# Intrastromal Corneal Ring Segments Combined with Collagen Cross Linking for the Treatment of Keratoconus. A Comparison of Intacs Vs Kerarings

## Abstract

**Purpose:** To compare the results of Intacs with Kerarings when used in combination with collagen cross-linking for the treatment of keratoconus

**Setting:** Queen Victoria Hospital, East Grinstead, UK

**Design:** Retrospective case series

**Methods:** A retrospective review of the case notes of keratoconic patients treated with a combination of collagen cross-linking and a intra-stromal corneal ring segments. The pre and post-operative visual acuities and topographical measurements were recorded.

**Results:** Both types of ring segment were associated with an improvement in visual acuities and topographical measurements. The average improvement in unaided acuity was 0.12 LogMar in the Intacs cases and 0.14 LogMar in the Keraring cases. The results in cases in which intacs were used were better than those for Kerarings but this did not reach statistical significance. There were more post operative complications in the intacs group.

**Conclusion:** Collagen cross-linking combined with intra-stromal corneal ring segments is an effective treatment for the early stages of keratoconus. There were no significant differences in the results of intacs cases compared to kerarings.

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**Abbreviations:** ISCRS: Intrastromal Corneal Ring Segments; PMMA: Poly-Methyl Methacrylate; SK: Severe Keratoconus

## Introduction

Keratoconus is a corneal ectasia which affects approximately 1 in 200 people [1]. It is characterized by changes in corneal collagen structure and organization which leads to progressive stretching and thinning of the cornea [2]. This causes a reduction in vision secondary to increasing myopia and irregular astigmatism. The severity of the condition can vary from mild irregular astigmatism to severe thinning and protrusion of the cornea with scarring [3].

Historically the main treatments for keratoconus have centred around spectacle and contact lens correction. The presence of corneal scarring, significant thinning and intolerance to contact lens wear are indications for corneal transplantation [4]. In the last decade, corneal collagen crosslinking has been shown to arrest the progression of keratoconus [5,6]. With this treatment, the corneal surface is treated with topical riboflavin and exposed to ultra-violet Aradiation of 370 nm wavelengths and an irradiance of 3mW/cm2 for 30 minutes [7]. This treatment increases the stiffness of the cornea by causing the addition of new covalent bonds between and within the corneal collagen fibrils [8], subsequently improving the shape and refractive properties of the cornea.

Intrastromal corneal ring segments (ISCRS) are small devices which can be implanted into the cornea in an attempt to reduce the steepness of the curvature of the cornea in keratoconus and subsequently achieve better visual acuity [9]. They were initially designed to correct low levels of myopia [10] and have more recently been shown to flatten the central part of the cornea in keratoconus. They are sited in tunnels created with either a diamond knife or laser, at an approximate depth of 70% in the corneal stroma [11]. Generally, two segments are implanted superiorly and inferiorly to manage symmetrical patterns of corneal thinning, whereas one segment may be used if the thinning follows an asymmetric pattern [11]. It has been shown that there is a greater improvement in vision when ISCRS is combined with CXL compared to using ISCRS alone [12]. The aim of our paper is to compare the results of CXL/Intacs with CXL/Keraring for the treatment of Keratoconus.

## Methods

A retrospective review of the case notes of keratoconic patients treated with a combination of CXL and a ISCRS was performed for patients at Queen Victoria Hospital, East Grinstead. The surgeries were performed by 5 different surgeons with 2 of these performing the vast majority of procedures. All procedures were planned according to respective company's pre surgical planning guides.

### ISCRS Technique

Intacs consist of a pair of semicircular pieces of poly-methyl methacrylate (PMMA) with an arc length of 150' and a hexagonal transverse shape, external diameter of 8.10 mm and internal diameter of 6.77 mm with different thicknesses (0.25-0.45 mm) in 0.05 mm increments. There is an additional Intacs design named severe keratoconus (SK) with an inner diameter of 6.00 mm, oval cross section and two different thicknesses (0.40, 0.45 mm). Intacs is manufactured by Addition Technology Inc., Des Plaines, IL, USA [13]. Kerarings are available as 90-210° segments made of PMMA. They are triangular in cross-section with a 600 micron base and an apical diameter of 5 mm. They come in variable thickness (0.15, 0.20, 0.25, 0.30 and 0.35 mm) in 0.05 mm steps [14]. They are produced by Mediphacos in Belo Horizonte, Brazil. Data from Pentacam scans and subjective refraction (where possible) were used to plan the positioning of ring segments. Tunnels were formed in the cornea using IntraLase® FS Laser (Abbott Laboratories Inc. Abbott Park, Illinois, USA).

