

# Continuous Intracorneal Ring Implantation in Keratoconus: Efficacy, Predictive Factors, and Complications

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**Purpose:** To examine the clinical outcomes, predictors of visual improvement and complications of continuous intracorneal ring (ICCR) implantation in patients with keratoconus and confirmed contact-lens intolerance (CLI).

**Methods:** This nonrandomized, multi-centric, retrospective cohort study examined visual, keratometric and clinical outcomes evaluated after a minimum follow-up of 2 months. Among the inclusion criteria for the standard treatment group (STG) were corrected distance visual acuity (CDVA) <20/25 Snellen, no central corneal scars, minimum corneal thickness >350µm, and central mean keratometry reading (meanK) <55 diopters. All other eyes were classified as non-standard treatment group.

**Results:** A total of 118 eyes of 118 patients with aged  $32 \pm 11$  years were included in this study. At a median follow-up of 161 days (interquartile range: 111–372 days) ICCR implantation improved the CDVA from a mean of 0.38 to 0.15 logMAR ( $p < 0.0001$ ). Our correlation analysis showed lower preoperative CDVA to be the single best predictor of CDVA improvement, with eyes of a CDVA of 20/80 or lower improving by  $4.3 \pm 2.0$  lines on average. Eyes with a meanK >55 diopters gained  $9.04 \pm 4.83$  lines in UDVA and  $2.86 \pm 3.09$  lines in CDVA. However, postoperatively these eyes had a CDVA of  $0.32 \pm 0.21$  logMAR which is significantly inferior to the STG outcome ( $p = 0.001372$ ). Fifteen eyes (12.7%) had to undergo a ring exchange procedure because of refractive under- (9 eyes) or overcorrection (6 eyes). Two eyes (1.7%) experienced medical complications.

**Conclusion:** This study confirms the inclusion criteria of ICCR implantation in KC eyes with CDVA <20/25 and CLI. Particularly in eyes with a preoperative CDVA <20/80 and a meanK <55 diopters, ICCR implantation should be considered due to its reversibility and low rates of serious complications. The main challenge remains in the low predictability of the magnitude of this improvement in eyes with CDVA >20/30.

**Keywords:** keratoconus, MyoRing, continuous intracorneal ring, intracorneal continuous ring

## Introduction

In the last 20 years, the range of treatment modalities for Keratoconus (KC) has vastly expanded. Novel contact-lens types<sup>1</sup> can significantly improve visual acuity by correcting both lower- and higher-order aberrations. A central problem, however, is that, due to irregularities of the corneal surface, many patients begin to experience CL intolerance (CLI) and surgical measures become necessary.<sup>2</sup>

Classical corneal crosslinking (CXL) is an established surgical first step to halt KC by stabilizing the cornea and thereby prevents further ectasia and decreases in visual acuity.<sup>3–6</sup>

To improve vision in a clinically significant manner, the minimally invasive embedding of intracorneal implants have become increasingly popular. Intracorneal ring segments (ICRS) and 360° intracorneal continuous rings (ICCR) have been developed by different manufacturers and have shown their efficacy in significantly improving visual acuity in eyes with KC and in postponing or completely eliminating the need for keratoplasty.<sup>7–9</sup> The reported advantages of ICCR

compared to ICRS are the more robust improvement of spherical aberrations,<sup>7</sup> increased biomechanical stability<sup>10,11</sup> and their sustained effectiveness in progressive KC.<sup>8,12–15</sup>

However, a recent systematic review and meta-analysis on ICCR implantation in KC highlighted the need for high-powered studies, mainly due to heterogeneity in corrected distance visual acuity (CDVA) outcome.<sup>9</sup> Furthermore, only few studies have reported on the surgical complications occurring after ICCR implantation and even less have reported on the need for repeated surgery to address over or under correction.<sup>16,17</sup>

To provide further insight into the efficacy of this treatment option and its complications for patients with KC, we retrospectively examined the data collected at three different centers. All treatments were planned in coordination with the manufacturer's reading center, and all patients met the same inclusion and exclusion criteria for ICCR implantation.

## Materials and Methods

This retrospective case-series was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the ethics committee of the Hamburg medical association in April 2019 with the approval number PV6017. All patients provided informed consent for anonymized data analyses.

### Patient Selection

Patients were diagnosed with KC based on their medical history, slit-lamp examination results, and corneal topography and tomography findings (irregular astigmatism displayed by one or more of the following findings: a steepest K value  $\geq 47$  diopters (D); an inferior-superior K-value difference (I-S value) of  $>1.5$  D and/or a skewed topographical axis. Patients aged 16 years or older with a thinnest pachymetry reading  $>350$   $\mu\text{m}$ , a CDVA  $<20/25$ , and without central corneal scarring were considered for ICCR implantation. Only patients with persistent contact-lens intolerance after multiple fitting attempts, one of which must have been done at specialized contact lens institute were included in the study. To prevent aniseikonia, patients with a projected postoperative anisometropia  $>4$  D were considered ineligible for surgery. The "keratometric limit" beyond which we expected an ICCR to be insufficient for visual rehabilitation was set to a mean central simulated keratometry reading ( $\text{meanK} = \frac{\text{SIMK1} + \text{SIMK2}}{2}$ ) of 55 D.<sup>14</sup> When patients met these criteria, the decision to perform ICCR implantation was based on the degree of subjective visual impairment. In some cases, we deviated from this treatment algorithm and included patients that did not meet all the aforementioned criteria. The eyes of these patients were defined as the non-standard treatment group (NSG). Surgery was performed for these patients when the alternative treatment (laser-assisted therapeutic keratectomy with CXL<sup>18</sup> or keratoplasty) was not feasible for the patient.

