Clinical outcomes after intracorneal ring segment implantation for keratoconus management in corneas with mild apical haze

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Abstract
Purpose: The implantation of intracorneal ring segments represents an effective and safe therapeutic option for visual improvement in patients with keratoconus. The presence of corneal opacities is considered an exclusion criterion for this operation.
Methods: This is a retrospective cohort study of six eyes of six keratoconus patients at Queen Victoria Hospital, East Grinstead, UK, between January 2012 and December 2016. Femtosecond laser-assisted intracorneal ring segment implantation was performed in six eyes with apical corneal haze. Preoperative and postoperative visual acuity, keratometry readings, as well as corneal pachymetry were compared at 6-month follow-up.
Results: Uncorrected visual acuity (UCVA) [LogMAR] improved significantly from median 1.05 [95% confidence interval (CI): 0.83–0.13] preoperatively to 0.9 (95% CI: 0.63–1.00) at 6 months postoperatively (p = 0.03). Corrected visual acuity (CDVA) also improved significantly from median 0.75 (95% CI: 0.43–1.00) preoperatively to 0.4 (95% CI: 0.23–0.50) at 6 months postoperatively (p = 0.03). Keratometric readings, K-max (diopters) and K-mean (diopters), decreased significantly from 54.5 and 47.85 preoperatively to 53.45 and 46.42 postoperatively, respectively (p = 0.03). Corneal pachymetry showed no significant changes postoperatively.
Conclusion: The results of this study show that the presence of apical haze should not exclude the implantation of intracorneal ring segments in patients with keratoconus.

Keywords: apical haze, intracorneal ring segment, keratoconus

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Introduction
Keratoconus is a bilateral, asymmetrical and progressive corneal disorder with multifactorial etiologies causing corneal thinning and steepening which can lead to irregular astigmatism with or without myopia.1-3 In its early stages, conservative therapy with spectacles and rigid contact lenses is usually sufficient. Until the turn of the century, corneal transplantation was the only option for visual acuity improvement in young patients with moderate to advanced keratoconus characterized by severe irregular astigmatism and stromal opacities.4,5 Nowadays, there are minimally invasive procedures for visual improvement, such as the implantation of intracorneal ring segments (ICRSs) in cases of contact lens intolerance.6-8 Initially, ICRSs were used in myopic patients; in 2000, Colin described their use for the first time in patients with keratoconus.6,7 They provide a safe and effective treatment option for visual improvement caused by irregular astigmatism in these patients and can delay the need for corneal transplantation by stabilizing the topographic...
regularity and improving the uncorrected visual acuity (UCVA) and corrected visual acuity (CDVA). ICRSs flatten the central cornea by acting through ‘arc shortening effect’ on corneal stroma with advantages of proven stability, safety and reversibility. ICRS, particularly KERARING (Mediphacos Inc., Belo Horizonte, Brazil) has a triangular cross-sectional profile with an arc length ranging between 90° and 325° and inner and outer diameter of 5.40 and 6.60 mm, respectively, and can be implanted in up to 80% of corneal thickness. Previously, ICRS implantation through manual tunnel dissection has been reported to have various complications, including epithelial defects, infectious keratitis, stromal edema, incision extension, persistent wound gaping and corneal perforation. Nowadays, femtosecond-assisted tunnel creation has proven efficacy and safety avoiding most of the complications encountered by manual methods. The indications for the implantation of these polymethyl methacrylate (PMMA) segments include CDVA less than 0.6 in the decimal scale, intolerance to contact lenses, clear cornea and a minimum pachymetry of 450 µm in the implantation area. The presence of corneal opacities is considered an exclusion criterion for the use of ICRSs. The aim of this study was to evaluate the clinical outcomes after ICRS implantation for keratoconus with corneal apical haze. To our knowledge, this study is the first study to report the visual and safety outcomes of femtosecond-assisted KERARING implantation in keratoconic eyes with apical haze.

Methods

Study design
This is a retrospective, noncomparative study of six patients with keratoconus and corneal apical haze who underwent femtosecond laser-assisted (Ziemer Z6, Ziemer, Biehl, CH) KERARING insertion at Queen Victoria Hospital, East Grinstead, UK, between January 2012 and December 2016.

Outcome measures
Primary outcome measures of uncorrected distance visual acuity (UCVA), corrected distance visual acuity (CDVA), Keratometry parameters (K-max, K-mean) and thinnest corneal pachymetry were evaluated preoperatively and at 6 months after KERARING insertion.

Inclusion and exclusion criteria
Inclusion criteria were keratoconic eyes with contact lens intolerance, apical corneal haze, CDVA of 0.6 LogMar or less and minimum pachymetry of 450 µm at the implantation area and 350 µm centrally. Eyes with advance keratoconus and corneal leucoma were excluded. In all eyes, ICRS implantation was performed no sooner than 6 months after collagen cross-linking (CXL). Corneal haze following CXL is reported to be temporary and tends to resolve within first 4 months after CXL. No further haze-related changes occur beyond 6 months following CXL. All patients were counselled and a written consent was taken for the procedure. All eyes have had corneal cross-linking prior to the implantation of KERARING.

Assessment
A complete ophthalmological examination was performed including slit lamp biomicroscopy and tonometry. All patients were assessed objectively for corneal haze, and all the patients were classified as haze grade 2 according to the Fantes grading scale.

Data analysis
Data analysis was performed using software SPSS for Windows version 23.0 (IBM, Armonk, NY, USA). Wilcoxon test was applied for statistical analysis with calculation of median value. Values of $p < 0.05$ were considered statistically significant.

