

Original Article

Intrastromal corneal ring segments: visual outcomes from a large case series

Guilherme Ferrara MD,^{1,2} Leonardo Torquetti MD PhD,¹ Paulo Ferrara MD PhD¹ and Jesús Merayo-Llodes MD PhD²

¹Paulo Ferrara Eye Clinic, Belo Horizonte, Brazil; and ²Fernandez-Vega Eye Institute, Oviedo, Spain

ABSTRACT

Background: To evaluate the clinical safety and efficacy of implanted Ferrara intrastromal corneal ring segments in a large sample of patients with ectatic corneal disease.

Design: Retrospective, consecutive case series.

Samples: A total of 1073 eyes of 810 patients consecutively operated from January 2006 to July 2008 were evaluated.

Methods: Two groups were created according to the type of ring implanted: Group 1 – patients implanted with the 160° of arc ring – and Group 2 – patients implanted with the 210° of arc ring.

Main Outcome Measures: Uncorrected visual acuity, best-corrected visual acuity, keratometry, asphericity and pachymetry at the thinnest point of the cornea. All patients were evaluated using a corneal tomography (Pentacam, Oculus, Inc., Lynnwood, WA, USA).

Results: For Group 1 patients, uncorrected visual acuity increased to 20/80, best-corrected visual acuity increased to 20/40, asphericity decreased to -0.35 , spherical equivalent decreased to -2.26 D and keratometry decreased to 45.72 D ($P < 0.001$ for each compared with preoperative values). For Group 2 patients, uncorrected visual acuity increased to 20/130, best-corrected visual acuity increased to

20/60, asphericity decreased to -0.56 , spherical equivalent decreased to -4.14 D and keratometry decreased to 48.10 D ($P < 0.001$ for each compared with preoperative values). The 210° intrastromal corneal ring segments reduced keratometry and asphericity more than the 160° intrastromal corneal ring segments did. The complication rate was 3.82%.

Conclusions: Ferrara intrastromal corneal ring segments implantation is safe and effective and has a low complication rate. It can effectively reduce the corneal steepening and improve uncorrected visual acuity and best-corrected visual acuity in patients with keratoconus.

Key words: cornea, corneal topography, keratoconus.

INTRODUCTION

Ferrara pioneered the technique of intrastromal corneal ring segment (ICRS) implantation in keratoconus.¹ ICRS are polymethylmethacrylate devices that have now been successfully used for the management of keratoconus,^{2–6} pellucid marginal degeneration,⁷ postoperative corneal ectasia,^{8,9} myopia^{10,11} and high postkeratoplasty astigmatism.¹² ICRS implantation is a safe, reversible alternative to keratoplasty and does not affect the central visual axis of the cornea. The goal of ring segment implantation is to improve visual acuity and to delay or avoid corneal grafts in patients with keratoconus.

■ **Correspondence:** Dr Guilherme Ferrara, Contorno Avenue 4747, Suite 615, Lifercenter, Funcionários, Belo Horizonte, MG 30110-031, Brasil. Email: guilherme@ferrararing.com.br

Received 9 July 2011; accepted 15 August 2011.

Competing/conflicts of interest: No stated conflict of interest.

Funding sources: Dr Paulo Ferrara, Dr Guilherme Ferrara and Dr Jesús Merayo-Llodes have financial interest in the Ferrara Ring. Dr Leonardo Torquetti has no financial interest.

The changes in corneal structure induced by additive technologies can be roughly predicted by the Barraquer thickness law.^{13,14} This law states that when material is added to the periphery of the cornea or an equal amount of material is removed from the central area, a flattening effect is achieved. In contrast, when material is added to the centre or removed from the corneal periphery, the surface curvature is steepened. The corrective result varies in direct proportion to the thickness of the implant and in inverse proportion to its diameter. The thicker and the smaller the diameter of the device, the higher the corrective result.^{13,14}

The purpose of this study was to evaluate the visual and topographic outcomes of the Ferrara ICRS for the treatment of keratoconus and keratectasia in a large sample of patients.

METHODS

This study was approved by the institutional review board of Dr Paulo Ferrara Eye Clinic, Belo Horizonte, MG, Brazil and followed the tenets of the Declaration of Helsinki. The procedures were fully explained to each patient, and each provided written informed consent.

In the present study, 1073 eyes of 810 consecutive surgical patients from January 2006 to July 2008 were retrospectively evaluated. The patients were divided into two groups according to the type of keratectasia and ring implanted. Patients with keratoconus and keratectasias of the oval- or bowtie-type^{15,16} were designated as Group 1 ($n = 972$ eyes, Table 1) and implanted with ICRS with 160° of arc (160-ICRS, Ferrara e Hijos, Boecillo, Spain). Patients with the nipple-type keratectasia^{15,16} were designated as Group 2 ($n = 101$ eyes) and were implanted with ICRS with 210° of arc (210-ICRS). Only cases of primary ectasias were included in this study.

