**The Effect of Intracorneal Ring Segments Implantation for Keratoconus on In Vivo Corneal Biomechanics Assessed With the Corvis ST**

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## ABSTRACT

**PURPOSE:** To evaluate the effect of the implantation of intracorneal ring segments (ICRS) in keratoconus on the dynamic corneal response (DCR) parameters obtained with the Corvis ST (Oculus Optikgeräte GmbH).

**METHODS:** This prospective clinical study included patients who underwent ICRS implantation for keratoconus over a period of 1 year. On the day of the surgery and at least 1 month after ICRS implantation, the following measurements were made: corrected and uncorrected distance visual acuity, corneal tomography indices with the Pentacam (Oculus Optikgeräte GmbH), biomechanically corrected intraocular pressure (bIOP), Corvis ST DCR parameters, integrated inverse concave radius (1/R), deformation amplitude ratio (DA ratio), stiffness parameter at first applanation (SP-A1), stress–strain index (SSI), and highest concavity radius (HRC).

**RESULTS:** Fifty-one eyes of 40 patients were included with a median follow-up time of 3 months (interquartile ratio [IQR]: 2 to 6 months). Statistical analysis showed that ICRS implantation did not affect corneal biomechanical measurements evaluated with the Corvis ST, which was demonstrated by non-significant changes in the SP-A1 (*P* = .637), 1/R (*P* = .647), HRC (*P* = .177), DA ratio (*P* = .735), and SSI (*P* = .501). Addition-

ally, the results showed that bIOP measurements were not significantly affected by ICRS implantation (*P* = .113).

**CONCLUSIONS:** ICRS implantation does not affect corneal biomechanical measurements in early follow-up.

eratoconus is an asymmetrical, progressive bi-lateral corneal disease that causes thinning and irregular steepening of the cornea.1 The “pri-mum movens” of the pathogenesis of keratoconus is a focal reduction in corneal biomechanics2 that, together with eye rubbing,3 starts a cycle of decompensation that leads to increased curvature and reduced corneal pachymetry. There are several principles for the treatment of keratoconus, which vary depending on visual acuity and evidence of progression. One of the most common and accepted treatments for keratoconus is intracorneal ring segments (ICRS) implantation, which results in long-term improvement of corneal shape and refraction, an increase of visual acuity, and an excellent safety profile.4-8

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Although there is evidence that ICRS implants alone can improve the shape of the cornea and stop disease progression, even in the long term,7,9-12 the exact mechanism for which the cycle of biomechanical decompensation of keratoconus is interrupted has not been investigated. Although the placement of ICRS does not intrinsically alter corneal tissue, the change in the curvature pattern and the redistribution of stress leads to improvement over time and is hypothesized to stabilize the disease.2,13

Therefore, there is an unmet need in the current literature on the effect of ICRS implantation alone on in vivo corneal biomechanical measurement. Theoretically, an instrument that measures the intrinsic material properties of the cornea should not be influenced by ICRS implantation; therefore, the preoperative and postoperative measurements should not be different. However, ICRS are made of a stiff material that can influence the examination.

Much research has been conducted over the past two decades to assess corneal biomechanics in vivo. These efforts first resulted in the biomechanical parameters produced by the Ocular Response Analyzer (G3; Reichert Technologies), namely corneal resistance factor and corneal hysteresis, which were shown to correlate with the cornea’s geometric stiffness and the viscoelasticity of the tissue, respectively.14 Previous studies did not show significant changes in corneal hysteresis or corneal resistance factor after ICRS implantation.15

This was followed by the development of the Corvis ST (Oculus Optikgeräte GmbH) and its dynamic corneal response (DCR) parameters, which correlate with corneal overall stiffness.16-18 A recent development has been the stress-strain index (SSI), which estimates the stress-strain behavior of corneal tissue independent of intraocular pressure (IOP) and thickness.19

This study assessed the effect of ICRS implantation in patients with keratoconus using measurements from the Corvis ST’s biomechanical indices obtained before and after surgery.

