BJO Online First, published on June 28, 2010 as 10.1136/bjo.2010.179580

Sequential versus concurrent KERARINGS insertion and corneal collagen cross-linking for keratoconus

Tamer M El-Raggal

Ophthalmology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to
Associate Professor Tamer M El-Raggal, Ain Shams University, Apartment 13, 2 Nakhla El-Moteae street — Heliopolis, Cairo 11361, Egypt; telragal@hotmail.com

Presented in ESCRS meeting held in Berlin, Germany, September 2008. Presented in ASCRS meeting held in San Francisco, CA, USA, April 2009 and awarded Best Paper of Session (BPOS).

Accepted 20 March 2010

ABSTRACT
Purpose To evaluate the safety and efficacy of combined intracorneal ring segments (KERARINGS) insertion and corneal collagen cross-linking (CXL) performed in one session or two sessions and to present the refractive outcomes.
Setting Magrabi Eye Hospital, Cairo, Egypt.
Methods This prospective comparative study included 16 eyes of 10 patients with progressive mild to moderate keratoconus that were randomly divided into two groups. Group 1 included nine eyes that underwent KERARINGS insertion followed by CXL 6 montsh later; group 2 included seven eyes that underwent the two procedures at the same day. In both groups channel creation was performed using the femtosecond laser (Intralase FS 60).
Results There was statistically significant improvement in both groups' uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), with significant reduction in refractive error and keratometric values ($p<0.05$). There was no statistically significant difference between both groups regarding the changes in UDVA, CDVA and refractive error ($p>0.05$). However, group 2 revealed more statistically significant reduction of keratometric values on topographical examination ($p=0.046$). The stromal haze that developed in both groups was more marked and persistent in group 2 than in group 1.
Conclusion Combined KERARINGS insertion and CXL can be performed safely in one or two sessions. However, the same-session procedure appears to be more effective regarding the improvement in the corneal shape.

INTRODUCTION
Keratoconus is a progressive non-inflammatory ectatic disease of the cornea with onset generally at puberty. Its prevalence in the general population is reported to be about 1 in 2000.[1]

Changes in corneal collagen structure[2 3] and intercellular matrix, as well as apoptosis and necrosis of keratocytes, exclusively involving the central anterior stroma and the Bowman's membrane are documented in structurally weakened corneal tissue typical of keratoconus.[4–8]

The biomechanical properties of cornea depend on the characteristics of collagen fibres,[2 3] interfibril bonds[5] and their spatial–structural disposition.[4] Biomechanical resistance of cornea of keratoconus patients is half that seen in normal corneas. Cross-linking stabilises stromal collagen, increasing the biomechanical stability of the cornea.[9]

The technique of corneal collagen cross-linking (CXL) consists of photo-polymerisation of stromal fibres by the combined action of a photosensitising substance (riboflavin or vitamin B_2) and ultraviolet type A rays (UVA).[10] Photo-polymerisation increases the rigidity of corneal collagen.[11] The aim is to slow or arrest progression to delay or avoid keratoplasty.[10]

Intracorneal ring segments have been proposed and investigated as an additive surgical procedure for keratoconus correction, which provides an interesting alternative aimed at delaying if not avoiding corneal grafting.[12–14] They act by an 'arc-shortening effect' on the corneal lamellae and flatten the central cornea.[15] The main advantage of intracorneal ring segments is the fact that the surgical process does not affect the corneal visual axis.[16–19]

A combination of these modalities would provide better results because these procedures complement each other.

The aim of this study was to evaluate the safety and efficacy of combined intracorneal ring segments (KERARINGS; Mediphacos Inc., Belo Horizonte, Brazil) insertion by femtosecond laser and CXL performed in one session or two sessions and to present the refractive outcomes.

PATIENTS AND METHODS
Patients
The inclusion criteria included: patients with progressive keratoconus (those with keratometric values increased ≥1 D over 1 year) who were contact-lens intolerant with clear cornea (no apical scarring). The maximum keratometric reading (K) was <60 D and the minimal corneal thickness was >450 μm, scotopic pupil diameter was <5 mm with the absence of any other ocular or systemic disease. The exclusion criteria included: corneal opacity, corneal dystrophy, atopy, collagen, auto-immune or other systemic disease, and pregnancy. Patients who failed to attend the follow-up visits were also excluded.