### CXL Technique

Corneal collagen cross linking was performed using our previously published novel technique where the epithelium is disrupted rather than completely removed [15]. Each patient initially had 4 drops of Ofloxacin 0.3% and 2 drops of Pilocarpine 2% instilled into the eye to be treated. Topical anaesthesia of the cornea was then achieved by instilling benoxinate into the eye every 5 min. After inserting the eyelid speculum, the corneal epithelium over the complete corneal surface was disrupted using the Daya Epithelial Disruptor (Duckworth and Kent, Hertfordshire, UK). A solution of isotonic riboflavin 0.1% with dextran was applied to the corneal surface every 3 min for a minimum total of 30 min, and continued until riboflavin was observed within the anterior chamber with slit-lamp biomicroscopy using cobalt blue light. Adhering to the recently published "rapid" CXL protocol [16]. The eye was subsequently irradiated for 9 min, with UVA at a working distance of 54 mm and an irradiance of 10 $mW/cm^2$ using a VEGA CBM X-Linker (CSO). During this time, riboflavin 0.1% with dextran was applied to the eye every 2 min.

For those patients with thin corneas, hypotonic riboflavin 0.1% without dextran was used in place of the isotonic solution. In these patients, corneal thickness was re-measured before irradiation, and crosslinking was commenced when a minimum central corneal thickness of 400 µm was reached. The average time between the ISCRS procedure and CXL procedure was 3 months (range 1-18 months). Visual acuity measurements, subjective refraction and Pentacam measurements (K readings and corneal astigmatism) were recorded at pre-operative and post-operative (1,3,6,9 and 12 months) visits. Post-operative times were recorded from the date of the second procedure. Statistical comparisons between pre-operative and post-operative values were performed using the Wilcoxon test for UCVA, BCVA, K2, Kmean and Kmax values. Changes in these outcome measures were compared using t-tests with a P value of less than 0.05 considered statistically significant.

## Results

Data was collected from 34 patients receiving CXL/Intacs and 26 patients receiving CXL/Kerarings. The average age of the patients receiving Intacs was 26 (range 16-42). 27 were male and 7 were female. 18 were right eyes and 16 were left eyes. When assessed by the Modified Krumeich classification of Keratoconus 15 were grade I (44%), 10 were grade II (29%), 4 were grade III (12%) and 5 were grade IV (15%). The average age of the patients receiving Kerarings was 31 (range 14-57). 22 were male and 4 were female. 18 were right eyes and 8 were left eyes. When assessed by the Modified Krumeich classification of Keratoconus 14 were grade I (53%), 6 were grade II (23%), 3 were grade III (12%) and 3 were grade IV (12%).

The mean time between ISCRS and CXL procedures was 35 days in the Intacs group and 26 in the Keraring group. In the intacs group there were 3 post operative complications. 2 patients had the Intacs removed (one due to infection and due to erosion). The third patient was found to have poor vision post operatively and had the intacs repositioned which resulted in an improvement in vision. One patient in the Keraring group had to have the implants removed as a result of erosion through the cornea. In the Intacs group the mean UCVA improved from 0.81 LogMAR (±0.30) preoperatively to 0.69 (±0.27) at 6 months post operative (p=0.037) whilst the mean BCVA remained unchanged at 0.36 LogMAR. In the Kerarring group the mean UCVA improved from 0.80 LogMAR (±0.26) to 0.66 (±0.27) at 6 months post operative (p=0.031). The mean BCVA improved from 0.23 LogMAR (±0.19) to 0.2 (±0.25) at 6 months post operative (p=0.60).

In the Intacs group the mean K2 improved from 51.07D (±6.33) preoperatively to 49.08D (±5.45) at 6 months post operative (p=0.007). In the Keraring group the mean K2 improved from 49.56D (±4.81) to 49.13 (±3.92) at 6 months post operative (p=0.57). In the Intacs group the mean Kmean improved from 49.25D (±4.14) preoperatively to 46.97D (±4.32) at 6 months post operative (p=0.004). In the Keraring group the mean Kmean improved from 48.29D (±4.50) to 46.78D (±4.07) at 6 months post operative (p=0.004). In the intacs group the mean Kmax improved from 60.41D (±7.90) preoperatively to 58.68D (±7.44) at 6 months post operative (p=0.101). In the Keraring group the mean Kmax improved from 58.28D (±7.34) to 56.97D (±5.56) at 6 months post operative (p=0.016).