The primary aim of the surgery was visual rehabilitation, ie an improvement of the best spectacle-corrected distance visual acuity (CDVA). Additional aims can be halting the progression of KC by stabilizing the corneal after unsuccessful CXL and to reduce anisometropia, thereby improving functional binocular CDVA. In this trial, however, eyes with previous CXL were not included.

Postoperatively, beside a consult on the first postoperative day, patients were scheduled for a follow-up 2–3 months after ICCR implantation. At this follow-up visit, a definitive evaluation of the surgical effect can be made and the need for potential ring-exchange can be assessed.<sup>19</sup> Only patients who realized their follow-up at least 2 months after surgery were included in the study. If, at follow-up, both the physician in charge and the manufacturer's reading center considered the visual rehabilitation to have been maximized with the ring size employed, the patient was enrolled in the study. When a second surgery was performed to exchange a ring due to refractive over- or under-correction or due to complications, we included the preoperative values of the first surgery and the postoperative values of the last surgery in the analysis. A subgroup analysis was done to compare eyes undergoing single and those undergoing two surgeries. Patients scheduled for a ring exchange at the time of data collection were excluded. We also excluded all eyes that had previously undergone ocular surgery including CXL. To avoid biasing our analysis by treating two eyes within the same patient as independent, we only included one of two eyes (selected at random) when patients had undergone surgery for both eyes.

### Instruments and Procedures

Topography and tomography were performed on all patients using two different Scheimpflug-Placido camera systems (Pentacam HR, Oculus and Galilei G6, Ziemer Ophthalmic Systems AG). To implant the ICCR (MyoRing), an intra-corneal

pocket with a diameter of 8.7 mm was created at a corneal depth of 300  $\mu\text{m}$ . Pocket creation was carried out either using mechanical dissection with a microkeratome (Pocketmaker<sup>®</sup>, DIOPTEx GmbH, Austria) or a femtosecond laser (Femto LDV Z8<sup>®</sup>, Ziemer Ophthalmic Systems AG, Port, Switzerland) at the surgeon's discretion. The correct MyoRing dimensions were provided by the manufacturer (DIOPTEx GmbH, Linz, Austria) based on a mathematical corneal model after uploading the relevant parameters to an online database. The treatments were performed by one of three surgeons (AD, SL, JS). All steps have been described in previous publications.<sup>11,13</sup>

## Main Outcome Measures

Our primary outcome measures were the improvement of uncorrected distance visual acuity (UDVA) and CDVA as measured in logMAR chart lines. UDVA and best spectacle-CDVA were measured using a decimal scale and transformed into logMAR values for statistical analysis. As previous authors have done, the safety Index was defined as follows: the quotient between the postoperative CDVA and the preoperative CDVA.<sup>20</sup>

The rate of intraoperative and/or postoperative complications were also cataloged. Simulated central K values (SIM K1=steep, SIM K2=flat and meanK) were determined in the central 1–4-mm zone with a refractive index of  $n=1.3375$  with the axial (sagittal) curvature map. Kmax and thinnest Pachymetry were determined on an 8-mm zone of the anterior surface.

## Follow-Up

Follow-up examinations included slit-lamp examinations, assessments UDVA and CDVA, corneal topography and tomography, and corneal optical coherence tomography (OCT) examinations to assess the implantation depth of the ring. KC progression was assessed using tangential (instantaneous) anterior curvature maps and manifest refraction.

## Statistical Analysis

We calculated the median, mean, standard deviation (SD) and interquartile range of all continuous variables for the included eyes. Where applicable, the data are presented as the mean  $\pm$  standard deviation (SD) while non-normally distributed data are represented using the median and interquartile range (Q25:Q75).

All available variables were tested for normality using a conjunction of a graphical quantile–quantile test, and the Shapiro–Wilk test. We used the two variations of the *t*-test to assess for significant differences between variables sampled from a Gaussian distribution. Non-normally distributed data were analyzed using the Wilcoxon signed rank test for matched pairs (before and after) and the Mann–Whitney *U*-Test for independent samples.

Correlational analyses were computed with the appropriate parametric (Pearson) or non-parametric (Spearman) test using Bonferroni correction. The threshold for statistical significance was set at  $p < 0.05$ . All statistical analyses were performed using the programming language Python 3.7 run on PycharmEdu2019 (JetBrains, Czech Republic) for Microsoft Windows.

For statistical analysis, all visual acuities were converted to logarithm of minimum angle of resolution (logMAR). The visual acuities of counting finger, hand motion, and light perception were converted to 0.014, 0.005 and 0.001 in decimal notation respectively as described in previous studies.<sup>21</sup>

## Results

In total, 140 eyes of KC patients with full preoperative data were considered for the study. We excluded four eyes that were still scheduled for a ring exchange; one eye had previous penetrating keratoplasty; seven eyes of patients with bilateral surgery were randomly excluded to avoid overestimating the statistical power of our analysis. Finally, we excluded 10 eyes in which the final follow-up was performed before the completion of 60 days. We therefore included 118 eyes in our analysis. No patient was lost to follow-up.

Overall, the median age of patients was  $32 \pm 11$  years with 17 eyes (14%) having to undergo additional surgeries. Visual acuity improvements postoperatively were  $6.0 \pm 4.8$  lines in UDVA and  $2.3 \pm 2.1$  lines in CDVA. The median follow-up period was 161 days (111:372).

Descriptive statistics on pre- and postoperative parameter values are displayed in Table 1. The statistics on the differences between pre- and postoperative values are displayed in Table 2.