## PATIENTS AND METHODS

In this prospective, single-center clinical study, we included patients with keratoconus who underwent Ferrara type ICRS implantation (AJL Ophthalmic) at the Fernández-Vega Ophthalmological Institute, Oviedo, Spain, between January 2019 and December 2020. The inclusion criteria were diagnosis of keratoconus, no previous corneal surgery, indication to undergo ICRS implantation, and signed informed consent.

The exclusion criteria included a history of herpetic keratitis, dry eye, previous corneal infection, and concomitant ocular or systemic autoimmune disease. Other exclusion criteria were pregnancy or breastfeeding, the presence of central or paracentral opacities, and the use of rigid contact lenses within the 4 weeks preceding the baseline evaluation. The ethics committee of the Fernández-Vega Ophthalmological Institute approved this prospective research study, which was conducted in accordance with the standards set out in the tenets of the 1964 Declaration of Helsinki and revised in 2013.

**Intracorneal rIngs surgery**

The ICRS were implanted following the previous reported studies.4,5,7,9,10 Prior to surgery, 0.5% proparacaine, 0.3% ciprofloxacin, and 0.2% oxybuprocaine HCI were administered. Subsequently, the center of the pupil was identified, corneal thickness in the area of the implantation (5or 6-mm diameter) was measured with ultrasonic pachymetry, and a disposable suction ring was placed on the cornea. A circumferential channel and incision was then created at 70% of corneal thickness using a 60-kHz IntraLase infrared neodymium glass femtosecond laser (Johnson & Johnson) at a wavelength of 1,053 nm. The 3-mm diameter (spot size) laser beam was optically focused by computer scanners at a predetermined intrastromal depth of 70% from the anterior corneal surface. The laser beam was programmed to create a channel with a 4.8-mm inner diameter and 5.6-mm outer diameter for a 5-mm area implantation and an inner diameter of 6-mm and an outer diameter of 7.2-mm for 6-mm area implantation. The power used to create the channel and incision was 5 mJ in all eyes. The ICRS were then implanted and set into their final position with the aid of a Sinskey hook that engaged two positioning holes, one at each end of the segment.

Postoperatively, patients were prescribed a combination of antibiotics and steroid eye drops (Tobradex; Alcon Laboratories, Inc) administered three times a day for 2 weeks, tapering over another 2 weeks.

**outcome measures**

At baseline (day of the surgery) and over at least 1 month (accepted range: 1 to 12 months) after ICRS implantation, the following measurements were recorded: corrected distance visual acuity (CDVA), corneal tomography with the Pentacam (Oculus Optikgeräte GmbH), biomechanically corrected IOP20 (bIOP), and the DCR parameters of the Corvis ST. The bIOP is an intraocular pressure estimate derived using finite element simulations and intended to eliminate the influence of central corneal thickness (CCT), age, and other corneal biomechanical parameters on IOP measurements.20

**Dcr parameters of the corvIs st**

As described previously,17,21-23 the Corvis ST applies a metered, collimated air puff with a fixed, symmetrical profile on the corneal apex, which induces the cornea to deform through two phases. In the first phase, the cornea moves inward, experiences its first applanation,

(Heinrich-Heine-Universität). The minimum total sample size was 26, which was based on a previously published study that showed a significant change in HCR of 0.8225 with an alpha value of 0.05 and power of 0.95. All data samples were first analyzed using the Shapiro-Wilk test.

Paired *t* test or Wilcoxon signed-rank tests for paired data were used, when appropriate, to assess the significance of differences between preoperative and postoperative data using the same level of significance (*P* < .05) in all cases.

and continues to deform until it reaches the highest concavity point. Then, as the air pressure decreases, the cornea undergoes a second applanation before finally returning to its natural state of rest. During this process, the instrument camera takes 4,330 frames per second along an 8-mm wide horizontal meridian.

