Original Article

Postoperative corneal remodeling after corneal allograft intrastromal ring segment (CAIRS) implantation for keratoconus: An OCT study

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Objectives: To demonstrate corneal remodeling after corneal allograft intrastromal ring segment (CAIRS) with an anterior-segment optical coherence tomography (AS-OCT). **Design:** A prospective observational single-center study. **Methods:** This observational study included keratoconus patients who underwent CAIRS implantation into a stromal tunnel. Topographical, refractive, and visual changes were obtained from the patient records. Epithelial thickness (ET), anterior stromal thickness (AST), allograft corneal ring thickness (ACRT), and posterior stromal thickness (PST) were measured on the first day and 1, 3, 6, and 12 months postoperatively using AS-OCT. **Results:** The study included 35 eyes of 27 patients with advanced keratoconus. The mean keratometry decreased from 48.26 ± 4.78 D to 44.50 ± 4.42 D at 1-year postoperatively ($P = 0.004$), mean corrected distance visual acuity increased from 0.29 ± 0.18 to 0.70 ± 0.24 ($P < 0.001$), and spherical equivalent (SE) decreased from −6.94 ± 4.32 D to −1.44 ± 4.44 D ($P < 0.001$). The mean AST decreased by 17.39 ± 5.78 µm in the postoperative 1st month compared to 1st day after surgery ($P = 0.040$). No statistically significant variations were observed in AST after the first month. There was no statistically significant difference in the mean ET, ACRT, and PST measurements between follow-up times. Significant negative correlations were found between SE change and ET (r = −0.543, $P = 0.023$) and between K1 change and ACRT (r = −0.548, $P = 0.008$). **Conclusion:** CAIRS is an effective treatment method to improve visual acuity and keratometry measurements and does not cause significant changes in graft thickness or recipient corneal epithelial and stromal thicknesses during the 1-year follow-up period. The observed correlations between SE, keratometry, and corneal thickness suggest that epithelial and stromal remodeling play crucial roles in postoperative outcomes of CAIRS.

Access this article online
Website:
https://journals.lww.com/ijo
DOI:
10.4103/IJO.IJO_2107_24
Quick Response Code:

Key words: Anterior-segment optical coherence tomography, corneal allograft intrastromal ring segment implantation, corneal remodeling, keratoconus

Keratoconus is a progressive corneal ectatic disease characterized by progressive protrusion and thinning of the cornea, causing irregular astigmatism and visual impairment.[1] Treatment strategies for visual rehabilitation vary according to the disease stage, ranging from spectacles and contact lenses in early stages to more invasive interventions such as intracorneal ring segments (ICRS), corneal crosslinking, and phakic intraocular lens implantation. In advanced keratoconus, where conservative treatments fail, lamellar or penetrating keratoplasty is often required.[2]

For ICRS, synthetic (usually polymethyl methacrylate (PMMA)) materials have been widely used to flatten the corneal curvature and improve visual acuity, which changes the cornea curvature. They can be more easily implanted into the cornea with femtosecond laser assistance. However, there may still be complications such as extrusion, migration, corneal haze, corneal melting, and endothelial perforation due to poor bio-integration within the cornea.[3,4] Although long-term graft survival is good, corneal transplantation may be associated with complications such as graft rejection, infection, wound dehiscence, and high astigmatism that will affect the final result of the surgery.[5] The need for highly specialized corneal surgeons also limits their accessibility.[6] To address these challenges, Jacob *et al*.[7] introduced corneal allogenic intrastromal ring segments (CAIRS) as a safer alternative to synthetic segments, demonstrating efficacy in keratoconus management. Similar to the technique used by Jacob *et al*.,[7] implantation of a recently introduced allograft material, Keranatural™, to the cornea with Istanbul nomogram has been found to be a safe and effective method to enhance the visual performance of keratoconus patients.[8,9]

Corneal epithelial and stromal remodeling plays an important role in screening refractive surgery candidates, early diagnosis of keratoconus, and the determination of

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Received: 31-Aug-2024 Accepted: 04-Nov-2024
Published: 27-Dec-2024

Cite this article as: Yakut B, Tanriverdi C, Keskin Perk FF, Nacaroglu SA, Altinbas M, Kilic A. Postoperative corneal remodeling after corneal allograft intrastromal ring segment (CAIRS) implantation for keratoconus: An OCT study. Indian J Ophthalmol 2025;73:382-8.

corneal crosslinking outcomes.[10-13] Given the importance of corneal remodeling in keratoconus treatment, this study aims to evaluate the changes in corneal epithelial and stromal thicknesses after CAIRS implantation by using anterior-segment optical coherence tomography (AS-OCT). In addition to visual and refractive outcomes, the study includes a detailed analysis of correlations between preoperative and postoperative parameters, offering insights into the mechanisms driving these changes.

