Six-month results of the Multicenter Phase I Study of Excimer Laser Myopic Keratomileusis

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ABSTRACT

We report six-month results of the Summit Technology Myopic Keratomileusis Phase I multicenter study. Fifty-seven eyes of 57 patients had keratomileusis to correct high myopia. A microkeratome was used for the primary keratectomy and the excimer laser was used to ablate the stroma of the resected lenticle (cap) or the stromal bed (in situ). At six months, 31 of the 47 eyes available for follow-up (65.9%) had uncorrected visual acuity of 20/40 or better; 16 (34.0%) had uncorrected acuity of 20/25 or better. Thirty-seven eyes (78.7%) maintained the same (± one Snellen line) best corrected visual acuity as before surgery; seven (14.9%) lost two lines and three (6.4%) lost more than two lines. In addition to the six-month multicenter study results, we report two year results in a subset of 28 eyes (22 from the multicenter study and six fellow eyes). At six months, 17 of the 24 eyes available for follow-up (70.9%) had uncorrected visual acuity of 20/40 or better and nine (37.5%) had uncorrected acuity of 20/25 or better, including eyes that had worse than 20/80 best corrected visual acuity preoperatively. At 24 months, five of the seven eyes available for follow-up (71.4%) had uncorrected acuity of 20/25 or better. Only one patient lost two lines of best corrected vision at six months and no patient lost more than two lines; at 24 months, all patients maintained (± one line) best corrected vision. Our findings suggest that myopic keratomileusis performed with the microkeratome, using the excimer laser for the refractive cut, is a safe, effective, and relatively predictable way to correct high myopia in the 6.0 to 25.0 diopter range. With longer follow-up, the accuracy of the refractive correction, as well as best corrected visual acuity and uncorrected visual acuity, continues to improve.

Key Words: excimer laser, high myopia, keratomileusis, microkeratome

More than 30 years ago, Barraquer developed myopic keratomileusis (MKM) to correct high myopia. His technique begins with a "primary keratectomy" in which an anterior corneal lenticle is resected with a microkeratome. For the "refractive keratectomy," the lenticle is frozen with a cryolathe and the myopic correction carved with a lathe similar to a contact lens lathe. The frozen lenticle is then thawed and sutured back in place with an eight-bite, antitorque suture.[1] Problems of the technique include mastering the use of the microkeratome and cryolathe and persistent corneal haze from the biological damage that occurs during freezing.[1,2]

To lessen the risk of damage, Krumeich developed planar nonfreeze keratomileusis, in which the primary keratectomy is performed with a microkeratome and the refractive keratectomy performed on the lenticle without freezing the tissue. The technique is still difficult; however, the corneas clear much more quickly. Refractive predictability is only fair (J. Krumeich, M.D., "Myopic Keratomileusis," presented at the First International Congress on Keratomileusis, Venice, September 1990).

Ruiz and Barraquer created an in situ keratomileusis technique that also requires two keratectomies.[1,3] The

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primary keratectomy, as in the Barraquer and Krumeich procedures, creates a planar disc, which is set aside as the refractive keratectomy is performed on the exposed stromal bed. Although the planar lenticle was originally replaced and sutured,[3] the technique has evolved into a no-suture method. The procedure is now known as automated lamellar keratoplasty, as the movement of the microkeratome across the cornea is mechanical rather than manual.

In 1983, Trokel and Srinivasan first suggested using an argon–fluoride (193 nm) excimer laser to correct refractive errors.[4–7] Photorefractive keratectomy (PRK) using the excimer laser has proven effective in correcting low to moderate myopia from 1.50 diopters (D) to 6.00 D. Excessive scarring and regression of effect was shown in early studies in which correction of higher amounts of myopia was tried.[8,9]

In 1989, Buratto conceived a new technique to achieve refractive correction using the microkeratome to perform the primary planar keratectomy and the excimer laser to sculpt the back of the lenticle (cap) or the bed in situ. The results have been excellent.[10–13] The excimer laser provides greater refractive predictability than previously used mechanical techniques.[3,14] Based on the reported and published success of the Buratto technique, in June 1991 Summit Technology began the FDA-approved, Multicenter Phase I Study of Excimer Laser Myopic Keratomileusis in the United States.

We report the six-month results of this study, as well as two-year results in a subset.

MATERIALS AND METHODS

To be included in the Excimer Laser Myopic Keratomileusis Phase I Study, patients had to be 21 years or older with a stable refraction and contact lens intolerance. Correction of 6.0 D to 25.0 D of myopia was attempted. Excluded were patients with unstable myopia, dry eyes, poorly controlled glaucoma, treatable retinal pathology, connective tissue disorders, previous refractive surgery on the eye to be treated, K-readings less than 37.5 or greater than 47.0, and central corneal thickness less than 450 μm. Informed consent was obtained according to standardized Summit and FDA protocols.

