USE OF THE 193-NM EXCIMER LASER FOR MYOPIC PHOTOREFRACTIVE KERATECTOMY IN SIGHTED EYES: A MULTICENTER STUDY*

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INTRODUCTION

THE USE OF THE 193-NM EXCIMER LASER FOR BOTH REFRACTIVE AND therapeutic purposes was first suggested by Trokel and associates[1] and Taylor and associates.[2] Early studies described the use of the excimer laser in animal models,[3-5] in blind and partially sighted eyes,[6,7] and more recently in fully sighted eyes.[8] We have reported our initial results at 6

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months in six sighted patients who underwent myopic excimer photorefractive keratectomy (PRK).[9] We report herein the results of a multicenter study of PRK in myopic eyes using the Taunton Technologies excimer laser.

METHODS

PATIENT SELECTION

Patients were selected according to guidelines from the US Food and Drug Administration (FDA)[10] under an Investigational Device Exemption and with Institutional Review Board oversight for these phase II and phase IIA studies. Informed consent was obtained from each patient after extensive discussion. Because of anisometropia occurring after excimer PRK, the ability to successfully wear a contact lens in the fellow eye was required for patients with high myopia.

Patients under 18 years of age or with abnormal corneas, severe dry eyes, blepharitis, and/or lagophthalmos were excluded. Only one eye from each patient was treated. Patient data are summarized in Table I.

INSTRUMENTATION

The laser used at all sites was the Taunton Technologies model LV 2000. This laser has been fully described by Taylor and associates[2] and by our group.[9,11] It utilizes an argon-fluorine gas mixture to produce a 193-nm wavelength output at 10 Hz, and it was adjusted to deliver a fluence of 100 to 120 mJ/cm^2. The entire laser system has a computer control module with an interactive menu, real-time monitoring of procedure parameters, and an integrated digital keratoscope. During the procedure, the patient is supine. Using a head restraint system and three-axis alignment, the eye is positioned by viewing through an integrated binocular surgical microscope as well as multiple video images. The laser was calibrated prior to each treatment session by measuring beam output and beam profile analysis. The desired dioptric change was entered into the computer control console. The maximum beam diameter was 5.2 to 6 mm, depending on the particular machine.

PREOPERATIVE AND POSTOPERATIVE EXAMINATION

All patients received complete ophthalmologic examinations, including slit lamp photography, corneoscopy, corneal topography, ultrasonic pachymetry, digital keratoscopy, and endothelial cell counts, the details of which have been fully described elsewhere.[9,11] Contrast sensitivity test-

TABLE I: DATA ON 31 PATIENTS WHO UNDERWENT PRK

CENTER	PATIENT	DATE OF SURGERY	AGE	SEX
2	1	7/26/89	47	M
	2	8/2/89	51	F
	3	8/7/89	27	F
	4	8/7/89	25	M
	5	8/16/89	45	M
	6	8/16/89	44	M
	7*	4/16/90	33	F
	8*	4/23/90	31	F
	9*	4/23/90	60	M
	10*	4/16/90	31	F
	11*	4/16/90	42	F
	12	5/14/90	36	M
	13	5/14/90	24	F
	14	5/21/90	33	F
	15	5/21/90	34	M
	16	5/21/90	47	F
	17	6/21/90	42	F
3	18	5/16/90	37	F
	19	5/16/90	49	M
	20	5/16/90	46	M
	21	5/23/90	30	F
	22	5/23/90	30	M
	23	5/23/90	39	F
4	24	5/10/90	25	M
	25	5/10/90	36	M
	26	5/10/90	41	F
	27	5/10/90	35	M
	28	5/10/90	63	M
	29	5/11/90	40	M
	30	5/11/90	40	M
	31	5/11/90	33	F

*Calibration error in energy output occurred during procedure.

ing was performed with use of both the Pelli Robson (Pergamon Press, UK) and the MCT 8000 (Visitec Consultants, Dayton, OH).

Corneal sensation was tested with a Cochet and Bonnet aesthesiometer (Luneau Co, France). All refractions, manifest and cycloplegic, were done by one clinical coordinator at each center at similar levels of illumination. Corneal haze was evaluated on a qualitative scale (5 grades) and documented with standardized slit lamp photography, including tangential broad beam, thin slit at 45°, broad beam at 45°, and diffuse views. This testing was repeated at 3, 6, and 12 months.

SURGICAL PROCEDURE

At the time of surgery, intravenous access and cardiac monitoring were

established. Oral diazepam, 5 to 10 mg (depending on age, body weight, and general health), was used in some patients. The nonoperated eye was taped closed. Several drops of 1% proparacaine hydrochloride were instilled. In phase II, the visual axis was marked with the patient fixating on the filament of a Zeiss operating microscope. The center of the pupil was marked with a Sinskey hook. This was then modified in phase IIA with the use of an internal fixation target within the laser coaxial to a point midway between the two objective lenses of the operating microscope and marking the patient's cornea over the center of the entrance pupil, as suggested by Uozato and Guyton.[12]

A 6-mm Weck trephine, premarked with blue dye, was centered on the epithelial impression made by the Sinskey hook (Storz, St Louis) and was then used to mark the epithelium. Peribulbar anesthesia (5 ml of a 50:50 mixture of 2% or 4% lidocaine and 0.75% bupivacaine hydrochloride [Marcaine HCl]) was then given. The epithelium was gently removed using a Tooke knife (Storz). While visualizing the patient's eye through the microscope and video monitors, the surgeon aligned the corneal apex to the laser plane by adjusting table travel in the X, Y, and Z directions. The eye was fixated with either a 0.12 forceps or Thornton ring, or was not fixated at all. The laser then delivered a series of pulses, predetermined through a rotating series of 15 apertures, lasting 20 to 30 seconds. This has been called the "recipe."

POSTOPERATIVE REGIMEN

Following ablation, tobramycin-dexamethasone drops (TobraDex, Alcon, Ft Worth, TX) and 5% homatropine hydrobromide drops (Isopto Homatropine, Alcon) were instilled and the eye ws patched overnight. In many cases, a disposable soft contact lens Vistakon Acuvue (Johnson & Johnson, Claremont, CA) was placed in addition to the patching. In some cases, the contact lens was kept in place for the first three weeks to promote epithelialization. In some cases, eyes were patched overnight. Patients were given 0.1% fluorometholone (FML Liquifilm, Allergan, Irvine, CA) every 2 hours on the first postoperative day and for the first week, then four times daily for the first month, twice daily for the second month, and gradually tapered over the next 4 to 5 months. Tobramycin 0.3% solution (Tobrex, Alcon) was administered four times daily until the epithelium was healed.

Statistical comparisons were determined with a Student's *t*-test. All mean values are presented with standard deviations.

RESULTS

Between July 26, 1989, and May 23, 1990, 31 patients (16 males and 15 females) underwent PRK under FDA Protocol II and IIA at three clinical centers. Patient ages ranged from 24 to 63 years (mean, 38.5 ± 9.6 years) (Table I). Except for one patient who missed an appointment at 1 week, all patients were seen at 1, 3, and 6 weeks and 3 and 6 months. The phase IIA patients were seen at 1 year. Preoperative refractions ranged from −15.00 + 6.00 × 130 to −4.00 spherical equivalent. Attempted corrections, usually aiming for emmetropia, ranged from 4.0 to 12.0 D of flattening.

Most patients experienced moderate to severe postoperative pain, which usually improved rapidly after 24 hours. Preoperative patient counseling, cycloplegics, ice packs, and oral narcotics were helpful. The epithelium was generally healed by 4 to 5 days postoperatively, and no recurrent erosions were observed.

Refractive errors at each follow-up visit are listed in Table II. The refractive changes after excimer PRK at each center are shown in Fig 1. Mean spherical equivalent was −6.49 ± 1.75 D preoperatively and −1.85 ± 2.46 D 6 months postoperatively. For most patients, the attempted correction was designed to achieve emmetropia. The distribution of preoperative and 6-month postoperative spherical equivalent of the manifest refraction is displayed in Fig 2. At 6 months, 67% (8 of 12) of the eyes with preoperative spherical equivalency between −3.12 and −6.00 (moderate myopia group), achieved spherical equivalent refraction of plano to −1.00 D, but in the −6.12 to −12.00 preoperative refraction group (high myopia group) only 16% (3 of 19) ended in that range, and 26% (5 of 19) ended between −1.12 and −2.00 D (Fig 2B).

At 6 weeks, 80.6% of the patients had postoperative spherical equivalent refraction within 2.0 D, and at 6 months, only 67.7% were within 2.0 D.

Attempted and achieved corrections at 6 weeks and 6 months are shown in Fig 3. No statistically significant astigmatism was induced or reduced following PRK. The mean cylinder was 0.77 ± 1.12 D preoperatively, and 0.81 ± 1.11 D 6 months postoperatively ($P = 0.747$).

Improvement or worsening of visual acuity was defined as a change of two or more Snellen lines of best corrected acuity. The changes in best corrected visual acuity are outlined in Fig 4. At 6 months postoperatively, all the patients had the same visual acuity ± 1 line as preoperatively.