Inclusion criteria were contact lens intolerance and/or evidence of ectasia progression as measured by worsening of uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA), progressive intolerance to contact lens wear and progressive corneal steepening documented by topographical changes. Two or more lines of UCVA and/or BCVA worsening and at least 2 diopters (D) of increase in mean keratometry as measured with a Pentacam (Pentacam HR, Oculus, Inc., Lynnwood, WA, USA) were required to define progression of the disease. Exclusion criteria included any of the following discovered during the preoperative examination: advanced keratoconus with curvatures over 62 D, significant apical opacity and scarring, hydrops, corneas with thickness below 300 μm in the ring track as evaluated by Pentacam pachymetry, and intense unresolved atopia, which is more appro-

Table 1. Demographic data for Groups 1 and 2

	Group 1	Group 2
Eyes (n)	972	101
Age (years)	29.4 \pm 9.4 (range 17 to 59)	30.2 \pm 8.7 (range 14 to 64)
Sex (male/female)	57/43	51/49
Follow-up (months)	23.8 \pm 12.2	22.9 \pm 15.1

Group 1 patients were implanted with the 160° arc ring (160-intrastromal corneal ring segments [ICRS]), Group 2 patients were implanted with the 210° arc ring (210-ICRS). P -values >0.05 for all variables.

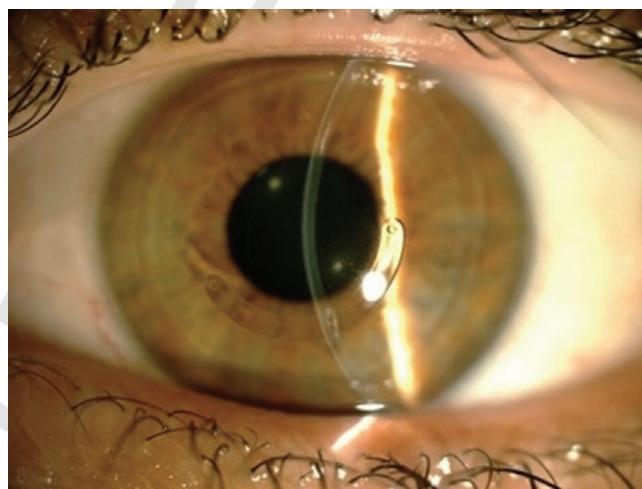


Figure 1. Day 1 postoperative slit-lamp examination.

priately treated before implantation. Pregnant or nursing women and patients with evidence of any systemic disease that would increase the risk of surgery were also excluded from the study.

Clinical measurements

A complete ophthalmologic examination was performed before surgery and included UCVA and BCVA assessment, biomicroscopy, funduscopy, tonometry, corneal topography, pachymetric map and asphericity measurement using the Pentacam HR. All clinical examinations were performed in a standardized manner by an experienced examiner (PF).

On the first postoperative day, slit-lamp biomicroscopic examination was performed (Fig. 1). Healing of the wound and migration of the segments were evaluated. At the last follow-up examination, manifest refraction, UCVA, BCVA, slit-lamp and topographic examinations were performed.

Surgical technique

All surgeries were performed by the same surgeon (PF) using the manual technique. The arc and thick-

ness of the ICRS were selected according to a previously described nomogram that is based on the position of the keratoconus on the cornea, topographic astigmatism and the pachymetric map.^{4,5} The nomogram determines the ring thickness to be implanted (Fig. 2). The surgery was performed under topical anaesthesia after miosis was achieved with 2% pilocarpine. An eyelid speculum was used to expose the eye, and 2.5% povidone-iodine eye drops were instilled onto the cornea and conjunctival cul-de-sac. The visual axis was marked by pressing a Sinskey hook on the central corneal epithelium while asking the patient to fixate on the corneal light reflex of the microscope light. Using a marker tinted with gentian violet, a 5.0-mm optical zone and incision site were aligned to the desired axis in which the incision would be made. This incision site was always the steepest topographic axis of the cornea given by the Pentacam.

A square diamond blade was set at 80% of corneal thickness as determined by the pachymetric map at the incision site. Using a 'stromal spreader', a pocket was formed in each side of the incision. Two 270° semicircular dissecting spatulas, clock-

wise and counterclockwise, were consecutively inserted through the incision and gently pushed with some quick, rotary 'back-and-forth' tunnelling movements. Following channel creation, the ring segments were inserted using a modified McPherson forceps. The rings were properly positioned with the aid of the Sinskey hook.

