

# CXL ALONE VERSUS IN COMBINATION WITH THE STARE-X PROTOCOL



Selection of the right technique can halt keratoconus and reduce aberrations.

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The goal of CXL therapy is not only to strengthen the cornea to slow or stop the progression of keratoconus, but also to induce apex flattening and improve corneal symmetry, which can lead to refractive improvement.

Conventional accelerated CXL protocols demonstrate a medium- to long-term improvement in visual acuity and topographic and aberrometric parameters,<sup>1,2</sup> but the results are highly variable because of the uneven collagen biological response to photodynamic reaction. The goal of this article is to guide surgeons and help them choose the best approach: a single CXL procedure or CXL in combination with transepithelial PRK (CXL-plus) to stabilize keratoconus and reduce aberrations, especially coma. In this regard, we will discuss the selective transepithelial ablation for regularization of ectasia (STARE-X) protocol for treating corneal ectatic disorders.

## FUNDAMENTAL THERAPEUTIC STRATEGY MUST BE INFLUENCED BY THE PATIENT'S HISTORY, BEHAVIOR, AND AGE

CXL is strongly suggested for patients under age 18 years who are diagnosed with keratoconus, rub their eyes excessively, and have a history of ocular allergy.<sup>3,4</sup> CXL alone is an effective option for patients with BCVA better than 20/40 and a low degree of comatic aberrations

because the goal is to halt keratoconus progression while the patient still has good visual acuity. Treating ocular allergy and encouraging patients to stop eye rubbing will also help to reduce external factors that are actively involved in keratoconus progression (see *Case Report*).

## FUNDAMENTAL INCREASE THE SAFETY OF EPITHELIUM-OFF CXL USING AN ACCELERATED PROTOCOL AND CUSTOMIZING DOSAGE AND ENERGY TO THE PATIENT'S CORNEAL PACHYMETRY, ESPECIALLY IN THINNER CORNEAS

Accelerated, customized CXL treatment can be performed safely in normal and thin corneas (< 400  $\mu\text{m}$ ) with different UV-A power and exposure time. The use of hydroxypropyl methylcellulose riboflavin solution is mandatory when managing thin corneas to help prevent corneal dehydration induced by dextran.<sup>5-8</sup> The nomogram in Figure 1 shows the depth of the demarcation line after CXL is performed with different energy levels and a fixed UV-A dose of 5.4 J.<sup>9</sup>

Our advice to improve the safety of this treatment is to consider a CXL protocol that will produce a demarcation line at least 100  $\mu\text{m}$  away from the endothelium. For this reason, it is better to avoid the Dresden protocol (3 mW/cm<sup>2</sup>, 5.4 J energy) in corneas thinner than 400  $\mu\text{m}$  (Figure 1).

## FUNDAMENTAL IN EARLY-STAGE KERATOCONUS, CONSIDER THE DIFFERENCE BETWEEN CENTRAL AND PERIPHERAL CONES BEFORE PLANNING TREATMENT, ESPECIALLY WHEN USING AN OLD CXL MACHINE

Several studies have shown that cone location is one of the most important parameters involved in corneal flattening after CXL performed with the Dresden protocol. Greenstain et al<sup>9</sup> demonstrated that, after CXL, more topographic flattening occurs in eyes with centrally located cones, and the least flattening effect of the cone occurs when the cone is located peripherally.<sup>10</sup> This cone-location effect is found in eyes with both keratoconus and ectasia with an average difference of more than 2.00 D.

The flat irradiation beam delivered by older CXL machines does not work well with the curvilinear shape of the cornea. Studies examining energy absorption profiles demonstrated a significant difference (> 4 J) between the central and peripheral cornea, creating an uneven energy delivery profile (Figure 2).<sup>11</sup> If a flat beam profile irradiates a convex surface (ie, the cornea), the central area will absorb more energy because it is closer to the energy source compared with the periphery. The other issue is that, in eyes with keratoconus, the location of the cone apex is typically in the paracentral and peripheral cornea (2 mm from the corneal center).

