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Results of Phase III Excimer Laser Photorefractive Keratectomy for Myopia

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Objective: The purpose of the study is to determine safety and efficacy outcomes of excimer laser photorefractive keratectomy (PRK) for the treatment of mild-to-moderate myopia.

Design: A prospective, multicenter, phase III clinical trial.

Participants: A total of 701 eyes of 701 patients were entered in the study; 612 eyes were examined at 2 years after surgery.

Intervention: Intervention was photorefractive keratectomy using the Summit ExciMed UV200LA excimer laser (Summit Technology, Inc., Waltham, MA). The treatment zone diameter used was 4.5 mm in 251 eyes (35.8%) and 5 mm in 450 eyes (64.2%). Attempted corrections ranged from 1.50 to 6.00 diopters (D).

Main Outcome Measures: Predictability and stability of refraction, uncorrected and spectacle-corrected visual acuity, refractive and keratometric astigmatism, corneal haze, contrast sensitivity, subjective reported problems of glare and halo, and patient satisfaction were the parameters measured.

Results: At 2 years, 407 (66.5%) eyes achieved 20/20 or better uncorrected visual acuity and 564 (92.5%) eyes achieved 20/40 or better visual acuity. Three hundred thirty-six (54.9%) eyes were within 0.5 D and 476 (77.8%) eyes were within 1.0 D of attempted correction. Stability of refraction improved with time; 86.8% of eyes were stable within 1.0 D from 6 to 12 months, 94% were stable from 12 to 18 months, and 96.3% were stable from 18 to 24 months. There was no evidence of progressive or late myopic or hyperopic refractive shifts.

One hundred fourteen (18.6%) eyes gained 2 or more lines of spectacle-corrected visual acuity, whereas 42 (6.9%) eyes lost 2 or more lines; however, of the latter, 32 (76.2%) had spectacle-corrected visual acuity of 20/25 or better and 39 (92.9%) eyes had 20/40 or better. Four hundred forty-two (72.2%) corneas were clear, 138 (22.5%) showed trace haze, 20 (3.3%) mild haze, 9 (1.5%) moderate haze, and 3 (0.5%) marked haze. On patient questionnaires, 87 (29.7%) patients reported worsening of glare from preoperative baseline; 133 (50.1%) reported worsening of halo symptoms from baseline.

Conclusions: Photorefractive keratectomy appears effective for myopic corrections of −1.50 to −6.00 D. Uncorrected visual acuity is maximized in most eyes by 3 months, although some patients require between 6 months and 1 year to attain their best postoperative uncorrected visual acuity and some may require from 1 to 2 years for stabilization of refraction. Refraction stabilizes progressively without evidence of late myopic or hyperopic refractive shifts. Optical sequelae of glare and halo occur in some patients treated with a 4.5- or 5-mm treatment zone. *Ophthalmology 1997;104:1535–1553*

Development of photorefractive keratectomy (PRK) dates from 1981 with the work of Taboada et al[1] and, subsequently, with the recognition by Trokel et al[2] that the 193-nm ultraviolet (UV) argon fluoride excimer laser could be used to excise corneal tissue. Initially it was proposed that the excimer be used as a "laser scalpel" to create linear excisions for "excimer radial keratotomy."[3,4] However, the excimer laser was found to be a poor substitute for the diamond scalpel because it removes, rather than incises, tissue.[5-7] A more promising application of the excimer laser was found to be reshaping of the corneal curvature by removal of graded amounts of tissue from the anterior stroma, a procedure termed photorefractive keratectomy (PRK).[8] Initial animal studies indicated little thermal or mechanical effect to the tissue adjacent to the ablation and that the healing of corneas was normal.[9-14] Therefore, as the design of lasers and delivery systems matured, confidence was gained that sighted ametropic human eyes could be treated successfully for refractive errors.[15]

Phase I of United States clinical trials with the Summit ExciMed UV200LA excimer (Summit Technology, Inc., Waltham, MA) laser began in 1989 with the treatment of 16 blind and 2 sighted eyes that were scheduled for enucleation. The results provided evidence that the procedure was not overtly harmful. The phase IIA investigation of 20 amblyopic or anisometropic eyes began in January 1990. In the fall of 1990, 100 otherwise healthy myopic eyes of 100 patients were treated as part of the phase IIB study.[16] These promising results allowed phase III clinical trials to begin on June 17, 1991. The clinical information obtained from these trials formed the basis on which premarket approval of the Summit Technology, Inc, excimer laser for the correction of myopia was granted in the United States on October 20, 1995. The laser ultimately was approved with a beam diameter of 6 mm.

Few studies to date report long-term results and stability of PRK in a well-controlled, prospective clinical investigation. We report herein the results of PRK in 701 myopic eyes of 701 patients enrolled in the phase III clinical study of PRK using the Summit ExciMed UV200LA excimer laser with a 4.5- or 5-mm diameter ablation zone and a single-pass expanding diaphragm technique with follow-up of 2 years.

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Patients and Methods

Study Design

As part of the phase III multicenter clinical study of the Summit Technology, Inc. excimer laser conducted in accordance with U.S. Food and Drug Administration regulations, a prospective study of 701 eyes of 701 patients was performed to assess the safety and efficacy of PRK for the treatment of myopia.[17] The treatments were performed at ten clinical centers between June 1991 and March 1992. This article reports the 2-year examination results on the first eye treated of each patient.

All study centers conformed to standardized patient entry criteria under a U.S. Food and Drug Administration Investigational Device Exemption granted to Summit Technology, Inc. Approvals from appropriate institutional review boards were obtained, and all patients gave their informed consent.

Patient Selection

All patients entered in the study were 21 years of age or older and had between −1.25 and −7.25 diopters (D) of myopia (manifest refraction spherical equivalent) and less than or equal to 1.50 D of refractive astigmatism. Attempted corrections ranged from 1.50 to 6.00 D. The study protocol allowed planned undercorrections or overcorrections of 1.0 D or less (one patient did receive a planned undercorrection of 1.25 D). Patients were excluded if they had previous ocular surgery, previous or current ocular disease including evidence of keratoconus, or systemic diseases that might influence wound healing.

Photorefractive Keratectomy Procedure

Photorefractive keratectomy was performed with the Summit ExciMed UV200LA excimer laser system. Laser parameters included a repetition rate of 10 Hz, radiant exposure at the corneal plane of 180 mJ/cm^2, and pulse duration of 14 nsec, resulting in an ablation rate of corneal stromal tissue of approximately 0.25 μm per pulse. For patients with a pupil size less than or equal to 5 mm at an illumination of 21 lux, a 4.5-mm treatment zone was used, and for those with a pupil size greater than 5 mm, a 5-mm treatment zone was used. Treatment zone size was 4.5 mm (35.8%) in 251 cases and 5 mm (64.2%) in 450 cases.

The standardized PRK procedure used is explained in detail elsewhere.[18] In brief, to ensure appropriate laser energy and beam homogeneity, ablation and beam profile characteristics were tested at the beginning of each treatment day by the rate and pattern of ablation of a 100-μm thick gelatin filter (Kodak #1497890, Rochester, NY) and

standardized ablations on a polymethylmethacrylate disc. The operative eye received two drops of pilocarpine 1% approximately 30 minutes before the procedure and topical anesthetic drops. With the patient in the supine position, the laser was focused on the cornea by adjusting the position of the patient in the vertical direction until the two converging helium–neon aiming beams were coincident on the anterior corneal surface. The ablation was centered over the entrance pupil as suggested by Uozato and Guyton.[19] The centration procedure and accuracy of centration in this study are published elsewhere.[20]

Two training sessions were performed to familiarize the patient with the procedure and to ensure proper fixation subsequently. The first training session involved the application of methylcellulose 1% to the cornea before ablation to block the incoming laser beam. The second session was performed on dry epithelium using 25 pulses of the laser at its maximum aperture. After the second training session, the optical zone was marked around the entrance pupil with a 6-mm optical zone marker, the epithelium within this area was removed with a microsurgical blade, and the laser ablation was performed.

Postoperative Management

After surgery, a combination antibiotic–steroid ointment (tobramycin–dexamethasone) and a patch were applied. Per the study protocol, the ointment was continued up to 5 times daily until the cornea had re-epithelialized. Fluorometholone 1% drops then were administered five times daily for 1 month. The dosage then was reduced to fluorometholone 0.1% drops four times daily for 1 month and then three times daily for 1 month. Corticosteroid dosage after the completion of the third month was at the discretion of the individual surgeon based on the patient's refraction and degree of corneal haze. Bandage soft contact lenses and topical nonsteroidal anti-inflammatory agents were not used in any cases.

Patient Examinations

Patients were seen before surgery and after surgery on days 1 and 3 and at 1 week if slit-lamp examination results on day 3 showed that the cornea had not re-epithelialized completely. They again were examined 1, 2, 3, 4, 6, 9, 12, 18, and 24 months after the procedure.

Preoperative and follow-up visits included a detailed ophthalmologic examination with manifest refraction by two independent observers at each visit and cycloplegic refraction at 6 months, 1 year, and 2 years. By the study protocol, the refractions needed to be within 1.0 D; if not, refractions were repeated until the differences were reconciled. Planned undercorrections or overcorrections of 1.0 D or less were allowed at the surgeon's discretion per the study protocol and, generally, the least myopic refraction was chosen to avoid overcorrection. Visual acuity was measured under controlled lighting conditions to produce a 2- to 4-mm and a 6- to 8-mm pupillary diameter by trained technicians using a back-illuminated Early Treatment Diabetic Retinopathy Study chart (Lighthouse for the Blind, New York, NY). Manual keratometry,[21] glare testing with the Brightness Acuity Tester (Mentor, Norwell, MA) using the medium setting, and anterior segment photography also were performed at designated examinations. Contrast sensitivity was measured with the VectorVision CSV-1000 chart (Dayton, OH), which displays sine wave gratings at spatial frequencies of 3, 6, 12, and 18 cyc/deg. Thresholds were determined with both undilated and dilated pupils at a distance of 2.4 m. Computer-assisted videokeratography was performed at five study centers (EyeSys Laboratories, Houston, TX). Contact lens wear was discontinued at least 2 weeks before the preoperative examination for rigid lens wearers and at least 1 week for soft contact lens wearers.