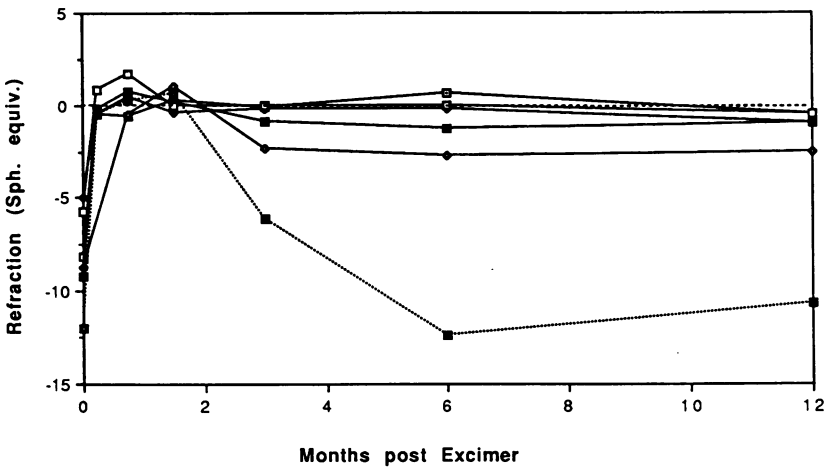
Figure 5 illustrates the change in uncorrected visual acuity at 6 months after PRK. Preoperative uncorrected visual acuity ranged from finger counting to 20/200. All but three patients (9.7%) had improved uncorrected vision following excimer PRK. Six patients (19.3%) had 20/20

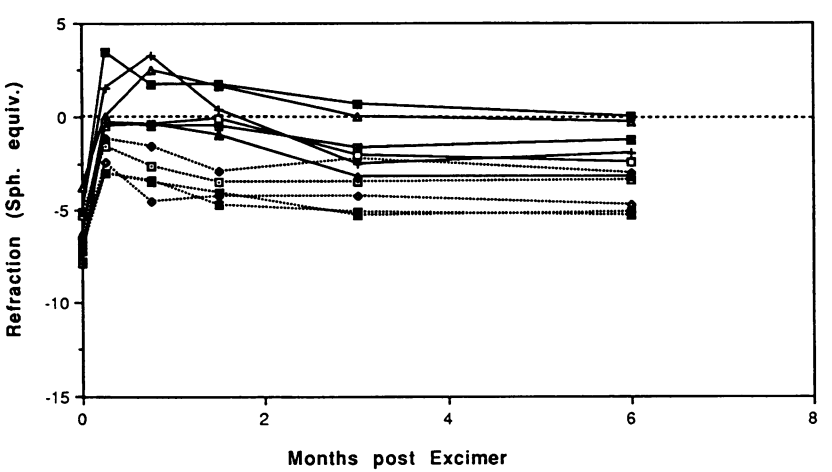
TABLE II: PREOPERATIVE AND POSTOPERATIVE REFRACTION OF 31 PATIENTS WHO UNDERWENT PRK

CENTER	PATIENT	PREOPERATIVE	1 WEEK	3 WEEKS	6 WEEKS	3 MONTHS	6 MONTHS	1 YEAR
2	1	−8.50+0.75×140	−0.50 sph	−1.25+1.25×120	Plano+0.50×110	−0.25+0.25×120	+0.25+0.75×125	−0.75+0.50×110
	2	−5.00 sph	−1.00+1.00×14	+0.25+0.50×85	−0.75+0.75×80	−0.25 sph	−0.25 sph	−1.00 sph
	3	−15.00+6.00×130	−2.75+4.50×105	−1.50+3.50×122	−1.25+3.75×90	−9.00+5.75×115	−15.00+6.00×115	−11.75+2.25×120
	4	−8.75 sph	NA*	−1.00+1.00×10	+0.50+1.00×12	−2.75+0.75×165	−2.75 sph	−2.50 sph
	5	−10.25+2.00×90	−0.75+1.00×120	+0.50+0.40×110	−0.25+0.75×90	−1.24+0.75×95	−1.75+1.00×90	−1.75+1.60×90
	6	−6.00+0.50×115	+0.50+0.75×60	+1.25+1.00×120	−0.25+0.50×100	Plano	Plano	−0.50 sph
	7†	−5.75+1.00×25	−2.00+1.00×20	−3.00+0.75×30	−3.50 sph	−3.50 sph	−3.50+0.50×10	
	8†	−7.50+1.50×75	−1.50+0.75×90	−2.00+1.00×70	−3.25+0.75×180	−2.75+1.00×75	−3.75+1.50×80	
	9†	−7.00+0.50×90	−3.00 sph	−4.00+1.25×90	−5.00+0.50×90	−5.25+0.25×75	−5.50+0.50×75	
	10†	−7.00 sph	−2.75+0.75×90	−4.50 sph	−4.25 sph	−4.25 sph	−4.75 sph	
	11†	−7.25 sph	−3.75+1.50×107	−4.25+1.50×75	−4.25+0.50×90	−5.25+0.25×90		
	12	−8.25+1.00×90	−0.50 sph	−1.00+1.25×85	−0.75+1.25×90	−3.00+2.00×90	−3.25+1.75×110	
	13	−6.25 sph	−0.25 sph	−0.50+0.25×95	−1.00 sph	−3.50+0.75×90	−3.25+0.25×105	
	14	−4.00+0.50×80	Plano	+2.00+1.00×90	+1.25+0.75×82	−0.50+1.00×90	−0.75+1.00×90	
	15	−5.25+0.25×90	+3.25+0.50×180	+1.75 sph	+1.75 sph	+0.50+0.25×90	Plano	
	16	−5.25+0.25×90	Plano+3.00×123	+2.00+2.50×133	Plano+0.75×122	−3.50+2.00×115	−2.25+0.75×114	
	17	−8.00+0.25×90	−0.25 sph	−1.00+1.00×140	−1.00+1.00×140	−2.25+1.25×120	−2.00+1.50×125	
3	18	−7.50+0.50×120	−1.50+0.75×10	−0.75+0.75×165	+1.50+2.00×90	+1.00+1.50×90	Plano+1.00×90	
	19	−7.50+0.50×100	+0.50+1.00×25	−0.50+0.75×45	−0.75+1.50×50	Plano+1.00×55	−0.50+1.25×55	
	20	−6.75+1.25×90	−1.25 sph	−2.75+0.25×105	−1.50+1.25×88	−0.25+0.75×90	−0.75 sph	
	21	−5.25+1.00×90	−1.50 sph	−1.00+1.00×162	−0.50+1.00×115	−1.00+1.00×105	−3.25+2.00×110	
	22	−6.25 sph	−2.25+0.75×80	−1.00+1.50×140	−0.50+0.50×110	−1.50+0.50×110	−1.50+0.50×140	
	23	−7.00+1.25×60	−2.00 sph	−0.50+0.50×171	Plano+0.50×85	−0.50+0.50×65	−0.50+0.75×65	
4	24	−4.25+0.50×57	Plano	Plano	Plano	−0.50+0.25×45	−1.00+0.50×43	
	25	−4.00 sph	Plano+0.75×130	+0.50 sph	+0.50 sph	−0.50 sph	−0.50 sph	
	26	−8.25+1.25×96	+1.00+1.25×96	−0.50+2.50×82	−0.50+1.75×100	Plano+0.50×90	−0.25+0.50×99	
	27	−6.75+0.50×88	+1.00+1.75×46	−0.25+0.75×45	Plano	−1.00 sph	−1.25 sph	
	28	−5.00+1.00×168	+1.00+0.75×65	−1.75 sph	−1.00 sph	−1.75+0.75×100	−1.50+1.00×167	
	29	−8.00 sph	+0.50+2.00×91	−0.75+1.00×110	−1.75 sph	−2.00 sph	−2.00 sph	
	30	−6.25+1.75×120	−0.50+1.75×120	+1.00+2.25+120	−1.75+2.50×130	−1.75+1.50×120	−1.75+2.00×124	
	31	−5.50 sph	−1.75+2.00×157	Plano	Plano	−2.00+0.50×135	−1.25 sph	

*NA, not available.

†Calibration error in energy output occurred during procedure, resulting in undercorrection.