**Table 1** Descriptive Statistics

Parameter	Preoperative Values		Postoperative Values		p
	n	Mean ± SD	n	Mean ± SD	
UDVA (logMAR)	118	0.99 ± 0.45	118	0.39 ± 0.3	<0.0001
CDVA (logMAR)	118	0.38 ± 0.23	118	0.15 ± 0.15	<0.0001
Sph (D)	106	-2.5(-4.94:-0.06)*	107	0.82 ± 2.32	<0.0001
Cyl (D)	106	-3.82 ± 2.32	107	-1.5(-3.0: -0.75)	<0.0001
SE (D)	106	-4.0(-7.0: -2.03)	107	-0.19 ± 2.2	<0.0001
K1 preop (D)	118	47.38 ± 4.18	111	42.35 ± 2.58	<0.0001
K2 preop (D)	118	50.59 ± 4.85	111	45.75 ± 3.16	<0.0001
meanK (D)	118	48.98 ± 4.23	111	44.05 ± 2.66	<0.0001
topoAsti (D)	118	3.82 ± 2.49	111	2.9(1.96: 4.39)*	0.1195
Kmax preop (D)**	118	57.58 ± 7.67	112	53.70(48.68: 57.32)*	<0.0001
min. Pachy (µm)	117	445.18 ± 41.22	110	450.24 ± 45.67	0.3837

**Notes:** \*Denotes median (interquartile range) for variables that are not normally distributed as \*\*Preoperative and postoperative values for Kmax could be located at completely different points in the cornea.

**Abbreviations:** logMAR, logarithm of the minimum angle of resolution; D, Diopter; SD, standard deviation; Sph, refractive sphere; Cyl, refractive cylinder; SE, spherical equivalent; K1, flat meridian of anterior simulated keratometry, K2, steep meridian of anterior simulated keratometry min. Pachy, thinnest pachymetry reading; Kmax, maximum keratometry reading; topo Asti, topographical astigmatism.

**Table 2** Difference Between Preoperative and Postoperative Values

Parameter	n	Mean ± SD	p
Δ UDVA (logMAR)	118	-0.6 ± 0.48	<0.0001
Δ CDVA (logMAR)	118	-0.22 ± 0.21	<0.0001
Δ Sph (D)	97	3.74 ± 3.78	<0.0001
Δ Cyl (D)	97	1.84 ± 2.58	<0.0001
Δ SE (D)	97	3.88(1.75 to 7.0)*	<0.0001
Δ K1 preop (D)	111	-4.93 ± 3.25	<0.0001
Δ K2 preop (D)	111	-4.62 ± 3.61	<0.0001
Δ meanK (D)	111	-4.78 ± 3.1	<0.0001
Δ topoAsti (D)	111	-0.28 ± 2.44	0.1195
Δ Kmax preop (D)**	112	-3.91 ± 6.75	<0.0001
Δ min. Pachy (µm)	109	4.73 ± 25.53	0.3837

**Notes:** \*Denotes values that are not normally distributed in the format median (interquartile range) \*\*Preoperative and postoperative values for Kmax could be located at completely different points in the cornea. \*\*Preoperative and postoperative values for Kmax could be located at completely different points in the cornea. Δ is the difference between the postoperative and the preoperative value of the same parameter.

**Abbreviations:** logMAR, logarithm of the minimum angle of resolution; D, Diopter; SD, standard deviation; Sph, refractive sphere; Cyl, refractive cylinder; SE, spherical equivalent; K1, flat meridian of anterior simulated keratometry, K2, steep meridian of anterior simulated keratometry min. Pachy, thinnest pachymetry reading; Kmax, maximum keratometry reading; topo Asti, topographical astigmatism.

Figure 1 depicts the postoperative changes in distance visual acuity lines for each eye. Figure 2 shows the CDVA improvement in all eyes with respect to the day of follow-up at which this was measured.

### Subgroup Analyses – Multiple Surgeries and Non-Standard Treatment Group

Among the eyes that underwent multiple surgeries, 17 underwent one additional treatment. One eye had three surgeries overall. The reasons for reoperation are listed under the subheading Complications.

The outcomes comparing eyes that only underwent one surgery and the ones undergoing multiple surgeries are listed in Table 3.

We performed another subgroup analysis for the 14 eyes in the NSG. Alternative treatments were not feasible for those patients. Eight of 14 eyes were classified as non-standard for their meanK being above our threshold of 55 d with meanK at  $59.18 \pm 3.29$  and Kmax at  $73.48 \pm 11.82$ . These eyes gained  $9.04 \pm 4.83$  lines in UDVA and  $2.86 \pm 3.09$  lines in CDVA with a postoperative vision of  $0.32 \pm 0.21$  CDVA significantly worse than STG eyes ( $p=0.001372$ ). One patient had a min. pachy of  $346\mu\text{m}$  and had a femto-laser assisted pocket creation at  $290\mu\text{m}$ . Five eyes only had mild KC findings with preoperative CDVA  $>20/25$  and Kmax values below 47D. Three of those patients were treated with the main objective of improving UDVA in myopic patients. Two of the mild KC patients underwent ICCR implantation to relieve anisometropia due to asymmetrical KC. All comparisons between STG and NSG can be found in Table 4.

