Original Article

Long-term course of contrast sensitivity in eyes after laser-assisted *in-situ* keratomileusis for myopia

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Purpose: To evaluate the long-term contrast sensitivity (CS) after laser *in-situ* keratomileusis (LASIK) for myopia. **Methods:** This retrospective, single-center, cohort study involved 190 eyes of 95 patients who underwent bilateral LASIK between January 2001 and October 2007. This study includes patients who underwent CS and higher-order aberration (HOA) measurements in a five-year postoperative period. For all enrolled patients, visual acuity, refractive error (RE) in diopters (D), CS at 3-, 6-, 12-, and 18-cycles per degree (cpd), and HOA in a 4 mm area of the dilated pupil were measured before surgery and 6 months, 1 year, and 5 years after it. **Results:** The mean RE measured before the surgery and after 6 months, 1 year, and 5 years after was -6.08 ± 2.50D, −0.26 ± 0.65D, −0.28 ± 0.65D, and −0.48 ± 0.80D, respectively. There were no clinically significant changes between preoperative results and the measures taken 6 months, 1 year, and 5 years after surgery. The slight increase in HOA had little effect on CS over the mid to long-term postoperative period. **Conclusion:** Our findings show that CS does not clinically change post LASIK. Although we were unable to identify the specific mechanism, we theorize that after LASIK there is a possibility for the compensation of HOA.

Key words: Contrast sensitivity, excimer laser, laser *in-situ* keratomileusis, long-term course, refractive surgery

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Contrast sensitivity (CS) testing is used to examine a patient's ability to visually distinguish between finer and finer increments of light versus dark (i.e., contrast). Measurement of CS allows ophthalmologists to research form perception more generally than measuring visual acuity (VA), as it involves the use of a high contrast chart, with the measurements being performed quantitatively over a wide area.[1,2] Since vision in human eyes is 'band pass' filtered, CS decreases not only in the high-frequency region [18-cycles per degree (cpd)], but also in the low-frequency region (3-cpd).[3] It has been reported that CS improves by reducing higher-order aberrations (HOA) of the eye.[4,5]

Laser *in-situ* keratomileusis (LASIK) is a standard method used for refractive surgery.[6,7] Due to the change in cornea shape that occurs post LASIK, it induces statistically significant HOA in 4 mm pupils and a relatively greater amount of HOA in larger pupils.[8,9] However, the underlying mechanism, by which the increase of specific HOA affects visual function, has yet to be elucidated.[10,11] The findings of some previous studies have suggested that CS decreases during the early period post LASIK,[12] yet recovers within 3 or 6 months postoperative.[13] However, only a few previous studies have focused on investigating the long-term course of CS post LASIK.[14]

The purpose of this study was to evaluate the long-term CS post LASIK for the treatment of myopia. According to our data, this is the first study investigating the long-term course of CS up until 5 years post LASIK.

Methods

This retrospective, single-center, cohort study involved 190 eyes of 95 patients who underwent bilateral myopic and myopic astigmatism LASIK between January 2001 and October 2007. In the study, we involved patients who were able to undergo repeated CS measurements until 5 years postoperative.

In each eye, CS at 3-, 6-, 12-, and 18-cpd at 4 m was measured using a CS testing instrument (CSV-1000; VectorVision, Greenville, OH) prior to surgery and 6 months, 1 year, and 5 years postoperative. Before every measurement, the refractive error was corrected when needed and CS testing was performed. In addition, VA and refractive error (RE) in diopters (D) were measured using Landolt C charts. HOA in a 4-mm area of the pupil dilated with 0.5% tropicamide/phenylephrine hydrochloride eye drops (Mydrin-P® Ophthalmic Solution; Santen Pharmaceutical Co., Ltd., Osaka, Japan) was measured using an optical diagnostic instrument (OPD-Scan; Nidek Co. Ltd., Gamagori, Japan). The obtained measurement data was fitted to a six-order Zernike polynomial, and total HOA, 3rd-order HOA (Z3), 4th-order HOA (Z4), and spherical aberration (SA) were then calculated.

