mathrm{hFs}, \tag{1}$$

where h is the difference between the corneal and spectacle plane (vertex distance in meters) and Fs the back-vertex power of the corrective lens at the spectacle plane. The following equation was used to convert visual acuity from the spectacle plane to the corneal plane: $\mathrm{logMAR}_{\mathrm{cornea}} = \mathrm{logMAR}_{\mathrm{spec}} - \mathrm{logRM}$ [26].

Photopic corrected distance and uncorrected contrast sensitivity (CCS and UCS) measurements were performed at 12 cycles per degree (cpd), using randomly oriented sinusoidal arrays at 4 meters. Photopic best-corrected and uncorrected contrast sensitivities were also measured with the introduction of glare. To generate glare, oncoming headlights were simulated by attaching 2.5 watt halogen floodlights to each side of the computer screen [26].

A "tolerance to blur" measurement was also performed (corrected sensitivity to blur, CSB). The subjective depth of field criteria used was unacceptable blur. This is the level of blur that the patient would refuse to accept if he had to endure it permanently. The average generally observed is about 1.4 D [45–47]. During the evaluation, the subjects wore their spherocylindrical correction and held in front of their eyes an artificial pupil of 3 mm that was subjectively adjusted to maximize the contrasts.

Starting systematically from the clear image (Figure 2) as a reference, defocalization was added to each new slide (0.05 μm or about 0.055D). The subject had to say "stop" as soon as the image was no longer acceptable according to the criterion of unacceptable blur described by Atchison [46, 48].

The illumination of the room where the tests were carried out was about 350 lux. The luminance of the screen that projects the contrast sensitivity, visual acuity, and simulated images for the depth of field measurement has been systematically calibrated to about 100 candelas per m [2].

All patients completed two French versions of vision quality questionnaires: (QOV) [49] (range: 0 excellent quality of vision to 100 very poor quality of vision) and Ocular Surface Disease Index (OSDI) which was developed to quantify the specific impact of dry eye disease on vision-targeted health-related quality of life (range: 0 normal to 100 severe dry eye) [50] preoperatively and one, three, and six months postoperatively. The overall OSDI score defined the ocular surface as normal (0–12 points) or as having mild (13–22 points), moderate (23–32 points), or severe (33–100 points) disease.

All these parameters were measured preoperatively on day 1 and 1 month, 3 months, and 6 months postoperatively. Each measured parameter was verified by the examiner prior to recording. All measurements were performed by the same operator (IS).

2.4. Statistical Analysis. Statistical analysis was performed with commercial software (SPSS v. 13.0; SPSS Inc., Chicago, IL). We used paired and unpaired Student's t-test to compare the outcomes in this population. ANOVA test was also used to compare means. Pearson correlation analyses were also used. A calculated p value <0.05 was considered statistically significant. Data are presented as the mean ± standard deviation.

Astigmatism plots were generated using AstigPLOT® software (EB Eye). The average magnitude and the axis of cylinders were computed using vector calculations. The astigmatism plots were represented with a positive cylinder magnitude convention.

3. Results

3.1. Demographics. 60 myopic eyes of 30 patients were included in the study. The mean preoperative spherical equivalent was −4.5 ± 2.2 D (ranging from −9.3 D to −0.8 D). 43 eyes of 60 (72%) had a SE higher (more myope) than −3.00 D, and 3 eyes among 60 had a SE lower or equal to 1 diopter. The mean age was 30.4 ± 4.2 years (ranging from 21.3 to 38.7 years). Data are further detailed in Table 1.

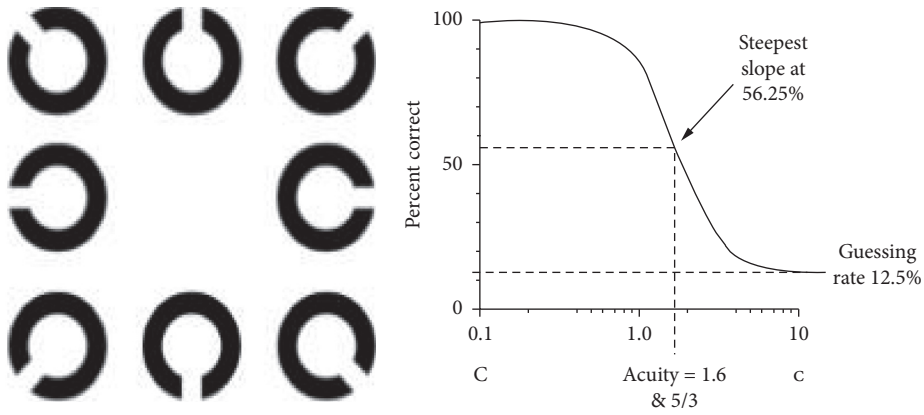


Figure 1: (a) Landolt rings displayed during the visual acuity test. 8 orientations were possible: left, top left, top, top right, right, bottom right, bottom, and bottom left. (b) Psychometric function used by the Freiburg test. The probability of correct answers depends on the size of the optotype. Visual acuity is 16/10 (−0.2 logMAR) [44].

Figure 2: Black-and-white (HEV) images presented for tolerance/sensitivity to blur.

3.2. Anatomical Changes. Six months postoperatively, the cornea became flatter (44.27 ± 1.61 D preoperatively to 40.51 ± 1.67 D at 6 months postoperatively). There was a significant difference between the average corneal power before and after LASIK (paired t-test, $t = 17.50$; $p < 0.001$) (Figure 3(a)).

There was no correlation between the average keratometric power and the patient's age, refractive spherical equivalent, and the initial central mean pachymetry, before and after the surgery (ex: correlation between preop keratometry and age, $r^2 = 0.184$; $p = 0.160$).

The mean corneal pachymetry was $575.08 \pm 29.41\,\mu$m, $457.16 \pm 68.59\,\mu$m, $479.42 \pm 58.97\,\mu$m, $492.49 \pm 53.18\,\mu$m, and $495.03 \pm 53.79\,\mu$m, respectively, preoperatively one day and 1 month, 3 months, and 6 months postoperatively. 6 months postoperatively, the pachymetry was significantly lower than preoperatively (paired t-test, $t = 15.03$; $p < 0.001$).

Six months postoperatively, the mean decrease in keratometry was 3.76 ± 1.66 D while the mean decrease in pachymetry was $80.04 \pm 41.26\,\mu$m. The difference in pachymetry at 6 months postoperatively correlated positively ($r^2 = 0.74$; $p < 0.001$) with the Munnerlyn formula pachymetry estimation (Figure 4).

On day one after LASIK, corneal asphericity as expressed by the Q factor became significantly more oblate ($Q = -0.18 \pm 0.10$ (SD) (range: −0.38 to 0.05)) preoperatively and $Q = 0.19 \pm 0.30$ (SD) (range: −0.29 to 0.98) one day after surgery ($t = -9.52$; $p < 0.001$). There was no significant difference in the Q factor at different time points after surgery ($t = -0.31$; $p = 0.98$) (Figure 3(b)).

There was no correlation between the preoperative spherical equivalent and the preoperative corneal asphericity measured ($r = -0.003$; $p = 0.98$). There was no correlation between the initial mean central pachymetry and the corneal asphericity ($r = 0.206$; $p = 0.18$).

3.3. Safety and Predictability

3.3.1. Quality of Vision Outcomes. Figure 5 shows that, after LASIK, monocular 90% and 10% CDVA increased slightly but not significantly (paired t-test, $t = 2.07$; $p = 0.053$ and $t = 1.62$; $p = 0.11$, respectively), while monocular corrected contrast sensitivity and corrected sensitivity to blur remained unchanged (paired t-test, $t = -0.75$; $p = 0.46$ and $t = -0.36$; $p = 0.72$, respectively). The CCS with glare was lower than the CCS by 0.1 u.log.

Table 2 shows the safety and predictability of LASIK in terms of quality of vision outcomes. Although there was no difference in the quality of vision outcomes (CDVA and CSB) preoperatively between high (cylinder ≥ 1.5 D) and low astigmatic eyes (cylinder < 1.50 D) except for the CCS (where the high astigmatic eyes CCS was smaller than the low astigmatic one (ANOVA, $p = 0.016$)), there were differences postoperatively. No significant difference was found between groups in CSB.

3.3.2. Refractive Spherical Equivalent Outcomes and Magnitude of Astigmatism. Figures 6(a) and 6(b) show predictability of the manifest SE (scattergram of attempted versus achieved manifest SE). There was a strong and statistically significant correlation between the laser attempted SE and the achieved SE ($r^2 = 0.98$; $p < 0.001$). The postoperative SE was independent from the preoperative SE ($r^2 = 0.0098$; $p < 0.001$) (Figure 6(c)), and there were no statistically significant differences in the SE 6 months postoperatively between high astigmatic eyes and low astigmatic ones (ANOVA, $p = 0.98$). Figure 6(d) displays the distribution of preoperative and 6 months postoperative SE.

Table 1: Demographic data.

	Total	Low cylinder (<1.50 D)	High cylinder (≥1.50 D)
Number of patients	30	24	6
Number of eyes	60	49	11
Right/left	30/30	24/25	6/5
Age (years)			
Mean ± standard deviation	30.4 ± 4.2	30.8 ± 4.2	28.7 ± 4.4
Minimum/maximum	21.3/38.7	21.3/38.7	21.3/36.6
% female/% male	63%/37%	67%/33%	45%/55%
% of the contact lens carrier	70%	78%	36%
Refractive spherical equivalent (D)			
Mean ± standard deviation	−4 5 ± 2.2	−4.6 ± 2.2	−3.8 ± 1.9
Minimum/maximum	−9 3/−0 8	−9.3/−0.8	−6.6/−1.3
Refractive cylinder (D)			
Mean ± standard deviation	−0 8 ± 0.8	−0.5 ± 0.3	−2.1 ± 0.7
Minimum/maximum	0.0/−3.3	0.0/−1.3	−1.5/−3.3

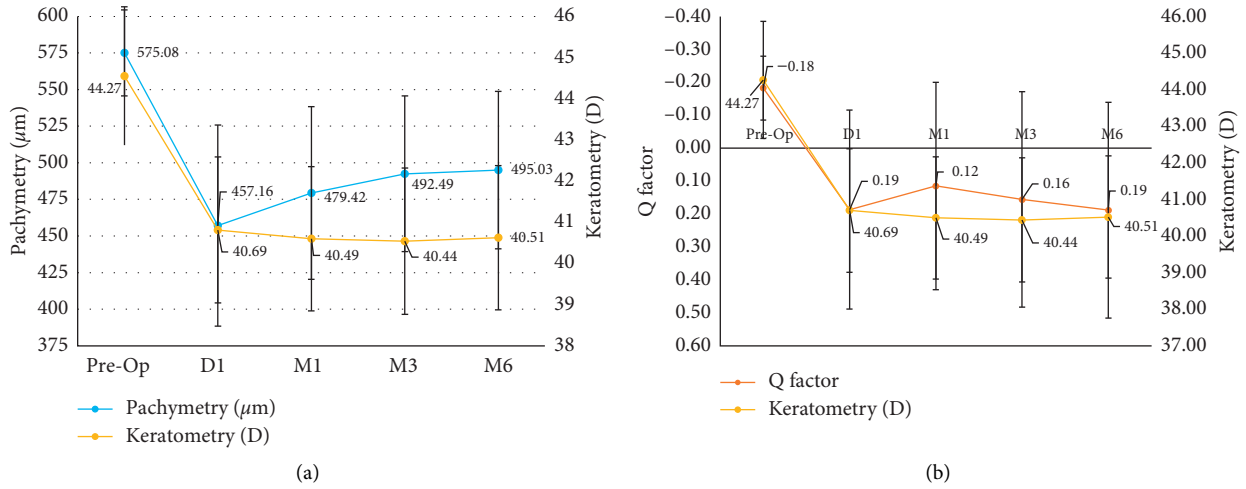


Figure 3: Evolution of anatomical parameters after myopic LASIK. (a) Evolution of pachymetry with regard to keratometry. (b) Evolution of keratometry with regard to asphericity.

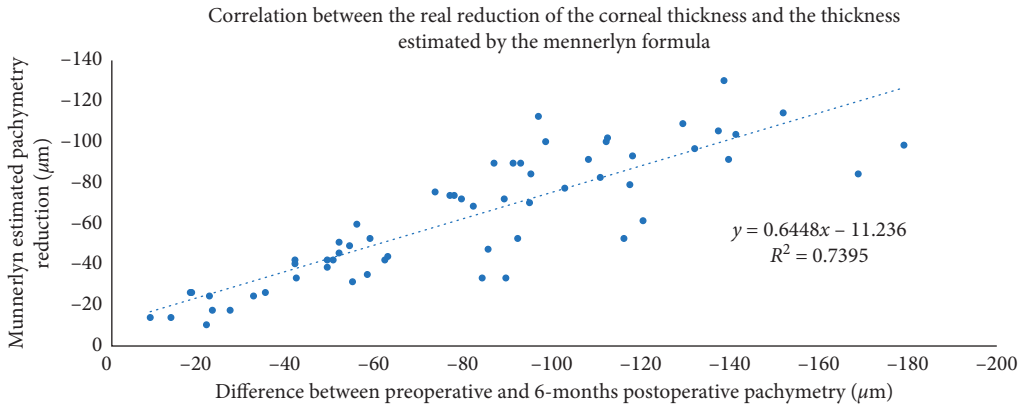


Figure 4: Positive correlation between the real reduction of the corneal thickness and the thickness estimated by the Munnerlyn formula.

Astigmatism is an optical aberration which is mainly caused by the toricity of a refractive surface. Although topography instruments measure toricity (not astigmatism), we will use the terms "astigmatism" and "toricity" interchangeably. The magnitude of the astigmatism was calculated as follows.

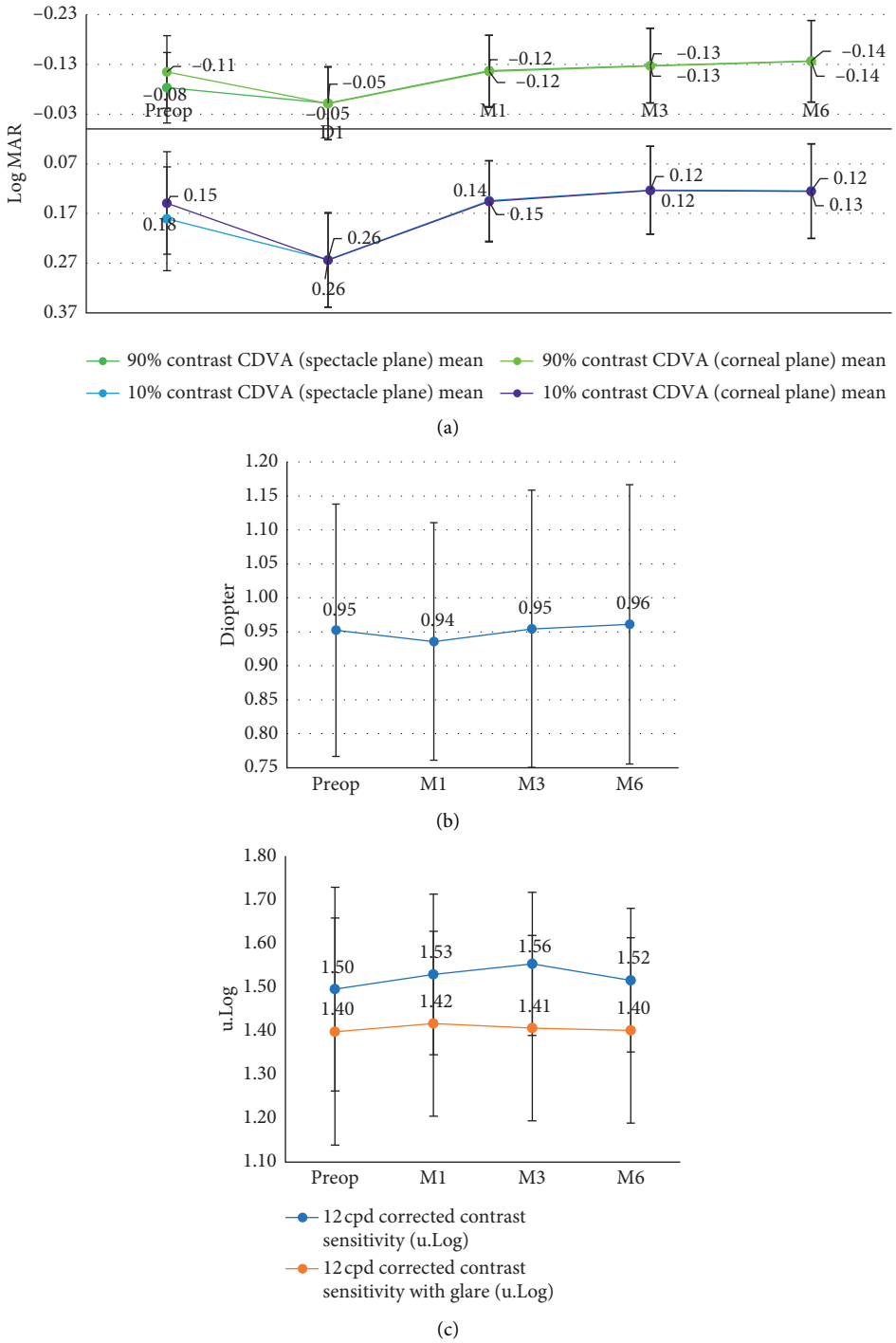


Figure 5: Evolution of visual outcomes after myopic LASIK. (a) Evolution of 90% and 10% contrast CDVA in the spectacle and the corneal planes. (b) Evolution of the corrected sensitivity to blur. (c) Evolution of 12 cpd corrected contrast sensitivity and 12 cpd corrected contrast sensitivity and 12 cpd corrected contrast sensitivity with glare.

In the 5 mm ring zone, the difference in simulated keratometry (sim-K) of the steepest and the flattest hemimeridians was calculated as the "sim-K difference" by topography software. The magnitude of the astigmatism was computed as the variation between the "sim-K difference" values. The average refractive astigmatism value decreased from 0.40 D preoperatively to 0.05 D 6 months postoperatively. And the corneal astigmatism decreased from 0.51 D to 0.19 D after LASIK. Before and after LASIK, the astigmatism was predominantly with the rule (WTR) except for the total refractive astigmatism which was oriented against the rule at 6 months (Figure 7(b)).

Table 2: Differences between high (cylinder ≥ 1.5 D) and low astigmatic eyes (cylinder < 1.50 D) in 90% and 10% corrected distance visual acuity (CDVA), in corrected contrast sensitivity and corrected contrast sensitivity with glare (CCS at 12 cycles per degree), and in corrected sensitivity to blur (CSB).

Safety	1 day postoperative ($n = 60$)			1 month postoperative ($n = 60$)			3 months postoperative ($n = 60$)			6 months postoperative ($n = 60$)		
	Percentage (95% CI)			Percentage (95% CI)			Percentage (95% CI)			Percentage (95% CI)		
	High astigmatism	Low astigmatism	p^*	Low astigmatism	Low astigmatism	p^*	High astigmatism	Low astigmatism	p^*	High astigmatism	Low astigmatism	p^*
CDVA												
Loss of 3 lines or more (90% contrast)	9%	4%	**0 039***			**0.037***			0.137			**0.005***
Loss of 2 lines (90% contrast)	27%	8%		9%				4%			2%	
Loss of 1 line (90% contrast)	36%	33%		27%	20%		36%	18%		55%	12%	
No loss or gain of lines (90% contrast)	18%	49%		45%	51%		55%	43%		45%	45%	
Gain of 1 line (90% contrast)	9%	6%		18%	27%		9%	29%			33%	
Gain of 2 lines (90% contrast)					2%			6%			8%	
Gain of 3 lines or more (90% contrast)												
Loss of 3 lines or more (10% contrast)	18%	14%	**0.008***	9%	2%	**0.035***		2%	0.751*		2%	0.08
Loss of 2 lines (10% contrast)	36%	18%		9%				8%			4%	
Loss of 1 line (10% contrast)	36%	22%		18%	22%		18%	16%		36%	18%	
No loss or gain of lines (10% contrast)	9%	37%		36%	41%		36%	27%		18%	27%	
Gain of 1 line (10% contrast)		8%		18%	27%		36%	31%		45%	39%	
Gain of 2 lines (10% contrast)					8%		9%	16%			8%	
Gain of 3 lines or more (10% contrast)				9%							2%	
CCS (12 cpd)												
Loss of 0.4 u.log or more	9%	31%	0.191	9%	6%	**0.001***	9%	4%	**0.001***	9%	2%	**0.001***
Loss of 0.1 to 0.4 u.log	64%	45%		27%	29%		9%	31%		18%	35%	
No loss or gain	9%	6%		27%	18%		18%	16%		36%	18%	
Gain of 0.1 to 0.4 u.log	18%	16%		27%	37%		55%	33%		27%	41%	
Gain of 0.4 u.log or more		2%		9%	10%		9%	16%		9%	4%	
Loss of 0.4 u.log or more (with glare)	—	—		9%	2%	**0.001***	9%	4%	**0.001***	9%	6%	**0.001***

Table 2: Continued.

Safety	1 day postoperative ($n = 60$) Percentage (95% CI)			1 month postoperative ($n = 60$) Percentage (95% CI)			3 months postoperative ($n = 60$) Percentage (95% CI)			6 months postoperative ($n = 60$) Percentage (95% CI)		
	High astigmatism	Low astigmatism	p^*	Low astigmatism	Low astigmatism	p^*	High astigmatism	Low astigmatism	p^*	High astigmatism	Low astigmatism	p^*
Loss of 0.1 to 0.4 u.log (with glare)	—	—		36%	37%		18%	37%		36%	33%	
No loss or gain (with glare)	—	—		18%	18%		27%	14%		18%	12%	
Gain of 0.1 to 0.4 u.log (with glare)	—	—		18%	37%		27%	37%		27%	43%	
Gain of 0.4 u.log or more (with glare)				18%	6%		18%	8%		9%	6%	
CSB												
Loss of 0.3 D or more					10%	0.197		8%	0.108		8%	0.29
Loss of 0.1 to 0.3 D				9%	29%			39%		9%	45%	
No loss or gain				36%	31%		18%	14%		9%	12%	
Gain of 0.1 to 0.3 D				45%	29%		73%	35%		73%	22%	
Gain of 0.3 D or more				9%	2%		9%	4%		9%	12%	

*Significant.

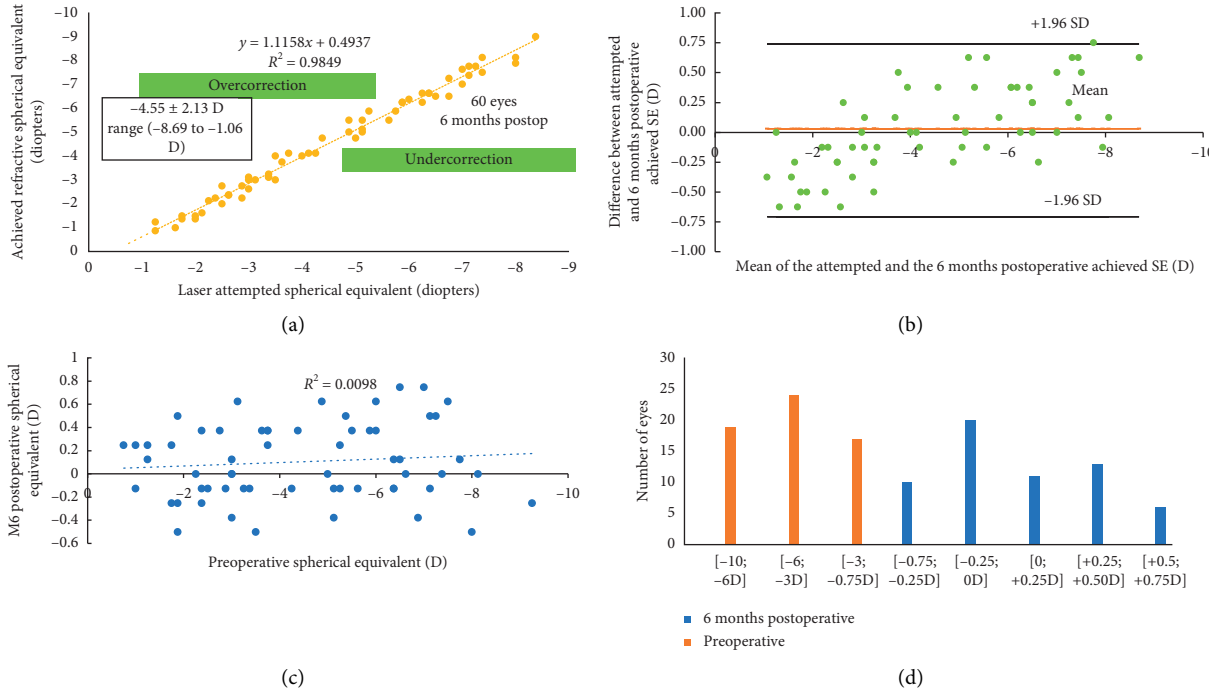


Figure 6: Refractive spherical equivalent (SE) outcomes: distribution of achieved SE outcomes after LASIK at 6 months (a), Bland–Altman distribution of attempted SE (b), correlation between preoperative SE and 6 months postoperative SE (c), and distribution of manifest SE preoperatively and 6 months postoperatively (d).

