

WAVEFRONT-GUIDED LASER IN SITU KERATOMILEUSIS (LASIK) VERSUS WAVEFRONT-GUIDED PHOTOREFRACTIVE KERATECTOMY (PRK): A PROSPECTIVE RANDOMIZED EYE-TO-EYE COMPARISON (AN AMERICAN OPHTHALMOLOGICAL SOCIETY THESIS)

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ABSTRACT

Purpose: To compare the safety and efficacy of wavefront-guided laser in situ keratomileusis (LASIK) vs photorefractive keratectomy (PRK) in a prospective randomized clinical trial.

Methods: A cohort of 68 eyes of 34 patients with -0.75 to -8.13 diopters (D) of myopia (spherical equivalent) were randomized to receive either wavefront-guided PRK or LASIK in the fellow eye using the VISX CustomVue laser. Patients were evaluated at 1 day, 1 week, and months 1, 3, 6, and 12.

Results: At 1 month, uncorrected visual acuity (UCVA), best spectacle-corrected visual acuity (BSCVA), 5% and 25% contrast sensitivity, induction of higher-order aberrations (HOAs), and subjective symptoms of vision clarity, vision fluctuation, ghosting, and overall self-assessment of vision were worse ($P < 0.05$) in the PRK group. By 3 months, these differences had resolved ($P > 0.05$). At 1 year, mean spherical equivalent was reduced 94% to -0.27 ± 0.31 D in the LASIK group and reduced 96% to -0.17 ± 0.41 D in the PRK group. At 1 year, 91% of eyes were within ± 0.50 D and 97% were within ± 1.0 D in the PRK group. At 1 year, 88% of eyes were within ± 0.50 D and 97% were within ± 1.0 D in the LASIK group. At 1 year, 97% of eyes in the PRK group and 94% of eyes in the LASIK group achieved an UCVA of 20/20 or better ($P = 0.72$). Refractive stability was achieved in both PRK and LASIK groups after 1 month. There were no intraoperative or postoperative flap complications in the LASIK group. There were no instances of corneal haze in the PRK group.

Conclusions: Wavefront-guided LASIK and PRK are safe and effective at reducing myopia. At 1 month postoperatively, LASIK demonstrates an advantage over PRK in UCVA, BSCVA, low-contrast acuity, induction of total HOAs, and several subjective symptoms. At postoperative month 3, these differences between PRK and LASIK results had resolved.

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INTRODUCTION

Keratorefractive surgery has evolved over the last decade. Initial attempts at correcting simple spherocylinder refractive errors with incisional corneal surgery (radial keratotomy, arcuate keratotomy)^{1,2} and first-generation excimer laser surgery were reasonably effective for many lower-level refractive errors.³⁻¹⁰ The evolution of more complex laser technology has resulted in increasingly accurate and predictable results and has expanded the indications for refractive surgery. Improved quality of results has also been driven by the emergence of both diagnostic and therapeutic wavefront technology.¹¹⁻²⁰ Wavefront technology allowed the customization of the refractive procedure, minimized degradation of the quality of the vision (ie, contrast sensitivity) that can occur with conventional corneal refractive surgery, and has been important in allowing us to come a step closer to achieving the possibility of the "holy grail" of vision free from optical aberrations. Although the advantages of wavefront-guided treatment over conventional treatments are clear,²¹⁻²⁷ the distinction between wavefront-guided laser in situ keratomileusis (LASIK) and wavefront-guided photorefractive keratectomy (PRK) is less obvious. In this prospective, randomized clinical trial, we evaluate the 1-year results of wavefront-guided LASIK vs wavefront-guided PRK in fellow eyes with myopia.

With the widespread adoption of LASIK and PRK surgery, there has been increased scrutiny given to potential complications and untoward side effects of the two procedures.²⁸⁻³⁹ In particular, there has been a great deal of interest in measuring patient satisfaction rates after LASIK and PRK surgery.³⁹⁻⁴⁸ Quality of life and quality of vision following keratorefractive surgery have been closely linked to uncorrected visual acuity (UCVA) results. However, both contrast sensitivity and higher-order aberrations (HOAs) have been shown to play a role in patient satisfaction and quality of vision.⁴⁹⁻⁶² With these issues in mind, we designed this study to measure patient satisfaction, contrast sensitivity, and HOAs in addition to the standard refractive surgical outcomes normally measured in clinical studies. We wanted to study if there were any significant differences in any of the outcome measures between LASIK and PRK to determine whether one procedure offers any advantages or disadvantages over the other.

METHODS

Sixty-eight eyes of 34 patients with myopia with or without astigmatism were randomized to receive either wavefront-guided PRK or wavefront-guided LASIK in the fellow eye with the VISX Star CustomVue S4 IR excimer laser (Abbott Medical Optics, Santa Ana, California). Eyes were randomized according to a computer-generated randomization schedule. Randomization was performed by assigning the dominant eye to receive wavefront-guided LASIK or wavefront-guided PRK and the fellow nondominant eye to receive the alternative procedure. Inclusion criteria included a stable refraction with a change of less than 0.50 diopters (D) of sphere or cylinder in the last year, discontinuation of soft contact lens wear at least 7 days prior to preoperative evaluation, best-corrected visual acuity of 20/20 or better, age older than 21, and ability to participate in follow-up examinations for at least 12 months following refractive surgery.

From Stanford University School of Medicine, Palo Alto, California (Dr Manche), and University of California San Diego School of Medicine and Shiley Eye Center, La Jolla, California (Dr Haw).

Patients were excluded for use of rigid gas permeable contact lenses, severe dry eye or blepharitis, corneal pathology (recurrent erosion, basement membrane disease, keratoconus, irregular corneal mires on central keratometry), corneal pachymetry in which the LASIK procedure would result in less than 250 μm of remaining posterior corneal thickness below the flap postoperatively, baseline standard manifest refraction with a difference of 0.75 D or more in sphere power or 0.50 D in cylinder power as compared to the baseline standard cycloplegic refraction, history of herpes zoster or herpes simplex, corneal warpage, and certain systemic diseases or conditions (connective tissue disease, diabetes, pregnancy, lactation, immunocompromised state, severe atopy). Also excluded were patients with sensitivity to planned study concomitant medications and patients participating in a clinical trial for another ophthalmic drug or device. Each patient signed an informed consent form approved by the Stanford University Institutional Review Board before enrollment.

Patients who met the preceding criteria underwent a comprehensive preoperative evaluation, including a history and examination with slit-lamp biomicroscopy, Goldmann applanation tonometry, infrared pupilometry (Neuroptics, Irvine, California) under photopic and scotopic lighting conditions, dilated fundus examination, manifest and cycloplegic refraction using Early Treatment Diabetic Retinopathy Study (ETDRS) charts, VISX WaveScan WaveFront (Abbott Medical Optics, Santa Ana, California), and computerized corneal topography. Patients also completed a measurement of best-corrected visual acuity under controlled ambient conditions with 5% and 25% contrast sensitivity conditions (Precision Vision, La Salle, Illinois). Patients completed a questionnaire detailing subjective symptoms, which included a quantitative grading on a scale of 0 (no symptoms) to 10 (severe symptoms) for each of the following symptoms: glare under night and day conditions, haze, halos, clarity under night and day conditions, dry eye symptom frequency and severity, gritty or scratchy sensation, vision fluctuation, and ghosting (see Appendix). Patients were also asked to grade their overall vision. In this scoring system, 0 was for "excellent" vision. The questionnaire used in this study has been employed and validated in previous contralateral eye studies.^{38,62} The questionnaire was administered preoperatively and at postoperative months 1, 3, 6, and 12. The LASIK and PRK surgeries were performed in a bilateral simultaneous fashion. Therefore, any learning curve would be negated because of the simultaneous fashion of the surgery and completion of the questionnaire during the same session.

Wavefront aberrations were measured with an undilated pupil (>6.0 mm). All eyes had pupil sizes that measured ≥ 6 mm preoperatively and postoperatively. Higher-order aberrations were subject to variability secondary to measuring at different diameters; hence we used aberrometry images that were within 0.25 mm of the preoperative measurement for data analysis. Although luminance was not measured, all measurements were made in the same room with the same dark lighting conditions for all patients and all measurements. To assess aberrometry readings, six readings of each eye were taken on each visit before and after surgery. The best acquisition of the six readings was determined by the clearest centroid image. The best-acquired image was used as a standard study analysis for the aberrometry data before and after PRK and LASIK surgery.

Topical proparacaine hydrochloride 0.5% (Ophthetic; Allergan, Irvine, California), moxifloxacin hydrochloride ophthalmic solution 0.5% (Vigamox; Alcon, Fort Worth, Texas), and ketorolac tromethamine ophthalmic solution 0.4% (Acular LS; Allergan, Irvine, California) were administered immediately before the procedure.