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When the preoperative corneal topography was deemed normal, and the residual corneal bed was more than 250 μm in depth, LASIK was performed using the EC-5000 (Nidek) excimer laser, the VISX™ (Abbott Medical Optics Inc., Abbot Park, IL) excimer laser, and the Technolas® 217z (Bausch and Lomb, Rochester, NY) excimer laser in 84 eyes, 86 eyes, and 20 eyes, respectively. A mechanical microkeratome was used for flap creation in the LASIK procedure. The correction limit was up to -10D. From 3 days before surgery, all patients were administered 0.5% cefmenoxime hydrochloride eye drops (Bestron®; Senju Pharmaceutical Co. Ltd., Osaka, Japan) 4-times daily and 100 mg of oral cefcapene pivoxil hydrochloride hydrate (Flomox®; Shionogi and Co., Ltd., Osaka, Japan) 3-times daily. For 1-week postoperative, all patients were initially administrated 0.1% fluorometholone eye drops (Flumetholon® Ophthalmic Suspension 0.1; Santen Pharmaceutical) and 0.3% gatifloxacin hydrate eye drops (Gatiflo® Ophthalmic Solution; Senju Pharmaceutical) 4-times daily.

CS and VA were subjected to a logarithmic transformation and analyzed as a continuous variate with log CS and logMAR. The mixed-effect model was used to analyze the CS shift between measurements obtained preoperatively and 6 months, 1 year, and 5 years postoperatively. By using identification (ID) number as a random effect, we used both eyes of the same person for analysis. The confidence interval was 95%.

For stability, the mixed-effect model was also used to analyze the postoperative study variables (i.e., VA, RE, and HOA) between measurements obtained 6 months, 1 year, and 5 years, postoperatively. The relationship between the change in pre- and post-LASIK CS, and change in HOA was examined by linear correlation analysis.

For outlier cases where the contrast sensitivity decreased by 2 standard deviation (SD) or more from the average value after 6 months after the operation. Outlier cases in 6 postoperative months defined that comparing to the preoperative level the contrast sensitivity has decreased from the average by 2 or more SD. Individual changes for outlier cases in 1 year and 5 years postoperatively were evaluated.

Statistical analysis was performed with JMP pro version 14 software for Windows (SAS Institute Inc., Cary, NC). Written consent was obtained from all the participants. The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional ethics committee.

Results

This study involved 190 eyes (110 male eyes and 80 female eyes; mean patient age: 35.8 ± 8.6 years; range: 20-57 years). Average logMAR uncorrected distance visual acuity (UDVA) was 1.30 ± 0.27 (mean ± SD range: 0.30 ~ 2.00). The mean preoperative spherical equivalent (SE) RE was -6.08 ± 2.50D (range: -1.38 ~ -15.88D). The mean preoperative spherical refractive error and astigmatism was -5.6 ± 2.48D (range: -0.25 ~ -15.00D) and -1.00 ± 0.72D (range: 0 ~ -4.50D), respectively. In all eyes, VA and RE were measured before surgery and at each postoperative period. CS and HOA measurements were obtained in 154 eyes at 6 months postoperative and only 188 eyes at 1-year postoperative.

Our findings showed no clinically significant change between preoperative and 6 months, 1 year, and 5 years postoperative CSs [Fig. 1]. The difference of log CS between preoperative and 6 months, 1 year, and 5 years postoperative results was less than -0.087 [Table 1]. The maximum confidential interval (CI) (95%) was from -0.087 to 0.00008 at 18 cpd in 6 months from preoperative.

Post LASIK surgery, the UDVA improved and the RE decreased. Six months postoperatively logMAR UDVA was -0.07 ± 0.20 (range: 1 ~ −0.30) and SE was −0.16 ± 0.36D (range: −1.75 ~ 0.5D). In the time interval from 6 months post-op to 5 years post-op, UDVA decreased significantly and mean logMAR change was 0.040 [95% confidence interval (CI) −0.009 to −0.070]. During that same period, myopia progressed, and the mean SE refractive change was 0.311D [95% CI 0.527 to 0.095] [Table 2].

Table 1: Average Difference of contrast sensitivity (CS)

	Log CS shift	95% CI	
		Lower limit	Upper limit
3 cycles/deg			
6M-Pre	0.007	-0.027	0.042
1Y-Pre	−0.017	−0.049	0.016
5Y-Pre*	−0.033	−0.065	−0.0004
6 cycles/deg			
6M-Pre	−0.025	−0.060	0.010
1Y-Pre*	−0.037	−0.070	−0.004
5Y-Pre	−0.026	−0.058	0.007
12 cycles/deg			
6M-Pre	0.0006	−0.048	0.050
1Y-Pre	0.004	−0.042	0.050
5Y-Pre	−0.016	−0.061	0.030
18 cycles/deg			
6M-Pre	−0.044	−0.087	0.00008
1Y-Pre	−0.011	−0.052	0.0308
5Y-Pre	−0.018	−0.059	0.023

The CS shift and the 95% confidence interval (CI) were obtained by subtracting the preoperative value from the postoperative value of log CS. The data for 3, 6, 12, and 18 cycles/degree are shown. *P<0.05