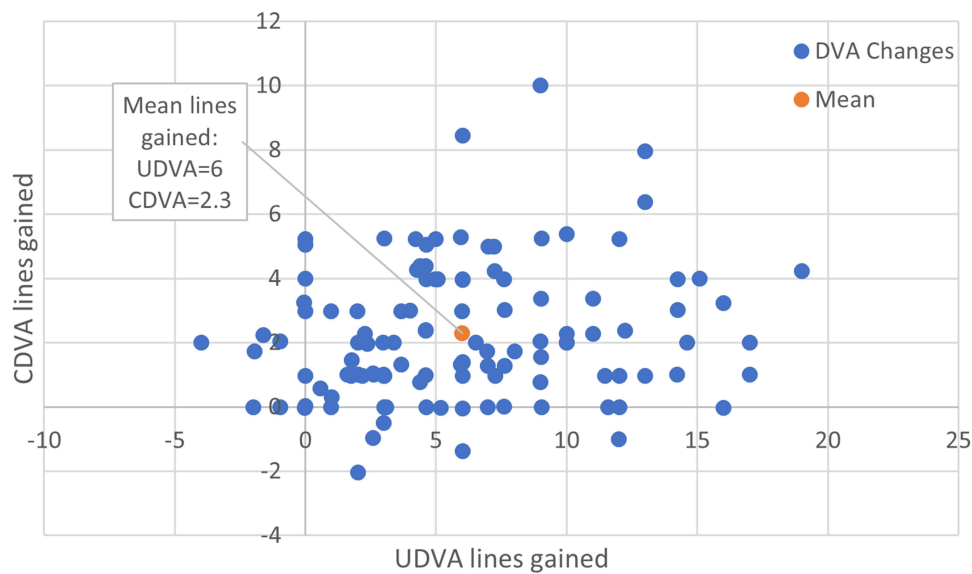


Figure 1 Simultaneously displayed changes in UDVA and CDVA. Mean: Denotes the simultaneous representation of mean changes in UDVA (6 lines) and mean changes in CDVA (2.3 lines).

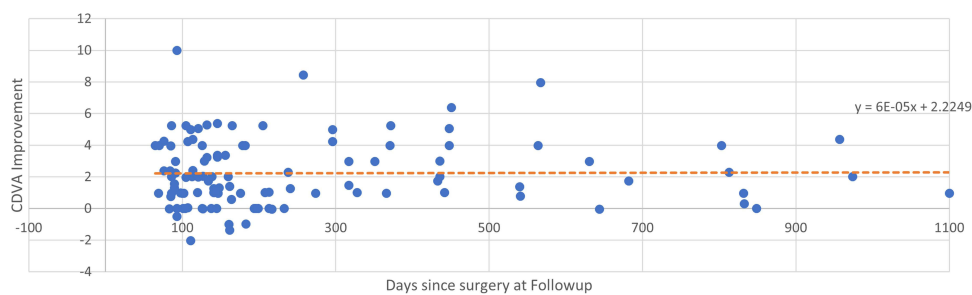


Figure 2 CDVA changes across time. The relationship between the day of last follow-up and the CDVA change after surgery of different eyes included in the study is displayed. The upper right corner shows the mathematical equation of the trendline in scientific notation:  $y = 6 * 10^{-5} * x + 2.2$ .

**Table 3** Subgroup Comparison Multiple Surgeries versus Single Surgery Eyes

Parameter	Single Surgery Eyes		Multiple Surgeries (Compounded Outcome)		p
	n	Mean ± SD	n	Mean ± SD	
Age (years)	101	32.27 ± 10.78	17	32.59 ± 10.81	0.9106
Surgeries	101	1.0 (1.0: 1.0)*	17	2.0 (2.0: 2.0)*	<0.0001
Safety Index	101	1.59 (1.25: 2.5)*	17	1.55 ± 0.76	0.0465
Follow-up (days)	101	156.0 (107.0: 351.0)*	17	213.0 (142.0: 564.0)*	0.0845
UDVA Lines gained	101	6.3 ± 4.8	17	3.0 (1.7: 5.0)*	0.012
CDVA Lines gained	101	2.4 ± 2.0	17	1.6 ± 2.0	0.1396
<b>Preoperative values</b>					
UDVA (logMAR)	101	1.0 ± 0.42	17	0.7 (0.7: 1.3)*	0.1518
CDVA (logMAR)	101	0.38 ± 0.23	17	0.3 (0.2: 0.4)*	0.3967
Sph (D)	90	-3.39 ± 4.01	16	-0.12 (-3.12: 0.26)*	0.0214
Cyl (D)	90	-3.5 (-5.75: -2.0)*	16	-3.66 ± 1.99	0.7614
SE (D)	90	-5.32 ± 4.19	16	-2.12 (-5.09: -1.44)*	0.0316
K1 preop (D)	101	47.62 ± 4.24	17	45.97 ± 3.47	0.1343
K2 preop (D)	101	50.4 (47.3: 53.41)*	17	48.9 ± 3.29	0.0608
meanK (D)	101	49.24 ± 4.31	17	47.44 ± 3.28	0.1047
topoAsti (D)	101	3.95 ± 2.6	17	3.06 ± 1.41	0.1737
Kmax preop (D)	101	57.3 (52.4: 61.6)*	17	55.67 ± 4.31	0.1486
min. Pachy (µm)	100	443 ± 40	17	458 ± 47	0.1722
<b>Postoperative values</b>					
UDVA (logMAR)	101	0.37 ± 0.25	17	0.53 ± 0.47	0.0372
CDVA (logMAR)	101	0.15 ± 0.15	17	0.2 ± 0.18	0.1532
Sph (D)	90	0.91 ± 2.4	17	0.32 ± 1.7	0.3447
Cyl (D)	90	-1.98 ± 1.8	17	-2.13 ± 1.87	0.7496
SE (D)	90	-0.08 ± 2.27	17	-0.74 ± 1.64	0.2591
K1 preop (D)	95	42.4 ± 2.48	16	42.08 ± 3.06	0.6435
K2 preop (D)	95	45.79 ± 3.13	16	45.52 ± 3.32	0.7559
meanK (D)	95	44.1 ± 2.59	16	43.8 ± 3.04	0.683
topoAsti (D)	95	2.9 (1.9: 4.32)*	16	3.45 ± 1.94	0.3941
Kmax preop (D)	96	53.86 ± 6.13	16	52.73 ± 6.15	0.4998
min. Pachy (µm)	95	450 ± 46	15	450 ± 46	0.983

**Notes:** This table compares eyes having had one surgery (group 1) and those having had multiple surgeries (group 2). Postoperative values for eyes in group 2 are the outcomes after all surgeries. \*Non-normally distributed data are displayed as median (25th percentile:75th percentile).

