NEW TECHNIQUE

Topography-guided Transepithelial Surface Ablation Followed by Corneal Collagen Cross-linking Performed in a Single Combined Procedure for the Treatment of Keratoconus and Pellucid Marginal Degeneration

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ABSTRACT

PURPOSE: To evaluate a combination of topography-guided custom ablation and corneal collagen cross-linking (CXL) in a single procedure for the treatment of keratectasia.

METHODS: Twelve eyes of 12 patients with keratectasia were treated with topography-guided custom ablation and CXL. Topography-guided custom ablation was performed using a transepithelial technique with the iVIS Suite 1 kHz flying spot excimer laser. Collagen cross-linking was performed immediately after topography-guided custom ablation, according to standard protocol. Postoperative follow-up examinations were performed at 1, 3, 6, and 12 months. Uncorrected visual acuity (UCVA), best spectacle-corrected visual acuity (BSCVA), refractive change, corneal topography, and pachymetry were analyzed pre- and postoperatively.

RESULTS: Mean UCVA increased from 20/1000 preoperatively to 20/125 12 months postoperatively. Mean BSCVA increased from 20/57 to 20/35, with no loss of lines of visual acuity. Mean astigmatism was reduced from 5.40±2.13 diopters (D) to 2.70±1.44 D, and keratometric asymmetry decreased from 6.38±1.02 D to 2.76±0.73 D. Only minor changes in posterior corneal surface elevation and stability of refraction were found, confirming that no progression of ectasia occurred during the observation time.

CONCLUSIONS: A combination of topography-guided custom ablation and CXL improved patients' visual, refractive, and topography outcomes and halted the progression of keratectasia within the observation period of 12 months. This method may postpone or eliminate the need for corneal transplantation in suitable cases with keratectasia. [*J Refract Surg*. 2009;xx:xxx-xxx.]

Keratectasia is often accompanied by visually disturbing irregular astigmatism, which leads to serious deterioration of vision. Traditionally, it has been treated by invasive procedures such as corneal transplantation[1] and, to some extent, by implantation of intracorneal ring segments.[2] A combination of topography-guided custom ablation—to improve vision—and corneal collagen cross-linking (CXL)—to make that visual improvement last—was first attempted by Kanellopoulos and Binder.[3] However, they applied CXL first and did not perform topography-guided custom ablation until 12 months later. The current study describes a combined procedure where topography-guided custom ablation is performed first, immediately followed by CXL.

PATIENTS AND METHODS

Twelve eyes of 12 patients (8 men, 4 women) were treated with topography-guided custom ablation and CXL at the University Hospital of North Norway, Tromsø, Norway. Mean patient age was 39.8±11.9 years (range: 26 to 62 years). Six cases were diagnosed as keratoconus and 6 as pellucid marginal degeneration. The inclusion criteria were diagnosis of keratectasia, best spectacle-corrected visual acuity (BSCVA) worse than 20/30 that could not be further improved by use of soft contact lenses, and no previous eye surgery. Exclusion criteria were corneal thickness <400 µm; keratometric readings >60.00 diopters (D); other active ocular disease; patients who were immunocompromised, pregnant, or who had atopic syndrome; known sensitivity to study medication;

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intraocular pressure >23 mmHg; history of glaucoma; or glaucoma suspects. The study was approved by the regional ethics committee, and patients signed informed consent concerning the new combined treatment.

Preoperative examination consisted of slit-lamp microscopy, Scheimpflug-based corneal topography/tomography (Precisio; Ligi, Taranto, Italy), visual acuity/manifest refraction (NIDEK RT 2100 system; NIDEK Co Ltd, Aichi, Japan), dynamic pupillometry (pMetrics, Ligi), Goldmann applanation tonometry, and central ultrasound pachymetry (Corneo-Gage Plus; Sonogage Inc, Cleveland, Ohio). Precisio was used for measurement of 1) anterior corneal elevation (used for topography-guided custom ablation), 2) keratometric asymmetry within the central 3 mm (for assessment of the corneal optical irregularity), and 3) maximum posterior corneal surface elevation above the floating best-fit sphere fitted at a 10-mm diameter (for assessment of corneal biomechanical stability).

A procedure consisting of transepithelial topography-guided custom ablation followed immediately by CXL (in the same session) was performed. Topography-guided custom ablation was performed using iVIS Suite (Ligi), which consists of the iRES laser, Scheimpflug-topographer/tomographer, dynamic pupillometer, and Corneal Interactive Programmed Topographic Ablation (CIPTA) software. With the iVIS topography-guided custom ablation system, the patient's refraction, corneal elevation data, and pupillometry data are imported into CIPTA software, which then compiles an ablation that transforms the actual corneal shape into a regularized aspheric shape of a desired curvature within a desired treatment zone. The CIPTA software fully customizes the ablation including parameters such as tilt, centration, and asphericity of the targeted corneal surface, as well as the size and shape of the optical and transition zones.