At the preoperative and 6-month, 12-month, 18-month, and 2-year postoperative visits, patients were asked to fill out a self-administered questionnaire. In general, questionnaires were completed without explanations by study personnel; however, explanations were given if requested by the patient. As part of this questionnaire, patients were asked to assess subjective glare and halo sequelae in the first eye operated on on a 0-to-5 scale where 0 indicated an absence of such symptoms and 5 indicated the worst symptomatology. Subjective patient satisfaction also was assessed on a 0-to-5 scale, where 5 indicated the most satisfaction with the procedure. Anterior stromal haze was graded subjectively during slit-lamp biomicroscopy and reported as one of five standardized categories: clear, trace (haze only seen with broad-beam illumination), mild (haze visible by slit-beam illumination), moderate (haze somewhat obscuring iris detail), and marked (haze markedly obscuring iris detail).[22] Any complications or adverse reactions were noted.

Data Acquisition and Analysis

Data were entered at each investigational site onto standardized data collection forms by either the investigator or trained technicians. All visual acuity measurements were reported on the logarithm of the minimum angle of resolution (LogMAR) scale.[23] Outcome of predictability was defined as achieved minus attempted correction. Stability of the postoperative refraction was assessed by comparing the manifest refraction spherical equivalent at different follow-up examinations.

Data from the collection forms were compiled at Summit Technology and entered into a database program customized for this application. Statistical analysis was performed using the Statistical Analysis System 6.07 (SAS Institute, Inc, Cary, NC). Descriptive statistics were compiled and are presented herein. To compare patients lost to follow-up at 2 years with those on whom data were available, bivariate analyses included the chi-square test for proportions, the Mantel–Haensel chi-square test for trends, and Fisher's exact two-tailed test for cases in which the incidence in any one cell was less than 5%. Multivariate models of characteristics associated with the principal clinical outcomes of PRK including postoperative uncorrected vision, predictability, and postoperative refractive stability are reported elsewhere.[24]

Results

Preoperative Characteristics

A total of 701 eyes of 701 patients entered the study cohort. Clinical data were available on 612 (87%) at 2 years after PRK. The mean age of the 612 patients observed was 38 years. One hundred forty-one patients (23%) were 21 to 30 years of age, 242 (40%) were 31 to 40 years of age, 179 (29%) were 41 to 50 years of age, 41 (7%) were 51 to 60 years of age, and 9 (2%) were older than 60 years of age. Three hundred thirty-four (55%) were male; 278 (45%) were female.

Preoperative manifest spherical equivalent refraction ranged from −1.25 to −7.25 D (mean, −4.21 D; standard deviation [SD], 1.32 D). Manifest refractive cylinder ranged from 0 to 1.75 D (mean, 0.51 D). Pupil diameter at low-light conditions (21 lux) ranged from 2 to 9 mm (mean, 5.6 mm; SD, 1.9 mm), and at 322 lux ranged from 2 to 6.5 mm (mean, 3.5 mm; SD, 0.89 mm). Three hundred seventy-eight patients (61.8%) wore contact lenses before surgery.

Patients Lost to Follow-up

To investigate the potential bias that the 89 patients not examined at 2 years differed from the 612 patients present for 2-year follow-up, 2 analyses were performed. First, comparing patients lost to follow-up with those examined at 2 years, there were no differences at baseline in age, gender, preoperative uncorrected or spectacle-corrected visual acuity, manifest refraction spherical equivalent, attempted correction, or refractive astigmatism.

Second, those patients lost to follow-up were compared to the remainder of the cohort at the time of their last follow-up examination. Regarding the outcomes of predictability and uncorrected visual acuity, the patients lost to 2-year follow-up had outcomes that were statistically indistinguishable from the 612 patients who did present for the 2-year examination. Specifically, at 6 months, 21 (87.5%) of the 24 patients subsequently lost to follow-up had an uncorrected visual acuity of 20/40 or better and 16 patients (66.7%) had a predictability within 1.0 D of attempted correction; in comparison, 595 (92.2%) of the 645 patients followed up after 6 months had an uncorrected visual acuity of 20/40 or better and 464 (72%) had a predictability within 1.0 D. At 12 months, all 22 (100%) of the 22 patients lost to follow-up had an uncorrected visual acuity of 20/40 or better and 17 (77.3%) had a predictability within 1.0 D of attempted correction; in comparison, 525 (90.8%) of the 578 patients followed up after 12 months had an uncorrected visual acuity of 20/40 or better and 436 (75.6%), of the 577 patients with predictability data available were within 1.0 D of attempted correction. Similarly at 18 months, all 28 (100%) of the 28 patients lost to follow-up had an uncorrected visual acuity of 20/40 or better and 24 patients (85.7%) had a predictability within 1.0 D of attempted correction; in comparison, 465 (93.8%) of the 496 patients followed up after 18 months had an uncorrected visual acuity of 20/40 or better and 395 (79.8%) had a predictability within 1.0 D.

Based on these analyses of preoperative characteristics and postoperative results, there is no evidence that these patients lost from the original cohort differed significantly from those examined at 2 years. Moreover, of the subgroup of patients who received subsequent procedures (see below), only one (1.7%) was lost to follow-up.

Laser Procedure Characteristics

Attempted corrections ranged from 1.50 to 6.00 D with a mean of 4.24 diopters (SD, 1.25 D) (Fig 1). Excimer laser beam diameter in patients with 2-year data available was 4.5 mm (32%) in 198 eyes and 5 mm (68%) in 414 eyes. Six hundred fifty-two procedures (93%) were carried out within 5 minutes of the start of the epithelium removal. Total time for the PRK procedure from insertion to removal of the lid speculum was 7 minutes or less in 172 eyes (28%), 7 to 10 minutes in 176 (29%), 10 to 13 minutes in 135 (22%), and more than 13 minutes in 123 eyes (20%).

Subsequent Procedures

Sixty (9.8%) of the 612 patients seen at the 2-year follow-up visit had had 1 or more additional refractive procedures on the study eye during the time of observation. Twenty-one (35%) of these had a second PRK, 2 (3.3%) had radial keratotomy, 22 (36.7%) had astigmatic keratotomy, 23 (38.3%) had mechanical epithelial debridement, and 1 (1.7%) had automated lamellar keratoplasty. One patient had anterior stromal micropuncture.

Predictability and Stability of Refractive Change

Before surgery, the mean manifest spherical equivalent refraction was −4.21 D (SD, 1.32 D). The mean attempted correction was 4.07 D. Thus, in general, emmetropia or a slight undercorrection was the goal of the procedure.

The predictability of the procedure, as defined by the achieved minus attempted correction, is seen in Table 1 and Figure 2. At 2 years after PRK, 336 eyes (54.9%) were within 0.5 D, 476 eyes (77.8%) were within 1.0 D, and 579 eyes (94.6%) were within 2.0 D of attempted correction. Seventy-five eyes (12.3%) were overcorrected by more than +1.0 D and 61 eyes (10%) were undercorrected by more than −1.0 D. Those patients who underwent more than one procedure were more likely to be less predictable. Whereas 447 (81%) of the 552 eyes of patients who underwent only 1 procedure achieved within 1.0 D of the attempted correction, only 30 (50%) of the 60 eyes of patients having more than 1 procedure obtained this goal ($P < 0.001$).

The actual refractive outcome at different timepoints is seen in Table 2 and the change in refraction over time is illustrated in Figure 3. An early mean overcorrection occurred followed by regression and stabilization of the refractive effect. At 1 month, the mean manifest refraction was +1.58 D (SD, 1.16 D), at 3 months +0.75 D (SD,

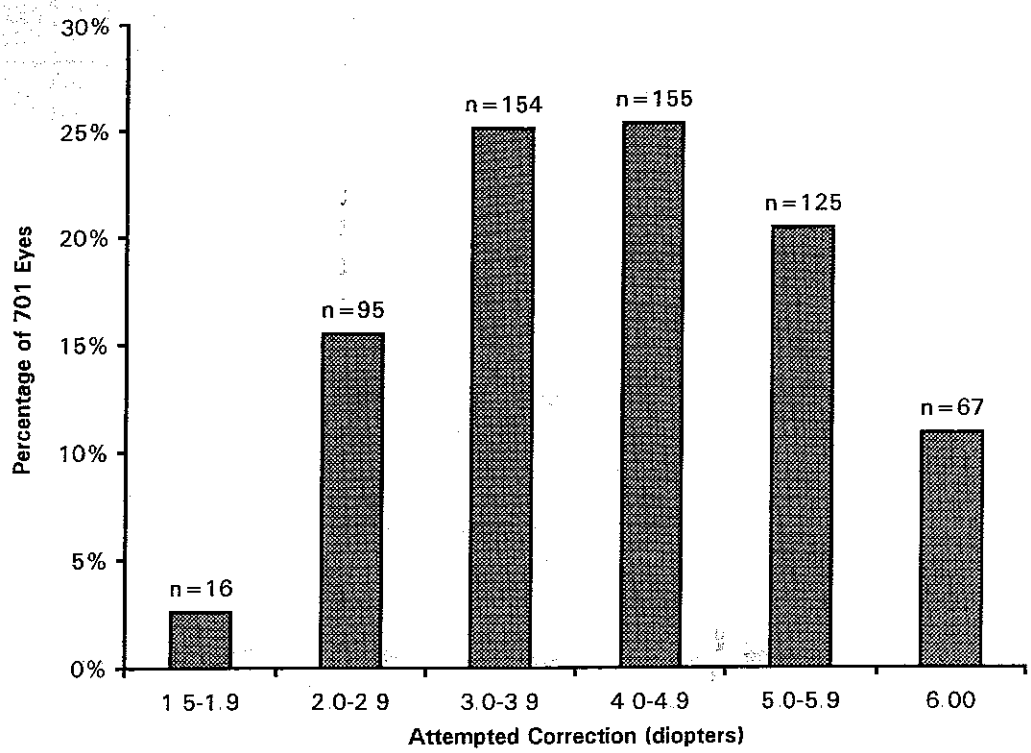


Figure 1. Attempted refractive correction stratified to 1.0-diopter subgroups.