Figure 7 represents the magnitude and orientation of the refractive and anterior corneal astigmatism preoperatively and 6 months postoperatively. We found a difference of 0.58 D (for the refractive astigmatism) and 0.33 D (for the corneal astigmatism) between the two analysed periods.

There was no correlation between the 6-month postoperative cylinder value and the preoperative cylinder ($r^2 = 0.0013$; $p < 0.001$).

3.3.3. Corneal and Total Aberrations' Analysis on a 5.5 mm Pupil. Figure 8 and Table 3 show the very slight but significant increase in total, corneal, and internal ocular aberrations after LASIK surgery. The most important increase in corneal and total HOAs seems to be attributed to the increase of corneal coma (Figure 9). The total spherical aberration increased very slightly but significantly (0.034 ± 0.063; $p < 0.001$).

We found no correlations between total, corneal, and internal spherical aberrations after LASIK and preoperative SE ($r^2 = 0.03$; $p < 0.001$, $r^2 = 0.012$; $p < 0.001$, and $r^2 = 0.009$; $p < 0.001$, respectively). No predictive factor for the increase in postoperative HOAs was found (low r^2, $p > 0.05$). However, we found a positive correlation between total preoperative HOAs and M6 postoperative HOAs ($r^2 = 0.573$; $p < 0.001$).

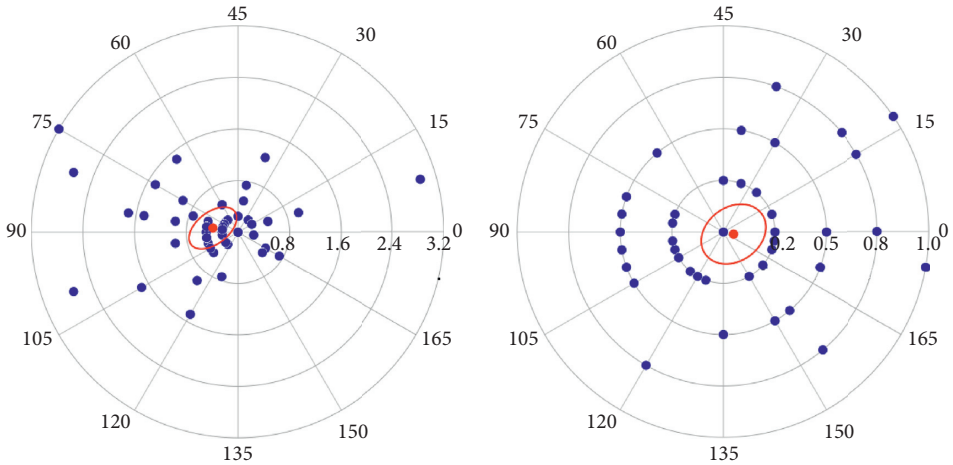
3.4. Efficacy, Stability, and Satisfaction. One day after LASIK surgery, the mean refractive spherical equivalent and keratometry were $+0.14 \pm 0.52$ D and 40.49 ± 1.70 D, respectively, and remained stable up to 6 months follow-up (Figure 10).

Six months postoperatively, 62% of eyes achieved high-contrast UDVA of −0.1 log MAR or better versus 42% CDVA before undergoing LASIK. Uncorrected CCS appeared unchanged 6 months postoperatively compared to corrected CCS in both normal and glare illumination conditions (Figure 11).

In both populations (preoperative contact lens wearers and nonwearers), QoV score was unchanged from preoperative levels (paired t-test, $p = 0.262$). The same observation was made for the OSDI questionnaire although it increased and then decreased significantly between preoperative and 6 months postoperative follow-up (Figures 12(a) and 12(c)). Figures 12(b) and 12(d) show that 6 months after LASIK, dry eye symptoms were more related to the QoV score than corneal HOAs, which may explain the lower quality of vision. We found no correlation between the QoV score at 6-month follow-up and the preoperative spherical equivalent ($r^2 = 0.0004$; $p < 0.001$).

4. Discussion

This study aims to explore the midterm post-myopic LASIK refractive surgery clinical results with the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA) by evaluating changes in ocular anatomical parameters, visual performance, and quality of vision. To the best of the authors' knowledge, there are few comprehensive studies that evaluate anatomical changes of

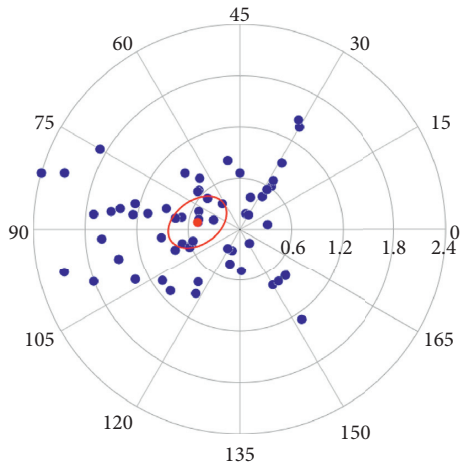


Arithmetic mean: 0.76 ± 0.76
Mean: 0.40 (±1.00) D at 85 (±15)°

(a)

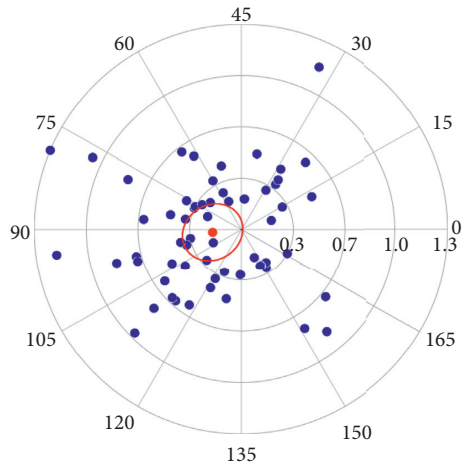
Arithmetic mean: 0.35 ± 0.24
Mean: 0.05 (±0.43) D at 174 (±19)°

(b)



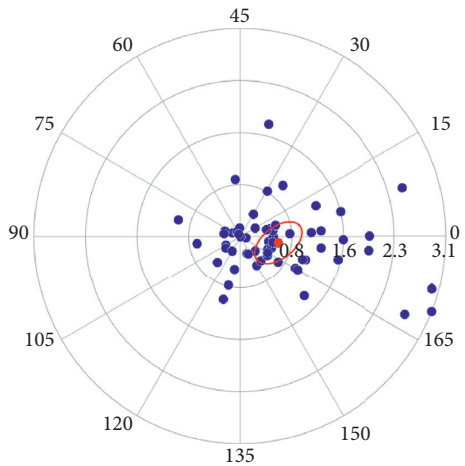
Arithmetic mean: 0.91 ± 0.53
Mean: 0.51 (±0.92) D at 85 (±17)°

(c)



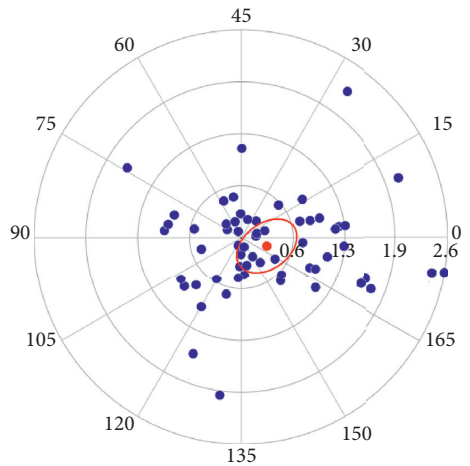
Arithmetic mean: 0.50 ± 0.27
Mean: 0.19 (±0.54) D at 93 (±21)°

(d)



Arithmetic mean: 0.84 ± 0.73
Mean: 0.58 (±0.95) D at 176 (±15)°

(e)



Arithmetic mean: 0.85 ± 0.60
Mean: 0.33 (±1.00) D at 171 (±17)°

(f)

Figure 7: Preoperative refractive astigmatism (a), 6 months postoperative refractive astigmatism (b), preoperative corneal astigmatism (c), and 6 months postoperative corneal astigmatism (d). Difference between preoperative and 6 months postoperative refractive astigmatism (e) and corneal astigmatism (f).

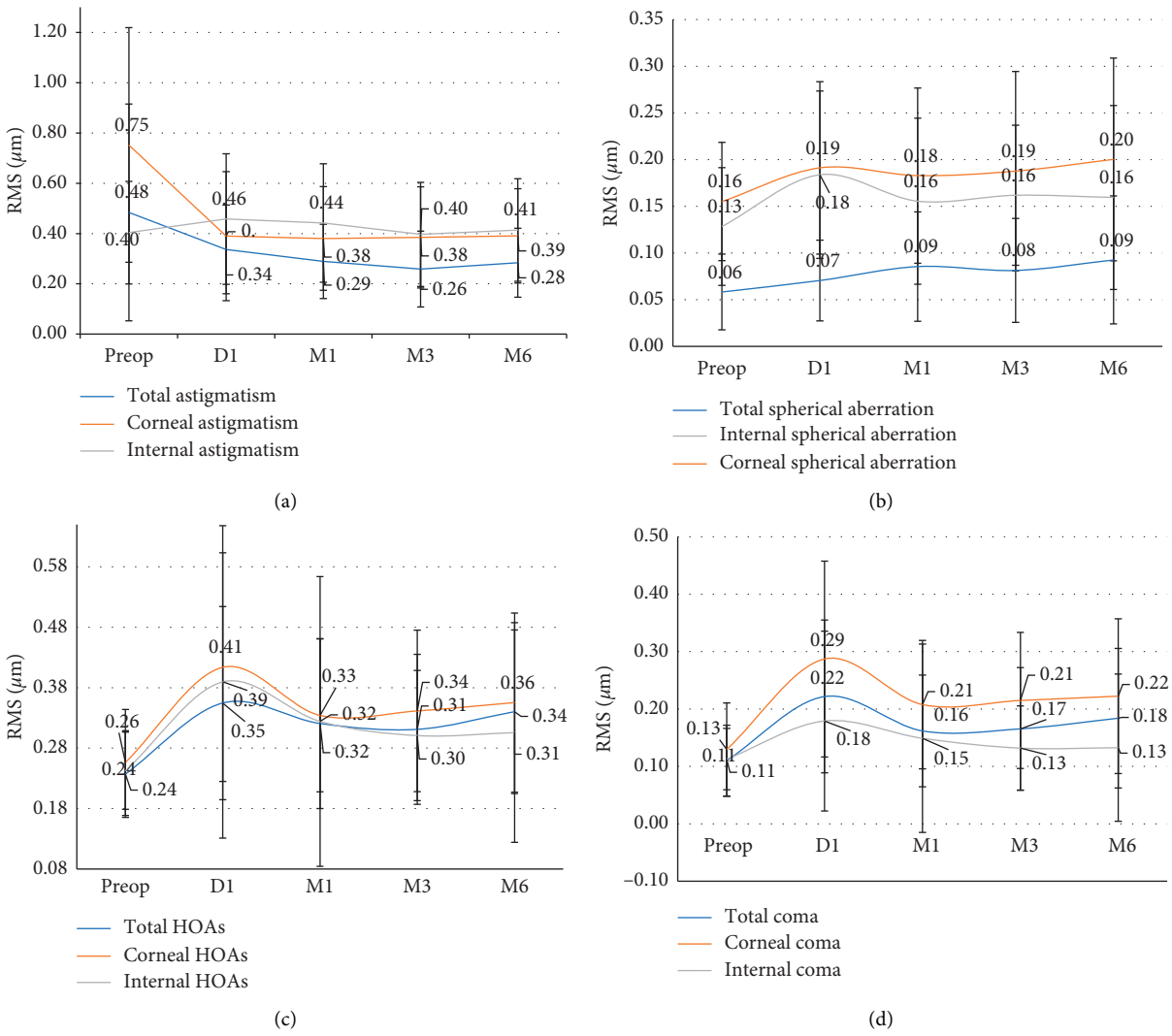


Figure 8: Evolution of RMS ocular total, corneal, and internal aberrations (μm): astigmatism evolution (a), spherical aberration evolution (Zernike SA4 + SA12) (b), high-order aberrations (HOAs: 3rd order and higher) (c), and coma evolution (d).

Table 3: Evolution of RMS ocular total, corneal, and internal aberrations (μm).

Aberrations (RMS in μm)	Preoperative Mean ± SD	6 months postoperative Mean ± SD	Difference Mean ± SD	p
Total high-order aberrations (HOAs)	0.237 ± 0.072	0.340 ± 0.135	0.103 ± 0.111	$p < 0.001^*$
Total coma	0.11 ± 0.062	0.184 ± 0.121	0.074 ± 0.108	$p < 0.001^*$
Total spherical aberrations (SA4 + SA12)	0.058 ± 0.04	0.093 ± 0.069	0.034 ± 0.063	$p < 0.001^*$
Corneal high-order aberrations (HOAs)	0.256 ± 0.088	0.355 ± 0.148	0.099 ± 0.115	$p < 0.001^*$
Corneal coma	0.130 ± 0.081	0.222 ± 0.135	0.093 ± 0.118	$p < 0.001^*$
Corneal spherical aberrations (SA4 + SA12)	0.155 ± 0.063	0.200 ± 0.109	0.045 ± 0.082	$p < 0.001^*$
Internal high-order aberrations (HOAs)	0.243 ± 0.064	0.306 ± 0.182	0.063 ± 0.175	$p < 0.01^*$
Internal coma	0.113 ± 0.053	0.133 ± 0.128	0.02 ± 0.128	$p = 0.26$
Internal spherical aberrations (SA4 + SA12)	0.128 ± 0.063	0.159 ± 0.099	0.031 ± 0.10	$p = 0.027^*$

*Significant.

the eye and report outcomes following myopic femtosecond LASIK performed with this Refractive Suite [16, 51–54].

4.1. Anatomical Changes. The pachymetry decreased noticeably on D1 and then increased again until 6 months postoperatively. These results could be explained by the fact

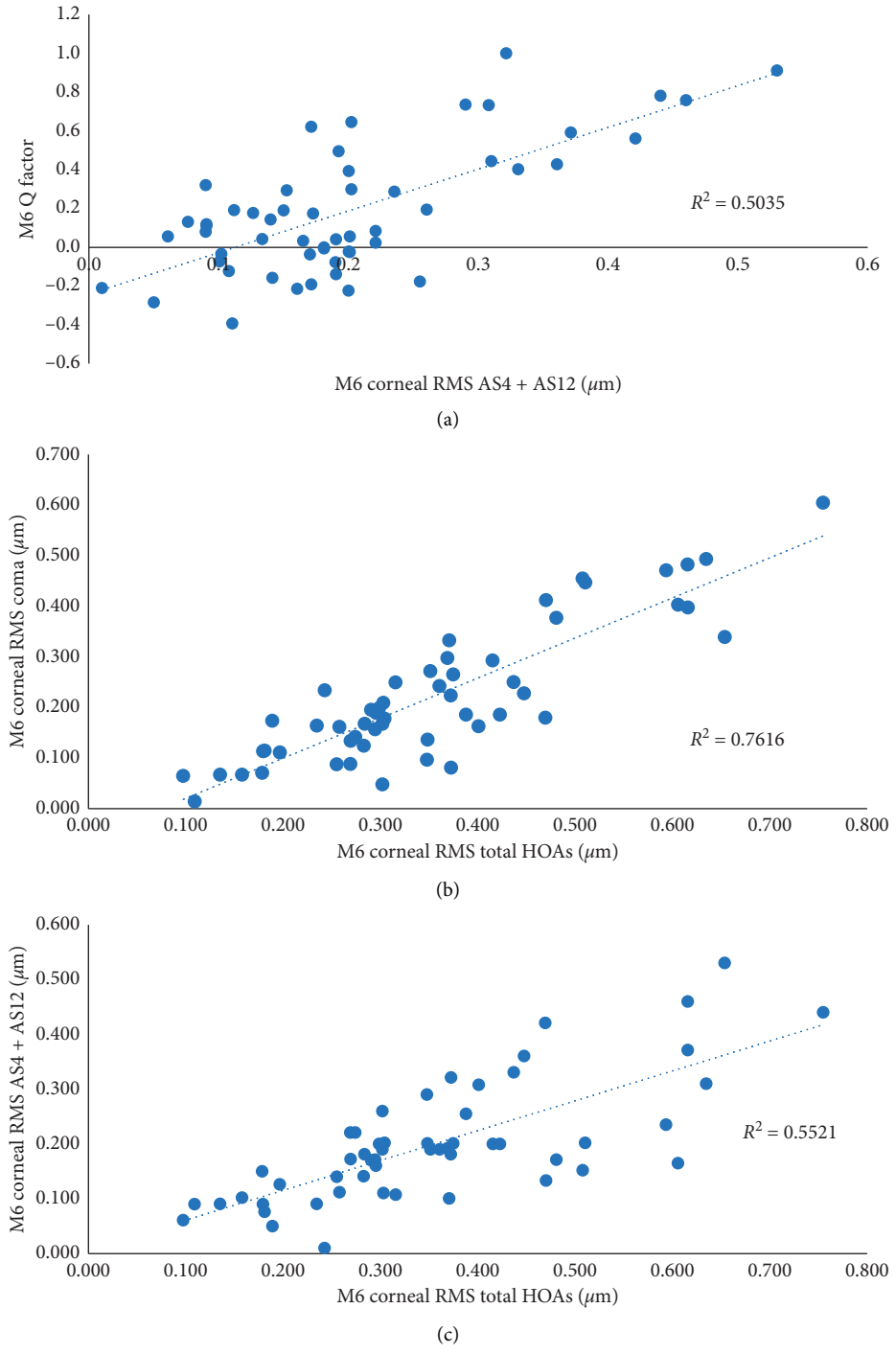


Figure 9: Relationship between spherical corneal aberrations and Q factor (a), between corneal HOAs and corneal coma (b), and between corneal HOAs and corneal spherical aberrations (c).

that Orbscan IIz® (Bausch & Lomb®, USA), which uses a scanning-slit topography system-based measurement of the corneal tomography, largely underestimates the real thickness of the cornea at D1 because of the oedema generated by LASIK [51]. The oedema disappears few days after the LASIK procedure, and the estimation of the pachymetry becomes closer to the real one. Indeed, it is well known that the post-LASIK accuracy of Orbscan II is poorer compared to other devices, but it still gives a good indication on the "pachymetric dynamics." As a matter of fact, this constitutes a limit of our study. However, Hassan Hashemi and Shiva Mehravaran, in a paper published in the JCRS in 2007, concluded that although Pentacam seems to show better agreement than Orbscan II, especially after refractive surgery, it is not advisable to use different devices interchangeably in every clinical situation [55].

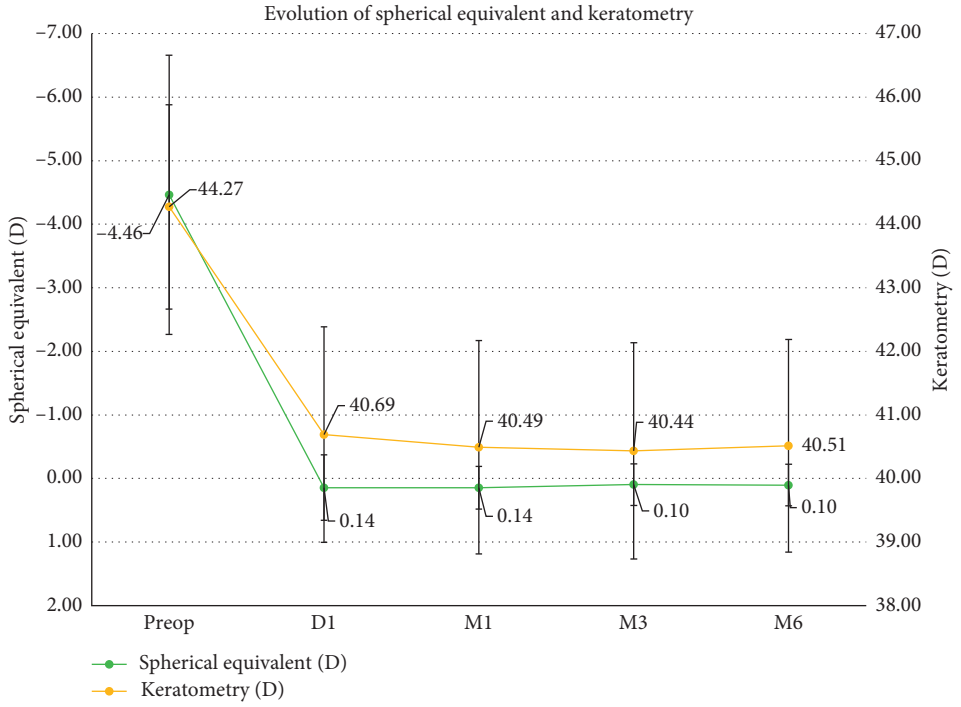


Figure 10: Stability of keratometry and spherical equivalent refraction after LASIK between 1 day and 6 months.

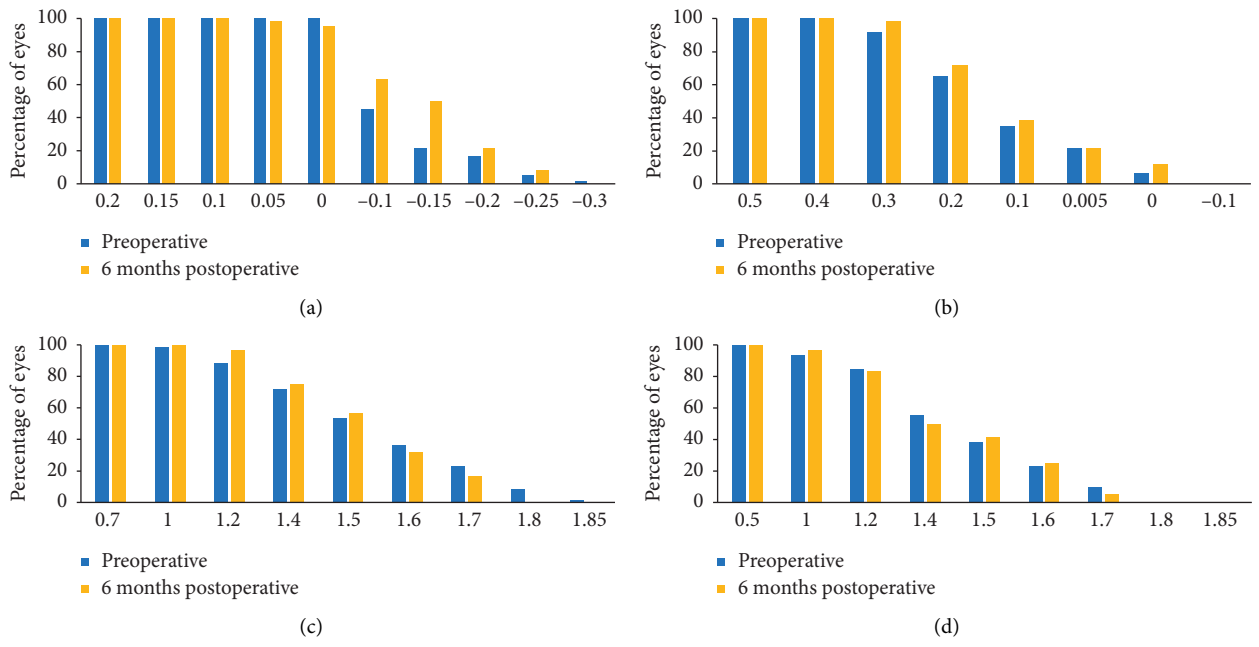


Figure 11: Changes in 90% contrast (a) and 10% (b) uncorrected distance visual acuity and uncorrected contrast sensitivity (c) and uncorrected contrast sensitivity with glare (d) at 6 months of follow-up after LASIK.