Anesthesia methods evolved over the three-year study from general, to retrobulbar or peribulbar, to topical. A drop of 1% pilocarpine was administered preoperatively. A 3 mm marker coated with gentian violet was used to mark the central cornea over the entrance pupil. A peripheral 10 mm corneal mark was made, along with a radial mark for subsequent realignment of the lenticle. In all but two cases, the primary keratectomy was made with the automated microkeratome of Ruiz (Steinway/Chiron, Inc., Boca Raton, FL). The BKS 1000 microkeratome was used for two procedures, as described by Krumeich.[2] In the early part of the study, the excimer ablation refractive correction was to be performed on the cap; thus, a 300 μm lenticle was desired and the 300 μm plate selected for the microkeratome. The planned resection diameter of the lenticle was to be 7.2 mm. During later phases of the study, the primary resection was decreased to 160 μm and the subsequent excimer ablation performed in the bed (in situ).

The refractive excimer correction was performed with the Summit Excimed UV 200LA laser (Summit Technology, Waltham, MA). The repetition rate was 10 Hz with an ablation zone of 5.0 mm, except for three cases in which the ablation zone was decreased to 4.5 mm to allow for higher refractive correction. The fluence of the laser was factory set at 180 mJ/cm^2, with an ablation of 0.25 μm/pulse. The computer software was designed for myopic keratomileusis and thus allowed ablations up to 25 D. When the ablation was performed on the lenticle, the lenticle was placed stromal side up in an antidesiccation chamber supplied with the Chiron automated microkeratome. The aiming helium–neon (He–Ne) beams were centered on the center of the 3 mm pupillary zone mark, and the excimer ablation for the appropriate amount of myopic correction was performed 5 mm from the ablation zone. About 10 μm of tissue was removed for each diopter of desired correction.

If the primary resection was too thin, or if an in situ correction was planned, the patient was brought to the excimer laser. The ablation, performed in the stromal bed, was centered on the pupil with the patient fixating on the green fixation light and the divergent He–Ne beams focused on the 3 o'clock and 9 o'clock pupillary margins. Then the planar lenticle was replaced.

Four eyes were done in situ; in the remaining 53, the lenticle was treated. After both types of procedures in the 20 eyes treated in the early part of the study, the lenticle was repositioned on the corneal bed and sutured in place with an eight-bite, antitorque, 10-0 nylon suture. In the later part of the study, most patients were not sutured; the air-drying technique allowed the lenticle to adhere to the bed.

Postoperatively, a pressure patch was placed if the lenticle was sutured or the lids were taped shut if a no-stitch technique was used. Re-epithelialization was usually complete the morning after surgery, and topical antibiotics and steroids were administered and tapered over two to three weeks at the surgeon's discretion. When the eight-bite, antitorque suture was used, it was removed ten to 14 days postoperatively.

Patients were examined at 1 day; 1 week; and 1, 2, 3, 6, 9, 12, and 24 months after surgery, according to the protocol. At each examination, uncorrected visual acuity and manifest refraction with best spectacle corrected visual acuity were measured (Snellen and ETDRS charts) with small and large pupils controlled by room lighting conditions. Best corrected visual acuity with glare using the Brightness Acuity Test on medium intensity, keratometry readings, intraocular pressure, corneal status, and complications were recorded.

RESULTS

In the Summit Technology Myopic Keratomileusis Phase I study, 57 eyes of 57 patients (28 female) were treated between June 22, 1991, and September 9, 1993. We report the six-month results for all 57 eyes and two-year results for a subset of 22 consecutive patients (28 eyes) treated by the medical monitor (S.F.B.).

Mean age of the patients was 35.8 years (range 21 to 51 years; SD = 8.5). Attempted correction for the 57 eyes in the primary study ranged from 6.0 D to 19.0 D (Figure 1). The number of laser pulses delivered ranged from 240 to 676 (average 360.5 pulses). Mean diameter of the primary keratectomy was 7.4 mm (range 5.0 mm to 9.0 mm). The (primary resection) lenticle thickness ranged from 150 μm to 400 μm, with a small number intentionally made thin for planned in situ ablation.

In the multicenter study, the ablation was performed on the lenticle in 53 cases and in situ in four cases. Mean ablation depth was 90.7 μm (range 61 μm to 167 μm; SD = 24.9). Surgery lasted from 24 to 75 minutes (mean 41.2 minutes).

