Intracorneal Ring Segments Implantation Followed by Same-day Topography-guided PRK and Corneal Collagen CXL in Low to Moderate Keratoconus

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ABSTRACT

PURPOSE: To evaluate the safety and efficacy of intrastromal corneal ring segments (ICRS) implantation followed by same-day topography-guided photorefractive keratectomy (PRK) and ultraviolet-A/riboflavin collagen cross-linking (CXL) in patients with low to moderate keratoconus.

METHODS: Patients with low to moderate keratoconus and contact lens intolerance were included in the study. All patients first underwent femtosecond laser–enabled placement of ICRS (Keraring, Mediphacos) (first step). Same-day topography-guided PRK and CXL (second step) were subsequently performed in all patients after the refraction was stable (average 6 months [range: 3 to 11 months]).

RESULTS: Thirteen eyes from 13 patients were included in the study. Based on values before the first step and 6 months after the second step, significant improvements were noted in uncorrected distance visual acuity (0.7±0.32 logMAR vs 0.08±0.08 logMAR), corrected distance visual acuity (CDVA) (0.16±0.19 logMAR vs 0.02±0.04 logMAR), sphere (−3.65±3.08 diopters [D] vs 0.06±1.6 D), astigmatism (−3.31±1.5 D vs −0.98±0.75 D), average K (47.28±1.99 D vs 41.42±3.22 D), and coma (2.36±1.23 μm vs 1.47±0.68 μm) ($P<.05$). Approximately 63% of eyes gained ≥2 lines of CDVA, whereas no change in CDVA was reported in ~27% of eyes. No eyes lost lines of CDVA.

CONCLUSIONS: The combination of ICRS implantation followed by sequential same-day topography-guided PRK/CXL may be a reasonable option for improving visual acuity in patients with low to moderate keratoconus. [*J Refract Surg*. 2013;29(1):59-63.]

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Corneal collagen cross-linking (CXL) has emerged as an effective technique in halting the progression of keratoconus and pellucid marginal degeneration.[1,2] Current long-term follow-up studies have shown that CXL may prevent topographic and refractive progression and, to some extent, improve visual acuity and astigmatism and induce corneal flattening.[1,3]

Few studies have reported the combined effect of CXL with the insertion of intracorneal ring segments (ICRS) in patients with keratoconus. These studies have demonstrated an overall additive effect of CXL and ICRS on visual acuity and keratometry.[4-6] The potential association of photorefractive keratectomy (PRK) and CXL has also been described previously.[7-11] However, few studies have reported the combined effect of the three procedures (ICRS, CXL, and PRK).[6,12]

The purpose of our study was to evaluate the efficacy and safety of ICRS implantation followed, after reaching refractive stability, by same-day topography-guided PRK and CXL for visual rehabilitation in patients with low to moderate keratoconus.

PATIENTS AND METHODS

Patient Population

Patients with keratoconus were included in this prospective, interventional, nonrandomized, noncontrolled study. All patients underwent ICRS implantation followed by same-day topography-guided PRK and CXL after achieving refractive stability following ICRS implantation. Inclusion criteria were intolerance to contact lenses, low to moderate keratoconus, and observed progression over the previous 6 months. Grading of keratoconus was based on Amsler-Krumeich classification.

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TABLE 1

Preoperative Patient Demographics

Variable	Mean±SD (Range)
UDVA (logMAR)	0.7±0.32 (0 to 1)
CDVA (logMAR)	0.16±0.19 (−0.1 to 0.54)
Steep K (D)	49.27±1.98 (47.23 to 52.19)
Flat K (D)	45.82±2.82 (42.27 to 52.3)
Sim K (D)	47.28±1.99 (45.39 to 51.33)
Maximum K	49.27±1.98 (47.23 to 51.19)
Sphere (D)	−3.65±3.08 (−9.00 to +3.00)
Cylinder (D)	3.31±1.50 (1.00 to 6.00)
Topographic astigmatism (D)	−3.9575±2.37 (−9.92 to −1.46)
Spherical equivalent refraction	−5.03±2.93 (−10.50 to 1.25)
Coma (μm)	2.36±1.23 (1.4 to 4.54)
Corneal thickness at thinnest location (μm)	468±29.06 (404 to 507)

SD = standard deviation, UDVA = uncorrected distance visual acuity, CDVA = corrected distance visual acuity, K = keratometry

Progression was defined as one or more of the following changes over a period of 6 months: an increase of ⩾1.00 diopter (D) in maximum keratometry, an increase of ⩾1.00 D in manifest cylinder, and an increase of ⩾0.50 D in manifest refraction spherical equivalent (MRSE). All patients were seeking to correct their refractive error and were adequately informed about the aim and expected results of this type of refractive surgery. All patients signed a consent form. This study was approved by the local ethical committee.