Otherwise, Smadja et al. [51] reported in 2012 that posterior steepening and a shift toward prolateness of the corneal posterior surface were observed very early after myopic LASIK, with a tendency to return toward the preoperative level between 1 month and 3 months. Finally, it has also been described in the literature that there is an epithelial hyperplasia that occurs gradually a few weeks after LASIK [52, 56]. In other words, the increase of pachymetry from D1 to M6 could be partly due to the ability of the epithelium to reshape the operated corneal surface and keep the refraction stable, but without an actual impact on the keratometry if the hyperplasia occurs

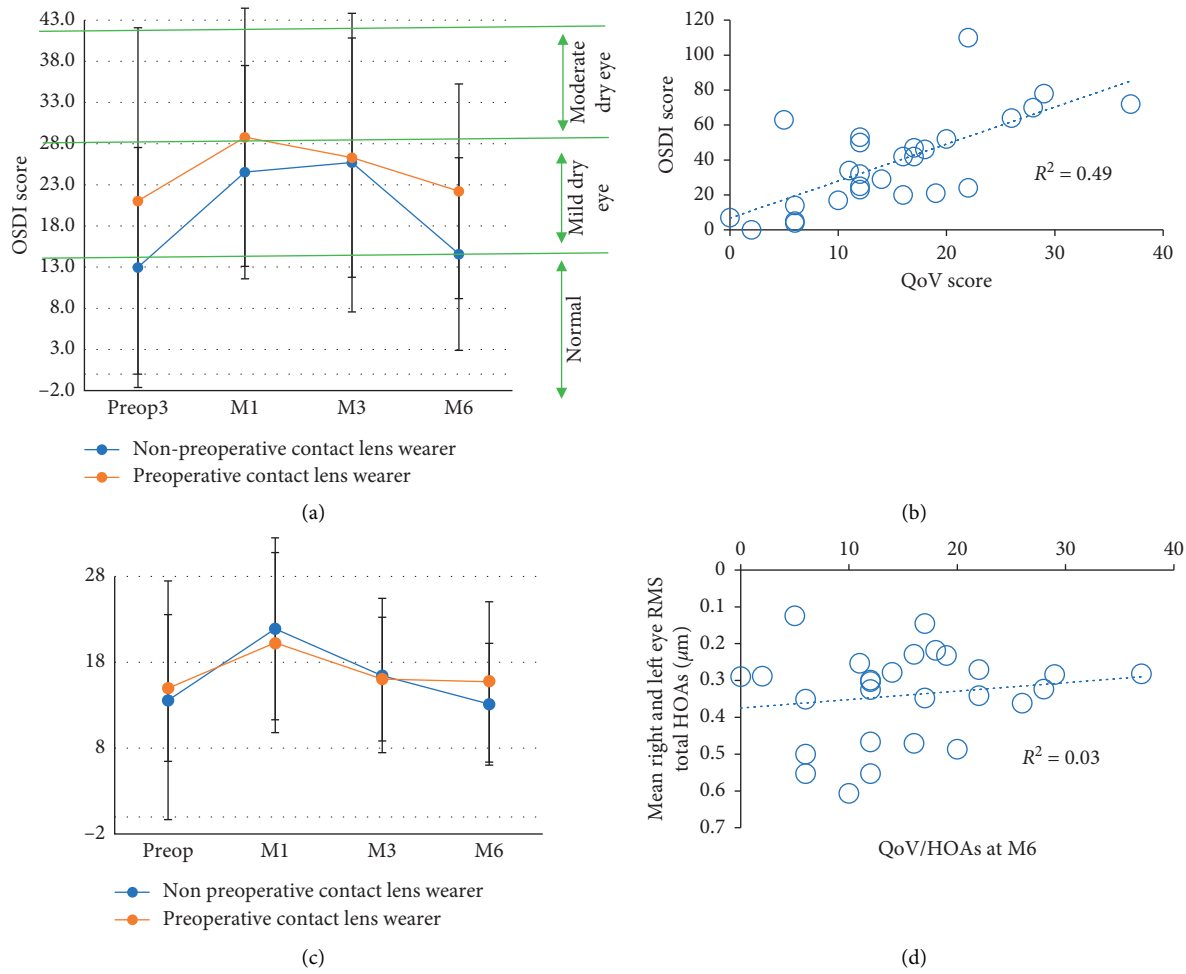


Figure 12: Evolution of QoV (a) and OSDI (c) scores and relationship between the QoV score and the OSDI score (b) and total HOAs (d).

uniformly in the operated zone, which is the case in the present study.

Figure 4 shows that, in our study, the excimer laser ablated more in the central cornea than the Munnerlyn formula planes by a factor of 16%. Indeed, as the Munnerlyn formula does not consider possible variations in corneal asphericity, actual aspheric treatments induce a slightly different central ablation depth (and ablate more in the peripheries) which allows to maintain a level of postoperative spherical aberration close to preoperative levels [57–60].

One day after LASIK, the corneal asphericity expressed by the Q factor became significantly more oblate, and Figure 9 shows that even as the asphericity changed, the spherical aberration calculated on a 5.5 mm pupil increased very slightly ($+0.034 \pm 0.063$). This result is consistent with the increased ablation in the central and peripheral cornea to maintain a low level of positive spherical aberration induced by the surgery [61].

4.2. Safety and Predictability

4.2.1. Quality of Vision Outcomes. Figure 5 shows results are consistent with the literature [15, 53]. However, regarding contrast sensitivity, it would have been preferable to study additional spatial frequencies. Indeed, Tuan [15] reported differences in outcomes between different spatial frequencies. We chose to test only the spatial frequency at 12 cpd to ensure the patient remained in comfortable conditions and without overexertion (and thus distortion of the results) due to the long examination sessions (2 hours).

Although there was no difference in the quality of vision outcomes (CDVA and CSB) preoperatively between high (cylinder ≥ 1.5 D) and low astigmatic eyes (cylinder$<$ 1.50 D) except for the CCS (where the high astigmatic eyes CCS was smaller than the low astigmatic one (ANOVA, $p = 0.016$)) and no difference in 6 months postoperative residual SE, the high astigmatic eyes had a poorer postoperative CDVA and CCS. This may be due to underoptimized astigmatism ablation profiles and/or nomogram of the excimer. However, we can highlight that the low number of high astigmatic eyes (cyl >1.5 D, only 11 eyes) constitutes a limitation in our study. Indeed, even if the result was statistically significant, we were not sure that we could make robust generalized conclusions for these eyes with astig >1.5 D.

4.2.2. Refractive Spherical Equivalent Outcomes and Astigmatism. The outcomes showed an extremely high predictability and accuracy (Figures 6(a) and 6(b)). These

results are consistent with those reported previously by Kanellopoulos and Asimellis [53]. Furthermore, we found that postoperative residual SE was independent from the preoperative degree of myopia and that the high and low astigmatic eyes had the same residual SE. The 6-month postoperative refractive and corneal residual cylinders were low, and we did not find any correlation between the preoperative refractive cylinder and 6-month postoperative cylinder. This suggests that this LASIK technique is predictable in all cases in our sample of eyes. However, it must be noted that our sample did not include eyes with very high amount of astigmatism (maximum included: −3.25 D).

4.2.3. Corneal and Total Aberrations' Analysis on a 5.5 mm Pupil. We note that the evolution profile of coma corresponds to the evolution profile of total, corneal, and internal high-order aberrations (Figure 8 and Table 3). Furthermore, the most important increase in corneal and total HOAs seems to be attributed to the increase of corneal coma (Figure 9). Our results were comparable with those reported by Glydenkerne et al. [62] on a 5 mm pupil. Coma corresponds to a treatment decentration. It is possible then that the increased amount of coma may have been induced by the choice of the centration strategy (i.e., 50% decentration towards the corneal vertex) we planned for all patients.

On a 5.5 mm pupil diameter, the total spherical aberration was well controlled (increased very slightly but significantly (0.034 ± 0.063, $p < 0.001$)) due to the aspheric ablation profiles. These findings indicate that the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA) aspheric ablation profile seems to limit the increase in postoperative HOAs [61].

Again, our results were comparable with those described by Krueger and Chan [57], but highly different from those reported by Glydenkerne et al. [62] and Bühren et al. [54], where the increase measured on a smaller pupil (5 mm) was, respectively, 0.15 ± 0.084 and 0.153 measured on 6 mm pupil PMMA lenses that received excimer aspheric ablation profile. This is probably due to the less aspheric ablation profile of the excimer laser used.

Moreover, we found that the spherical aberration at M6 was independent from the amount of the corrected myopia (no correlations between total, corneal, and internal spherical aberrations after LASIK and preoperative spherical equivalent ($r^2 = 0.03$, $p < 0.001$, $r^2 = 0.012$, $p < 0.001$, and $r^2 = 0.009$, $p < 0.001$, respectively)), which is consistent with the optimized aspheric profile we mentioned previously.

However, we found a positive correlation between total preoperative HOAs and M6 postoperative HOAs ($r^2 = 0.573$, $p < 0.001$). Again, this is in favour of a minimal impact of excimer ablation on the increase of HOAs.

Finally, the internal aberrations can be computed by subtracting corneal from total aberration coefficients. Figure 8 and Table 3 show the internal aberrations before and after LASIK surgery. We found a very slight but significant increase in internal ocular aberrations studied (except for internal coma) after LASIK surgery. This increase was higher at D1 postoperatively and then decreased between 1 and 6 months after surgery. Although the LASIK procedure is performed on the anterior surface of the cornea, internal aberrations follow the same evolution profile as corneal and total aberrations. In a previous study [29], Marcos et al. came to the same conclusion. They described their experience in control subjects who had undergone a surgical procedure performed in two different experimental sessions (separated by at least 1 month, as in the surgical eyes) which did not reveal statistically significant changes in the internal aberrations across sessions. This indicated that possible changes across sessions in the accommodative state or decentrations of corneal topography data cannot account for the observed differences in the internal optics found between pre- and post-LASIK results. Therefore, we can conclude that these changes must be attributable to the surgery and specifically to a biomechanical reaction of the posterior surface of the cornea to the surgery [29, 51].

4.3. Efficacy, Stability, and Satisfaction. 6 months after surgery, 62% of eyes achieved high-contrast UDVA of −0.1 log MAR or better versus 42% CDVA before undergoing LASIK. Uncorrected CCS appeared unchanged 6 months postoperatively compared to the corrected CCS in both normal and glare illumination conditions (Figure 11). LASIK surgery showed good outcomes in terms of efficacy and stability.

Furthermore, in both preoperative contact lens wearers and nonwearers, the QoV score did not change from the preoperative level (paired t-test; $p = 0.262$). Ocular dryness increased significantly after surgery and returned to the baseline level at M6 (Figures 12(a) and 12(c)). Figures 12(b) and 12(d) show that 6 months after LASIK, QoV score was more related to dry eye symptoms than to corneal HOAs. The quality of vision at M6 did not depend on the preoperative degree of myopia ($r^2 = 0.0004$; $p < 0.001$) neither on the M6 SE ($r^2 = 0.0013$; $p < 0.001$). Therefore, we can assume that the patient's quality of vision depends more on the postoperative dry eye disease generated by the laser than on the induced HOAs (which are low in this study) or the patient's initial spherical equivalent correction.

Therefore, we can conclude that LASIK surgery for correction of myopia performed with the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA) showed good postoperative outcomes and good safety, predictability, efficiency, and stability of postoperative outcomes. These results are likely due to good control of spherical aberration with high performance of aspheric ablation profiles, as well as the use of large optical zones. In addition, our results suggest a change in the shape of the posterior corneal surface as a result of the surgery. Finally, we believe that improvement is required in two main areas: (1) an increase in the predictability of outcomes in eyes with high astigmatism and (2) improved solutions for the issue of ocular dryness.

Our data analysis was limited to 6-month follow-up. Further studies are necessary to investigate potential changes occurring after this time period.

Data Availability

The data set is available at the Rothschild foundation hospital and could be provided if needed.

Additional Points

What Was Known. LASIK surgery for moderate to high myopia, performed with the WaveLight® Refractive Suite, showed good postoperative outcomes, with demonstrated safety, predictability, efficiency, and stability. This is probably due to well-controlled spherical aberration and the use of large optical zones. *What This Paper Adds.* Prior to this paper, there was no exhaustive study performed on the anatomical and visual outcomes after LASIK in moderate to high myopia with the WaveLight® Refractive Suite (Alcon® Laboratories Inc., USA) on a large sample of patients with such an accurate methodology. We have demonstrated that the patient's quality of vision depends more on the postoperative dry eye disease generated by the laser than on the induced HOAs.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Long-Term Evaluation of Capsulotomy Shape and Posterior Capsule Opacification after Low-Energy Bimanual Femtosecond Laser-Assisted Cataract Surgery

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Purpose. To evaluate capsulotomy shape and posterior capsule opacification (PCO) during an 18-month follow-up for bimanual femtosecond laser-assisted cataract surgery (FLACS). *Methods*. 74 eyes operated by a well-trained surgeon with bimanual FLACS technique using low-energy LDV Z8 (Ziemer Ophthalmic Systems AG, Port, Switzerland) were included in the study. The follow-up period was 18 ± 2 months. Another 91 eyes, which underwent standard bimanual microincision cataract surgery (B-MICS), served as a control group. In all cases, a BunnyLens AF (Hanita Lenses, Israel) intraocular lens was implanted in the bag. A digital image of the capsule with slit-lamp retroillumination was performed in all patients at 18 months of follow-up. Image analysis software (ImageJ) was used to evaluate the shape of the capsulotomy in terms of diameter, area, and circularity. PCO score was evaluated using EPCO 2000 software. Best corrected visual acuity (BCVA) and endothelial cell count (ECC) were evaluated before and after surgery at 1 and 18 ± 2 months. *Results*. At 18 months, mean capsulotomy diameter was 5.34 ± 0.21 mm while capsulorhexis was 5.87 ± 0.37 mm ($p < 0.001$) and the deviation area from baseline was $1.13 \pm 1.76\,\text{mm}^2$ in FLACS and $2.67 \pm 1.69\,\text{mm}^2$ in B-MICS ($p < 0.001$). Capsulotomy circularity was 0.94 ± 0.04 while capsulorhexis was 0.83 ± 0.07 ($p < 0.001$). EPCO score was 0.050 ± 0.081 in the FLACS group and 0.122 ± 0.239 in the B-MICS group ($p = 0.03$). The mean BCVA improvement was significant in both groups, without a significant difference at 18 months. We noticed a statistically significant difference in endothelial cell loss at 18 months (FLACS 12.4% and B-MICS 18.1%; $p = 0.017$). *Conclusions*. Bimanual FLACS is a safe and effective technique, as determined in a long-term follow-up. Capsulotomy shape presented higher stability and circularity in the FLACS group over the 18-month observation period. FLACS resulted in lower PCO scores and endothelial cell loss at 18 months in comparison to B-MICS standard technique.

1. Introduction

Age-related cataract is the second cause of moderate-to-severe vision impairment among the global population after uncorrected refractive errors. The strong impact of cataract in the public health justifies ophthalmological community interest in increasing precision and safety in cataract surgery [1].

In recent years, the use of a femtosecond laser has been introduced to assist the surgeon during cataract surgery. Even though femtosecond laser-assisted cataract surgery (FLACS) does not seem to show any significant difference with respect to refractive and visual outcomes when compared to standard phacoemulsification, recent studies showed better accuracy and reproducibility in the execution of corneal incisions, highly precise anterior capsulotomies, and nucleus fragmentation/liquefaction associated with a lower phacoemulsification energy and limited manipulation inside the eye [2–5].

The femtosecond laser LDV Z8 (Ziemer Ophthalmic Systems AG, Port, Switzerland) is a nonapplanating liquid patient interface femtolaser system characterized by high

frequency and low energy [6]. It allows overlapping of very small laser spots creating a precise cut with minor gas bubbles and inflammation comparing to other femtolaser machines. It is entirely mobile, and its small dimensions allow surgeons to carry out the whole surgical operation in the same operating room, avoiding questionable patient transfer.

Bimanual microincision cataract surgery (B-MICS) is a variant of traditional coaxial phacoemulsification characterized by its incisional microinvasiveness (1.4 mm incisions) [7, 8]. The increased stability of the anterior chamber, the separation of the aspiration and the infusion probe together with the small instrument size, and greater visibility of the surgical field make it a safe and effective technique to be used in combination with a femtosecond laser [9–11].

It is well established that a perfect circular and properly sized capsulotomy is essential for stable results over time and better intraocular lens (IOL) position, especially for "premium" cataract surgery (multifocal and toric IOLs) [12]. Moreover, a better IOL overlapping with the anterior capsule has seen to cause less posterior capsule opacification (PCO) [13].

In a recent study, with a 3-month follow-up period, we demonstrated that the low-energy/high-frequency properties of the LDV Z8 laser pulse, combined with the overlapped pulse-pattern, resulted in highly continuous morphology of capsule edges. [14]. In addition, a higher apoptosis induction (Caspase-3 analysis) of the epithelial cells of the capsule edge has been demonstrated at confocal immunofluorescence in FLACS in comparison to manually performed capsulorhexis in standard cataract surgery [14, 15], which could reduce the incidence of PCO during the follow-up.

To our knowledge, currently there are no studies investigating PCO incidence and capsulotomy shape in FLACS with a low-energy/high-frequency femtosecond laser.

The aim of the study was to evaluate the shape of anterior capsulotomy and PCO incidence during an 18-month follow-up for bimanual FLACS with a low-energy femtosecond laser, comparing the results with a control group of standard B-MICS interventions. Secondary outcomes were best corrected visual acuity (BCVA) and endothelial cell count evaluated preoperatively and at 18-month follow-up.

2. Methods

We retrospectively reviewed the data of 165 eyes who underwent cataract surgery at the Institute of Ophthalmology of the University of Modena and Reggio Emilia between March 2016 and July 2018. Seventy-four eyes underwent bimanual cataract surgery using FLACS technique (FLACS); 91 eyes, operated with the B-MICS standard technique, were chosen as a control group. All surgeries were carried out by the same expert surgeon (GMC). Patients in both groups were similar in age, gender, and lens LOCS III score (Table 1). The study was approved by the Ethics Committee of the University of Modena and Reggio Emilia (Modena, Italy) and was conducted in compliance with the Declaration of Helsinki. Informed consent was obtained before surgery.

Exclusion criteria included eyes with previous surgery, complicated cataracts (e.g., hard cataracts, traumatic cataract, and pseudoexfoliation syndrome), insufficient mydriasis (<4 mm), concomitant eye pathologies (e.g., uveitis, glaucoma, corneal opacities, and diabetic retinopathy), low endothelial cell count (<1500 cells/mm^2), and monocular patients.

A detailed clinical history evaluation was carried out on all the patients prior to surgery with best corrected visual acuity (BCVA) examination, anterior segment biomicroscopy, and fundus examination. Biometry was performed with IOL Master (Carl Zeiss Meditec, Jena, Germany) and corneal microscopy with a Noncon Robo-CA (Konan Medical Inc., Hyogo, Japan).

Patients applied nonsteroidal anti-inflammatory drug (NSAID) drops preoperatively 3 times a day for 3 days before surgery in both groups.

A consistent mydriasis was obtained before surgery with the instillation of atropine 1.0%, phenylephrine 10%, and cyclopentolate 1%, and a locoregional anaesthesia was carried out with peribulbar block (1.5 ml of lidocaine 2% and 1.5 ml of bupivacaine 0.5%). All interventions were performed using the same phacoemulsifying machine (Faros, Oertli Instruments AG, Berneck, Switzerland). Standard B-MICS and FLACS surgery using the bimanual technique with the LDV Z8 and IOL implantation through a 1.4 mm incision have been previously described [11].

FLACS capsulotomy diameter was 5.2 mm in all cases. The surgeon implanted the same model of hydrophilic acrylic BunnyLensAF IOL (Hanita Lenses, Israel) in all eyes.

BCVA and endothelial cell count (ECC) were evaluated after surgery at 1 and at 18 ± 2 months using the instruments previously described. In particular, ECC was evaluated by manually counting a group of cells and then providing a rapid morphometric automated endothelial analysis by the machine. The same experienced doctor carried out all these examinations.

Digital retroilluminated images of the pseudophakic anterior segments of the eyes were taken at day-1 and again at 18 ± 2 months postoperative follow-up visit using a camera connected to the slit lamp. Images of the capsule were taken following dilation of the pupil in all patients.

Image analysis software (ImageJ) was used to evaluate the shape of the capsulotomy.

ImageJ is biomedical imaging software for scientific image analysis, which is available as a free download from an open platform [16, 17].

Capsulotomy/capsulorhexis analysis was carried out in three phases: firstly, the scale was defined by measuring the size in pixels for a feature of known true size. In this case, the 6 mm IOL optic plate diameter was first calculated on an image. The number of pixels that corresponded to 6 mm was calculated. Then, the contour of the anterior capsule edge was defined by the operator. Finally, through an automated analysis, the software calculated the major and minor diameter (mm), the area (mm^2), and the coefficient of circularity (from 0 = lower circularity to 1 = perfect circularity). (Figure 1).

Table 1: Comparison of demographic data at baseline for both groups.

	Group A (FLACS)	Group B (B-MICS)	p value*
Eyes *(n)*	74	91	—
Mean age *(y)* ± *SD*	73.19 ± 6.88	74.70 ± 8.32	$p > 0.05$
Right/left eyes *(n)*	40/34	52/39	$p > 0.05$
Male/female *(n)*	24/32 (56)	22/41 (63)	$p > 0.05$
Cataract grade (LOCS III)	2.37 ± 0.49	2.49 ± 0.50	$p > 0.05$

PCO score was evaluated using the computer-based software Evaluation of Posterior Capsule Opacification 2000 (EPCO2000) at 18 ± 2 months of follow-up. This software is based on the morphological assessment of PCO and allows a quantitative and qualitative evaluation of the amount of IOL surface affected by opacification, as previously described [18].

The EPCO2000 software was used to evaluate each image providing a final PCO score for every eye examined. The PCO score for each eye is calculated by multiplying the density of the opacification, graded from 0 (none) to 4 (severe), by the fractional PCO area involved behind the entire IOL optics. Density areas were identified and marked interactively on the computer screen by the same expert observer who was blinded to the surgical procedure used (Figure 2).

The neodymium-yttrium-aluminum-garnet (Nd : YAG) laser capsulotomy rate was recorded.

An Excel database (Microsoft Excel 2010 and Microsoft Office Professional Plus 2010) was used to record all data; for data analysis, we used Stata 13.1 software (StataCorp LP, College Station, TX, USA) with Student's t-test and the Wilcoxon rank sum test. A post hoc power analysis was applied to verify the features of two groups. Statistical significance was indicated by a p value <0.05.

3. Results

Group A consisted of 74 eyes (40 right eyes and 34 left eyes) of 42 patients (24 males and 32 females); the average age was 74.83 ± 5.29 years.

Group B was made up of 91 eyes (52 right eyes and 39 left eyes) of 63 patients (22 males and 41 females); the average age was 75.94 ± 8.95 years.

The two groups were homogeneous and comparable for age and gender with no statistical and clinical differences (Table 1). No intraoperative complications were recorded. A BunnyLens AF IOL was implanted in all eyes. All IOLs were implanted in the capsular bag.

Demography of the study population is summarized in Table 1. Results in both groups are reported in Tables 2–4.

3.1. Continuous Curvilinear Capsulotomy/Capsulorhexis (CCC). Concerning anterior capsule opening diameters, our analysis showed that FLACS capsulotomy presented lower changes in mean diameter and mean area over an 18-month follow-up than B-MICS capsulorhexis.

In particular, capsulotomy diameter variation was 0.14 ± 0.21 mm while that of capsulorhexis was 0.29 ± 0.19 mm ($p < 0.001$). We registered a lower mean area variation in FLACS (1.13 ± 1.76 mm^2) than in B-MICS (2.67 ± 1.69 mm^2) ($p < 0.001$).

Moreover, the circularity index at 18 months was 0.94 ± 0.04 in FLACS while 0.83 ± 0.07 in B-MICS ($p < 0.001$). All the results are shown in Table 2 and Figure 3.

3.2. PCO Incidence. PCO score in FLACS was lower (0.050 ± 0.081) than B-MICS (0.122 ± 0.239), and the difference was statistically significant ($p = 0.03$). PCO was registered in 5 cases out of 71 (6.8%) for FLACS and 27 cases out of 91 (29.7%) for B-MICS.