For PRK, the epithelium was removed using an Amoils epithelial scrubber (Innovative Excimer Solutions, Inc, Toronto, Canada) to create a central 8.0-mm zone centered over the pupil. Photoablation was achieved using the VISX Star CustomVue S4 IR excimer laser system. Autocentration and iris recognition were used in all cases. No mitomycin C was used in any of the cases. All surgeries were performed at Stanford University Eye Laser Center by a single surgeon (E.E.M.). For eyes undergoing PRK, a bandage contact lens (Acuvue Oasys; Johnson & Johnson Vision Care, Inc, New Brunswick, New Jersey) was placed until the epithelium was healed. Postoperative medications included topical moxifloxacin 0.5% (Alcon, Fort Worth, Texas) until the epithelium was healed and fluorometholone ophthalmic solution 0.1 % (FML; Allergan, Irvine, California) four times a day for 2 weeks and then two times a day for 2 weeks.

LASIK flaps were created using the 60-kHz IntraLase FS (Abbott Medical Optics, Santa Ana, California). A 9.2-mm diameter, superior hinge with 100 μm programmed flap depth setting was used in all cases. Intraoperative ultrasonic pachymetry (Sonogage, Cleveland, Ohio) was performed in all LASIK cases. Postoperative medications included topical moxifloxacin four times daily for 4 days and prednisolone acetate 1.0 % (Pred Forte; Allergan, Irvine, California) four times daily for 7 days.

Patients were prospectively evaluated at 1 day, 1 week, 1 month, 3 months, 6 months, and 12 months. Primary outcome measures included UCVA, refractive stability, predictability, contrast sensitivity, aberrometry, subjective questionnaire, loss of best spectacle-corrected visual acuity (BSCVA), and adverse event profile. Statistical analysis was performed using a two-tailed, paired *t* test and the Microsoft Excel ToolPak Software (Microsoft Corporation, Redmond, Washington). Normal distribution of the preoperative and postoperative data was confirmed by Kolmogorov-Smirnov and Shapiro-Wilk tests at each time interval ($P > 0.05$ at all time intervals). For all statistics, a *P* value of < 0.05 was considered statistically significant.

RESULTS

The PRK and LASIK groups were similar in regard to preoperative refraction and total HOAs (Table 1). The LASIK group underwent correction for -4.83 ± 1.89 D (range, -2.0 to -8.75 D) of myopia with $+0.74 \pm 0.73$ D (range, 0 to +2.50 D) of astigmatism with a spherical equivalent of -4.46 ± 1.94 D (range, -1.25 to -8.13 D). The PRK group underwent correction for -4.81 ± 2.06 D (range, -1.50 to -8.75 D) of myopia, $+0.85 \pm 0.62$ D (range, 0 to +2.50 D) of astigmatism with a spherical equivalent of -4.39 ± 2.02 D (range, -0.75 to -8.00 D). Mean age was 39 ± 7.3 years (range, 26 to 52 years) with 44% ($n = 15$) males and 56% ($n = 19$) females. There was no patient lost to follow-up ($n = 34$) on postoperative day 1, postoperative week 1, and postoperative month 1. Three patients were lost

to follow-up on the third postoperative month follow-up and sixth postoperative month follow-up. One patient was lost to follow-up at the 1-year follow-up (Table 2).

TABLE 1. AVERAGE PREOPERATIVE REFRACTIVE ERRORS FOR LASIK AND PRK GROUPS*

	LASIK	PRK
Sphere (D)	-4.83 ± 1.89 D (range, -2.0 to -8.75 D)	-4.81 ± 2.06 D (range, -1.50 to -8.75 D)
Astigmatism (D)	+0.74 ± 0.73 D (range, 0.0 to +2.50 D)	0.85 ± 0.62 D (range, 0.0 to +2.50 D)
Spherical equivalent (D)	-4.46 ± 1.94 D (range, -1.25 to -8.13 D)	-4.39 ± 2.02 D (range, -0.75 to -8.00 D)
RMS error (µm)	0.30 ± 0.11 µm (range, 0.10 to 0.52 µm)	0.33 ± 0.16 µm (range, 0.09 to 0.85 µm)

LASIK, laser in situ keratomileusis; PRK, photorefractive keratectomy; RMS, root-mean-square.
*There is no statistically significant difference between each group.

TABLE 2. REFRACTIVE RESULTS AT DESIGNATED INTERVALS FOR LASIK AND PRK GROUPS*

	PREOP		1 MO		3 MO		6 MO		12 MO	
	LASIK	PRK	LASIK	PRK	LASIK	PRK	LASIK	PRK	LASIK	PRK
Sphere (D)	-4.83 ± 1.89	-4.81 ± 2.06	-0.29 ± 0.27	-0.50 ± 0.43	-0.31 ± 0.28	-0.27 ± 0.39	-0.38 ± 0.26	-0.30 ± 0.36	-0.39 ± 0.35	-0.28 ± 0.42
Cylinder (D)	+0.74 ± 0.73	+0.85 ± 0.62	+0.23 ± 0.22	+0.51 ± 0.47	+0.19 ± 0.26	+0.25 ± 0.25	+0.17 ± 0.23	+0.26 ± 0.27	+0.23 ± 0.29	+0.25 ± 0.25
Spherical Equiv (D)	-4.46 ± 1.94	-4.39 ± 2.02	-0.18 ± 0.28	-0.25 ± 0.35	-0.21 ± 0.28	-0.14 ± 0.40	-0.30 ± 0.27	-0.16 ± 0.36	-0.27 ± 0.31	-0.17 ± 0.41
% Follow-Up (No. of Eyes)	100 (34)	100 (34)	100 (34)	100 (34)	91 (31)	91 (31)	97 (33)	97 (33)	97 (33)	97 (33)

LASIK, laser in situ keratomileusis; PRK, photorefractive keratectomy.

*Mean and standard deviation.

Preoperatively, the average corneal thickness by ultrasonic pachymetry was 542 ± 28 µm (range, 489 to 624 µm) in the LASIK group and 544 ± 29 µm (range, 489 to 615 µm) in the PRK group. In the LASIK group, mean stromal bed was 455 ± 33 µm (range, 403 to 549 µm) with a mean flap thickness of 92 ± 15 µm (range, 60 to 125 µm). The calculated mean ablation depth was 74 ± 24 µm (range, 34 to 122 µm) in the LASIK group and 73 ± 26 µm (range, 30 to 122 µm) in the PRK group.

REFRACTIVE ACCURACY

In the first month, 96% of the mean spherical equivalent was corrected in the LASIK group to -0.18 D ± 0.28 D (range, -0.82 to +0.50 D) and 97% of eyes were within ±0.50 D of attempted correction (Table 2, Figure 1). In the PRK group, the mean spherical equivalent was corrected 94% to -0.25 D ± 0.35 D (range, +0.50 to -1.0 D) and 82 % of eyes were within ± 0.50 D of attempted correction. One hundred percent of eyes were within ±1.0 D of attempted correction for both the PRK and LASIK groups. At 1 month, mean residual sphere was -0.29 ± 0.27 (range, +0.25 to -1.0 D) and mean astigmatism was 0.23 ± 0.22 D (range, 0 to +0.75 D) in the LASIK group. The corresponding values for the PRK group were -0.50 ± 0.43 D (range, +0.50 to -1.50 D) and 0.51 ± 0.47 D (range, 0 to +1.75 D). PRK eyes demonstrated a statistically significant higher mean cylinder ($P=0.0009$) and higher mean sphere ($P=0.004$) as compared to fellow LASIK eyes at 1 month.

At the 3-month follow-up, 96% of the mean spherical equivalent was corrected in the LASIK group to -0.21 ± 0.28 D (range, +0.25 to -1.0 D), 97% of eyes were within ±0.50 D of attempted correction, and 100% of eyes were within ±1.0 D of attempted correction. In the PRK group, 97 % of the mean spherical equivalent was corrected to -0.14 ± 0.40 D (range, +0.62 to -1.12 D), 94% of eyes were within ±0.50 D of attempted correction, and 97% were within ±1.0 D of attempted correction. The difference in refractive accuracy between the PRK group and the LASIK group was not statistically significant for ±0.50 D of attempted correction ($P=0.43$) or for ±1.0 D of attempted correction ($P=0.41$). Mean residual sphere was -0.31 ± 0.28 D (range, 0 to -1.25 D) and mean astigmatism was +0.19 ± 0.26 D (range, 0 to +1.0 D) in the LASIK group. In the PRK group, the corresponding values were -0.27 ±

0.39 D (range, +0.50 to -1.25 D) and $+0.25 \pm 0.25$ D (range, 0 to +0.75 D).

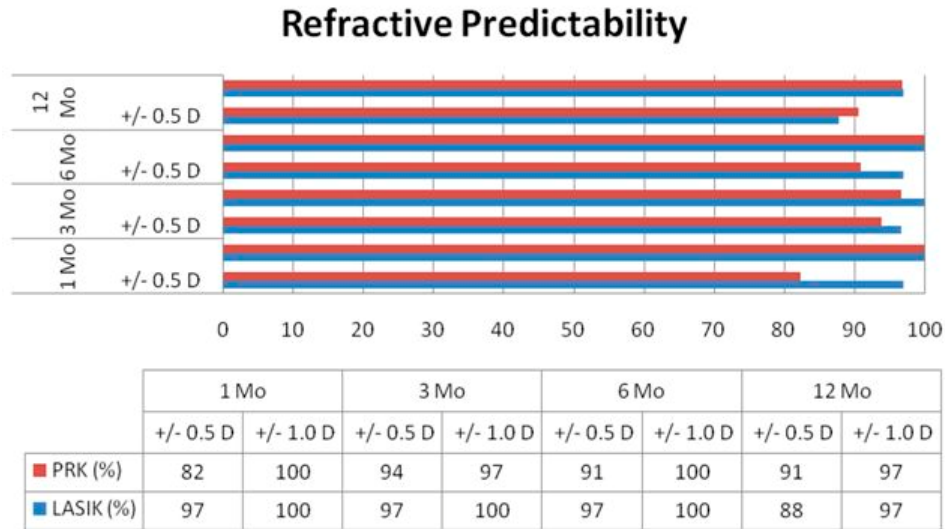


FIGURE 1

Percentage of eyes within ± 0.50 (diopters) D and ± 1.0 D of attempted correction for the photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) groups at 1 month, 3 months, 6 months, and 12 months following their procedure.