Refraction (Sph. equiv.)
5
0
-5
-10
-15
0
2
4
6
8
10
12
Months post Excimer


Refraction (Sph. equiv.)
5
0
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-10
-15
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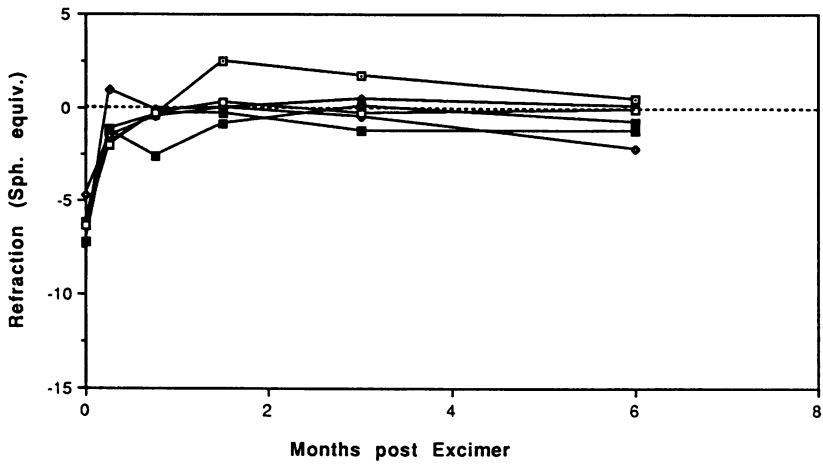
2
4
6
8
Months post Excimer



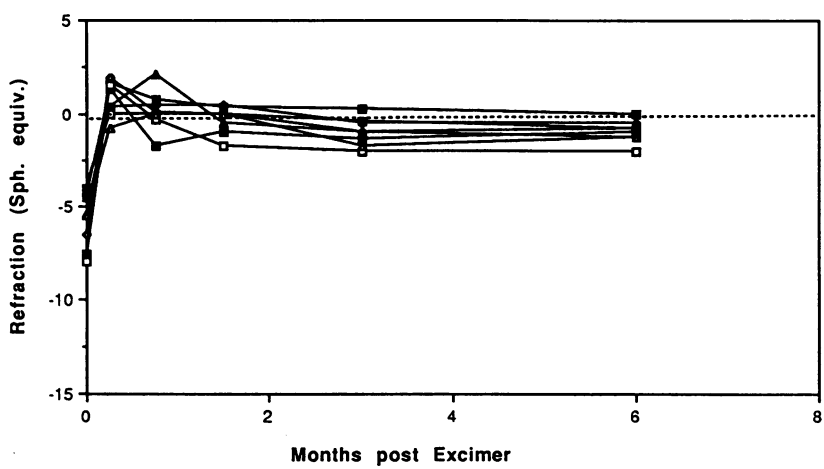


FIGURE 1
Change in refraction over time after excimer PRK. A: Phase II, center 2 (Minnesota). B: Phase IIA, center 2. *Dotted lines* represent 5 cases of undercorrection due to calibration problem. C: Phase IIA, center 3 (Kentucky). D: Phase IIA, center 4 (Florida).

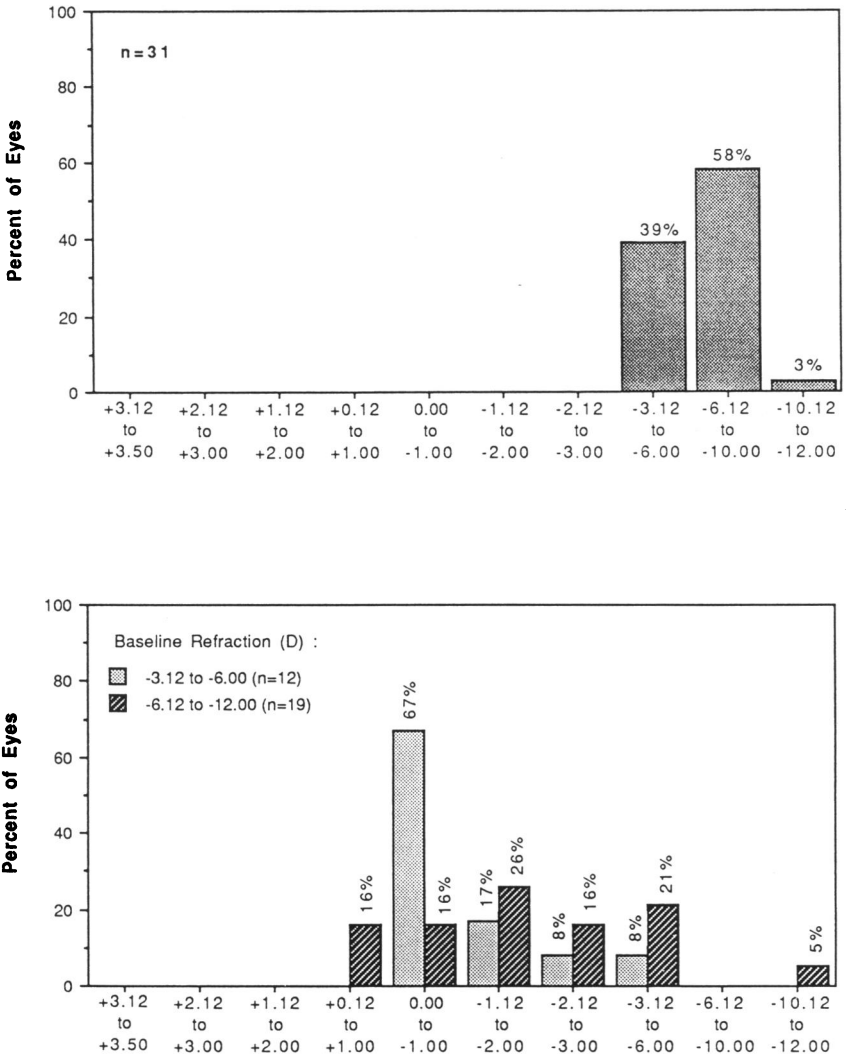


FIGURE 2

A: Distribution of baseline spherical equivalent refractive errors in 31 eyes before excimer PRK, revealing majority of eyes had refractive errors between −6.12 and −10.00 spherical equivalent. B: Distribution of spherical equivalent refractive errors 6 months postoperatively, subdivided by baseline refraction of −3.12 to −6.00 or −6.12 to −12.00 spherical equivalents.

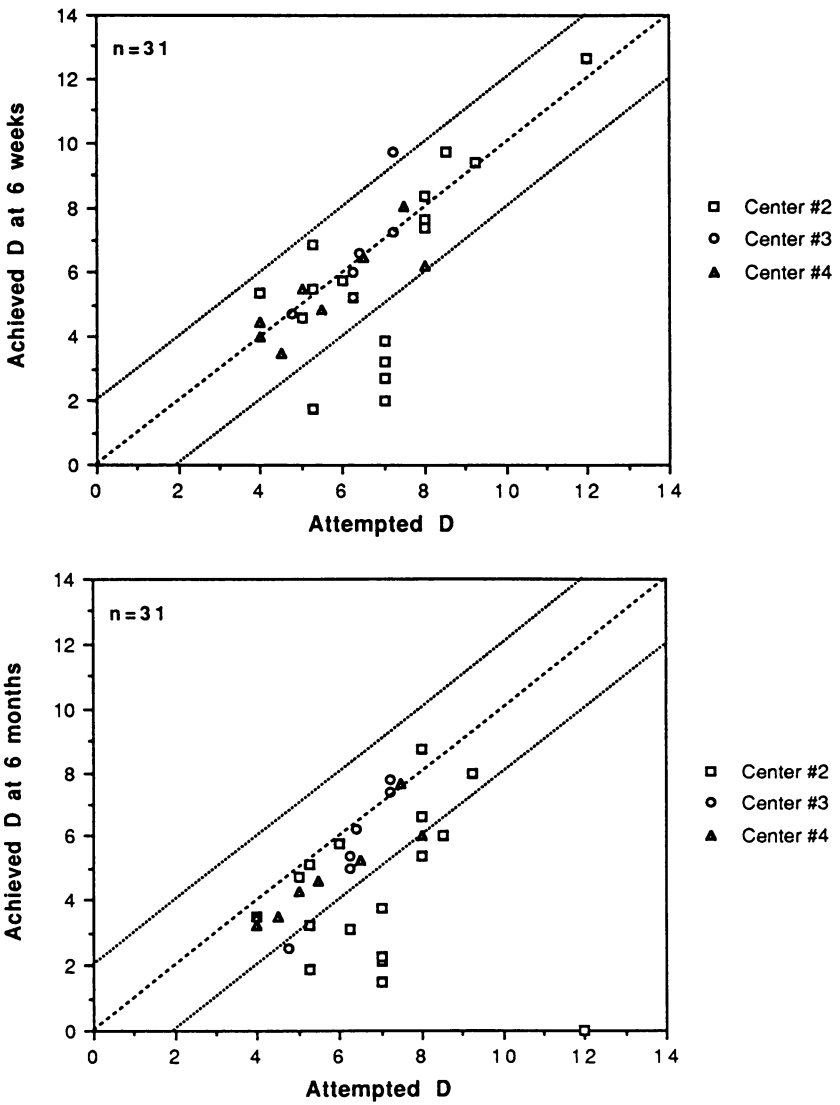


FIGURE 3
Attempted correction (spherical equivalent) plotted against achieved correction (spherical equivalent) in 31 eyes at 6 weeks (A) or 6 months (B) after excimer PRK.