Table 2: Stability of the postoperative value

	Average difference	95% CI	
		Upper limit	Lower limit
UDVA (logMAR)			
6M-1Y	0.001	0.030	−0.032
6M-5Y	−0.040	−0.009	−0.070
SE (D)			
6M-1Y	0.116	0.332	−0.100
6M-5Y	0.311	0.527	0.095
HOA (um)			
6M-1Y	0.004	0.023	−0.014
6M-5Y	−0.005	0.013	−0.023

The average value and the 95% confidence interval (CI) obtained by subtracting the 1- or 5-year post LASIK value from the 6-months postoperative value of logMAR, spherical equivalent error (SE), total higher-order aberration (HOA) in 4 mm pupils. D: Diopters

Six months post LASIK, mean HOA slightly increased, and the average value of total HOA before and 6 months post-op LASIK were 0.155 ± 0.076 um (range: 0.05 ~ 0.545) and 0.217 ± 0.093 um (range: 0.083 ~ 0.623), respectively. No significant change in total HOA was observed later in the 5-year postoperative period [Table 2].

The correlation coefficient was calculated by using the 6 months, 1 year, and 5 years of CS shift and HOA shift. The change of correlation coefficient in CS and HOA is as follows: at 6 months, 3 cpd was −0.08, 6 cpd was −0.076, 12 cpd was −0.12 and 18 cpd was −0.1. At 1 year, 3 cpd was −0.08, 6 cpd was −0.076, 12 cpd was −0.12 and 18 cpd was −0.1. At 5 years, 3 cpd was −0.079, 6 cpd was −0.061, 12 cpd was −0.145 and 18 cpd was −0.151.

For outlier cases where the contrast sensitivity decreased by 2 SD or more from the average value after 6 months after the operation, 3 cpd 1 case 2 eyes, 12 cpd 3 cases 3 eyes, 18 cpd 1 case 1 eye were observed. There was one eye in which 3, 12, and 18 cpd was decreasing, so in total it was 4 eyes. All eyes improved in either cycle, after 1 year or 5 years period [Table 3].

Discussion

The findings of this study showed that in all frequencies, CS at 1-year and 5-years post LASIK were not lower than before surgery and that the slight increase in HOA had little effect on CS over the mid to long-term postoperative period.

It has been previously reported that post LASIK there is a possibility for a decrease in CS due to changes in the shape of the cornea and an increase in HOA. Holladay *et al*. reported that in myopia cases, CS decreases until 6 months post LASIK surgery due to the oblate corneal shape that occurs.[13] Yamane *et al*. reported that CS decreases at all frequencies at 1-month postsurgery, and that this change correlates with an increase in HOA.[12] In this study, the CS at 1 year and 5 years postoperative was significantly reduced by 6-cpd and 3-cpd. Although this change was statistically significant ($P < 0.05$), it was not clinically significant. CS remained nearly constant throughout the study period. The lasers used in this study had a wider ablation diameter than that in the previous report, and thus may have had less effect on visual function.[15] In this study, we provide a more profound overview compared to previous papers due to the longer observation period.

Although HOA was found to have slightly increased post LASIK, the CS was mostly constant. The mean spherical RE was 0.06 μm, which is equivalent to 0.1D.[16] Thus, this HOA change may be too little to produce a change in CS.[17,18] Due to the few changes observed in HOA, we hypothesize the change in susceptibility to aberration occurs in the central