Surgeries

As a first step, all patients underwent femtosecond laser–enabled (IntraLase FS; Abbott Medical Optics, Abbott Park, Illinois) placement of ICRS (Keraring; Mediphacos, Belo Horizonte, Brazil). Segments sizes were determined according to the nomogram provided by the manufacturer. Depth of the ring channels was set at 75% to 80% of the thinnest pachymetry reading. At the end of the surgery, antibiotic and corticosteroid eye drops were administered, a soft bandage contact lens (BCL) was placed, and the eye was examined at the slit-lamp. The BCL was removed after the epithelial defect at the site of incision had closed (3 to 5 days postoperative). Postoperative medication included antibiotic/corticosteroid (tobramycin/dexamethasone) drops four times daily until the BCL was removed.

After the refraction was stable, the patient was scheduled for the second step, which was a sequential topography-guided PRK/CXL treatment performed on the same day. The average time between the first step (ICRS implantation) and the second step (topography-guided PRK/CXL) was 6.18±2.75 months (range: 3 to 11 months). Refractive stability was determined by stable residual refractive error and K-readings in two consecutive visits at least 1 month apart.

The Schwind Amaris laser platform (Schwind eye-tech-solutions, Kleinostheim, Germany) was used to perform phototherapeutic keratectomy (PTK) to remove 50 μm of the central 6.5 mm of corneal epithelium, and subsequently to perform all topography-guided PRK procedures. Topography-guided PRK treatments with a 6-mm optical zone were performed to normalize the cornea by reducing irregular astigmatism while treating part of the refractive error. Based on previous studies,[8] a limited topography-guided PRK treatment (maximum 50 μm of stromal ablation) was chosen to minimize tissue ablation and reduce the risk of iatrogenic ectasia. Mitomycin C 0.02 mg/mL was then applied for 30 seconds for all topography-guided PRK procedures.

Immediately after topography-guided PRK, CXL was performed according to the methodology described by Wollensak et al.[13] Riboflavin (0.1% in 20% dextran T500 solution) was administered topically every 2 minutes for 30 minutes. Riboflavin absorption throughout the corneal stroma and anterior chamber was confirmed by slit-lamp examination. Isotonic riboflavin was used whenever the stromal bed thickness was >400 μm; otherwise, hypotonic riboflavin (0.1% with no dextran) was used for 10 minutes to swell the cornea to reach at least 400 μm. The cornea was aligned and exposed to ultraviolet A 365 nm light for 30 minutes at an irradiance of 3.0 mW/cm^2. During ultraviolet A exposure, riboflavin administration was continued every 2 minutes.

At the end of the surgery, antibiotic and corticosteroid eye drops were administered, a BCL was placed, and the eye was examined at the slit-lamp. The BCL was removed after the epithelial defect at the incision site had closed (3 to 5 days postoperative). Postoperative medication included diclofenc sodium 0.1 drops for 2 days and antibiotic/corticosteroid (tobramycin/dexamethasone) drops four times daily until the BCL was removed.

Outcome Measures

Uncorrected distance visual acuity (UDVA [logMAR]); corrected distance visual acuity (CDVA [logMAR]);