Maximum ablation depth was 60 µm, whereas the minimal postoperative corneal thickness was 400 µm. To optimize the visual outcome under these constraints, the CIPTA "restored morphological axis" and "minimal ablation" strategies were used. The mechanism of action of the former is described elsewhere.[4] In the minimal ablation strategy, the software suggests a curvature change that results in maximal reduction of the irregularities with the least possible amount of tissue consumption.

The CIPTA-generated ablation plan is transferred to the high-resolution, 0.6-mm dual flying-spot iRES excimer laser, which delivers an effective frequency of up to 1 kHz (2×<500 Hz) and employs a high-speed eye-tracking system with dynamic intraoperative cyclotorsional compensation based on iris recognition. In addition to its constant frequency per area delivery, the laser's fluence and shot pattern are optimized to minimize the ablation rate difference between corneal epithelium and stroma, making the transepithelial treatment the system's recommended surgical technique.[4] Transepithelial treatment consists of two parts: a lamellar ablation for epithelial removal, and a custom ablation for corneal stromal regularization to a desired curvature and toricity. In practice, these two ablations are summed and executed as a single continuous ablation.

Surgical protocol describing the use of medication before and during the excimer laser treatment is described elsewhere.[5] Immediately after the ablation, the pachymetric measurements were taken and the stroma was saturated by topically applied 0.1% riboflavin-5-phosphate and 20% dextran solution, as one drop every 3 minutes. In cases where the measurements of the minimal corneal thickness showed values <400 µm, hypotonic 0.1% riboflavin solution was applied until slight corneal edema and 400-µm thickness were achieved. After the corneal saturation was confirmed by presence of fluorescent flare in the anterior chamber, the cornea was irradiated by ultraviolet A (UVA) light for 30 minutes. A timer controlled UVA-illuminator (UV-X; IROC, Zurich, Switzerland) provided a homogeneous UVA (365 nm) light with 3 mW/cm^2 power within a circle of 9 mm in diameter. After the irradiation, non-preserved chloramphenicol (Novartis, Basel, Switzerland) eye drops were applied, as well as a bandage contact lens (Acuvue Oasys; Johnson & Johnson Vision Care Inc, Jacksonville, Fla), which was worn for 4 to 7 days. Dexamethasone with chloramphenicol (Novartis) eye drops were used four times daily for the first 2 weeks, and then replaced by a low potency steroid rimexolone 1% (Vexol; Alcon Laboratories Inc, Ft Worth, Tex) three times daily for another 2 weeks, and twice daily for the last 2 weeks. Valium 5 mg before sleep was prescribed for the first 3 days. Chilled 0.2% hyaluronic acid (for lubrication and lavage purposes) was used every 10 minutes for the remainder of the day after surgery and later as needed. Patients were seen on postoperative day 4 to 7 (upon bandage contact lens removal) and 1, 3, 6, and 12 months after surgery.

To calculate visual acuity averages and changes, all visual acuity measurements were converted from Snellen values to the logarithm of the minimum angle of resolution (logMAR) back to Snellen values. Vector analysis was used to analyze the changes of spherocylinders according to the Alpins' method.[6] The refractive outcome of astigmatism was represented as magnitude of error and angle of error.

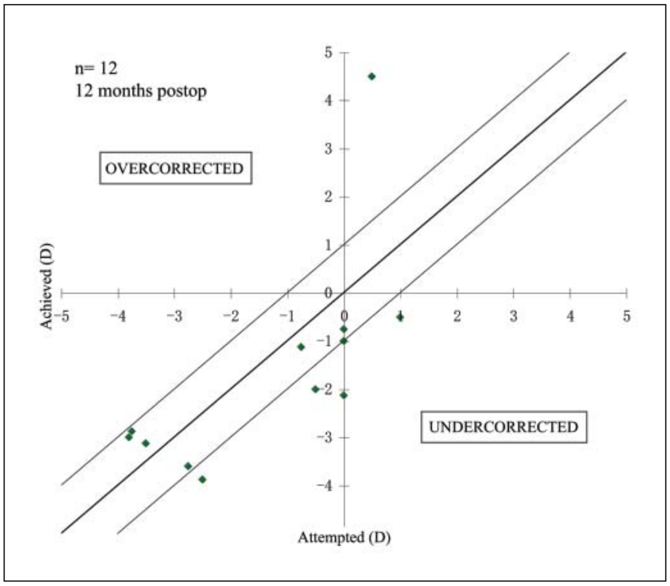

Figure 1. Attempted versus achieved spherical equivalent refraction 12 months after surgery in 12 eyes that underwent combined topography-guided custom ablation and corneal collagen cross-linking for the treatment of keratectasia.