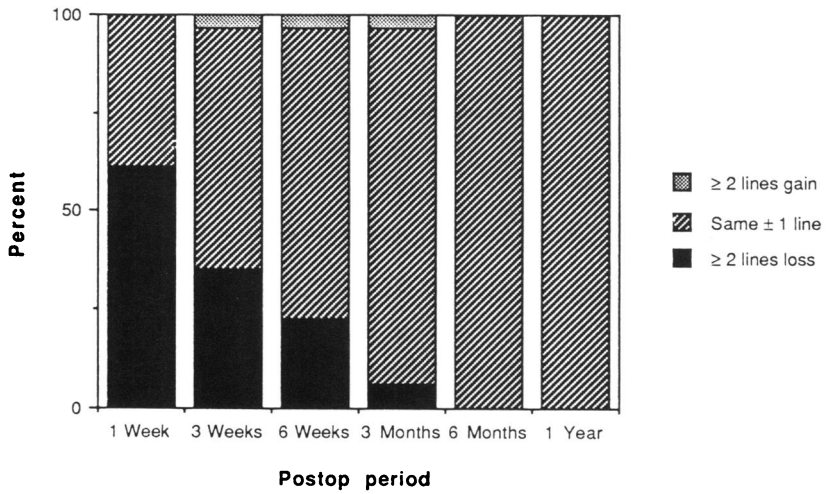


FIGURE 4
Changes in Snellen visual acuity in 31 patients, compared with preoperative vision, at 1 week, 3 weeks, 6 weeks, 3 months, 6 months, and 1 year after excimer PRK.

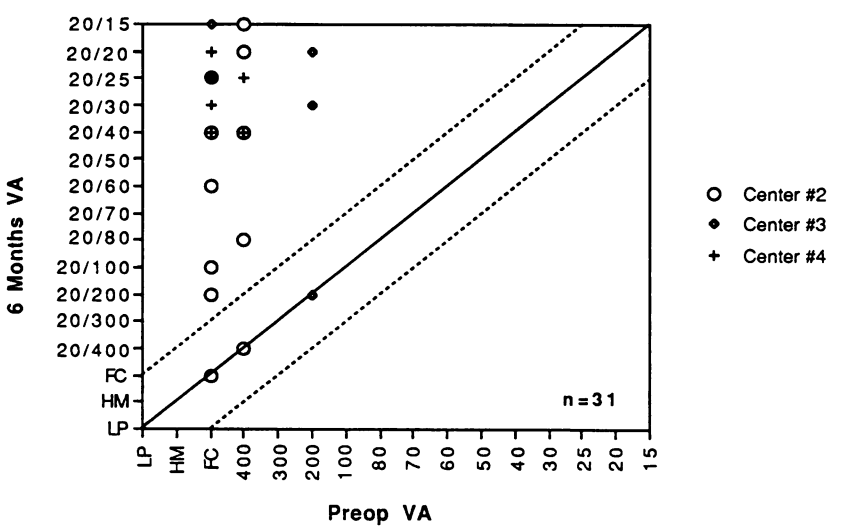


FIGURE 5
Preoperative uncorrected vision versus postoperative uncorrected vision at 6 months after excimer PRK (31 eyes).

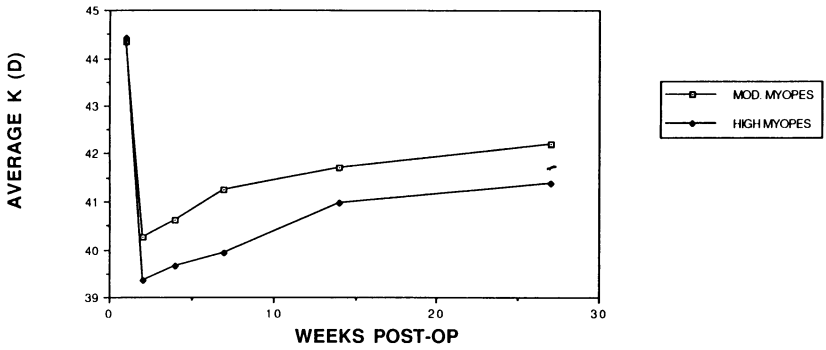


FIGURE 6
Average keratometry values measured preoperatively and at various postoperative intervals in 31 eyes. Cases were subdivided into moderate myopia (−3.12 to −6.00 D) (n = 15) and high myopia (−6.12 to −12.00 D) (n = 16).

acuity or better, 14 patients (45.2%) had 20/40 or better, 4 patients (12.9%) had 20/100 or better, and 7 patients (22.6%) had 20/200 or worse. No patient had a deterioration in uncorrected visual acuity.

Keratometry was performed at each visit, and the mean keratometry readings at each visit were averaged (Fig 6). The cases were subdivided into moderate myopia (−3.12 to −6.00 D) and higher myopia (−6.12 to −12.00 D) groups, similar to Fig 2B. Significant corneal flattening was observed in both groups, with marked steepening between weeks 1 and 6 and more gradual steepening continuing through the 6-month visit. There was no consistent correlation between the amount of flattening as measured by the keratometer and the amount of final change of refractive error (6 months or 1 year).

INTRAOCULAR CHANGES

There were no intraocular effects noted except for two instances of elevated intraocular pressure (mid-20s), which returned to normal after topical FML was discontinued.

Mean endothelial cell count was 2663 ± 429 cells/mm preoperatively, and 2708 ± 434 cells/mm 3 months postoperatively (P = 0.57). Central corneal thickness measurements were performed at each follow-up visit. There was statistically significant reduction between the preoperative and all postoperative corneal thickness measurements ($P < 0.001$), but no statistically significant difference was found between different postoperative measurements (P = 0.134 to 0.951).

CORNEAL TOPOGRAPHY

All patients underwent digital keratometry using the built-in digital topography system. An example of this has been previously reported by our group.[9] These maps confirmed the central area of corneal flattening, and, in general, a good correlation was seen between the topographic map and refraction data.

CONTRAST SENSITIVITY

No statistically significant difference was found between contrast sensitivity visual acuity preoperatively and 3 months postoperatively ($P = 0.092$).

CORNEAL SENSITIVITY

Corneal sensitivity was 4.6 ± 1.4 preoperatively and 4.7 ± 1.5 at 3 months postoperatively ($P = 0.706$), showing no significant change.

CORNEAL HAZE

Quantitative grading of corneal haze, especially at minimal levels, is difficult, and numerical grades are not very meaningful. Qualitatively, similar results were seen in phase IIA, as described by Zabel and associates[9] in a preliminary report of our phase II patients and as reported by Seiler and associates.[8] A fine reticulation was noted at the epithelial stromal interface and in the anterior 25 μm of the stroma at the end of the first and second weeks. At low magnification, the reticulation was confluent and of uniform density across the excimer bed. On occasion, there were some areas of increased density. When viewed under high magnification, a stellate substructure could be discerned within the area of reticulation. A very diffuse nebular haze and patchy granularity were seen in some patients, as viewed by sclerotic scatter. By the third week, the stromal granularity had usually resolved, and the fine reticulation became attenuated by the sixth week. All these changes gradually diminished in most patients over time. By the 6-month visit, this haze was gone in may patients and minimal in all the other patients except for one who had discontinued steroids at 3 weeks. All the investigators agreed that the fine reticulations did not interfere with vision.

DISCUSSION

Ophthalmologists have been developing surgical methods of correcting refractive errors for the last 100 years. In 1985, Waring[13] reviewed 15 different techniques, and more recently, Thompson[14] pointed out that

because of unsolved problems with predictability, unstable refractions, lack of adjustability, or irreversibility, these procedures have not gained widespread acceptance. The excimer laser offers yet another new technology and technique for the permanent reduction of myopia. Its success or failure will depend on whether PRK can be proven to be safe, effective, predictable, stable, and easily performed. The reader of this study and other studies on this technology needs to be able to compare these results to the results of other refractive procedures, including the excimer. Waring[15] has proposed guidelines for the presentation of results from refractive procedures to enable a more rational comparison. We have made efforts here to present our data in this suggested format to facilitate these comparisons.

Some rough comparisons can be made between these data and results from radial keratotomy as reported in the 1-year results of the prospective evaluation of radial keratotomy (PERK) study.[16] At 1 year, 38% of eyes in the PERK study with a baseline refraction of −4.50 to −8.00 D had achieved corrections between −1.00 and +1.00 D. In this small series of excimer PRK, 41% (10 of 24) achieved the same correction. If the five cases of undercorrection due to the calibration error were omitted (cases 7 through 11), 58% of these higher myopes would achieve correction within 1 D of emmetropia. We saw no evidence of diurnal shifts of refraction or progressive myopia or hyperopia after 3 months. A larger series of patients, with follow-up of several years, will eventually be needed to determine if small amounts of regression occur. In contrast to radial keratotomy, there were minimal problems with glare sensitivity and virtually no chance of perforations. PRK eyes had no recurrent erosions or structural weakening, both of which have been seen with radial keratotomy.