TABLE 2

Postoperative Visual and Refractive Outcomes

	Preop (Baseline)	After ICRS	*P* Value*	After PRK/CXL	*P* Value*	*P* Value†
UDVA (logMAR)	0.7±0.32 (0 to 1)	0.23±0.14 (0 to 0.4)	<.05	0.08±0.08 (0 to 0.16)	<.05	<.05
CDVA (logMAR)	0.07±0.09 (0 to 0.3)	0.16±0.19 (−0.1 to 0.54)	>.05	0.02±0.04 (0 to 0.1)	<.05	>.05
Flat K (D)	46.04±2.48 (41.50 to 50.65)	49.27±1.98 (47.23 to 52.19)	<.05	43.02±2.45 (39.37 to 46.86)	<.05	<.05
Steep K (D)	43.31±2.01 (40.66 to 48.69)	45.82±2.82 (42.27 to 52.3)	<.05	40.78±2.25 (36.67 to 44.6)	<.05	<.05
Sim K (D)	44.97±2.52 (40.20 to 49.76)	47.28 ±1.99 (45.39 to 51.33)	<.05	41.42±3.22 (34.62 to 46.29)	<.05	<.05
Maximum K (D)	46.04±2.42 (41.50 to 50.65)	49.27±1.98 (47.23 to 51.19)	<.05	43.03±2.45 (39.37 to 46.86)	<.05	<.05
Sphere (D)	−1.33±1.51 (−3.25 to +0.50)	−3.65±3.08 (−9.00 to +3.00)	<.05	0.06±1.60 (−2.50 to −4.50)	<.05	<.05
Manifest astigmatism (D)	−1.81±1.49 (−0.50 to −6.00)	−3.31±1.50 (−1.00 to −6.00)	<.05	−0.98±0.75 (−3.00 to 0)	<.05	<.05
Topographic astigmatism (D)	2.08±0.93 (0.76 to 3.68)	3.96±2.37 (1.46 to 9.92)	<.05	2.06±1.02 (1.00 to 3.75)	<.05	>.05
Spherical equivalent (D)	−2.24 ±1.38 (−4.00 to −0.125)	−5.03±2.93 (−10.50 to 1.25)	<.05	−0.48±1.32 (−3.00 to +3.00)	<.05	<.05
Coma (μm)	1.73±1.08 (1 to 3.9)	2.36±1.23 (1.4 to 4.54)	>.05	1.47±0.68 (0.7 to 2.9)	<.05	<.05

ICRS = intracorneal ring segment implantation, PRK = photorefractive keratectomy, CXL = corneal collagen cross-linking, UDVA = uncorrected distance visual acuity, CDVA = corrected distance visual acuity, preop = preoperative, K = keratometry
**Baseline vs after ICRS.*
†Baseline vs after PRK/CXL.

MRSE; mean, steep, and flat topographical keratometry (K) values; and corneal coma were recorded for each patient at baseline, last follow-up after ICRS placement but prior to topography-guided PRK/CXL, and 6 months after topography-guided PRK/CXL.

Safety index was calculated by the ratio postoperative ICRS placement CDVA/baseline CDVA (in logMAR). Efficacy index was calculated by the ratio postoperative ICRS placement UDVA/baseline CDVA (in logMAR).

Statistical Analysis

GraphPad Prism version 5.03 software (GraphPad, San Diego, California) was used to perform the statistical analysis. The results in outcome measures after ICRS and PRK/CXL were analyzed using the paired two-tailed design. The results were considered statistically significant for $P<.05$. The correlation between UDVA and CDVA after PRK/CXL and the preoperative baseline demographics were studied using the Pearson correlation coefficient.

RESULTS

Thirteen eyes from 13 patients were included. Table 1 summarizes the preoperative conditions in the eyes analyzed. Table 2 summarizes the postoperative visual and refractive outcomes after ICRS and 6 months after PRK/CXL.

After ICRS, a significant improvement was noted in UDVA, keratometry values, and all components of the refractive error. No significant change was noted in CDVA and coma ($P>.05$).

Additional significant changes were seen at 6 months after PRK/CXL in comparison with the results after ICRS. A significant improvement was noted in the same parameters. No significant change was noted in CDVA, topographic astigmatism, or coma ($P>.05$).

All outcome measures showed significant changes ($P<.05$) when the final results were compared with baseline data (Fig 1). After PRK/CXL, UDVA was available in 11 of 13 eyes. Safety and efficacy indexes for the 11 eyes were 0.154 and 0.62, respectively. As shown in Figure 2, approximately 63% of eyes gained ⩾2 lines in CDVA, whereas no change in CDVA was noted in approximately 27% of eyes. Figure 3 illustrates the efficacy of the two-step procedure.

