

Topography-guided Hyperopic LASIK With and Without High Irradiance Collagen Cross-linking: Initial Comparative Clinical Findings in a Contralateral Eye Study of 34 Consecutive Patients

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ABSTRACT

PURPOSE: To evaluate the safety and efficacy of intrastromally applied collagen cross-linking (CXL) in a comparative contralateral eye study of topography-guided femtosecond laser-assisted hyperopic LASIK.

METHODS: Thirty-four consecutive patients with hyperopia and hyperopic astigmatism elected to have bilateral topography-guided LASIK and were randomized to receive a single drop of 0.1% sodium phosphate riboflavin solution under the flap followed by 3-minute exposure of 10 mW/cm² ultraviolet A (UVA) light with the flap realigned in one eye (CXL group) and no intrastromal CXL in the contralateral eye (no CXL group). All eyes were treated with the WaveLight FS200 femtosecond laser and WaveLight EX500 excimer laser (Alcon Laboratories Inc). Refractive error and keratometric, topographic, and tomographic measurements were evaluated over mean follow-up of 23 months.

RESULTS: Preoperatively, mean spherical equivalent refraction was $+3.15 \pm 1.46$ diopters (D) and $+3.40 \pm 1.78$ D with a mean cylinder of 1.20 ± 1.18 D and 1.40 ± 1.80 D and mean uncorrected distance visual acuity (UDVA) (decimal) of 0.1 ± 0.26 and 0.1 ± 0.25 in the CXL and no CXL groups, respectively. At 2 years postoperatively, mean spherical equivalent refraction was -0.20 ± 0.56 D and $+0.20 \pm 0.40$ D with mean cylinder of 0.65 ± 0.56 D and 0.76 ± 0.72 D and mean UDVA of 0.95 ± 0.15 and 0.85 ± 0.23 in the CXL and no CXL groups, respectively. Eyes with CXL demonstrated a mean regression from treatment of $+0.22 \pm 0.31$ D, whereas eyes without CXL showed a statistically significant greater regression of $+0.72 \pm 0.19$ D ($P = .0001$).

CONCLUSIONS: Topography-guided hyperopic LASIK with or without intrastromal CXL is safe and effective, with greater long-term efficacy (less regression) in eyes with CXL. Our data suggest that the regression seen with hyperopic LASIK may be related to biomechanical changes in corneal shape over time. [*J Refract Surg.* 2012;28(11 Suppl):S837-S840.]
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The evolution of laser vision correction technology has made the treatment of myopia, hyperopia, and astigmatism more accurate. Numerous studies of hyperopic LASIK have been reported,¹⁻⁷ and as the WaveLight Allegretto Wave laser (Alcon Laboratories Inc, Ft Worth, Texas) was introduced, reports of wavefront-optimized hyperopic LASIK have also been published.^{8,9} We previously reported the use of topography-guided excimer laser ablations for hyperopia and their advantage in correcting angle kappa.^{10,11}

Recently, we published a report on a large cohort of topography-guided hyperopic LASIK with long-term follow-up.¹² In this study, we found a higher level of safety and efficacy when treating hyperopia and hyperopic astigmatism with topography-guided LASIK. Nevertheless, between 1 and 2 years postoperatively a consistent level of regression was noted. We theorized that this was due to a progressive flattening effect, and not due to latent hyperopia and/or accommodation loss, because the regression was consistent with a reduction of the amount of “steepening” of corneal shape achieved initially.

We also introduced the concept of high irradiance, short exposure corneal collagen cross-linking (CXL)¹³ and prophylactic CXL in myopic LASIK several years ago,¹⁴ and recently reported the long-term safety and efficacy of these therapies. In the present study, we have attempted to evaluate the effect of “prophylactic” CXL in the long-term stability and safety of hyperopic topography-guided LASIK.

PATIENTS AND METHODS

All patients signed informed consent prior to treatment following the protocol set forth by the Declaration of Helsinki.

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Dr Kanellopoulos is a consultant to Alcon Laboratories Inc. Dr Kahn has no financial interest in the materials presented herein.