1.02 D), at 6 months +0.35 D (SD, 1.03 D), at 1 year +0.06 D (SD, 1.02 D), and at 2 years −0.08 D (SD, 1.04 D).

Table 3 further quantifies the stability of postoperative refraction by comparing spherical equivalent refraction at different timepoints after PRK using definitions of stability of either 0.5 D or 1.0 D difference in manifest refraction spherical equivalent between follow-up visits. From the 6- to 12-month examinations, for instance, 66.8% of eyes were stable within 0.5 D and 86.8% were stable within 1.0 D.

Stability of refraction improved with time. Whereas 86.8% of eyes were stable within 1.0 D from the 6- to 12-month examination, 94% were stable from the 12- to 18-month examination, and 96.3% were similarly stable from the 18- to 24-month examination. There were more myopic than hyperopic changes early in the postoperative course; this decreased with time. There was no evidence of progressive or late myopic or hyperopic refractive shifts.

Astigmatism

There was little difference in the mean manifest refractive astigmatism or keratometric cylinder between the preoperative values and all postoperative measurements (Table 4). The distribution of refractive and keratometric astigmatism at baseline and at 2 years after surgery, as well as the change

Table 1. Predictability (Achieved − Attempted Correction) after Photorefractive Keratectomy: No. (%) of Eyes

Range	1 mo (n = 690)	3 mos (n = 664)	6 mos (n = 669)	1 yr (n = 599)	2 yrs (n = 612)
±0.50 D	106 (15.4)	216 (32.5)	318 (47.5)	313 (52.3)	336 (54.9)
±1.00 D	201 (29.1)	369 (55.6)	482 (72.1)	455 (76.0)	476 (77.8)
±1.50 D	293 (42.5)	488 (73.5)	556 (83.1)	520 (86.8)	548 (89.5)
±2.00 D	420 (60.9)	586 (88.3)	611 (91.3)	560 (93.5)	579 (94.6)
±3.00 D	612 (88.7)	647 (97.4)	654 (97.8)	585 (97.7)	600 (98.0)
±4.00 D	666 (96.5)	660 (99.4)	663 (99.1)	597 (99.7)	605 (98.9)
±5.00 D	685 (99.3)	664 (100.0)	669 (100.0)	599 (100.0)	610 (99.7)
±6.00 D	690 (100.0)	—	—	—	612 (100.0)
Overcorrected >1.0 D	483 (70.0)	269 (40.5)	158 (23.6)	96 (16.0)	75 (12.3)
Undercorrected >1.0 D	4 (0.6%)	17 (2.6)	27 (4.0)	47 (7.8)	61 (10.0)

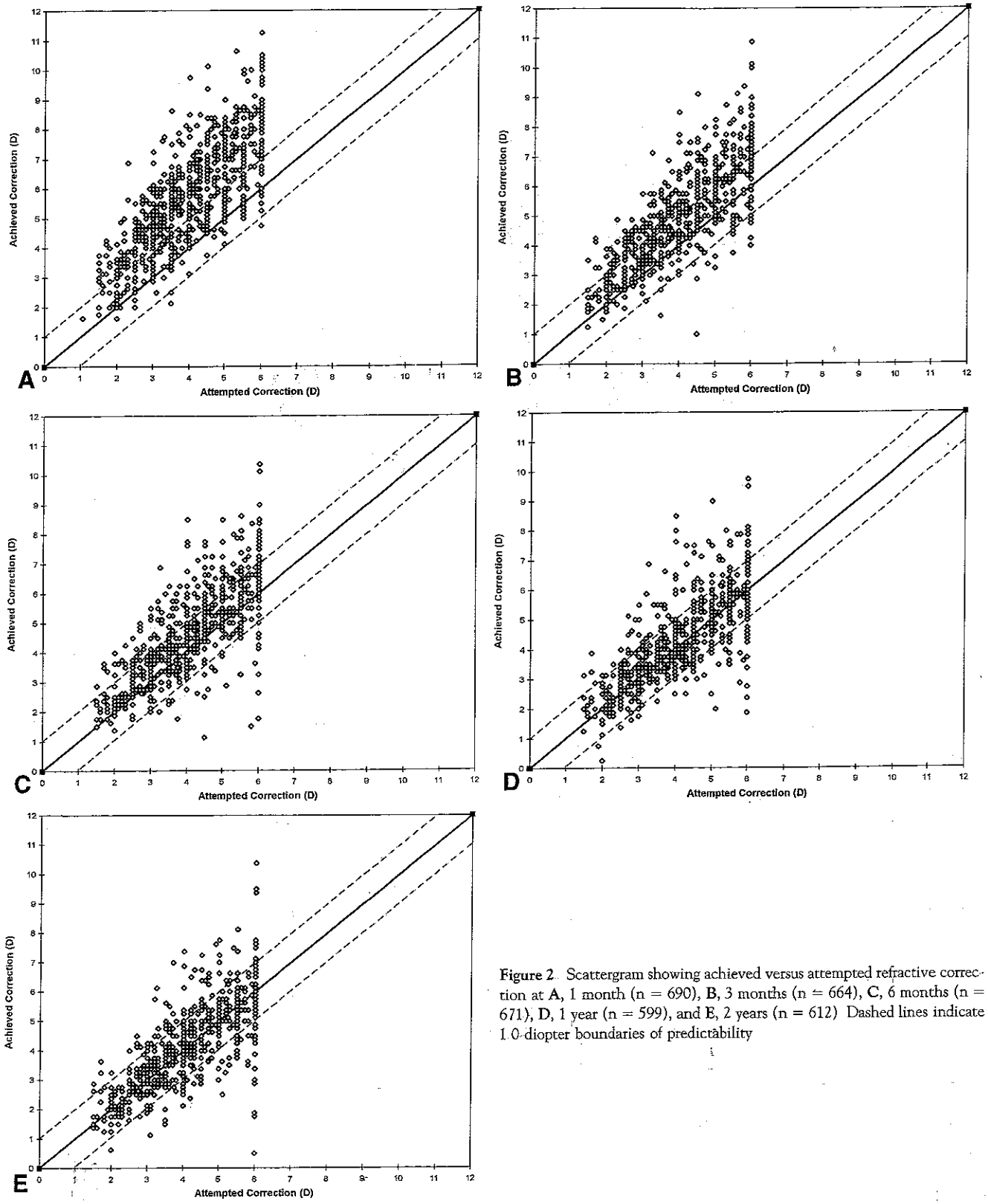


Figure 2 Scattergram showing achieved versus attempted refractive correction at **A**, 1 month (n = 690), **B**, 3 months (n = 664), **C**, 6 months (n = 671), **D**, 1 year (n = 599), and **E**, 2 years (n = 612) Dashed lines indicate 1.0-diopter boundaries of predictability

Table 2. Actual Refractive Outcome after Photorefractive Keratectomy: No. (%) of Eyes

Manifest Refraction Spherical Equivalent	1 mo (n = 690)	3 mos (n = 664)	6 mos (n = 669)	1 yr (n = 599)	2 yrs (n = 612)
+5.01 to +5.50	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
+4.51 to +5.00	5 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
+4.01 to +4.50	7 (1.0)	1 (0.2)	2 (0.3)	0 (0.0)	1 (0.2)
+3.51 to +4.00	16 (2.3)	3 (0.5)	1 (0.2)	2 (0.3)	0 (0.0)
+3.01 to +3.50	25 (3.6)	4 (0.6)	1 (0.2)	4 (0.7)	1 (0.2)
+2.51 to +3.00	81 (11.7)	20 (3.0)	11 (1.6)	6 (1.0)	4 (0.7)
+2.01 to +2.50	87 (12.6)	27 (4.1)	20 (3.0)	10 (1.7)	7 (1.1)
+1.51 to +2.00	130 (18.8)	68 (10.2)	35 (5.2)	21 (3.5)	14 (2.3)
+1.01 to +1.50	99 (14.4)	107 (16.1)	53 (7.9)	29 (4.8)	30 (4.9)
+0.51 to +1.00	88 (12.8)	128 (19.3)	123 (18.4)	58 (9.7)	59 (9.6)
+0.50 to −0.50	137 (19.9)	256 (38.6)	345 (51.6)	351 (58.5)	364 (59.4)
−0.51 to −1.00	9 (1.3)	29 (4.4)	44 (6.6)	57 (9.5)	62 (10.1)
−1.01 to −1.50	3 (0.4)	11 (1.7)	14 (2.1)	34 (5.7)	35 (5.7)
−1.51 to −2.00	1 (0.2)	5 (0.8)	9 (1.3)	13 (2.2)	15 (2.5)
−2.01 to −2.50	0 (0.0)	1 (0.2)	5 (0.8)	4 (0.7)	10 (1.6)
−2.51 to −3.00	0 (0.0)	2 (0.3)	1 (0.2)	6 (1.0)	3 (0.5)
−3.01 to −3.50	0 (0.0)	1 (0.2)	2 (0.3)	2 (0.3)	1 (0.2)
−3.51 to −4.00	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
−4.01 to −4.50	0 (0.0)	0 (0.0)	2 (0.3)	1 (0.2)	2 (0.3)
−4.51 to −5.00	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.5)
−5.01 to −6.00	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
−6.01 to −7.00	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

in astigmatism, is presented in Table 5. One hundred fifty-one eyes (24.3%) showed a decrease in refractive astigmatism of more than 0.25 D, 351 (56.6%) changed by 0.25 D or less, and 119 (19.1%) had an increase in refractive astigmatism of more than 0.25 D (Fig 4). One hundred thirty-seven eyes (22.2%) showed a decrease in keratometric astigmatism of more than 0.25 D, 311 (50.5%) changed by 0.25 D or less, and 168 (27.2%) had an increase in keratometric astigmatism of more than 0.25 D (Fig 4).

Uncorrected and Spectacle-corrected Visual Acuity

At 2 years after PRK, 407 (66.5%) of 612 eyes saw 20/20 or better uncorrected visual acuity and 564 (92.5%) saw 20/40 or better visual acuity (Table 6). There was little change in the cumulative percentage of eyes at 20/40 or better or 20/20 or better visual acuity after 6 months. Those eyes that underwent more than one procedure were less likely to have good postoperative uncorrected visual acuity. Whereas only 30 (5.4%) of the 552 eyes that underwent only 1 procedure achieved worse than 20/40 uncorrected visual acuity, 18 (30%) of the 60 eyes having more than 1 procedure were worse than 20/40 ($P < 0.0001$) visual acuity.