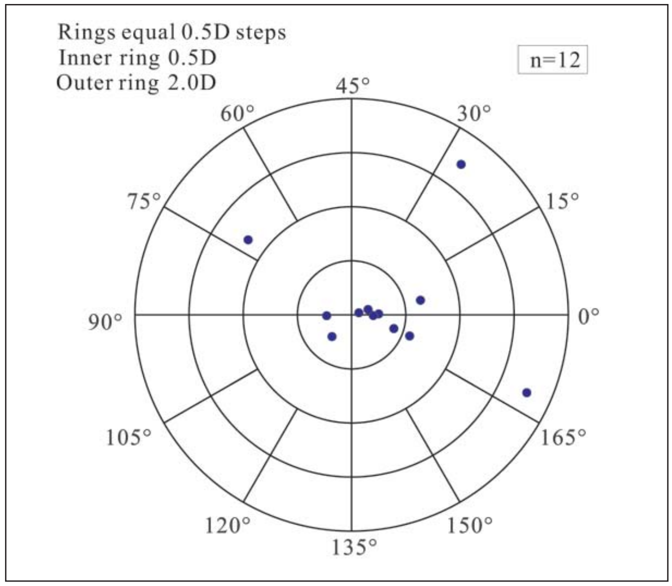

Figure 2. Double angle plot of magnitude and angle of error of astigmatism correction 12 months after surgery in 12 eyes that underwent combined topography-guided custom ablation and corneal collagen cross-linking for the treatment of keratectasia. Left and right deviations from zero-point show over- and undercorrections, whereas superior and inferior deviations show clockwise and counterclockwise angle error.

RESULTS

Mean preoperative uncorrected visual acuity (UCVA) was 20/1000 (range: 20/2000 to 20/200), and mean preoperative BSCVA was 20/60 (range: 20/200 to 20/30). Mean preoperative spherical equivalent refraction was +2.32±2.34 D, mean preoperative cylinder was 5.40±2.13 D, and mean keratometric asymmetry was 6.38±1.02 D.

Mean attempted spherical equivalent refraction correction was +0.99±1.50 D (range: +4.13 to +0.50 D), mean attempted cylinder correction was 2.92±1.59 D (range: 2.00 to 7.00 D), and mean maximum ablation depth was 54±7.3 µm (range: 39 to 60 µm).

At 12 months postoperative, mean UCVA increased to 20/125 and mean BSCVA increased to 20/35, whereas mean spherical equivalent refraction was reduced to +1.63±2.24 D, mean cylinder to 2.70±1.44 D, and mean keratometric asymmetry to 2.76±0.73 D. Figure 1 is a scattergram of attempted versus achieved spherical equivalent refraction, whereas a polar diagram shows the vector analysis of astigmatism correction (Fig 2). The Table shows preoperative and 12-month postoperative data for all 12 patients. None of the eyes lost lines of BSCVA, whereas 10 eyes gained 1 to 4 lines (Fig 3). Safety index was 1.60. Stability of spherical equivalent refraction is shown in Figure 4. In 4 (33%) of 12 eyes, spherical equivalent refraction changed ⩾1.00 D (P=.00). The increase of the posterior float elevation within the follow-up time was within 11 µm, confirming no progression of ectasia.

There were no complications other than bandage contact lens loss on postoperative day 1 in three cases, with consequent pain. No postoperative haze graded higher than 1 was observed at any of the follow-up examinations. Figures 5 to 10 show preoperative anterior and posterior elevation maps, pachymetry and curvature maps, as well as postoperative curvature maps of patients 1 and 2.

DISCUSSION

Corneal transplantation for keratectasia is a difficult procedure with a long and uncertain visual recovery.[7] The idea of an alternative treatment with a chance to postpone or replace transplantation and improve vision was appealing to the patients in the current study and they expressed a strong motivation for the new combined procedure presented herein.

Corneal collagen cross-linking has been clinically available for a number of years.[8,9] It stiffens the stroma and halts the ectatic process, but it does not directly address the patient's refractive error. The spherocylindrical change that it causes is limited, ranging typically from a slight steepening to approximately 2.00 D of flattening,[8] varying seemingly unpredictably from case to case. Excimer laser correction of the refractive errors in keratectasia has been previously attempted with variable success concerning predictability and stability.[10-25]

Topography-guided custom ablation seems to be a suitable treatment for regularizing visually disturb-

TABLE

Characteristics of 12 Eyes of 12 Patients Who Underwent Topography-guided Custom Ablation and Corneal Collagen Cross-linking for the Treatment of Keratectasia