The postoperative regimen consisted of moxifloxacin 0.5% (Vigamox, Alcon, Fort Worth, TX, USA) and dexamethasone 0.1% (Maxidex, Alcon) eye drops four times daily for 2 weeks. The patients were instructed to avoid rubbing the eye and to frequently use preservative-free artificial tears (Oftane 0.4%, Alcon). The patients were examined postoperatively at 1 day, 1 month, 3 months, 6 months and 1 year after the surgery. After the first year, the patients were evaluated annually. The mean follow-up time was based on the time of the last visit.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA) was used for descriptive statistics, including means \pm standard deviations, and to test group differences for continuous variables. Student's *t*-test for paired data was used to compare preoperative and postoperative data. Statistical analysis was done using independent sample *t*-tests to compare variables between Groups 1 and 2. *P*-values less than 0.05 were considered statistically significant.

RESULTS

The mean follow-up times for Groups 1 and 2 were 23.8 ± 12.2 months and 22.9 ± 15.1 months, respectively (Table 1). The mean UCVA in Group 1 increased from 20/220 to 20/80 ($P = 0.00001$, Table 2). For Group 2, the mean UCVA increased from 20/350 to 20/130 ($P = 0.001$). The mean BCVA in Group 1 increased from 20/100 to 20/40 ($P = 0.00023$, Table 2), whereas in Group 2, it increased

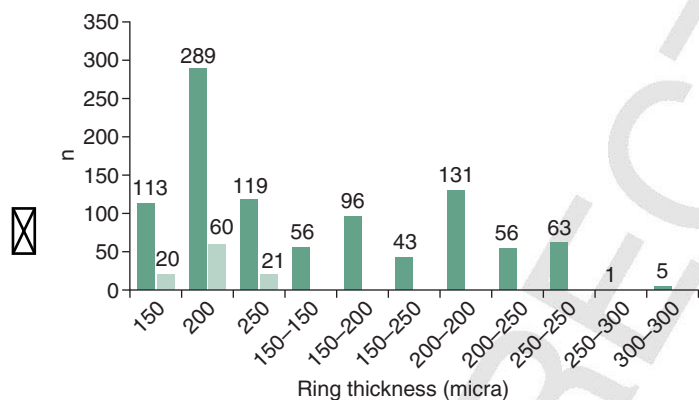


Figure 2. Distribution of implanted intrastromal corneal ring segment (ICRS) rings according to thickness and arc. Blue bars, 160-ICRS; Red bars, 210-ICRS.

Table 2. Preoperative and last follow-up examination data of patients implanted with the Ferrara ICRS

	Group 1			Group 2			Unpaired <i>t</i> -test (between groups)
	Preoperative	Postoperative	<i>P</i> [†]	Preoperative	Postoperative	<i>P</i> [‡]	<i>P</i>
UCVA	20/220	20/80	0.00001	20/350	20/130	0.001	0.038
BCVA	20/100	20/40	0.00023	20/110	20/60	0.0003	0.0034
Asphericity	-0.88 ± 0.52	-0.35 ± 0.55	0.00004	-1.17 ± 0.47	-0.56 ± 0.56	0.00004	0.0031
Spherical equivalent (D)	-3.99 ± 4.22	-2.26 ± 3.09	0.0002	-8.52 ± 5.63	-4.14 ± 4.37	0.0002	0.0010
Keratometry (D)	49.18 ± 4.42	45.72 ± 3.72	0.00003	51.92 ± 5.91	48.10 ± 4.96	0.0001	0.0001
Pachymetry (μ m)	448 ± 44.8	465 ± 49.2	0.0001	418 ± 53.4	435 ± 56.6	0.0002	0.0001

[†]Preoperative Group 1 versus Postoperative Group 1. [‡]Preoperative Group 2 versus Postoperative Group 2. BCVA, best-corrected visual acuity; ICRS, intrastromal corneal ring segments; UCVA, uncorrected visual acuity.

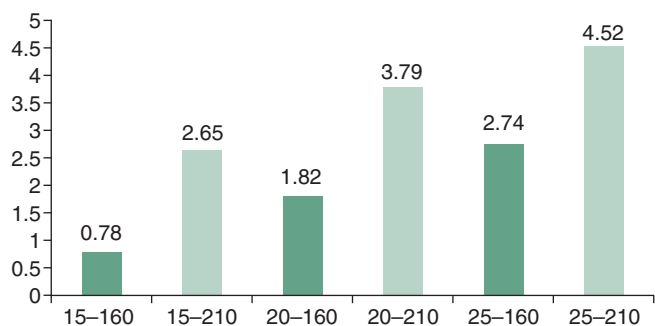


Figure 3. Effect of ring thickness on mean keratometry. The mean decrease in keratometry from preoperative to postoperative values at the last follow-up visit was greater for thicker rings. Blue bars, 160-intrastromal corneal ring segments (ICRS); Red bars, 210-ICRS. The numbers 15, 20 and 25 on the bottom of the chart, before the numbers 160 and 210, refer to ring thickness: 15 = 150 micra, 20 = 200 micra and 25 = 250 micra.

