New Approaches for Corneal Remodelling for Refractive Surgery

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A NUMBER of new technologies are becoming available to refractive surgeons for the treatment of corneal irregularities such as keratoconus and post-LASIK keratectasia and irregular astigmatism. The new approaches involve the remodelling of the cornea through biochemical techniques, intracorneal implants, and laser ablation, according to a series of presentations at a symposium at the 9th ESCRs winter refractive Surgery Meeting. Theo Seiler MD told the symposium that a technique called collagen cross-linking might halt and even slightly reverse the progression of keratoconus. The technique strengthens lamellar fibres, thereby restoring the cornea’s structural integrity, he said.

“We can now by medical and therapeutic means transform keratoconus into the forme fruste state,” Theo Seiler MD

Keratoconus is a condition in which the tensile strength of the cornea’s lamellar fibres diminish to about half of their normal values, causing the cornea to assume a conical shape with an off-centre apex, and resulting in irregular astigmatism, he noted.

The condition generally first appears when a patient is between 10 and 20 years of age. In most cases the deformation of the cornea progresses up to a certain point and then stops as mysteriously as it began. When this occurs, the condition is called forme fruste keratoconus.

However, in the case of “frank” keratoconus the condition becomes progressively worse for several decades, perhaps even for the lifetime of the patient, although the progression slows over time. Topography studies suggest that forme fruste keratoconus has an incidence of about 5:1,000, while progressive keratoconus has an incidence of about 1:2,000.

With collagen cross-linking it may be possible to transform the progressive form of keratoconus into the more benign, forme fruste keratoconus.

Cross-linking technique

Collagen cross-linking stiffens collagen by creating new chemical bonds between collagen molecules. It occurs naturally as a consequence of ageing and diabetes. In fact, type 1 diabetes provides complete protection against keratoconus, Dr Seiler said.

After experimenting with several techniques to induce collagen cross-linking in human corneal tissue, Dr Seiler and his associates decided that the application of riboflavin (vitamin B2) combined with UV radiation offered the most favourable safety/efficacy ratio. In that technique the ultraviolet light causes riboflavin to release oxygen radicals, which in turn create new cross-linking bonds between lamellar fibres and within the collagen molecules, he explained.

Dr Seiler’s procedure involves the scraping of the epithelium from the central 9.0 mm of the cornea, the application of riboflavin in 20% dextrane, and irradiation of the area with 3mW/cm2 of ultraviolet light at a wavelength of 365 nm for 30 minutes. “Based on animal experiments and early clinical experience we found that these parameters happened to be the best combination for an optimal stiffening effect on the collagen fibres of the cornea to provide a biochemical forces, he said, adding: “Clinical trials confirm efficacy of collagen cross-linking.”

Clinical results so far suggest that not only does the collagen cross-linking achieved in this way halt the progression of keratoconus, but it also causes keratoconic corneas to assume a more normal shape with consequent improvements in visual acuity.

In a study involving 26 eyes of 25 keratoconus patients who underwent the cross-linking treatment, corneal topography showed progression halted in every case after a follow-up of one to five years (mean 2.4 years).

In addition, maximal K-readings decreased by a mean of 1.38 D (p<0.01) and were significantly reduced in 65% of the cases. Furthermore, visual acuity improved by a mean of 1.3 lines (p<0.01).

“We can now by medical and therapeutic means transform keratoconus into the forme fruste state,” he announced.

Intracorneal ring segments

Mark Swanson MD, Swann Institute, Sonora, Mexico told the symposium that intracorneal ring segments not only halt the progression of keratoconus but also correct the irregular astigmatic error in eyes with condition. The devices achieve their effect through a synergism of mechanical, biomechanical, and biochemical forces, he said, adding: “InTACS provide a tool to remodel the collagen fibres of the cornea to provide a better optical surface. They achieve this through the rearrangement of the cross-linking pattern of the bundles of collagen fibres, supported by the mechanical forces the rings exert from the mid-periphery of the cornea. In this way they provide a secondary limbus to strengthen the whole cornea.”

InTACS are clear PMMA micro-thin prescription inserts. They have an arc length of 150° and are hexagonal in cross-section. They have two positioning holes and are implanted at an angulation of 31° to follow the corneal curvature.

The ring segments are placed at 230mm corneal depth in the peripheral cornea, and the central cornea is flattened. The rings are manufactured in different thicknesses. Thicker rings produce a...
greater degree of corneal flattening. The implants are currently recommended for the treatment of up to -4.50 D of myopia with up to 2.0 D astigmatism, forme fruste and progressive keratoconus, post-LASIK keratectasia, and as an adjunct to ablative refractive procedures in patients with thin corneas. The channels for implantation of the inserts can be created manually or with a femtosecond laser. The inserts may then be implanted with specially designed instrumentation. In astigmatic eyes the incision for insertion is made on the steepest meridian. "INTACS exert forces on the flattest axis to remodel the architecture of the cornea over time, adjusting the cornea toward normal prolate optics."