Most eyes were re-epithelialized the morning following surgery after the patch or tape was removed; 51 were re-epithelialized by 72 hours and 54 by 96 hours. Two patients with perforated lenticles during the procedure had delayed re-epithelialization.

Corneal Haze

Unlike PRK, in which subepithelial reticular corneal haze is anticipated, excimer MKM rarely causes corneal haze within the interface. In the multicenter group at six months, seven eyes had trace haze and three eyes had mild haze, as defined in the Summit protocol.

Refraction

In the multicenter study, mean preoperative spherical equivalent was −10.70 D (range −6.13 to −21.75 D; SD = 3.29). At the six-month follow-up (n = 47), manifest spherical equivalent was −0.63 (range −6.50 to +6.63; SD = 2.41) (Figure 2).

In the subset, mean preoperative spherical equivalent was −10.94 D (range −6.13 to −21.75 D; SD = 0.54). At six months (n = 24), the manifest spherical equivalent was −0.002 (range −5.87 to +2.63; SD = 1.22). At 12 months (n = 14), the spherical equivalent was −0.69 (range −6.75 to +1.75; SD = 1.38), and at 24 months (n = 7), the spherical equivalent was −0.23 (range −1.75 to +1.88; SD = 1.01) (Figures 3 to 6).

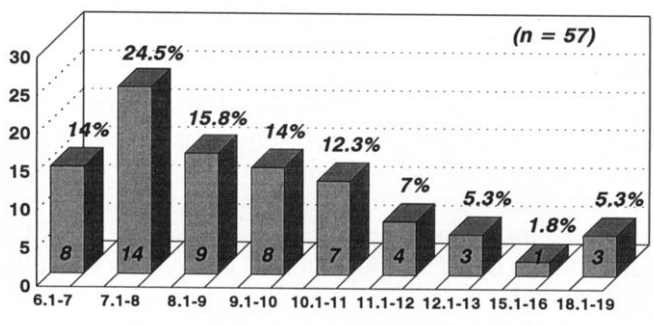

Fig. 1. (Brint) Distribution of attempted correction in the multicenter study.

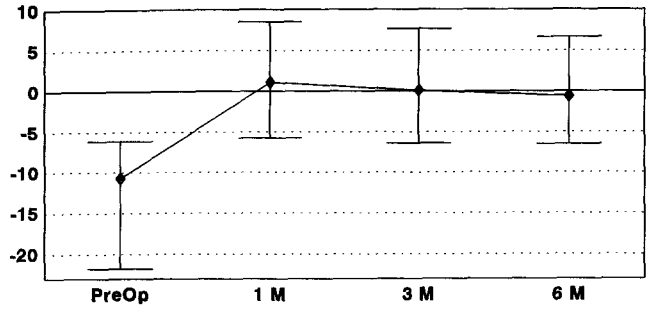

Fig. 2. (Brint) Mean spherical equivalent over time in the multicenter study.

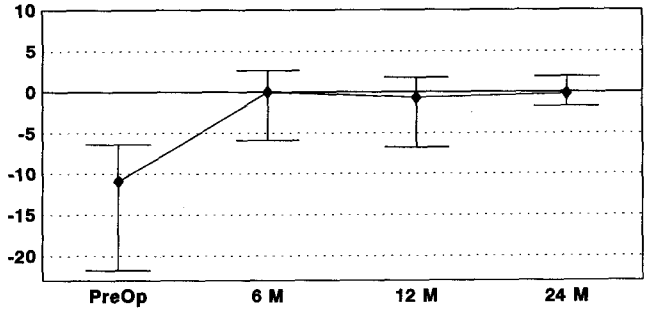

Fig. 3. (Brint) Mean spherical equivalent over time in the subset.

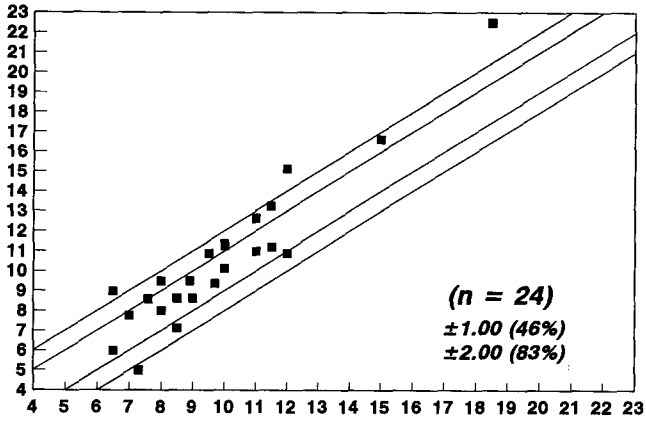

Fig. 4. (Brint) Attempted versus achieved corrections at six months in the subset.