This prospective comparative study included 16 eyes of 10 patients (six women and four men) with progressive mild to moderate keratoconus who were operated upon by insertion of KERARINGS and CXL in Magrabi Eye Hospital in Cairo.

The age of the patients ranged from 22 to 36 (mean 27.9±4.8) years with uncorrected distance visual acuity (UDVA) ranging from 0.05 to 0.3 (mean 0.13±0.07) and best corrected distance visual acuity (CDVA) from 0.2 to 0.5 (mean 0.34±0.12). The spherical error (SE) ranged from −1.50 to −7.0 (mean −4.06±1.51) D while the cylindrical error ranged from 3.75 to 6.50 (mean 5.36±0.86) D.

The eyes were randomly divided into two groups: group 1 included nine eyes that underwent KERARINGS insertion followed by CXL 6 month later; group 2 included seven eyes that underwent the two procedures at the same day. In both groups channel creation was performed using the femtosecond laser (Intralase FS 60 kHz; IntraLase Corp., Abbot Medical Optics, Santa Ana, California, USA).

According to the Amsler–Krumeich classification, in group 1 there was one eye with stage I keratoconus (mean K value <48.00 D), seven eyes with stage II (mean K value 48.00–53.00 D) and one eye with stage III (mean K value 53.00–55.00 D). In group 2, there was one eye with stage I, five eyes with stage II and one eye with stage III keratoconus.

Methods

The KERARING segments (Mediphacos Inc.) are made of polymethylmethacrylate (PMMA) Perspex CQ acrylic segments that were originally designed by Paulo Ferrara. They vary in thickness from 150 to 350 μm. The segment has 160° (range 90–210°) of arc.

We used the nomogram provided by KERARINGS manufacturer[20]; the choice of insertion of one or two segments was determined according to the distribution of ectatic area on the corneal surface, whereas the thickness of the segment was determined according to the distribution of the ectatic area as well as the SE.

Preoperative evaluation included UDVA, CDVA, refraction, slit lamp and fundus examination. Corneal topography (TMS-3; Tomey Inc, Nagoya, Japan) and corneal thickness measurement using ultrasonic pachymetry (Nidek Co Ltd, Gamagori, Japan) were also performed.

The surgical procedure was done under topical anaesthesia. The tunnel was performed at 80% of the corneal thickness with the aid of femtosecond laser (Intralase FS 60 kHz), which is an infrared, neodymium glass femtosecond laser with a wavelength of 1053 nm. This beam induces photodisruption to form a dissection plane.

An inner diameter of 5.0 mm and outer diameter of 5.8 mm was programmed with the laser software with an incision length of 1.4 mm performed on the steepest topographical axis, and entry cut thickness of 1 μm. In all eyes, the power used to create the tunnel and the incision was 1.5 mJ.

After placement of a lid speculum, marking the centre of the pupil and measuring the corneal thickness by ultrasonic pachymeter at the area of implantation (5 mm diameter) was done.

Using a disposable Intralase cone, we lowered the contact glass onto the cornea until the peripheral meniscus was eliminated and adequate pressure was achieved. Final centration was achieved manually and confirmed using the laser's display. The laser was engaged to create the channels.

Once the corneal channel was made, the entrance of the channel was located using a spatula, and the ring segment was used to dissect the channel. We did not wait for the disappearance of the bubbles. The intracorneal ring segments were implanted under full aseptic conditions with special forceps and the segments were placed in the final position with a Sinskey hook without the need for suturing to close the wound.

In group 1, the surgery was terminated at that step and a bandage contact lens (AcuVue; Johnson & Johnson Vision Care Inc, New Brunswick, NJ, USA) was applied for 1 day. The postoperative treatment included a combination of antibiotic and steroid eye drops (Tobradex; Alcon, Puurs, Belgium) and artificial tears (Refresh tears; Allergan Inc, Irvine, CA, USA,) four times daily with tapering of the dose over 1 month. CXL was then performed 6 months after the original surgery. In group 2, CXL was performed immediately after the KERARING insertion procedure under topical anaesthesia.

