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UVA cross-linking may stabilize cornea after refractive surgery

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By: Lynda Charters
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San Diego—Regression after refractive surgery may be reduced by using ultraviolet A (UVA) cross-linking techniques to stabilize the cornea. The preliminary results of UVA cross-linking after refractive procedures demonstrated that regression stopped in the near term and appeared to be without adverse effects.

"Nearly all refractive procedures that involve the cornea impair the mechanical properties of the cornea," said **Theo Seiler, MD, PhD,** professor and chairman, department of ophthalmology, University of Zurich, and Institute of Refractive and Ophthalmic Surgery, and his colleague, **Tobias Koller, MD,** also of the Institute of Refractive and Ophthalmic Surgery, Zurich, Switzerland.

Stiffening of the cornea by means of ultraviolet A cross-linking is a new approach with new applications.

"Some procedures—such as LASIK and PRK—thin the cornea and weaken the tissue strength as a side effect. In other procedures—such as automated lamellar keratoplasty and RK—the goal is to weaken the corneal integrity," said Dr. Seiler at the American Society of Cataract and Refractive Surgery annual meeting.

"When biomechanical weakening is such a powerful tool, biomechanical stiffening should also have its own applications," he added.

The corneal tissue can be stiffened by cross-linking, which is not a new technique. Stiffening is a well-known technique in materials science that is used to increase the elastic properties of a material by inducing new intermolecular bonds that in turn increase the molecular strength of the tissue, Dr. Seiler explained.

"Stiffening of the cornea is also a physiologic effect that occurs during aging and in patients with diabetes," Dr. Seiler said. "Cross-links in corneal collagen can be induced enzymatically, with irradiation, or by means of aldehydes. When we investigated the various techniques of cross-linking, we found that a combination of UV radiation and photo-activation by means of riboflavin was the most effective and the least harmful procedure."

Dr. Koller

He explained that when using this technique experimentally the elastic modulus of the rabbit cornea was increased by a factor of 1.4 to 1.6, and the same result was found even in cadaver eyes.

In a prospective study carried out at sites in Zurich and Dresden, Germany, Dr. Seiler and colleagues treated 26 eyes of patients, who had progressive keratoconus, with riboflavin 0.1% drops and then irradiated the eyes with UV light at a wavelength of 365 nm for 30 minutes. A custom cocktail of artificial tears/anesthetic/cross-linker/bio-vital solutions was instilled every 5 minutes throughout the 30-minute UVA exposure to maintain hydration, anesthesia, and lenticular/retinal protection.

Dr. Seiler

In all of these cases, the progression was verified pre-treatment. The patients were followed for up to 4 years.

"This was a safe procedure because the endothelial cell count density and the clarity of the lens and cornea remained unchanged," Dr. Seiler said. "Based on the results of corneal topography the progression stopped in every case."

He explained that this method may provide an immediate response to the problem of biomechanical regression.

'Time of flight' measurement

"However, we cannot wait for years to determine if cross-linking is effective. Herekar Satish, PhD, developed a 'time of flight' measurement of the ultrasound velocity to determine the change in the elastic modulus of the cornea," Dr. Seiler said.

"Dr. Satish first treated half of a porcine cornea with riboflavin cross-linking and the other half was left untreated. Dr. Satish measured the time of flight required in the two halves of the cornea," he said. "There was a highly significant difference between the treated and the untreated halves of the cornea."

This method documents the effect of stiffening immediately postoperatively

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This treatment appears to be particularly applicable to patients who are suspected of having forme fruste keratoconus or those with a correction that exceeds -8 D.

"These patients may benefit from stiffening of the cornea because keratectasia would not develop," Dr. Seiler said. "Thicker corneas may benefit from this treatment by extending the range of correction and perhaps allowing treatment of higher corrections once the cornea is more stable and has greater biomechanical strength."

Early treatments of iatrogenic keratectasia after LASIK performed at the University of Dresden seem to be effective in preventing further progression of the central keratoconus.

An intriguing idea, Dr. Seiler said, is the prevention of biomechanical regression after laser thermokeratoplasty (LTK), the only drawback of which is a high rate of regression. The same is true for the other types of thermokeratoplasty.

"If we assume that there are biomechanical changes in the stroma in higher corrections (as proposed by Cynthia Roberts, PhD), the changes can be stabilized by using a cross-linking procedure," Dr. Seiler said. "Finally, corneal cross-linking is based on the collagen molecule, which is also present in the sclera. Cross-linking of the myopic sclera may stop progression in early cases."