**Abbreviations:** logMAR: logarithm of the minimum angle of resolution; D: Diopter; SD: standard deviation; Sph: refractive sphere; Cyl: refractive cylinder; SE: spherical equivalent; K1: flat meridian of anterior simulated keratometry, K2: steep meridian of anterior simulated keratometry min. Pachy: thinnest pachymetry reading; Kmax: maximum keratometry reading; topo Asti: topographical astigmatism.

**Table 4** Standard Treatment Group Vs Non-Standard Treatment Group

Parameter	STG		NSG		p
	n	Mean $\pm$ SD	n	Mean $\pm$ SD	
Age (years)	104	32.65 $\pm$ 10.94	14	29.79 $\pm$ 9.95	0.35438
Safety Index	104	1.91 $\pm$ 1.21	14	2.29 $\pm$ 1.82	0.29502
Follow-up (days)	104	362.2 $\pm$ 511.41	14	313.57 $\pm$ 274.38	0.72831
UDVA Lines gained	104	5.68 $\pm$ 4.75	14	8.05 $\pm$ 4.73	0.08217
CDVA Lines gained	104	2.3 $\pm$ 1.95	14	1.85 $\pm$ 2.92	0.44447
<b>Preoperative values</b>					
UDVA (logMAR)	104	-3.04 $\pm$ 4.11	14	-4.6 $\pm$ 4.54	0.10173
CDVA (logMAR)	104	-3.96 $\pm$ 2.28	14	-2.71 $\pm$ 2.6	0.95539
Sph (D)	94	-5.02 $\pm$ 4.22	12	-5.96 $\pm$ 5.25	0.22119
Cyl (D)	94	46.8 $\pm$ 3.4	12	51.68 $\pm$ 6.68	0.07968
SE (D)	94	49.94 $\pm$ 3.64	12	55.39 $\pm$ 8.95	0.48187
K1 preop (D)	104	48.37 $\pm$ 3.16	14	53.54 $\pm$ 7.6	0.00002
K2 preop (D)	104	3.84 $\pm$ 2.18	14	3.71 $\pm$ 4.28	0.00005
meanK (D)	104	56.89 $\pm$ 5.48	14	62.75 $\pm$ 16.23	0.00001
topoAsti (D)	104	445.85 $\pm$ 37.39	14	440.21 $\pm$ 65.54	0.85997
Kmax preop (D)	104	-3.04 $\pm$ 4.11	14	-4.6 $\pm$ 4.54	0.00700
min. Pachy ( $\mu$ m)	104	-3.96 $\pm$ 2.28	14	-2.71 $\pm$ 2.6	0.63450
<b>Postoperative values</b>					
UDVA (logMAR)	104	0.39 $\pm$ 0.3	14	0.37 $\pm$ 0.31	0.74838
CDVA (logMAR)	104	0.15 $\pm$ 0.14	14	0.2 $\pm$ 0.22	0.26807
Sph (D)	94	0.86 $\pm$ 2.37	13	0.48 $\pm$ 2.08	0.58280
Cyl (D)	94	-2.06 $\pm$ 1.87	13	-1.6 $\pm$ 1.38	0.39278
SE (D)	94	-0.17 $\pm$ 2.25	13	-0.32 $\pm$ 1.98	0.82006
K1 preop (D)	98	42.17 $\pm$ 2.41	14	43.77 $\pm$ 3.45	0.03546
K2 preop (D)	98	45.58 $\pm$ 3.1	14	47.04 $\pm$ 3.54	0.12008
meanK (D)	98	43.87 $\pm$ 2.53	14	45.4 $\pm$ 3.42	0.05224
topoAsti (D)	98	3.48 $\pm$ 2.22	14	3.27 $\pm$ 1.4	0.75159
Kmax preop (D)	98	53.8 $\pm$ 6.05	14	52.99 $\pm$ 7.2	0.64962
min. Pachy ( $\mu$ m)	97	450.89 $\pm$ 43.48	14	445.38 $\pm$ 62.94	0.68664

**Notes:** This table compares eyes in the standard treatment group (STG) and non-standard treatment group (NSG). STG fit all the classical inclusion criteria, while NSG eyes received treatment when the alternative treatment keratoplasty or laser-assisted topography was not feasible for the patient or the primary aim was not to improve CDVA.

**Abbreviations:** logMAR, logarithm of the minimum angle of resolution; D, Diopter; SD, standard deviation; Sph, refractive sphere; Cyl, refractive cylinder; SE, spherical equivalent; K1, flat meridian of anterior simulated keratometry, K2, steep meridian of anterior simulated keratometry min. Pachy, thinnest pachymetry reading; Kmax, maximum keratometry reading; topo Asti, topographical astigmatism.

## Correlation Analysis

Table 5 shows the correlation of preoperative parameters with the UDVA lines gained and CDVA lines gained. The Pearson  $r$  correlation coefficients are found in the columns of “UDVA lines correlation coefficient” and “CDVA lines correlation coefficient”, respectively. The single best predictor of CDVA lines gained is preoperative CDVA. In Figure 3 one can observe the CDVA lines gained for each eye with respect to the preoperative CDVA in the same eye, further underlining the significant correlation between both variables.

## Exemplary Case

To illustrate a typical outcome, we chose a typical patient with regards to UDVA and CDVA improvements. All his preoperative parameter values except age lie within half a standard deviation from the median. The patients’ age is within one standard deviation from the median. In the concerned eye, the preoperative unaided vision was 20/200 with a CDVA of 20/70. UDVA improved by 4.6 lines (study average: 5.9) to 20/70 while his CDVA improved by 2.4 lines (study average: 2.1) to 20/40. Figure 4 shows a top-to-bottom comparison of the curvature maps one week before and 3.5 months after surgery in our exemplary case.