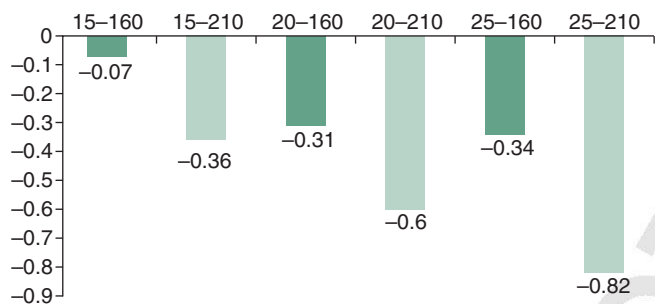


Figure 4. Effect of ring thickness on mean asphericity. The mean decrease in asphericity from preoperative to postoperative values at the last follow-up visit was greater for thicker rings. Blue bars, 160 – intrastromal corneal ring segments (ICRS); Red bars, 210 – ICRS and thickness implanted. The numbers 15, 20 and 25 on the bottom of the chart, before the numbers 160 and 210, refer to ring thickness: 15 = 150 micra, 20 = 200 micra and 25 = 250 micra.

from 20/110 to 20/60 ($P = 0.0003$). Asphericity changed in Group 1 from -0.88 to -0.35 ($P = 0.001$) and from -1.17 to -0.56 in Group 2 ($P = 0.000$).

For Group 1 patients, the preoperative spherical equivalent, -3.99 D, was reduced to -2.26 D at the last postoperative examination and the keratometry decreased from 49.18 to 45.72 D (both $P < 0.001$, Table 2). Simultaneously, the pachymetry at the thinnest point increased from 448 to 465 μm ($P < 0.001$). For Group 2 patients, the spherical equivalent decreased from -8.52 to -4.14 D and the keratometric values decreased from 51.92 to 48.10 D (both $P < 0.001$, Table 2). Simultaneously, the pachymetry at the thinnest point increased from 418 to 435 μm ($P < 0.001$).

The mean keratometry values decreased between the preoperative and postoperative periods (Fig. 3), and the thicker rings induced larger reductions. The

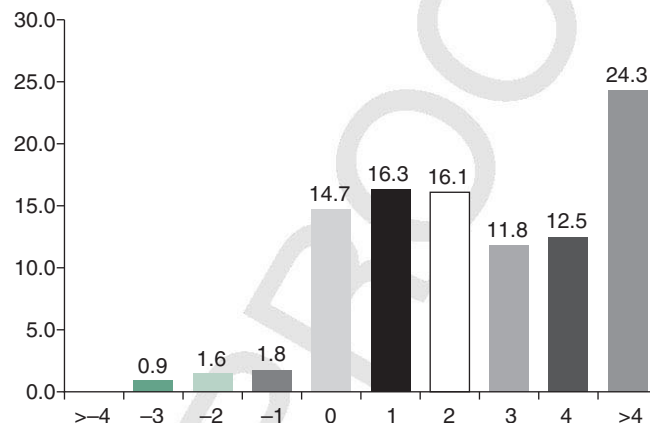


Figure 5. Best-corrected visual acuity lines gain/lost in Group 1 (%).

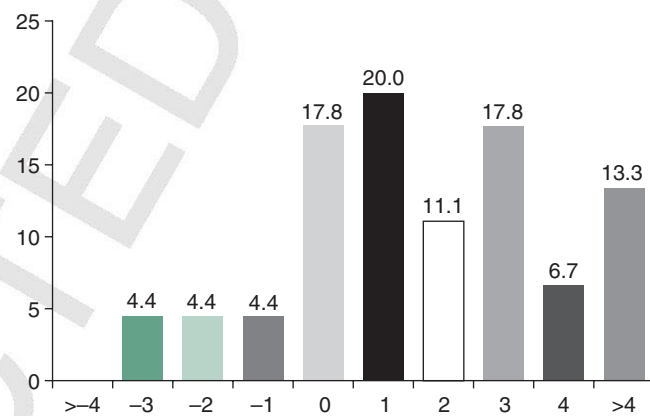


Figure 6. Best-corrected visual acuity lines gain/lost in Group 2 (%).

210-ICRS caused larger changes in mean keratometry than did the 160-ICRS (Table 2). Asphericity values changed between the preoperative and postoperative periods (Fig. 4), and the thicker the ring, the larger the asphericity change. Also, the 210-ICRS caused larger changes in asphericity than the 160-ICRS did (Table 2).