Patient No.	Age (y)	Diagnosis	Time	UCVA	Manifest Refraction
1	29	Keratoconus	Preop	20/800	−0.75 −6.00 × 132
			Postop	20/125	−2.00 −1.75 × 115
2	62	PMD	Preop	20/2000	+6.00 −11.00 × 92
			Postop	20/50	+0.00 −4.25 × 90
3	42	Keratoconus	Preop	20/2000	+2.50 −5.00 × 180
			Postop	20/200	+0.00 −4.00 × 160
4	29	Keratoconus	Preop	20/600	−1.75 −4.25 × 64
			Postop	20/60	−2.00 −2.00 × 65
5	45	PMD	Preop	20/1000	+0.25 −6.25 × 117
			Postop	20/50	+0.25 −2.50 × 100
6	30	Keratoconus	Preop	20/1000	−4.75 −4.25 × 67
			Postop	20/200	−3.00 −1.25 × 65
7	49	Keratoconus	Preop	20/200	+2.50 −3.00 × 17
			Postop	20/400	+5.00 −1.00 × 40
8	26	Keratoconus	Preop	20/400	−2.75 −3.50 × 175
			Postop	20/200	−3.25 −1.25 × 25
9	27	Keratoconus	Preop	20/600	+1.25 −3.50 × 145
			Postop	20/60	+0.50 −2.00 × 140
10	55	PMD	Preop	20/600	−0.25 −6.50 × 88
			Postop	20/100	−1.75 −2.75 × 114
11	38	PMD	Preop	20/1000	+1.25 −6.00 × 75
			Postop	20/125	+1.50 −5.25 × 70
12	46	PMD	Preop	20/600	+1.00 −5.50 × 100
			Postop	20/400	+1.50 −4.50 × 105

UCVA = uncorrected visual acuity, BSCVA = best spectacle-corrected visual acuity, asymmetry = keratometric asymmetry within the central 3 mm from vertex, PFE = maximum postoperative float elevation, PMD = pellucid marginal degeneration

ing irregular astigmatism[26] in non-ectatic corneas with sufficient thickness, but it is commonly considered contraindicated in unstable corneas with keratectasia because of the danger of worsening of the corneal structural stability and its consequences, caused by tissue removal. Topography-guided custom ablation and CXL combines the benefits of both treatments with the potential for creating a safe and stable optical improvement of the irregular keratectatic cornea in a less invasive fashion than the currently available treatment options. In the study by Kanellopoulos and Binder,[3] performing laser ablation 12 months after CXL caused a reduction in strength in the ablation area by ablating the superficial (supposedly the most strengthened) part of the CXL-treated cornea. Therefore in the current study, the order was reversed and CXL was performed immediately after topography-guided custom ablation to strengthen the stroma at a uniform depth, before the ectatic process had a chance to progress. Another advantage of this single combined procedure compared to the sequential procedure of Kanellopoulos is that the patient avoids two deepithelializations. The risk of haze, which can occur after surface ablation due to keratocyte activation,[27] may be lower if the surface ablation is performed in close proximity to CXL, due to temporary keratocyte loss during the first months after CXL.[28] This constitutes the third advantage of performing topography-guided custom ablation and CXL in a single procedure.

Performing laser ablation and CXL in a single pro-

BSCVA	Asymmetry (D)	PFE (μm)	Pachymetry (μm)	Attempted Correction	Ablation Depth (μm)
20/50	8.5	95	454	−2.00 +4.00 × 42	44
20/20	3.2	91	420		
20/50	7.3	105	538	−3.00 −7.00 × 2	60
20/30	4.3	95	481		
20/200	6.4	91	483	−0.25 +1.50 × 90	39
20/80	3.6	92	389		
20/40	6.6	92	484	−1.10 +2.05 × 154	58
20/30	2.7	94	431		
20/60	5.8	100	512	−0.75 −4.25 × 117	59
20/25	2.1	111	445		
20/80	6.5	87	499	−2.75 −2.75 × 67	56
20/30	2.2	92	433		
20/40	5.6	99	483	−0.50 +2.00 × 107	52
20/40	3.2	98	414		
20/30	4.8	95	540	−0.75 −2.50 × 175	58
20/25	1.7	93	484		
20/50	5.3	88	485	−0.75 −1.50 × 144	45
20/40	2.3	92	433		
20/30	5.7	94	565	−1.75 +3.50 × 178	60
20/30	2.2	99	499		
20/125	7.3	102	552	−0.25 −1.47 × 75	57
20/60	2.8	111	479		
20/125	6.3	92	548	−0.50 −2.50 × 100	60
20/50	2.8	98	475		

cedure raises the question of distinguishing their individual effects on the refraction and ectatic process. The refractive effects on cases with keratectasia, when performed separately, have already been investigated for both laser ablation[10-15] and CXL,[8] whereas the effect of CXL when performed immediately after the laser ablation requires extensive clinical studies. To date, only the surgeon's clinical judgment can be used to determine the safe depth of the laser ablation, which when followed by CXL, will not result in further ectasia. However, development of reliable and standardized measurements of corneal biomechanical properties can lead to more objective surgical planning.