## Complications

In all, 15 eyes (12.7%) had to undergo a ring exchange procedure because of refractive under- (9 eyes) or overcorrection (6 eyes). One eye developed a corneal herpes simplex infection, which warranted explantation 8 months post-operatively. Re-implantation of the ICCR as performed 4 months later. Nevertheless, the patient gained 6.0 lines in UDVA and 3.9 lines in CDVA as a combined result of all procedures.

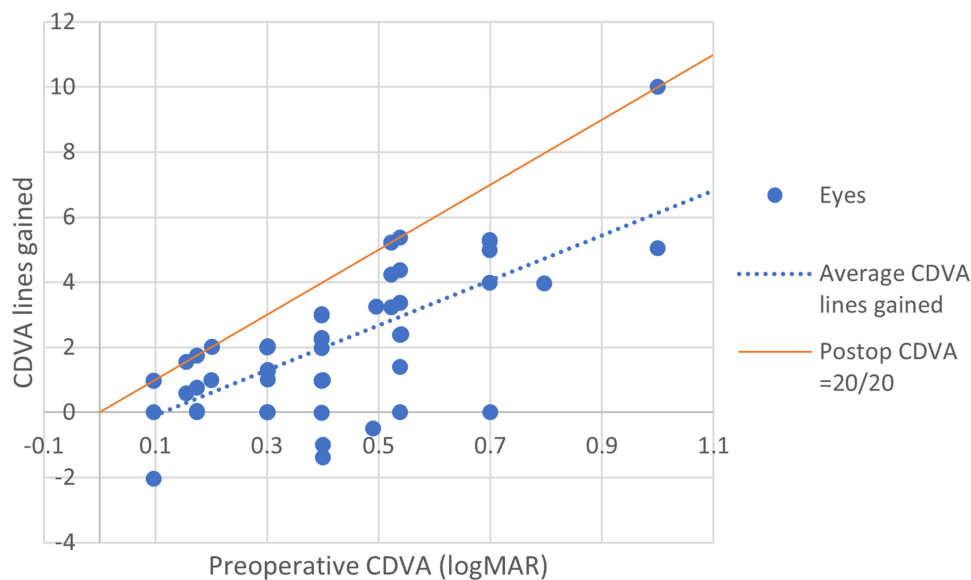
**Table 5** Correlation of Preoperative Parameters with UDVA Lines Gained and CDVA Lines Gained

Preoperative Parameter	UDVA Lines Correlation Coefficient	p	CDVA Lines Correlation Coefficient	p
Age (year)	0.15	0.1121	0.04	0.642
UDVA (logMAR)	0.79	<0.0001	0.09	0.3414
CDVA (logMAR)	0.06	0.5228	0.75	<0.0001
Sph (D)	-0.44*	<0.0001	-0.24*	0.0116
Cyl (D)	0.05	0.646	-0.16	0.0915
SE (D)	-0.44*	<0.0001	-0.3*	0.0016
K1 preop (D)	0.31	0.0006	0.27	0.0034
K2 preop (D)	0.14	0.1181	0.33	0.0002
meanK (D)	0.24	0.0101	0.32	0.0004
topoAsti (D)	-0.03	0.7739	0.15	0.0954
Kmax preop (D)	0.12	0.2109	0.35	0.0001
min. Pachy ( $\mu$ m)	-0.19	0.0442	-0.34	0.0002

**Notes:** This table displays how preoperative parameters correlate with the postoperative gains in UDVA and CDVA lines. The correlation coefficient denotes the Pearson  $r$  coefficient or in the case of non-normally distributed variables the Spearman rank  $\rho$  coefficient (\*). A Bernoulli-adjusted alpha’ would yield significant correlations for p-values equal or below: 0.0042.

**Abbreviations:** logMAR, logarithm of the minimum angle of resolution; D, Diopter; Sph, refractive sphere; Cyl, refractive cylinder; SE, spherical equivalent; K1, flat meridian of anterior simulated keratometry, K2, steep meridian of anterior simulated keratometry min. Pachy, thinnest pachymetry reading; Kmax, maximum keratometry reading; topo Asti, topographical astigmatism.





**Figure 3** CDVA lines distribution and correlation with preoperative CDVA. The orange line denotes the number of lines necessary to achieve a postoperative vision of 20/20 Snellen. The blue dotted line is a trendline, achieved by linear regression with conventional least squares as loss function. This trendline can be understood as the average CDVA lines improvement for a given preoperative CDVA.

In one case, the surgical pocket created using the PocketMaker was too superficial. Initially, the patient had good postoperative vision; however, a month after surgery after minor trauma to the eye with a pillowcase, the patient started experiencing persistent epiphora. Four months after surgery, the ICCR was explanted due to the risk of extrusion. This eye gained 2.0 lines of UDVA but lost 2.0 lines of CDVA.

No eye included developed post-operative KC progression, epithelial ingrowth, or any signs of sterile inflammatory responses due to the implant or the surgical trauma.

## Discussion

In this study, all analyzed visual acuity and topography parameters improved significantly ( $p < 0.001$ ) with the exception of the thinnest pachymetry value (min. pachy) and topographical astigmatism (topoAsti).

