

# Answering Your Patients' Questions About Cross-Linking

Many centers worldwide are now offering cross-linking as a first-line treatment for conditions such as keratoconus, corneal ectasia, and pellucid marginal degeneration.

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Interest in corneal collagen cross-linking is increasing rapidly in the United States. Corneal cross-linking was first used to treat keratoconic patients in the 1990s soon after animal studies demonstrated promising results. According to one estimate, roughly 400 centers across the globe now offer cross-linking as a first-line treatment for keratoconus, corneal ectasia, and pellucid marginal degeneration (Ray Stein, MD, personal communication, 2009). International experience that includes some long-term studies has been very positive.<sup>1-6</sup> Due to the current regulatory environment and other factors, the United States is perhaps the only developed country that does not have cross-linking available as a routine, noninvestigational procedure at this time.

Keratoconus is not an uncommon disease: its prevalence ranges between one in 500 to one in 10,000.<sup>7</sup> Most corneal specialists believe that the condition actually occurs more often than these estimates, because technology is now able to detect this disease at earlier stages and in more subtle forms. One such device is the Pentacam Comprehensive Eye Scanner (Oculus, Inc., Lynnwood, WA), which can measure the back surface of the cornea.<sup>8</sup>

Cross-linking is relatively straightforward. The surgeon instills riboflavin (vitamin B2) eye drops after epithelial removal, as in preparation for PRK. These drops are instilled for 30 minutes, and anesthetic eye drops are used to enhance the patient's comfort during the procedure. After the riboflavin has saturated the cornea, the surgeon applies the UV light source—calibrated to provide a steady irradiance of light—for 30 minutes to each eye. For patients who have corneas between 300 and 400  $\mu\text{m}$  thick, a hypotonic riboflavin solution can be used to swell the cornea to greater than 400  $\mu\text{m}$  before treatment. This process pro-

TECTS the endothelium, lens, and other intraocular structures by ensuring that only safe levels of UV light penetrate to the deeper corneal layers. A bandage contact lens is sometimes placed on the eye immediately after surgery, and antibiotic and nonsteroidal eye drops are then instilled. The surgeon observes the patient postoperatively until the epithelium is intact (generally 2-5 days), and then he or she follows the patient with serial refractions, topography, and other measurements over the ensuing months and years.

As with many conditions, the earlier the patient is treated, the better the results are. In some countries, cross-linking is used for patients as young as 10 years who are found to have forme fruste (preclinical) or frank (clinical) keratoconus. This first-line treatment makes it much less likely that these patients will develop severe irregular astigmatism and ultimately require corneal transplantation.<sup>3</sup> If cross-linking is performed early, it may be possible to prevent the development of keratoconus in some eyes with preclinical signs of keratoconus. Patients who have keratoconus can also benefit from cross-linking treatment. Roughly 60% to 70% of patients experience a significant improvement in their BSCVA after treatment.<sup>2</sup> In our experience, patients usually move one "step" up what we refer to as the *vision-correction spectrum*. In other words, if they are intolerant of their rigid contact lenses and are headed toward a corneal transplant, we can often avoid transplantation and restore their comfort with contact lenses. If they are doing well in rigid lenses, we can sometimes get them into soft lenses. If they are wearing soft lenses well, we are often able to provide better vision with glasses.

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## CXL-USA STUDY GROUP: PATIENTS' FREQUENTLY ASKED QUESTIONS

### What is cross-linking?

Corneal collagen cross-linking is a technique that was first used in 1998 to treat patients with a disease called *keratoconus*. In keratoconus, the cornea (the front clear window of the eye) becomes weak and thin. Instead of keeping its normal round shape, corneas with keratoconus can bulge forward into the shape of a cone, which causes poor vision. Cross-linking is now being performed on patients with this condition at approximately 400 centers throughout the world. Through a research study, our practice is now able to provide this investigational treatment to our patients using advanced technology for cross-linking.

### What does cross-linking do?

Corneal collagen cross-linking strengthens the cornea by allowing it to form new cross-links between the collagen fibers. These new cross-links help strengthen the cornea, which stops the thinning process and further loss of vision. Cross-linking works by adding "cross-beams" between the weak layers of the cornea in keratoconic eyes.