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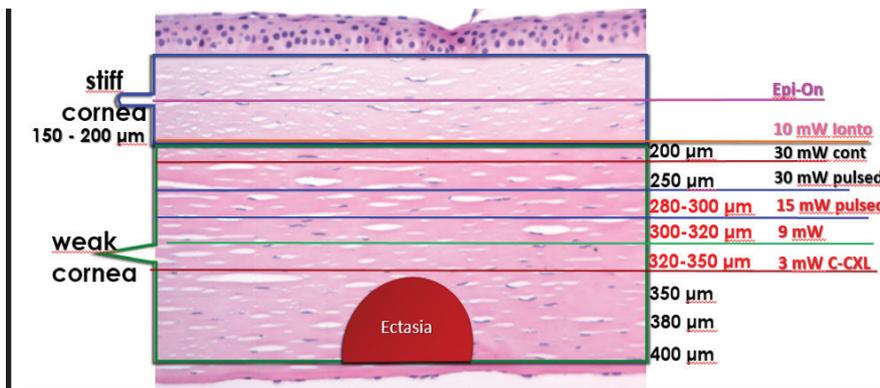


Figure 1. The depth of the demarcation line after CXL with different energy levels and a fixed UV-A dose of 5.4 J.

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The result is that a CXL procedure performed with an older machine centered on the cornea will produce more cross-linking (and flattening) effect on the central cornea than the cone apex.

The uneven energy delivery with older CXL machines can be understood looking at demarcation line depth 10 to 15 days after CXL: The line is deeper in the center and gradually becomes superficial toward the periphery (Figure 2). This is not useful in terms of coma reduction because, in most cases of keratoconus, the apex is 2 mm away from the corneal vertex.

Top-hat or umbrella-like beams produced by newer CXL machines significantly improve energy management, delivering a more even amount of radiation from center to periphery and, thus, improving the crosslinking effect in the apex zone (Figure 2).<sup>11</sup> More than this, in the STARE-X CXL protocol, the beam is centered on the

posterior elevation apex, eventually covering the limbus with a sponge if the beam diameter exceeds the corneal limbus. Demarcation line depth after this protocol is more even from center to periphery (Figure 2).<sup>11</sup> A customized and cone-centered irradiation profile will lead to more effective crosslinking, more flattening in the apex zone, and a better refractive effect.

#### FUNDAMENTAL 4 CONSIDER THE STARE-X PROTOCOL FOR ECTATIC CORNEAS WITH A HIGH DEGREE OF COMATIC ABERRATION

The combination of accelerated CXL and corneal wavefront-guided transepithelial PRK should be considered in patients with a high degree of comatic aberration (root mean square, > 1 at 5 mm pupil diameter). We perform the STARE-X protocol using the Amaris excimer laser (Schwind eye-tech-solutions); the

ablation is customized using corneal wavefront data acquired by the Sirius corneal tomograph (CSO), which combines a Scheimpflug camera, a Placido-disc topographer, and pupillometry. The KXL System (Avedro) is used to deliver the CXL treatment.

STARE-X protocol parameters for all treatments are as follows: maximum stromal ablation depth less than 50 µm; maximum optimization for saving ablation depth, as calculated by excimer laser software; maximum correction of coma aberration, eventually reducing spherical and cylinder refraction to not exceed the 50-µm ablation depth limit; epithelium removal of 55 µm in the center and 65 µm in the periphery of the selected ablation zone (we suggest to not extend over 6.5 mm to reduce ablation volume); and ablation offset up to 1 mm from corneal vertex in the direction of the cone apex as measured manually on topography. These settings allow the surgeon to center the ablation more on the cone with respect to the corneal vertex, reducing stromal ablation over the cone apex and further reducing coma aberrations (Figure 3).

#### FUNDAMENTAL 5 CONSIDER LASER EPITHELIUM REMOVAL ALONE IN THINNER CORNEAS WITH A HIGH DEGREE OF ABERRATION AND A CORNEAL APEX GREATER THAN 53.00 D

In patients with keratoconus, the epithelium is normally thinner on the cone apex, acting as a masking agent for smoothing anterior elevation irregularities. Previous studies show an average thinning of 10 to 13 µm at 1.2 mm from the corneal vertex between normal corneas and those with keratoconus.<sup>12,13</sup> This means that a 55- to 65-µm epithelial ablation in the apex zone will remove about 15 to 20 µm of stromal tissue. This is crucial information to consider, especially if removal of the epithelium or further topography-guided stromal regularization is planned, to not exceed the ablation depth target. This is the