In both groups the protocol for CXL was as following: the epithelium was mechanically scraped within the central 7.0 mm diameter area. Next, riboflavin (0.1% solution, 10 mg riboflavin 5-phosphate in 10 ml dextran 20% solution) was applied every 3 min for 30 min until the stroma was completely saturated and aqueous was stained yellow.

Ultraviolet-A irradiation was performed using a commercially available UVA system (UVX; Pescheke Meditrade, GmbH, Switzerland). Before treatment, the intended 3 mW/cm^2 surface irradiance (5.4 J/cm^2 surface dose after 30 min) was checked using a UVA meter (LaserMate-Q; LASER 2000, Wessling, Germany). During treatment, riboflavin solution was applied every 3 min to ensure saturation and balanced salt solution (BSS) was applied every 5 min to moisten the cornea. A drop of Lomefloxacin 0.3% (Okacin; Novartis Ophthalmics, Basle, Switzerland) and a bandage contact lens were applied at the end of the surgery.

Postoperative treatment included Okacin eye drops 4 times daily and diclofenac 0.1% eye drops (Voltaren; Novartis,) three times daily for 2 weeks. Artificial tears were also used four times daily for 1 month. In case of exaggerated stromal haze, fluorometholone (FML; Allergan) eye drops were used three times daily for 2 weeks.

All patients included were followed up after 3 days for contact lens removal then after 1 week, and 1, 3, 6, 9 and 12 months after the final intervention for UDVA, CDVA, refraction, slit lamp examination and topographical profile.

Corneal haze was quantified subjectively on slit lamp by using a scale from 0 to 3 as follows: 0=no haze, totally transparent; 1+=slight corneal haze, slight loss of transparency; 2+=moderate haze, iris details seen; and 3+=exaggerated haze, iris details are hardly seen.

Statistical analysis was done using SPSS statistical software (SPSS Inc, Chicago, IL, USA). Paired Student t test was used to study the changes among each individual group. Independent sample t test was used to compare the preoperative data and the postoperative changes in the two groups.

Results

Sixteen eyes of 10 patients with grade I, II and III keratoconus (according to the Amsler-Krumeich classification) were included in this study. The eyes were randomly divided into two groups.

There were no statistically significant differences between the two groups regarding the preoperative UDVA (p=0.62), CDVA

Table 1 Changes recorded in group 1 after KERARING insertion and after CXL

Group 1	Preoperative		Post KERARING		Post CXL	
Mean UDVA	0.13±0.08		0.33±0.13		0.40±0.14	
Mean CDVA	0.36±0.12		0.70±0.15		0.72±0.15	
Mean spherical error	−4.10±1.58		−2.25±1.25		−1.58±1.27	
Mean cylindrical error	5.53±0.83		4.89±0.86		4.67±0.96	
Keratometric values	Ks	Kf	Ks	Kf	Ks	Kf
	53.28±2.45	47.56±2.53	50.84±2.13	45.47±2.49	49.94±2.16	44.69±2.29

CDVA, corrected distance visual acuity; CXL, collagen cross-linking; Kf, flat keratometric reading; Ks, steep keratometric reading; UDVA, uncorrected distance visual acuity.

 El-Raggal TM. *Br J Ophthalmol* (2010). doi:10.1136/bjo.2010.179580

Table 2 Changes in the UDVA

Mean UDVA	Preoperative	Postoperative	p Value
Group 1	0.13±0.08	0.40±0.14	<0.001
Group 2	0.11±0.06	0.40±0.15	0.0056

UDVA, uncorrected distance visual acuity.

(p=0.65), spherical error (p=0.89), cylindrical error (p=0.39) and mean K value (p=0.85).

Intra-operative complications were not encountered either during KERARING insertion or during CXL.

Two segments of 300 and 200 μm were inserted in the cornea of two eyes of group 1 and 2 eyes of group 2. Two equal segments of 250 μm were inserted in the cornea of three eyes of group 1 and two eyes of group 2. Two segments of 250 and 150 μm were inserted in the cornea of three eyes of group 1 and three eyes of group 2. One segment of 250 μm was inserted in the cornea of one eye of group 1.