### How effective is cross-linking?

Many research studies have shown that cross-linking prevents further vision loss in more than 95% of patients, with 60% to 70% of patients having improved vision.<sup>1-5</sup>

### How long does cross-linking treatment last?

Based on cross-linking study results over more than a decade, the beneficial effects of corneal cross-linking appear to last for a long time, and there is evidence that this strengthening effect will be permanent.

### Is cross-linking new?

Corneal collagen cross-linking has been performed since 1998. The results and safety profile of cross-linking have been very positive in numerous studies throughout the world.<sup>1-6</sup> The cross-linking procedure is now routinely performed on patients as young as 10 years in Europe to prevent the development of keratoconus.

### What is keratoconus?

Keratoconus is a common disease that has been estimated to occur in one in 500 Americans. In keratoconus, the cornea becomes weak, progressively thins, and becomes irregular in shape, producing high levels of astigmatism. Instead of a relatively round shape for good focus, the cornea can become conical. This can interfere with the individual's ability to see clearly. Often, patients with kerato-

conus require glasses and then contact lenses. If the condition becomes severe, a corneal transplant may be required.

### What do ladders and keratoconus have in common?

In keratoconus, the cornea has a weakened structure with too few cross-links or support beams. This weakened structure allows the cornea to bulge outward. The cross-linking procedure adds cross-links or "ladder rungs" to the cornea, making it more stable, holding its shape, and focusing power better.

### Can cross-linking prevent the need for a corneal transplant?

Many studies have shown that cross-linking can often prevent the need for a corneal transplant and allow patients to wear contact lenses or glasses more comfortably and safely again.<sup>1-5</sup>

### Is cross-linking like LASIK?

No, LASIK reduces or, in some cases, eliminates the patient's need for glasses or contact lenses by removing corneal tissue. The cross-linking treatment does not remove tissue. The purpose of cross-linking is to prevent further deterioration of vision for most patients and potentially to improve their vision. Patients will typically require a lower eyeglass prescription and can have an easier time being fit with contact lenses.

### Can a corneal transplant be done after cross-linking?

If cross-linking does not prevent the need for a corneal transplant, then a corneal transplant can generally be performed.

### Does cross-linking need to be repeated?

In many studies, the vast majority of patients responds to a single cross-linking treatment and does not need to have the procedure repeated. For the occasional patient in whom this treatment is not successful, cross-linking can often be repeated.

### Does insurance cover cross-linking treatment?

Insurance generally does not cover cross-linking treatment because it is investigational in the United States.

### Is financing available?

Convenient, affordable financing is available to help our patients get the treatment they need before their keratoconus or other similar condition progresses to the point where they can no longer have cross-linking.

**CXL-USA STUDY GROUP: PATIENTS' FREQUENTLY ASKED QUESTIONS (CONTINUED)****Can cross-linking be performed on everyone with keratoconus?**

To qualify for the cross-linking study, patients must be at least 18 years old, and their corneas cannot be too thin or too scarred for the procedure. During your consultation, we will determine if cross-linking might be an appropriate treatment option. Our practice offers a complimentary, 5-minute, no-touch, painless screening test to determine whether cross-linking might help stop your vision from getting worse or even improve it.

**Should my relatives be tested?**

As you may know, keratoconus often runs in families, so it is important to arrange a screening for all of the family members of patients with keratoconus. If the disease is caught early, there is a good chance that cross-linking can halt the progression of keratoconus and prevent the need for a corneal transplant and/or uncomfortable contact lens wear for many patients.

**How is cross-linking performed?**

The collagen cross-linking treatment is an outpatient procedure performed in the doctor's office using only numbing eye drops and a mild sedative like oral diazepam. You will need to lie flat on your back in a reclining chair and look up at a soft blue light during the treatment. To help prevent you from blinking, an eyelid retainer may be placed between your upper and lower eyelids. This is painless because of the numbing eye drops. The epithelium—a thin layer of clear, protective skin that covers the cornea—is prepared for the cross-linking procedure. Next, vitamin (riboflavin) eye drops are instilled in the eye, one drop every 2 minutes for about 30 minutes. The treatment concludes with another set of vitamin (riboflavin) eye drops instilled every 2 to 5 minutes for 30 minutes while you look at an ultraviolet (UV) light. It is generally easy to look at the light, because your eyes are numb, and we will be applying drops so your eyes will not feel dry. The UV light appears to have a soft blue color (Figure 1).