Nd : YAG laser capsulotomy at 18 months was necessary only in 1 case for FLACS and in 8 cases for B-MICS. Detailed results are reported in Table 3 and Figure 4.

3.3. Postoperative Results. In the FLACS group, at the 18-month follow-up mark, a mean BCVA improvement of 0.404 ± 0.346 LogMAR was observed and was statistically significant from baseline ($p < 0.001$). Similarly, in the B-MICS group, a mean BCVA improvement of 0.400 ± 0.261 LogMAR was observed ($p < 0.001$). However, the difference in the improvement of visual acuity between the two groups was not statistically significant ($p = 0.46$).

Regarding the ECC, at the 18-month follow-up visit, a mean endothelial cell loss of 288 ± 424 cells/mm^2 in Group A (12.4%) and of 443 ± 356 cells/mm^2 in Group B (18.1%) was observed and showed a reduction that was statistically significant between the two groups ($p = 0.017$) (Table 2).

4. Discussion

With the introduction of femtosecond laser technology, cataract surgery is experiencing a period of change and scientific fervor. The femtosecond laser does not only assist and facilitate cataract surgery but also standardizes some crucial steps: allowing precise and reproducible corneal microincisions, perfectly circular and centered anterior capsulotomies, and lens fragmentation, thus, ultimately leading to a reduction in ultrasound energy.

Recently, we published a paper about the safety and effectiveness of the combination of FLACS with bimanual technique [11]. However, the usefulness of FLACS is still debated since recent meta-analyses showed no statistically significant differences with standard manual cataract surgery in terms of visual and refractive outcomes and general complications [2–5]. Many surgeons maintain conflicting views on the effective large-scale spread of this surgical technique in the near future.

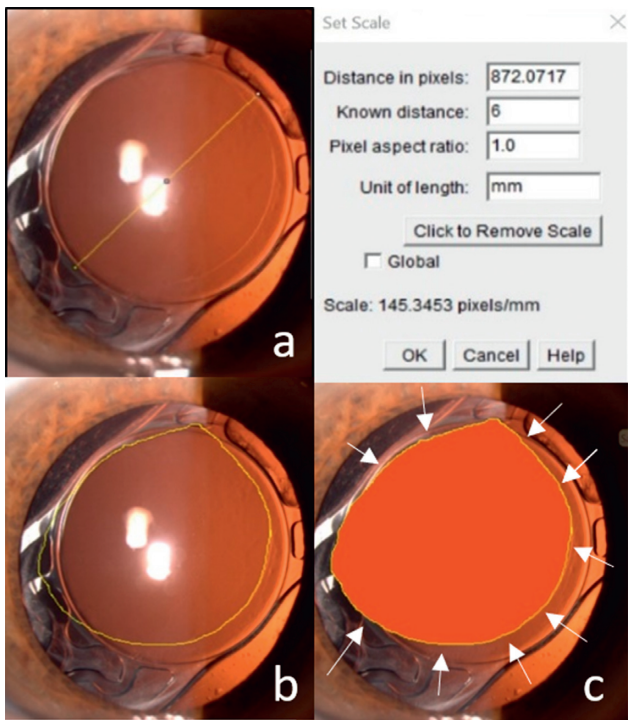

Figure 1: Anterior capsule opening analysis with ImageJ software. (a) Setting of the scale measuring the 6 mm IOL optic plate diameter as known true size. (b) Laying out of the contour of anterior capsule edge. (c) Software analysis (capsulotomy area indicated in red).

The interest of the scientific community is nowadays rather focused on the evaluation of long-term effects of FLACS as this procedure could have a positive influence on IOL stability and PCO incidence over time in comparison to the standard technique.

A recent study reported a more precise and stable capsulotomy in FLACS patients in a 12-month follow-up period using a high-energy/low-frequency femtosecond laser platform in comparison to a control group [19].

In this study, we investigated long-term (18 months) results obtained by an expert surgeon with bimanual FLACS technique with a low-energy/high-frequency femtolaser in terms of capsulotomy shape and PCO incidence. We also evaluated visual outcomes and endothelial cell loss at 18 months after surgery. We compared results with a control group. Up to date, there are no studies on a long-term evaluation of FLACS treated with a low-energy/high-frequency femtosecond laser.

Recent scientific investigations have proven that FLACS capsulotomies are more predictable, regular, and better-centered than manual ones, leading to safer surgery and a positive influence on visual recovery and patient satisfaction [20]. Moreover, the regularity of the capsulotomy/rhexis shape and size influences the position of the IOL and the predictability of the calculated power for the IOL [21, 22]. It is well known that if the CCC is too small, it can cause a hyperopic outcome caused by a posteriorly pushed IOL due to an excessive anterior capsular overlap. If it is too large, the IOL can be positioned too anteriorly resulting in a myopic shift. Moreover, if the capsulotomy is not well-centered, the IOL can be tilted causing astigmatism or a compromised retinal image [23]. In addition, a capsulotomy, which is centered on the optical axis of the lens with a diameter of 5.25 mm, optimizes prevention of PCO, consistency of effective lens position (ELP), and capsular strength [12].

In our study, we found that FLACS capsulotomy presented a significantly higher stability of the capsulotomy diameter and area at 18 months after surgery. Moreover, the FLACS group had a significantly higher circularity than B-MICS capsulorhexis.

Our findings are in line with results reported in the literature showing significant centration and stability of FLACS capsulotomy over time in comparison to standard phacoemulsification. In particular, Pathier et al. [19] evaluated the diameter of the rhexis, its centration, and the position of the IOL in 33 patients who underwent FLACS in one eye and traditional phacoemulsification in the other; they found that in the FLACS group, the laser capsulotomies were more precise, centered, and stable over time.

Similar results were found by Friedman et al., who showed higher symmetry, centering, and circularity in the FLACS group compared to the controls [24]. Berk et al. in a recent study evaluated 995 cases of FLACS and 883 cases of traditional phacoemulsification after three weeks from surgery, highlighting more precisely centered, circular, and reproducible capsulotomies in the first group [25].

High-energy/low-frequency femtolasers were used in the above mentioned studies. It is known that laser pulse energy influences the strength of the capsulotomies, which increases with decreasing the energy [24]. Previous research with the low-energy/high-frequency Ziemer Z8 showed, similar to our results, median circularity 0.98 [0.97–0.99] ($n = 6$) with FLACS, better accuracy when compared to manual capsulorhexis and importantly very smooth capsulotomy edges due to low energy [26]. In contrast to ours, the research was undertaken using human donor eyes and no follow-up examination was possible.

We also observed a better IOL overlapping with capsulotomy than in manual capsulorhexis. Complete overlap of the IOL optic by the anterior capsule edge is a well-known enhancement of the barrier effect to lens epithelial cell growth. Hollick et al. [27] have long ago reported and confirmed significantly less PCO with a capsulorhexis completely covering the edge of the IOL optic.

Posterior capsule opacification (PCO) remains one of the main long-term complications after cataract surgery, especially when hydrophilic IOLs are concerned, often seen as one of the most common causes of nonrefractive decrease in vision [28, 29]. In our study, PCO score and incidence were significantly reduced in the FLACS group compared to the standard phaco group.

In the literature, uncertain data about this controversial topic are found. Kovacs et al. observed a lower PCO incidence at 18–26 months in the femtolaser group in comparison to standard phacoemulsification [13]. On the other hand, some recent investigations reported results in contrast with this evidence [25, 30].

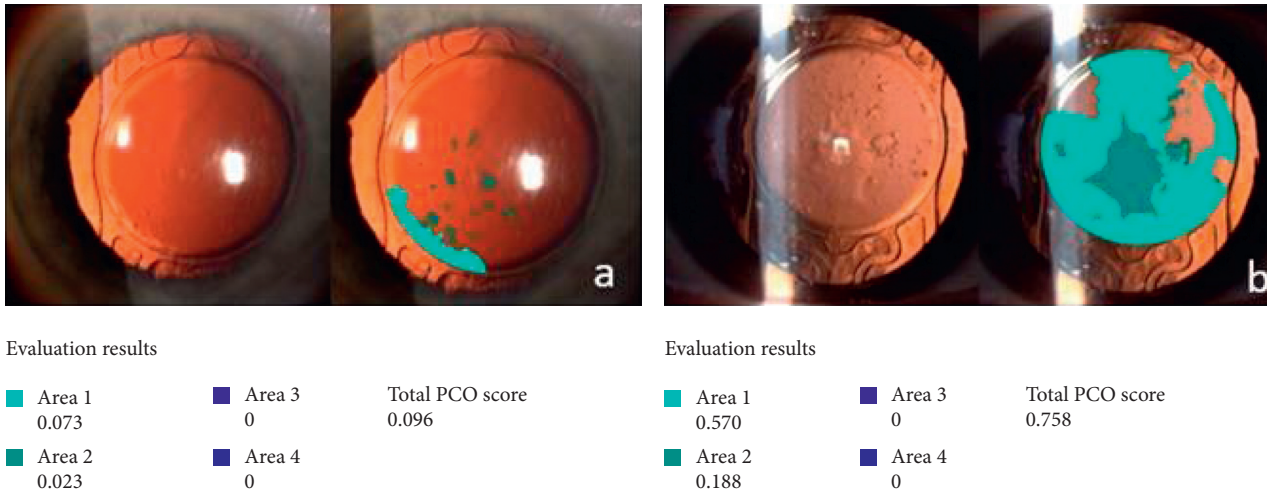

Figure 2: PCO analysis with EPCO2000 software in two study cases: (a) FLACS, patients (*n*), 41; (b) B-MICS, patients (*n*), 52. *Note.* Left pictures are from the slit lamp (native image), and right pictures are those from the correspondent software analysis (evaluated image). Evaluation results and legend for each single image are on the left.

Table 2: CCC diameter and area, BCVA, and ECD results at baseline and 18 months for the two groups.

	FLACS			B-MICS		
	Baseline	18 months	Difference	Baseline	18 months	Difference
CCC diameter (mm)	5.20	5.34 ± 0.21	**0.14 ± 0.21**	5.60 ± 0.40	5.87 ± 0.37	**0.29 ± 0.19**
CCC area (mm^2)	21.24	22.37 ± 1.69	**1.13 ± 1.76**	24.93 ± 3.50	27.16 ± 3.75	**2.67 ± 1.69**
BCVA (logMar)	0.420 ± 0.342	0.016 ± 0.065	**0.404 ± 0.346**	0.443 ± 0.238	0.043 ± 0.020	**0.400 ± 0.261**
Endothelial cell density (cells/mm^2)	2290 ± 466	2007 ± 230	**288 ± 424**	2448 ± 337	2005 ± 489	**443 ± 356**

Table 3: PCO score and percentage of PCO cases and YAG laser in the two groups.

	FLACS (74)	B-MICS (91)
PCO score	0.050 ± 0.081	0.122 ± 0.239
Total cases with PCO	6.8% (5 cases)	29.7% (27 cases)
Nd : YAG laser	1.4% (1 cases)	8.8% (8 cases)

PCO reduction could be attributed to a well-centered capsulotomy or to the lens epithelial cell apoptosis at the margin of the capsulotomy as previously described [14]. With regards to cell apoptosis and loss, different reports exist, but all are in agreement that the low-energy minimizes cell loss and reduces peripheral damage along the capsulotomy [31–33]. Thus, the cell loss at the capsulotomy margin alone cannot explain the lower occurrence of the PCO in low-energy FLACS.

It is well demonstrated that FLACS procedures performed with high-energy lasers are associated with higher prostaglandin and cytokine concentrations and higher rates of anterior capsule damage [34], whereas reduced inflammation could also decrease the risk of PCO induction, and Liu et al. found only low amounts of interleukin (IL)-1α and -1β in the anterior chamber aqueous humour of patients who underwent FLACS with the low-energy Z8 [35]. The IL-1α of 0.5 ± 0.2 pg/ml was only slightly higher compared to manual surgery (0.05 ± 0.05 pg/ml), and the IL-1β showed almost similar values for the FLACS and manual surgery: 0.5 ± 0.3 pg/ml and 0.5 ± 0.4 pg/ml respectively. The numbers reported with high-energy lasers are up to 25.6 pg/ml [36].

Interleukin-1 receptor antagonist has been shown to suppress the proliferation of lens epithelial cells [37], and this might provide an explanation to our findings and support a favorable view of low-energy FLACS in the aspect of the occurrence of postoperative PCO [38]. For these reasons, we suppose that a low-energy femtosecond laser could give even more advantages in terms of a reduction of PCO occurrence in FLACS.

Regarding postoperative results, we registered a significant improvement in mean BCVA in both groups, as previously found for FLACS [2–5, 39], without any significant difference between the two groups. As for endothelial cell loss, the results obtained in our study showed a reduced loss in the FLACS group than in the control group, and this difference was statistically significant. This is likely due to the reduction in phaco energy, which has been shown to harm the endothelium. The positive impact of FLACS on the endothelium has been widely reported in the literature regardless of the femtolaser system used [11, 40–45] even though recently a few papers reported on no significant differences in endothelial cell loss between the two techniques [46, 47]. The present study reports on a longer follow-up period, and the results are obtained from a low-energy femtosecond laser, which is a first report according to our knowledge.

A limitation of our study was its retrospective nature: a randomized prospective clinical trial and another blind observer for PCO and capsulotomy evaluations should be

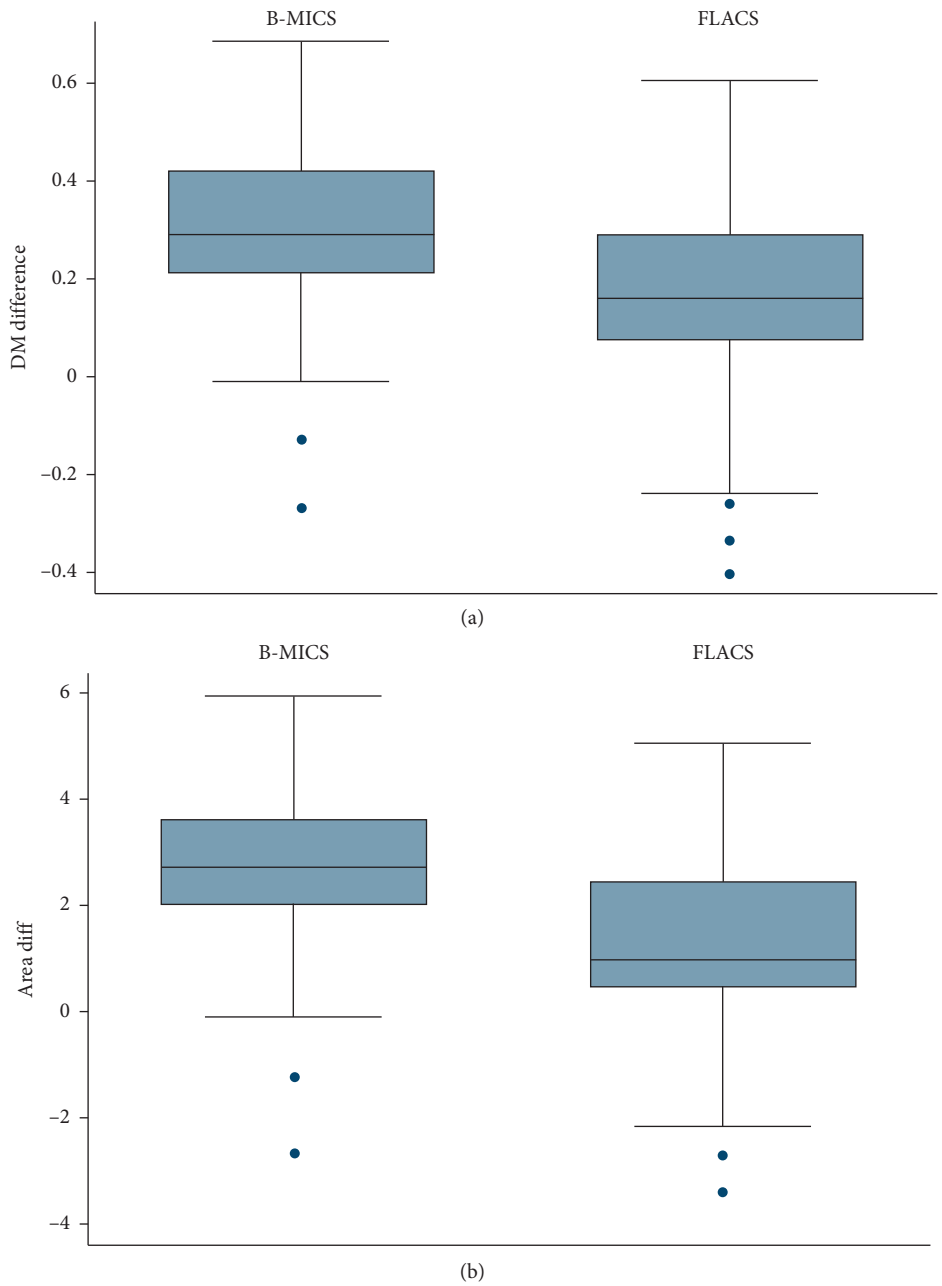

Figure 3: Box plot with whiskers indicating 95% confidence intervals for diameter (a) and area (b) variation in an 18-month follow-up period. DM = diameter.

preferred. Another limitation was that data collection at 18-month follow-up was not at that precise time-point for every patient but varied ±2 months. Moreover, endothelial cell loss was not assessed by a blind observer.

In conclusion, low-energy femtosecond laser technology in conjunction with the advantages of B-MICS technique shows good results in cataract surgery in a long-term follow-up. FLACS with LDV Z8 showed a more stable capsulotomy shape and a higher circularity, when compared to standard capsulorhexis, and registered a significantly decreased PCO score with a lower YAG laser incidence than in the standard phacoemulsification group. These findings have a significant impact on cataract surgery as stable capsulotomy influences the IOL centration. Furthermore, a low incidence of PCO reduces the need for a YAG-laser procedure, which is expensive and has related risks such as retinal tear or detachment. Moreover, a reduced endothelial cell loss in FLACS was also retrospectively confirmed in our 18-month follow-up study.

Further studies will be needed to confirm the data, in particular the analysis of visual outcomes after toric, multifocal, or trifocal IOL implantation or in complicated cases such as endothelial disease, weak zonules, or other ocular

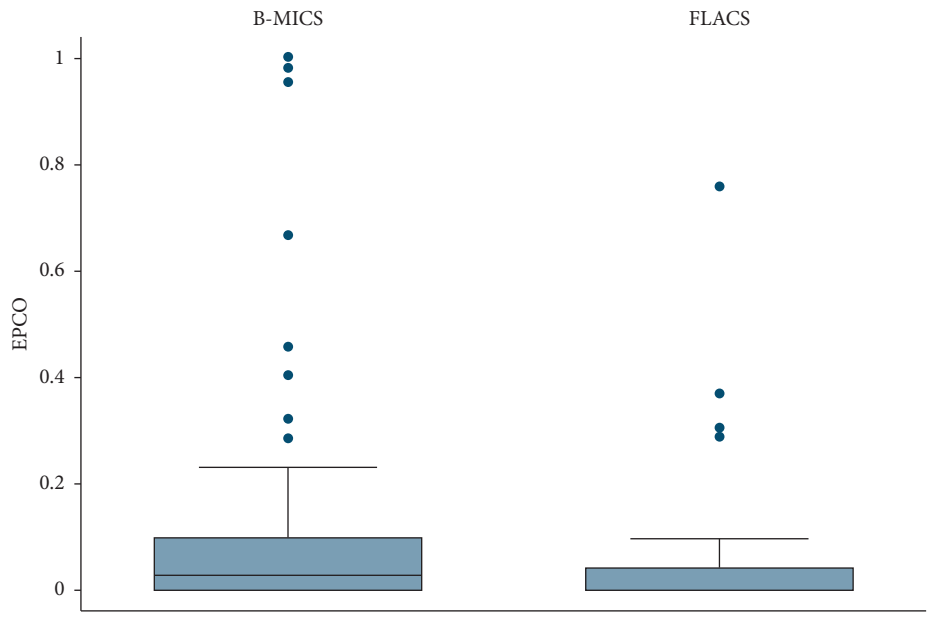

Figure 4: Box plot with whiskers indicating 95% confidence intervals for EPCO score variation in an 18-month follow-up period.

Table 4: Summary of study findings at 18 months with statistical significance of the comparison.

	FLACS	B-MICS	p value
CCC differential diameter (mm)	0.14 ± 0.21	0.29 ± 0.19	<0.001
CCC differential area (mm^2)	1.13 ± 1.76	2.67 ± 1.69	<0.001
Circularity index (0-1)	0.94 ± 0.04\	0.83 ± 0.07	<0.001
Visual gain BCVA (logMar)	0.404 ± 0.346	0.400 ± 0.261	$p = 0.46$
Endotelial cell loss (cell/mm^2)	288 ± 424	443 ± 356	$p = 0.017$
EPCO	0.050 ± 0.081	0.122 ± 0.239	$p = 0.03$

conditions in which overall reduced energy and mechanical manipulation should be needed Table 4.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Disclosure

Preliminary results are presented as a poster presentation at the XXXVI Annual Meeting of the ESCRS, Vienna (Austria), September 2018.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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Research Article

Preliminary Results of a Novel Standardized Technique of Femtosecond Laser-Assisted Deep Anterior Lamellar Keratoplasty for Keratoconus

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Purpose. To evaluate the feasibility and the initial outcomes of a novel standardized surgical technique of femtosecond laser- (FSL-) assisted big-bubble deep anterior lamellar keratoplasty (BBDALK) for eyes with keratoconus. *Methods*. This prospective interventional case series included 11 consecutive FSL-assisted BBDALK procedures performed for the eyes with keratoconus from September 2019 to December 2019. The FSL was used to create (i) an intrastromal channel incision (1.7 mm in length, 4.6 mm in width, 80% depth, and cut energy of 1.70 μJ) and (ii) a 9.0 mm diameter circular lamellar side cut 65 μm above the endothelium (cut energy of 0.90 μJ) intersecting the intrastromal incision. In the operating room, a blunt dissector was used to open the intrastromal channel incision, through which a blunt spatula was inserted, tangentially advanced towards the center of the cornea, and replaced with a blunt cannula for pneumatic dissection. The subsequent surgical steps did not differ from the conventional technique. Main outcome measures were the success rate of pneumatic dissection and the percentage of intraoperative complications. *Results*. Eleven eyes of 11 patients (6 males and 5 females; mean age: 34.54 ± 13.23 years) underwent FSL-assisted DALK. Using the FSL, both corneal incisions (lamellar side cut and intrastromal channel incision) were successfully created in all cases without the need for repeat docking or additional dissection. Pneumatic dissection with type 1 bubble formation succeeded in all 11 eyes (100%). DALK surgery was completed uneventfully in all cases. Descemet membrane perforation did not occur in any case, and no procedure was converted to penetrating keratoplasty. *Conclusion*. Using standardized FSL parameters for both incision design and cut energy in BBDALK surgery, pneumatic dissection can be achieved in a very high rate of cases with minimal risk of intraoperative complications.

1. Introduction

Deep anterior lamellar keratoplasty (DALK) has been recognized as the first-line surgical procedure for eyes with corneal stromal disease but healthy endothelium [1, 2]. The main advantages of DALK over penetrating keratoplasty (PK) include the elimination of endothelial rejection, reduced endothelial cell loss, and improved long-term graft survival [3–8]. Furthermore, since DALK is essentially an extraocular procedure, the complications associated with an open-sky surgery are avoided [1, 8, 9].

However, based on the 2019 statistical report of the Eye Bank Association of America [10], the general popularity of DALK has remained limited with only 11% of corneal transplants for keratoconus performed using DALK compared to 89% with PK. Though several techniques for DALK have been proposed [1], there has been a slow adoption among corneal surgeons, mainly due to technical challenges

in achieving a smooth and regular graft-host interface compatible with optimal vision [11].

Currently, one of the most commonly used methods is the big-bubble (BB) technique, which involves intrastromal injection of air to obtain a cleavage plane between the deep stroma and either the pre-Descemetic layer (PDL) through a type 1 bubble or Descemet's membrane (DM) through a type 2 bubble [12]. Although successful pneumatic dissection results in favourable visual and refractive outcomes, the success rate of pneumatic dissection is variable even in the hands of experienced surgeons ranging from 64 to 91%, depending on the technique employed and/or the type and severity of underlying corneal disease [13–18].