Our results showed relatively good safety, efficacy, and predictability, if the amount and type of preoperative error are taken into consideration. The change in spherical equivalent refraction between 6 and 12 months was statistically significant; however, it did not change more than 1.00 D in nine cases. The change may be explained either by corneal structural changes, continuous epithelial remodeling, or even the patient's adaptation to the new optical conditions.

In the current study, transepithelial surface topography-guided custom ablation was chosen instead of traditional surface ablation to avoid potential custom ablation planning error due to epithelial remodeling, which is a common characteristic of irregular astigmatism[29] (eg, epithelial thinning over the cone in keratoconus). Mechanical or alcohol epithelial removal, used in traditional surface ablation, would in cases where epithelial

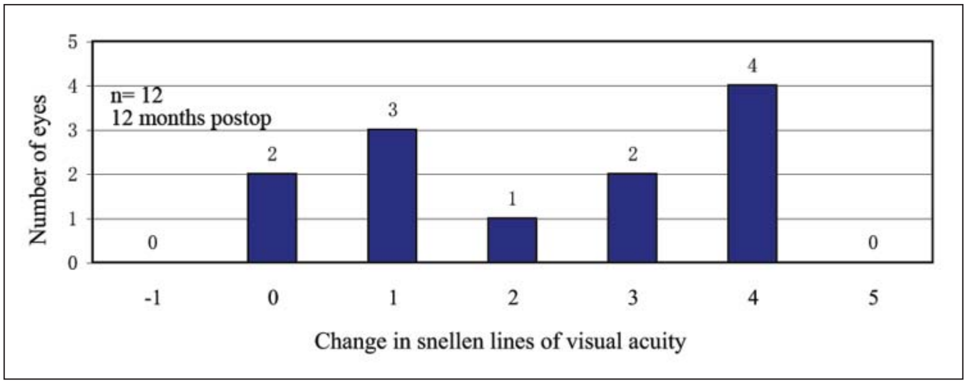

Figure 3. Gain/loss of best spectacle-corrected Snellen visual acuity 12 months after surgery in 12 eyes that underwent combined topography-guided custom ablation and corneal collagen cross-linking for the treatment of keratectasia.

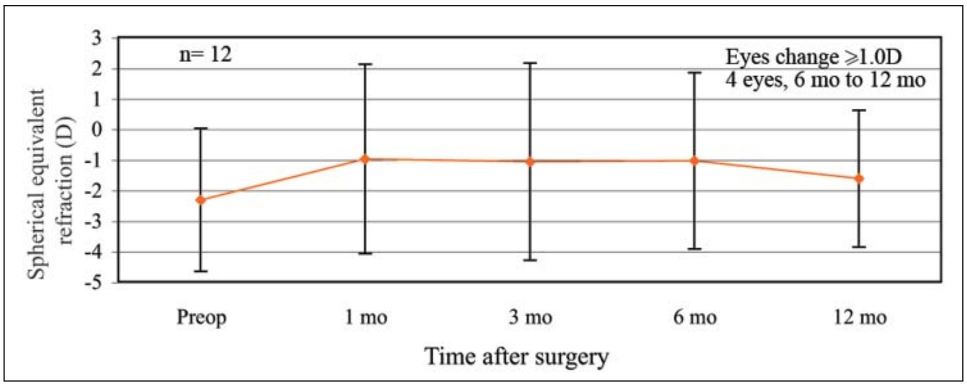

Figure 4. Mean manifest spherical equivalent before and 1, 3, 6, and 12 months after surgery in 12 eyes that underwent combined topography-guided custom ablation and corneal collagen cross-linking for the treatment of keratectasia.

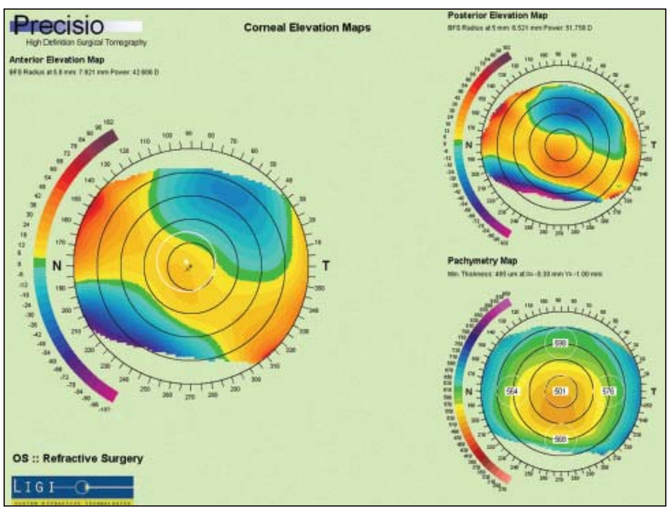

Figure 5. *Patient 1.* Precisio preoperative maps of **left)** anterior elevation, **upper right)** posterior elevation, and **lower right)** pachymetry.