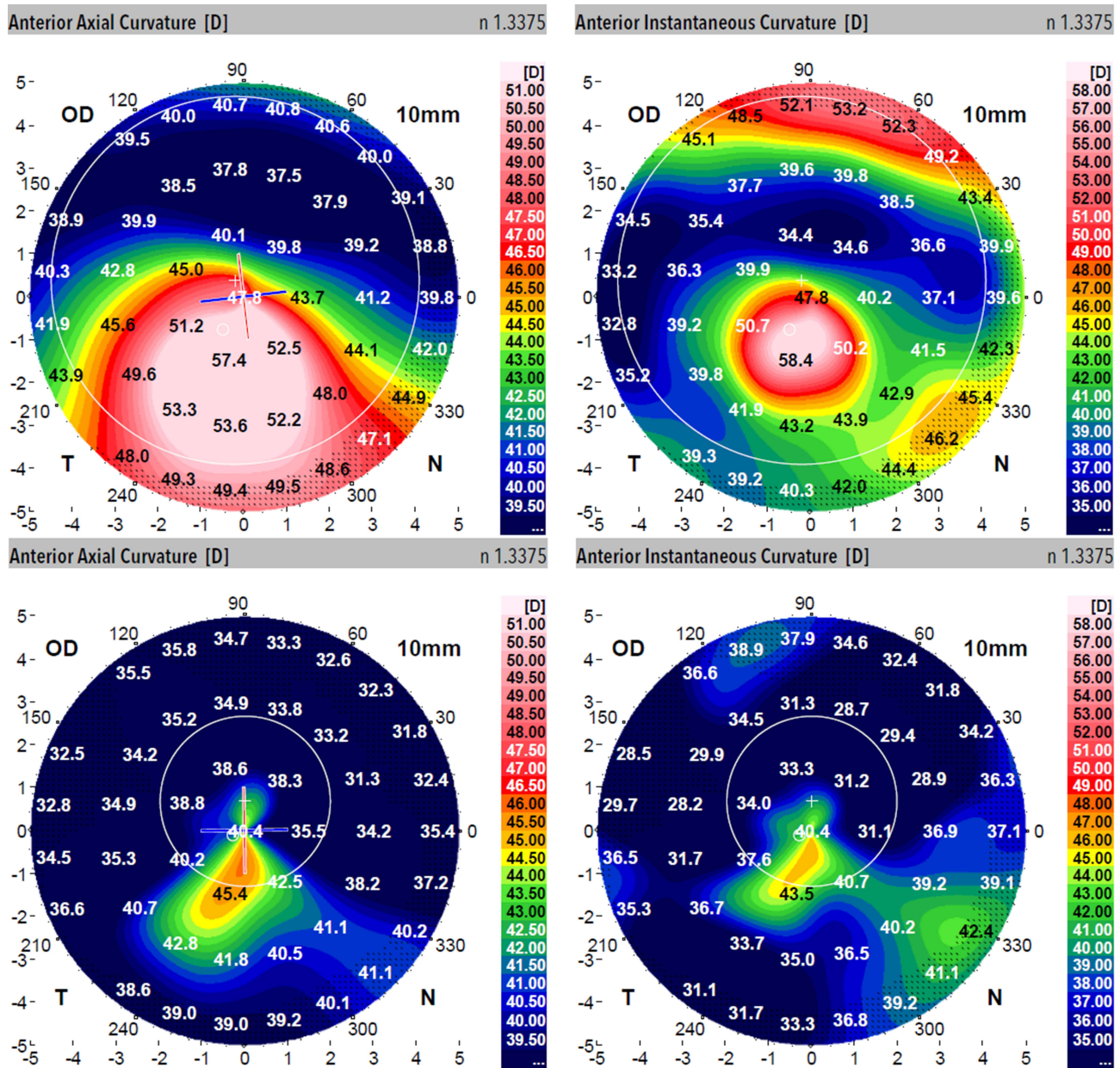
The mean improvement in CDVA, was highly variable, with a standard deviation of 2.1 lines ranging from  $-2.0$  to 10 Lines as can be seen in [Figure 3](#). This underlines our further need for improving selection criteria by performing subgroup analyses.

Our subgroup analysis showed eyes with a higher SE were more likely to require reoperation (group 2). Eyes in group 2 had a tendency for inferior compounded CDVA gains compared to group 1 ( $p=0.13958$ ).

Our correlation analysis showed preoperative vision to be the single most useful predictor of postoperative improvement in vision. In other words, high potential for improvement in CDVA was associated with a greater gain in CDVA lines. For instance, the eyes in the upper quartile of preoperative CDVA (as measured in logMAR) were eyes with a CDVA of 20/80 and lower, as measured in Snellen. These eyes gained  $4.3 \pm 2.0$  lines in CDVA on average ([Appendix A of Supplemental Data](#)).

Our analyses further demonstrated that the degree of myopia predicts the average improvement in UDVA ([Table 5](#)), which is in line with the results in previous studies.<sup>16,22</sup> What has not been published before, is that preoperative myopia correlates weakly but significantly with the CDVA improvement ( $r_{SE}=-0.3$  and  $p=0.0116$ ) before applying an optional Bonferroni correction.<sup>23</sup> This further corroborates the link between our diverging outcomes in Group 1 and 2 and higher myopia in group 1.

The inverse correlation between SE and CDVA lines gained, could in part or entirely be explained by the correlation of myopia with advanced KC and hence, high potential for improvement. To investigate whether these correlations



**Figure 4** Curvature Maps before and after MyoRing implantation. Top-to-bottom comparison of the curvature of anterior axial and anterior instantaneous curvature maps one week before (top) and 3.5 months after MyoRing implantation (bottom) in an average patient.

reflected inherently positive biomechanical properties and held irrespective of potential for improvement, we did a post hoc correlation analysis between these variables and one we named the “achieved CDVA potential”.

$$\text{Achieved CDVA potential} = \frac{\text{CDVA Lines gained}}{\text{CDVA Lines to achieve 1.0}}$$

This post hoc analysis demonstrated a weak inverse correlation that was not statistically significant ([Appendix B in Supplemental Data](#)). Further research is therefore necessary to elucidate the role of SE and a host of other parameters, as predictive factors for postoperative CDVA outcomes.