At the 6-month follow-up, 94% of the mean spherical equivalent was corrected in the LASIK group to a mean spherical equivalent of -0.30 ± 0.27 D (range, +0.12 to -0.75 D), and 97% of eyes were within ± 0.50 D of attempted correction. In the PRK group, the mean spherical equivalent was reduced 96% to -0.16 ± 0.36 D (range, +1.0 to -0.62 D), and 91% of eyes were within ± 0.50 D of attempted correction. In both the PRK and LASIK group, 100% of eyes were within ± 1.0 D of attempted correction at the 6-month follow-up. The difference in refractive accuracy between the PRK group and the LASIK group was not statistically significant for ± 0.50 D of attempted correction ($P=0.27$) or for ± 1.0 D of attempted correction ($P=0.39$). Mean residual sphere was -0.38 ± 0.26 D (range, 0 to -0.75 D) and mean astigmatism was $+0.17 \pm 0.23$ D (range, 0 to +0.75 D) in the LASIK group. The corresponding values in the PRK group were -0.30 ± 0.36 D (range, +1.0 to -0.75 D) and $+0.26 \pm 0.27$ D (range, 0 to +0.75 D).

At 12 months, the mean spherical equivalent was reduced 94% to -0.27 ± 0.31 D in the LASIK group. The mean spherical equivalent was reduced 96% to $-0.17 \text{ D} \pm 0.41$ D during the same interval for the PRK group. Ninety-one percent of eyes were within ± 0.50 D of attempted correction and 97% were within ± 1.0 D of attempted correction in the PRK group at 12 months (Figure 2). The respective values for the LASIK group were 88% and 97%. The difference in refractive accuracy between the PRK group and the LASIK group was not statistically significant for ± 0.50 D of attempted correction ($P=0.68$) or for ± 1.0 D of attempted correction ($P=0.78$). Mean residual sphere was -0.39 ± 0.35 D (range, +0.25 to -1.25 D) and mean astigmatism was $+0.23 \pm 0.29$ D (range, 0 to +0.75 D) in the LASIK group. The corresponding values in the PRK group were -0.28 ± 0.42 D (range, +0.75 to -1.75 D) and $+0.25 \pm 0.25$ D (range, 0 to +0.75 D).

Stability was achieved after 1 month for both the PRK and LASIK groups (Figure 3). There was less than ± 0.05 D change in the mean spherical equivalent in both the LASIK group and PRK group for each of the measured postoperative intervals after the first postoperative month. The largest change in the mean spherical equivalent occurred between 1 and 3 months for the PRK group (± 0.11 D) and between 3 and 6 months for the LASIK group (± 0.09 D). There were no statistically significant differences in stability between the PRK and LASIK groups at the 3-month ($P=0.64$), 6-month ($P=0.68$), and 12-month ($P=0.62$) visits. In the PRK group, one eye (3%) with high myopia (preoperative mean spherical equivalent -8.0 D) underwent late regression (after the 6-month follow-up) of more than 1 D at 12 months.

UNCORRECTED VISUAL ACUITY

In the LASIK group, UCVA (mean, logMAR scale) was significantly improved by the first postoperative day and remained stable throughout all postoperative intervals (Figure 4). In contrast, the PRK group required 3 months before matching the LASIK group. Uncorrected visual acuity (mean, logMAR scale) was significantly better in the LASIK group on the first postoperative day ($P<0.01$), first postoperative week ($P<0.01$), and first postoperative month ($P<0.01$). After 3 months, there was no statistically significant difference between the LASIK and PRK groups. The percentage of eyes with the designated UCVA is demonstrated for each of the postoperative intervals for the LASIK and PRK groups in Figure 5. At 12 months in the LASIK group, UCVA of 20/40 or better was achieved in 100% of eyes and 20/20 or better in 94% of eyes. In the PRK group, UCVA of 20/40 or better was achieved in 100% of

eyes and 20/20 or better in 97% of eyes. The difference in the percentage of eyes achieving an UCVA of 20/20 or better between the two groups was not statistically significant ($P=0.72$). Eighty-eight percent of eyes demonstrated an UCVA of better than 20/20 in the LASIK group and 82% of eyes in the PRK group at 12 months.

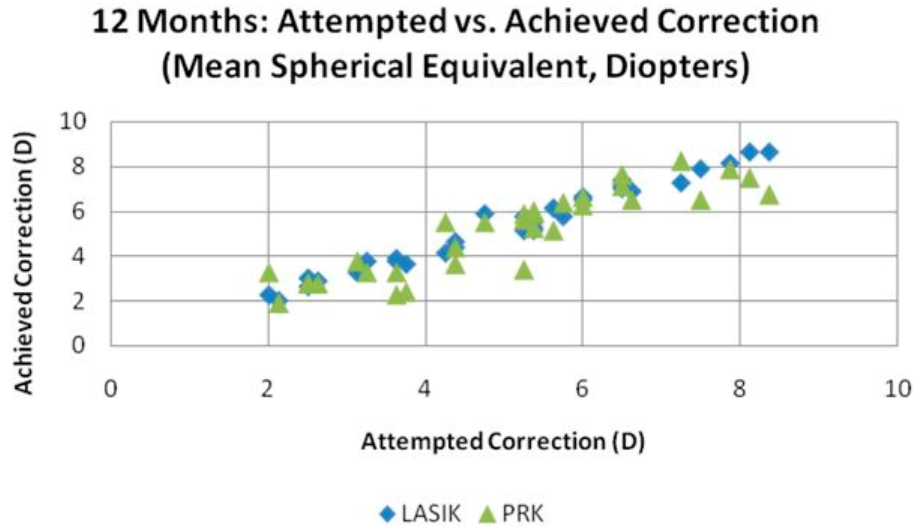


FIGURE 2

Attempted vs achieved correction (mean spherical equivalent, diopters) for the LASIK and PRK groups at the 12 month-postoperative visit. In the LASIK group 88% of eyes were within ± 0.5 D of attempted correction and 97% of eyes were within ± 1.0 D of attempted correction. In the PRK group 91% of eyes were within ± 0.5 D of attempted correction and 97% were within ± 1.0 D of attempted correction.

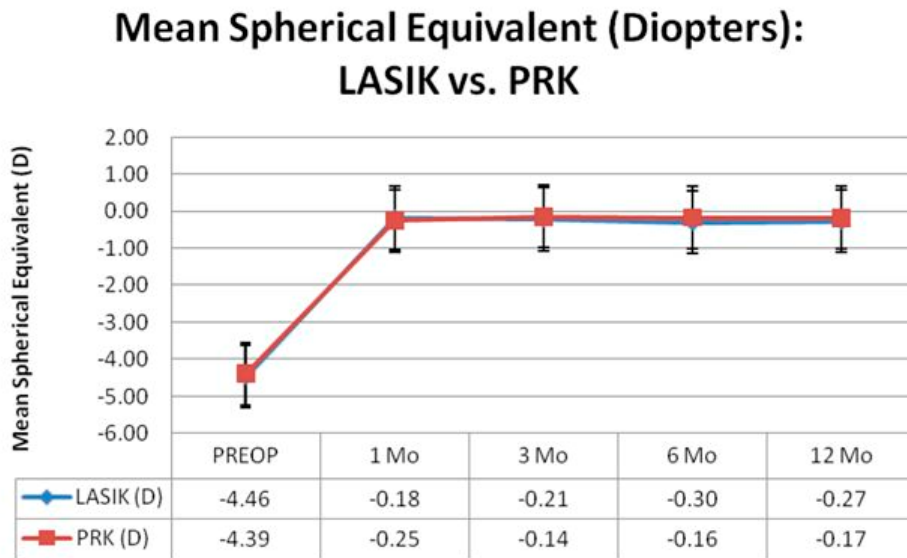


FIGURE 3

Mean spherical equivalent (diopters) over each of the postoperative periods. Refractive stability was achieved at 1 month for both LASIK and PRK groups. Standard error bars are shown.