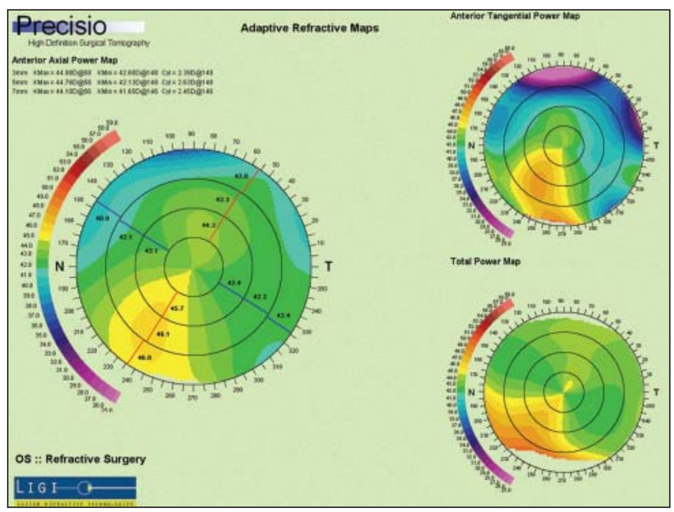

Figure 6. *Patient 1.* Precisio preoperative anterior keratometric maps: **left)** axial, **upper right)** tangential, and **lower right)** power.

remodeling has occurred, reveal an irregular stromal surface that would no longer match the preoperative corneal topography upon which the custom ablation had been planned, causing a potentially significant ablation error.[26] The transepithelial approach circumvents such error by adding a lamellar component to the custom ablation thus translating the targeted corneal surface (calculated by topography-guided custom ablation software) below the lowest point of the epithelium. Additionally, with the custom transepithelial approach the area of epithelial removal corresponds directly to the area of the custom ablation, with a consequence that only the absolutely necessary amount of epithelium is removed. This is less invasive than traditional surface ablation and it shortens the reepithelialization time.

AUTHOR CONTRIBUTIONS

Study concept and design (A.S., T.A.N., Q.W.); data collection (A.S., J.Z., X.C.); analysis and interpretation of data (A.S., J.Z., T.A.N., S.C.); drafting of the manuscript (A.S., J.Z., T.A.N.); critical revision

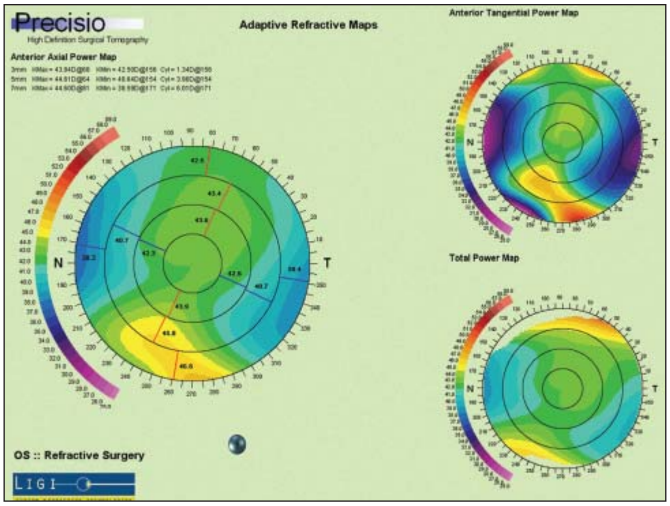

Figure 7. *Patient 1.* Precisio postoperative anterior keratometric maps: **left)** axial, **upper right)** tangential, and **lower right)** power.

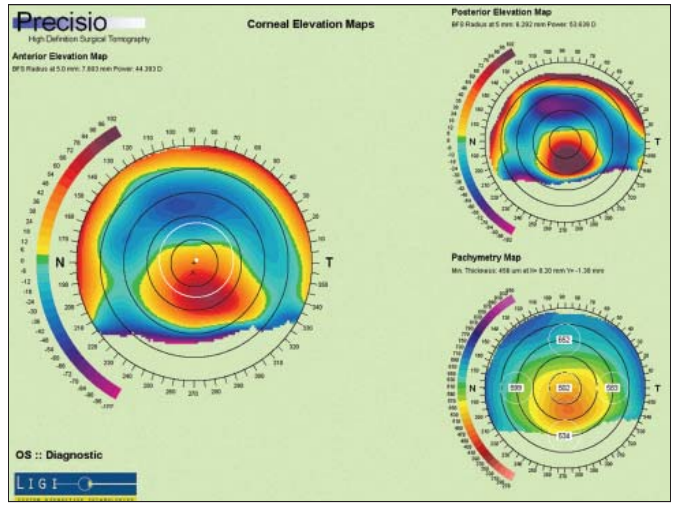

Figure 8. *Patient 2.* Precisio preoperative map of **left)** anterior elevation, **upper right)** posterior elevation, and **lower right)** pachymetry.