In group 1, after KERARING insertion and before CXL, there was statistically significant improvement of UDVA (p=0.002) and CDVA (p<0.001); reduction of both spherical (p<0.001) and cylindrical errors (p=0.016); and decrease in keratometric readings (p<0.001 for both Ks (steep K) and Kf (flat K)).

After CXL, there was another statistically significant improvement in UDVA (p=0.02), reduction of spherical error (p<0.001) and decrease in keratometric readings (p<0.001 for Ks and p=0.003 for Kf), with no significant change in CDVA (p=0.169) and cylindrical error (p=0.121). Table 1 shows the changes recorded in group 1 after KERARING insertion and then after CXL.

The final postoperative results were as follows.

Visual acuity

UDVA

There was a statistically significant improvement in the final UDVA from the preoperative values in the two groups (p<0.001 and p<0.0056 in group 1 and 2, respectively). There was no statistically significant difference between both groups regarding the UDVA improvement (p=1.00). Table 2 shows the mean UCVA changes in the two groups.

CDVA

There was a statistically significant improvement in the final CDVA from the preoperative values in the two groups (p<0.001 in the two groups). There was no statistically significant difference between both groups regarding the improvement in CDVA (p=0.59). Table 3 shows the mean CDVA changes in the two groups.

Refractive error

Spherical error

There was a highly statistically significant reduction of the spherical error from the preoperative values in the two groups (p<0.001 in the two groups). There was no statistically significant difference between both groups regarding the spherical error reduction (p=0.88). Table 4 shows the mean spherical error changes in the two groups.

Table 3 Changes in the CDVA

Mean CDVA	Preoperative	Postoperative	p Value
Group 1	0.36±0.12	0.72±0.15	<0.001
Group 2	0.33±0.11	0.69±0.11	<0.001

CDVA, corrected distance visual acuity.

Table 4 Changes in the spherical error

Mean spherical error	Preoperative	Postoperative	p Value
Group 1	−4.1±1.58	−1.58±1.27	<0.001
Group 2	−4.0±1.53	−1.46±1.83	<0.001

Cylindrical error

There was a statistically significant reduction in the cylindrical error from the preoperative values in the two groups (p=0.018 and 0.045 in group 1 and 2, respectively). There was no statistically significant difference between both groups regarding the cylindrical error reduction (p=0.42). Table 5 shows the mean cylindrical error changes in the two groups.

Keratometry (K reading)

There was a statistically significant reduction in the mean keratometric reading from the preoperative values in the two groups (p<0.001 in the two groups). Both Ks and Kf were significantly reduced.

There was a statistically significant difference between both groups regarding the mean keratometric reduction with a greater reduction in group 2 (figure 1) than in group 1 (p= 0.046). Tables 6 and 7 show the changes in keratometric values in the two groups.

Postoperative complications

Very minimal intracorneal channel deposits were present in one eye in group 1 and were visually insignificant.

Stromal haze developed in all eyes of the two groups but was more marked and persistent in group 2 (3+ haze in six eyes that took 4–5 weeks to clear) than group 1 (3+ haze in one eye that took 3 weeks to clear), but finally resolved without sequelae in both groups.

Other complications such as infection and extrusion of KERARINGS were not recorded in this series. Removal of the rings was not needed in any eye.

Stability of the visual acuity and refraction

The follow-up period in these eyes revealed nearly stable visual and refractive outcome for 12 months after the surgery. There was no statistically significant changes in the UDVA, CDVA, SE or cylindrical error between 6 and 12 months after the surgery.