Uncorrected Visual Acuity (logmar, mean): LASIK vs PRK

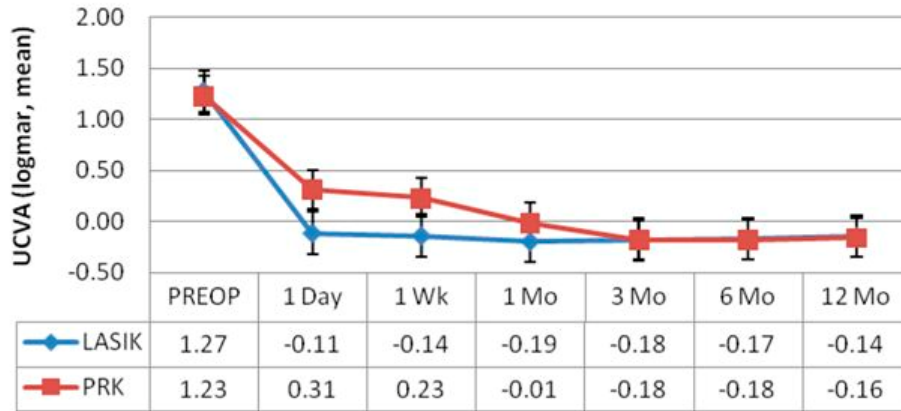


FIGURE 4

Uncorrected visual acuity (UCVA, logMAR, mean) for LASIK and PRK groups for each postoperative interval. Standard error bars are shown.

Uncorrected Visual Acuity

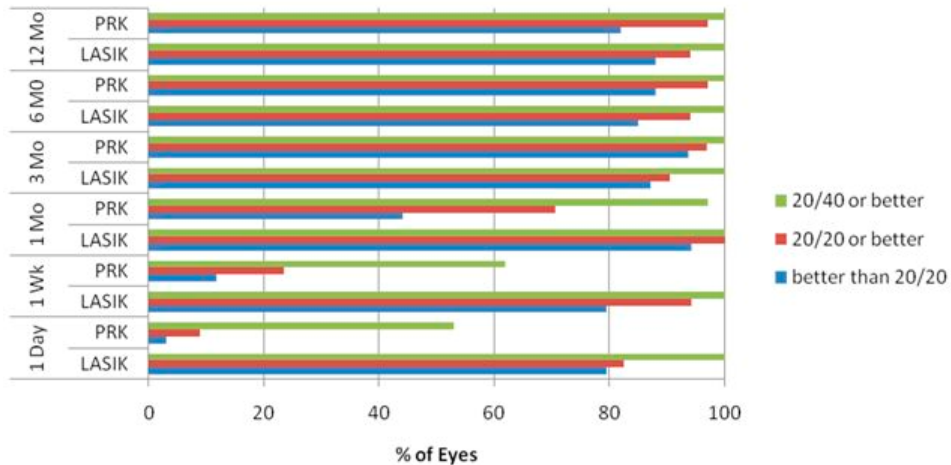


FIGURE 5

Percentage of eyes with the designated uncorrected visual acuity (UCVA) at each postoperative interval for both the LASIK and PRK groups.

BEST SPECTACLE-CORRECTED VISUAL ACUITY

In both the LASIK and PRK groups, there was an improvement in the mean BSCVA at 12 months (logMAR scale, mean BSCVA) (Figure 6). There was a statistically significant ($P=0.003$) temporary decline in BSCVA at 1 month in the PRK group. By 3 months, the difference in the mean BSCVA between the PRK and LASIK groups had resolved. The improvement in BSCVA was realized at 1 month postoperatively and remained consistent throughout the 12-month follow-up period in the LASIK group. In both LASIK and PRK groups, no eyes lost 2 or more lines of BSCVA (Figure 7). In the LASIK group, 1 eye (3%) lost 1 line, 18 eyes (55%) had no change, 10 eyes (30%) gained 1 line, and 4 eyes (12%) gained 1 or more lines of BSCVA at 12 months. In the PRK group, 2 eyes (6%) lost 1 line, 21 eyes (64%) had no change, 9 eyes (27%) gained 1 line, and 1 eye (3%) gained 1 or more lines of BSCVA at 12 months.

Best Corrected Visual Acuity (logmar, mean): LASIK vs PRK

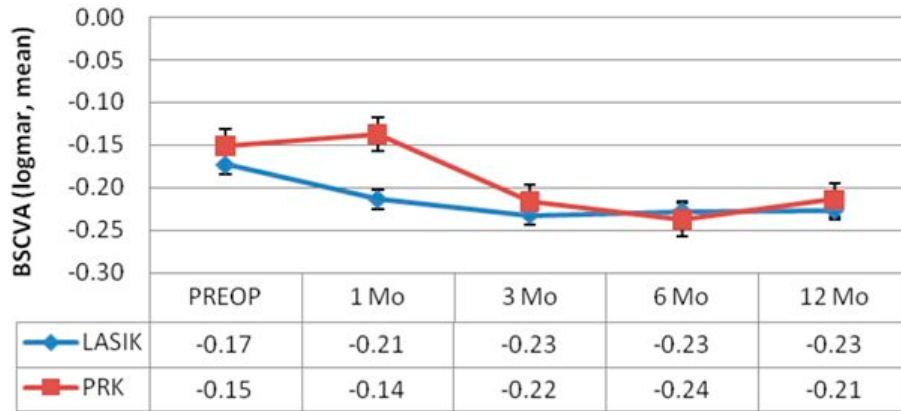


FIGURE 6

Best spectacle-corrected visual acuity (BSCVA) (logMAR, mean) for LASIK and PRK groups for each postoperative interval. Standard error bars are shown.

Change in Best Spectacle Corrected Visual Acuity (BSCVA) at 12 Months

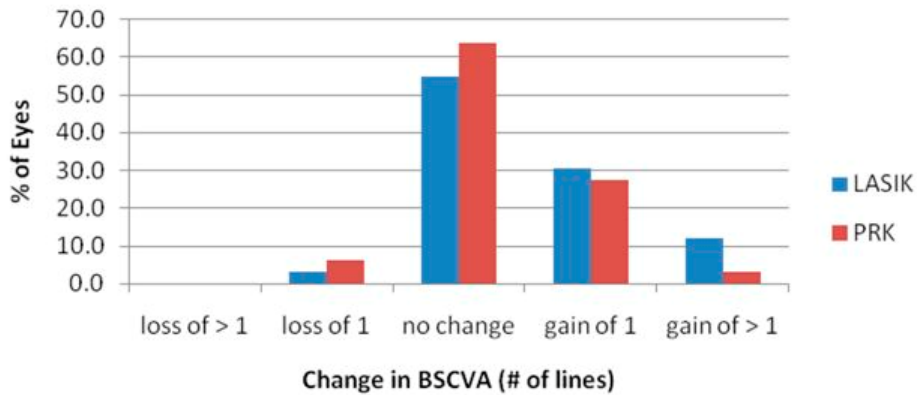


FIGURE 7

Change in best spectacle-corrected visual acuity (BSCVA; number of lines) at 12 months postoperatively. The percentage of eyes (%) is demonstrated for the LASIK and PRK groups. No eyes in the LASIK or PRK groups lost more than 1 line of BSCVA.

CONTRAST SENSITIVITY BSCVA

The BSCVA (mean, logMAR scale) was better than the preoperative BSCVA in all postoperative intervals (1, 3, 6, and 12 months) in the LASIK group under both 5% and 25% contrast sensitivity conditions (Figures 8 and 9). BSCVA (mean, logMAR scale) under 5% contrast sensitivity and 25% contrast sensitivity conditions exhibited a decline in the PRK group at 1 month before mirroring the LASIK groups at 3, 6, and 12 months. The difference between PRK and LASIK groups at postoperative month 1 was significant in both the 5% contrast sensitivity condition ($P=0.006$) and 25% contrast sensitivity condition ($P=0.0002$). The differences in 5% contrast acuity between the two groups was not statistically significant at postoperative month 3 ($P=0.48$), postoperative month 6 ($P=0.54$), and postoperative month 12 ($P=0.32$). The differences in 25% contrast acuity between the two groups was not statistically significant at postoperative month 3 ($P=0.36$), postoperative month 6 ($P=0.24$), and postoperative month 12 ($P=0.35$). After 1 month, the PRK group demonstrated a better BSCVA (mean, logMAR scale) than the corresponding preoperative measurement in all

measured intervals (3, 6, and 12 months) in both the 5% and 25% contrast sensitivity conditions. After the 1-month postoperative visit, there were no statistically significant differences in 5% or 25% contrast acuity between the LASIK and PRK groups.

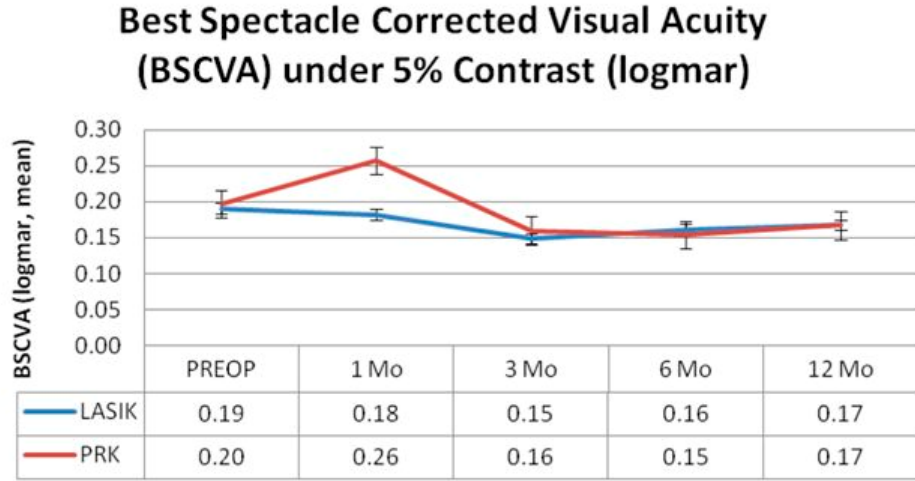


FIGURE 8

Best spectacle-corrected visual acuity (logMAR, mean) for LASIK and PRK groups for each postoperative interval under 5% contrast conditions. Standard error bars are shown.