Patient 3, who had an almost complete regression, had several unique preexisting problems, which have previously been described.[9] She had myopic epikeratophakia that was not successful and then had removal of the epikeratophakia lenticule. Her preoperative refraction was −15 + 6.00 × 130. She became pregnant approximately 2 weeks after PRK and discontinued using corticosteroids. After initial encouraging results, she rapidly regressed between the 6th and 12th weeks, and significant epithelial hypertrophy and haze also developed. Although her haze was the most significant of the series, her best corrected vision was unchanged. Within the last several months, this patient had her epithelium mechanically removed, but the refractive error did not change after reepithelialization. The central haze was, however, resolved, and best corrected vision improved to 20/25. On histologic examination, the plaque-like

corneal scar was made up exclusively of corneal epithelium and has not returned 3 months after debridement. Epithelial hyperplasia, although exaggerated in this patient, has been described by other investigators[17,18] and may be associated with regressions and variations in refractive results.

The epithelium was routinely removed prior to PRK to help improve predictability of the procedure. It is feasible and easier to perform PRK through the intact epithelium. However, the absence of accurate clinical methods for evaluation of epithelial layer thickness would make the programming of this value problematic. With a beam diameter of 5.6 mm, ablation of 10 μ produces approximately 1 D of refractive change. The average thickness of the corneal epithelium is 0.5 mm but may vary by ± 10 to 15 mm. We believe this variation could induce significant errors if the epithelium was ablated by the laser rather than removed prior to PRK.

Corneal hydration may be an important factor that needs to be explored. Liu and associates[19] have detailed some of the variables involved with variable amounts of corneal hydration and correctly point out that increased stromal hydration may lead to decreased ablation per pulse. The Taunton laser system utilizes an effluent removal system, placed near the operative eye, which moves considerable air over the cornea, resulting in significant drying of the cornea. Seemingly minor deviations in surgical technique, such as the use of balanced salt solution or topical anesthetic on the cornea prior to the ablation, will influence the state of corneal hydration and possibly cause variations in the ablation rate.

Peribulbar anesthesia was used in these phase II and phase IIA patients. In subseqauent clinical trials utilizing the newer model of the Taunton laser (model 2015), we have found that PRK can be safely performed with use of topical anesthesia. This has a number of benefits, beyond the obvious increased safety factor of not having to inject near larger myopic eyes. The patients are able to fixate on an internal fixation light, and improved centration is obtained. Paradoxically, the patients seem to have less postoperative pain and topical anesthesia than after peribulbar or retrobulbar blocks.

The location of the optical zone in PRK is extremely important. In his excellent review, Maloney[20] emphasized that an optical zone that is too small or decentered may decrease acuity, lessen contrast sensitivity, or produce glare. Uozato and Guyton[12] have clearly presented the case for centering the procedure over the entrance pupil while the patient is fixating on a target coaxially placed with the surgeon's sighting eye.

The maximum ablation diameter in this study was 5.2 to 6.0 mm. The

larger beam diameter has a number of clinical advantages, including reduced night glare and less critical centering requirements. Our patients had minimal complaints concerning halos or night glare. This is in contrast to Seiler, who reported significant halos or night glare problems in his patients when utilizing a 3.5-mm beam with an earlier prototype of Summit Technologies excimer laser (Summit Technologies, Watertown, MA) (personal communication, 1991). This problem was mostly resolved with a 4.5-mm beam diameter.

The initial reluctance of some investigators to use a larger-diameter ablation zone is understandable and stems from the requirement for a deeper ablation depth with the larger-diameter beam. However, it is our impression that the presence of clinically significant corneal haze is not correlated with the depth of ablation and, in fact, is not a problem at any depth of ablation performed in this series. The latest model of the Taunton excimer has a 6.0-mm beam diameter, and the ideal diameter may prove to be 7.0 mm or larger.

The undercorrected patients at Center 2 were the probable result of performing the procedure at a fluence 30% to 35% lower than desired. The desired fluence for the Taunton machine is 100 to 124 mJ/cm^2. The laser was calibrated before every treatment session. Among the calibration tests was analysis of beam energy levels with an oscilloscope measuring device placed in a special holder under the beam pathway. A defect in this measuring device was subsequently discovered and remedied. The ideal optimal fluence to perform PRK is not known. The VISX excimer laser (model 2020, VISC Co) utilizes a higher fluence of 160 mJ/cm^2, with similar clinical results. We have since modified the calibration techniques by ablating standardized discs of plastic at a uniform fluence and measuring the depth of the central cut in microns.

Corneal haze, once thought to be a potential risk of excimer PRK,[21,22] has not proven to be a significant problem. The transient period of faint reticulated haze is the result of fibroblastic keratocytes beneath the epithelium,[23] and experimental studies have confirmed the presence of types III and VI collagen.[24] Tuft and associates[25] demonstrated in rabbits that this new collagen formation may diminish after topical corticosteroid treatment. This provides the rationale for the use of intensive topical corticosteroids in our patients. There is presently no available data to indicate whether less intensive topical corticosteroids, used for a shorter duration, would be equally efficacious. In cases of overcorrection, it is our clinical impression from these and more recently performed cases that rapidly decreasing or discontinuing corticosteroids may induce increased corneal haze and a small myopic shift, sometimes seen within a week.

Seiler and associates[8] have reported similar findings. If topical steroids are discontinued for modulation of refraction or because of ocular hypertension, the patient should be observed closely for regression and/or increased corneal haze.

These preliminary studies show the safety and efficacy of the 193-nm excimer laser for the reduction of moderate myopia. Considerable additional study will be needed before the excimer laser can be used on the small but significant segment of the myopic population who desire surgical correction of myopia.

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REFERENCES

1. Trokel SL, Srinivasan R, Braren B: Excimer laser surgery of the cornea. *Am J Ophthalmol* 1983; 96:710-715.
2. Taylor DM, L'Esperance FA Jr, DelPero RA, et al: Human excimer laser lamellar keratectomy: A clinical study. *Ophthalmology* 1989; 96:654-664.
3. McDonald M, Beuerman R, Falzoni W: Preliminary experience with the excimer laser for area ablation of rabbit corneas. *Invest Ophthalmol Vis Sci* 1987; 28:275.
4. Puliafito CA, Steinert RF, Deutsch TF, et al: Excimer laser ablation of the cornea and lens: Experimental studies. *Ophthalmology* 1985; 92:741-748.
5. McDonald MB, Frantz J, Klyce S, et al: One year refractive results of central photorefractive keratectomy for myopia in the nonhuman primate cornea. *Arch Ophthalmol* 1990; 108:40-47.
6. McDonald MB, Frantz JM, Klyce SD, et al: Central photorefractive keratectomy for myopia. *Arch Ophthalmol* 1990; 108:799-808.
7. McDonald MB, Liu JC, Andrade H, et al: Clinical results of 193 nm excimer laser central photorefractive keratectomy for myopia: The partially sighted and sighted eye studies. *Invest Ophthalmol Vis Sci* (Suppl) 1990; 31:245.
8. Seiler T, Kahle G, Kriegerowski M: Excimer laser (193 nm) myopic keratomileusis in sighted and blind human eyes. *Refract Corneal Surg* 1990; 6:165-173.

9. Zabel RW, Sher NA, Ostrov CS, et al: Myopic excimer laser keratectomy: A preliminary report. *Refract Corneal Surg* 1990; 6:329-334.
10. Draft clinical guidance for the preparation and contents of an investigational device exemption (IDE) application for excimer laser devices used in ophthalmic surgery for myopic photorefractive keratectomy (PRK). Office of Device Evaluation, Division of Ophthalmic Devices, Food and Drug Administration. *Refract Corneal Surg* 1990; 6:265-269.
11. Sher NA, Bowers RA, Zabel RW, et al: The clinical use of the 193 nm excimer laser in the treatment of corneal scars. *Arch Ophthalmol* 1991; 109:491-498.
12. Uozato H, Guyton DL: Centering corneal surgical procedures. *Am J Ophthalmol* 1987; 103:264-275.
13. Waring GO: Making sense of keratospeak. *Arch Ophthalmol* 1985; 5:362-367.
14. Thompson KP: Will the excimer laser resolve the unsolved problems with refractive surgery. *Refract Corneal Surg* 1990; 6:315-317.
15. Waring GO: Conventional standards for reporting results of refractive surgery. *Refract Corneal Surg* 1989; 5:285-287.
16. Waring GO, Lynn MJ, Gelender H, et al: Results of the prospective evaluation of radial keratotomy (PERK) study one year after surgery. *Ophthalmology* 1985; 92:177-207.
17. Tuft SJ, Zabel RW, Marshall J: Corneal repair following keratectomy. *Invest Ophthalmol Vis Sci* 1989; 30:1769-1777.
18. Goodman GL, Trokel SL, Stark WJ, et al: Corneal healing following laser refractive keratectomy. *Arch Ophthalmol* 1989; 107:1799-1803.
19. Liu JC, McDonald MD, Varnell R, et al: Myopic excimer laser photorefractive keratectomy: An analysis of clinical correlations. *Refract Corneal Surg* 1990; 6:321-328.
20. Maloney RK: Corneal topography and optical zone location in photorefractive keratectomy. *Refract Corneal Surg* 1990; 6:363-371.
21. Marshall J, Trokel S, Rothery S, et al: Photoablative reprofiling of the cornea using the excimer laser: Photorefractive keratectomy. *Lasers Ophthalmol* 1986; 1:21-48.
22. Hanna KD, Pouliquen Y, Waring GO, et al: Corneal wound healing after excimer laser ablation in rabbits. *Invest Ophthalmol Vis Sci* (Suppl) 1988; 29:390.
23. Fantes FE, Hanna KD, Waring GO, et al: Wound healing after excimer laser keratomeleusis (photorefractive keratectomy) in monkeys. *Arch Ophthalmol* 1990; 108:665-672.
24. Malley DS, Steiner RF, Puliafitio CA, et al: Immunofluorescence study of corneal wound healing after excimer laser anterior keratectomy in the monkey eye. *Arch Ophthalmol* 1990; 108:1316-1322.
25. Tuft S, Zabel R, Marshall J: Corneal repair following keratotomy. *Invest Ophthalmol Vis Sci* 1989; 30:1769-1777.