**Prospective study**

Dr. Joseph Colin told the symposium that in the prospective study, which involved 100 eyes of 100 patients with keratoconus and clear corneas, implantation of INTACS provided stable improvements in vision in the majority of eyes. He noted that in select keratoconus patients, the implants might obviate the need for corneal transplantation.

"INTACS are safe for treating keratoconus. Some 70% of eyes demonstrated improved objective visual outcomes. The majority of eyes remained stable from one to two years postoperatively. Two years is not very long in these young patients but I think it’s promising," he added. INTACS were successfully implanted in all eyes without any intraoperative complications. However, removal of the implant was necessary in two eyes at five and eight months postoperatively because of extrusion of one INTACS segment at the site of the incision.

In addition, two patients underwent removal of the implant between one and two years postoperatively because of unsatisfactory visual results and subsequently underwent penetrating keratoplasty. Another 14 eyes were lost to follow-up.

**Most gain lines in visual acuity, some lose lines**

Of the remaining 82 eyes, 80.5% had an improvement of UCVA and 68.3% had an improvement of BCVA at two years’ follow-up. Furthermore, the proportion with BCVA of 20/40 or better at one and two years’ follow-up was 32.2% and 33.3%, respectively, compared to only 15.5% preoperatively, and 56% had an improvement of MRSE of 1.0 D or more. Mean logMAR UCVA improved from 1.0 preoperatively to 2.0 and 4.9 at one and two years, respectively. Mean logMAR BCVA improved from 3.4 preoperatively to 4.6 and 4.9 at one and two years, respectively.

In addition, 41.5% gained one or two lines of UCVA, 25.6% gained three or four lines, and 13.4% gained five or more lines. Similarly, as regards BCVA, 35.4% gained one or two lines, 25.6% gained three or four lines, and 7.3% gained five or more lines. However, 3.6% of eyes lost 1-4 lines of UCVA and 15.7% lost 1-4 lines of BCVA.

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Cylinder improved from preoperative values of -4.62 D to -3.87 D at one year and -2.12 D at two years. Sphere improved from preoperative values of -4.62 D to -2.12 D at one year and -2.18 at two years.
“We must learn more about this very severe complication of modern refractive surgery. Participation in this survey will help us determine the risk factors and find the best ways to prevent it.”

Joseph Colin MD

Three of four eyes with keratectasia treated with INTACS showed significant improvements in uncorrected and best-corrected visual acuity. That is, logMAR UCVA improved from 0.1 to 4.0 to 0.1, and logMAR BCVA improved from 0.1 to 2.0 to 0.1. One eye did not improve.

Dr. Colin said he has achieved good results through implantation of INTACS in eyes with post-LASIK keratectasia. His procedure involves dissecting the channel for ring implantation under the LASIK flap. He then places one inferior segment at a depth of 300-400 microns.

“The implantation of Ferarra rings is a procedure which has the objective of correcting the irregularities. The rings displace the corneal apex to its physiological position in front of the pupil in keratoconic corneas and preserves positive corneal asphericity.”

Unlike INTACS, Ferarra rings are triangular in cross section. In this way they produce a prismatic effect, which directs reflected light away from visual pathway. The implants also have a smaller optical zone, made possible by the prismatic design, which prevents halos and edge glare. Moreover, Ferarra rings are smaller than INTACS and positioned more centrally, they can correct the same amount of refractive error with thinner rings.

When treating keratoconic patients, Dr. Ferrara always makes the incision at the steepest meridian and first implants one segment, and only places a second segment if necessary to achieve optimal correction. The amount of correction can be modified by changing the positioning of the ring or by exchanging the ring with one of a different thickness.

“We have implanted the Ferarra rings to centre them on the visual axis rather than the pupillary axis. That is why the ring has to remain at the base of the cornea. The tips of the ring will flatten the central portion of the ring and the body of the rings will steepen the cornea thus correcting astigmatism.”

By repositioning the cornea the implants also reduce higher-order aberrations, he noted.

“The thing is patients with a high amount of residual ametropia we can still very good improvements of uncorrected visual acuity.”

Since their introduction in 1996, the rings have been implanted in over 4,000 patients worldwide. Currently 148 Brazilian surgeons and 187 surgeons in other countries perform implantation of the ring segments.

The results of the survey will be published in the Journal of Cataract and Refractive Surgery and EuroTimes.

Ferrara Rings

Ferrara rings are another intracorneal implant which can restore keratoconic corneas to a visually more optimal shape, said Paulo Ferrara MD.

Like INTACS, the rings are composed of two PMMA segments that have one hole in each segment to facilitate ring manipulation during the implantation procedure. They also work by essentially the same principle as INTACS.

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