Before surgery, best spectacle-corrected visual acuity was 20/20 or better in 576 eyes (94.1%), 20/25 or better in 608 (99.3%), and 20/40 or better visual acuity in all eyes. At the 2-year examination (n = 611), 114 (18.7%)

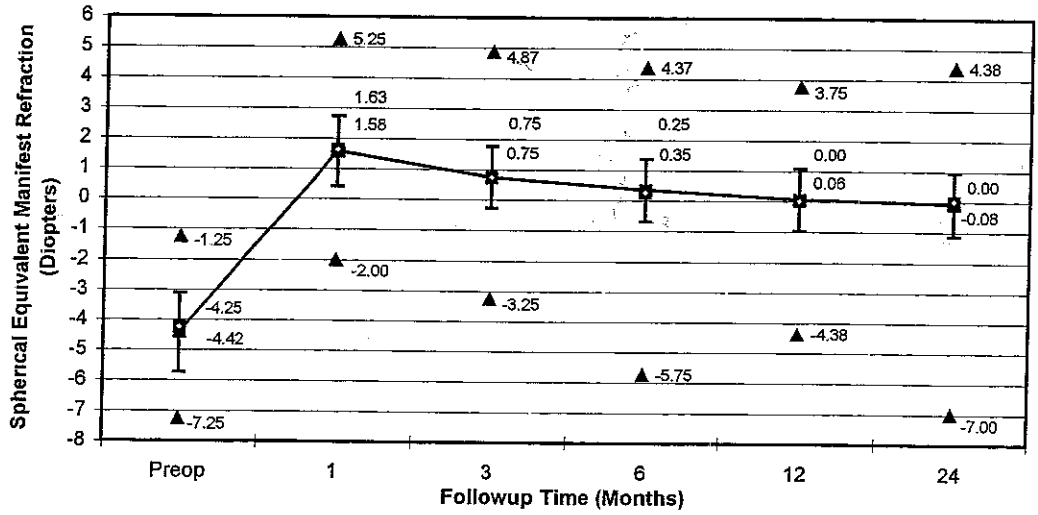


Figure 3. Change in refraction over time. Each black square (■) represents the mean spherical equivalent refraction, white diamonds (◇) within the black squares indicate the median refraction, vertical bars indicate the standard deviation, and black triangles (▲) indicate the range of refraction. For each timepoint, the actual values are noted from top to bottom = maximum, median, mean, and minimum spherical equivalent refraction.

Table 3. Stability of Refraction after Photorefractive Keratectomy between Examinations: No. (%)

Change	Time of Examinations		
	6–12 mos (n = 546)	*12–18 mos (n = 463)*	*18–24 mos (n = 463)*
Hyperopic shift > +0.5 D	36 (6.6)	39 (8.4)	37 (8.0)
Change ≤ 0.5 D	365 (66.8)	352 (76.0)	388 (83.8)
Myopic shift > −0.5 D	145 (26.6)	72 (15.6)	38 (8.2)
Hyperopic shift > +1.0 D	17 (3.1)	7 (1.5)	9 (1.9)
Change ≤ 1.0 D	474 (86.8)	435 (94.0)	446 (96.3)
Myopic shift > −1.0 D	55 (10.1)	21 (4.5)	8 (1.7)

eyes had gained 2 or more lines of spectacle-corrected visual acuity, whereas 42 (6.9%) had lost 2 or more Snellen lines (Table 7). Spectacle-corrected visual acuity was 20/20 or better in 587 (96.1%) eyes. Of the 42 eyes that lost 2 or more lines of spectacle-corrected visual acuity, 25 (59.5%) saw 20/20 or better, 32 (76.2%) saw 20/25 or better, 37 (88.1%) saw 20/32 or better, and 39 (92.9%) saw 20/40 or better (Fig 5).

Three eyes (0.5%) had spectacle-corrected visual acuity worse than 20/40. The first patient initially was undercorrected and underwent a repeat PRK 7 months after surgery, but myopia recurred with a spherical equivalent manifest refraction of −5.0 D at 2 years with moderate corneal haze, irregular astigmatism, and spectacle-corrected visual acuity of 20/80. After the 2-year examination, another PRK retreatment was performed, and at this patient's follow-up visit, spectacle-corrected visual acuity had improved to 20/16. The second patient had an epithelial abrasion during applanation tonometry at the 1-month examination and at 6 and 14 months had mechanical corneal scrapings to remove irregular epithelium. Spectacle-corrected visual acuity at 2 years was 20/200. At 26 months, an excimer laser phototherapeutic keratectomy procedure was performed to remove corneal haze, resulting in spectacle-corrected visual acuity of 20/32. The third patient had a macular cyst develop, which was not noted at the preoperative examination, with spectacle-corrected visual acuity of 20/80. The same condition was noted in the untreated fellow eye and, thus, probably was not related to PRK.

Epithelialization

Nine eyes (1.3%) had completely epithelialized by 24 hours, 112 (16%) between 24 and 36 hours, 177 (25.2%) between 37 and 48 hours, 336 (47.9%) between 49 and 72 hours, 49 (7%) between 73 and 96 hours, and 15 (2.1%) between 97 and 192 hours. There were no cases of persistent epithelial defects, recurrent epithelial erosions within the treatment zone, or sterile corneal ulceration. One patient underwent anterior stromal micropuncture for an epithelial defect that occurred outside of the treatment zone after the 1-year examination.

Intraocular Pressure

On preoperative examination, the average intraocular pressure (IOP) was 15.1 mmHg (range, 7–25 mmHg; SD, 2.8). At 1 month follow-up, the average IOP was 16.2 mmHg (range, 7–46 mmHg; SD, 4.2); at 3 months, the average IOP was 15.9 mmHg (range, 5–42; SD, 4.1); at 6 months, the average IOP was 14.7 (range, 6–38; SD, 3.1); at 1 year, the average IOP was 14 (range, 5–22; SD, 3); at 2 years, the average IOP was 14.2 (range, 6–24; SD, 2.8).

Corneal Haze

Generally, there was progressive clearing of the corneas during the 2 years after surgery (Table 8, Fig 6). At 2 years, 442 (72.2%) corneas were clear (0+), 138 (22.5%)

Table 4. Refractive and Keratometric Astigmatism after Photorefractive Keratectomy

Time (mos)	No. of Eyes	Refractive (D)			Keratometric (D)		
		Mean	*SD*	*Range*	*Mean*	*SD*	*Range*
Preoperative	701	0.44	0.38	0.0 to 1.75	0.71	0.50	0 to 3.75
1	691	0.45	0.51	0.0 to 3.0	0.86	0.67	0.0 to 6.0
3	664	0.40	0.47	0.0 to 2.75	0.82	0.65	0.0 to 6.9
6	669	0.42	0.48	0.0 to 3.0	0.80	0.61	0.0 to 6.0
12	600	0.43	0.46	0.0 to 2.5	0.81	0.81	0.0 to 10.4
24	612	0.42	0.45	0.0 to 3.0	0.77	0.57	0.0 to 2.0

Table 5. Net Change in Refractive and Keratometric Astigmatism 2 Years after Photorefractive Keratectomy: No. (%) of Eyes

Magnitude or Change* in Astigmatism (D)	Refractive			Keratometric		
	Baseline	*2 yrs*	*Change*	*Baseline*	*2 yrs*	*Change*
−1.76 to −2.25	NA	NA	0 (0.0)	NA	NA	1 (0.2)
−1.26 to −1.75	NA	NA	1 (0.2)	NA	NA	4 (0.6)
−0.76 to −1.25	NA	NA	27 (4.3)	NA	NA	19 (3.1)
−0.26 to −0.75	NA	NA	123 (19.8)	NA	NA	113 (18.3)
0.0 to 0.25 (change = −0.25 to 0.25)	262 (42.3)	326 (52.6)	351 (56.6)	160 (25.8)	173 (28.1)	311 (50.5)
0.26 to 0.75	267 (43.1)	182 (29.4)	94 (15.1)	243 (39.3)	190 (30.8)	124 (20.1)
0.76 to 1.25	84 (13.5)	96 (15.5)	23 (3.7)	149 (24.1)	160 (25.9)	30 (4.9)
1.26 to 1.75	7 (1.1)	15 (2.4)	2 (0.3)	54 (8.7)	61 (9.9)	7 (1.1)
1.76 to 2.25	0 (0.0)	1 (0.2)	0 (0.0)	11 (1.8)	26 (4.2)	5 (0.8)
2.26 to 2.75	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.0)	2 (0.3)
2.76 to 3.25	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
3.26 to 3.75	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

NA = not applicable

* Negative numbers indicate decrease in magnitude of astigmatism; positive numbers indicate increase in magnitude of astigmatism.

showed trace haze (1+), 20 (3.3%) showed mild haze (2+), 9 (1.5%) showed a moderate haze (3+), and 3 (0.5%) showed a marked haze (4+).

Five hundred ninety-two eyes had both 6- and 12-month haze data available. One hundred seventy-four (29.4%) eyes showed an improvement in haze grade from the 6- to the 12-month examination; 2 eyes (0.3%) improved by 3 grades and 14 eyes (2.4%) improved by 2 grades. There was no change in 352 eyes (59.4%). Sixty-six eyes (11.1%) showed worsening of haze; 2 eyes (0.3%) worsened by 3 grades (both from clear to moderate) and 3 eyes (0.5%) worsened by 2 grades (Fig 7A). Similarly, 557 eyes (94.1%) had both 1- and 2-year haze data available. One hundred twenty (21.5%) of eyes showed an improvement in haze grade from the 1-year to 2-year examinations; 2 eyes (0.4%) improved by 3 grade steps and 21 (3.8%) improved by 2 grades. There was no change in 377 eyes (67.7%). Sixty eyes (10.8%) showed worsening of haze; during this period, no eyes worsened by 3 grades and 2 eyes (0.4%) worsened by 2 grades (Fig 7B).