Patients in Group 1 had better preoperative and postoperative UCVA and BCVA than patients in Group 2 (Table 2). The changes in keratometry, asphericity, spherical equivalent and pachymetry were larger in Group 2 than in Group 1 (Table 2). Regarding lines gain/loss, 81% of patients of Group 1 gained at least two lines of BCVA. In Group 2, 49% of patients gained at least two lines of BCVA. (Figs 5,6).

Complications

The complication rate after Ferrara ICRS implantation was low, 3.82% (Table 3). The main com-

Table 3. Complication rate after ICRS implantation

Complication	Treatment	Eyes (%)
Undercorrection	Implantation of additional segment	16 (1.49)
Overcorrection	Segment removal and reimplantation	11 (1.02)
Extrusion	Segment removal	6 (0.56)
Malposition	Segment repositioning	4 (0.37)
Progressive corneal steepening	Keratoplasty	2 (0.18)
Ring neovascularization	Bevacizumab	2 (0.18)
Total		41 (3.82)

ICRS, intrastromal corneal ring segments.

Table 4. Preoperative and last follow-up examination data of patients who underwent follow-up surgery for removal, exchange or additional ICRS implantation

	Preoperative	Postoperative	P
UCVA	20/300	20/80	0.005
BCVA	20/160	20/50	0.0002
Asphericity	-0.84 ± 0.74	-0.35 ± 0.81	0.15
Spherical equivalent (D)	-4.64 ± 4.87	-3.04 ± 3.45	0.137
Keratometry (D)	49.33 ± 4.19	46.16 ± 3.90	0.0001
Pachymetry (µm)	450 ± 42.9	469 ± 40.8	0.0001

n = 37 eyes, 34 from Groups 1 and 3 from Group 2. BCVA, best-corrected visual acuity; ICRS, intrastromal corneal ring segments; UCVA, uncorrected visual acuity.

plication, 16 cases, was undercorrection, requiring implantation of an additional segment. One eye each of 37 patients (34 in Group 1 and 3 in Group 2) underwent follow-up surgery (Table 4) to remove (n = 6), exchange (n = 11), reposition (n = 4) or insert an additional ICRS (n = 16). For those patients, there were significant improvement between the preoperative values and the final follow-up values for UCVA, BCVA, keratometry and pachymetry. Asphericity and spherical equivalent for these patients did not improve significantly.

DISCUSSION

Modern treatment of keratoconus and keratectasia includes the implantation of ICRS that can effectively reduce corneal steepening and improve UCVA and BCVA. The Ferrara ring nomogram requires the keratoconus type, oval, bowtie or nipple, to determine the arc segment, 160° or 210°, which will be implanted. Longer arc ring segments provide more keratometry reduction and less astigmatism reduction. In the nipple type of keratoconus, Group 2 in this study, the cornea is usually very steep with relatively low astigmatism. Therefore, for this

type of keratoconus, the 210° ring segments are the most appropriate. They provide significant flattening without a large concomitant induction of astigmatism.³

Our postoperative results showed a significant improvement in UCVA and BCVA. These results are in concordance with most similar papers;^{1,2,4,17-19} however, this is the first study to describe the clinical outcomes in a large sample of consecutive surgical patients. To the best of our knowledge, this study has the largest sample of patients implanted with ICRS ever published. Our data reinforce the reproducibility and efficacy of the technique.^{20,21}

Miranda *et al.* obtained a significant reduction in the postoperative central corneal curvature, and the BCVA and UCVA improved in 87.1 and 80.6% of the eyes, respectively.²² Siganos *et al.* showed an increase of the UCVA from 20/285 preoperatively to 20/100 and 20/60 after 1 and 6 months, respectively.² The BCVA improved from 20/55 preoperatively to 20/40 and 20/33 after 1 and 6 months, respectively. Kwitko and Severo reported that after implantation of Ferrara rings in keratoconus eyes, the BCVA improved in 86.4% of eyes, was unchanged in 1.9% and worsened in 11.7%.³ The UCVA improved in 86.4% of eyes, was unchanged in 7.8% and worsened in 5.8%. The mean corneal curvature was reduced from 48.76 D to 43.17 D.

When comparing our results with studies using other types of ICRS (e.g. Intacs and Keraring), we found similar outcomes. Alio' *et al.* performed a retrospective study to evaluate the long-term (up to 48 months) results after Intacs implantation in patients with keratoconus.²³ After 6 months, the mean UCVA increased significantly (P < 0.01) from 0.46 (20/50) preoperatively to 0.66 (20/30), and the average keratometry decreased by 3.13 D. Coskunseven *et al.* evaluated the results Keraring ICRS in 50 eyes of patients with keratoconus.²⁰ Of these, 47 had UCVA of 20/40 (range: counting fingers to 20/30). At the last follow-up examination, 14 of the 50 eyes had a UCVA of 20/40 or better (range: counting fingers to 20/25). Nine eyes maintained the preoperative BCVA, whereas 39 eyes experienced a BCVA gain of one to four lines.