Visual Acuity

In the multicenter study, preoperative uncorrected visual acuity ranged from 20/200 to 20/800; 47 eyes had an uncorrected acuity of 20/800 or worse. Preoperative best corrected acuity was 20/60 or worse in five eyes. At

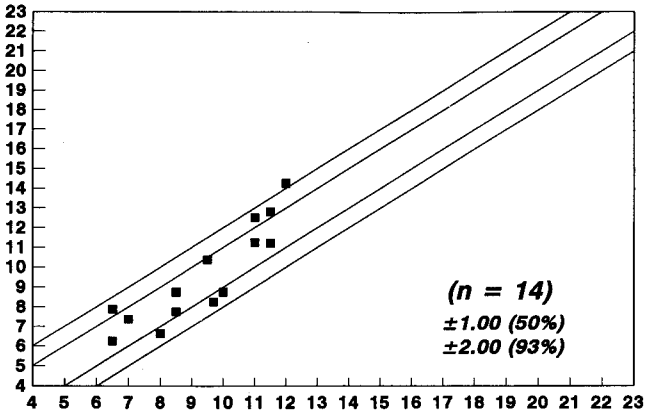

Fig. 5. (Brint) Attempted versus achieved corrections at 12 months in the subset.

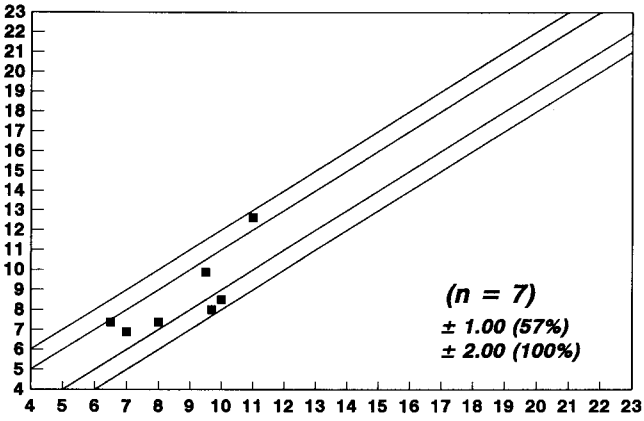

Fig. 6. (Brint) Attempted versus achieved corrections at 24 months in the subset.

six months (n = 47), 31 eyes (65.9%) had 20/40 or better uncorrected visual acuity; 16 (34.1%) had an uncorrected acuity of 20/25 or better (Table 1).

In the subset, four eyes had preoperative best corrected acuity of 20/80 or worse. At six months (n = 24), 17 eyes (70.9%) had 20/40 or better uncorrected visual acuity and nine (37.5%) had 20/25 or better uncorrected acuity, including the eyes that had 20/80 or worse best corrected acuity preoperatively. At 12 months (n = 14), six eyes (42.8%) had uncorrected acuity of 20/25 or better. At 24 months (n = 7), five eyes (71.4%) had uncorrected acuity of 20/25 or better, demonstrating continued improvement in uncorrected visual acuity with longer follow-up (Table 2).

In the multicenter study, at six months the best corrected postoperative visual acuity was within one Snellen line of the preoperative best corrected acuity in 37 eyes (79.0%). Seven eyes (15.0%) had a decrease of two Snellen lines; three (6.0%) had a decrease of more than two Snellen lines.

In the subset, at six months only one eye (3.0%) had lost two lines of best corrected visual acuity; no eye lost more than two lines.

Table 1. Six-month postoperative uncorrected visual acuity in the multicenter study (n = 47).

Visual Acuity	Number of Eyes
20/20 or better	10
20/25	6
20/30	8
20/40	7
20/50	2
20/62.5–20/80	6
20/100–20/125	2
20/200	5
20/500	1

Table 2. Postoperative uncorrected visual acuity at six, 12, and 24 months in the subset.

	Number of Eyes		
Visual Acuity	6 Months (n = 24)	12 Months (n = 14)	24 Months (n = 7)
≤20/20	5	3	3
20/25	4	3	2
20/30	4	—	—
20/40	4	1	—
20/50	1	3	—
20/60	2	—	—
20/80	—	1	—
20/100	1	—	—
20/200	3	3	2

Keratometry

Mean preoperative refractive cylinder was 1.36 D (range 0 to −4.00 D). At six months, the mean postoperative cylinder was 1.42 (range 0 to 7.50; SD = 1.31) (Figure 7). In the multicenter study, no eyes had preoperative irregular astigmatism; however, 10 eyes (21.0%) had irregular astigmatism at the six-month postoperative follow-up visit.