DISCUSSION

DR GEORGE O. WARING III. Doctor Lindstrom and colleagues report the use of the Taunton argon fluoride (193-nm) excimer laser for performing photorefractive keratectomy (PRK) to treat myopia.

Peribulbar anesthesia was used, which I think is unnecessary in these circumstances. It means that the surgeon must control the fixation of the eye manually. I would like to know the authors' experience with use of peribulbar anesthesia, compared with use of topical anesthesia alone, and which of the two methods they prefer.

Centering these surgical procedures is difficult, and the authors describe a fixation target within the laser coaxial to a point midway between the two objective lenses. It would be nice to know more detail about this method and

whether or not it was useful in maintaining fixation during surgery.

The authors used a disposable soft contact lens immediately after surgery in addition to patching. They do not indicate how long the soft contact lens was left in place. Do they think that the lens increased or decreased underlying stromal edema, the rate of epithelial healing, patient comfort, and the final refractive result? What base curve was used?

Moderate to severe postoperative pain is described, and this would be expected from the large epithelial debridement and the ultraviolet "burn" of the cornea. Do the authors think this pain is different from that experienced by radial keratotomy patients?

For eyes with baseline refractions of approximately 3 to 6 D, 67% were within 1 D of emmetropia at 6 months after surgery, none of the eyes being overcorrected. Doctor Lindstrom and colleagues have reported the results of four-incision radial keratotomy on a series of eyes with -1.50 to -5.00 D of myopia. At 6 months, 24 of 26 eyes (92%) and at 1 year, 29 of 32 eyes (91%) had refractions within 1 D of emmetropia. I would be interested in hearing the authors' comparison of their experience with PRK and with radial keratotomy for eyes in approximately the same range of myopia.

The stability of refraction after 3 months seems quite good in the reported eyes. There is little overcorrection in the first few weeks after the surgery. Such an overcorrection in the first few weeks after the surgery. Such an overcorrection has been described by investigators using other instruments, such as the Summit and the VISX instruments. How do the authors account for this difference? do they think the soft contact lens or the intensive topical corticosteroids have something to do with this?

Subepithelial fibrosis occurs in eyes after PRK producing clinical haze. Studies in animals have demonstrated that this results from the deposition of type III collagen and keratin sulfate both of which are gradually remodeled and become more normal over approximately 3 to 24 months after surgery. The clinical haze that is present lasts for a few months. The authors describe the appearance of a diffuse, fine, reticulated haze in the first and second week in the anterior stroma. Others have described the appearance of the haze as more delayed response, appearing at 1 month or so. Can the authors distinguish the early subepithelial edema that is associated with the initial epithelial wound healing from the later production of the subepithelial wound healing extracellular matrix? They describe attenuation of the haze by 6 weeks. Other observers have seen this as late as 3 to 6 months. I wonder if the intensive topical steroids affect this more rapid disappearance of the haze.

Videokeratography is reported briefly. Were the ablation zones round and central? Were some eccentric? Was there induced astigmatism?

Contrast sensitivity was tested using two instruments, but it is not indicated whether this was done with the pupil constricted or dilated. The most sensitive tests would be with the pupil dilated. Can the authors tell us about this circumstance that simulates contrast under nighttime or scotopic conditions?

The authors discuss the effluent removal system placed near the operated eye,

which moves considerable air over the cornea and dries the surface. Other systems do not use an effluent removal system. Could the authors comment on the necessity of this system and on its possible effect on the accuracy of the procedure?

The ablation diameter in this study was 5.2 to 6.0 mm, larger than the 4.5 to 5.0 mm in some other studies. The authors suggest that the larger diameter might decrease the halos and night glare; I wonder if the larger zone might also create better contours of the cornea to diminish early fluctuations in wound healing. The authors speculate that a 7-mm or larger diameter ablation zone might be preferable, and I would like to know why they have that opinion.

The authors candidly observe that some less-than-desirable outcomes were achieved because of technical problems. At one center, the fluence was 30% to 50% lower than desired. This emphasizes the need for optimal technical support while using these lasers, since most physicians are not comfortable calibrating and aligning these lasers.

I personally have experience with ten myopic patients treated with the Summit Technology laser under the phase IIB protocol of the FDA investigation. The preoperative refractions ranged from −2.50 to −6.75 D (mean, −4.25 D). Treatment parameters included a radiant exposure (fluence) at the cornea of 180 mJ/cm^2, an ablation rate of 0.25 μ/pulse, a repetition rate of 10 Hz, and a maximum ablation rone diameter of 4.5 mm. Surgery was done under topical anesthesia with patient fixation. A slightly eccentric ablation occurred in one of the ten eyes.

Postoperatively, topical dexamethasone was used four time daily for 1 month, followed by topical fluorometholone four times for another month, with gradual tapering over the third and fourth months. Videokeratography showed central flattening of the cornea with concentric mires producing aspherical curves.

At 4 months after surgery, nine eyes had a spherical equivalent manifest refraction within ± 0.50 D; the remaining eye had a refraction of +1.50 sphere. Uncorrected visual acuity was 20/25 or better in all ten eyes. The subepithelial haze had a grading of 0 in one eye, trace in six eyes, and mild in three eyes at 4 months, and was not considered to be a significant clinical problem. Would Doctor Lindstrom please comment on the differences among results of the various instruments?

There is no question that the different excimer lasers can achieve different results in a similar clinical population, and part of the challenge of this new technology is for the manufacturers and the surgeon-users to figure out the best set of parameters in each laser to achieve optimal results. Some advantages over radial keratotomy are obvious: The cornea is not weakened by deep incisions, and therefore one would expect a more stable refraction over time without a continued effect of the surgery in the hyperopic direction that has been seen after radial keratotomy. However, it is unknown when subepithelial wound healing after PRK ceases, and this could introduce some instability into the refractive correction over time. The cornea is not weakened, so that corneal perforation from trauma is not a danger after PRK. However, it has not yet been shown that PRK is more

accurate than radial keratotomy, because corneal wound healing plays a role in the outcome of both types of refractive surgery. Longer follow-up is needed to answer this question. In addition, complications from PRK occur in the central cornea and can be devastating to a patient's visual acuity, whereas complications from radial keratotomy usually occur in the paracentral and peripheral cornea and may less directly affect the patient's visual function. Adjustments after radial keratotomy using a staged surgical approach are commonplace and have the ability to fine-tune a patient's results to the desired level (eg, monovision). Under the FDA excimer laser protocols, repeated ablations are not allowed, and there is little information about whether or not adjustability is possible with myopic PRK.

We all look forward to the commencement of the phase III trials in the United States, in which each company will treat 700 patients and follow them for 2 years. Doctor Lindstrom is to be lauded for his honest and careful approach to the evaluation of this technology.

DR STEVEN G. KRAMER. Thanks very much, Doctor Blodi. I had a comment about the first lecture, but I think I may have forgotten it after hearing the second lecture.

My feeling about new technologies is that in the early phases, reports are about observations rather than data, and the comments are largely editorial. So I would congratulate both speakers on their observations and their editorial comments. That is not as critical as it sounds because I am going to join in by making a few comments of my own.

Let me first give Doctor Lindstrom a couple of questions. One concern I have about central invasion of the cornea is, "what about the permanent loss of Bowman's membrane?" Would you speculate on the long-term effects of that? Doctor Waring showed us the scarring reaction that occurs in the central cornea. So the added scarring as well as the permanent loss of Bowman's membrane are conceivably long-term problems. I also wonder whether you think there is any likelihood of steroid-related complications when intensive post-laser steroids are needed.

Let me also speak to some of the other problems that appear to be persistent with this procedure. The presence of corneal haze continues to worry us all. There is the possibility of regression as is true in all refractive surgery, and that has been particularly disappointing in the case of the excimer laser for high myopes as Doctor Lindstrom's observations tend to support. We hoped this might be a refractive procedure that would be very helpful in highly myopic eyes, ones that we would like very much to help. It turns out, however, that the attractive results tend to be in eyes with low myopia.