Using intraoperative optical coherence tomography (OCT) imaging, we have previously demonstrated that what is critical for successful BB formation is the depth at which pneumatic dissection is attempted. When the cannula reaches within 100 μm of the posterior corneal surface, the likelihood of successful big-bubble formation exceeds 90% [19]. Based on this surgical principle, the femtosecond laser (FSL) has been proposed to make intracorneal incisions of appropriate depth, which in turn serve as a guide for cannular insertion and subsequent pneumatic dissection. In this pilot study, we evaluate the feasibility and initial outcomes of the first series of keratoconus eyes operated on with this novel standardized technique of FSL-assisted BB-DALK.

2. Materials and Methods

This prospective interventional case series evaluated the outcomes of consecutive FSL-assisted BBDALK procedures performed in eyes with keratoconus from September 2019 to December 2019 at a single tertiary referral center (Department of Ophthalmology, University of Magna Graecia, Catanzaro, Italy). The study adhered the tenets of the 2013 Declaration of Helsinki and was approved by the local ethics committee (Comitato Etico Regione Calabria—Sezione Area Centro). Written informed consent for the surgery and research was obtained from all participants.

All cases required corneal transplantation for unsatisfactory corrected distance visual acuity (CDVA) due to significant refractive errors and/or poor tolerance to rigid gas permeable contact lenses. Eyes with previous hydrops, evident lesions at the level of DM and endothelium, and history of trauma or other ocular diseases were excluded. Preoperatively, all patients underwent a complete ophthalmologic evaluation including CDVA testing, slit-lamp examination, and anterior segment optical coherence tomography (AS-OCT, Casia; Tomey, Tokyo, Japan). CDVA was recorded using the Snellen visual acuity chart. All operated patients were evaluated 6 months after surgery. The main outcomes were the success rate of pneumatic dissection as well as the percentage of intraoperative complications. Secondary outcomes were postoperative complications, final CDVA, and refractive results.

2.1. Surgical Technique. FSL-assisted BB-DALK surgery was performed in all eyes by a single high-volume corneal surgeon (V. S.) as demonstrated in Video 1 (Supplemental Digital Content). In all cases, anaesthesia and akinesia were obtained by means of peribulbar injection of 10 mL of a 0.75% ropivacaine solution. A single drop of tropicamide 1% (Visumidriatic 1%, Visufarma, Roma, Italy) was instilled preoperatively to induce pharmacologic mydriasis and improve intraoperative visualization [20]. All laser treatments were performed using the Victus FSL platform (Bausch & Lomb, Bridgewater, NJ, USA). The FSL parameters of the corneal incisions were calibrated based on the corneal thickness in the area of intended cuts using the real-time swept-source OCT imaging integrated into the FSL platform. Applying the software developed and approved for intracorneal ring segment (ICRS) implantation, the intrastromal channel incision parameters were set to 1.7 mm in length, 4.6 mm in width, and 80% depth at the superior cornea, usually at 10-11o'clock position, using 1.70 μJ of cutting energy. The inner edge of this channel was 3.0 mm from the center of the cornea. Using 0.90 μJ of cutting energy, the 9.0 mm diameter circular lamellar side cut was designed to intersect with the first planar incision, leaving a residual thickness of 65 μm above the endothelium (Figure 1(a)).

In the operating room, a blunt dissector (Model JDBB01, E. Janach, Como, Italy) was used to open the intrastromal channel incision. The blunt spatula (Model AE-2900, Asico, Westmont, USA) was inserted through the intrastromal channel and advanced tangentially to the cornea posterior surface towards the center of the cornea, maintaining the same depth of the entrance plane. The spatula was then replaced with a blunt 27-gauge Fontana cannula (Model J2641.58, E. Janach, Como, Italy), and pneumatic dissection was attempted (Figure 1(b)). Following debulking of about 80% of the anterior stroma, the roof of the bubble was incised using a 30° blade under viscoelastic (IAL-F, Fidia, Padova, Italy) protection. The slit of the incised bubble was enlarged through blunt Vannas scissors, and removal of the bubble roof was completed using corneal scissors. The donor cornea was punched from the endothelial side with a Barron donor punch (Katena Products, Inc., Parsippany, NJ, USA) to the same diameter as the recipient cornea (9.0 mm). After staining with 0.06% trypan blue dye (VisionBlue; D.O.R.C., Zuidland, the Netherlands), DM and endothelium were gently stripped off using a dry Weck-Cel sponge. Four interrupted 10-0 nylon sutures initially secured the graft into the recipient bed, and the graft was sutured into the recipient bed with 16-bite double running, 10-0 nylon suture. The astigmatism was checked under the guidance of a microscope-mounted digital keratoscope (Figure 1(c)).

Starting the following day, betamethasone 0.2% and chloramphenicol 0.5% eye drops were administered every 2 hours for 1 week. Subsequently, antibiotic treatment was discontinued while dexamethasone 1 mg/ml was prescribed 4 times daily and then slowly tapered off during the following 6 months.

2.2. Data Analysis. Statistical analysis was performed using SPSS Statistics (SPSS, Inc., Chicago, IL) for data analysis. Values were expressed as mean ± standard deviation (SD).

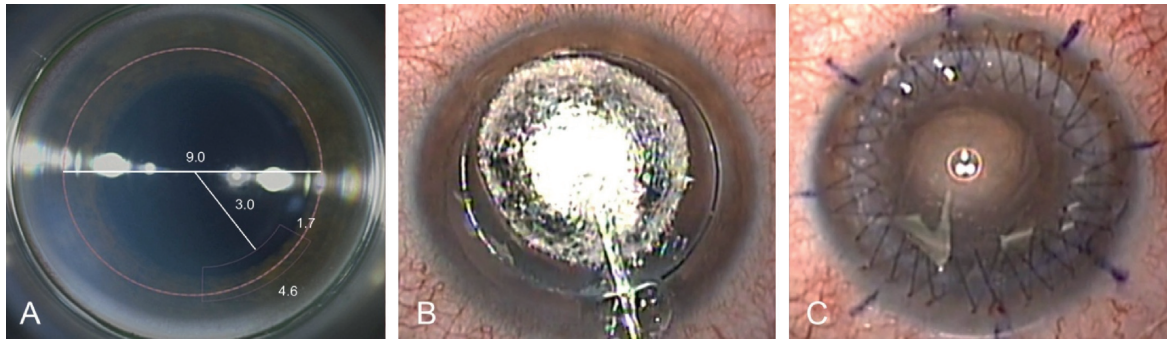

Figure 1: Intraoperative and postoperative images of a representative patient who underwent femtosecond laser- (FSL-) assisted big-bubble deep anterior lamellar keratoplasty: (a) shape and size of FSL incisions; (b) successful formation of big bubble; (c) end of the surgery with keratoscopy control of final astigmatism.

The Wilcoxon signed-rank test was used to compare the continuous variables. A p value less than 0.05 was considered statistically significant.

3. Results

This series included 11 eyes of 11 patients that underwent FSL-assisted DALK. The mean age at the time of surgery was 34.54 ± 13.23 years, and 6 patients (55%) were males. Based on the Amsler–Krumeich classification, 4 cases (36%) were classified as stage II, 5 (45%) as stage III, and 2 (18%) as stage IV. All cases had a follow-up of at least 6 months (7.2 ± 1.5 months).

Utilizing the FSL, both corneal incisions (lamellar side cut and intrastromal channel) were successfully created in all cases without the need for repeat docking or additional dissection. Pneumatic dissection with type 1 bubble formation succeeded in all 11 eyes (100%). DALK was completed uneventfully in all cases. DM perforation did not occur in any case, and no procedure was converted to PK.

Preoperative mean Snellen CDVA significantly increased from 0.34 ± 0.11 to 0.58 ± 0.07 at final follow-up ($p < 0.001$), while mean keratometric astigmatism and mean K steep significantly decreased from 3.71 ± 1.95 to 2.40 ± 0.57 diopters (D) ($p = 0.04$) and from 55.20 ± 3.09 to 45.60 ± 1.35 D ($p < 0.001$), respectively. Complete attachment of the donor lamella was achieved with corneal clarity restored in all cases. No episode of double anterior chamber formation, immunologic rejection, graft failure, or any other postoperative complications was observed.

4. Discussion

Although DALK has clear advantages over PK in terms of graft survival, technical challenges of the procedure along with poor reproducibility still limit its widespread adoption among corneal surgeons [21, 22]. Injecting air at the proper depth using a reproducible technique represents the significant surgical challenge, especially among novice corneal surgeons [23].

Though several studies have described the use of FSL for the creation of an intrastromal channel for the air injection [24–27], FSL settings for DALK have not been standardized thus far. Unlike FSL-based procedures for cataract surgery and ICRS, no dedicated software has been developed, possibly due to technical challenges and concerns regarding the safety and efficacy of FSL for creating DALK incisions. In fact, laboratory studies have demonstrated that FSL creates uneven interfaces at greater corneal depths (as required during DALK surgery) and may possibly induce endothelial cell damage [28–30].

In this study, we have demonstrated the feasibility of FSL-assisted BB-DALK according to our standardized technique. Firstly, the FSL has allowed to create precise and large-diameter side cut incision. At the 9 mm optical zone, the cornea tends to be less affected by ectasia and more regular with less variability in zonal pachymetry. Consequently, a deeper incision based on the thinnest point pachymetry is created and could account for the consistent surgical outcomes observed. Secondly, the FSL has allowed the creation of accurate and reproducible intrastromal incisions that represents a deep entrance plane for the advancement of the cannula at the appropriate depth, thereby resulting in high rates of successful big-bubble formation in this series. Unlike conventional DALK using manually calibrated trephines, FSL allows a precise deep trephination, which is associated with high rates of successful pneumatic dissection independent of surgical experience [18], eliminating the risk of perforation in this surgical step. Interestingly, pneumatic dissection resulted in the formation of a type 1 bubble in all cases. The presence of PDL confers additional strength to the floor of the bubble and accounts for the absence of intraoperative and postoperative complications observed in this series despite the inclusion of eyes with more advanced stages of keratoconus [11, 31]. Although the FSL settings used were originally developed for ICRS implantation, the modifications presented in this series could represent a major improvement in the DALK technique.

Another important feature of this procedure is the design of the intrastromal channel. Instead of a straight narrow tunnel, we created a large intrastromal pocket that is more easily identifiable by the surgeon in the operating room. Additionally, a large stromal pocket

would allow insertion of the cannula through a different intrastromal tunnel in case of failure of the first attempt. In order to prevent air from escaping through the large intrastromal channel, before injecting air for bubble formation, the cannula was advanced tangential to the corneal posterior surface maintaining the same depth of the entrance plane. Though limited follow-up is currently available, the significant improvements of CDVA and keratometric outcomes in this series seem to support other studies that have reported stable and faster wound healing after FSL-assisted DALK [32, 33]. However, although the visual and refractive outcomes of FSL-assisted DALK have been reported as comparable to conventional DALK, further studies are required to evaluate long-term differences.

Besides FSL, other approaches have been described to assist surgeons during BB-DALK and improve the success of the pneumatic dissection. For instance, ultrasound pachymetry and intraoperative OCT are helpful tools to achieve a proper depth of air injection [34–36]. However, the former approach appears less precise and standardized compared to our technique and requires dedicated instruments such as a corneal pachymeter and a micrometer-controlled knife [34]. The latter approach is useful in cases with decreased visualization under the operating microscope, but the main limitation is represented by the obstruction of the OCT image acquisition by metallic instruments [35]. As demonstrated by our preliminary results, FSL may help to overcome these limitations, thereby improving the pneumatic dissection success rate while maintaining high standards of safety. In addition, this technology may increase the safety and reproducibility of the circular lamellar trephination.

Although the present case series is an appealing attempt at standardizing FSL-assisted BB-DALK, there are some limitations in this study. Firstly, this is a pilot study with limited sample size and no control group. Larger studies are required to validate these data, and randomized clinical trials are desirable to establish the superiority of this approach over the conventional DALK. Moreover, long-term longitudinal observation is required to evaluate the influence of FSL-assisted DALK on postoperative refractive and visual outcomes. Though the laser setting used in this series was developed for ICRS implantation, the promising initial surgical outcomes of FSL-assisted DALK support the need for the development of dedicated settings for DALK. With greater understanding of the principles behind successful BB formation [19], FSL settings can be further optimized by improving the reproducibility and overall outcomes of the procedure.

In conclusion, using standardized FSL parameters for both incision design and cut energy in DALK surgery, pneumatic dissection can be achieved in a very high rate of cases with minimal risk of intraoperative complications.

Data Availability

The data used to support the findings of this study are included within the article.

Disclosure

This article was presented at the 38th Congress of the European Society of Cataract and Refractive Surgery (ESCRS), 2–4 October, 2020.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Andrea Lucisano and Giuseppe Giannaccare contributed equally to the work and should be considered co-first authors.

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Supplementary Materials

Channel incision parameters are set to 1.7 mm in length, 4.6 mm in width, and 80% depth at the superior cornea. A 9.0 mm diameter circular lamellar side cut is designed. In the operating room, a blunt spatula is inserted, then it is replaced with a blunt 27-gauge cannula, and pneumatic dissection is attempted. Subsequently, the bubble roof is removed. In the donor cornea, the Descemet membrane and endothelium are stripped off after staining with trypan blue dye. Finally, the graft is sutured into the recipient bed with 16-bite double running sutures. The astigmatism is checked under the guidance of a microscope-mounted keratoscope. (*Supplementary Materials*)

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Research Article

Clinical Observation of Silicon Hydrogel Contact Lens Fitted Immediately after Small Incision Lenticule Extraction (SMILE)

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Purpose. To examine the immediate use of bandage contact lenses (BCLs) for improving patient comfort after small incision lenticule extraction (SMILE) surgery. *Methods*. This is a prospective randomized controlled study in which one hundred and seventy-eight patients undergoing SMILE were randomly allocated to three groups: group A wore BCLs for 8 hours postsurgery, group B wore BCLs for 24 hours postsurgery, and group C did not wear any BCLs postsurgery. Eight subjective symptoms including photophobia, tearing, pain, foreign body sensation, burning, blurred vision, sting, and dry eyes were prospectively evaluated at 2 hours, 4 hours, 8 hours, and 24 hours, using a questionnaire with a total score of 24. The scores of symptoms and signs were compared between the three groups. *Results*. There was a statistically significant time effect on scoring, which implicated a decline in symptoms over time after surgery ($P < 0.001$). There was also a significant interaction between time and the treatment group ($P < 0.01$). The total symptom score of groups A and B (5.85 ± 3.97 and 5.99 ± 4.67, respectively) was significantly lower than that of group C at 2 hours postsurgery (7.35 ± 4.86, $P < 0.05$), especially in tearing and pain ($P < 0.05$). The level of corneal oedema at 24 hours postsurgery was also statistically significantly different between the three groups ($P < 0.001$), and the post hoc test showed that groups A and B were lower than group C ($P < 0.01$). *Conclusion*. Silicon hydrogel BCLs applied immediately after SMILE surgery can relieve postsurgical symptoms of tearing and pain, improving overall patient comfort, and reduce corneal oedema. This trial is registered with ChiCTR-ONRC-13003114. *Precis*. The application of silicone hydrogel bandage contact lenses immediately after SMILE surgery has the potential to improve patient comfort, corneal healing, and patient satisfaction following SMILE.

1. Introduction

Refractive surgery has seen continual improvement over the last few decades, with a number of new procedures now being performed worldwide. Advances in technology have made refractive surgeries less invasive, more predictable, and capable of achieving better visual outcomes and less patient discomfort. One of the latest surgical techniques, small incision lenticule extraction (SMILE), has become popular due to its excellent predictability, stability, small incision required, and reduced complications [1–3]. However, despite its advantages, quite a few number of patients complain of ocular discomfort after surgery, including tearing, difficulty with eye opening, and so on. Improved methods for reducing the stimulative symptoms associated with SMILE require continuous exploration.

Bandage contact lenses (BCLs) are often used to promote corneal wound healing and reduce patient discomfort after laser refractive surgery [4–6], particularly following procedures such as photorefractive keratectomy (PRK) and laser epithelial keratomileusis (LASEK). As there are many different types of contact lens materials and designs available on the market, researchers have been investigating the most suitable type of contact lens to be used after laser refractive surgery [7–9]. Conventional hydrogel BCLs had low oxygen transmissibility, which might potentially cause hypoxic

complications of the cornea when prescribed using a continuous wear modality [6, 10]. Silicone hydrogel (SiH) materials, on the other hand, have a higher oxygen transmissibility property, which has been shown to enhance corneal wound healing after refractive surgeries [11–13], and have been approved by the Food and Drug Administration (FDA) to be used as a BCL for a continuous wear modality [14].

We identified no literature reporting on the clinical application of SiH BCLs after SMILE surgery so far. Hence, the purpose of this research was to investigate the safety and efficacy of immediate use of SiH BCLs after SMILE surgery in reducing patients' discomfort, such that to provide the clinical basis for its use in the postoperative setting.

2. Method and Subjects

2.1. Participants. This prospective randomized controlled study was approved by the ethics committee of the Eye and ENT Hospital affiliated with Fudan institutional review board and was carried out in accordance with the tenets of the Declaration of Helsinki. After a detailed explanation of the study design, written informed consent was obtained from all participants.

The sample size for this study was determined using the formula: $n = (\Psi^2 (\sum S_i^2/K))/[\sum (X_i - \overline{X})^2/(K-1)]$ based on the statistics provided in the referenced article [10], where the mean symptom score was $X_i = 0.76$, 0.31, and 0.20, and the reference standard deviation was $S_i = 1.19$, 0.55, and 0.52. Assuming an alpha of 0.05 and a beta of 10%, the sample size was calculated as $n = 2.57^2(1.989/3)/[0.176/(3-1)] = 49$, assuming a lost to follow-up rate of 20%, and 60 participants are required in each group, making a total of 180 participants.

One hundred and eighty patients who presented to the Eye and ENT Hospital of Fudan University for SMILE surgery between December 2017 and September 2018 were recruited in the study. The inclusion criteria for this study were as follows: aged 18 years and above and cessation of contact lens wear for at least 2 weeks for soft contact lens wearers, 8 weeks for rigid contact lens wearers, and over 3 months for orthokeratology contact lens wearers. Subjects were excluded if their tear film break up time is less than 10 seconds or if they presented with any anterior ocular diseases, such as keratoconus and inflammatory eye diseases, systemic connective tissue disease or autoinflammatory diseases, and unstable mental health.

The participants were randomly allocated to three groups. There were 178 subjects (354 eyes) included in the analysis: group A had 59 subjects (118 eyes), group B had 60 subjects (120 eyes), and group C had 59 subjects (116 eyes) who served as the control. Two subjects were excluded as they failed to show up at follow-up visits.

The average age of all the subjects was 27.1 ± 5.9 years (range, 18 to 40 years), with 113 being male and 65 being female. The average refractive error of all participants was -5.18 ± 1.72 DS (range, -9.50 to -0.50 DS). The average presurgical astigmatism of all the participants was -0.92 ± 0.67 DC (range, -6.00 to -0.25 DC). The average corneal ablation depth (thickness of lenticule) was $114.85 \pm 24.81\,\mu$m (range, 50 to 160 μm). There were no significant differences in the demographic data between the three groups, as represented in Table 1.

2.2. Study Protocol. All participants underwent routine preoperative examinations including anterior eye examination, refraction, intraocular pressure, and corneal topography. The SMILE procedure was performed as described by Zhao et al. [15, 16], by an experienced surgeon who performs over 2000 SMILE surgeries annually. All participants were given 3 drops of topical anaesthesia (0.4% bupivacaine hydrochloride) prior to laser surgery. SMILE was performed using the 500 Hz VisuMax® laser system (Carl Zeiss Meditic AG). The lenticule was removed via a 2 mm arcuate incision at the superior limbus. The corneal cap thickness was set as 120 μm, and the lenticule diameter was between 6.0 and 6.8 mm, adjusted to the thickness of the lenticule.

Following surgery, all participants were given 1 drop of Tobradex (Alcon, USA), and participants in groups A and B were then fitted with a SiH BCL (Acuvue Oasys, senofilcon A, 38% water content, 147 Dk/L, 14.0 mm diameter, 8.80 mm base curve, and 0.07 mm central thickness, Johnson and Johnson, USA). Lens fitting was evaluated immediately after the insertion of BCLs, with a good centration and modest movement being confirmed in all cases.

Group A participants had their contact lenses removed 8 hours after surgery, and group B participants had their contact lenses removed 24 hours after surgery with sterilized microforceps. All participants were given topical tobramycin and fluorometholone acetate eye drops (0.1%) every 3 hours after surgery on the operation day. Lens stability and movement was confirmed 8 hours after surgery, and all the subjects were reviewed at 24 hours after operation. Uncorrected visual acuity (UCVA) was measured using a Snellen visual chart and recorded as logMAR.

2.3. Scoring. Participants' subjective symptoms and postoperative comfort were measured using a self-administered standardized survey [6] conducted at 2 hours, 4 hours, 8 hours, and 24 hours after surgery. Participants were required to return the questionnaire at the 24 hour review time. The questionnaire inquired about 8 symptoms, including photophobia, tearing, pain, foreign body sensation, burning, blurred vision, sting, and dry eyes. Each symptom was scored using a grading scale of 0–3 points, with 0 being no symptoms, and 1, 2, 3 indicating mild, moderate, and severe symptoms, respectively. The total score was recorded as the final symptom score.

Participants' eyes were examined for corneal oedema and conjunctival redness at the 24-hour follow-up visit. The severity of these signs was assessed under a slit-lamp microscope by the same ophthalmologist who was masked from the participant's group allocation. The clinical signs were scored using a 0–3 point scale. The higher the score, the more severe the corneal oedema and conjunctival injection.

Table 1: Participants' baseline demographics.

Group	n	Age	Gender Females (%)	Spherical power (D)	Cylindrical power (D)	Ablation depth (μm)
A	59	27.17 ± 5.91	38 (62.3)	5.15 ± 1.77	0.94 ± 0.58	114.98 ± 23.27
B	60	26.98 ± 5.91	36 (60.0)	4.94 ± 1.54	0.87 ± 0.67	112.55 ± 25.48
C	59	27.23 ± 6.05	39 (66.1)	5.45 ± 1.80	0.96 ± 0.77	116.88 ± 25.74
F/χ^2		0.026	0.545	2.419	0.474	0.767
P		0.974	0.761	0.091	0.623	0.465

(Mean ± SD, $N = 178$). Group A: wore BCLs for 8 hours, group B: wore BCLs for 24 hours, and group C: no BCL wear.

2.4. Statistical Analysis. Statistical analyses were conducted using SPSS 20.0. Data are expressed as mean ± SD, frequency, and percentage. Participants' baseline demographic details were compared using one way-ANOVA and chi-square testing. Repeated measures ANOVA with an intragroup factor of time and an intergroup factor of treatment modality was applied to analyze the scores of patients' subjective symptoms and objective signs after surgery. Pairwise comparisons were carried out using Bonferroni corrections. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Participant Subjective Symptom Score. The overall subjective symptom scores are displayed in Table 2 and Figure 1. Repeated measures ANOVA showed a statistically significant time effect, which implicated a decline in symptoms over time after surgery ($P < 0.001$); the interaction between time and the treatment group was also statistically significant ($P < 0.01$). All three groups showed the highest symptom scores at 2 hours postsurgery, which declined at 4, 8, and 24 hours; scores in group C decreased faster than those in the other two groups from 2 to 4 hours postsurgery. Multiple comparisons showed that at 2 hours postsurgery, groups A and B had statistically significantly lower symptom scores than group C ($P = 0.012$ and $P = 0.020$, respectively), while no significant differences were seen between groups A and B ($P = 0.814$). There were no significant differences in symptom scores between groups at all other time points (all $P > 0.05$).

The most reported postsurgical symptoms were blurred vision, photophobia, and tearing. At 2 hours postsurgery, among the 58 participants in group C, 68.8% experienced glare, 61.7% experienced tearing, 51.3% experienced varying degrees of pain, and 92.2% complained of blurred vision; both groups A and B had lower tearing ($P = 0.027$ and $P = 0.005$, respectively) and pain symptom scores ($P = 0.036$ and $P = 0.048$, respectively) than group C at that time. Table 3 presents the symptom scores in all groups.