Discussion

CXL is one of the first treatments for keratoconus that addresses the underlying cause of corneal weakening. It was reported that CXL leads to a mean of 2.00 D of topographical flattening. Implantation of intracorneal ring segments is another modality that is useful in mechanically flattening a portion of the cone. Based on these findings, a combination of intracorneal rings and CXL procedures lead to a synergistic flattening effect in patients with keratoconus.[21]

Intracorneal ring segments flatten the conic cornea and shift the decentralised corneal apex more centrally. These segments

Table 5 Changes in the cylindrical error

Mean cylindrical error	Preoperative	Postoperative	p Value
Group 1	5.53±0.83	4.67±0.96	0.018
Group 2	5.14±0.90	4.29±0.82	0.045

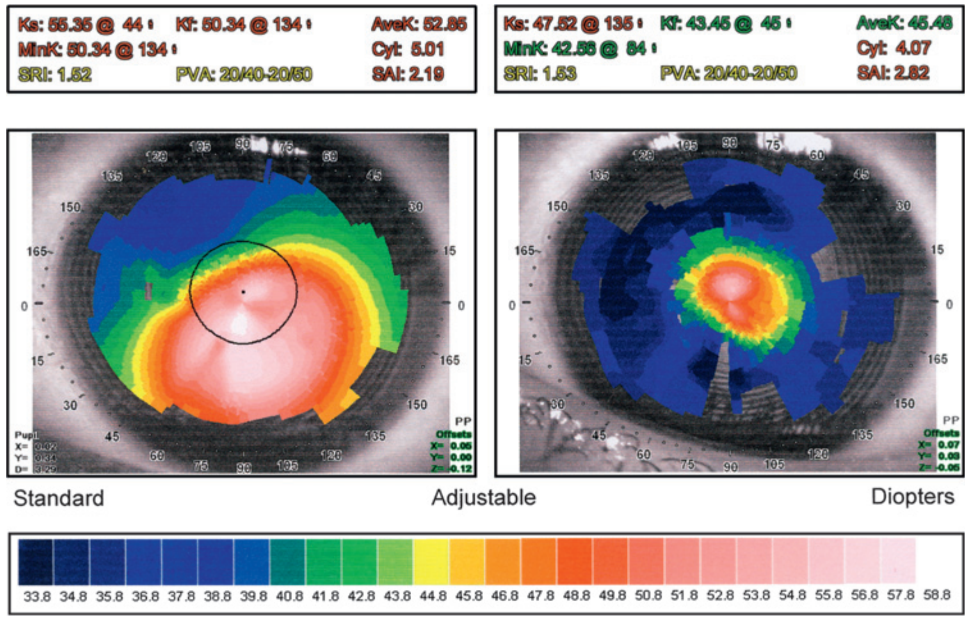

Figure 1 Preoperative (left) and postoperative (right) topography of case 1 in group 2. Notice the marked reduction of both K for steep (Ks) and K for flat (Kf) with more centration of the cone and reduction of corneal cylinder of about 1 D.

may be implanted using a mechanical method; however, the advent of the femtosecond laser now enables surgeons to create intracorneal ring tunnels using laser energy.[22]

Intracorneal ring segment implantation is an effective method for the improvement of UDVA and CDVA in keratoconic eyes. The inhibiting effect of intracorneal ring segment on keratoconus progression is still unclear; however, the addition of CXL to the procedure stops the progression of the disease and provides greater improvements than KERARINGS implantation alone.

In a retrospective case series, Chan *et al*[21] compared the results of eyes that underwent intracorneal ring segment implantation with eyes that underwent a combined treatment of intracorneal ring segment implantation followed by CXL. Significantly greater improvements in cylinder and maximal K values were reported in the combined treatment group.

CXL has an additive effect on intracorneal ring segments implantation in keratoconic eyes and may be considered as an enhancement and stabilising procedure. CXL after Intacs resulted in improvement of both UDVA and CDVA, with a greater reduction of keratometric readings.[23]

Intacs SK implantation and subsequent CXL may be alternatives in the treatment of post-laser-assisted in situ keratomileusis (LASIK) ectasia with resultant improvement of CDVA and reduction of manifest refraction.[24]

In our study, there was statistically significant improvement in UDVA and CDVA in both groups, with significant reduction in refractive error and keratometric values.

To our knowledge, this is one of the very few published articles studying the sequence of combined intracorneal rings and CXL, and up till now there has been no approved protocol on which surgical intervention has to be done first.