Contrast Sensitivity

At the 1-, 3-, 6-, 12-, and 24-month postoperative examinations with the pupil undilated, the log mean contrast sensitivity for all spatial frequencies was within 1 SD of the preoperative baseline. Changes of such magnitude are not considered to have a clinically significant effect.[25] The greatest loss was 0.26 log unit, which occurred at 18 cyc/deg at the 1-month postoperative examination. At the 1-month examination, the change in log mean contrast sensitivity was −0.10, −0.17, −0.26, and −0.21 at 3, 6, 12, and 18 cyc/deg, respectively; at the 6-month examination, the change was −0.05, −0.13, −0.18, and −0.14 at 3, 6, 12, and 18 cyc/deg; at the 1-year examination, the change was −0.06, −0.11, −0.14, and −0.11 at 3, 6, 12, and 18 cyc/deg; at the 2-year examination, the change in log mean contrast sensitivity was −0.07, −0.14, −0.17, and −0.15 at 3, 6, 12, and 18 cyc/deg, respectively.

For eyes with the pupil dilated, the log mean contrast sensitivity for all spatial frequencies at 6, 12, and 24 months was similarly within 1 SD of the preoperative baseline. At the 6-month examination, the change in log mean contrast sensitivity was −0.07, −0.12, −0.15, and −0.12 at 3, 6, 12 and 18 cyc/deg, respectively; at the 2-year examination, the change was −0.12, −0.17, −0.20, and −0.18, at 3, 6, 12, and 18 cyc/deg, respectively. The greatest loss was 0.18 log unit, which occurred at 12 cyc/deg at the 2-year examination. These differences represent less than two contrast steps on the Vector Vision chart.

Glare and Halo Index

Before surgery, the glare index (reported on a scale of 0–5 where 0 represented no glare and 5 represented the worst glare) averaged 1.46 for patients wearing glasses (n = 627) and 1.51 for patients wearing contact lenses (n = 438). After surgery, the glare index averaged 1.27 at 6 months (n = 652), 1.24 at 1 year (n = 585), and 1.29 at 2 years (n = 603) (Table 9). The halo index also was reported on a scale of 0 to 5. Before surgery, the halo index averaged 1.00 for patients wearing glasses (n = 627) and 1.43 for patients wearing contact lenses (n = 438). After surgery, halo averaged 1.87 at 6 months (n = 652), 1.64 at 1 year (n = 585), and 1.53 at 2 years (n = 603) (Table 10).

Two hundred ninety-two eyes had both preoperative and 2-year survey information on glare. One hundred eleven (38.1%) patients reported less glare, 94 (32.2%) reported no change, and 87 (29.7%) reported worsening of glare from before surgery (Fig 8A). Two hundred sixty-

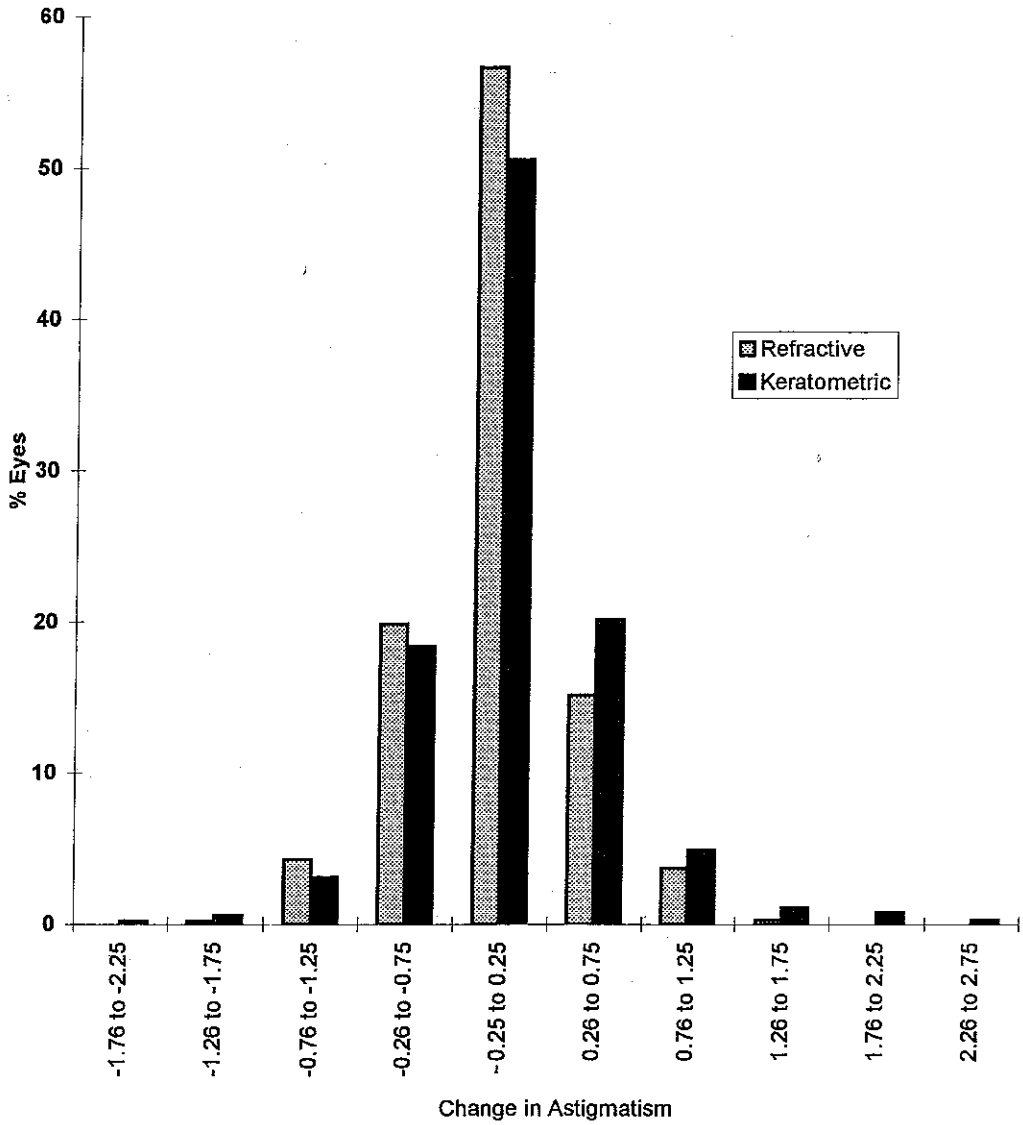


Figure 4. Change in refractive (gray columns) and keratometric (black columns) astigmatism 2 years after photorefractive keratectomy. Negative numbers indicate decreased astigmatism, and positive numbers indicate increased astigmatism

five eyes had both preoperative and 2-year examination information on halo. Sixty-three (23.7%) patients reported less halo, 69 (26%) reported no change, and 133 (50.1%) reported worsening of halo (Fig 8B).

Videokeratography

Analysis of videokeratography on a subset of 200 eyes of 200 patients in this study have been published previously. The mean decentration of the treatment zone from center of the entrance pupil of 0.46 mm (range, 0.00–1.44 mm).[20] Distinct qualitative patterns of corneal topography also were identified and the effect on clinical outcomes have been described previously.[18]

Adverse Reactions

No unanticipated adverse reactions such as microbial keratitis, endophalmitis, corneal melting or perforation, corneal decompensation, hyphema, hypopyon, cataract, or retinal lesions were found in this study.

Postoperative Pain

In the postoperative patient survey, immediate postoperative pain was rated from 0 to 5 where 5 represented the most severe pain. The mean pain score for the first 24 hours after PRK was 2.99 (SD, 0.47). Of 652 patients completing the questionnaire, 63 (9.7%) patients rated pain as 0, 63 (9.7%) as 1, 81 (12.4%) as 2, 125 (19.2%) as 3, 139 (21.3%) as 4, and 159 (24.3%) as 5. Twenty-two (3.4%) did not respond to the questionnaire.

Patient Subjective Satisfaction

At the 2-year follow-up examination, patient satisfaction with the procedure was reported subjectively from grade 0 (very dissatisfied) to 5 (very satisfied); it averaged 4.03.

Table 6. Uncorrected Visual Acuity (UCVA) after Photorefractive Keratectomy: No. (%) of Eyes*

UCVA	Preoperative (n = 701)	1 mo (n = 691)	3 mos (n = 664)	6 mos (n = 669)	1 yr (n = 600)	2 yrs (n = 612)
20/10	0 (0.0)	2 (0.3)	12 (1.8)	12 (1.8)	14 (2.3)	13 (2.1)
20/12.5	0 (0.0)	11 (1.9)	50 (9.3)	73 (12.7)	68 (13.7)	56 (11.3)
20/16	0 (0.0)	56 (10.0)	107 (25.5)	129 (32.0)	132 (35.7)	141 (34.3)
20/20	0 (0.0)	126 (28.2)	196 (55.0)	199 (61.7)	187 (66.8)	197 (66.5)
20/25	0 (0.0)	105 (43.4)	97 (69.6)	106 (77.6)	71 (78.7)	88 (80.9)
20/32	0 (0.0)	97 (57.5)	69 (80.0)	65 (87.3)	40 (85.3)	38 (87.1)
20/40	1 (0.1)	70 (67.6)	52 (87.8)	32 (92.1)	35 (91.2)	31 (92.2)
20/50	1 (0.3)	69 (77.6)	28 (92.0)	15 (94.3)	19 (94.3)	14 (94.4)
20/62.5	9 (1.6)	52 (85.1)	17 (94.6)	10 (95.8)	10 (96.0)	9 (95.9)
20/80	17 (4.0)	54 (92.9)	16 (97.0)	14 (97.9)	7 (97.1)	7 (97.1)
20/100	29 (8.1)	23 (96.2)	15 (99.2)	7 (99.0)	7 (98.3)	4 (97.7)
20/125	26 (11.8)	6 (97.1)	1 (99.4)	1 (99.1)	3 (98.8)	3 (98.2)
20/160	50 (19.0)	6 (98.0)	1 (99.5)	1 (99.3)	1 (99.0)	1 (98.4)
20/200	166 (42.7)	13 (99.9)	3 (100.0)	4 (99.7)	3 (99.5)	7 (99.5)
20/400	215 (73.3)	0 (0.0)	0 (0.0)	1 (100.0)	2 (99.2)	0 (99.5)
<20/400	187 (26.7)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)	3 (4.9)

* Cumulative percentage

More than half (53.8%) of the patients reported a satisfaction level of 5, whereas 23 (3.8%) reported a satisfaction grade of 0 (Table 11).