3.2. Corneal Oedema. On physical signs, there were also differences observed between the three groups. There was a statistically significant difference in corneal oedema at 24 hours postsurgery in all 3 groups ($P < 0.001$), with the post hoc test showing less corneal oedema in groups A and B compared to group C ($P < 0.001$ and $P = 0.001$); there was no significant difference between groups A and B ($P = 0.472$). Corneal oedema was recorded in 14.1% of the participants in group C, 4.9% in group B, and absent in group A. There were no statistically significant differences in limbal hyperemia between the three groups ($F = 2.442$, $P = 0.089$). Table 4 represents the scores of clinical signs in all three groups.

3.3. Uncorrected Visual Acuity Postsurgery. There were no statistically significant differences in UCVA between the three groups ($F = 0.087$, $P = 0.917$). UCVA was -0.00 ± 0.11 in group A (BCL removed at 8 hours postsurgery), -0.03 ± 0.11 in group B (BCL removed at 24 hours postsurgery), and -0.00 ± 0.11 in group C (no BCL wear postsurgery).

4. Discussion

Corneal wound healing and postsurgical comfort are important issues concerning corneal refractive surgeries. The use of BCLs in refractive surgeries such as PRK and LASEK has been proven to be effective and safe [4, 5]. Studies have also shown that BCLs applied immediately after LASIK can reduce flap complications and patient discomfort after surgery [6, 17]. As SMILE is a relatively new type of refractive surgery, the clinical use of BCLs for the improvement of patients' comfort is not fully understood and requires further assessment.

The results of this study showed that the main subjective symptoms after SMILE surgery were blurred vision, photophobia, tearing, and foreign body sensation. The symptom scores were highest at 2 hours postsurgery, which then gradually reduced over time. This reduction in symptom scores over time reflects what is already known and expected and is similar to the findings reported by previous studies investigating other types of corneal refractive surgery. However, in the present study, the observed trend was slightly different to previous studies. For example, Orucov et al. [6] reported that pain, tearing, and discomfort are most prominent at 4 hours after LASIK when compared to 1 hour postsurgery. O'Doherty et al. [18] also found that Epi-LASIK and PRK patients who wore BCLs postsurgery experienced a gradual rise in pain symptoms in the early postoperative period, which peaked at 4 hours postsurgery, whilst their LASIK patients experienced the greatest discomfort at 2 hours postsurgery. This postsurgical pain is often related to corneal nerve ending exposure as well as the mechanical friction of the eyelid over the surgical site; however, this pain often subsides at 24 hours postsurgery. This difference in symptom change over time could be due to that SMILE, and

Table 2: Comparison of the total symptom scores after SMILE between the 3 groups at different postsurgery time points.

Group	n	2 h	4 h	8 h	24 h	Time effect F	Group effect F	Time x group F
A	59	5.85 ± 3.86	3.63 ± 2.52	2.59 ± 1.71	1.62 ± 1.37			
B	60	5.99 ± 4.35	4.43 ± 3.62	3.11 ± 2.55	1.98 ± 1.49			
C	59	7.35 ± 4.44*	4.30 ± 3.31	3.02 ± 2.36	2.03 ± 1.60	310.182	3.055	3.877
F		4.534	2.177	1.807	2.618			
P		0.011*	0.115	0.166	0.074	0.000**	0.048	0.001*

(Mean ± SD, $N = 178$). Group A: wore BCLs for 8 hours, group B: wore BCLs for 24 hours, and group C: no BCL wear. $^{*}P < 0.05$;$^{**}P < 0.001$.

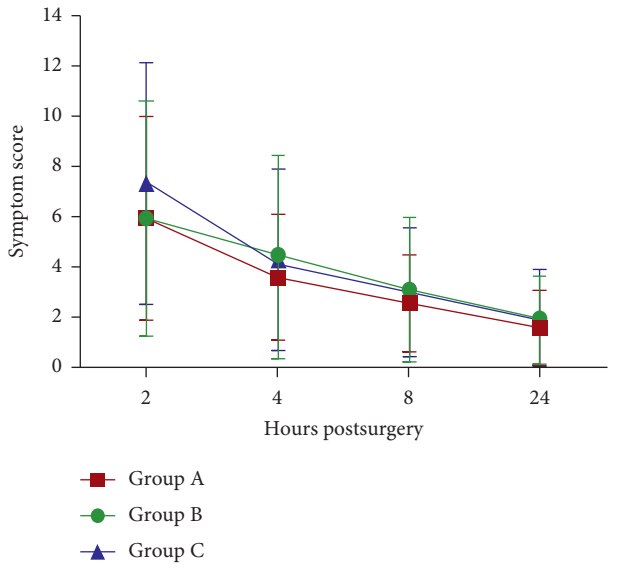

Figure 1: The total symptom scores after SMILE among the 3 groups at different postsurgery time points.

unlike most refractive surgeries, it is a flapless laser refractive procedure, with the benefit of creating only a small corneal wound with minimal corneal nerve damage. However, the separation of the anterior and posterior stroma, as well as the process of removing the lenticule has the potential to cause disruption to the surrounding corneal tissue, thereby affecting the corneal surface [19] and inducing patients' postsurgical discomfort.

In the present study, patients who wore BCL after surgery had lower scores of total symptoms and tearing and pain at 2 hours than those without BCLs. This indicated that the utilization of a SiH BCL can help alleviate early stage pain and tearing symptoms from the SMILE procedure. Orucov et al. [6] showed that BCL application after LASIK was effective in reducing early burning, pain, and tearing symptoms; patients who wore BCLs for 1 hour or 1 day postsurgery had significantly lower symptoms than those without BCLs at 4 hours and the following morning. Ahmed and Breslin [20] showed that most LASIK patients who wore BCLs within 3 hours postsurgery reported better ocular comfort than those without BCLs. The effect of using BCLs to relieve pain and discomfort after LASEK surgery was previously confirmed [13, 21]. Xie et al. [13] found that LASIK patients who wore silicone hydrogel contact lenses postsurgery had reduced pain and photophobia than hydrogel contact lenses. BCLs can aid in the protection of the exposed corneal wound and nerve endings, reducing the irritation that arises from blinking. The present study demonstrated that the wearing of SiH BCLs for a short period after SMILE can reduce ocular symptoms and improve overall comfort of patients, which shows the novelty of this study.

This study also found that the BCL wearing group had lower corneal oedema scores than the no BCL wearing group at 24 hours postsurgery. SMILE has been shown to yield low incidences of postoperative complications. Zhang et al. [3] reported no incidences of corneal swelling in their 45 subjects who had undergone SMILE surgeries. The present study found mild corneal oedema 24 hours postsurgery in some patients, which may be partly caused by the suction ring used during surgery. The BCLs used in the present study utilized a silicone hydrogel material, which has a high oxygen transmissibility. This effectively avoided hypoxic complications such as limbal injection and corneal swelling from overnight lens wear as demonstrated by Fonn et al. [10, 22, 23] who found reduced levels of corneal oedema with SiH CLs (range, 2%–5%) when in contrast with conventional low Dk lens (10% to 15%). It has been shown that in LASIK patients, the speed of corneal epithelium healing was faster in SiH CL wearers (4.1 ± 0.3 days) when compared to hydrogel lens wearers (4.3 ± 0.8 days) [13]; whilst another study showed that eighty percent of eyes with a SiH CLs versus 63% of eyes with hydrogels had grade 1 epithelial recovery at 5 days postsurgery [12]. Gao et al. [17] also found that the corneal thickness of eyes in silicone hydrogel lens were thinner than those wearing hydrogel lens at 1 day after Sub-Bowman keratomileusis (SBK) surgery. More investigations are needed to confirm if SiH BCLs may further assist, as the results of this study suggested, in preventing or alleviating corneal oedema related with surgery procedures after SMILE.

The present study used a SiH lens with a base curve (BC) of 8.80 mm (Acuvue Oasys, Johnson and Johnson). The lens demonstrated excellent centration with adequate movement, which was suitable for post-SMILE patients. Previous studies have examined the applications of the same lens for post PRK and LASEK conditions and have compared it with two other SiH CLs; the results showed that this lens was superior when it comes to patients' comfort [24]. A comparison between the two base curves available for this lens has also been carried out: the 8.80 mm BC was found to be more suitable for the postsurgical flatter cornea as compared to 8.40 mm BC and was effective in alleviating postsurgical pain

Table 3: The scores of symptoms after SMILE in all 3 groups.

Symptom	Time after surgery (h)	Group A	Group B	Group C	F	P
Blurred vision	2	1.46 ± 0.74	1.52 ± 0.75	1.53 ± 0.80	0.306	0.736
	4	1.17 ± 0.60	1.29 ± 0.69	1.19 ± 0.70	1.079	0.341
	8	0.99 ± 0.61	1.15 ± 0.64	1.00 ± 0.57	2.534	0.081
	24	0.80 ± 0.59	0.92 ± 0.60	0.82 ± 0.52	1.574	0.209
Photophobia	2	1.18 ± 1.02	1.03 ± 1.13	1.31 ± 1.14	1.755	0.174
	4	0.69 ± 0.87	0.59 ± 0.77	0.67 ± 0.77	0.434	0.649
	8	0.34 ± 0.57	0.34 ± 0.60	0.37 ± 0.52	0.106	0.900
	24	0.16 ± 0.36	0.11 ± 0.31	0.24 ± 0.43	3.686	0.018*
Tearing	2	0.92 ± 1.04	0.83 ± 1.11	1.23 ± 1.16	4.474	0.012*
	4	0.38 ± 0.63	0.47 ± 0.79	0.36 ± 0.64	0.755	0.471
	8	0.07 ± 0.25	0.15 ± 0.40	0.10 ± 0.32	1.754	0.175
	24	0.04 ± 0.20	0.06 ± 0.23	0.05 ± 0.22	0.134	0.875
Pain	2	0.50 ± 0.73	0.61 ± 0.81	0.83 ± 0.96	3.524	0.031*
	4	0.18 ± 0.43	0.36 ± 0.74	0.31 ± 0.55	2.791	0.063
	8	0.18 ± 0.42	0.19 ± 0.47	0.29 ± 0.56	1.844	0.160
	24	0.04 ± 0.20	0.06 ± 0.23	0.08 ± 0.27	0.727	0.484
Foreign body sensation	2	0.44 ± 0.72	0.64 ± 0.84	0.70 ± 0.93	2.977	0.049*
	4	0.38 ± 0.53	0.61 ± 0.75	0.53 ± 0.67	3.683	0.027*
	8	0.30 ± 0.53	0.53 ± 0.63	0.42 ± 0.62	4.158	0.016*
	24	0.20 ± 0.44	0.40 ± 0.58	0.25 ± 0.45	4.769	0.009*
Burning	2	0.42 ± 0.70	0.44 ± 0.81	0.59 ± 0.76	1.529	0.218
	4	0.07 ± 0.25	0.25 ± 0.61	0.31 ± 0.58	6.173	0.003*
	8	0.06 ± 0.24	0.14 ± 0.47	0.14 ± 0.34	1.560	0.212
	24	0.01 ± 0.09	0.05 ± 0.22	0.08 ± 0.27	3.378	0.037*
Sting	2	0.39 ± 0.73	0.46 ± 0.85	0.56 ± 0.83	1.165	0.313
	4	0.15 ± 0.40	0.30 ± 0.69	0.32 ± 0.60	2.968	0.053
	8	0.16 ± 0.39	0.19 ± 0.47	0.21 ± 0.46	0.349	0.706
	24	0.04 ± 0.27	0.05 ± 0.22	0.08 ± 0.27	0.657	0.519
Dry eyes	2	0.43 ± 0.60	0.49 ± 0.67	0.59 ± 0.82	1.567	0.210
	4	0.47 ± 0.68	0.51 ± 0.62	0.67 ± 0.65	3.039	0.049*
	8	0.46 ± 0.53	0.46 ± 0.70	0.52 ± 0.63	0.389	0.678
	24	0.35 ± 0.51	0.39 ± 0.55	0.50 ± 0.63	1.919	0.148

(Mean ± SD, $N = 178$). Group A: wore BCLs for 8 hours, group B: wore BCLs for 24 hours, and group C: no BCL wear. *$P < 0.05$.

Table 4: Clinical sign scores at 24 hours after surgery in the 3 groups.

Groups	n	Limbal hyperemia (% of subjects)	Corneal oedema (% of subjects)
A	59	0.03 ± 0.16 (2.5)	0.00 ± 0.00 (0.0)
B	61	0.12 ± 0.32 (11.0)	0.03 ± 0.18 (4.9)
C	58	0.07 ± 0.24 (5.6)	0.22 ± 0.42 (14.1)
F		2.442	10.780
P		0.089	0.000**

(Mean ± SD, $N = 178$). Group A: wore BCLs for 8 hours, group B: wore BCLs for 24 hours, group C: no BCL wear. **$P < 0.001$.

as well as reducing the incidence of lens loss [4]. Plaka et al. [11] found that the 8.80 mm BC lens was also superior to the 8.40 mm BC lens in terms of UCVA at 4 days after operation in their Epi-LASIK patients.

To our knowledge, this is the first randomized clinical trial aimed at investigating the efficacy of SiH BCLs used postoperatively to reduce patient discomfort in the population underwent SMILE surgery, which provide insightful findings for clinical practice in this field. Second, the outcome assessor was blinded to the group allocation, therefore, the credibility of results was ensured. Moreover, the effectiveness of SiH BCLs was comprehensively evaluated, which has been rarely reported in previous study.

The limitation in the current study is that the subjective symptoms were only observed in a short time frame of 2–24 hours postsurgery.

To conclude, short-term wearing of SiH BCLs after SMILE is effective in relieving pain and tearing symptoms and thus improves patient ocular comfort. It is recommended to use the bandage contact lens for short-term, 4–24

hours, after SMILE, which could improve patient satisfaction. In addition, bandage contact lens wearing may also reduce corneal oedema after surgery, which could be further investigated.

Data Availability

The data used to support this study are available from the corresponding author upon request.

Ethical Approval

This prospective randomized controlled study was approved by the ethics committee of the Eye and ENT Hospital affiliated with Fudan institutional review board with ethical code KJ2010-18. It was carried out in accordance with the tenets of the Declaration of Helsinki.

Consent

After a detailed explanation of the study design, written informed consent was obtained from all participants.

Disclosure

The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Jifang Wang is the first author.

Acknowledgments

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Review Article

Application of Femtosecond Laser in Anterior Segment Surgery

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Femtosecond laser (FSL) is a near-infrared laser that can create reliable and reproducible tissue cutting with minimal damage to adjacent tissue. As the laser can also create incisions with various orientations, depths, and shapes, it is expected to be a useful tool for anterior segment surgery, such as cornea, refractive, and cataract surgery. In this review, the authors will introduce the application of FSL in various anterior segment surgeries and discuss the results of studies regarding the efficacy and safety of FSL in cornea, refractive, and cataract surgery. Experimental studies regarding the potential use of FSL will also be introduced. The studies discussed in this review suggest that FSL may be a useful tool for improving the prognosis and safety of surgeries of the anterior segment.

1. Introduction

Femtosecond laser (FSL) is a neodymium glass (Nd:glass) laser employing ultrashort pulse durations in the femtosecond time domain (1 femtosecond = 10^{-15} sec), allowing tissue cutting with substantially reduced energy, compared with other ophthalmic laser pulses, e.g., nanosecond time domain (10^{-9} sec), argon, excimer, and neodymium yttrium aluminium garnet (Nd:YAG) lasers [1]. Such reduction in energy may result in confined tissue effect with minimal collateral damage to adjacent tissues [2].

With wavelengths in the near-infrared spectrum (1053 nm), FSL is neither absorbed by optically transparent tissues, such as cornea and lens, at low power densities, nor affected by corneal magnification [1, 2]. Infrared lasers undergo substantially reduced attenuation compared to visible wavelength lasers, and to a certain degree, FSL can transmit through haze media, such as opacified or edematous corneas.

Like the Nd:YAG laser, FSL uses a process of photodisruption, whereas argon and excimer lasers employ photocoagulation and photoablation, respectively [2]. The precisely focused FSL can increase the power density, on a targeted structure depth [3], and can cut tissue via photodisruption, which is the process of generating a plasma of free electrons and ionized molecules that rapidly expands and collapses to produce microcavitation bubbles and acoustic shock waves, resulting in incisions and separation of the target tissue [1, 4]. FSL is not only able to produce consistent and reproducible tissue incisions, but it can also allow the creation of various shapes of incisions, such as circular, decagonal, and zigzag shapes [1, 2].

The application of FSL in ophthalmic surgery was first introduced in 2001 [3]. Since then, it has been increasingly used in anterior segment surgery [3]. In corneal transplantation, FSL is applicable for customized trephination in penetrating keratoplasty (PK) and deep anterior lamellar keratoplasty (DALK) [3, 4]. It can also be used in the preparation of donor tissue for endothelial keratoplasty (EK) [3].

FSL is currently used for refractive surgery worldwide, including the creation of flaps in laser-assisted in situ

keratomileusis (LASIK) and refractive lenticule extraction (ReLEx) [5]. FSL has also been increasingly used for cataract surgery, as it has been shown to improve the reliability and reproducibility for creation of corneal wound and anterior capsulotomy and reduce phacoemulsification energy for lens fragmentation [6].

In this review, we aim to provide information on the application of FSL in anterior segment surgery, including cornea, refractive, and cataract surgeries.

2. Femtosecond Laser in Keratoplasty

2.1. Femtosecond Laser-Assisted PK. FSL is able to create customized trephination cuts, such as top-hat, zigzag, and mushroom configurations, to improve biomechanical wound integrity and facilitate wound healing after PK and DALK [4]. Theoretically, corneal trephination using FSL can enable the creation of more structurally stable and predictable wound configuration by providing more accurate fit with larger contact area between the donor and host (Figure 1) [7]. This may conceivably result in reduced wound distortion and enhanced wound tensile strength, decreasing surgically induced astigmatism and facilitating wound healing and visual recovery [4, 7].

Previous studies revealed that the FSL-assisted KP with the two most popular trephination patterns, the "top-hat" and "zigzag" configuration, enabled faster visual recovery with better best-corrected visual acuity (BCVA), less astigmatism, and faster suture removal than manual PK [7–12], although graft failure and rejection rates were similar to those for manual PK [8]. In comparison between the "top-hat" and "zigzag" incisions, the two patterns showed comparable visual and refractive outcomes, endothelial cell counts, and wound healing [13]. However, Chamberlain et al. [14] showed that the improvement in astigmatism with FSL-assisted PK was not significant after 6 months postoperatively, and no significant improvement in BCVA was found at any time point [14]. FSL-assisted PK with "mushroom" configuration also resulted in reduced astigmatism [15] and was suggested to be a viable option for pediatric patients, as it combined the refractive advantage of a larger anterior diameter with an immunologic advantage of smaller posterior graft [16].

2.2. Femtosecond Laser-Assisted DALK. With the ability to perform predictable and precise dissections at a variety of orientations and depths, while providing stable donor-host apposition, FSL is also envisaged to be a useful tool for lamellar keratoplasty procedures [17, 18]. Theoretically, FSL may be advantageous in DALK, as it enables the removal of anterior stromal lamella and formation of big bubble without difficulty [19], as well as improving wound integrity and healing [17].

FSL can be used for the preparation of both the recipient and donor tissues [6]. In the recipient cornea, FSL first creates an anterior lamellar cut at a predetermined depth and then performs a peripheral circular trephination cut, from the lamellar interface plane to just above the corneal epithelium [3, 6, 17]. The donor tissue is prepared in a similar fashion using a corneoscleral button mounted on an artificial anterior chamber (AC), which is transferred and sutured onto the host lamellar bed using either continuous or interrupted 10-0 nylon sutures [17]. The surgical procedures of our DALK case using FSL are demonstrated in Figure 2.

A case series study demonstrated that FSL-assisted DALK was an efficient and safe procedure for visual recovery in patients with anterior corneal diseases [20]. FSL-assisted DALK with mushroom configuration enabled faster visual recovery than manual DALK [21, 22], although the final BCVA was comparable [21]. Salouti et al. [23] recently reported that FSL-assisted DALK was advantageous for reducing residual myopia and restoring corneal anatomy compared with manual DALK in patients with keratoconus, although postoperative BCVA and astigmatism were comparable.

2.3. Femtosecond Laser-Assisted EK. FSL can also allow for a more reliable, predictable, and precise preparation of donor and recipient tissues for EK [6]. In recipient cornea, the posterior trephination cut starts from the AC and progresses anteriorly through Descemet's membrane, and the lamellar dissection is performed on the posterior stroma [3]. The donor cut is performed in a similar fashion using a corneoscleral button mounted on an artificial AC [3].

Early results demonstrated that FSL-assisted EK showed worse visual outcome and higher endothelial cell loss than manual PK, although it had significantly reduced postoperative astigmatism [24]. The authors concluded that a modification of donor tissue insertion technique was needed to prevent endothelial cell loss [24].

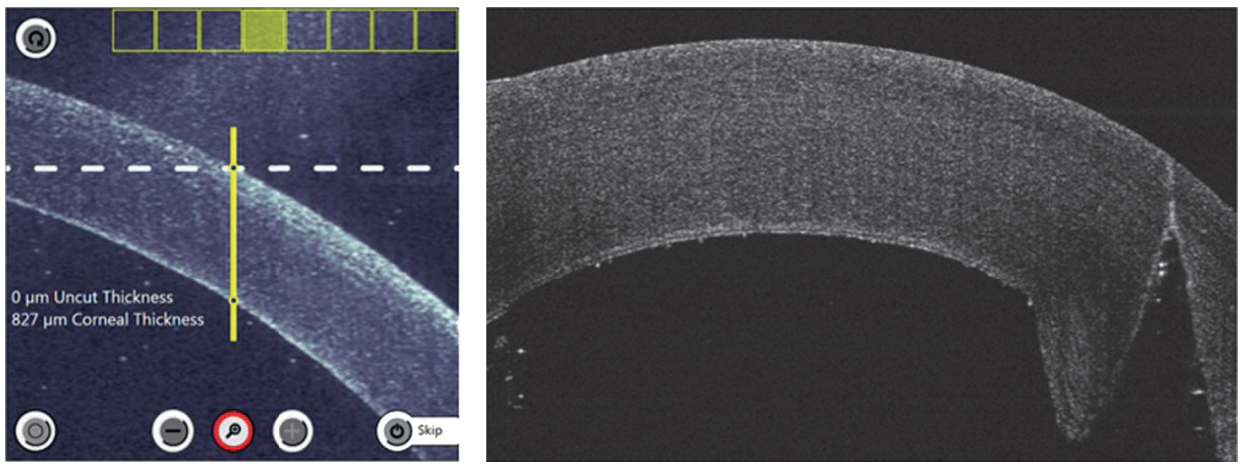
Recent studies reported that FSL-assisted Descemet's membrane EK (DMEK) had a visual outcome comparable to manual DMEK, with a significantly reduced rate of graft detachment, rebubbling, and endothelial cell loss [25, 26]. Sorkin et al. [27] suggested that FSL-assisted DMEK might be a safe and effective option in patients with failed PK, resulting in substantially reduced detachment and rebubbling rates and trend towards reduced primary failure than manual DMEK.

However, FSL has a limitation that it can increase operating time and elevate the costs of tissue cutting and the surgical procedure in all kinds of keratoplasty.

3. Femtosecond Laser in Refractive Surgery

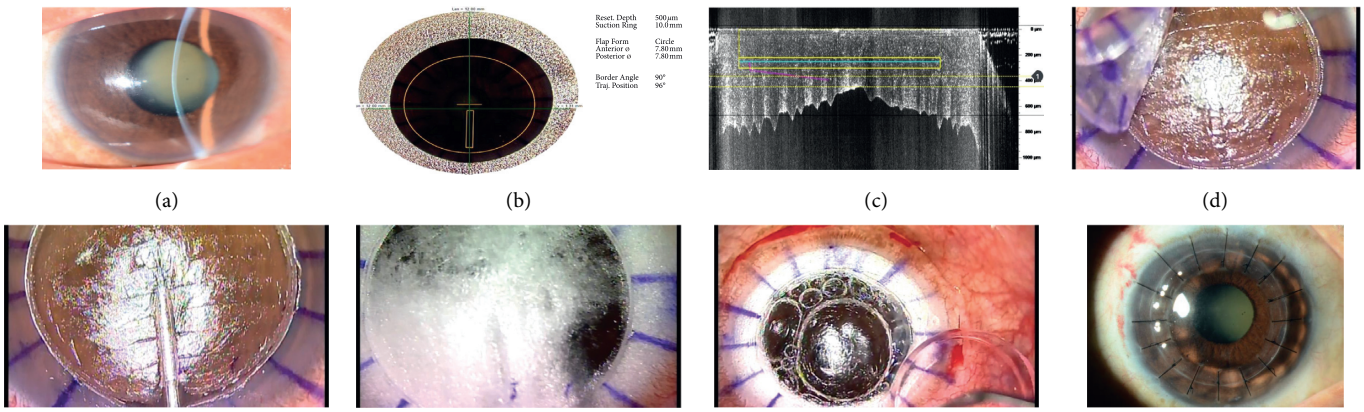
3.1. FSL-Assisted Laser In Situ Keratomileusis (FSL-LASIK). The application of FSL in LASIK flap creation has rapidly gained popularity since its introduction in 2002 [3]. The FSL first performs lamellar dissection at a predetermined depth in the anterior stroma, creating circular vertical cuts in a posterior to anterior direction [3]. Using an instrument, such as an iris sweep, the flap interface is swept across and the flap is lifted [3].