The mean improvement in UCVA at 6 months in the Intacs group was 0.12 LogMAR and 0.14 LogMAR in the Kerarring group (p=0.84). The mean improvement in BCVA at 6 months in the Intacs group was 0 LogMAR and 0.03 LogMAR in the Kerarring group (p=0.82). The mean improvement in K2 readings at 6 months in the Intacs group was 1.99D and 0.43D in the Kerarring group (p= 0.24). The mean improvement in Kmean at 6 months in the Intacs group was 2.28D and 1.51D in the Keraring group (p=0.41). The mean improvement in Kmax at 6 months in the Intacs group was 1.73D in the Intacs group and 1.31D in the Kerarring group (p=0.75) See Figure 1.

| | Intacs | Kerarring | P value |
|---|---|---|---|
| Mean improvement in UCVA (LogMAR) | 0.12 (±0.23) | 0.14 (±0.23) | 0.84 |
| Mean improvement in BCVA (LogMAR) | 0 (±0.40) | 0.03 (±0.21) | 0.82 |
| Mean improvement in K2 (D) | 1.99 (±4.70) | 0.43 (±2.40) | 0.24 |
| Mean improvement in Kmean (D) | 2.28 (±3.40) | 1.51 (±1.60) | 0.41 |
| Mean improvement in Kmax (D) | 1.73 (±4.30) | 1.31 (±3.70) | 0.75 |

**Figure 1:** Comparison of mean improvements at 6 months with Intacs and Kerarring.

## Discussion

Both Kerarings and Intacs have been shown to be an effective method of improving vision when used in isolation for patients with keratoconus. In 2014 Torquetti et al. [17] published data showing that Kerarings could effectively improve UDVA and CDVA in patients with keratoconus. Fahd et al. [18] showed Intacs to be safe and effective when used to treat eyes with moderate to severe keratoconus. However, recent data has suggested that there is regression in visual, refractive and topographic measures 5 years after ISCRS implantation [19]. This regression is to be expected as although the ISCRS flatten the cornea, they do not prevent the progression of the disease itself. CXL has therefore been used in combination with ISCRS to address this and provide the maximal visual improvement for the patient [20-22].

Our data shows ISCRS (INTACS and Kerarings) combined with CXL treatment to be a safe and effective treatment for keratoconus. We found both INTACS and Kerarings combined with CXL to produce a significant improvement in UCVA and topographic measurements. The mean improvement in UCVA and BCVA were similar in INTACS and Kerarring groups. We found that the topographical measures improved more in the INTACS group but this did not reach statistical significance. Our findings with Kerarings are similar to those reported by El Awady et al. [20] who assessed the outcomes of Kerarings followed by CXL treatments in 13 patients (21 eyes) with keratoconus. The mean time between implantation of Keraring and CXL treatment was 4.56±3.2 months. The mean pre-operative UDVA improved from 0.05±0.02 (Decimal acuity) to 0.23±0.17 post-operatively which is a gain of approximately 0.4 LogMAR units. This improvement in UDVA is slightly greater than our results with Keraring/CXL (0.14 LogMAR units). Our Intacs results are comparable to those reported by Ertan et al. [23] in 2009. In this paper 25 keratoconic eyes (17 patients) were treated with Intacs implantation and subsequent CXL treatment (average time between procedures 3.98 months). The UCVA improved on average by 3.1 Snellen lines and mean K improved by 2.57D.

There is currently no consensus on the best time to administer CXL after ISCRS implantation. Our average time between procedures was 35 days in patients with Intacs and 26 days in patients with Kerarings. Liu et al. [24] compared the results of ISCRS/immediate sequential CXL with ISCRS/delayed CXL (9-33 months) and found no significant difference between the results. Future modifications of the ISCRS/CXL treatment are likely to include methods to attempt to further improve the UDVA. There is already some published data on combining the procedure with topography guided transepithelial PRK in a so called "three step procedure". In a report of 16 eyes (10 patients) using this treatment the mean UDVA improved from 1.14±0.36 LogMAR pre-operatively to 0.25±0.13 at 6 months ($p<0.5$) [25].

There has also been an effort to avoid the post operative pain associated with removing the patient's epithelium during the CXL procedure. Many groups have published reports of performing "epithelium on" CXL but none have shown comparable results to "epithelium off" [26]. The corneal tunnels formed as part of the implantation procedure for ISCRS does provide an alternative method for applying the riboflavin to the cornea during the CXL treatment. Kilic et al injected the riboflavin into the corneal channel made for ISCRS insertion in 131 eyes (105 patients) and reported a mean improvement in UDVA of 0.26±0.16 logMAR [27,28] . These results are comparable to similar studies using transepithelial ("epithelium on") administration of riboflavin but not as good as those reported with "epithelium off".

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