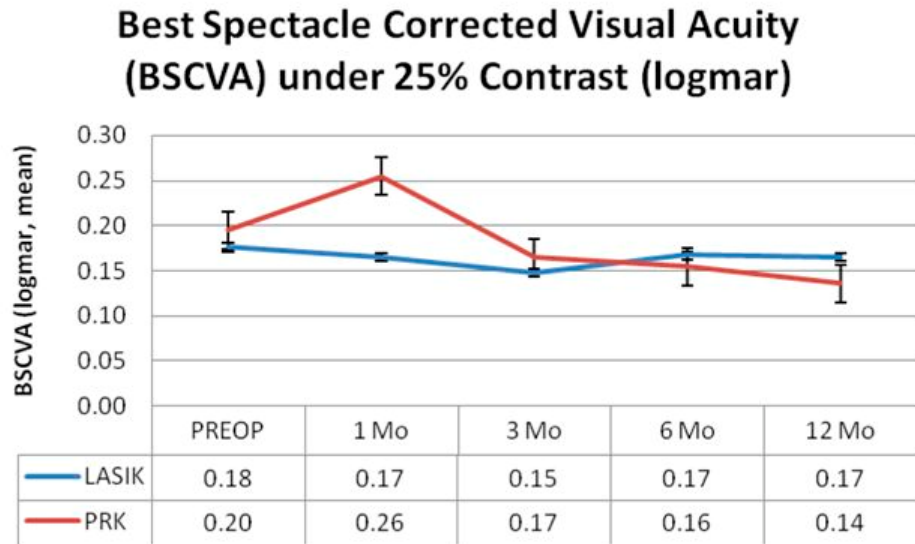


FIGURE 9

Best spectacle-corrected visual acuity (logMAR, mean) for LASIK and PRK groups for each postoperative interval under 25% contrast conditions. Standard error bars are shown.

HIGHER-ORDER ABERRATION (HOA)

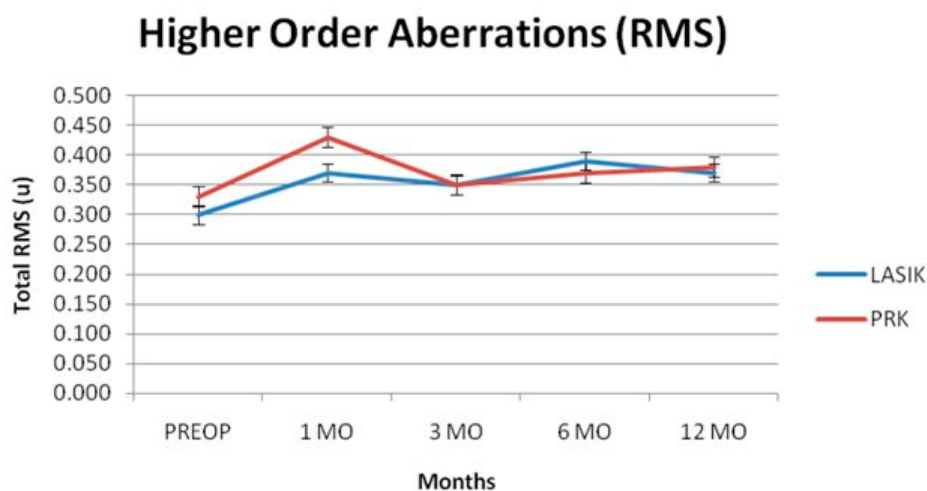
Coma, trefoil, spherical aberration, and total HOA root-mean-square (RMS) for each of the measured postoperative intervals are shown in Table 3 for both the LASIK and PRK groups. At 12 months there was significant increase in coma ($P=0.014$) and total HOA ($P=0.04$) for the LASIK group as compared to preoperative levels. In the PRK group, there was a significant increase in spherical aberration ($P=0.007$) from the preoperative level and a trend toward an increase in total HOA ($P=0.06$)

The mean total HOAs increased from the preoperative levels in all measured postoperative intervals (1, 3, 6, and 12 months) for both the LASIK and PRK groups (Figure 10). At 1 month, the PRK group demonstrated a statistically significant increase in the mean total HOA ($P=0.04$) but by 3 months was similar to the corresponding measurement in the LASIK group. However, there was no difference in total HOA between the LASIK and PRK groups at 12 months postoperatively.

TABLE 3. HIGHER-ORDER ABERRATIONS AT DESIGNATED INTERVALS FOR LASIK AND PRK GROUPS.

	PREOP		1 MO		3 MO		6 MO		12 MO	
	LASIK	PRK	LASIK	PRK	LASIK	PRK	LASIK	PRK	LASIK	PRK
Coma	0.14 ± 0.08	0.18 ± 0.11	0.22 ± 0.15	0.19 ± 0.10	0.21 ± 0.12	0.19 ± 0.08	0.23 ± 0.15	0.17 ± 0.09	0.22 ± 0.17	0.21 ± 0.10
Trefoil	0.15 ± 0.09	0.16 ± 0.11	0.11 ± 0.11	0.16 ± 0.09	0.10 ± 0.06	0.12 ± 0.12	0.13 ± 0.09	0.12 ± 0.07	0.11 ± 0.06	0.14 ± 0.07
Spherical aberration	0.08 ± 0.13	0.08 ± 0.14	0.12 ± 0.17	0.08 ± 0.21	0.09 ± 0.17	0.11 ± 0.20	0.12 ± 0.21	0.17 ± 0.20	0.12 ± 0.17	0.15 ± 0.18
RMS (μm)	0.30 ± 0.11	0.33 ± 0.16	0.37 ± 0.20	0.43 ± 0.15	0.35 ± 0.15	0.35 ± 0.12	0.39 ± 0.17	0.37 ± 0.13	0.37 ± 0.18	0.38 ± 0.13

LASIK, laser in situ keratomileusis; PRK, photorefractive keratectomy; RMS, root-mean-square.

**FIGURE 10**

Higher-order aberrations, root-mean-square (RMS, μm) over each of the designated postoperative intervals for the LASIK and PRK groups. Standard error bars are shown.

SURVEY: SUBJECTIVE SYMPTOMS

Subjective symptoms of glare increased in the LASIK and PRK groups under both day and night conditions at 1 month before improving close to preoperative levels (Figure 11). There was no significant difference in subjective glare symptoms between the LASIK and PRK groups under both day and night conditions after month 1.

Subjective symptoms of haze increased in both the LASIK and PRK groups (Figure 12). The 6-month increase in mean haze symptoms in the LASIK subgroup was skewed by a single eye that experienced severe subjective symptoms of haze (9 of 10). This eye had an UCVA of 20/16.

Subjective symptoms of halos increased in the LASIK and PRK groups at 1 month before improving close to preoperative levels (Figure 13). There was no significant difference in subjective halo symptoms between the LASIK and PRK groups after month 1.

Subjective symptoms of vision clarity in day and night conditions declined at 1 month from preoperative levels in both the LASIK and PRK groups but improved steadily at 12 months (Figure 14). The PRK group demonstrated a significant decline as compared to the LASIK group at 1 month under both the day ($P=0.001$) and night ($P=0.001$) conditions. There was no difference between the LASIK and PRK groups at 3, 6, and 12 months.

The severity and frequency of dry eye symptoms were worse at 1 month postoperatively in both the LASIK and PRK groups before improving steadily over 3-, 6-, and 12-month intervals (Figure 15). However, there was no difference in the severity and frequency of dry eye symptoms between the LASIK and PRK groups after postoperative month 1.

Subjective symptoms of gritty and scratchy sensation increased in the LASIK and PRK groups at 1 month before improving to preoperative levels (Figure 16). There was no significant difference in subjective gritty and scratchy sensation symptoms between the LASIK and PRK groups after month 1.

Subjective symptoms of vision fluctuation increased at 1 month from preoperative levels in both the LASIK and PRK groups but improved steadily at 12 months (Figure 17). The PRK group demonstrated a significant increase in vision fluctuation as compared to the LASIK group at 1 month ($P=0.003$). There was no difference between the LASIK and PRK groups at 3, 6, and 12 months.