Discussion

Study Design

There have been a number of well-designed published studies reporting the results of excimer laser PRK.[22,26–33] This report has the advantages of a prospective, multicenter design with rigorous control of case selection, examination methodologies, surgical technique, postoperative care, and patient follow-up. Although procedures in this study used a 4.5- or 5-mm treatment zone, the PRK procedure now approved in the United States uses a 6-mm beam diameter. Furthermore, the postoperative regimen in this study was restricted to patching with topical antibiotic and corticosteroid; neither topical nonsteroidal antiinflammatory agents nor bandage soft contact lenses were used.

This report presents the essential outcomes of this phase III study with attention to stability of refraction over a 2-year follow-up period. Further in-depth analyses of this patient cohort include a multivariate statistical analysis of preoperative and procedure characteristics influencing clinical outcomes,[24] effects on the corneal endothelium,[34] corneal topography,[18] and treatment zone centration,[20] and are published elsewhere.

Table 7. Change in Spectacle-corrected Visual Acuity after Photorefractive Keratectomy (PRK): No. (%) of Eyes

Change in Snellen Lines	Time after PRK: 6 mos (n = 665)	1 yr (n = 599)	2 yrs (n = 611)
−12	0 (0.0)	0 (0.0)	1 (0.2)
−6	0 (0.0)	1 (0.2)	2 (0.3)
−5	1 (0.2)	0 (0.0)	1 (0.2)
−4	1 (0.2)	1 (0.2)	0 (0.0)
−3	2 (0.3)	3 (0.5)	6 (1.0)
−2	16 (2.4)	12 (2.0)	32 (5.2)
±1	537 (80.6)	473 (78.8)	455 (74.4)
+2	84 (12.6)	80 (13.4)	77 (12.6)
+3	23 (3.5)	26 (4.3)	36 (5.9)
+4	1 (0.2)	2 (0.3)	0 (0.0)
+5	0 (0.0)	1 (0.2)	1 (0.2)

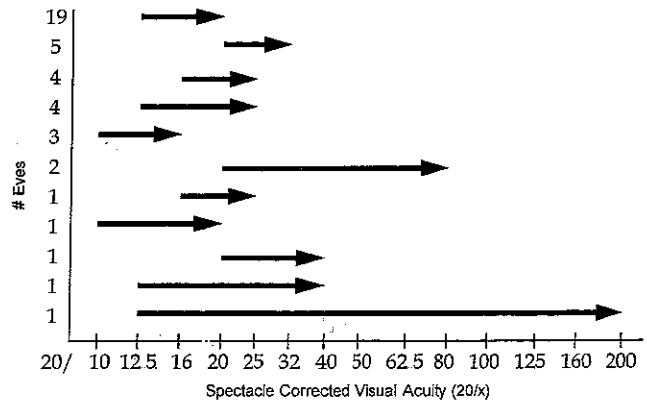


Figure 5. Change in spectacle-corrected visual acuity for eyes losing 2 or more Snellen lines at 2 years

Table 8. Anterior Stromal Haze after Photorefractive Keratectomy (PRK): No. (%) of Eyes

	Time after PRK				
Haze Grade	*1 mo* (*n* = 691)	*3 mos* (*n* = 664)	*6 mos* (*n* = 669)	*1 yr* (*n* = 600)	*2 yrs* (*n* = 612)
Clear	115 (16.6)	170 (25.6)	307 (45.8)	373 (62.1)	442 (72.2)
Trace	411 (59.5)	393 (59.1)	276 (41.3)	163 (27.2)	138 (22.5)
Mild	148 (21.4)	81 (12.2)	62 (9.3)	40 (6.7)	20 (3.3)
Moderate	15 (2.2)	17 (2.6)	24 (3.6)	24 (4.0)	9 (1.5)
Marked	2 (0.3)	3 (0.5)	0 (0.0)	0 (0.0)	3 (0.5)

Efficacy of Photorefractive Keratectomy

The goal of any refractive surgery procedure is to decrease the patient's dependency on glasses and contact lenses for a variety of life's activities by improving uncorrected visual acuity and general visual function. In addition, the accuracy and predictability of the procedure, as well as its stability over time, are important outcomes that show a procedure's efficacy. Whether the outcome is a "success," however, depends on the patient's subjective needs and expectations. A person with 6.0 D of myopia who enjoys swimming may be quite pleased with a residual refractive error of 1.0 D and 20/40 uncorrected visual acuity; an accountant with 3.0 D of myopia may be displeased with a +1.0 D outcome and 20/30 distance acuity, but diminished near-point function. Thus, in practice, patients need to be assessed on an individual basis. Population statistics, however, are invaluable to guide patient education and the informed consent procedure as well as to elucidate the efficacy of the procedure in general.

Uncorrected Visual Acuity. Approximately two thirds of eyes achieved 20/20 or better uncorrected visual acuity after surgery; approximately 80% were 20/25 or better visual acuity and more than 90% were 20/40 or better visual acuity. Previously published data on this patient cohort[24] have shown postoperative uncorrected visual acuity to be associated independently with attempted correction as well as patient age.

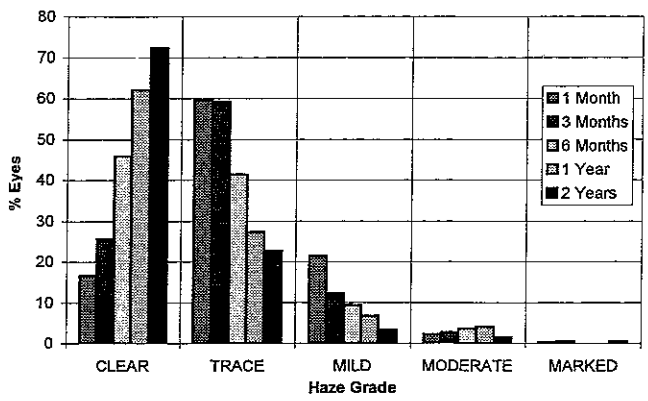


Figure 6. Corneal stromal haze grade (scale = 0–5) at different timepoints after photorefractive keratectomy

Predictability and Stability. Both for patient care and in evaluation of new refractive surgery technologies, it is necessary to know when the "final result" is attained. Uncorrected visual acuity was maximized in most eyes by 3 months and remained stable thereafter, although some patients did require between 6 months and 1 year to attain their best postoperative uncorrected visual acuity (Table 6). Thereafter, uncorrected visual acuity remained stable, with the proportion of patients with either 20/20 or better or 20/40 or better uncorrected visual acuity remaining consistent at 1 and 2 years.

Looking at predictability and stability of refractive result, PRK in this study using a 4.5- or 5-mm ablation zone generally was associated with early overcorrection and subsequent regression and stabilization of the refractive effect. Whereas there was a mean regression of 0.83 D from 1 to 3 months, the mean regression from 3 to 6 months was 0.40 D, from 6 months to 1 year was 0.29 D, and from 1 year to 2 years, the mean regression was 0.14 D (Fig 3). Furthermore, there were more overcorrections than undercorrections through 1 year (Table 1) but a mitigating tendency toward myopic shifts through 18 months (Table 3). From 18 to 24 months, stability further improved with a decrease in the proportion of myopic shifts, and there remained a small, but now equivalent, likelihood of myopic and hyperopic changes. The actual refractive outcome (Table 2) was stable from the 1-year examination and afterward.

Viewing these data in toto, it can be concluded that stability of refraction after PRK in this study continually improves with time and that, in general, the ultimate refractive outcome is achieved between 1 and 2 years. There is no evidence of progressive or late myopic or hyperopic shifts. This finding is corroborated by the work of Epstein et al[35] who similarly showed refractive stability after 18 months in 495 eyes treated with ablation zones of 4.3 or 4.5 mm. Depending on refractive stability of an individual eye, the appropriate timing of fellow eye treatment may vary; the surgeon should wait until the first eye is stable before proceeding with fellow eye treatment. In a previously published multivariate analysis of this same patient cohort,[24] we found an independent association of stability of refraction with attempted correction; that is, eyes with higher attempted corrections, in general, take longer to stabilize. Thus, the interval between first and second eye treatments may need to be relatively longer for patients with higher degrees of myopia.