Surgical technique
The ICRS calculation was performed on the nomogram provided by the manufacturer (KERARING; Mediphacos Inc.). Implantation of one to two segments was decided from nomogram based on the distribution of ectatic area on the corneal surface. The thickness of the rings was calculated according to the spherical equivalent (SE) in addition to the distribution of ectatic area on the corneal surface. Pupil centre was marked on the slit lamp and the desired implantation site within the central 5-mm optical zone according to the nomogram calculations. All eyes were operated under topical anaesthesia using tetracaine hydrochloride 1.0%
and proxymetacaine hydrochloride 0.5%. A disposable suction ring was placed and centred with reference to pupil centre mark to avoid decentration at the start of the procedure. The entry cut was made at the steepest topographic axis, and tunnels of inner diameter of 4.4 mm and outer diameter of 5.6 mm and at 80% corneal stromal depth were created using femtosecond laser (9 Ziemer Z6, Ziemer, Biehl, CH). In all eyes, the femtosecond laser was used to create the tunnels within 15 s. Intracorneal rings were then implanted under sterile conditions with special forceps, and Sinskey hook was utilized to adjust the final position of the implantation through the guiding holes at the end of the ring segments. No corneal sutures were placed at the end of procedure.

Postoperative topical treatment included dexamethasone sodium phosphate 0.1% for 4 weeks and chloramphenicol 0.5% eye drops for 2 weeks. Patients were reviewed 1 week postoperatively with slit lamp biomicroscopy for wound healing and evaluation of segment migration, UCVA, CDVA, keratometry and corneal pachymetry. These steps were repeated at each 1-, 3- and 6-month postoperative reviews.

**Results**

Six eyes of six keratoconic patients (four men and two women) received KERARING insertion. Median age was 33 years (range: 28–38 years). Table 1 shows the preoperative and final postoperative data on vision and keratometry in six keratoconic eyes with apical haze after implantation of KERARING.

The mean preoperative SE was $-7.5 \pm 3.0$ D (sphere $-4.5 \pm 2.75$ D, cylinder $-6.25 \pm 3.25$ D) and postoperative SE was $-5.5 \pm 3.25$ D (sphere $-3.25 \pm 3.0$ D, cylinder $-4.75 \pm 3.0$ D) with a statistically significant difference between the two ($p < 0.05$). No intraoperative and postoperative complications occurred in the six eyes included in the study at 6-month follow-up.

Figure 1 shows the preoperative and 6-month postoperative UCVA and CDVA changes in the six patients included in the study.

Figure 2 highlights the presence of apical corneal haze in the anterior segment photo of patient 5 taken 6 months after KERARING insertion.

**Discussion**

The visual rehabilitation process in keratoconus patients is complex and can be initiated successfully with conservative measures like the use of rigid contact lenses. If contact lenses are not sufficient or no longer tolerated in patients with keratoconus, minimally invasive procedures such
as the implantation of ICRSs are indicated. 6,7 ICRSs were first implanted in human eyes in early 90s, and later on adapted to use in keratoconic eyes by Colin and associates in the form of Intacs. 18,19 It has proven to be a safe and reversible procedure regularizing the corneal topography and keratometric readings leading to avoidance of much invasive surgical procedures like keratoplasty in keratoconic eyes. 4,5 KERARING has smaller apical diameter of 5.0 mm than Intacs, thus theoretically has greater efficacy in flattening the cornea but poses greater surgical challenge for being inserted in more central and thinner corneal zone. This challenge is generally overcome by the introduction of femtosecond laser-assisted incisions and tunnel formation. 12 Selecting the appropriate patient to offer this management option is challenging and highly crucial for postoperative visual success. A full ophthalmological examination including UCVA, CDVA, accurate corneal topography, aberrometry without rigid contact lens usage, corneal pachymetric map and corneal

Figure 1. Uncorrected and corrected visual acuity changes after KERARING insertion in the six patients. CDVA, corrected visual acuity; UCVA, uncorrected visual acuity.

Figure 2. Anterior segment photos of patient 5 following 6 months of ICRS insertion and the presence of corneal haze.
biomechanics assessment is required. The presence of corneal opacities is considered an exclusion criterion in the literature for this operation. No study to date has demonstrated the clinical outcomes after ICRS implantation in patients with keratoconus and apical haze.

Our study showed significant keratometric improvement, as well as significant increase in both UCVA and CDVA 6 months postoperatively after ICRS implantation in patients with keratoconus and apical corneal haze. As keratoconus is a progressive corneal ectatic disease, the stability of ICRS implantation results depends on the disease progression at the time of procedure. In stable disease, long-term results of ICRS implantation are promising but variable.19 Various studies reported that the combination of ICRS and corneal CXL leads to better visual outcomes by producing more flattening of the cornea and effectively reducing astigmatism20,21 than those offered by ICRS alone.22 However, the order of sequentially performing these two procedures remains controversial in producing better visual, refractive and topographic outcomes.23,24 All patients in our study had received corneal CXL 6 months or more prior to the ICRS implantation was offered, and none of them showed any signs of disease progression at the time of procedure.

Even if the clinical relevance is limited due to the small number of cases, our results show that the presence of mild apical opacity should not necessarily exclude the implantation of ICRSs in patients with keratoconus. Further studies with larger number of patients are required, validate this conclusion.

Our study showed significant keratometric amelioration and visual improvement after ICRS implantation in patients with keratoconus and mild corneal apical haze at 6 months postoperatively. These results suggest that the presence of mild corneal apical haze should not necessarily exclude the use of ICRSs in patients with keratoconus.

Authors’ note
The above findings the findings were partially presented in a meeting abstract https://online library.wiley.com/doi/abs/10.1111/j.1755-3768.2019.5419.

Conflict of interest statement
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Ethical statement
The study adhered to the tenets of the Declaration of Helsinki, and was approved as a retrospective audit by our local institutional review board at Queen Victoria Hospital, UK, with approval number of 536.

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