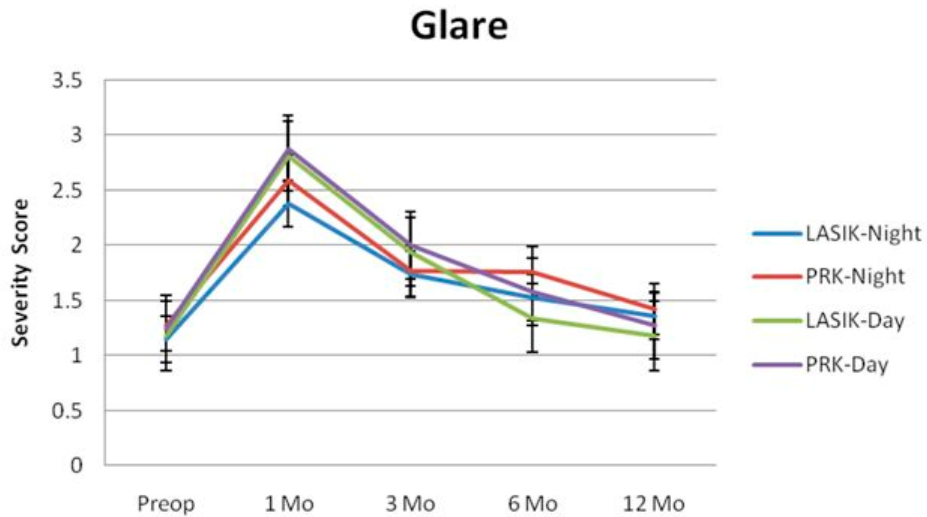


FIGURE 11

Glare symptoms for each of the designated postoperative intervals for LASIK and PRK eyes during the day and night. Standard error bars are shown.

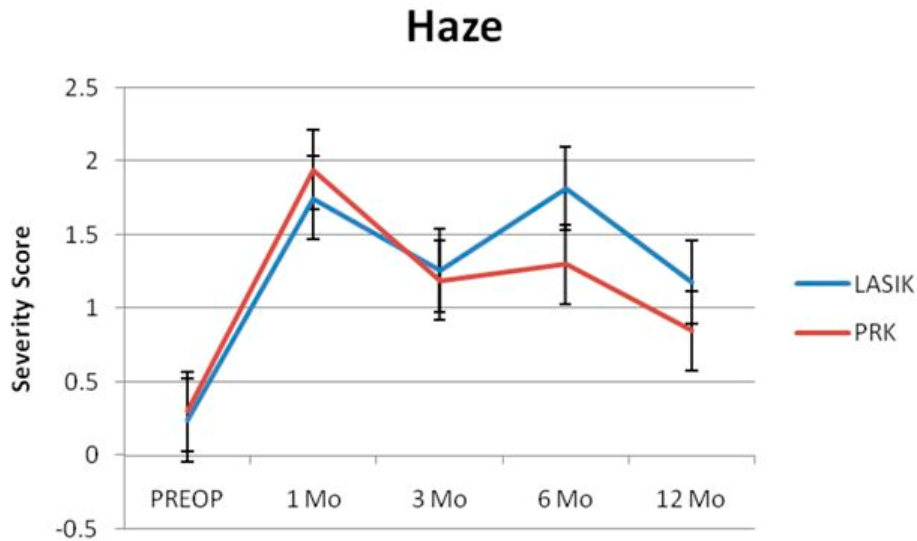


FIGURE 12

Haze symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

Subjective symptoms of ghosting increased at 1 month postoperatively for both the LASIK and PRK groups before improving at the 12-month postoperative interval (Figure 18). Ghosting in the PRK group was significantly worse than in the LASIK group at 1 month ($P=0.02$). At 3, 6, and 12 months, there was no difference in subjective symptoms of ghosting between the PRK and LASIK groups.

The LASIK group demonstrated improved overall vision as compared to the preoperative level at all measured intervals (1 month, 3 months, 6 months, and 12 months) (Figure 19). The PRK group initially declined from the preoperative level at 1 month before improving beyond the preoperative level at 3, 6, and 12 months. The difference between the LASIK and PRK groups was statistically significant only at 1 month postoperatively ($P=0.02$).

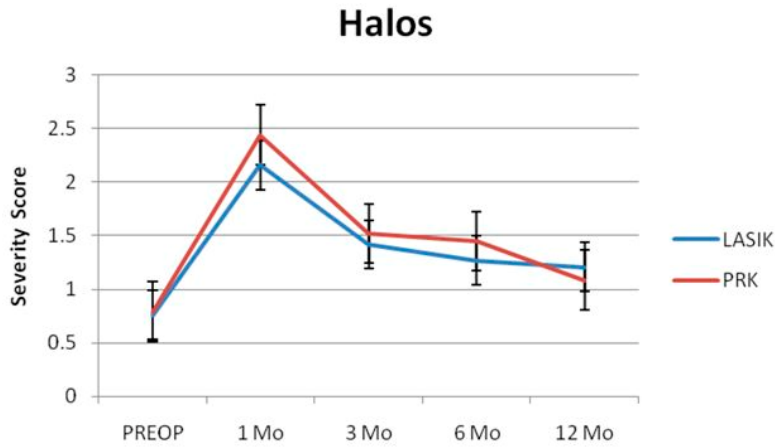


FIGURE 13

Halo symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

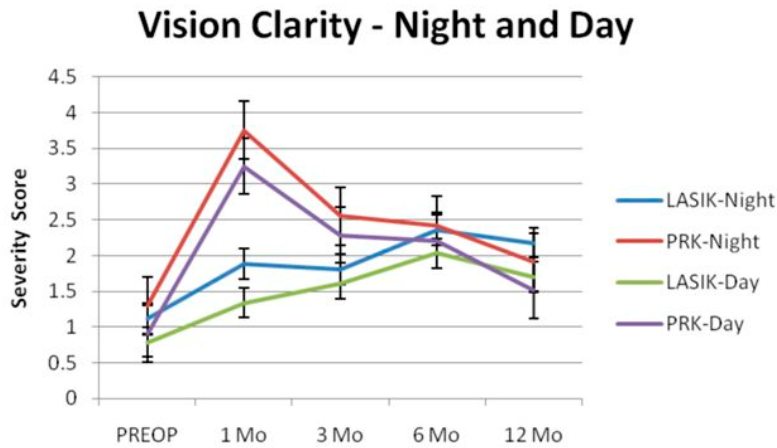


FIGURE 14

Vision clarity symptoms for each of the designated postoperative intervals for LASIK and PRK eyes during the night and day. Standard error bars are shown.

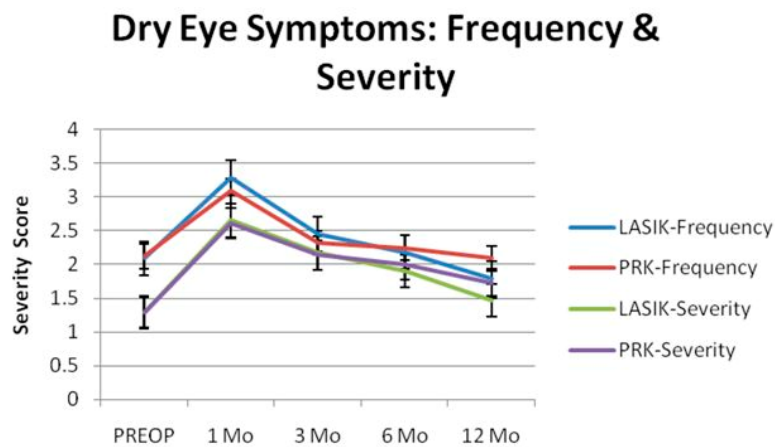


FIGURE 15

Frequency and severity of dry eye symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

