

# Effectiveness of CXL Combined With LASIK

Is this a promising new modality to prevent refractive regression and ectasia?

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LASIK is the most common form of refractive surgery, but, despite important technical advances, some limitations remain. Of specific concern are ectasia and refractive regression.<sup>1-3</sup>

## REGRESSION

The correction achieved with LASIK is not always stable, and in some cases refractive regression can occur.<sup>1,4</sup> Studies have shown that the risk of regression is between 5.5% and 27.7%.<sup>4</sup> In a study of 615 eyes, Chen et al found that multiple factors influenced regression, including preoperative manifest refraction spherical equivalent (MRSE), mean preoperative central corneal curvature, optic zone size, undercorrection, and age.<sup>4</sup>

Another study evaluating the long-term outcomes of LASIK for high myopia reported that corneal changes occurred over a period of 10 years in almost 10% of cases.<sup>5</sup> We and others postulate that the combination of LASIK and corneal collagen crosslinking (CXL) may be able to stabilize LASIK results over a longer period.<sup>2</sup>

## ECTASIA

Post-LASIK ectasia can develop in as little as 1 week or as long as a few years after the initial procedure. When it manifests, patients typically present with increased myopia and astigmatism, loss of distance UCVA, and, often, loss of distance BCVA.<sup>1</sup> Many treatment options are available,<sup>2,6,7</sup> but in some cases a corneal transplant is still necessary.<sup>6</sup>

Post-LASIK ectasia is relatively rare. In the literature, the incidence is about 0.04% to 0.6%;<sup>1</sup> however, accurate clinical studies on this topic are lacking.

Preventing ectasia is naturally more desirable than having to treat it, and CXL has emerged as a promising new technique aimed at slowing or stopping its progression.<sup>1</sup> Clinical results indicate that BCVA and corneal curvature in patients with keratoconus improved or remained stable after CXL (maximum follow-up, 6 years).<sup>8</sup>

## COMBINATION TREATMENTS

Today, some surgeons combine refractive surgery and CXL to maximize postoperative results. There are two popular combinations: CXL plus LASIK for refractive correction in healthy eyes and CXL plus PRK in eyes with keratoconus or ectasia. This article focuses on the combination of CXL and LASIK.

**CXL plus LASIK.** CXL is used to improve refractive correction after LASIK in healthy eyes. The function of CXL is to stabilize the cornea, which may have become destabilized as a result of the creation of the corneal flap.<sup>9</sup>

**CXL plus PRK.** PRK is used to improve the CXL process in eyes with keratoconus or ectasia.

Corneal biochemical response has been associated with the pathophysiology of regression after LASIK; therefore, modifying the biochemical properties of the cornea may result in positive treatment outcomes.<sup>3</sup> When CXL is combined with LASIK, the refractive correction should remain stable over time, and post-LASIK ectasia may be prevented.

## TAKE-HOME MESSAGE

- Patients with post-LASIK ectasia typically present with increased myopia and astigmatism, loss of distance UCVA, and, possibly, loss of distance BCVA.
- When CXL is combined with hyperopic LASIK, refractive correction could potentially remain more stable over time.
- The decision to perform LASIK plus CXL should be based on the patient's risk of developing ectasia: In low-risk patients, LASIK and CXL might be considered, although this combination is currently clinically experimental; in high-risk patients, a surface ablation procedure such as PRK in combination with CXL should be preferred.

Moreover, due to the increased stability of the postoperative result, patients who would normally be excluded from LASIK—those with a higher risk of ectasia—can be treated.<sup>10</sup> Although current results are encouraging, this concept is still in a clinical investigational phase.

## CONSIDERATIONS

**Possible complications.** Similar to a standalone LASIK procedure, LASIK plus CXL also carries the risk of flap-related problems and epithelial ingrowth (0.92%).<sup>11-13</sup> Furthermore, the flap is more difficult to relift after the combined procedure than after LASIK alone;<sup>10</sup> this means that retreatments are possible only with PRK.

**Patient selection.** Inclusion criteria for LASIK plus CXL should be based on the additional risks and benefits to patients and the additional resources required for the procedure.