The DCR parameters evaluated in the current study were determined by the Corvis ST operating software based on the corneal deformation profile and included the integrated inverse concave radius (1/R), deformation amplitude ratio (DA ratio), stiffness parameter at first applanation (SP-A1), SSI, and highest concavity radius (HCR). Specifically, the 1/R and DA ratio were included in the analysis because they demonstrated an association with corneal biomechanics and reduced the dependence on IOP.17 SP-A1, which measures overall corneal stiffness, was also evaluated.24 Finally, the SSI measures the stress–strain behavior of the cornea.19 A previous study demonstrated the SSI’s independence from the corneal thickness and IOP and its correlation with age.19 The HCR was also evaluated as in a previous study, and it was found to be significantly different before and after ICRS implantation.25

**statIstIcal analysIs**

Statistical analysis was performed using the SPSS statistics software (version 26.0; IBM Corporation). Data were described as mean and standard deviation. Sample size was calculated with G Power 3.1.9.3 software.

## RESULTS

Fifty-one eyes of 40 patients, (8 women and 32 men) were included in this prospective study. The median follow-up time was 3 months (interquartile range [IQR]: 2 to 6 months) and the median age at the time of surgery was 27.5 years (IQR: 22.0 to 47.5 years). As described by Fernandez-Vega-Cueto et al,10 the baseline keratoconus phenotypes of the study participants were the following: 32 croissant, 26 duck, 26 hyperprolate, and 14 snowman. **Table 1** shows details of implanted rings and demographics.

**visual, RefractIve, anD corneal tomographIc outcomes**

The mean uncorrected distance visual acuity (UDVA) improved from 0.93 ± 0.60 logMAR preoperatively to

0.47 ± 0.43 logMAR postoperatively (*P* < .0001), and the mean CDVA changed from 0.12 ± 0.13 to 0.06 ± 0.06 logMAR (*P* < .0001). The efficacy index (mean postoperative UDVA/mean preoperative CDVA) was 0.59. Postoperatively, the CDVA improved by one or more lines in 52.9% of eyes, and none of the patients lost lines of CDVA. The safety index (ratio of postoperative to preoperative CDVA) was 1.11. Spherical equivalent decreased from a preoperative value of -2.59 ± 2.63 to

-1.77 ± 2.16 diopters (D) postoperatively (*P* < .0001). In turn, the refractive cylinder improved from -3.65 ±

1.93 to 1.98 ± 1.69 D (*P* < .0001). Similarly, maximum keratometry decreased significantly (*P* = .006, **Table 2**), but the minimum thickness did not (*P* = .328, **Table 2**). Statistical analysis showed that numerous topographical indices significantly improved following ICRS implantation: steep keratometry (*P* = .001), surface variance index (*P* = .002), vertical asymmetry index (*P* = .007), keratoconus index (*P* < .001), and

height decentration index (*P* < .001) (**Table 2**).

**corneal BIomechanIcal results**

Mean preoperative and postoperative DCR values are summarized in **Table 3**.

The main result of the current study was the lack of significant changes in Corvis ST corneal biomechanical measurements following ICRS implantation. That was demonstrated by non-significant changes in SP-A1 (*P* = .637), 1/R (*P* = .647), HCR (*P* = .177), DA ratio (*P* = .735), and SSI (*P* = .501). Additionally, the statistical analysis showed that bIOP measurements were not significantly affected by ICRS implantation (*P* = .113).