FSL has the following advantages in flap creation over the mechanical microkeratome: (1) wide variability of flap parameters, such as flap thickness and diameter, side cut



(a) (b)

Figure 1: Penetrating keratoplasty with full-thickness trephination using Ziemer Z8 platform in a porcine eye model. (a) The inbuilt OCT scans in eight meridians and the depth of the laser cut can be adjusted. The yellow line indicates the pathway of laser cutting. The cutting pattern can be customized. (b) Postcutting OCT scans showing full-thickness trephination.



(a) (b) (c) (d)

(e) (f) (g) (h)

Figure 2: FSL-assisted DALK with Ziemer Z8 laser. (a) Preoperative anterior segment photograph of a patient with keratoconus. (b) Inbuilt intraoperative OCT for surgical planning. (c) Purple line: tunnel cut and second solid yellow line: lamellar cut. (d) Removal of anterior cap. (e) The cannula was inserted into the laser-created intrastromal tunnel for air bubble injection. (f) Injecting air for big bubble technique. (g) DM sparing and DALK graft. (h) 3 months postoperatively.

angle, hinge length, and position [28, 29]; (2) more precise and predictable flap thickness and position that result in improved flap safety [28, 29]; (3) decreased risk of flap-related complications, such as free caps, buttonholes, short flaps, and irregular cuts [28]; and (4) flaps with uniform thickness with a planar shape that is different from the mechanical flap with meniscus shape [3].

Meta-analysis studies concluded that FSL-LASIK has good visual outcome and safety comparable to LASIK with microkeratomes and may have improved predictability of flap thickness and refractive error [30, 31].

Regarding complications, diffuse lamellar keratitis is the most common but is generally mild and self-limited [30]. FSL is also associated with several unique complications. First, confluent cavitation gas bubbles during intrastromal laser treatment can result in opaque bubble layer (OBL) in the deep stromal bed that may interfere with iris registration and pupil localization [3]. Second, seepage of gas bubbles into the subepithelial space can cause flap buttonholes [32]. Although it is extremely rare, leakage of gas bubbles into the AC may hamper the centration of the laser beam [33]. Third, transient light-sensitivity syndrome is characterized by severe photophobia with good visual acuity and absence of abnormalities on ophthalmologic examination [34]. It usually occurs 2 to 6 weeks postoperatively and improves in a week with topical corticosteroids [34]. Finally, rainbow glare may be an optical side effect of light scatter from the back surface of the interface after FSL-LASIK, which could be prevented by using the improved focusing optics of higher numeric aperture [30, 35].

3.2. Refractive Lenticule Extraction (ReLEx). FSL-LASIK requires both FSL for flap creation and an excimer laser for corneal stromal ablation [5]. Femtosecond lenticule

extraction (FLEx) was introduced as a new method that requires only FSL [36], which was further developed into small incision lenticule extraction (SMILE) [5]. Subsequently, the overall terminology "refractive lenticule extraction (ReLEx)" was suggested to include these two procedures [5].

In FLEx, a corneal flap is created using FSL [36]. However, FLEx involves intrastromal dissection using FSL and extraction of a refractive lenticule instead of stromal ablation as in FSL-LASIK [36]. In SMILE, the flap is not created and the refractive lenticule is extracted through small peripheral corneal incision constructed by FSL [5]. Theoretically, SMILE can improve corneal biomechanical stability by avoiding corneal flap creation [36].

In SMILE, after initial docking of the eye with the interface cone and suction fixation, the FSL creates a posterior surface of the lenticule, a lenticule side cut, an anterior surface, and a small incision [37, 38]. Then, a manual dissector is inserted into the pocket through the incision, which is used to separate the lenticule along the anterior and posterior surface [37, 38]. The lenticule is then extracted through the incision using removal forceps (Figure 3) [37, 38].

Lenticule dissection and extraction is the most challenging step and can lead to complications, such as tear of anterior cap or side cut, posterior stromal damage, and partially or completely retained lenticule [39]. However, these complications are related to inexperience and may decrease with the learning curve [37, 39]. Complications, including suction loss, incisional bleeding, OBL, and inaccurate laser pulse placement, have also been reported; however, these can mostly be resolved with appropriate management [40].

Studies suggest that both FLEx and SMILE show good visual and refractive outcomes, safety, and predictability profiles [5, 41, 42]. SMILE was reported to have good efficacy and safety comparable to FSL-LASIK, and milder higher-order aberrations and spherical aberration, higher contrast sensitivity, and fewer dry eye symptoms than FSL-LASIK [43–46] A meta-analysis study indicated that SMILE may be advantageous over FSL-LASIK due to its association with a lower risk of flap-related complications, faster corneal nerve recovery, reduced corneal nerve injury, and higher-order aberrations, despite its comparable safety, efficacy, and predictability levels to FSL-LASIK [36].

4. Femtosecond Laser-Assisted Cataract Surgery (FLACS)

FSL has currently four applications in cataract surgery: corneal wound construction, anterior capsulotomy, lens fragmentation, and limbal relaxing incisions (LRIs) [5]. It is envisioned to improve the safety and efficacy of the cataract surgery [1, 47].

4.1. Corneal Wound Construction. The optimal construction of clear corneal incision (CCI) with adequate length and architecture is important for wound safety and prevention of complications associated with wound leakage, such as induced astigmatism, iris prolapse, hypotony, and endophthalmitis [1, 48]. However, manual CCI is sometimes difficult and less predictable in terms of length and shape [49] and is more prone to injuries of Descemet's membrane and gaping of the internal wound, which can result in delayed healing and increased risk of corneal decompensation [50]. FSL allows CCIs to be leak-proof and self-sealing with greater reproducibility and safety [48, 51], which may result in better wound integrity and sealability than manual CCI [1, 52].

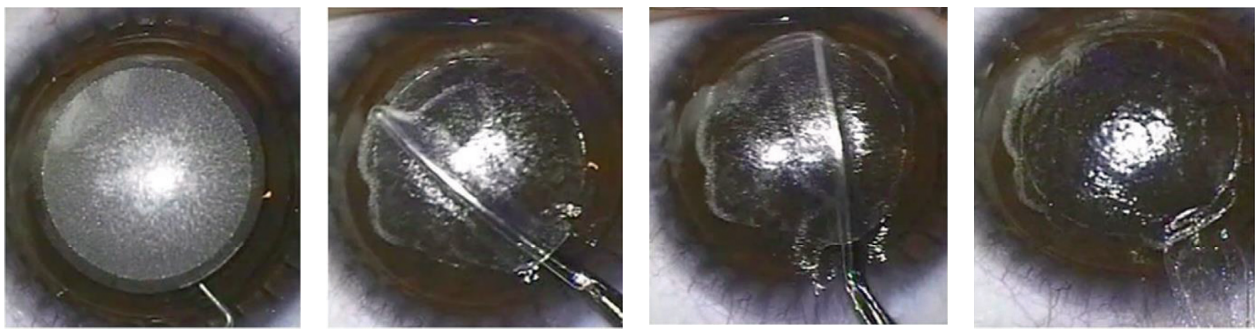
4.2. Anterior Capsulotomy. Anterior capsulotomy with appropriate size and circularity is important for the positioning and performance of the intraocular lens (IOL) [53, 54]. It is also closely related to the effective lens position (ELP), which is a major determinant of IOL power calculation [55]. Inadequate size or circularity of the capsulotomy can cause tilting, decentration, or rotation of IOL and changes in ELP that can result in worse visual and refractive outcomes, with more profound effects with multifocal and toric IOLs [1, 56].

However, manual capsulorhexis is one of the most technically challenging skills in cataract surgery [57], with increased difficulty in cases with shallow AC, capsular fibrosis, weak zonule, and mature or pediatric cataracts [54]. Although creation of capsulotomy with good size, circularity, and centration has been increasingly emphasized, manual capsulorhexis is associated with substantial unpredictability and variability even for experienced surgeons [54, 58].

FSL is shown to allow for more reliable and reproducible anterior capsulotomy with enhanced centration and circularity than manual capsulorhexis [48, 54, 58–60]. FSL can substantially reduce the risk of IOL tilting or decentration, which is particularly important for multifocal IOL [59, 61]. Animal studies revealed that FSL might be associated with increased tensile strength of the capsular opening [58, 62]. FSL is also advantageous in achieving complete overlap between the anterior capsule and IOL optic, which is important for IOL centration and prevents posterior capsular opacification, compared to manual capsulorhexis [54, 60]. Dick et al. [63] reported that FLACS achieved earlier capsular bag stabilization, suggesting that it may allow for more predictable ELP, IOL power calculations, and refractive outcomes [63, 64].

FSL has another advantage. It is not influenced by the axial length, pupil size, and corneal magnification, whereas manual capsulorhexis is dependent on these factors [60].

4.3. Lens Fragmentation. Ultrasound energy within the AC causes oxidative stress and increases the risk of injury to the iris, capsule, and cornea [65]. FLACS involves the pretreatment of the lens using liquefaction or fragmentation to segment or soften the cataract [2]; thus, it can reduce the amount of ultrasound energy and intraocular manipulation during phacoemulsification [51, 58, 66–68]. Hence, FLACS is predicted to reduce the risk of posterior capsular rupture and corneal endothelial cell injury [49, 67].



(a) (b) (c) (d)

Figure 3: Small incision lenticule extraction (SMILE). (a) Small arcuate incision, anterior and posterior lenticule planes are cut by FSL. (b) Dissection of anterior lenticule plane, followed by (c) dissection of posterior lenticule plane. (d) Extraction of lenticule from small incision.

Studies have revealed that FLACS substantially reduced phacoemulsification energy and effective phacoemulsification time (EPT) compared with conventional cataract surgery [51, 58, 66]. FLACS has also been reported to be associated with decreased corneal swelling and endothelial cell loss, which might be correlated with reduction of EPT [66, 69, 70].

4.4. Limbal Relaxing Incisions. With its potential ability to create precise and accurate LRIs, FSL can theoretically overcome the limitations of manual LRIs, which include technical difficulty and unpredictability, and as such, it is expected to be widely used for the correction of astigmatism [1, 2]. Chan et al. [71] suggested that arcuate keratotomy using FSL might be helpful for the management of low to moderate astigmatism after cataract surgery. Yoo et al. [72] reported that FSL-assisted arcuate keratotomy could be a safe procedure with comparable efficacy to toric IOL for reducing residual astigmatism after cataract surgery.

4.5. Learning Curve. The FLACS technique does require a significant learning curve, as demonstrated by Bali et al. [73], who studied the first 200 cases. Suction breaks occurred in 2.5% of cases (5 eyes), which led to an abortion of the remaining laser procedure [73]. Small anterior capsular tags were found in 10.5% of cases (21 eyes), which led to anterior radial tears in 4% (8 eyes) [73]. Posterior capsular ruptures and posterior lens dislocation occurred in 3.5% (7 eyes) and 2% (4 eyes), respectively [73]. Although these complication rates may appear even higher compared with conventional phacoemulsification, it should be noted that the report is describing the learning curve of FLACS [73]. Conventional phacoemulsification also requires a significant learning curve, as pointed out by Martin and Burton [74] the rate of vitreous loss fell from 4.0% in the first 300 cases to 0.7% in the last 300 cases, over the course of 3000 conventional phacoemulsification cases [74]. In a report of a course of the first 1500 FLACS cases, Roberts et al. [75] revealed that the incidence of anterior and posterior capsular tears significantly decreased from 7.5% (15 eyes) in the first 200 cases to 0.62% (8 eyes) in the latter 1300 cases, indicating the safety of FLACS after learning curve [75]. Other studies also reported the rate of anterior capsule tear to be in the range of 0.21%–0.43% [76, 77], suggesting that the capsular complication rate of FLACS might be lower compared with that of conventional surgery reported in the literature [78].

4.6. Clinical Outcome. Kránitz et al. [61] reported that the FLACS group demonstrated significantly better BCVA than the conventional surgery group, suggesting that the better BCVA showed a correlation with less IOL tilting and decentration [61] Filkorn et al. [79] showed that the FLACS group had greater predictability of IOL power calculation, with greater differences especially in the long (axial length >26.0 mm) and short (axial length <22.0 mm) eyes [79]. Mihältz et al. [80] revealed that FSL capsulotomy led to significantly reduced internal optical aberrations compared with manual capsulotomy, which might result in better optical quality [80]. Lee et al. [81] recently demonstrated that FLACS was associated with greater predictability in the astigmatic change, lower internal aberrations, and increased patient satisfaction [81].

By contrast, several studies reported that FLAC did not show any significant improvement in the refractive and visual outcomes [51, 82–84], although the reduction in EPT might validate the safety and efficacy of FLACS [84]. Roberts et al. [85] recently revealed that FLACS showed a significant reduction in posterior capsule ruptures, although it did not result in any significant differences with respect to the visual outcome, refractive error, and corneal endothelial injury.

FLACS is also suggested to be associated with decreased aqueous flare as a measure of postoperative intraocular inflammation [86, 87], which might be correlated with reduction in EPT [87]. Although FSL capsulotomy can increase the inflammatory cytokines and prostaglandin levels in AC [88, 89], the reduction of EPT energy may contribute to the reduction in postoperative AC inflammation [89]. FLACS also resulted in a significant reduction in thickness of 1.5 mm inner macular ring during the early postoperative period, suggesting that FLACS may be associated with milder postoperative inflammation and can be beneficial for patients at risk of postoperative inflammation and macular edema [1, 90].

FLACS can improve the outcomes in complicated cases, such as trauma cases with anterior capsule rupture or lens

subluxation associated with Marfan syndrome [91, 92]. It is also advantageous in eyes with shallow ACs over conventional cataract surgery, offering milder AC inflammation and better visual outcome [93]. Successful FLACS after implantation of the Malyugin ring in the case of acute phacomorphic glaucoma with mature cataract and shallow AC has also been reported [94].

FSL can improve the safety of anterior capsulotomy in intumescent white cataract [64, 95]. In a study of 25 eyes with white cataract, Conrad-Hengerer et al. [95] reported that FLACS allowed for an uneventful IOL implantation in all cases, although radial tear and incomplete capsulotomy button occurred in 2 eyes (8%) and 3 eyes (12%), respectively.

In pediatric cataract, elasticity of the lens capsule renders the capsulorhexis more challenging and unpredictable, often leading to decentered, inadequate sizes of capsulotomy and even radial tears [49]. Hence, FLACS may play an important role in the improvement of the efficacy and safety of pediatric cataract surgery, especially with respect to the creation of anterior capsulotomy with good diameter and centration [49]. Dick et al. [96] reported the successful use of FLACS for both anterior and posterior capsulotomies in 4 children aged 9 months to 7 years. Fung et al. [97] recently introduced the use of the mobile FSL platform in anterior capsulotomy for pediatric cases, suggesting that FLACS can be applied in patients receiving surgery under general anesthesia [97].

4.7. Limitations and Complications. Corneal opacification can interfere with the absorption of the laser and cause dispersion of laser energy [1]. Hence, significant corneal opacity may hinder FLACS; however, the degree of opacity that causes significant scattering of FSL has not yet been elucidated [51]. As FSL capsulotomy requires mydriation of 7-8 mm, poor dilatation, posterior synechiae, and corectopia have been considered relative contraindication [49]. However, poor dilation can be addressed using implantation of pupil expanders, such as the Malyugin ring [49, 94].

Posterior subcapsular cataracts were also considered contraindication, due to the safety margin requirement for FLACS being at least 400 μm from the posterior capsule [68]. However, Titiyal et al. [98] introduced a technique of FLACS with a hybrid pattern of cylinder and chop in which remaining outer rings acting as a protective cushion and manual hydrodissection and hydrodelineation were avoided and suggested that the techniques may be effective in cases of posterior polar cataract.

FLACS can be associated with an increased risk of capsular block syndrome, in which posterior capsule rupture and lens dislocation can occur following hydrodissection [99]. FSL lens fragmentation produces intralenticular gas, which induces nuclear volume expansion and formation of a seal between capsulotomy and the expanded nucleus. This restricts the decompression inside the lens, resulting in pressure rise on the posterior capsule and posterior capsular rupture [1, 99]. However, it can be prevented with measures, such as decompressing the AC and lens capsule before and during hydrodissection, dividing the hemispheres before hydrodissection, and performing a gentle and slow hydrodissection [1, 99].

Poor docking before laser procedure is associated with tilting of the lens, which can lead to capsular tag, incomplete capsulotomy, and incomplete lens fragmentation [49, 73]. However, these complications diminish throughout the learning curve and have also been prevented by technical developments on the interface [49, 73]. Subconjunctival hemorrhage caused by the suction ring is frequently found; however, it resolves spontaneously in 1-2 weeks [49].

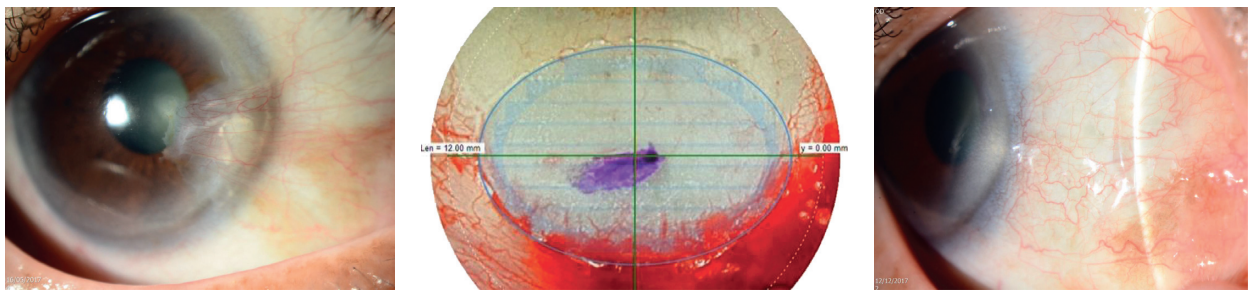
Despite the potential advantages of FLACS, it has a limitation that it is not cost-effective at its current cost, because of the cost of equipment and maintenance of laser [100, 101]. FSL can also slow operating room flow for cataract surgery and increase operating time. Moreover, there are contradictory reports of the clinical comparisons between FLACS and conventional phacoemulsification surgery. A meta-analysis study concluded that FLACS was not superior to conventional phacoemulsification surgery in terms of intraoperative and postoperative complications [102]. A Cochrane systematic review including 16 randomized clinical trials that compared FLACS with conventional phacoemulsification surgery also failed to determine the superiority of FLACS [103]. Therefore, further development of FLACS would be needed to provide significant improvement in safety and efficacy and to reduce costs to keep health systems sustainable.

5. Femtosecond Laser in Other Anterior Segment Surgeries

5.1. Astigmatic Keratotomy and Arcuate Wedge Resection. FSL can lessen the burden and increase precision when performing corneal astigmatic surgery, such as arcuate keratotomy or wedge resection [104, 105]. Arcuate keratotomy performed with FSL was effective and predictable in reducing postkeratoplasty astigmatism and tended to have reduced misalignment of treatment and complications including corneal perforation [104, 105]. Ghanem and Azar [106] introduced a technique using FSL to perform corneal wedge resection, which resulted in significant improvement of astigmatism [106].

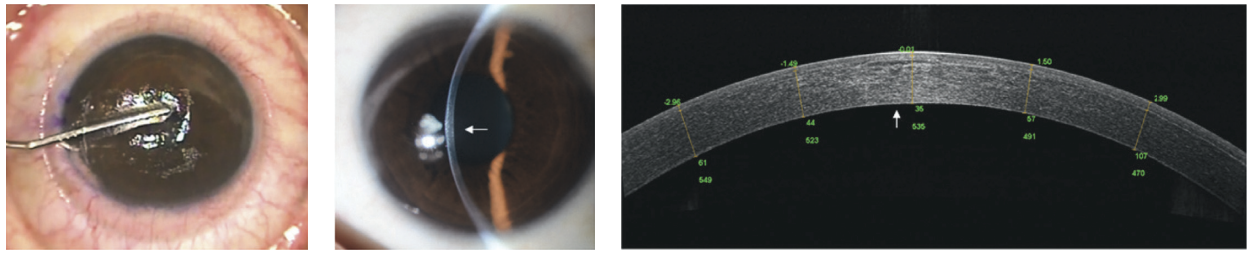
5.2. Intracorneal Ring Segments. Intracorneal ring segments are implanted in the midperipheral cornea stroma for correction of myopia ≤ -3.5 diopters, milder cases of keratoconus without central scarring and post-LASIK ectasia [3, 6, 107].

FSL may be programmed to precisely create uniform channels at a specific depth for safer insertion of the segments [6]. The use of FSL for channel creation was reported to be as effective as mechanical dissection for mild to moderate cases of keratoconus and post-LASIK keratectasia [108]. Piñero et al. [109] reported that ring segment insertion using FSL had comparable visual and refractive outcomes to mechanical expander, and FSL showed more favorable aberrometric correction [109].



(a) (b) (c)

Figure 4: Pterygium excision and FSL-assisted conjunctival autograft preparation. (a) Preoperative anterior segment photograph. (b) Laser handpiece docking at superior bulbar conjunctiva to harvest the conjunctival autograft. The depth of the lamellar cut, and the size of autograph, can be adjusted intraoperatively. (c) At postoperative 6 months. No recurrence with good cosmetic outcome.



(a) (b) (c)

Figure 5: Implantation of the inlay derived from SMILE lenticule for the treatment of presbyopia. (a) Dissection of intrastromal pocket for inlay implantation. (b) At postoperative 6 months. The inlay was in the central cornea without eliciting stromal haze or inflammatory response. (c) Postoperative 6 months OCT showing the position of implanted inlay.

5.3. Experimental Studies regarding Potential Application of the FSL. FSL is also suggested to enable an adjustment of IOL power by increasing hydrophilicity of the target areas within the optic, creating a refractive index shaping lens within an existing IOL [110, 111]. An *in vitro* study revealed that a negative refractive index change in the laser-treated optic areas resulting from the change in hydrophilicity might be the chemical basis for an alteration of the IOL power [112]. An experimental study using a hydrophobic acrylic IOL revealed that power adjustment using FSL produced a reliable refractive change [111]. An animal study also showed that IOL power adjustment using FSL might be a precise, reliable, and biocompatible method for the correction of refractive error after cataract surgery [110].

An experimental study showed that IOL fragmentation was feasible with FSL [113]. Anisimova et al. [114] introduced a case in which a one-piece acrylic hydrophobic IOL was successfully transected using FSL with low energy parameters for explantation via a small corneal incision. Bala et al. [115] also reported two cases in which FSL was used to transect hydrophilic acrylic IOL.

In vitro studies showed that the creation of gliding planes using FSL inside the crystalline lens tissue can enhance the deformation ability of the lens, suggesting that it can be a possible option for the treatment of presbyopia [116–118].

FSL can also enable automated, quick, and reliable preparation of an ultrathin conjunctival autografting, which might be helpful for further standardization of a surgical procedure for conjunctival reconstruction [119]. Our studies have shown the efficacy of FSL in the preparation of an ultrathin conjunctival autografting after excision of pterygium or conjunctival melanosis (Figure 4) [119–123]. Our study using a primate model suggested that biological corneal inlays derived from lenticules extracted from SMILE might be a viable option for the management of presbyopia (Figure 5) [124]. Potential application of FSL for tissue preparation for stromal keratophakia has also been introduced [125].

6. Conclusion

FSL is capable of precise, accurate, and predictable tissue cutting with minimal collateral tissue damage and can create customized incisions with various shapes [17, 18]. Therefore, the laser is expected to be helpful for surgeries of anterior segment tissues, including cornea and lens. So far, many studies have indicated that FSL can be a useful tool for the improvement of efficacy and safety of keratoplasty, refractive surgery, and cataract surgery. Moreover, experimental studies suggested the novel application of FSL, such as IOL power adjustment, IOL fragmentation, presbyopic correction, and pterygium surgery.