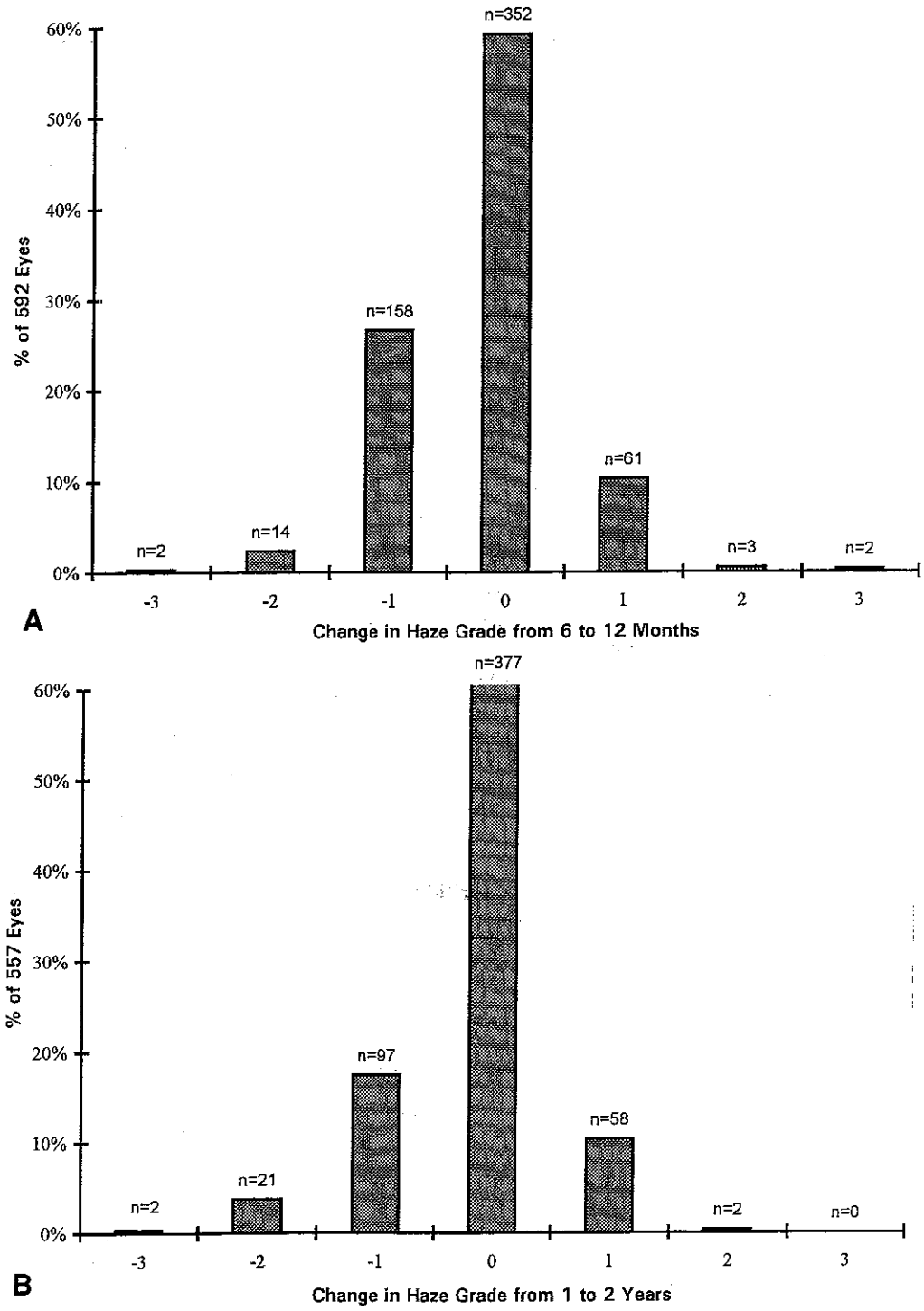


Figure 7. A, change in haze grade (scale = 0–5) from the 6- to 12-month examination. Positive numbers indicate worsening of haze by that number of units on the scale. B, change in haze grade from the 1- to 2-year examination.

The general trend of early overcorrection followed by progressively diminishing regression probably is secondary to wound remodeling. Both epithelial and stromal wound healing likely participate, with epithelial hyperplasia and the deposition of new collagen and glycosaminoglycans filling in the ablated area of stroma.[12] As suggested by other investigators, overcorrections may result from the lack of this typical healing and undercorrections from healing, which is more aggressive than expected.[36] Indeed, undercorrections often are associated with corneal haze.[36–38]

Unlike some reports of radial keratotomy, there does not appear to be a progressive hyperopic or myopic shift in PRK. This may be a result of the nature of the corneal wound. In radial keratotomy, collagen lamellae are incised with the subsequent production of contractile myo-

Table 9. Subjective Glare* after Photorefractive Keratectomy (PRK): No. (%) of Eyes

Glare Grade	Preoperative (with glasses) (n = 627)	Preoperative (with contact lens) (n = 438)	Time after PRK		
			6 mos (n = 652)	*1 yr (n = 585)*	*2 yrs (n = 603)*
0	156 (24.9)	121 (27.8)	235 (36.1)	191 (32.6)	209 (34.6)
1	120 (19.1)	76 (17.4)	161 (24.7)	170 (29.1)	178 (29.5)
2	86 (13.7)	60 (13.7)	85 (13.0)	79 (13.5)	77 (12.8)
3	90 (14.4)	65 (14.8)	74 (11.3)	63 (10.8)	58 (9.6)
4	58 (9.3)	43 (9.8)	48 (7.4)	34 (5.8)	41 (6.8)
5	24 (3.8)	20 (4.6)	17 (2.6)	14 (2.4)	21 (3.5)
No response	93 (14.8)	53 (12.1)	32 (4.9)	34 (5.8)	19 (3.2)

* Response to one question on subjective patient questionnaire with analog scale of 0 (none) to 5 (severe).

fibroblasts and lengthy wound remodeling, leading in some cases either to progressive contracture or relaxation of the wound with consequent refractive shifts.[39] Wound remodeling in PRK, in contrast, may exert diminishing effects with time and fewer late changes on the corneal curvature since the refractive change of PRK is mediated by a direct effect on corneal curvature rather than by biomechanical manipulation as in RK. Given this hypothesis of postoperative healing and the results of this study over 2 years, it is reasonable to speculate that changes in refraction after PRK generally will not occur after the eye initially has stabilized

Safety of Photorefractive Keratectomy

Although major adverse sequelae will be of obvious importance, more subtle side effects must be considered after any refractive surgical procedure. Thus, as in the evaluation of efficacy of PRK, an assessment of safety may be dependent on individual patient needs and expectations. Whereas a professional truckdriver may be troubled by any night-time glare or halo symptoms or an airplane pilot may not tolerate the least decrease in distance visual function, many patients likely will find side effects from the procedure tolerable given their improvement in uncorrected vision. Possible risks, therefore, must be discussed carefully with the individual patient and safety issues assessed accordingly.

General Complications. Epithelialization was complete by 4 days in most eyes, and there was no incidence of persistent epithelial defect, recurrent epithelial dysadhesion within the treatment zone, sterile stromal ulceration, or corneal infection. One patient underwent anterior stromal micropuncture for an epithelial defect, which occurred outside of the treatment zone. No sterile corneal infiltrates, as have been reported in patients treated after surgery with topical nonsteroidal anti-inflammatory drugs and bandage soft contact lenses,[40] were seen. Ocular pain for 1 to 3 days after surgery was moderate to severe in many patients; all received only topical corticosteroids and antibiotics. Patient discomfort has been reported to be significantly ameliorated with the use of nonsteroidal anti-inflammatory drugs and bandage contact lenses after PRK.[41]

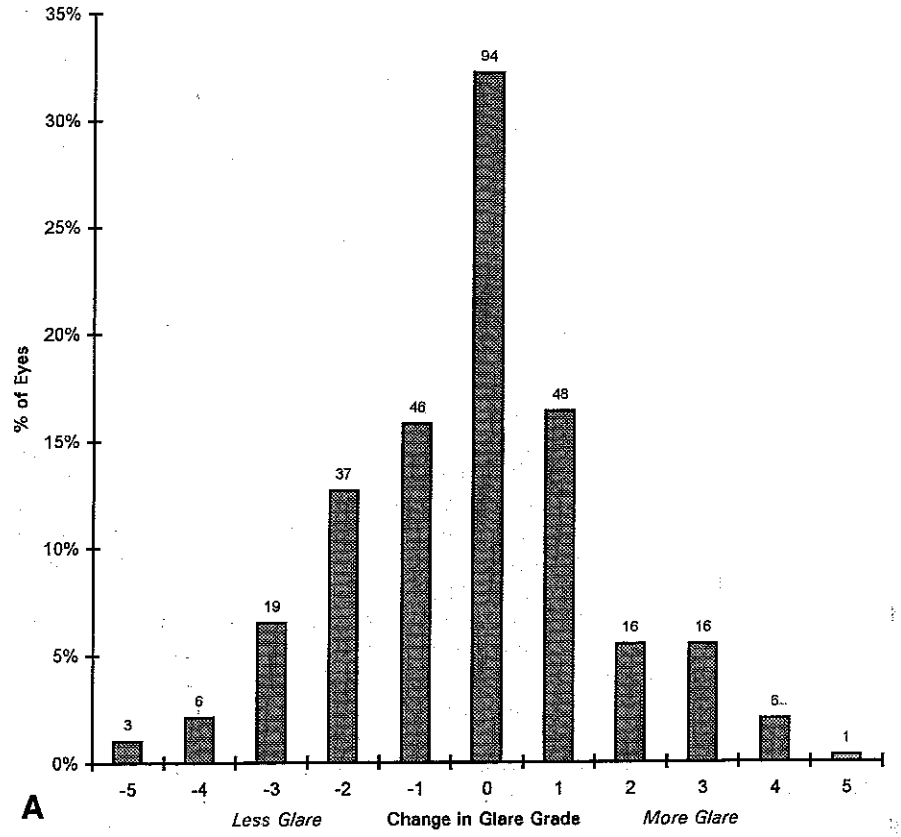
Transient increase in IOP may be of concern in some patients, especially those at risk of optic nerve damage.[42] At months 1, 3, and 6 after surgery, the maximum IOP seen was 46, 42, and 38 mmHg, respectively. Such increases, likely, result from corticosteroid effects and decrease on cessation of steroid; maximum IOP was 22 and 24 mmHg at 1 and 2 years after surgery, respectively.

Anterior stromal haze was seen in most patients during

Table 10. Subjective Halo* after Photorefractive Keratectomy (PRK): No. (%) of Eyes

Halo Grade	Preoperative (with glasses) (n = 627)	Preoperative (with contact lens) (n = 438)	Time after PRK		
			6 mos (n = 652)	*1 yr (n = 585)*	*2 yrs (n = 603)*
0	219 (35.0)	115 (26.3)	159 (24.4)	152 (26.0)	177 (29.4)
1	117 (18.7)	90 (20.6)	129 (19.8)	137 (23.4)	158 (26.2)
2	66 (10.5)	58 (13.2)	98 (15.0)	93 (15.9)	94 (15.6)
3	54 (8.6)	65 (14.8)	109 (16.7)	90 (15.4)	66 (10.9)
4	36 (5.7)	39 (8.9)	90 (13.8)	54 (9.2)	50 (8.3)
5	15 (2.4)	14 (3.2)	41 (6.3)	30 (5.1)	36 (6.0)
No response	120 (19.1)	57 (13.0)	26 (4.0)	29 (5.0)	22 (3.6)

* Response to one question on subjective patient questionnaire with analog scale of 0 (none) to 5 (severe).