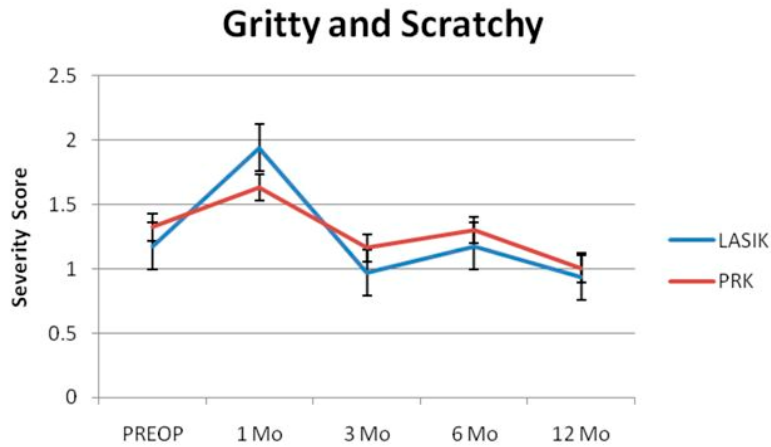


FIGURE 16

Gritty and scratchy symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

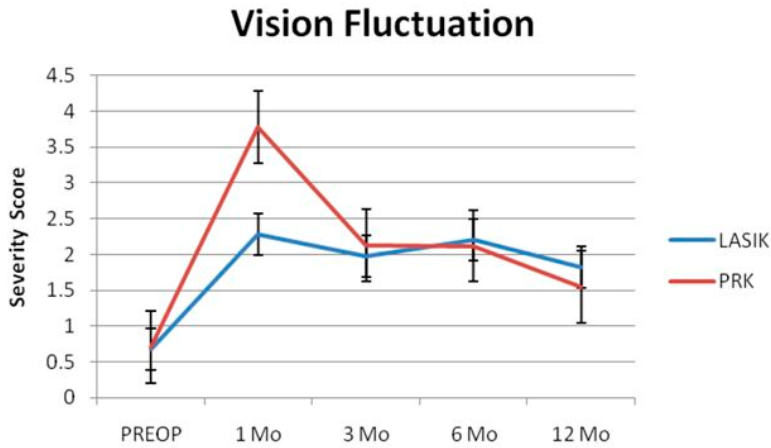


FIGURE 17

Fluctuation of vision symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

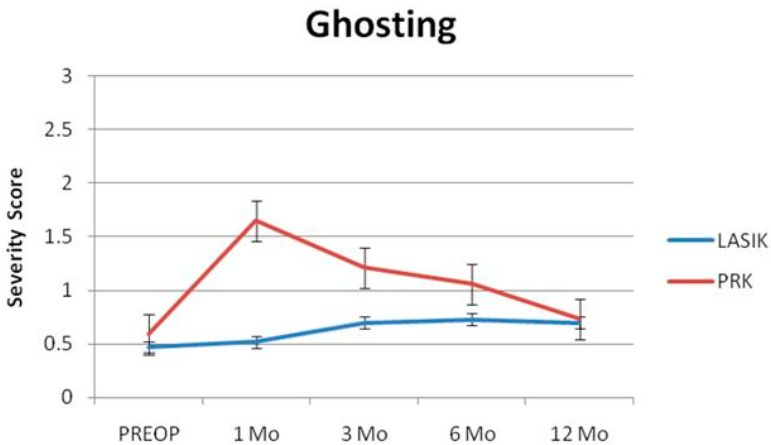
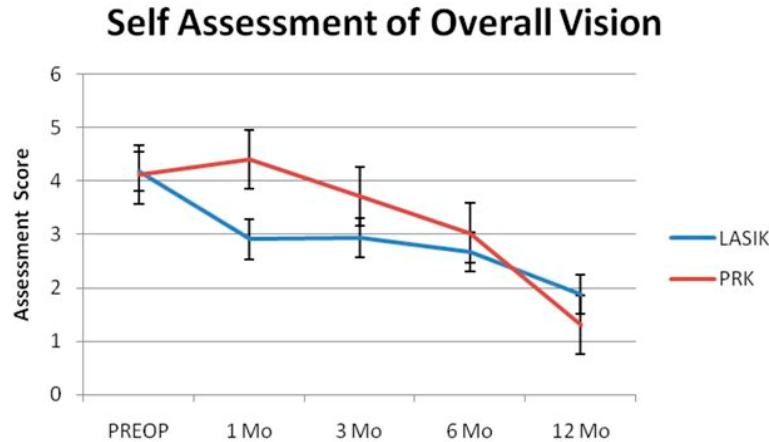


FIGURE 18

Ghosting symptoms for each of the designated postoperative intervals for LASIK and PRK eyes. Standard error bars are shown.

**FIGURE 19**

Self-assessment of overall vision for each of the designated postoperative intervals for LASIK and PRK eyes. “0” was described as “excellent” vision.

COMPLICATIONS

There were no intraoperative or postoperative flap complications in the LASIK group. There were no instances of corneal haze in the PRK group. The corneal epithelial defect was healed in all eyes in the PRK group within 5 days. No eyes were re-treated within the first 12 months. One eye (3 %) with high myopia (preoperative mean spherical equivalent -8.0) in the PRK group developed late-onset myopic regression of more than 1.0 D between 6 months and 12 months postoperatively.

DISCUSSION

In our study, wavefront-guided PRK and wavefront-guided LASIK were both effective at treating myopia with and without astigmatism. Both techniques demonstrated stable and predictable long-term results and significant improvement in UCVA at 1 year. In addition, both techniques demonstrated excellent safety profiles with no loss of BSCVA >2 lines, contrast sensitivity loss, or incidents of corneal haze/scarring or flap complications. We did note a loss of 1 line of BSCVA of 3% in the LASIK group and 6% in the PRK group. The difference in the loss of 1 line of BSCVA between the two groups was not statistically significant ($P=0.17$). Loss of 2 or more lines of BSCVA is the standard safety measurement required by the US Food and Drug Administration (FDA) when considering the approval of a refractive surgical procedure or device. A comprehensive review of all of the FDA-approved excimer lasers for LASIK and PRK showed a 5% to 11% loss of 1 line of BSCVA among the various platforms. The VISX CustomVue excimer laser used in our study had an 8.7% loss of 1 line of BSCVA after LASIK surgery in the FDA clinical trial that led to the device’s approval.⁶³ The original VISX excimer laser approved by the FDA had an 8.5% loss of 1 line of BSCVA after PRK surgery in the clinical trial that led to its approval.⁶⁴ It is difficult to compare our outcomes to those of other published studies because most studies report only 2 or more lines of BSCVA loss and do not provide the data on 1-line loss. A review of the PRK and LASIK literature with data on 1-line loss of BSCVA showed data quite similar to ours, with reported losses ranging from 6% to 19%.⁶⁵⁻⁶⁸ The most common cause of loss of BSCVA has been reported to be subclinical microstriae and superficial punctate keratitis in LASIK and corneal haze and superficial punctate keratitis in PRK.⁶⁶ Even though we did not report any complications in either group, it is likely that our loss of BSCVA was attributable to some of the same factors. However, in our study, there were several notable differences between PRK and fellow LASIK eyes.

When comparing wavefront-guided PRK vs wavefront-guided LASIK, there was an initial delay in optimal visual recovery in the PRK group, which is consistent with previous studies evaluating lamellar surgery vs surface ablations in fellow eyes.⁶⁶⁻⁶⁸ At 1 month, LASIK-treated eyes outperformed the fellow PRK-treated eyes in several subjective and objective categories: subjectively, patients experienced less visual clarity during both day and night, more vision fluctuation, and more ghosting/double vision in the PRK-treated eyes ($P < 0.05$) as compared to their LASIK-treated fellow eyes. In addition, patients rated their overall self-assessment of vision as poorer in the PRK-treated eye at 1 month ($P=0.02$). Many of these symptoms may be consistent with the residual lower-order aberrations, such as spherocylinder refractive error in the PRK-treated eyes. Although there was no difference ($P=0.24$) between the mean spherical equivalent between PRK- and LASIK-treated eyes at the 1-month visit, the PRK-treated eyes had a larger mean residual refractive error (ie, sphere $P=0.004$, and astigmatism $P=0.0009$) than the fellow LASIK-treated eye. In addition, there was a tendency toward more variability and higher standard deviation in the mean refractive error (sphere and cylinder) at 1 month in the PRK-treated eye as compared to the fellow LASIK-treated eye. This also translated into a poorer mean UCVA (logMAR scale, $P=0.000006$) in the PRK-treated eyes at the 1-month visit.

However, the difference in lower-order aberrations (ie, sphere, cylinder) at 1 month does not account for the difference in BSCVA

noted between PRK-treated and fellow LASIK-treated eyes. The LASIK-treated eyes outperformed the PRK-treated eyes in mean BSCVA under all testing conditions at 1 month: standard conditions (logMAR scale, $P=0.003$), 5% contrast sensitivity conditions (logMAR scale, $P=0.0006$), and 25% contrast sensitivity conditions (logMAR scale, $P=0.00002$). This may be consistent with differences in the induction of total HOAs between the PRK-treated and fellow LASIK-treated eyes. At 1 month, PRK-treated eyes had more induced total HOAs (mean, RMS, $P=0.04$) than the fellow LASIK-treated eyes. In several studies, the presence of total HOAs may correlate with poor performance on contrast sensitivity tests, increased coma related to symptoms of monocular diplopia and ghosting, and increased spherical aberrations correlating with glare and starburst.⁶⁹⁻⁷¹ Indeed, at 1 month, the PRK-treated eyes were also more likely to suffer from several subjective symptoms, such as poorer vision clarity in day and night, as well as ghosting, when compared to their LASIK-treated fellow eye. However, the differences in subjective symptoms, residual spherocylinder error, UCVA, and HOAs had completely resolved by 3 months. By 3 months, the differences in BSCVA under standard, 5% contrast sensitivity, and 25% contrast sensitivity conditions had also completely resolved. Our results were identical to the results of two other studies comparing wavefront-guided LASIK to wavefront-guided PRK.^{66,67} In contrast, Slade and associates⁶⁸ reported statistically significantly better 10% contrast sensitivity results in the wavefront-guided LASIK group compared to the wavefront-guided PRK group at all postoperative time intervals.