Coskunseven *et al*[25] found that after intracorneal ring segments (ICRS) implantation and before CXL, there was a statistically significant increase in UDVA and CDVA and a statistically significant decrease in SE, manifest cylinder and the mean K value. After additional treatment with CXL, there was a statistically significant decrease in SE and in mean K. There was also a statistically significant increase in UDVA. The increase in CDVA and the decrease in manifest cylinder were not statistically significant.

These findings were exactly similar to our results in group 1: after KERARING insertion we found a statistically significant improvement in UDVA and CDVA, a reduction of both SE and cylindrical error and a decrease in keratometric readings. After CXL, there was again a statistically significant improvement in UDVA, reduction in SE and decrease in keratometric readings, without significant change in CDVA or in cylindrical error.

Coskunseven *et al*[25] concluded that KERARING implantation followed by corneal CXL resulted in greater improvement in keratoconus than CXL followed by ICRS implantation.

In group 1, we performed KERARING insertion first, followed by CXR, as we believe that the effect of the rings in flattening and regularisation is maximum on thin keratoconic tissue rather than on rigid cross-linked cornea. In addition, our previous experience with Intralase for channel creation revealed that we have to increase the energy to create the channels in cross-linked corneas, which in some instances may result in increased corneal haze.

With regard to CXL first, some investigators found that CXL after doing corneal surgery results in exaggerated haze that may end in scarring. In our study the corneal haze was developed in both groups but was more exaggerated in group 2, which in some instances needed the use of weak steroid eye drops. All corneas had cleared by the end of the fifth week. At the end no

Table 6 Changes in the keratometric values

	Preoperative		Postoperative	
Keratometric values	**Ks**	**Kf**	**Ks**	**Kf**
Group 1	53.28±2.45	47.56±2.53	49.94±2.16	44.69±2.29
Group 2	52.68±2.55	47.64±3.17	46.94±2.14	42.93±1.96

Kf, flat keratometric reading; Ks, steep keratometric reading.

Table 7 Changes in the mean keratometric values

Mean keratometric values	Preoperative	Postoperative	p Value
Group 1	50.42±3.81	47.32±3.46	<0.001
Group 2	50.16±3.80	44.94±2.87	<0.001
p Value	0.852	0.046	

El-Raggal TM. *Br J Ophthalmol* (2010). doi:10.1136/bjo.2010.179580

eye in this study developed corneal opacities. Other complications were not encountered in this study.

Regarding the comparison between the two study groups, there was no significant difference between sequential and concurrent groups regarding changes in UDVA, CDVA and refractive error. However, group 2 had a more significant reduction of keratometric values on topographical examination.

The reason for greater corneal improvement in the concurrent group is not clear, but it can be hypothesised that the newly dissected femtosecond corneal channel may result in more pooling of riboflavin with resultant exaggerated flattening effect of CXL. This is in contrast to the healed channel that was potentially closed tightly on the ring. Other area that need studying include postoperative changes in the epithelium anatomy and/or function, and keratocyte apoptosis in the anterior stroma at the time of exaggerated haze with resultant changes in corneal remodelling.