No significant correlations were observed between the final UDVA and CDVA and the baseline parameters

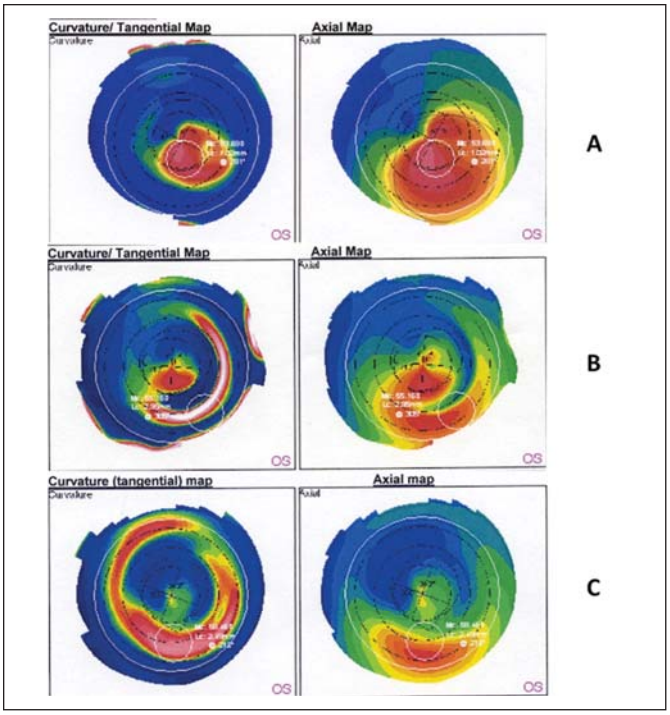


Figure 1. Representative corneal topography changes after intracorneal ring segments implantation **(B)** and topography-guided photorefractive keratectomy/crosslinking **(C)**. In this patient with keratoconus, the three procedures achieved a progressive flattening of the cone with consequent reduction of topographic astigmatism compared to baseline **(A)**.

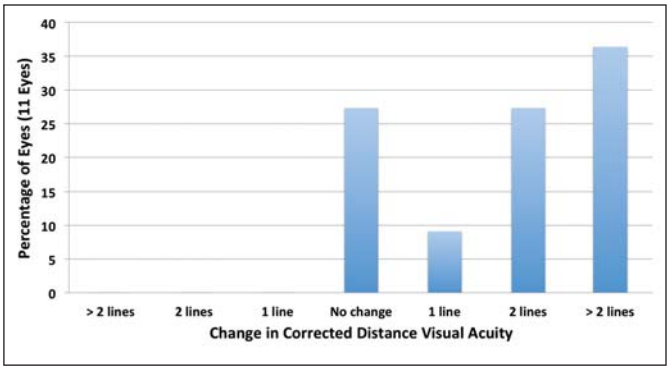
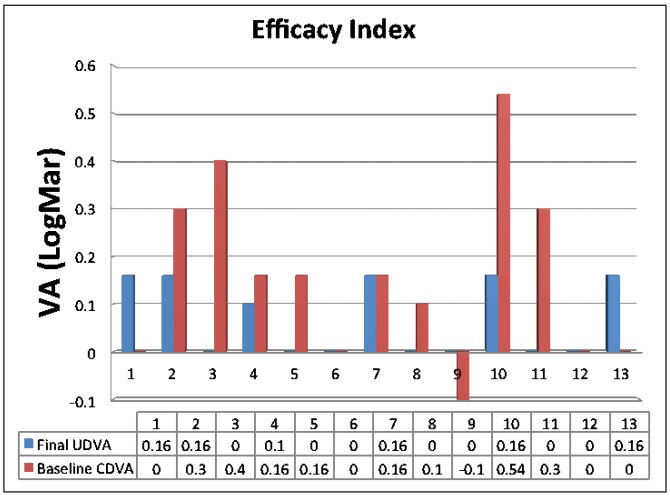


Figure 2. Safety index 6 months after the second step of 11 eyes that underwent intracorneal ring segment implantation followed by same-day topography-guided photorefractive keratectomy and corneal collagen cross-linking in low to moderate keratoconus.



	1	2	3	4	5	6	7	8	9	10	11	12	13
Final UDVA	0.16	0.16	0	0.1	0	0	0.16	0	0	0.16	0	0	0.16
Baseline CDVA	0	0.3	0.4	0.16	0.16	0	0.16	0.1	-0.1	0.54	0.3	0	0

Figure 3. Efficacy index 6 months after the second step of 11 eyes that underwent intracorneal ring segment implantation followed by same-day topography-guided photorefractive keratectomy and corneal collagen cross-linking in low to moderate keratoconus.