In our study, we found no statistical difference between wavefront LASIK-treated and fellow PRK-treated eyes among spherical aberration, trefoil, and coma during each of the postoperative periods. Although there was no difference in the mean total RMS between LASIK and PRK groups, there was a consistent trend toward more variability (higher standard deviation) in the wavefront-guided LASIK group than in the corresponding wavefront-guided PRK group at every postoperative time period between 1 and 12 months (Table 3). The observed trend was unrelated to mean pupil diameter, which was equivalent in our LASIK- and PRK-treated eyes (6.4 ± 0.9 mm in LASIK-treated eyes vs 6.2 ± 1.0 mm in the fellow PRK-treated eye; $P=0.08$). The variability may be consistent with the creation of the lamellar keratectomy during LASIK. Porter and colleagues⁷² reported an increase in HOAs of approximately 30% 2 months after creating a lamellar flap with a mechanical microkeratome. Moshirfar and colleagues⁶⁶ reported an increase in HOAs by a factor of 1.22 in PRK-treated eyes and an increase of 1.74 in LASIK-treated eyes in a prospective comparison of wavefront-guided PRK to wavefront-guided LASIK surgery. This difference was statistically significant ($P=0.005$). However, in agreement with our results, Slade and associates⁶⁸ reported no statistical significant difference in induced HOAs in a prospective comparison study of wavefront-guided PRK to wavefront-guided LASIK at 6 months ($P=0.23$). Other studies also found an increase in total HOAs following flap formation.⁷³⁻⁷⁶ In addition, the amount of induced HOAs from the flap creation may be dependent upon whether a microkeratome or femtosecond laser is employed to create the flap.^{75,76} One limitation of our study was the lack of analysis of HOAs at a standardized pupil size. The VISX Wavescan aberrometer does not control the pupil size and therefore cannot measure the aberrations for standardized pupil sizes in a cohort of eyes. The only way to perform an analysis using standardized pupil size is to utilize special software (Zernicke Tool Software, Abbott Medical Optics, Santa Ana, California). This software utilizes a mathematical algorithm that allows back calculation for HOA for standardized pupil size. This software is not commercially available and is available only as a research tool. In lieu of this software, we attempted to control for pupil size by analyzing aberrometry readings that were within $0.25 \mu\text{m}$ of the preoperative measurements. This technique has been validated in a previous published study.⁷⁷

Despite the ability to measure aberrations beyond the sixth order and the ability to precisely deliver excimer laser ablations based on these measurements, the outcomes of wavefront-guided PRK and wavefront-guided LASIK are significantly limited by the variable and physiologic effects of the excimer laser on tissue such as the cornea. In LASIK, creation of the lamellar flap, independent of excimer laser ablation, may induce aberrations that are unaccounted for during preoperative aberrometer readings.⁷⁴⁻⁷⁶ In addition, corneal surface healing following LASIK or PRK can result in overall smoothing of the corneal surface as the epithelium thickens over divots and thins over bumps.⁷⁸ This may partially negate the accuracy of micron and submicron wavefront-guided excimer laser technology.⁷⁹ Studies have suggested that this process plays a significant role in the interpersonal variability and refractive stability of the procedure and can significantly impact the results of ablation.⁷⁹⁻⁸¹ Therefore, the corneal biomechanical response to ablative surgery may significantly affect outcomes and should be taken into account when planning wavefront-guided excimer laser procedures.⁸⁰⁻⁸²

Adjunctive pharmacologic wound modulation during the perioperative period may have a potential role in minimizing variations on a cellular level following keratorefractive surgery.^{83,84} Topical steroids, topical anti-transforming growth factor beta, and topical nonsteroidal anti-inflammatory medications have been proposed or successfully used in various capacities to modulate the healing response and control regression of refractive effect or optical clarity.^{85,86} Topical intraoperative mitomycin C has also been used to minimize the variable healing response, improve optical clarity, and possibly maximize the effects of laser surgery in PRK.⁸⁷⁻⁹³ Wallau and Campos⁶⁸ evaluated the use of mitomycin C as an adjunctive treatment to PRK in comparison to LASIK treated fellow eyes.⁹⁴ In this study, 88 eyes of 44 patients with moderate myopia were randomized to PRK with 0.002% for 1 minute or LASIK in the fellow eye. In contrast to our results, Wallau and Campos found that eyes undergoing PRK with adjunctive intraoperative mitomycin C performed better than LASIK-treated eyes in many objective parameters, such as UCVA, BSCVA, contrast sensitivity, refractive outcomes, total RMS, defocus, astigmatism, and spherical aberrations at the 1-year follow-up. However, the investigators caution that further studies are indicated before widespread use of mitomycin C in keratorefractive surgery is encouraged.

In summary, both wavefront-guided PRK and wavefront-guided LASIK are safe and effective at reducing myopia with and without astigmatism. The decision to pursue wavefront-guided PRK vs wavefront-guided LASIK should be decided on an individual basis and

should take into consideration many factors unique to the individual patient. The advantages of each technique should be balanced by the potential risks of each individual procedure. LASIK provides a more comfortable and rapid visual recovery in terms of many subjective and objective criteria, although by 3 months, these differences have largely dissipated. PRK provides the advantages of a flap-free procedure (reduced potential for ectasia and flap complications) at the cost of a slower, more uncomfortable visual recovery. Regardless, both wavefront-guided PRK and wavefront-guided LASIK demonstrate promise in the correction of myopia with and without astigmatism. Avoiding the mechanical variations due to the creation of the lamellar flap (ie, LASIK) and the longer healing phase in PRK have potential benefits when dealing with the micron level of accuracy demonstrated by wavefront diagnostic and therapeutic modalities. In the future, we will have to reconcile with the biologic variability resulting from interpersonal variations in corneal wound healing. Unfortunately, advances in the clinically available pharmacologic and biologic wound-healing modulation techniques have not kept pace with advances in wavefront technology. In the future, improved methods of pharmacologically or biologically modulating the response of the cornea to the excimer laser could help us realize the full potential of wavefront technology. Despite this shortcoming, both wavefront-guided PRK and wavefront-guided LASIK are proving to be important and valuable approaches to managing patients with refractive errors.

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Author Contributions: *Design of the study* (E.M.); *Conduct of the study* (E.M.); *Collection* (E.M.), *management* (E.M.), *analysis* (E.M., W.H.), *and interpretation* (E.M., W.H.) *of the data*; *Preparation* (E.M., W.H.), *review* (E.M.), *and approval* (E.M.) *of the manuscript*.

Conformity With Author Information: Approved by the Stanford Institutional Review Board on August 8, 2006 (Stanford IRB protocol number 6934; ClinicalTrials.gov Identifier: NCT01140594). All subjects signed an informed consent that was HIPAA compliant.

APPENDIX

PATIENT QUESTIONNAIRE

1. People have difference experiences with their vision. Some people have problems with glare or light sensitivity. Please indicate whether you now—that is, within the last two weeks—have problems with glare or light sensitivity in the following situations. On a scale of 0 to 10 where 0 stands for “no glare” and 10 stands for “disabling glare,” how much trouble do you have with glare?

Glare	No glare	Disabling glare
At night	0....1....2....3....4....5....6....7....8....9....10	
During the day	0....1....2....3....4....5....6....7....8....9....10	

2. People have difference experiences with their vision. Some people have problems with hazy or foggy. vision. Please indicate whether you now—that is, within the last two weeks—have problems with hazy or foggy vision. On a scale of 0 to 10 where 0 stands for “no haze” and 10 stands for “disabling haze,” how much trouble do you have with haze?

Haze	No haze	Disabling haze
	0....1....2....3....4....5....6....7....8....9....10	

3. People have difference experiences with their vision. Some people have problems with halos, rings or star-bursts around objects or lights. Please indicate whether you now—that is, within the last two weeks—have problems with, halos, rings or starbursts. On a scale of 0 to 10 where 0 stands for “no halos” and 10 stands for “disabling halos,” how much trouble do you have with halos?

Halos	No halos	Disabling halos
	0...1...2...3...4...5...6...7...8...9...10	

4. People have difference experiences with their vision. Some people have problems with sharpness or clarity. Please indicate whether you now—that is, within the last two weeks—have problems with sharpness or clarity. On a scale of 0 to 10 where 0 stands for “no problems” and 10 stands for “disabling problems,” how much trouble do you have with sharpness or clarity?

Clarity	No problem	Disabling problem
At night	0...1...2...3...4...5...6...7...8...9...10	
During the day	0...1...2...3...4...5...6...7...8...9...10	

The next set of questions asks you to describe your vision as you go about your daily activities, both when you are at work and when you are not at work. Please enter your scores in the boxes provided for each eye.

5. My vision is excellent	Strongly agree	Strongly disagree
	0...1...2...3...4...5...6...7...8...9...10	
6. Do you have problems with dry eyes?	No problem	Disabling problem
	0...1...2...3...4...5...6...7...8...9...10	
7. If you do have problems with dry eyes, how severe is this problem?	No problem	Disabling problem
	0...1...2...3...4...5...6...7...8...9...10	
8. Do you have problems with gritty, scratchy or sandy feelings in your eyes?	None of the time	All of the time
	0...1...2...3...4...5...6...7...8...9...10	
9. Do you have problems with your vision fluctuating over the day?	None of the time	All of the time
	0...1...2...3...4...5...6...7...8...9...10	
10. Do you have difficulty because of double vision or ghost images?	No difficulty	Extreme difficulty
	0...1...2...3...4...5...6...7...8...9...10	

Questionnaire completed preoperatively and postoperatively at months 1, 3, 6, and 12. Patients completed a separate questionnaire for each eye.

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