CORNEA/EXTERNAL DISEASE
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# Collagen cross-linking shows promise for slowing keratoconus, ectasia

Corneal collagen cross-linking significantly improved keratometry and visual acuity 1 year after treatment in patients with keratoconus and corneal ectasia, a study found.

The goal of the study was to determine the efficacy of corneal collagen cross-linking in slowing the progression of keratoconus and ectasia after LASIK.

“Cross-linking, which is still an investigational procedure … would give ophthalmologists their first therapy for decreasing keratoconus progression,” lead study author Peter S. Hersh, MD, FACS, told *Ocular Surgery News*.

Cross-linking creates additional bonds between collagen molecules, which cause the cornea to stiffen. Dr. Hersh said the treatment could be groundbreaking in the management of keratoconus.

Study results were published in *Journal of Cataract and Refractive Surgery*.

## Patients, methods

Researchers evaluated 71 eyes of 58 patients who underwent standard corneal collagen cross-linking with ultraviolet A light and topical riboflavin 0.1%. Patients with corneas thinner than 400 µm also received hypotonic riboflavin 0.1% drops until the cornea was of adequate thickness.

Of the eyes included in the study, 49 had keratoconus and 22 had corneal ectasia. Researchers conducted follow-up examinations at 1, 3, 6 and 12 months after treatment.

The prospective, randomized, controlled clinical trial included a sham control group in addition to a fellow-eye control group.

The sham control group included 41 eyes that received riboflavin 0.1% alone and were followed for 3 months postoperatively. Dr. Hersh said patients with potentially treatable keratoconus underwent full cross-linking at 3 months due to ethical considerations and noted that the short-term follow-up period was a limitation of this group. Therefore, 30 eyes in a fellow-eye control group that did not receive any treatment were evaluated for comparison to treated eyes as well. Although these eyes completed the 12-month follow-up period, Dr. Hersh said that the comparative results were limited because the group was not randomized and the severity of keratoconus varied.

Patients were analyzed as a cohort and then individually within keratoconus or ectasia subgroups.

## Results, conclusions

Changes in uncorrected distance visual acuity, corrected distance visual acuity, maximum keratometry value and average keratometry value from baseline to 3 months were not significantly different between the treatment group and the sham control group at 3 months, the study said.

All groups, however, showed significant improvements in mean uncorrected distance visual acuity ($P = .04$) and corrected distance visual acuity ($P < .001$) 1 year after treatment. The entire cohort experienced the most improvement between baseline and 3 months and 3 months and 6 months, and researchers observed a plateau in improvement and stabilization for the remainder of the study.

According to Dr. Hersh, the healing process can take months to complete and is marked by periods of improvement, stabilization and sometimes early worsening of certain measures.

“The stabilization and improvement we are seeing in corneal steepness and distance corrected visual acuity represents the complete course of the actual cross-linking event and the subsequent wound healing that goes on afterward,” he said.

Maximum keratometry was considered the primary outcome because it gives some indication of the severity of the keratoconic cone, according to the study.

After 1 month, all groups showed a significant increase in maximum keratometry value, followed by significant decreases between 1 month and 3 months and 3 months and 6 months. No significant change was observed between 6 months and 12 months, which follows the same stabilization curve as the other measures, Dr. Hersh said.

At 12 months, the treatment group showed significant improvements in all outcome measures compared with the fellow-eye control group. On average, maximum keratometry flattened by 1.7 D, uncorrected visual acuity improved

from 20/137 to 20/117, and corrected distance visual acuity improved from 20/45 to 20/34. The researchers are currently analyzing changes in topography indices and wavefront measurements after cross-linking in this patient group.

## Future studies

Dr. Hersh and colleagues are conducting a number of studies to further evaluate the parameters of corneal collagen cross-linking. One trial aims to determine whether cross-linking and implanting Intacs (Addition Technology) should be done together or separately with a 3-month healing period in between.

Another study is evaluating the use of hypotonic riboflavin vs. the standard dextran formulation to determine whether hypotonic riboflavin provides a more consistent corneal thickness throughout the cross-linking procedure. Dr. Hersh said he hopes to present the results of both studies soon.

The researchers are also conducting a multivariate analysis that will determine the most appropriate and inappropriate candidates for corneal collagen cross-linking. They are looking for characteristics that could predict a stable or improved result, and preliminary results suggest that patients with higher keratometry readings, steeper cones and worse best corrected visual acuity may benefit more from the procedure. Final results are due later this spring, he said.

Dr. Hersh said that the research will look at other indicators of success or failure as well in order to determine the best candidates for cross-linking. *– by Courtney Preston*

**Reference:**


- Hersh PS, Greenstein SA, Fry KL. Corneal collagen crosslinking for keratoconus and corneal ectasia: one-year results. *J Cataract Refract Surg.* 2011;37(1):149-160.



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- Disclosure: Dr. Hersh is medical monitor to Avedro Inc.


**PERSPECTIVE**

Riboflavin UV cross-linking was first described by Seiler more than a decade ago. Since then, multiple studies have demonstrated its safety and efficacy in preventing the progression of keratoconus, but less is known about the role of this technology in the management of ectasia after refractive surgery. Hersh and colleagues have further corroborated the efficacy of riboflavin UV cross-linking in the treatment of keratoconus. Their findings showed improvements in uncorrected and best corrected visual acuity in the treated patients and continued worsening in the untreated control group. In addition, treated patients had a decrease in maximum and mean keratometry values. The results in the post-refractive ectasia group were also significant, but not as robust as in the keratoconus group. This study further documents the importance of riboflavin UV cross-linking, as well as the necessity of this technology to become routinely available in the United States.


**– Eric D. Donnenfeld, MD**
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