



## **Cross-linking results promising, but still preliminary** Indications, contraindications and complication rates are unclear, but prospective studies may reveal more information.

Cross-linking is increasingly proving to be a successful technique for strengthening the cornea and halting keratoconus progression. However, indications and contraindications cannot yet be established, according to Theo Seiler, MD, PhD, who developed this technique.



**Theo Seiler**

Pre-clinical studies began in 1993 and the first patient was treated in 1998. A pilot study started the following year, after the first patient was shown to have successful results and no complications.

“Prospective studies have only started in 2003, 2004. In the meantime, the technology has evolved, the protocols for treatment have come to a better definition and indications are slowly becoming clearer. However, we must wait a few more years to draw conclusions on the long-term results of the technique,” Dr. Seiler said at the European Society of Cataract and Refractive Surgeons meeting in Berlin.

So far, a few main points have emerged from 10 years of experience with the procedure.

### **Corneal biomechanics**

In Dresden, where Dr. Seiler’s first studies were based, and where now more than 400 eyes have been treated, it was demonstrated that cross-linking has an impact on corneal biomechanics, as it strengthens and stiffens the cornea. It was also shown that keratoconus progression is halted in all of the cases, and maximum keratometry readings decrease and visual acuity improves in a significant percentage of cases.

“It is a fact that we cannot fully explain, but that is probably due to the regularization of the corneal surface induced by the procedure,” Dr. Seiler said.

Oculus Pentacam scans show a significant reduction of all keratoconus indexes.

In Zurich, attempts were recently made with a “light” riboflavin solution to allow the treatment of thinner corneas by swelling them for the duration of the cross-linking procedure. However, current indications have gone back to the previous, standard riboflavin/dextran combination, and a minimum corneal thickness of 400 µm is recommended, Dr. Seiler said.

Some controversy was raised about the concomitant use of intracorneal rings, which were shown to be safe and to act synergistically with the cross-linking treatment, he said.

As the number of patients treated with cross-linking increases and the follow-up gets longer, it is possible to establish both the frequent and rare complications of this treatment, Dr. Seiler said.

Haze is fairly common, but it is a transient phenomenon that can be reversed with topical corticosteroids. Demarcation lines between cross-linked and non cross-linked areas are found in the majority of patients, indicating texture changes where the collagen fibers have been irradiated, he said.

### **Prospective studies**

The prospective studies mentioned by Dr. Seiler are currently ongoing in Europe. In 2006, the group in Siena, Italy, published its 6-month results. The original contribution of this study was to show by confocal microscopy that cross-linking causes keratocyte death in the irradiation area, but massive repopulation occurs over the following 6 months.

The Zurich, Milan and Brussels group compared the results of treated and untreated eyes in an intra-individual study.

“The different evolution of the two eyes was highly significant in demonstrating that the treatment halts keratoconus progression. At 2 years, the K-readings increased in the untreated eye and remained constant in the cross-linked eye,” Dr. Seiler said. “Also, we found that during the first year, the Pentacam keratoconus indexes started to increase in the untreated eye while they regularized, more or less, in the other eye. A reduction was found in nearly 60% of the treated eyes. The difference at 1 year was significant for index of surface variance, keratoconus index, central keratoconus index and index of height asymmetry.”

Besides transient haze, which occurred frequently in this study, a few rare complications were found, such as stromal scarring and keratitis.

“Severe complications are rare but can happen. Though minimally invasive, cross-linking is surgery, and like any other surgery, the risk is never zero. We are not yet able to establish a precise rate, but it should be less than 1%,” Dr. Seiler said. – *by Michela Cimberle*

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- Theo Seiler, MD, PhD, can be reached at Augenklinik Nordtrakt II, Frauenklinikstrasse 24, CH-8091 Zurich, Switzerland; 44-1-2554900; e-mail: [theo.seiler@iroc.ch](mailto:theo.seiler@iroc.ch).
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#### PERSPECTIVE

All studies on cross-linking seem to converge on the same encouraging results: Cross-linking halts keratoconus progression and improves both best corrected and uncorrected vision, keratometry readings, surface regularity and uniformity. In other words, it has a positive impact on all corneal parameters, including a significant decrease of aberrations. With the contribution of all those who are currently involved and with the longer follow-up of prospective studies, we will be able to evaluate the stability of these positive outcomes.

If results are up to our expectations, this technique will indeed change our current approach to keratoconus, reducing the number of corneal transplantations.

– **Aldo Caporossi, MD**

Head of Ophthalmology, Siena University School of Medicine, Italy