We found a significant increase in corneal thickness in both groups. In theory, this can be explained by corneal collagen remodelling induced by the implantation of the ICRS.^{24,25} By acting as 'spacers', the ring segments could interfere with corneal collagen turnover, with consequent increases in the corneal pachymetry.

We found a significant decrease in asphericity values after implantation of the ICRS. The postoperative value was -0.35 for Group 1 and -0.56 for Group 2. Most studies agree that human cornea asphericity values range from -0.01 to -0.80.²⁶⁻²⁸

Currently, the most commonly accepted value in a young adult population is approximately -0.23 .²⁹ The asphericity can be considered as one of markers of visual quality. Thus, returning it closer to 'normal' or at least reducing the excess prolateness usually found in keratoconus could be a predictor of improved visual quality.

For all the measured parameters, the results were better for Group 1 than Group 2. The type of keratoconus can explain the differences. The Group 2 patients had the nipple-type keratoconus that tends to be more aggressive and respond to the 'conventional' 160° ring segments with less efficacy than the oval-type keratoconus. Nipple-type keratoconus is better treated with long-arc ring segments, such as the 210° ring segments. Given the same thickness of ICRS, the 210° ring segments can provide greater changes in keratometry and asphericity than the 160° ring segments. The efficacy and safety of the 210° ring has been demonstrated.³

The incidence of complications found in this study was extremely low. This can be explained by two factors: (i) mastery of the technique; and (ii) nomogram evolution. After mastering the surgical technique, especially the deep incision and the well-constructed intrastromal tunnel, the technique-related complications become very infrequent. The nomogram has evolved based on the knowledge that thinner segments achieve the same or better results than the thicker segments used in the past.^{4,22} In some cases, an undercorrection or overcorrection was found; the cause for these changes are not well understood but probably are related to corneal biomechanics. The reason for insertion of additional ICRS was usually undercorrection, that is, a suboptimal reduction of corneal steepening after implantation of a single ICRS. One of the most feared complications of ICRS, ring extrusion, is now rare because the 350- μ m thick rings are no longer implanted. The pachymetry at the ring track must be at least double the ring thickness to be implanted.

We showed that the outcome of patients requiring follow-up surgery because of overcorrection or undercorrection, 3.4%, is acceptable. For these patients, there was improvement of UCVA, BCVA, keratometry and pachymetry. However, asphericity and spherical equivalent did not improve in these patients undergoing subsequent surgery, perhaps because of the scarring of corneal tissue and/or stroma secondary to the first procedure.

Kwitko and Severo reported Ferrara ICRS decentration in 3.9% of cases, segment extrusion in 19.6% and bacterial keratitis in 1.9%.² As the authors mentioned in their paper, the surgeon's learning curve and different healing processes in keratoconic corneas can cause the majority of complications related to the surgical technique. Once the surgical

procedure is mastered, the complications rate related to the surgery itself is very low, as demonstrated in the present study. To avoid surgery-related complications, the steps must be followed carefully, including constructing the stromal tunnel with the adjustable diamond knife set at 80% of local corneal thickness. This reduces the chance of a shallow tunnel and subsequent ring extrusion.

Extrusion of the ICRS usually occurs in patients with little stroma, overlying the implanted segments and when the ring is located close to the incision. As a general rule, it must be assumed that the thickest portion of a pair of segments in the stromal bed cannot exceed half the thickness of the cornea. If the desired ICRS thickness exceeds half the thickness of the cornea, then a thinner diameter ICRS must be selected even if the correction is likely to be smaller than desired. This should be considered as the 'pachymetry law' for ICRS implantation. Since this rule began to be followed, the incidence of extrusion has decreased significantly.³⁰

Kubaloglu *et al.* evaluated the clinical outcomes of keratoconus patients that had ICRS implantation in which the intrastromal tunnel was created manually, as we did in our study, and by femtosecond laser.³¹ After 1 year, there was significant improvement in UCVA, BCVA, keratometry, spherical equivalent, manifest sphere and cylinder in both groups. Importantly, there were no significant differences between the two groups regarding the visual or refractive results. After mastering the manual technique, the incidence of perioperative complications is extremely low, and this technique is both very safe and effective.

In conclusion, Ferrara ICRS implantation is an effective treatment for keratoconus and keratectasia. The procedure is minimally invasive and yields good visual, refractive and keratometric outcomes. Moreover, it is a safe technique and does not preclude any future additional treatment if necessary.