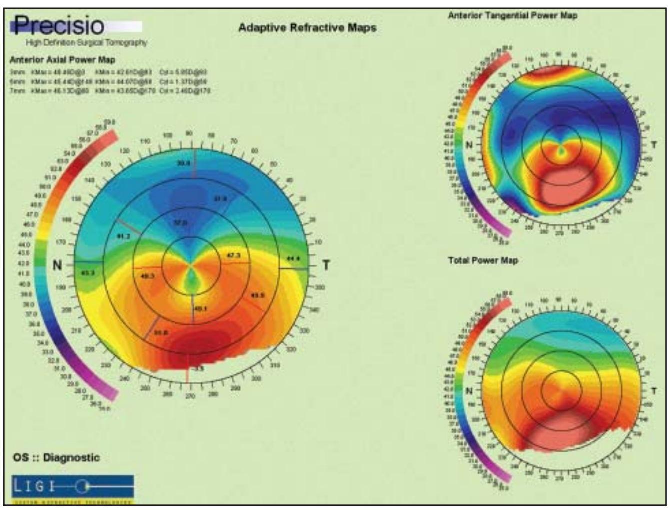

Figure 9. *Patient 2.* Precisio preoperative anterior keratometric maps: **left)** axial, **upper right)** tangential, and **lower right)** power.

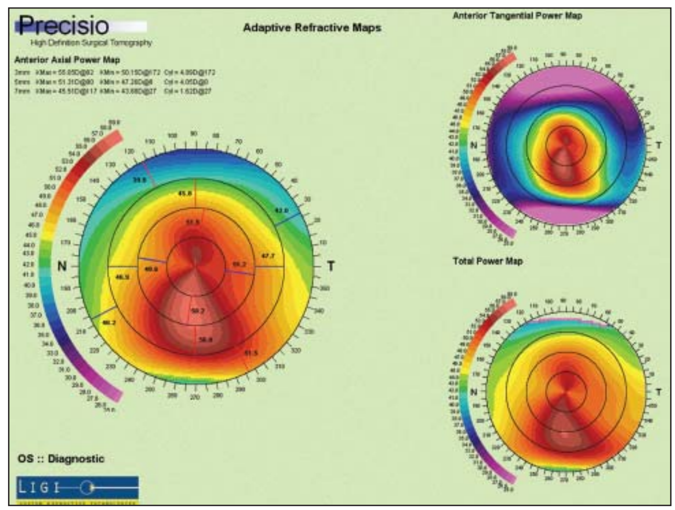

Figure 10. *Patient 2.* Precisio postoperative anterior keratometric maps: **left)** axial, **upper right)** tangential, and **lower right)** power.

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REFERENCES

1. Lim L, Pesudovs K, Coster DJ. Penetrating keratoplasty for keratoconus: visual outcome and success. *Ophthalmology*. 2000;107:1125-1131.
2. Kymionis GD, Siganos CS, Tsiklis NS, Anastasakis A, Yoo SH, Pallikaris AI, Astyrakakis N, Pallikaris IG. Long-term follow-up of Intacs in keratoconus. *Am J Ophthalmol*. 2007;143:236-244.
3. Kanellopoulos AJ, Binder PS. Collagen cross-linking (CCL) with sequential topography-guided PRK: a temporizing alternative for keratoconus to penetrating keratoplasty. *Cornea*. 2007;26:891-895.
4. Stojanovic A, Suput D. Strategic planning in topography-guided ablation of irregular astigmatism after laser refractive surgery. *J Refract Surg*. 2005;21:369-376.
5. Stojanovic A, Wang L, Jankov M, Nitter T, Wang Q. Wavefront optimized versus custom-Q treatments in surface ablation for myopic astigmatism with the WaveLight ALLEGRETTO laser. *J Refract Surg*. 2008;24:779-789.
6. Alpins NA. A new method of analyzing vectors for changes in astigmatism. *J Cataract Refract Surg*. 1993;19:524-533.
7. Claesson M, Armitage WJ, Fagerholm P, Stenevi U. Visual outcome in corneal grafts: a preliminary analysis of the Swedish Corneal Transplant Register. *Br J Ophthalmol*. 2002;86:174-180.
8. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol*. 2003;135:620-627.
9. Caporossi A, Baiocchi S, Mazzotta C, Traversi C, Caporossi T. Parasurgical therapy for keratoconus by riboflavin-ultraviolet type A rays induced cross-linking of corneal collagen: preliminary refractive results in an Italian study. *J Cataract Refract Surg*. 2006;32:837-845.
10. Fagerholm P, Fitzsimmons T, Ohman L, Orndahl M. Nebulae at keratoconus—the result after excimer laser removal. *Acta Ophthalmol (Copenh)*. 1993;71:830-832.