With technological development, FSL is envisaged to be an even more useful tool for various anterior segment surgeries, which will enable better prognosis and safety of these surgeries. However, the results must be validated through well-conducted clinical trials.

Conflicts of Interest

None of the authors have proprietary interests in the study or financial interests to disclose.

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Research Article

Extrusion of Femtosecond Laser-Implanted Intrastromal Corneal Ring Segments in Keratoconic Eyes: Prevalence, Risk Factors, and Clinical Outcomes

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Purpose. To evaluate the prevalence, possible risk factors, and clinical results of femtosecond laser implanted intrastromal corneal ring segment (ICRS) extrusion in keratoconic eyes. *Patients and Methods*. This is a retrospective observational study evaluating 333 eyes of 269 patients who were subjected to femtosecond laser-implanted Keraring ICRS in the Sohag Refractive Center, Sohag, Egypt, from January 2014 to January 2019. The study included eyes with channels created by a femtosecond laser (60 kHz IntraLase femtosecond system; Advanced Medical Optics, Santa Ana, California, USA) with implantation of Keraring intrastromal corneal ring segments (Mediphacos, Belo Horizonte, Brazil). Patient data and causes of Keraring extrusions were identified as being those rings that migrated or showed melting of the cornea with no other reason which required segment removal. *Results*. Seven eyes were found to fit the criteria of ring extrusion (2.1%) out of the 333 eyes which had Keraring implantation. All extruded rings were from patients with keratoconus grade 3, with eccentric cones, and with femtosecond creation of the tunnel. Four eyes belonging to 3 patients (57.1%) had a history of vernal Keratoconjunctivitis, yet they did not show signs of activity at the time of implantation. They reported excessive rubbing just before they presented with conjunctival hyperemia and foreign body sensation. Five eyes (71.4%) showed chronic sun exposure. The mean minimal corneal thickness was 401.85 μm (range 384–420 μm), while the mean maximum keratometry was 61 D (range 55.18–68.96 D). Most of the extruded rings had large arcs. Six eyes had crosslinking (CXL) at the same session of the Keraring implantation. The simultaneous CXL treatment is considered as a possible significant risk factor for ring extrusion. *Conclusion*. ICRS is an effective reversible option for patients with keratoconus who are intolerant to hard contact lenses, yet the choice of cases and ring segments is mandatory for satisfactory results. Moreover, meticulous history taking and examination reduces the incidence of complications including extrusion.

1. Introduction

Implantation of intrastromal corneal ring segments (ICRS) is an effective and reversible refractive technique for keratoconus management [1]. Different types of incomplete rings are used in the management of keratoconus: Intacs (AdditionTechnology, Inc.), Ferrara ring (Ferrara Ophthalmics Ltd.), and Keraring (Mediphacos Ltd.) [2].

The reversibility of ICRS implantation has been confirmed in keratoconic eyes and poses a major advantage as the technique of implantation does not involve tissue removal [3].

Despite the positive reports of ICRS implantation in managing corneal ectatic disease, some complications have been reported such as incomplete tunnel creation, anterior or posterior corneal perforation, epithelial defects, and segment extrusion [4–9].

Ring segment extrusion is one of the late complications of ICRS implantation, leading to ring explantation [7]. Different causes have been supposed as an etiology including ring segment migration and corneal melting which precede total ring segment extrusion [10].

Ring implantation by mechanical tunnel creation showed more common extrusion than tunnel creation

performed by the femtosecond laser (FS) [11]. Femtosecond laser-created corneal tunnels are an effective procedure to avoid late ring segment extrusion as it made the corneal ring implantation procedure faster, easier, and safer with precise depth of implantation [12].

The aim of our study is to evaluate the prevalence, possible risk factors, and clinical results of the femtosecond laser-implanted ICRS extrusion in keratoconic eyes.

2. Patients and Methods

This is a retrospective observational study evaluating 333 eyes of 269 patients who were implanted with Keraring ICRS in the Sohag Refractive Center, Sohag, Egypt, from January 2014 to January 2019. This study followed the tenets of Declaration of Helsinki, and Ethical Board Committee approval from the institution was obtained.

Patient data and causes of Keraring extrusions were identified as being those rings that migrated or showed melting of the cornea with no other obvious reason which required segment removal. Exclusion criteria included eyes with elective explantation for refractive dissatisfaction, infective or noninfective keratitis, or visual disturbance and ring implantation indications other than keratoconus and mechanical creation of the ring tunnel.

The study included eyes with channels created by a femtosecond laser (60 kHz IntraLase femtosecond system; Advanced Medical Optics, Santa Ana, California, USA) with implantation of Keraring intrastromal corneal ring segments (Mediphacos, Belo Horizonte, Brazil).

All patients had 1 or 2 Keraring ICRS implanted for the treatment of keratoconus (grade 1, 2, and 3 according to Amsler-Krumeich classification) following the Keraring nomogram rules. It was taken into consideration that the central cornea was clear and age range was between 18 and 40 years. The minimum corneal thickness at the implantation site was 350 μm at the thinnest corneal point and at least 400 μm at the incision site. All cases underwent full ophthalmological evaluation including uncorrected visual acuity (UCVA), best spectacle corrected visual acuity (BSCVA), slit-lamp biomicroscopy (dry eye grading) [13], manifest and cycloplegic refraction, and corneal tomography using Sirius Scheimpflug placido topography (Costruzione Strumenti Oftalmici, Florence, Italy).

2.1. Primary Implantation Procedure. The surgical procedures were performed by the two surgeons involved in this study under topical anesthesia and complete aseptic measures. The procedure was initiated by marking a reference point for centration (Purkinje reflex). Continuous circular stromal tunnel was created as recommended by ring manufacturers and previous studies [8, 14]. The incision axis was planned on the axis of the steepest keratometric reading at an 80% depth of the thinnest location as determined by optical and ultrasound pachymetry with inner diameter 5.00 mm, outer diameter 5.90 mm, entry cut length 1.40 mm, and entry cut thickness 1 mm. Incision was created at the steepest axis, with ring energy 1.9 mJ. After ring insertion, a soft bandage contact lens was applied. Postoperatively, topical moxifloxacin and prednisolone acetate eyedrops were used with topical preservative-free lubricants.

2.2. Explantation Procedure. Explantation of extruded ring segments was done under complete aseptic conditions. The extruded side of the segment was pulled out with corneal forceps. A Sinskey hook was introduced to grab the segment at its distal end near the wound until completely pulled out of the tunnel. In some cases where melting was established, the ring was removed from the area it protruded from. No sutures were used. A soft bandage contact was applied to allow healing of the empty tunnel. After all procedures, moxifloxacin and dexamethasone eyedrops were used 4 times a day along with lubricant eyedrops 5 times a day for 2 weeks. The analysis comprised data from pre- and postoperative months. The rate and causes of extrusions were reported and analyzed throughout the six years. Slit-lamp examination to evaluate the ICRS position and corneal integrity after explantation was performed. Subsequent postextrusion follow-up included UCVA, BCVA, manifest refraction, slit-lamp evaluation, and corneal tomography.

2.3. Corneal Crosslinking (CXL) Procedure. Eyes that showed progression over follow-up periods were subjected to crosslinking. Inclusion criteria for accelerated epithelium on CXL had thinnest corneal thickness of 400 μm. CXL was performed following the ring implantation in the same session. CXL steps were as follows: Dextran-free hypo-osmolar riboflavin drops which contain benzalkonium chloride to enhance epithelium permeability (ParaCel, Avedro, Waltham, Massachusetts, USA) was applied every 1.5 min for 4.5 min, followed by benzalkonium chloride-free riboflavin drops (VibexXtra, Avedro, Waltham, Massachusetts, USA) every 1.5 min for 6 min. Then, accelerated CXL was used for 2 min and 40 seconds in a pulsed mode (2 seconds on/1 second off) (KXL accelerated CXL System, Avedro, Waltham, Massachusetts, USA). The power used was 45 mW/cm^2 with a total energy radiated of 7.2 J/cm^2. A contact lens was then applied for one week and eyedrops were prescribed for 4 weeks in the form of artificial tears, steroids, and antibiotics.

3. Statistical Analysis

Statistical analysis was performed using SPSS for Windows software (version 15.0.1, SPSS, Inc.). Student's t test for paired data was used to compare the preoperative and postoperative data (keratometry, sphere, etc.). The Wilcoxon rank test was used for comparing the rate of extrusions throughout the five years.

4. Results

Seven eyes were found to fit the criteria of ring extrusion (2.1%) out of the 333 eyes which had Keraring implantation. The mean age of the patients in the extrusion group was 20.27 years ± 4.75 (SD) (range from 18 to 25 years), while mean age in the control group was 21.7 ± 5.3 with no

statistical difference between groups. Comparison between the refractive data between eyes with extrusion and eyes with no extrusion are represented in Table 1. There was no statistical difference on comparing the prering implantation refractive data in both groups as well as postimplantation data. Analysis of the refractive data of the seven eyes before ring extrusion and after extrusion is demonstrated in Table 2. The refractive effect of the rings was reversed as they were removed (Figure 1).

Table 3 summarizes the possible risk factors in the ring extruded cases. There was no history of trauma, and no report of infection was found. All extruded rings were from patients with keratoconus grade 3 with eccentric cones with femtosecond creation of the tunnel. Females showed higher contribution to these cases (6 out of the 7 eyes) (85.7%). Four eyes belonging to 3 patients (57.1%) had a history of vernal keratoconjunctivitis, yet they did not show signs of activity at the time of implantation. They reported excessive rubbing just before they presented with conjunctival hyperemia and foreign body sensation. Five eyes (71.4%) showed chronic sun exposure (more than 6 hours a day). All eyes suffered from dry eye disease with grades ranging from 2 to 3 in severity. The mean thinnest corneal thickness was 401.85 μm (range from 384 to 420 μm) while the mean maximum keratometry was 61 D (range 55.18–68.96 D). The mean time interval between Keraring implantation and extrusion was 6.6 months (range 3–12 months). Five eyes out of the seven had 2 rings implanted in the same eye. Also, five eyes had thick rings implanted 300/250, and the other 2 eyes had rings with a thickness of 250/250. Most of the extruded rings had large arcs. Six eyes had crosslinking (CXL) at the same session of the Keraring implantation.

Table 4 shows the difference between the group with extruded rings and the nonextruded group. Statistically significant difference was found in the following parameters: dry eye, stage of KC, site of the cone, eyes implanted with two rings, thicker rings, increasing ring arc, and simultaneous CXL session.

Ring migration, which is considered an early stage before extrusion, was noted in 4 eyes (57.1%), while corneal melting was found in 5 eyes (2 eyes with ring migration) (Figure 2). In the eyes with corneal melting, the edge of the ring would protrude through the stroma and not necessarily through the primary incision site. Two eyes showed corneal opacification after ring removal (Figure 3).

Eyes with extruded rings were no further managed by reimplantation of ICRS; 4 eyes were left with no further intervention and the rest proceeded to penetrate keratoplasty.

5. Discussion

In the current study, we are reporting the cases with Keraring ICRS extrusion in a case series of ICRS implantation. We were trying to detect potential risk factors and contributing parameters for ring extrusion to be taken into account to decrease such complication.

The rate of ring extrusion in the current study is 2.1%, while others reported 6.4% [10], 19.7% [15], and 30% [7]. The higher incidence can be explained that these rings were implanted in tunnels created by manual dissection. Ferrer et al. [16] reported ICRS extrusion in 28 eyes out of 250 (10.9%), where they found macrophages with extracellular matrix (ECM), cells, collagen, and exopolysaccharide in 68.8% of both ends of the extruded segments using scanning electron microscopy.

Also, in a study by Monteiro et al. [17], they compared the incidence of complications between manual and femtosecond laser-assisted surgery for ICRS implantation and found that there were complications in 18.11% of eyes of the manual group while in the femtosecond laser only 3.6% of eyes. In the manual group, ICRS spontaneous extrusion occurred in 5.66%.

The creation of the channels in our study was done by the femtosecond laser which rules out the uneven depth creation by mechanical dissectors which is reported by other studies. The shortest time that elapsed from the time of implantation till the time of extrusion was 3 months and the longest was 12 months. A study by Oatts et al. reported late extrusion as late as 20 years [18]. The interval elapsing between implantation and extrusion is not the same in all cases, and the mechanism remains elusive. In the seven eyes reported, no obvious local triggering effect and only spontaneous extrusion occurred. One attributing mechanism that might have a role is severe stromal thinning over the implanted rings despite being implanted at an appropriate depth. We also concluded that thicker rings implanted in thinner corneas might play a role in extrusion. The creation of the channels in our study was done by the femtosecond laser which rules out the uneven depth creation by mechanical dissectors which is reported by other studies.

CXL was noted to be associated with all seven cases reported. Six eyes had CXL in the same session which might draw the conclusion that CXL might play a role in the migration and later extrusion of the rings. On searching the literature, no studies were found that link CXL to such a complication which necessitates further research.

We also found that dry eye disease (DED) could also play a role as it was reported to be more prevalent in keratoconus [19]. This might be attributed to the alteration in diffusion of metabolites due to the formation of dellen over the rings along with biomechanical stress [18].

We understand that our study has limitation as there is lack of histologic studies of the explanted rings which might have aided in understanding the potential biomechanical cause. There are histologic reports of corneas removed for penetrating keratoplasty documenting the presence of hypoplasia of the epithelium surrounding the channel with decreased keratocytes density above and below the tunnel and collagen IV synthesis even up to 27 months following implantation. These findings proved to be reversible after 6 months [20].

Four eyes out of the seven had a history of chronic atopic keratoconjunctivitis (AKC) which has been linked to keratoconus [21]. One possible explanation is that the implanted rings can induce chronic foreign body sensation

Table 1: Refractive changes in all eyes comparing the eyes with extrusion with eyes of no extrusion and pre- and postimplantation of ICRS.

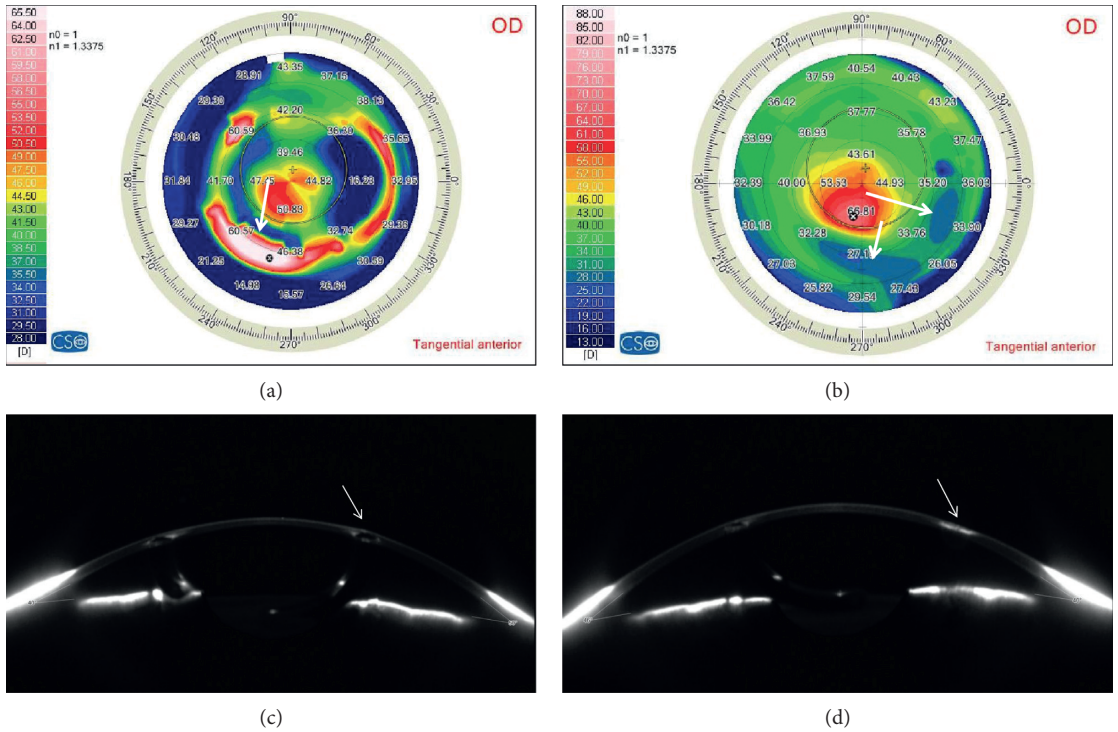
	Eyes with ring extrusion ($n = 7$)		Eyes with no extrusion ($n = 326$)		P value of preimplantation values in both groups	P value of postimplantation values in both groups
	Preimplantation	Postimplantation	Preimplantation	Postimplantation		
Sphere	7.1 ± 3.2	4.8 ± 2.1	8.2 ± 2.8	5.2 ± 2.1	0.53	0.44
Cylinder	6.5 ± 1.7	3.3 ± 1.9	6.1 ± 2.1	4.1 ± 1.4	0.35	0.43
UCVA (logMar)	1.2	0.8	1.2	0.7	0.93	0.81
BSCVA (logMar)	0.8	0.6	0.8	0.6	0.32	0.27
Thinnest CT (μm)	404	401	405	402	0.63	0.56
Max K (D)	61.1	56.3	61.7	57.2	0.23	0.33

UCVA, uncorrected visual acuity; BSCVA, best spectacle corrected visual acuity; CT, corneal thickness; K, keratometry.

Table 2: Refractive changes after extrusion.

	Prering extrusion	Postring extrusion
UCVA (logMar)	0.8	1.0
BSCVA (logMar)	0.4	0.8
Thinnest CT (μm)	404	401
Max K (D)	56	61

UCVA, uncorrected visual acuity; BSCVA, best spectacle corrected visual acuity; CT, corneal thickness; K, keratometry.



(a) (b)

(c) (d)

Figure 1: (a) Keratometry map before Keraring extrusion; the arrows pointing to the steepening correspond to the Kerarings. (b) Keratometry map after ring extrusion; the arrows pointing to the flattening correspond to the extruded rings. (c) Scheimpflug densitometry of implanted Kerarings. (d) Scheimpflug densitometry showing the scar at the site of extruded Keraring.

which triggers an inflammatory reaction with the release of MMP2 and MMP9 in the tear film. These enzymes play a role in degrading the basement membrane of the corneal epithelium [22]. This also can explain why not all rings extrude through the incision site and extrude through corneal melt.

Ring migration in our case series occurred more in long arc thick ring segments just before extrusion. In our

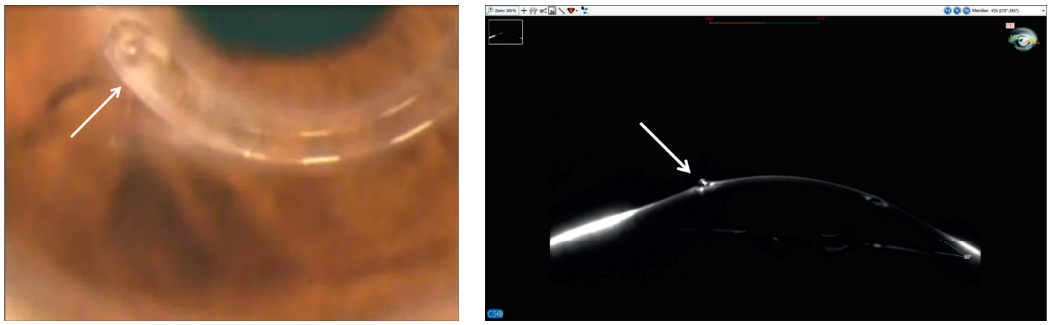
Table 3: Presumable risk factors in the ring extruded cases.

			Patient factors				Topography factors			Keraring factors				
Patient #	Age	Sex	Atopic association	Sun exposure	Dry eye severity level	Stage of KC	*K* max	Cone position	Minimal CT	Number of rings	Extrusion after mns	Ring thickness	Ring arc	CXL timing
1	25	F	+	−	2	3	58.57	Eccenteric	420	2	6	300–250	160–160	Same session
2	18	F	−	+	2	3	59.7	Eccenteric	410	2	3	300–300	160–160	Same session
3	18	F	−	+	3	3	61.22	Eccenteric	390	2	5	250–250	160–160	Same session
4	23	F	−	−	2	3	62.92	Eccenteric	402	2	8	300–300	210–90	Same session
5	20	F	+	+	3	3	55.18	Eccenteric	395	2	12	300–250	210–90	Same session
6	21	F	−	+	3	3	60.57	Eccenteric	384	2	12	300–250	160–160	Same session
7	19	M	+	+	3	3	68.96	Eccenteric	412	2	7	300–300	160–90	Sequential

F, female; M, male; KC, keratoconus; *K*, keratometry; CT, corneal thickness; CXL, crosslinking.

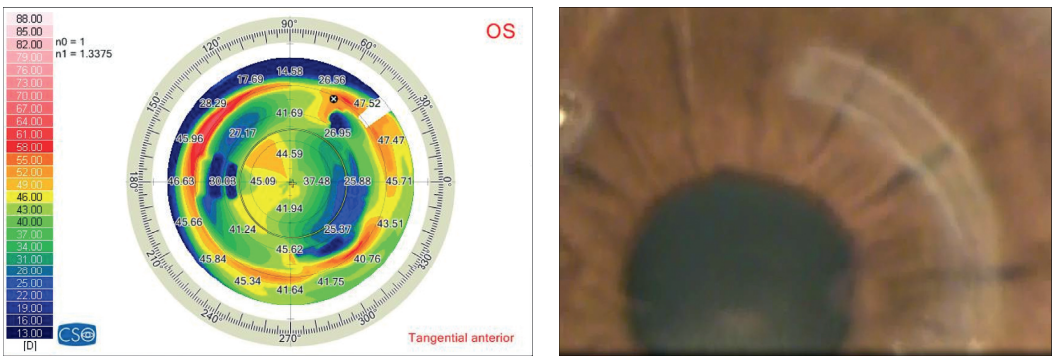
Table 4: Comparison of presumable risk factors between eyes with and without ring extrusion.

	Eyes with ring extrusion ($n = 7$)	Eyes with no extrusion ($n = 326$)	P value
Atopic association	3 (42.9%)	144 (44.1%)	0.33
Chronic sun exposure	5 (71.4%)	216 (66.3%)	0.085
Dry eye severity level			
0	—	48 (14.7%)	
1	—	50 (15.3%)	
2	3 (42.9%)	120 (36.8%)	0.044
3	4 (57.1%)	108 (33.1%)	0.03
Stage of KC			
Stage 1	—	84 (25.8%)	
Stage 2	—	112 (34.4%)	
Stage 3	7 (100%)	130 (39.9%)	0.02
K max			
<55 D	—	84 (25.8%)	
55–62 D	5 (71.4%)	144 (44.2%)	0.052
>62 D	2 (28.6%)	98 (30.1%)	0.063
Cone position			
Central	—	219 (67.2%)	
Eccentric	7 (100%)	107 (32.8%)	0.001
Number of rings			
One ring	—	194 (59.5%)	0.82
Two rings	7 (100%)	132 (40.5%)	0.001
Ring thickness			
300	8 (57.1%)	128 (27.9%)	0.03
250	6 (42.8%)	219 (47.8%)	0.087
200	—	111 (24.2%)	
Ring arc			
90	3 (21.4%)	105 (22.9%)	0.33
160	9 (64.2%)	288 (62.9%)	0.05
210	2 (14.2%)	65 (14.2%)	0.063
Same session CXL	6 (85.7%)	241 (73.9%)	0.01



(a) (b)

Figure 2: (a) Extruded Keraring. (b) Scheimpflug densitometry showing Keraring extrusion.



(a) (b)

Figure 3: (a) Keratometry map after Keraring extrusion showing corresponding corneal flattening. (b) Corneal scar corresponding to the site of extruded Kerarings.

experience, if a ring migrated in the range of 0.5 mm near the incision site, it should be followed closely with a trial of pushing it back into the tunnel for 2 mm to avoid dislodging if further movement occurred. Yet, if the movement recurred, explantation would be recommended.

In conclusion, ICRS use in the cases of KC is by far a viable option for patients who are intolerant to hard contact lenses, yet the choice of cases, meticulous preoperative evaluation, and timing of CXL are variables to be considered and well chosen for satisfactory long-term results.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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