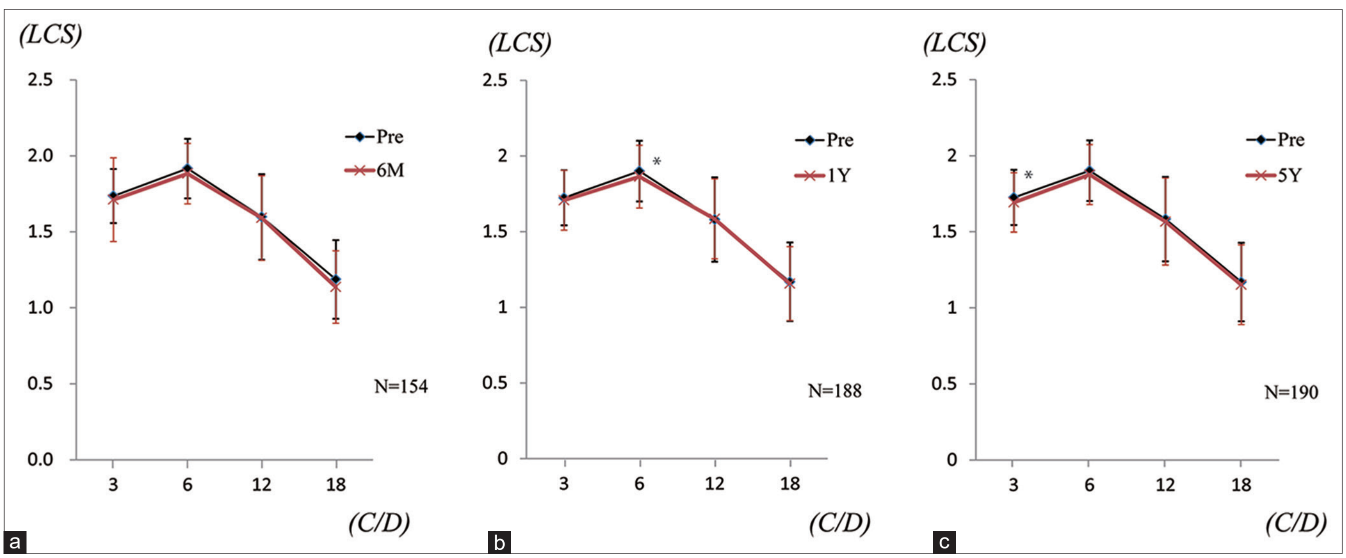

Figure 1: Comparison of log contrast sensitivity (CS) pre and post laser *in-situ* keratomileusis (LASIK) surgery: Pre LASIK and 6 months post LASIK (a), pre LASIK and 1-year post LASIK (b), and pre LASIK and 5 years post LASIK (c). In this current study, the CS at 1Y and 5Y postoperative was significantly reduced at 6-cpd and 3-cpd, respectively, compared with preoperative data. Although this change was statistically significant, it was not clinically significant. log CS: Log Contrast Sensitivity; C/D: Cycles/degree

Table 3: Subsequent process of outlier cases

No	eye	6M-Pre (logCS)				1Y-Pre (logCS)				5Y-Pre (logCS)			
		3 cpd	6 cpd	12 cpd	18 cpd	3 cpd	6 cpd	12 cpd	18 cpd	3 cpd	6 cpd	12 cpd	18 cpd
40	L	−0.29	−0.29	−0.64*	−0.27	−0.46	−0.62*	−0.46	−0.14	−0.45	−0.79*	−0.46	−0.41
98	R	0	0	−0.64*	−0.14	−0.44	−0.94*	−0.46	−0.74*	−0.14	−0.44	−0.46	−0.55
107	R	−0.75*	−0.32	−0.94*	−0.94*	−0.75*	−0.32	−0.94*	−0.46	−0.14	−0.14	−0.15	−0.14
	L	−0.75*	0	0	0.14	−0.3	−0.14	−0.15	−0.13	−0.75*	0	−0.15	0.14

Table 3 shows the outlier cases observed after 5 years, where the contrast sensitivity (CS) decreased by 2 or more standard deviations from the average change 6 months post LASIK (marked with *). The change of log CS for all eyes improved after 1Y post LASIK or 5Y post LASIK nervous system (neural adaptation).[19] In most changed cases, 6 months post-op one eye experienced over 2 SD decrease in log CS at 18 cpd, 1 year and 5 years post-op the CS improved dramatically [Table 3]. In this eye, the total HOA that was 0.27 µm before surgery, has increased to 0.42 µm in six months after surgery, then decreased to 0.35 µm in 1 year after surgery and 0.22 µm in 5 years after surgery. In each case, there are various patterns of increase of HOA and change of contrast sensitivity. Therefore, further study is required in the future.

One of the limitations of this study was that the CS measurements were obtained only in a brightly-lit place. Since there is more influence of HOA on the visual function in a dark light, we intend to carry out future studies assessing CS in the dark.[20,21] Another limitation was the type of equipment used to perform the LASIK operation, since the surgeries were performed 10 years ago. Today, the microkeratome has been replaced by the laser keratome,[22] and the laser ablation is mainly sophisticated wavefront-guided ablation.[23] The pupil diameter and the ablation diameter may affect the contrast sensitivity results, and the type of microkeratome and flap size may affect the change of HOAs. This study was not enough because these elements were not included. Because of the retrospective study, we have not been able to study these details. We continue to observe the long-term postoperative outcomes at our clinic, and we plan to conduct a prospective study using modern LASIK techniques and equipment with these details. We will compare the outcomes between this study and the modern refractive surgeries in the future.

Conclusion

The findings of this study show that CS does not significantly change post LASIK. We theorize that the small changes observed in the HOAs post LASIK could have minimal or no impact on the changes in CS. We also attribute the changes in CS to the possible compensatory role of the central nervous system over HOAs.

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Conflicts of interest

There are no conflicts of interest.

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