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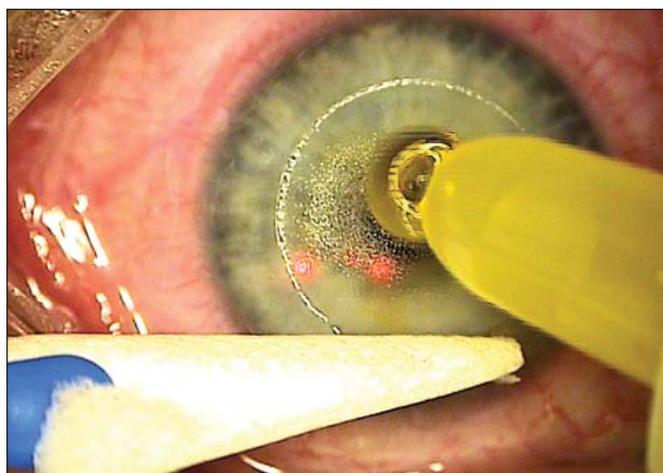


Figure 1. Riboflavin is instilled on the bare stromal bed. Care is taken to avoid contact with the folded LASIK flap.

Thirty-four patients (68 eyes) underwent bilateral topographic-guided hyperopic LASIK in our facility from March 2010 to October 2010, with one eye randomized (by coin toss) to receive prophylactic intrastromal CXL. Inclusion criteria were hyperopia of +0.25 to +8.00 diopters (D) and astigmatism up to -6.00 D with a spherical equivalent cycloplegic refraction ≤ 6.00 D. Exclusion criteria were previous corneal surgery, history of herpetic eye disease, corneal dystrophy, corneal scarring, keratoconus, severe dry eye, or collagen vascular diseases.

Preoperative evaluation included uncorrected distance visual acuity (UDVA), refraction (cycloplegic), corrected distance visual acuity (CDVA), slit-lamp examination including fundus evaluation, corneal imaging with Scheimflug corneal tomography (Oculus II, Alcon Laboratories Inc) and Placido disc-based topography (Vario, Alcon Laboratories Inc), ultrasound central corneal pachymetry with the NIDEK US-1800 (Echoscan, Achi, Japan), and wavefront analysis with the Allegretto-Wave Tscherning wavefront analyzer (WaveLight Technologie AG, Erlangen, Germany) measured at 6.5-mm pupil size. Contrast sensitivities were also measured using CSV-1000 (VectorVision, Arcanum, Ohio).

A custom nomogram-adjustment algorithm for determining the ablation treatment plan was used per our previous experience. As an important differentiator, this algorithm was used to compensate for the regression encountered in earlier cases; however, this nomogram-adjusted algorithm was not used in eyes randomized to receive intrastromal CXL.

SURGICAL TECHNIQUE

A disposable patient interface was used for flap creation in each eye treated with the FS200 femtosecond

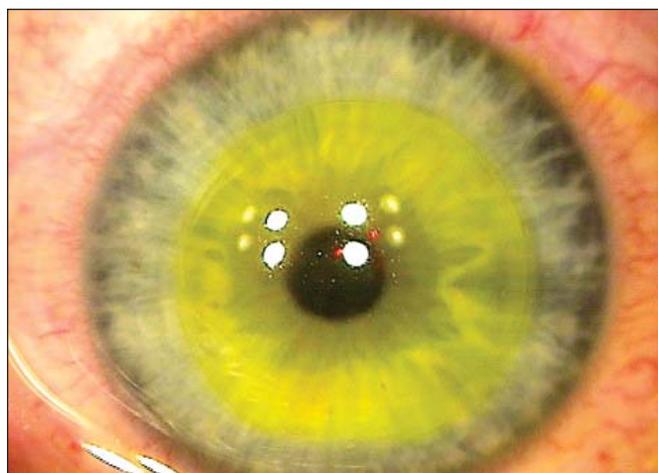


Figure 2. Repositioned LASIK flap. The yellow tinge seen within the corneal stroma is the riboflavin.

laser (Alcon Laboratories Inc). One drop of proparacaine 1% (Alcaine, Alcon Laboratories Inc) was instilled in the patient's eye just before the procedure. Eyelids were painted with povidone iodine antiseptic 10% (Betadine; Purdue Pharma L.P., Stamford, Connecticut), and the eye lashes were isolated with sterile plastic drapes (Tegaderm; 3M Health Care, St Paul, Minnesota). The femtosecond laser was used to cut the corneal flaps in all cases. The flaps were cut to expose a stromal bed at a diameter of at least 9.0 mm and depth of 135 μm , which was sufficiently large for the hyperopic (large diameter) ablation and its accompanying blend zone. The intraoperative flap diameter was measured with a surgical caliper, and pachymetry measurement of the residual stromal bed was done with the built-in optical pachymeter of the EX500. The 500-Hz EX excimer laser was used to perform the ablations in all cases using the topography-guided platform. Images were taken from the Oculus II as described previously.¹²