11. Gierek-Kalicka S, Wygledowska D, Mrukwa E. Preliminary report on the use of excimer laser in treating keratoconus. *Klin Oczna*. 1992;94:349-350.

12. Alpins N, Stamatelatos G. Customized photoastigmatic refractive keratectomy using combined topographic and refractive data for myopia and astigmatism in eyes with forme fruste and mild keratoconus. *J Cataract Refract Surg*. 2007;33:591-602.

13. Koller T, Iseli HP, Donitzky C, Ing D, Papadopoulos N, Seiler T. Topography-guided surface ablation for forme fruste keratoconus. *Ophthalmology*. 2006;113:2198-2202.

14. Tamayo GE, Serrano MG. Treatment of irregular astigmatism and keratoconus with the VISX C-CAP method. *Int Ophthalmol Clin*. 2003;43:103-110.

15. Kasparova EA, Kurenkov VV. Combination of photorefractive and phototherapeutic keratectomy in the treatment of keratoconus [Polish]. *Vestn Oftalmol*. 2000;116:10-12.

16. Bilgihan K, Ozdek SC, Konuk O, Akata F, Hasanreisoglu B. Results of photorefractive keratectomy in keratoconus suspects at 4 years. *J Refract Surg*. 2000;16:438-443.

17. Dausch D, Schröder E, Dausch S. Topography-controlled excimer laser photorefractive keratectomy. *J Refract Surg*. 2000;16:13-22.

18. Appiotti A, Gualdi M. Treatment of keratoconus with laser in situ keratomileusis, photorefractive keratectomy, and radial keratotomy. *J Refract Surg*. 1999;15:S240-S242.

19. Kremer I, Shochot Y, Kaplan A, Blumenthal M. Three year results of photoastigmatic refractive keratectomy for mild and atypical keratoconus. *J Cataract Refract Surg*. 1998;24:1581-1588.

20. Mortensen J, Carlsson K, Ohrström A. Excimer laser surgery for keratoconus. *J Cataract Refract Surg*. 1998;24:893-898.

21. Mortensen J, Ohrström A. Excimer laser photorefractive keratectomy for treatment of keratoconus. *J Refract Corneal Surg*. 1994;10:368-372.

22. Kasparova EA, Kasparov AA. Six-year experience with excimer laser surgery for primary keratoconus in Russia. *J Refract Surg*. 2003;19:250-254.

23. Cochener B, Le Floch G, Volant A, Colin J. Is there a role for excimer laser in the treatment of keratoconus? [French] *J Fr Ophtalmol*. 1997;20:758-766.

24. Ward MA, Artunduaga G, Thompson KP, Wilson LA, Stulting RD. Phototherapeutic keratectomy for the treatment of nodular subepithelial corneal scars in patients with keratoconus who are contact lens intolerant. *CLAO J*. 1995;21:130-132.

25. Cennamo G, Intravaja A, Boccuzzi D, Marotta G, Cennamo G. Treatment of keratoconus by topography-guided customized photorefractive keratectomy: two-year follow-up study. *J Refract Surg*. 2008;24:145-149.

26. Stojanovic A, Jankov M. Treatment of irregular astigmatism—developing an ideal corneal surface. In: Wang M, ed. *Irregular Astigmatism: Diagnosis and Treatment*. Thorofare, NJ: SLACK Inc; 2007:211-218.

27. Marshall J, Trokel SL, Rothery S, Krueger RR. Long-term healing of the central cornea after photorefractive keratectomy using an excimer laser. *Ophthalmology*. 1988;95:1411-1421.

28. Mazzotta C, Balestrazzi A, Traversi C, Baiocchi S, Caporossi T, Tommasi C, Caporossi A. Treatment of progressive keratoconus by riboflavin-UVA-induced cross-linking of corneal collagen: ultrastructural analysis by Heidelberg Retinal Tomograph II in vivo confocal microscopy in humans. *Cornea*. 2007;26:390-397.

29. Reinstein DZ, Archer T. Combined Artemis very high-frequency digital ultrasound-assisted transepithelial phototherapeutic keratectomy and wavefront-guided treatment following multiple corneal refractive procedures. *J Cataract Refract Surg*. 2006;32:1870-1876.