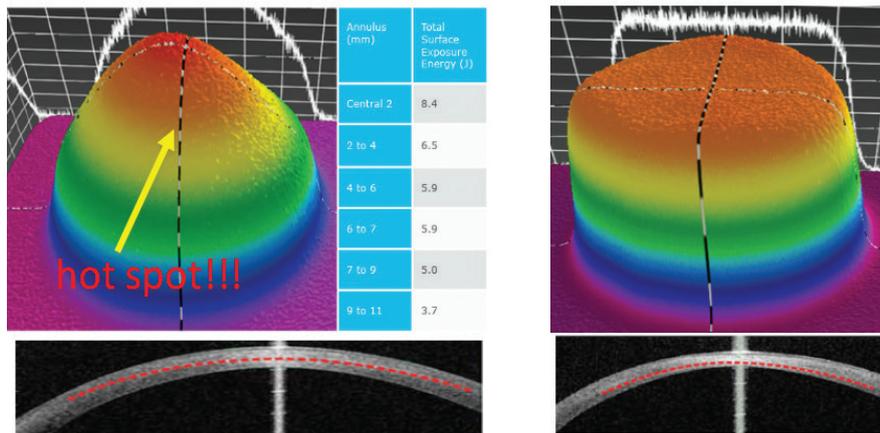


Figure 2. Uneven energy distribution and demarcation line during CXL performed with an old CXL machine (left). Homogeneous energy pattern and demarcation line in a cornea treated by a newer beam-optimized CXL machine (right).

reason why epithelium removal alone will flatten the cone apex and reduce comatic aberrations (Figures 4 and 5).

**CONCLUSION**

CXL alone represents an optimal solution for early ectasia in which the goal is to halt the progression of the condition in patients with good BCVA and few higher-order aberrations, preventing the need for an eventual corneal transplant.

The next challenge lies in how to manage keratoconus in patients with significant ectasia. The refraction of these patients is always difficult because spectacle correction is unable to improve high irregular astigmatism, especially in peripheral cones, and a comfortable contact lens fitting is sometimes hard or impossible to achieve and can cause corneal scarring or infection.

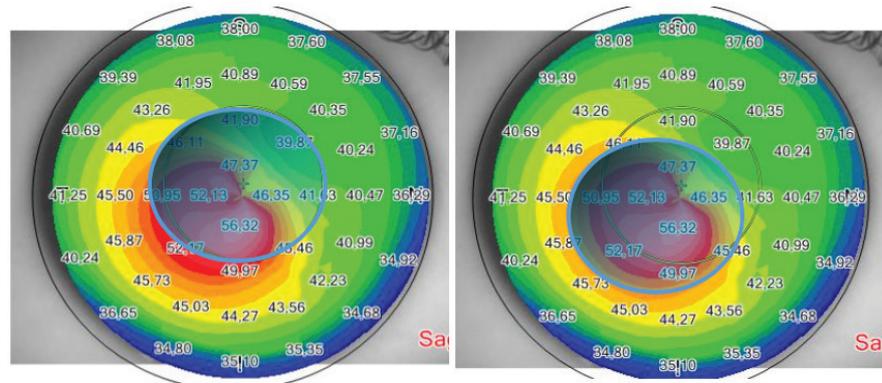


Figure 3. Corneal vertex-centered ablation (left) does not fully cover the apex zone and ablates tissue outside the corneal ectasia. Cone apex-centered ablation (right) fully covers the apex zone, saving nonectatic corneal tissue outside the cone.

The way to improve visual acuity in these patients is through corneal reshaping. In other words, the goal is to regularize the corneal geometry in the central 4-mm zone. This should reduce the vertical asymmetry and higher-order aberrations (especially coma) typically induced by ectasia.

The treatment of corneas with keratoconus using an excimer laser was historically considered inappropriate because it causes further corneal thinning and possible weakening of the corneal microstructure, leading to worsening of iatrogenic ectasia. Recent advances in technology have led to the

**CASE REPORT**

A 21-year-old man with progressive bilateral keratoconus was considered for treatment. His right eye was affected by a large paracentral ectasia with an apex of less than 55.00 D (see Figure 4 in main article). The patient became intolerant of his contact lens because of friction of a corneal apex. His BCVA was 0.6 logMAR.

Treating aberrations in very ectatic corneas using corneal wavefront data will always result in excessive ablation. For this reason, we opted for a mild treatment, planning a 6-mm epithelium removal decentered on the cone and accelerated CXL at 15 mw, 5.4 J, pulsed 1:1. At 6 months, we observed significant corneal flattening in the apex zone, reduction of comatic aberrations, and a mild reduction of corneal thickness (see Figure 5 in main article). BCVA was 0.18 logMAR and 0.1 logMAR using a new semirigid contact lens with a flatter profile. The patient reported improvements in visual acuity and night vision.