In conclusion, combined KERARINGS insertion and CXL can be performed safely in one session or two sessions. However, the same-session procedure is more effective regarding improvement in corneal shape. Further studies to refine the refractive outcome in terms of lower and higher order aberrations, to study the corneal biomechanical changes and to verify the long-term stability of using these approaches are warranted.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Magrabi Eye Hospital, Cairo-Egypt.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Rabinowitz YS.** Keratoconus. *Surv Ophthalmol* 1998;**42**:297–319.
2. **Tuori AJ,** Virtanen I, Aine E, *et al*. The immunohistochemical composition of corneal basement membrane in keratoconus. *Curr Eye Res* 1997;**16**:792–801.
3. **Cheng E,** Maruyama I, SundarRaj N, *et al*. Expression of type XII collagen and hemidesmosome-associated proteins in keratoconus corneas. *Curr Eye Res* 2001;**22**:333–40.
4. **Radner W,** Zehetmayer M, Skorpik C, *et al*. Altered organization of collagen in the apex of keratoconus corneas. *Ophthalmic Res* 1998;**30**:327–32.
5. **Kenney MC,** Nesburn AB, Burgeson RE, *et al*. Abnormalities of the extracellular matrix in keratoconus corneas. *Cornea* 1997;**16**:345–51.
6. **Wilson SE,** Kim WJ. Keratocyte apoptosis: implications on corneal wound healing, tissue organization, and disease. *Invest Ophthalmol Vis Sci* 1998;**39**:220–6.
7. **Kaldawy RM,** Wagner J, Ching S, *et al*. Evidence of apoptotic cell death in keratoconus. *Cornea* 2002;**21**:206–9.
8. **Scroggs MW,** Proia AD. Histopathological variation in keratoconus. *Cornea* 1992;**11**:553–9.
9. **Wollensak G,** Spoerl E, Wilsch M, *et al*. Endothelial cell damage after riboflavin–ultraviolet-A treatment in the rabbit. *J Cataract Refract Surg* 2003;**29**:1786–90.
10. **Wollensak G,** Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003;**135**:620–7.
11. **Wollensak G,** Spoerl E, Seiler T. Stress–strain measurements of human and porcine corneas after riboflavin–ultraviolet-A-induced crosslinking. *J Cataract Refract Surg* 2003;**29**:1780–5.
12. **Colin J,** Cochener B, Savary G, *et al*. Correcting keratoconus with intracorneal rings. *J Cataract Refract Surg* 2000;**26**:1117–22.
13. **Alió JL,** Shabayek MH, Artola A. Intracorneal ring segments for keratoconus correction: long-term follow-up. *J Cataract Refract Surg* 2006;**32**;978–85.
14. **Burris TE,** Ayer CT, Evensen DA, *et al*. Effects of intrastromal corneal ring size and thickness on corneal flattening in human eyes. *Refract Corneal Surg* 1991;**7**:46–50.
15. **Alió JL,** Artola A, Ruiz-Moreno JM, *et al*. Changes in keratoconic corneas after intracorneal ring segment explantation and reimplantation. *Ophthalmology* 2004;**111**:747–51.
16. **Alió JL,** Artola A, Hassanein A, *et al*. One or 2 INTACS segments for the correction of keratoconus. *J Cataract Refract Surg* 2005;**31**:943–53.
17. **Tunc Z,** Deveci N, Sener B, *et al*. Corneal ring segments (INTACS) for the treatment of asymmetrical astigmatism of the keratoconus: follow-up after 2 years [in French]. *J Fr Ophtalmol* 2003;**26**:824–30.
18. **Boxer Wachler BS,** Christie JP, Chandra NS, *et al*. INTACS for keratoconus. *Ophthalmology* 2003;**110**:1031–40.
19. **Colin J,** Cochener B, Savary G, *et al*. INTACS inserts for treating keratoconus: one-year results. *Ophthalmology* 2001;**108**:1409–14.
20. **Torquetti L,** Berbel RF, Ferrara P. Long-term follow-up of intrastromal corneal ring segments in keratoconus. *J Cataract Refract Surg* 2009;**35**:1768–73.
21. **Chan CC,** Sharma FM, Wachler BS. Effect of inferior-segment Intacs with and without C3-R on keratoconus. *J Cataract Refract Surg* 2007;**33**:75–80.
22. **Shabayek MH,** Alió JL. Intrastromal corneal ring segment implantation by femtosecond laser for keratoconus correction. *Ophthalmology* 2007;**114**:1643–52.
23. **Ertan A,** Karacal H, Kamburoğlu G. Refractive and topographic results of transepithelial cross-linking treatment in eyes with intacs. *Cornea* 2009;**28**:719–23.
24. **Kamburoglu G,** Ertan A. Intacs implantation with sequential collagen cross-linking treatment in postoperative LASIK ectasia. *J Refract Surg* 2008;**24**:S726–9.
25. **Coskunseven E,** Jankov MR II, Hafezi F, *et al*. Effect of treatment sequence in combined intrastromal corneal rings and corneal collagen crosslinking for keratoconus. *J Cataract Refract Surg* 2009;**35**:2084–91.