The decision to perform LASIK plus CXL should be based on the patient's risk for ectasia. Randleman and colleagues proposed a useful ectasia risk score for LASIK, and this measure can also be applied to the combined procedure.<sup>14,15</sup> The Ectasia Risk Score System (ERSS) is based on topography, residual stromal bed thickness, age, preoperative corneal thickness, and preoperative MRSE. The following recommendations are made based on an individual's risk score:

- Score of 0 to 2: Low risk; LASIK may be carried out, but the possibility that ectasia may develop is not excluded;<sup>14,15</sup>
- Score of 3: Moderate risk; LASIK may be carried out, but with caution; and
- Score of 4 or more: High risk; LASIK should not be carried out.

**Low risk.** In these eyes, the cornea is stable. If ectasia does occur, CXL can be effective.<sup>16</sup> Of patients in whom this occurs, only a small proportion might need further treatment, such as a corneal transplant.

In 90% of crosslinked eyes, haze is visible on slit-lamp examination and can be quantified by Scheimpflug imaging;<sup>17</sup> in most cases, it disappears by 1 year. Continuous and unpredictable corneal flattening after CXL has also been reported.<sup>9</sup> Yet these risks and known side effects of CXL are outweighed by the possible benefits for this group of patients and the unproven advantages of avoiding ectasia.

**Moderate and high risk.** In eyes with moderate and high risk for ectasia, the cornea is more unstable than in the low-risk group. Patients in the moderate- and high-risk groups are often contraindicated for LASIK due to the biomechanical instability of their corneas.

However, if LASIK is combined with CXL to strengthen the cornea, these patients might have a more marked benefit compared with patients in the low-risk group. In eyes in which ectasia has already developed, PRK plus CXL is the more appropriate treatment.

In summary, we suggest that LASIK plus CXL may be used if the ERSS score is 2 to 3 but not if the score is 0, 1, or greater than 4. In those with the lowest scores, LASIK alone can be considered, and in the highest score, PRK plus CXL should be considered.

**Technique.** Several variations of LASIK plus CXL techniques have been described.<sup>1-3,10</sup>

Derhartunian and Seiler<sup>10</sup> used femtosecond LASIK (90- $\mu$ m flap) and rapid CXL (2 minutes of intrastromal riboflavin 0.5% under the flap and 10 minutes of ultraviolet-A irradiation at 9 mW on the flap and corneal bed).

Following any treatment protocol, a bandage contact lens is placed on the cornea and the patient is prescribed topical steroids and antibiotics.

## CLINICAL DATA

Clinical data are lacking on the combined procedure of CXL plus LASIK, but research is ongoing and encouraging. A prospective pilot study evaluating accelerated CXL applied concurrently with LASIK (eight eyes of four patients with myopia or myopic astigmatism) found that, at 12 months, eyes treated with LASIK plus CXL had distance UCVA and manifest refraction equal to or better than patients treated with LASIK alone. There were no side effects with either procedure.<sup>1</sup>

In a larger study (43 consecutive cases) investigating prophylactic higher-fluence CXL immediately after LASIK in patients with high myopia and/or myopic astigmatism (defined as myopia greater than -6.00 D spherical equivalent), the combined procedure was a safe and effective treatment for refractive regression and potential ectasia.<sup>2</sup>

One should bear in mind that the demonstration of safety requires more eyes, and, therefore, a general conclusion that combined LASIK and CXL is safe cannot yet be drawn. The demonstration of effectiveness for avoiding ectasia has also not been clinically validated based on the number of eyes reported.

Most recently, Aslanides and Mukherjee<sup>3</sup> have reported that, in five eyes, simultaneous hyperopic LASIK plus CXL resulted in refractive stability through 4 years. The authors pointed out that this outcome was noteworthy given that the enrolled patients had higher hyperopia and astigmatism, relatively thin preoperative pachymetry, and high ERSS scores, which would have

increased their risk of biochemical changes. There was no clinical or topographic evidence of flap-related complications or late induced changes, and early stromal haze, which did not seem to limit visual recovery, resolved within 1 month.

## SUMMARY

Although the clinical evidence for the effectiveness of LASIK plus CXL is scant, there are promising indications that this combined procedure may ameliorate refractive regression and address the risk of post-LASIK ectasia in carefully selected patients. ■

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