As reported by a recent review,<sup>22</sup> reducing variability by improving inclusion criteria could yield considerably better outcomes for patients. The subgroup analysis between eyes undergoing standard and non-standard treatment showed a tendency for poorer postoperative vision (p= 0.26807). Particularly eyes with a meanK >55D had a significantly

inferior CDVA outcomes postoperatively ( $p=0.001372$ ) with their CDVA being under 20/40 Snellen. We therefore argue that for KC eyes classified as stage IV with Amsler–Krumeich classification, keratoplasty may be the more efficacious visual rehabilitation albeit with a different complications profile. The emergence of novel predictive models in the field of machine learning may be a worthwhile line of future research to further improve selection criteria.

There are large gaps in reporting the distribution of CDVA gains. Some publications with large sample sizes describe no eye losing a line and some report all eyes gaining vision and not a single eye losing a CDVA line.<sup>14,16,24</sup> With 20 eyes (17%) with CDVA lines change  $\leq 0$  at follow-up with 4 (3%) eyes losing one line or more in corrected vision, our findings suggest there may be large gaps in the reporting of CDVA gains distribution.

Very few publications have explicitly stated the percentage of eyes in which this enhancement surgery or ring centration was carried out. It has been reported that approximately 20% of eyes profit from a second procedure to adapt ring dimensions or positioning.<sup>14</sup> At 12.7%, our study found that eyes required these additional interventions less frequently.

In an attempt to compare studies analyzing results after complete ring (ICCR)- and ring segment-implantation, we found two reviews that were published since 2015. The first one, a systematic review by Izquierdo et al,<sup>7</sup> attributed improvements in UDVA and CDVA for all examined ICRS and ICCR after 1 year. However, they noted greater improvements in keratometry and more consistent correction of spherical aberration in patients treated with the ICCR compared with other ICRS. The second review, published by Park et al,<sup>25</sup> concluded that complete rings (ICCR) and near-complete ring segments of arc lengths of  $340^\circ$  and above achieved the most robust correction of spherical equivalent in comparison to regular ICRS.

Several comparative studies on this topic have been published since 2015 that were not included in either review.

A study by Yousif et al<sup>26</sup> comparing three intracorneal implant types found all three were effective at improving UDVA, CDVA, keratometry and corneal asphericity. They also reported a limited effect of 2-segment rings on advanced cases of KC at 6 months but a significant improvement with near-complete and complete rings.

A comparative study by Pashtaev et al<sup>27</sup> also demonstrated that ICCR treatment lead to a greater reduction in total corneal aberration, higher order aberrations (HOAs) and spherical aberration than the Keraring in KC eyes staged at Amsler–Krumeich III. Postoperative changes in Amsler–Krumeich II KC eyes were comparable in both groups.

Bamdad et al demonstrated superior reduction of asphericity and keratometry with MyoRing treatment as with the Keraring.<sup>27</sup>

Sammour et al<sup>28</sup> found that after 12 months the CDVA gains in eyes treated with the ICCR were significantly higher than those treated with the Ferrara Ring, mostly because of the regression of short-term (1 month) gains in the group treated with the Ferrara Ring.

Biomechanical considerations ascribing higher stabilization of the corneal by continuous rather than interrupted segments favor ICCR implantation.<sup>10,11</sup> This is particularly relevant since some publications report of regression to baseline of CDVA improvements 12 months after ICRS implantation, particularly in progressive KC.<sup>12,26,28–31</sup>

In light of the literature and our findings, we would suggest that the comparative advantages of ICCR to ICRS are its high suitability in advanced cases of KC, in eyes with low SE and possibly in progressive KC. Remaining purported advantages of some ICRS are possibly their particular suitability in KC with a highly asymmetric cone.

The current established modality to treat severe KC remains keratoplasty, with lamellar keratoplasty being the preferred option by many surgeons, because of the reduced risk of postoperative graft rejection compared with penetrating keratoplasty.<sup>32</sup> To our knowledge, only one study has intended to compare ICCR implantation with keratoplasty in KC.

A contralateral eye study by Yousif et al<sup>33</sup> with 30 patients comparing femtosecond assisted DALK and MyoRing implantation in patients with advanced to severe KC and a history of recent progression demonstrated that both techniques were effective at improving visual acuity and spherical and corneal aberrations with superior improvement of corneal asphericity and HOAs after DALK. The authors deemed it an acceptable substitute for keratoplasty in advanced KC. Yet, one needs to keep in mind that loss of visual acuity through central corneal scarring cannot be remediated by ICCR.

Further investigation is necessary to explore whether this comparability is reproducible, which could render ICCR a valid alternative in regions with insufficient capacities for corneal transplants.

A potential weakness of our study is that ICCR implantation was not thoroughly standardized as to the pocket creation method. Previous studies, however, have shown no significant differences in outcomes between femtosecond and manual dissection to create the stromal pocket.<sup>34–36</sup>

Despite the success demonstrated, a significant limitation is that patients were not systematically categorized using KC grading such as the Belin–Ambrosia ABCD classification. This renders comparison with the study population more arduous.

With 91% of eyes being followed up between 2 months and 3 years, only 29% of which were followed up 12 months or more, questions could remain as to the stability of the evaluated outcomes. Nonetheless, numerous other studies with follow-up periods of 1, 2, 3 and 5 years demonstrated stable refractive and keratometry outcomes with marginal improvement of HOAs beyond the first year.<sup>9,14,15,37–39</sup>

Furthermore, this work is also limited by the lack of its consideration of HOAs and qualitative photic phenomena, which play an important role in patients' quality of life.<sup>15,32</sup> Only one study to date has published any patient-centered outcomes such as satisfaction scores.<sup>40</sup> This is something that should be borne in mind in future studies.

The results of this study further confirm the efficacy of ICCR implantation as a treatment for KC. This promising technique comes with great benefits, particularly for KC patients with reduced preoperative vision (CDVA <20/70) and a low SE. The calculated safety index, low risk of complications and the reversibility of the treatment speak to its safety. The main challenge remains in the low predictability of the magnitude of this improvement in eyes with good spectacle corrected vision (CDVA >20/30).

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