At the completion of the excimer ablation, eyes that were randomized to receive CXL were given one drop of our custom 0.1% riboflavin sodium phosphate solution (Leiter's Pharmacy, San Francisco, California), on the bare stromal bed, which was left to soak for 60 seconds. Special care was taken not to allow the riboflavin solution to come in contact with the already folded LASIK flap (Fig 1). After 60 seconds of soaking, the LASIK flap was reflected into place and copiously irrigated and "ironed" in place with a Johnston applicator (Rhein Medical, Tampa, Florida) (Fig 2).

Immediately afterwards, one drop of Vigamox solution (Alcon Laboratories) was applied to the cornea and it was illuminated with 10 mW/cm^2 of 370-nm UV light with the KXL device (Avedro, Waltham, Massachusetts) for a total of 3 minutes. No additional drops

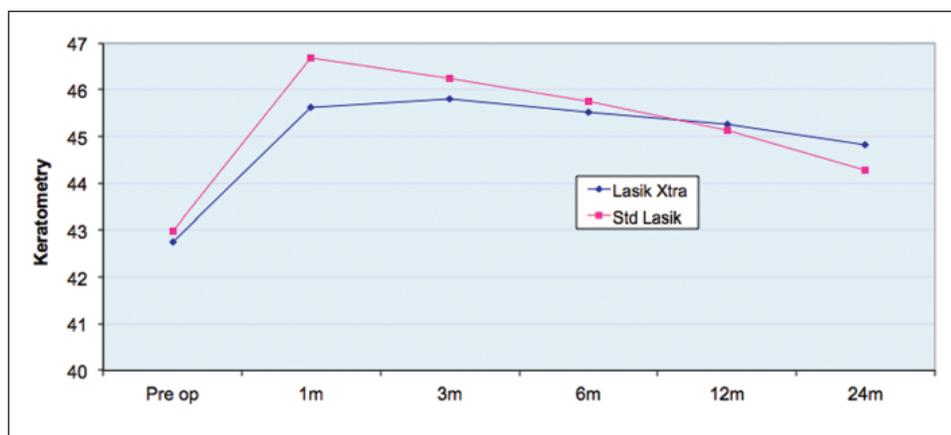


Figure 3. Pre- and postoperative comparison of the mean keratometric change in hyperopic eyes with intrastromal cross-linking (LASIK Xtra) and those without (Std LASIK) ($P=.001$).

of riboflavin were administered. The surface was kept moist with two to three drops of Vigamox during the 3-minute interval. A bandage contact lens was placed on the ocular surface, and the patient was prescribed Vigamox and 1% prednisolone acetate (PredForte; Allergan, Irvine, California) four times a day for 1 week. Patients were examined 30 minutes postoperatively to check for any flap irregularities or complications.

Postoperatively, UDVA, CDVA, corneal tomography and topography, and manifest and cycloplegic refraction were evaluated. These examinations were repeated during follow-up at 1 day, 1 week, and 1, 3, and 6 months, and every 6 months thereafter. All surgeries were performed by a single surgeon (A.J.K.) in an outpatient refractive surgery center in Athens, Greece. Measurements and data were obtained by the surgeon and his associate staff.

RESULTS

Preoperatively, mean spherical equivalent cycloplegic refraction (SE) was $+3.15 \pm 1.46$ D and $+3.40 \pm 1.78$ D with mean cylinder of 1.20 ± 1.18 D and 1.40 ± 1.80 and mean decimal UDVA of 0.1 ± 0.26 and 0.1 ± 0.25 in the CXL and no CXL groups, respectively. Postoperatively, mean SE at 2-year follow-up was -0.20 ± 0.56 D and $+0.20 \pm 0.40$ D with mean cylinder of 0.65 ± 0.56 D and 0.76 ± 0.72 D and mean decimal UDVA of 0.95 ± 0.15 and 0.85 ± 0.23 in the CXL and no CXL groups, respectively. Eyes with intrastromal CXL demonstrated a mean regression from treatment of $+0.22 \pm 0.31$, whereas the eyes that did not receive CXL showed a statistically significant greater regression of $+0.72 \pm 0.19$ ($P=.0001$).