The patient's fellow eye (left) was also affected by keratoconus and was treated 3 months later. BCVA at the most recent followup was 0.3 logMAR with -2.50 -2.00 x 70° (Figure 1). With a less pronounced ectasia and thicker cornea, we decided to treat comatic aberrations using a refraction of -0.50 -1.00 x 70°. We chose an optic zone of 5 mm decentered on the cone apex zone to save more corneal tissue and to better focus ablation and CXL effect in the cone area. The maximum depth of simulated ablation was 40 µm in the apex zone, followed by accelerated CXL at 15 mw, 5.4 J, pulsed 1:1. After 6 months, BCVA was 0.0 logMAR with -1.00 -0.50 x 60° with a residual corneal thickness up to 420 µm (Figure 2). The patient returned to using a soft, noncustomized contact lens and was enthusiastic about his dramatic improvements in visual acuity and halos at night.

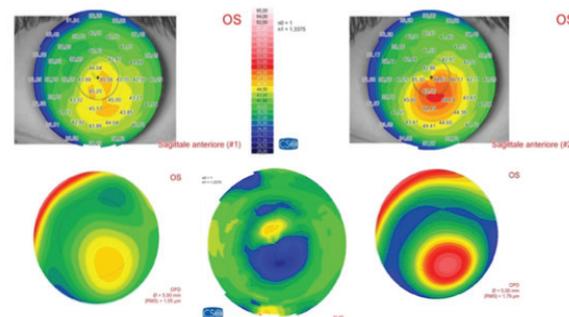


Figure 1. Preoperative sagittal and aberration maps (top and bottom right), postoperative sagittal and aberration maps (top and bottom left), and differential curvature map (bottom center) of a patient with keratoconus, thin corneas, and cone apex of 50.00 D treated with decentered corneal wavefront-guided transepithelial PRK plus accelerated CXL. A marked corneal flattening in the ectatic area was observed, associated with a strong reduction of comatic aberration.

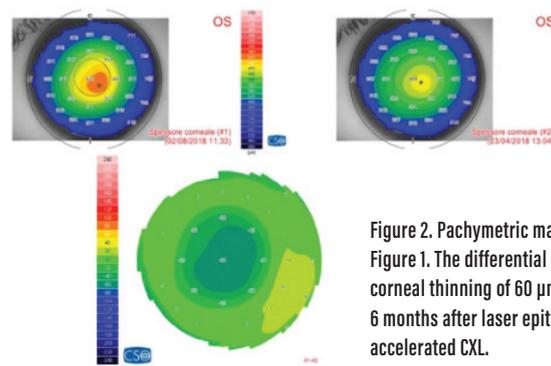
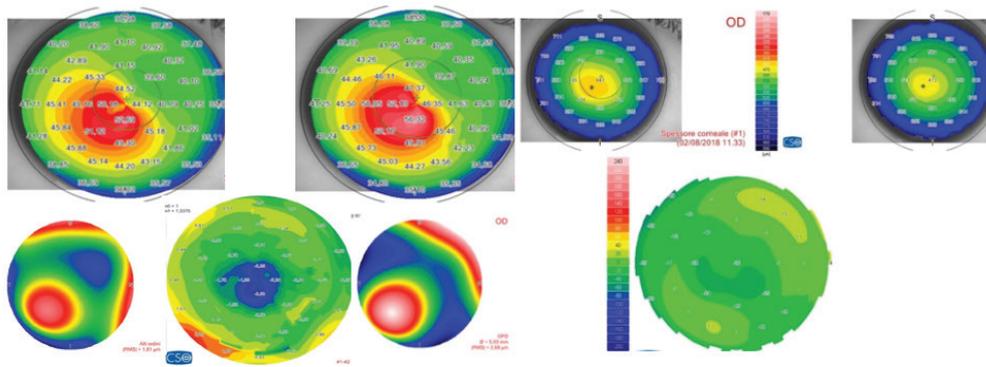


Figure 2. Pachymetric map of the patient in Figure 1. The differential map (bottom) shows corneal thinning of 60 µm in the apex zone 6 months after laser epithelium removal plus accelerated CXL.



**Figure 4.** Preoperative sagittal map and aberration map (top and bottom right), postoperative (top and bottom left), and differential curvature map (bottom center) of a patient with keratoconus, thin corneas, and cone apex of more than 55.00 D treated with decentered laser epithelium removal plus accelerated CXL.

**Figure 5.** Pachymetric map of the patient in Figure 4. The differential map (bottom) shows corneal thinning of 24  $\mu\text{m}$  in the apex zone 6 months after laser epithelium removal plus accelerated CXL.

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development of corneal wavefront-guided treatment which has improved the quality of laser treatment and introduced the concept of customized treatments.

The benefit of combined CXL plus refractive surgery is seen in the early postoperative period, regularizing the ectatic cornea and treating the new, reshaped cornea with CXL to further flatten the cornea in the medium to long term. ■

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