Another difficulty, of course, is the complexity and cost of the technology itself. Furthermore, with this procedure, the surgeon must become, in a sense, more an hypnotist than a technician in order to maintain the patient's fixation. The idea that the patient might look away and cause a terrible result is frightening.

I'll just close by mentioning another technology, one with no clinical data to support it at the moment, but an alternative approach that some of our colleagues

are developing. David Schanzlin, in particular, and Terry Burris have some nice experience in an experimental setting with an intracorneal ring. This is a PMMA device that is put peripherally in the cornea with a clever, hand-held corneal dissector causing a flattening of the cornea for myopia. It has some advantages in that the central cornea is not disturbed and the cost is orders of magnitude lower than an excimer laser.

DR JULES L. BAUM. One of the variables of refractive surgery is the variability of the correction in the individual patient, whether it be excimer or radial keratotomy. Why do we get such different responses in these patients? It may be because of individual differences in wound healing. We should not expect all patients to heal alike. Naively speaking, we all have different wound healing genes. We don't yet know what these wound healing genes are. Doctor Waring suggests differences in type 3 collagen. Perhaps, as an example, different people produce type 3 collagen, differently. Wouldn't it be nice if we knew this before the fact. I would like to suggest to those groups that are doing refractive or excimer surgery, that we collect blood, white cells, prospectively on all patients and freeze it away. Perhaps we can develop a nomogram, so that when a patient comes in preoperatively we take some blood, and knowing a little more about wound healing genes than we do now, we will be able to better quantitate the surgical procedure.

DR THOMAS O. WOOD. I understand with the excimer laser, the healing process electron microscopically is identical to any other injury to the cornea. I don't think we are going to be able to fool "Mother Nature" with the excimer laser. There are certain healing steps which produce scarring that the cornea goes through following any injury before it lays down new basement membrane (type 4 collagen).

My correction is about a -2.75 and having reached the half century mark it's a blessing. I think that myopia is not a disease, in our society, and we are possibly curing a process which becomes an asset over age 40, particularly when you are talking about -2.00 to -3.00 myopia.

DR DANIEL M. TAYLOR. I would like to congratulate Doctor Lindstrom on his very fine presentation and also Doctor Waring for his excellent discussion. They have both just summarized the findings of the FDA Phase II Excimer Laser Project on sighted eyes. Some of you may recall that Doctor L'Esperance and I did the initial Phase I study for the FDA on monkeys and blind human eyes. Following the successful completion of the study, we very carefully selected Doctor Lindstrom and several other individuals to carry out the phase II studies on sighted eyes. In the present environment of hype, emotion, and sometimes exaggerated claims, we knew that Doctor Lindstrom would carry out his studies in a highly professional manner and would very honestly report his results. This is exactly what he has done and the results appear promising. At this point, I would like to give you some follow-up on the original Phase I study, that Doctor L'Esperance and I performed.

Our excimer laser ablations on primates and blind human eyes were completed 3 years ago. We ablated approximately 100 eye bank eyes, 19 ablations on sighted eyes with corneal scarring. All of the 19 primate eyes continued to show some degree of scarring with up to 3 years follow-up in those not sacrificed earlier for pathologic specimens. None were treated postoperatively with steroids. The residual scarring in all of these patients would have been clinically significant if the monkeys were able to communicate their thoughts with us. Of the 11 blind eyes, pathologic specimens were obtained in 4. One is now deceased, and an additional patient is too critically ill to return for follow-up evaluations. The remaining five patients have now been followed for 3 years since their excimer ablation. All five of these patients continue to show mild degrees of corneal scarring. None have cleared completely, including the additional two patients who were lost to the study. All patients showed some evidence of regression due to normal healing mechanisms, consisting of epithelial hyperplasia and new collagen formation from activated keratocytes in the stromal bed. The initial excavations tended to fill in by approximately 30% to 50%, but tLe diopter regression was less, amounting to only 30% to 50%. After 6 months, the process seemed to stabilize and all eyes revealed permanent residual excavations or a flattening effect. Several eyes received steroids postoperatively, but not for prolonged periods. The normal healing mechanisms in primates seem to produce greater degrees of reaction with loss of excavation by as much as 50% to 80%. After 6 months, the changes appeared to stabilize and were permanent. Doctor Waring mentioned that their studies, and the observations of others, revealed that a great majority of the eyes seemed to clear almost completely and it is almost impossible for a nonbiased observer to differentiate between the ablated and the nonablated eyes of a given individual on slit lamp examination. We have not seen this almost complete clearing in our patients nor have we observed it in the eyes present at the 1989 meeting of the American Academy of Ophthalmology by the LSU group. The 1+ trace haze in three of the patients, and the $1^1/_2$+ haze in the remaining two would, in my judgment, be of clinical significance in discriminating individuals. They might be able to obtain 20/25 vision on a standard Snellen chart, but I feel certain that they would experience some glare and contrast sensitivity problems. This is consistent with our observation on eyes with minimal central corneal scarring or hazing from other pathologic conditions such as herpetic or foreign body scarring. These patients frequently complain of glare when the minimal scarring is centrally located and is barely detectable on slit lamp examination. These patients are able to read 20/20 on the Snellen chart, but may be somewhat more hesitant. It is interesting that both Doctor Lindstrom and Doctor Waring report that they have performed contrast sensitivity studies on patients treated with excimer laser and there is very little contrast sensitivity loss. Perhaps with more refined and sensitive tests, this will not be the case. In all fairness, it must be stated that there have been refinements in beam technology over the past 3 years, thus resulting in lesser degrees of corneal scarring then we observed in our series. Doctor L'Esperance and I were working with relatively primitive prototype equipment. It should also be stated that the prolonged utilization of steroids

postoperatively undoubtedly played a significant factor in scar reduction. It remains doubtful, however, that the normal healing mechanisms can be totally suppressed. For the moment, I would say that the jury is still out on this problem, and I agree with Doctor Waring who states that we are lucky to have an FDA that is very carefully monitoring these studies in the United States. In talking to FDA officials, it is my understanding that responsible authorities, in some of our foreign countries where there is no FDA and they are running wild with this new technology, are becoming increasingly concerned. Apparently, significant degrees of corneal scarring have been produced in some patients, and these responsible authorities are beginning to ask our FDA officials for copies of their excimer protocols.

Once again, my congratulations to Doctor Lindstrom and Doctor Waring for their excellent presentation.

DR GEORGE SPAETH. I would like to ask Doctor Lindstrom a question. The question is, is having myopia, having a disease?

DR FRANCIS A. L'ESPERANCE. First of all I would like to congratulate Doctors Lindstrom and Waring for both the comments and the excellent papers.

Just antidotally, the interesting thing about the pain was that the first three patients that we had (Doctor Taylor and I reported this series to the Society in 1988), the first patient was given a case of beer and he complained of no pain whatsoever for the first few days. The second patient was given a case of scotch and also complained of little discomfort. And the third person I think had three cases of scotch, but anyway, they did get through the initial painful period.

The other interesting thing with our patients was our third patient, who was done in August 1987 and which was the first seeing eye treated worldwide. This patient had 20/20 vision and had a nasally located malignant melanoma. After he was treated with a myopic correction which made him +3.25 D hyperopic, he was sent back to Syracuse. With that particular correction in Syracuse, he was brought back to 20/15 vision 14 days after the treatment. Then a few days after that the treated eye was enucleated. But he actually was the first human seeing eye that was treated by lamellar keratectomy.

The question I would like to ask, concerns the regression of the intended correction following treatment. Regression seems to be one of the biggest problems and I would like to have Doctor Lindstrom talk a little about that subject. What is his experience, what are his percentages, and how do they vary at particular dioptic levels. Again, I congratulate both Doctor Lindstrom and the discusser on their excellent presentations.

DR RICHARD L. LINDSTROM. Thank you. I wrote this all down, so hopefully I won't miss too many of the things I have been asked to comment on. As you know, Doctor Waring and I are good friends and are on the same team as far as trying to apply a scientific approach with two different groups who are looking at excimer results. Doctor Waring, I appreciate your comments.

The pattern of healing has been a little different with the Taunton instrument

than it was with the early work with the Summit instrument. The early work with the Summit instrument used significantly smaller optical zones, 3.5 initially and 4.5 later and they had more early overcorrection and significantly more difficulty with halos at night. The smallest optical zone we used in the Taunton series was 5.2 mm and many of our patients have a 6 mm optical zone. I think that may have influenced the clinical results, because we did have that smoother blend. With our instrument we are now capable of up to a 7 mm optical zone on some of the lower myopes.

I am not impressed that the bandage contact lens does anything other than give the patient some comfort and reassurance to see a little better a little faster. I don't believe it influences stromal healing. Although it may help epithelial stability.