($P>.05$) (Tables A and B, available as supplemental material in the PDF version of this article).

DISCUSSION

Placement of ICRS followed by combined topography-guided PRK/CXL appears to be safe and an effective option in select patients with keratoconus. The aim of our topography-guided PRK treatment was to normalize the cornea by reducing irregular astigmatism while treating part of the refractive error. To remove the minimum possible tissue, we decreased the effective optical zone diameter to 6 mm in all cases (compared to our usual treatment diameter of at least 6.5 mm in routine PRK and LASIK). We also planned 70% to 100% treatment of cylinder and sphere so as not to exceed 50 µm in planned stromal removal. Based on previous studies, we chose the value of 50 µm as the maximum ablation depth effected.[8]

The prior use of ICRS would induce corneal flattening and reduce keratometric astigmatism, allowing a controlled topography-guided PRK treatment to be performed with minimal tissue ablation.

Wavefront-guided ablation patterns are often misleading in keratoconus and seldom are applicable due to the high amount of aberrations present. On the contrary, topography-guided treatments can improve the corneal aspheric profile and are suitable for laser corrections on irregular and highly aberrated corneas.[8,14]

In their 2007 study, Kanellopoulos and Binder described CXL with sequential topography-guided PRK[7]; PRK was performed 12 months after CXL. Combined simultaneous topography-guided PRK followed by CXL has been described by Kymionis et al[10] and Kanellopoulos.[8] Kanellopoulos and Binder[7] conducted a large study that found topography-guided PRK and CXL improved UDVA, CDVA, MRSE, and keratometry and were more effective when applied on the same day.[8] Efficacy of sequential PRK/CXL on keratoconus and pellucid marginal degeneration was further confirmed in other studies.[9,10,15] Kymionis et al[6] described ICRS implantation with subsequent PRK/CXL treatment in a patient with pellucid marginal degeneration. They reported a significant improvement in final UDVA and CDVA.

Iovieno et al[12] conducted a two-step case series study including five eyes with keratoconus that underwent ICRS implantation followed by same-day PRK and CXL. Their results were promising, particularly after PRK/CXL. They reported that after ICRS implantation a significant improvement was noted only in CDVA, whereas significant improvements in all preoperative parameters were noted after PRK/CXL.

We conducted a relatively larger two-step case series, and our results showed significant improvements in all parameters after ICRS except for CDVA and coma, whereas all parameters significantly improved after PRK/CXL.

Several points make the comparison between the study by Iovieno et al[12] and ours difficult. First, the number of cases is different. Second, the type of ICRS implanted in their study was Intacs (Addition Technology, Des Plaines, Illinois), whereas we used the Keraring. Third, their baseline values were markedly different from ours. However, both studies showed good results in patients with low to moderate keratoconus.

There are some limitations to our study. The sample size is small. The period between the two steps is relatively short—there should be at least 6 months between procedures. In addition, the follow-up period after PRK/CXL is relatively short; patients should be observed for at least 12 months. Further studies with a larger number of eyes and longer period of follow-up are needed.

AUTHOR CONTRIBUTIONS

Study concept and design (W.A-.T); data collection (W.A-.T); analysis and interpretation of data (M.M.S.); drafting of the manuscript (M.M.S.); critical revision of the manuscript (W.A-.T, M.M.S.); statistical expertise (M.M.S.); supervision (W.A-.T)

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TABLE A

Correlation Between Final UDVA and Preoperative Demographics

	UDVA	
Demographic	**R**	***P* Value**
Maximum K	−0.01659	.95918
Sim K	−0.00062	.998462
Spherical equivalent	−0.48898	.106692
Sphere	−0.43268	.160059
Topographic astigmatism	−0.16659	.604839
Manifest astigmatism	−0.02637	.935169
K1	−0.01659	.95918
K2	−0.00473	.988367

UDVA = uncorrected distance visual acuity, K = keratometry

TABLE B

Correlation Between Final CDVA and Preoperative Demographics

	CDVA	
Demographic	**R**	***P* Value**
Maximum K	0.438092	.15431
Sim K	0.406596	.189637
Spherical Equivalent	0.348271	.267258
Sphere	0.335809	.285902
Topographic astigmatism	0.144714	.653626
Manifest astigmatism	−0.03687	.90942
K1	0.438092	.15431
K2	0.053325	.869267

CDVA = corrected distance visual acuity, K = keratometry