REFERENCES

1. Ferrara de A, Cunha P. Técnica cirúrgica para correção de miopia; Anel corneano intra-estromal. (Myopia correction with intrastromal corneal ring). *Rev Bras Oftalmol* 1995; **54**: 577–88.
2. Siganos D, Ferrara P, Chatzinikolas K *et al.* Ferrara intrastromal corneal rings for the correction of keratoconus. *J Cataract Refract Surg* 2002; **28**: 1947–51.
3. Kwitko S, Severo N. Ferrara intracorneal ring segments for keratoconus. *J Cataract Refract Surg* 2004; **30**: 812–20.
4. Ferrara P, Torquetti L. Clinical outcomes after implantation of a new intrastromal ring with a 210-degree of arch. *J Cataract Refract Surg* 2009; **35**: 1604–8.
5. Torquetti L, Ferrara P. Long term follow-up of intrastromal corneal ring segments in keratoconus. *J Cataract Refract Surg* 2009; **35**: 1768–73.

- 1 6. Ferrara P, Torquetti L. Ferrara ring. An overview. *Cataract Refract Surg Today Eur* 2009; ••: 27–30. 47
- 2 [6] 7. Rodrigues-Prats J, Galal A, Garcia-Lledo M *et al.* Intra- 48
- 3 corneal rings for the correction of pellucid marginal 49
- 4 degeneration. *J Cataract Refract Surg* 2003; 29: 1421–4. 50
- 5 8. Siganos CS, Kymionis GD, Astyrakakis N *et al.* Man- 51
- 6 agement of corneal ectasia after laser in situ keratom- 52
- 7 ileusis with INTACS. *J Refract Surg* 2002; 18: 43–6. 53
- 8 9. Silva FBD, Alves EAF, Cunha PFA. Utilização do Anel 54
- 9 de Ferrara na estabilização e correção da ectasia cor- 55
- 10 neana pós PRK. *Arq Bras Oftalmol* 2000; 63: 215–18. 56
- 11 10. Nose W, Neves RA, Burris TE *et al.* Intrastromal 57
- 12 corneal ring: 12-month sighted myopic eyes. *J Refract 58*
- 13 *Surg* 1996; 12: 20–8. 59
- 14 11. Schanzlin DJ, Asbell PA, Burris TE, Durrie DS. The 60
- 15 intrastromal ring segments; phase II results for the 61
- 16 correction of myopia. *Ophthalmology* 1997; 104: 1067– 62
- 17 78. 63
- 18 [7] 12. Ruckhofer J, Stoiber J, Twa MD *et al.* Correction of 64
- 19 astigmatism with short arc-length intrastromal corneal 65
- 20 ring segments: preliminary results. *Ophthalmology* 66
- 21 2003; 110: 516–24. 67
- 22 13. Barraquer JI. Queratoplastia refractiva, estudios e 68
- 23 informaciones. *Oftalmologicas* 1949; 2: 10–30. 69
- 24 [7] 14. Barraquer JI. Modification of refraction by means of 70
- 25 intracorneal inclusion. *Int Ophthalmol Clin* 1966; 6: 71
- 26 53–78. 72
- 27 15. Bogan SJ, Waring GO III, Ibrahim O *et al.* Classifica- 73
- 28 tion of normal corneal topography based on computer- 74
- 29 assisted videokeratography. *Arch Ophthalmol* 1990; 108: 75
- 30 945–9. 76
- 31 16. Rabinowitz YS, McDonnell PJ. Computer-assisted 77
- 32 corneal topography in keratoconus. *Refract Corneal Surg 78*
- 33 1989; 5: 400–8. 79
- 34 17. Colin J, Cochener B, Savary G, Malet F. Correcting 80
- 35 keratoconus with intracorneal rings. *J Cataract Refract 81*
- 36 *Surg* 2000; 26: 1117–22. 82
- 37 18. Colin J, Cochener B, Savary G *et al.* INTACS inserts for 83
- 38 treating keratoconus; one-year results. *Ophthalmology 84*
- 39 2001; 108: 1409–14. 85
- 40 19. Rodrigues-Prats J, Galal A, Garcia-Lledo M *et al.* Intra- 86
- 41 corneal rings for the correction of pellucid marginal 87
- 42 degeneration. *J Cataract Refract Surg* 2003; 29: 1421–4. 88
- 43 20. Coskunseven E, Kymionis GD, Tsiklis NS *et al.* One- 89
- 44 year results of intrastromal corneal ring segment 90
- 45 implantation (KeraRing) using femtosecond laser in 91
- 46 patients with keratoconus. *Am J Ophthalmol* 2008; 145: 92
- 775–9. 47
21. Zare MA, Hashemi H, Salari MR. Intracorneal ring 48
- segment implantation for the management of kerato- 49
- conus: safety and efficacy. *J Cataract Refract Surg* 2007; 50
- 33: 1886–91. 51
22. Miranda D, Sartori M, Francesconi C *et al.* Ferrara 52
- intrastromal corneal ring segments for severe 53
- keratoconus. *J Refract Surg* 2003; 19: 645–53. 54
23. Alio' JI, Shabayek MH, Artola A. Intracorneal ring 55
- segments for keratoconus correction: long-term 56
- follow-up. *J Cataract Refract Surg* 2006; 32: 978–85. 57
24. Flynn BP, Bhole AP, Saeidi N *et al.* Mechanical strain 58
- stabilizes reconstituted collagen fibrils against enzy- 59
- matic degradation by mammalian collagenase matrix 60
- metalloproteinase 8 (MMP-8). *PLoS ONE* 2010; 5: 61
- e12337. 62
25. Mackiewicz Z, Määttä M, Stenman M *et al.* Col- 63
- lagenolytic proteinases in keratoconus. *Cornea* 2006; 64
- 25: 603–10. 65
26. Davis WR, Raasch TW, Mitchell GL *et al.* Corneal 66
- asphericity and apical curvature in children: a cross- 67
- sectional and longitudinal evaluation. *Invest Ophthalmol 68*
- Vis Sci* 2005; 46: 1899–906. 69
27. Holmes-Higgin DK, Baker PC, Burris TE, Silvestrini 70
- TA. Characterization of the aspheric corneal surface 71
- with intrastromal corneal ring segments. *J Refract Surg 72*
- 1999; 15: 520–8. 73
28. Eghbali F, Yeung KK, Maloney RK. Topographic 74
- determination of corneal asphericity and its lack of 75
- effect on the refractive outcome of radial keratotomy. 76
- Am J Ophthalmol* 1995; ••: 275–80. 77
29. Yebra-Pimentel E, González-Méijome JM, Cerviño A 78
- et al.* Asfericidad corneal en una población de adultos 79
- jóvenes. Implicaciones clínicas. *Arch Soc Esp Oftalmol 80*
- 2004; 79: 385–92. 81
30. Torquetti L, Ferrara P. Reasons for intrastromal corneal 82
- ring segment explantation. *J Cataract Refract Surg* 2010; 83
- 36: 2014; author reply 2014–15. 84
31. Kubaloglu A, Sari ES, Cinar Y *et al.* Comparison of 85
- mechanical and femtosecond laser tunnel creation for 86
- intrastromal corneal ring segment implantation in 87
- keratoconus: prospective randomized clinical trial. 88
- J Cataract Refract Surg* 2010; 36: 1556–61. 89
32. Shetty R, Kurian M, Anand D *et al.* Intacs in advanced 90
- keratoconus. *Cornea* 2008; 27: 1022–9. 91
- [8] 92
- [9]
- [10]