## DISCUSSION

ICRS are known to improve corneal shape safely and effectively. Although ICRS do not alter the corneal structure, the implantation of the stiff rings (poly-methylmethacrylate is approximately 2,800 times stiffer than the cornea) can cause changes in corneal deformation in air-puff tonometry and may lead to changes in the biomechanics metrics measured by the Corvis ST. These possible changes were evaluated in this study. The first remarkable finding of the current study was that all visual and refractive outcomes significantly improved by more than three lines after surgery. These results, which agree with those previously reported,14,17 meant that corneal biomechanic parameters were evaluated in a sample of patients with successful ICRS implantation. The study found non-significant differences between preoperative and postoperative measurements of all corneal biomechanical DCR parameters provided by the Corvis ST, including the novel SSI, in all patients. These results indicate that the behavior of the cornea in the central region under the air puff was not affected by the placement of ICRS. Although the power of the study was sufficient to detect such a change, the study included almost twice the number of eyes suggested by the power calculations.26 Although these findings agree with the findings of Pinero et al15 and Dauwe et al,26 they contrasted with the results of Bamdad et al,25 who found a significant change in HCR between preoperative and postoperative of ICRS with a *P* value of .01. However, in that study, the alpha value would have been 0.01 if the Bonferroni correction were to be applied. Additionally, the inclusion of only 16 patients in Bamdad et al’s study limited the reproducibility of the study and the power of the analysis. To our knowledge, no other studies have evaluated the change in Corvis ST DCR parameters after ICRS implantation.

As a secondary finding, our results did not show significant changes in bIOP preoperatively and post-operatively, which proved the ability of the correction algorithm in estimating IOP after ICRS implantation. This result would be important for the treatment of patients with keratoconus with increased IOP following ICRS implantation. However, this result was not in agreement with Bamdad et al’s study, which found significant reductions in IOP evaluated with the Corvis ST.25 However, Bamad et al did not provide the Corvis ST software version, nor did they specify whether they evaluated Corvis ST IOP or bIOP.

Previous reports have attempted to explain why ICRS were able to stop keratoconus progression when they do not stiffen keratoconic corneas. It seems clear that the mechanism behind the long-term stable visual, refractive, and tomographic outcomes previously reported in both adult7,10 and pediatric9 populations were not related to an increase in corneal biomechanical properties similar to the effect of corneal cross-linking. Roberts2 proposed a stronger hypothesis and suggested that the redistribution of stresses and the changes in the curvature pattern could be behind the disease stabilization.2 As observed in earlier studies, ICRS alter the curvature pattern of the cornea (causing central flattening and peripheral steepening) and halt the biomechanical deterioration evident in the central steepening and thinning. The cornea is then hypothesized to respond viscoelasticly to the new biomechanical environment and remain stable over time.2,26 Additionally, after ICRS implantation, the cornea assumes a more regular surface with less over-elevated and depressed areas. This fact could lead to better tear film distribution and less corneal exposure. This corneal reshaping could also improve ocular surface homeostasis, minimizing inflammation and eye discomfort/ strain, and decreasing eye rubbing. It is also important to note that the experience of undergoing surgical intervention may affect patients’ behavior, making them aware of the importance of not rubbing their eyes.

The main strengths of the study include its prospective design, the large sample size relative to the power calculation, and the use of novel DCR parameters, which have been shown to be independent of IOP and tissue thickness. The main limitations of the study are the short-term follow-up and the fact that the Corvis ST measures only one horizontal meridian, whereas most ICRS are implanted inferiorly.

The current study shows that ICRS implantation does not affect IOP and corneal biomechanical measurements of the Corvis ST in the early follow-up period. These findings confirm the possibility to use the Corvis ST to assess long-term corneal biomechanical changes after ICRS implantation and to validate its use for IOP measurement.

## AUTHOR CONTRIBUTIONS

Study concept and design (RV, LF-V-C, AEliasy, JM-L, AElsheikh, JFA); data collection (AP-L, DM-C, CL); analysis and interpretation of data (RV, LF-V-C, AEliasy, JM-L, AElsheikh, JFA); writing the manuscript (RV); critical revision of the manuscript (LF-V-C, AP-L, AEliasy, JM-L, AElsheikh, DM-C, CL, JFA); statistical expertise (RV, AEliasy); administrative, technical, or material support (AP-L, DM-C, CL); supervision (LF-V-C, JM-L, AElsheikh, JFA).

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