Figure 3 shows the pre- and postoperative comparison of the mean keratometric change for each group. Overcorrection was seen in the no CXL group, as expected due to the added $+0.50$ D in the nomogram adjustment for this group, which seemed to decrease over the 2-year follow-up period. In eyes that received

adjunct intrastromal CXL, no overcorrection was noted and greater stability was achieved.

DISCUSSION

In previous studies, the potential advantage of using a topography-guided ablation profile in the correction of hyperopic refractive errors has been demonstrated with greater importance than myopic errors because of the presence of angle kappa in hyperopes.¹¹ When treating with wavefront-optimized or wavefront-guided ablation, the treatment pattern is centered on the entrance pupil, whereas with topographic-guided ablation, it is centered on the corneal apex. Although much debate surrounds the best location for centration, evidence suggests that the corneal apex may be more closely aligned to the visual axis, especially when compensating for angle kappa in hyperopes.¹⁵

In this study, we sought to evaluate the stability of these results after using intrastromal CXL. This, in theory, would act as a biomechanical modulator to the intrinsic corneal flattening response of hyperopic LASIK seen during long-term follow-up. The keratometric regression noted over the 2 years of follow-up in the eyes randomized to not receive adjunctive intrastromal CXL confirms, in our opinion, the above-mentioned intrinsic biomechanical mechanism of regression in hyperopic LASIK. We believe this to be an “expansion” or “stretching” of the severed midperipheral corneal fibers that have been ablated, resulting in progressive flattening of the steepened central cornea. Although the possibility of midperipheral thickening and central thinning of the epithelium might also play a role in the regression, the fact that it was statistically minimized in the eyes undergoing intrastromal CXL points more clearly to the biomechanical mechanism.

The implication of biomechanical modulation of postoperative hyperopic LASIK regression, so as to prevent progressive refractive instability over time, sets a new level of dynamic control on the outcomes of

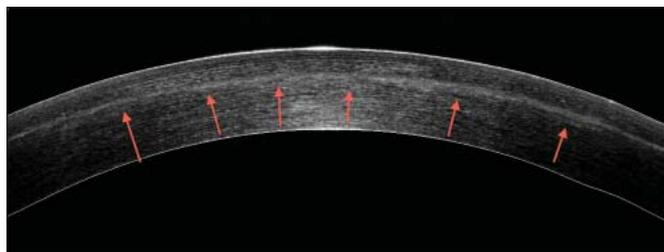


Figure 4. Corneal optical coherence tomography scan taken 3 months postoperatively of an eye that received intrastromal cross-linking (CXL) during hyperopic LASIK. The hyperreflective area around the LASIK flap interface (arrows) demonstrates the achieved CXL effect.

laser vision correction surgery, which previously was restricted to a static change in refractive error. Just as the dynamic change of refraction seen with progressive keratoconus requires CXL to prevent the instability and irregularity of ectasia, in a similar way, the dynamic refractive and topographic regression of hyperopic LASIK now seems to require CXL to maintain stability over time. This also may be true of myopic regression seen in high myopic treatments with thin corneas, and is the reason why some have advocated LASIK Xtra (LASIK + intrastromal CXL) for higher risk eyes.^{14,16}

Our preliminary data suggest that the combination of high irradiance, short exposure intrastromal CXL may offer a significant synergy in maintaining the long-term efficacy and stability of topography-guided hyperopic LASIK (Fig 4). However, we are unable to know or predict with certainty what will occur past 2 years based on these data. This synergy suggests that the regression of effect in hyperopic LASIK may be more related to corneal biomechanical changes than just a loss of residual accommodation, lens changes, or epithelial thickening. The use of CXL in association with LASIK may become another significant application of corneal CXL and further expand the science of modulating biomechanical change in refractive surgery.¹⁷ Finally, topography-guided LASIK with the EX500 excimer laser and FS200 femtosecond laser, with and without adjunctive intrastromal CXL, appears to be safe and effective in the correction of hyperopia and hyperopic astigmatism.

AUTHOR CONTRIBUTIONS

Study concept and design (A.J.K.); data collection (A.J.K.); analysis and interpretation of data (A.J.K., J.K.); drafting of the manuscript (A.J.K.); critical revision of the manuscript (A.J.K., J.K.); statistical expertise (A.J.K.); administrative, technical, or material support (A.J.K.); supervision (A.J.K.)

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