Toppan Best-set Premedia Limited	
Journal Code: CEO	Proofreader: Jason
Article No: 2698	Delivery date: 20 September 2011
Page Extent: 7	Copyeditor: Cindy

AUTHOR QUERY FORM

Dear Author,

During the preparation of your manuscript for publication, the questions listed below have arisen. Please attend to these matters and return this form with your proof.

Many thanks for your assistance.

Query References	Query	Remark
q1	AUTHOR: Please shorten the running head to no more than 40 characters including spaces, to follow journal style.	
q2	AUTHOR: 'corenal' has been changed to 'corneal'. Please check and confirm that this is correct.	
q3	AUTHOR: 'Kwitiko <i>et al.</i> ' has been changed to 'Kwitko and Severo' so that this citation matches the entry in the Reference List. Please check and confirm that this is correct.	
q4	AUTHOR: Should 'complications rate related' be changed to 'complication rates related'?	
q5	AUTHOR: 'Kubalgodlu <i>et al.</i> ' has been changed to 'Kubaloglu <i>et al.</i> ' so that this citation matches the entry in the Reference List. Please check and confirm that this is correct.	
q6	AUTHOR: Please check and confirm if the journal title is abbreviated correctly in Reference 6. Also, please supply the volume number for this reference.	
q7	AUTHOR: Please check and confirm if the journal title in Reference 13 is correct.	
q8	AUTHOR: If Reference 24 is not a one-page article, please supply the first and last pages for this article.	
q9	AUTHOR: Please supply the volume number for Reference 28.	
q10	AUTHOR: Reference 32 in the original file has not been cited in the text. Please indicate where it should be cited; or delete it from the Reference List.	
q11	AUTHOR: In the figures, commas that function as decimal points have been changed to full points. Please check and confirm if the changes made are correct.	
q12	AUTHOR: Please check and confirm if all instances of the unit micra should be changed to μm .	
q13	AUTHOR: Please provide a heading for the first column of Tables 1, 2 and 4.	