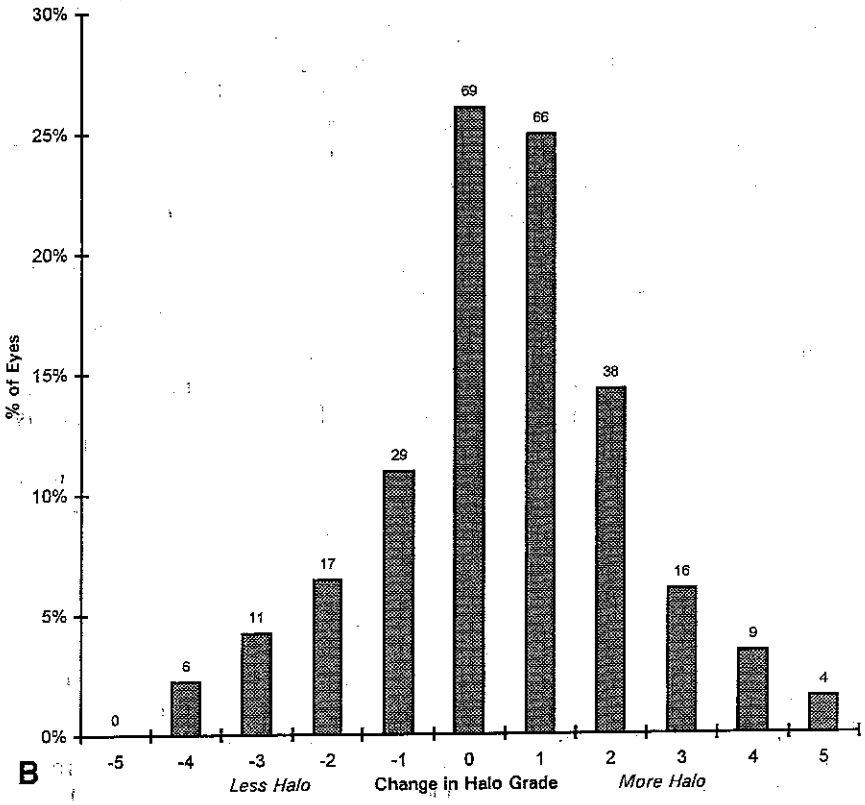


Figure 8. A, change in glare symptoms from preoperative to 2 years after photorefractive keratectomy taken from a subjective scale of 0 to 5. Negative numbers indicate a decrease in severity of the symptom from the preoperative value by that number of units on the scale and positive numbers indicate an increase in glare from the preoperative value. Numbers over columns indicate number of eyes. B, change in halo symptoms after photorefractive keratectomy.

Table 11. Subjective Patient Satisfaction* after Photorefractive Keratectomy (PRK): No. (%) of Eyes

Satisfaction Grade	Time after PRK		
	6 mos (n = 652)	1 yr (n = 585)	2 yrs (n = 603)
0	21 (3.2)	20 (3.4)	23 (3.8)
1	21 (3.2)	22 (3.8)	24 (4.0)
2	37 (5.7)	31 (5.3)	23 (3.8)
3	89 (13.7)	61 (10.4)	53 (8.8)
4	182 (27.9)	144 (24.6)	145 (24.0)
5	288 (44.1)	298 (51.0)	324 (53.8)
No response	14 (2.2)	9 (1.5)	11 (1.8)

* Response to one question on subjective patient questionnaire with analog scale of 0 (very dissatisfied) to 5 (very satisfied).

the early postoperative months after PRK and is likely associated with normal corneal wound healing as discussed above. The incidence and severity of corneal stromal haze, in general, diminished with time and reduced final visual acuity to below 20/40 in only two eyes. Two additional eyes showed an increase in haze from a grade of 0+ to 3+ from 6 to 12 months; no eyes showed such an increase in subepithelial haze after the 1-year examination (Fig 7). Although rare, this finding suggests that patients should be followed after corticosteroids are discontinued to detect a late increase in haze.[37,43] There also have been reports of focal subepithelial scarring causing localized topographic abnormalities associated with visual loss.[37,38] Such scars may be amenable to superficial keratectomy and more vigorous topical corticosteroid treatment during the healing period.[44–46]

In general, there was little change in both refractive and keratometric astigmatism 2 years after the procedure. However, approximately 5% of patients did show an improvement of astigmatism of 0.75 D or more, whereas a similar number showed worsening of 0.75 D or more. The worst change in magnitude of refractive astigmatism was 1.75 D; the worst change in keratometric astigmatism was 2.75 D. Changes in the overall corneal topography in a subgroup of the patients in this study have been published previously.[18]

Spectacle-corrected Visual Acuity. Spectacle-corrected visual acuity is one general indicator of a variety of changes in visual function after PRK. Spectacle-corrected visual acuity would be expected to increase slightly after any refractive surgery procedure because of image magnification inherent in correcting myopia at the corneal rather than spectacle plane.[47] Indeed, 18.2% and 18.7% of eyes gained two or more lines of visual acuity at 1 and 2 years, respectively. Although most eyes showed no change, 6.9% had lost two or more lines of spectacle-corrected visual acuity at 2 years. Of these eyes, a majority had better than 20/20 spectacle-corrected visual acuity before surgery and, in most cases, a decrease in spectacle-corrected visual acuity still left the patient with good visual acuity. In fact, only two eyes (0.3%) had both a spectacle-corrected visual acuity decrease of two lines or more and worse than 20/40 visual acuity as a result of the procedure. It is curious that the proportion of eyes losing two or more Snellen lines of spectacle-corrected visual acuity was greater at the 2-year examination than at 6 and 12 months. The reason for this finding is unclear; measurement error is a possible cause. Indeed, 548 patients subsequently were examined at 29 to 42 months to specifically analyze long-term changes in spectacle-corrected visual acuity; at this last follow-up examination, only 21 eyes (3.8%) had lost 2 or more lines of spectacle-corrected acuity, a proportion more in concordance with the 6- and 12-month values.

Loss of spectacle-corrected visual acuity after PRK could result from loss of corneal clarity and consequent light scatter[48] as well as from a variety of optical aberrations. Corneal haze is the etiology most easily diagnosed clinically; as noted, those two patients losing spectacle-corrected visual acuity to below 20/40 did so secondary to corneal scarring. It is more difficult to identify optical aberrations caused by change in corneal contour after PRK. General changes in corneal topography pattern,[18] decentration of the treatment zone,[20,49,50] surface irregularities and edge effects,[51,52] and changes in corneal asphericity[53,54] can all produce optical aberrations with reduced spectacle-corrected visual acuity in some patients.

Optical Side Effects. Glare and halo are side effects frequently reported by patients after PRK. Although there was little difference in the proportion of patients noticing glare and halo before and after PRK, individuals reported changes and a few patients improved or worsened substantially (Fig 8). For instance, nine patients (3.1%) reported a decrease in glare of 4 or 5 units on the 0 to 5 scale, whereas seven patients (2.4%) reported an increase in glare of 4 or 5 units. A similar finding was found for halo in which 6 patients (2.3%) reported a decrease of 4 or 5 units, whereas 13 patients (4.9%) noted an increase in halo of 4 or 5 units. It is thus important to apprise patients of the risks of postoperative glare and halo during informed consent.

Glare and halo may be caused by corneal haze and by a variety of changes in corneal contour, including edge effects and topographic irregularities in the treatment zone. Such optical side effects usually are worse when the pupil is larger than the edge of the functional optical zone and when the pinhole effect is least, most commonly at night.[50,55,56] It has been suggested that glare, halo, and other optical aberrations might be diminished using a larger ablation zone because this would place the edge of the zone outside most pupils.[57,58] At the 2-year examination in this study, the mean glare–halo index (index = maximum value of either glare or halo; scale = 0 to 5) was 1.89; the mean glare–halo index was 2.05 for the 4.5-mm treatment zone group and 1.79 for the 5-mm group, a difference that was found not to be statistically significant.[18] In a recent study using the Summit laser and a 6-mm optical zone, a mean glare–halo index of 1.33 was found.[59] Although these two studies are not directly comparable, the findings do suggest a diminution of such

optical symptoms with the larger treatment zone. This conclusion has been supported by other investigations.[49,57,60,61]

Comparison to Other Studies

As part of the phase IIB study of the Summit Technology ExciMed UV200LA excimer laser, Waring et al[16] reported the results of a prospective series of 100 patients. This investigation immediately preceded the phase III study reported herein as part of the U.S. Food and Drug Administration regulatory process for premarket approval of the laser for PRK. An ablation zone of 4.5 mm was used in all cases. In the 80 patients followed for 1 year, 36 (46%) achieved 20/20 or better uncorrected visual acuity and 61 (77%) achieved 20/40 or better visual acuity. Forty-two (53%), 60 (75%), and 74 (93%) of eyes were within 0.5 D, 1.0 D, and 2.0 D of attempted correction, respectively. Twelve percent of eyes lost two or more Snellen lines of spectacle-corrected vision. Improved outcomes, thus, are evident comparing the phase III and phase IIB results.

Two recent single-center, prospective studies report recent results of the Summit Technology OmniMed excimer laser using a 6-mm ablation zone. Schallhorn et al[62] reported 1-year results on 30 active-duty U.S. Navy personnel. Preoperative myopia ranged from −2.0 to −5.5 D. All eyes had an uncorrected visual acuity of 20/20 or better and 93% fell within 1.0 D of attempted correction. The excellent uncorrected vision in this study may, in part, have been a consequence of the relatively low degree of myopia in the patients treated and a preponderance of overcorrected versus undercorrected eyes in this relatively young, prepresbyopic patient cohort. Shah and Hersh[60] reported on 45 consecutive patients treated with the 6-minute ablation zone. Of these, 28 (62%) were 20/20 or better and 45 (100%) were 20/40 or better at the 6-month follow-up. Thirty-eight (84%) and 44 (98%) were within 0.5 D and 1.0 D of attempted correction, respectively. These studies, although of only a relatively small number of patients, suggest continuing improvement in clinical outcomes of PRK using this laser system.

The investigation reported herein shows that excimer laser PRK is an effective procedure for the treatment of mild-to-moderate myopia. Refraction after PRK stabilizes progressively and stability is achieved in most eyes between 1 and 2 years without evidence of progressive or late myopic or hyperopic refractive shifts. Corneal haze generally is present in the early postoperative period and subsides with time. Optical sequelae of glare and halo may occur in some patients. Further understanding of corneal optics, wound healing, the effects of ablation contour, and individual patient variation may produce even better outcomes of PRK in the future.

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