As far as the potential benefit of steroids in the rabbit they mainly effect the collagen deposition and not the epithelial hyperplasia. I expect as the studies continue that the steroids will, perhaps, be shown to be of some value in decreasing the amount of collagen that is deposited and the amount of hazing that we see. But I don't think it will eliminate the regression. I personally think the regression is primarily epithelial hyperplasia, in most cases. This will probably not be steroid responsive and, perhaps be somewhat unpredictable. I think if you created a facet or a flat spot on the cornea it fills in with epithelium and the cornea only wants to be so flat, it wants to have some curvature with a smooth surface and I think epithelial hyperplasia is the cornea response when overly flat. We saw that in myopic epikeratophakia and it certainly was my experience with the one patient who completely regressed that the etiology turned out to be primarily epithelial hyperplasia. I don't think we have anything that will modulate that other than perhaps larger optical zones, and that is why we have gone to 6 to 7 mm.

I was asked about centration, how good are we? I would say 100% of the patients have a decentered treatment zone. We are not good enough to have it perfectly centered in any patient. We have asked Doctor Maguire, at the Mayo Clinic, who is an individual who had done a lot of work with topography to help us study our patients and using computed anatomy topographic analysis. His work was published in the *Journal of Corneal & Refractive Surgery*. His work suggests that the leeway we have is about 1 mm. So we have to have the center of our treatment zone within 1 mm of the patient's visual axis and it turns out that that gives us some margin for error, but one of my patients was off more than that and had a degradation of visual quality both subjectively and objectively. So, centration is something that we will have to do well. I don't know what is the best way. We are now using patient fixation plus some assistance from the surgeon. If I looked at the future I think the patient is going to come in, the surgeon is going to evaluate him and then tell him to go back and be treated at the laser. It will be like driving into these automatic car washes, the patient will walk into the room and the computer will say "lay down and get on the table" and the table will snap the patient in under the laser and a voice will come out of the computer and it will say "please look at the green light" and the patient will look at the green light and they will automatically be centered underneath the laser. The surgeon or the technician will enter their myopia or maybe they will do it themselves and they will be

treated. And if they lose fixation the machine will shut off and when they refixate the machine will turn on again. Probably the surgeon won't even have to be in the same room. That is, perhaps, one of the interesting and exciting, but also confusing and frightening things about this technology. I see the future as having it be totally automatic, totally nonsurgeon dependent, at least during the procedure. There is, however, I think surgeon dependence on counseling and surgeon dependence on treating the patient postoperatively because they do have a significant corneal defect and need to be treated. But I think the treatment can all be automated and done much better than I can do it as an ophthalmologist, because I can't hold the eye perfectly stable. Eventually, the machine will do that.

We do create multifocal lenses. The cornea is aspheric when we start and is aspheric when we are done. It is just that it is aspheric in the opposite way. I don't think we fully understand yet what that means. We start out with a cornea that is usually steeper in the center and flatter in the periphery and we end up with one that is flatter in the center and steeper in the midperiphery. It is still aspheric. I'm not super impressed that the patient has a greater multifocal capability postoperatively than they do preoperatively. I think we have an aspheric cornea when we start and we have an aspheric cornea when we are done. Quite frankly I don't know which one is better but I'll bet that the one that was created by evolution is better than the one that we are creating. I will make a comment for Doctors Spaeth, Kramer, and Wood in just a minute.

With regard to clinical results, we did treat the higher myopes first and my hope was that this would work for the higher myope. It looks like it's not for high myopes, but for the lower myope. If you look at contact lens wear in the United States, 90% of the patients who opt for contact lenses are between −1.00 and −6.00 D. So it turns out that for the patient who doesn't want to be spectacle dependent and who is looking for an alternative, if you believe that one of those alternatives is a contact lens, which I do, 90% who don't want to wear glasses are between −1.00 and −6.00 D. So that means that excimer laser technology will be effective for 90% of the patients who are looking for an alternative even if it is only good up to −6.00 D. Since it looks like it is effective up to −5.00 or 6.00 D the vast majority of patients will be satisfactorily treated with this instrument, but certainly we know the higher myope is something we should try to approach with alternative techniques in the future.

Doctor Kramer, I do not think these are observations, I think this is good science. It is a prospective trial. We have designed it carefully, we are collecting data carefully and every kind of data that we can measure. I think we are trying to report it honestly. If you look at the surgeons involved, I think they all tried to report their results honestly. I would accept the criticism that we don't have adequate data and long enough follow-up to have definitive opinions and so I will agree that we are making observations with regard to having opinions. But I would not agree that it was not a well controlled scientific study. I think it is as well controlled as any clinical trial can be.

We have had complications with steroids. We have had two steroid responders. We can expect to have 5% to 6% of our patients to be gg, and so I expect about 6%

should be steroid responders. Our were not severe and we stopped the steroid with resolution of pressure. There have been patients in other studies who have had reactivation of herpes simplex. It looks like we can use a lower dose of steroid than we did with similar results. Recent work at LSU suggests that a lower dose of steroid can achieve almost the same result that we achieved with a higher dose of steroid. So we have to figure out what is the minimum dose of steroid that is effective, but we certainly will have complications. With any use of steroid one of those potential complications is poor patient compliance. That one bothers me, if steroids are required.

Doctor Baum asked about individual variability. I'm convinced that it is a legitimate concern. If we look at all the patients that have been done, something like 1% to 4% seem to respond differently. Some of those patients seem to get more scarring than we expect. I now have 1 patient of the 100 cases in our series, who has much more scarring than anyone else. It was not expected. In the LSU series they have two who have much more scarring than anyone expected. And in Seiler's group, early on of the 200 he reported, 3 patients had much more scarring than anyone expected. And so 1% to 2% may have more. Is that acceptable? I don't know. These are fairly young patients. I do not feel we have to collect blood in advance. I presume 99% of them will still be alive in 10 years, so I am guessing, I could collect the blood in 10 years if I know what it is I am going to study. So I am not certain collecting blood in advance is necessary. I am convinced there is a differential in wound healing and that is a problem, but I do not know how to screen for it. There is also a differential in preoperative corneal topography and it probably depends on what you start with as to what you get. We need to understand much more about the initial point of topography and we are just starting to get instruments that will help us study that problem.

Doctor Wood wants to know if we are trying to fool "Mother Nature." I played golf with Doctor Wood and he was trying to fool mother nature all day. I think Doctor Spaeth's comment may fall into the same category. Is trying to treat myopia trying to fool mother nature? Is myopia a disease? After being a refractive surgeon for 10 years, I am convinced it is to the patients. Now, whether or not it is to a given ophthalmologist is another question. The myopia is significant to the patient and I guess the thing that continues to drive me in refractive surgery is the patient's desires and the patient's responses. It certainly is a physical defect or perhaps a physical handicap. The change we make in the eye is a functional change and not a cosmetic change, we don't change the way the eye looks, other than the fact that maybe the patients look different without spectacles. We change the way the eye functions and maybe it's like treating dwarfism or giantism or something else like that. It certainly is not like treating cancer. I see it as a physical deficit or physical handicap and I feel that what I am doing is functional not cosmetic. On the other hand I don't know whether or not I would define it as a disease. Nonetheless, the patients seem to define it as a disease and I think we should listen to our patients.

What about pain? Doctor L'Esperance, I appreciate your comments and certainly your fine pioneering work. The pain is significant but manageable. I haven't used a case of beer or a case of scotch but I have used narcotics and one six pack.

Regression is greater with the high myopes. The flatter the cornea the greater the epithelial hyperplasia. That is a theory, that is not proven, but that is my current opinion and so I think the higher myopes regress more because we make the cornea flatter and we end up with thicker epithelium after the healing response.

In response to your comments, Doctor Taylor, you actually did play a role in recruiting me for the study and I appreciate that because I find it very interesting. Your results show more scarring, I think, than those of us who have worked more recently. I do not know if the laser is better, if we use different steroids, or what factor may be involved. When we look at our patients at 1 year, it really is difficult to differentiate the treated from the nontreated eye. We have surgeons visiting all the time. Some of them are very skeptical and I let them walk in and look at my patients and most of the time it is hard to differentiate at 1 year which eye was treated and which was not. Now that does not include that small number of outliers, 1% to 5%, where I can clearly see a scar on the eye even at 12 months. And so I am not sure about that group. But we do not have 100% persistent haze at 3 years like Doctor Taylor had in his early cases. Maybe we used more steroid or maybe we had a better homogenized beam in our laser. Our contrast sensitivity results are what they are, namely at 3 months postoperative there is no measurable loss of contrast. So again that suggests a clearer cornea than in the early work.

I also agree that we are fortunate to have an FDA. I was in Australia this last weekend. They are bringing six lasers into Australia in the next 6 months and they intend to treat thousands of patients. They have approximately 20 to 30 lasers in Italy and a lot of patients are being treated in very significant series before we really fully understand the technology. And so I am glad we do have an FDA, I am glad we worked together with them to create a quality protocol, and I do think you will see good data come out of studies in the United States.

Thank you for all the comments.