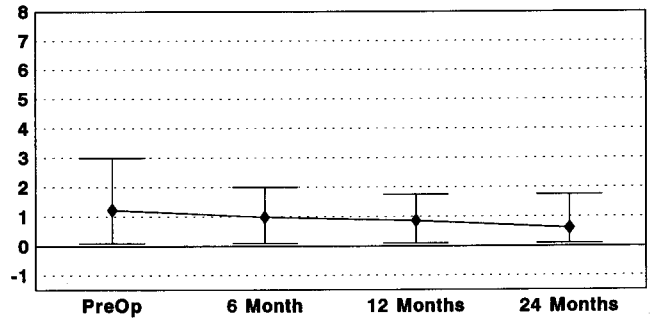

Fig. 7. (Brint) Mean cylinder over time in the subset.

The mean preoperative keratometry reading was 44.34 D. Mean keratometric astigmatism was 1.09 D. Six months after surgery, the mean keratometry reading was 38.75 D and the mean keratometric astigmatism 1.31 D (SD = 2.71) (Figure 8).

Complications

Other than the two perforated lenticles, no unanticipated adverse reactions were reported during the 57 MKM procedures in the multicenter study and during the six surgeries on the fellow eyes. One patient with a perforation had the lenticle removed and replaced with a previously ablated homograft lenticle five days after the original MKM procedure. The ablation of the homograft tissue was inadequate, and the patient remains highly myopic. One procedure was interrupted because the laser stopped firing during the procedure.

One eye had mild irregularity in Bowman's layer with mild opacification, and one showed mild wrinkling of Bowman's layer. Seven eyes had trace interface deposits and one eye had mild interface deposits. One eye had mild ghost image, and one eye had marked halo, as assessed by a patient questionnaire. One patient in the no-stitch group required repositioning of the lenticle three days after surgery.

DISCUSSION

The combination of using the microkeratome for the primary resection and excimer laser ablation, either on the cap or in situ, for the refractive correction seems to offer significant advantages over previous lamellar refractive techniques that require freezing of the tissue or a second planar refractive incision.

The excimer laser makes the performance of the refractive cut of the keratomileusis procedure more forgiving, as the centration of the ablation on either the previously marked center of the cap or the center of the pupil is superior to and more predictable than centration with a mechanical refractive cut. Ablation of the cap theoretically offers advantages over in situ ablation in that one is able to center the ablation perfectly over the previously placed 3 mm pupillary zone marker, and the issue of patient fixation or movement is negated. With in situ ablation, the surgeon must be concerned about eye movement and the patient's ability to fixate.

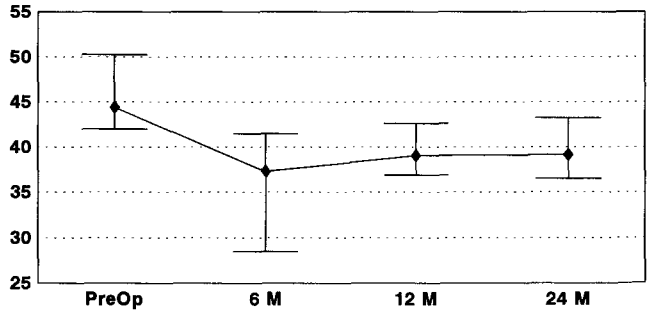

Fig. 8. (Brint) Change in mean keratometry over time in the subset.

In situ ablation, with the hinged primary resection (flap) technique, is a more rapid procedure, which can be performed entirely underneath the excimer laser's microscope. Regardless of which technique is used, postoperative rehabilitation is quicker and easier than after PRK because the epithelium and Bowman's layer are not disturbed. There appeared to be no difference in the results of these two techniques. Drops are required for two to three weeks, rather than months as with PRK, and pain is not significant because there is no extensive de-epithelialization.

The outcome of the procedures is most affected by the accuracy and ease of the microkeratome cut. When an even, smooth cut is achieved, the best and most predictable results are obtained. The use of the excimer laser for the refractive correction partially forgives even an irregular microkeratome resection, providing an adequate amount of tissue is removed to allow proper tissue ablation. The loss of early best corrected vision is probably due to irregular astigmatism and wound healing, which disappear with time.

At this point in the evolution of refractive surgery, the combination of the microkeratome and the excimer laser appears to be an ideal technique to correct myopia up to 20 D. The best predictability of any refractive procedure for high myopia has upper limits of −20 D to −23 D. The potential exists to expand the technique's use to correct combined myopia and astigmatism as well as hyperopia.

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