**How long does the procedure take?**

If two eyes are being treated at once, the procedure takes approximately 1.5 hours. If only one eye is being treated at a time, the procedure takes approximately 1 hour.

**Does the cross-linking procedure hurt?**

No, the cross-linking procedure is painless. Anesthetic eye drops are used to avoid any discomfort during the procedure.



Figure 1. The UV light used in collagen cross-linking appears to have a soft blue color.

**Can I have one eye treated at a time?**

Yes, your doctor will discuss with you the advantages and disadvantages of treating one eye or two eyes at a time.

**Can I have cross-linking if I already had a corneal transplant?**

Each patient and each patient's eyes are different. In some cases, cross-linking can be performed after corneal transplantation.

If cross-linking works for me and stops my vision from getting worse, can I have laser vision correction afterward?

Some patients may be able to have an excimer laser treatment or PRK to improve their vision without glasses after they have healed from the cross-linking procedure.

**Do I have to stop wearing contacts before having cross-linking?**

We recommend that you stay out of contact lenses for 1 or 2 weeks if possible before your consultation to see if you might benefit from cross-linking. This requirement can vary based on how difficult it is for you to see without your contacts. We often suggest patients not wear their lenses for 3 days before their cross-linking procedure.

**When can I resume wearing contact lenses?**

Most patients can return to wearing contact lenses 4 to 6 weeks after having the cross-linking procedure.

## CXL-USA STUDY GROUP: PATIENTS' FREQUENTLY ASKED QUESTIONS (CONTINUED)

### Will I need new glasses or contacts after cross-linking?

Because cross-linking often improves vision, patients usually find that their old contacts or glasses are too strong for them and they need to be refit with new glasses and/or contact lenses.

### When will I notice any improvement in my vision after cross-linking?

Most patients find that, right after the cross-linking treatment, their vision is actually worse than it was before the procedure. This decrease usually lasts roughly 3 to 6 weeks. Many patients start to notice positive effects 4 to 8 weeks after the procedure, and a major improvement in vision generally takes 3 to 6 months. In some studies, many patients' vision and astigmatism continue to improve for up to 5 years after cross-linking.

### When may I exercise and return to my usual activities after cross-linking?

Most people can do so after 5 to 7 days. Based on how quickly you are healing, your doctor can tell you when you can return to your usual activities. We want to help you be able to work or do other things you need and want to do as quickly as possible.

### What is astigmatism?

Astigmatism simply means that the front surface of the eye (the cornea or clear window in front of the eye) is shaped more like a football than like a basketball.

*For more information about keratoconus and/or our diagnostic screenings and treatments, please call our practice and ask to speak with a CXL coordinator or visit our Web site <http://cxlusa.com/>.*

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## THE CXL-USA STUDY GROUP

The CXL-USA Study Group is actively enrolling patients in a multicenter investigational study to gather data on the safety, efficacy, and optimal techniques for cross-linking. Current diagnostic criteria for enrollment include keratoconus (both clinical and preclinical forms), pellucid marginal degeneration, and post-LASIK ectasia. Some post-RK patients are being enrolled as well. Patients must be 18 years of age or older, and their thinnest corneal measurement must be 300  $\mu\text{m}$ . We look forward to expanding our indications for cross-linking to bullous keratopathy and corneal ulcers<sup>8</sup> in the near future.

Because more and more patients with corneal conditions are now seeking information about cross-linking and becoming interested in pursuing this option, the CXL-USA Study Group has developed a list of frequently asked questions (see *CXL-USA Study Group: Patients' Frequently Asked Questions*). We encourage clinicians to make this information available to patients who desire to learn more about their medical conditions and the best available treatment options. ■

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