Methods

This study was conducted in the (Ophthalmology Department of Medipol University Medical Faculty, Istanbul, Turkey) in accordance with the tenets of the Declaration of Helsinki. It was approved by the institutional ethics committee (document no.: E-10840098-772.02-5304). Informed consent was obtained from all patients.

Patients

The study inclusion criteria were keratoconus patients with a total corneal thickness of at least 350 μm at the thinnest point, a clear cornea, asymmetrical non-central cones, and documented contact lens intolerance history. All patients underwent a complete ophthalmological examination, including uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA) (Snellen, decimals), and anterior- and posterior-segment examination with a slit-lamp biomicroscope. The diagnosis of keratoconus and cone pattern were determined according to corneal tomography (Pentacam; Oculus Optikgerate GmbH). Exclusion criteria were defined as a history of corneal or intraocular surgery or viral keratitis, the presence of glaucoma or any retinal disease, connective tissue or systemic autoimmune diseases, and pregnancy or lactation during the study period.

Surgical method

The allograft corneal ring segments (ACRS) (KeraNatural™, Lions VisionGift, Portland, OR, USA) from human corneas were sourced and processed under the rigid ethical standards of the Uniform Anatomical Gift Act (UAGA), Food and Drug Administration (FDA), and the Eye Bank Association of America (EBAA). Each donor cornea was cleared for lamellar procedures in human use by an accredited eye bank. Then, ACRSs were processed and packed in an International Organization for Standardization (ISO)-certified eye bank clean room and sterilized to 10^{-6} sterility assurance level (SAL). The ACRSs have a 2-year shelf-life, and the grafts remain sterile and ready to be used even when stored at room temperature.

All the surgical procedures were performed by the same surgeon (A.K) under topical anesthesia according to the Istanbul nomogram.[8] The center of the pupil was marked in each patient. A corneal tunnel was created at the cone location for implantation of the allograft ring segment using the femtosecond laser (iFS® 150kH, Intralase, Abbott Medical Optics Inc, CA, USA). The inner and outer diameters of the tunnel were 4 mm and 7.5 mm, respectively, and the depth of the tunnel was 250 μm. The tunnel was then dissected with a modified C-hook separator. The ACRS was implanted as a single ring segment (160°) into the tunnel with modified C-hook forceps under a surgical microscope of a clinical excimer laser (VisX S4®, CustomVue, S4IR Abott Medical Optics Inc, CA, USA). Fine distention and centration were controlled, and the surgery was ended without any sutures. Postoperative treatment consisted of topical moxifloxacin 0.5% (Vigamox®, Alcon Laboratories, Fort Worth, TX) administered four times a day for 1 week along with 0.1% dexamethasone (Maxidex®, Alcon Laboratories, Belgium) and preservative-free artificial tears administered five times a day for 4 weeks. No intraoperative or postoperative complications were seen due to the surgery.

AS-OCT

All patients were examined with AS-OCT (Heidelberg Engineering, Germany), a spectral-domain OCT device with an anterior-segment module, on the first day and at 1, 3, 6, and 12 months postoperatively. This device allows high-resolution images of the cornea. Five evenly spaced horizontal lines 240 μm apart were used to scan the corneal apex. The scans were aligned on the typical vertex reflection on the central cornea. Measurements were acquired between 9 and 12 am to avoid the effect of diurnal variations. All measurements were performed by an experienced examiner according to the guidelines provided by the manufacturer. After central alignment was achieved and focus was adjusted, the patient was immediately asked to blink, followed by measurement when adequate eyelid opening was achieved. Examination quality was automatically controlled by the instrument for adequate coverage and accurate centering. Only correctly made acquisitions were used for analysis. Epithelial thickness (ET), anterior stromal thickness (AST), allograft corneal ring thickness (ACRT), and posterior stromal thickness (PST) measurements were obtained using the measuring tool and the cursor on the B-scan sections of the AS-OCT. These measurements were examined in the middle of the allograft ring segment and on the same scan by one investigator (C.T) blinded to the patient information.

Statistical analyses

The study data were analyzed statistically using SPSS package program version 25.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as mean and standard deviation (SD) values. The Shapiro-Wilk test was used to assess the normality of the data. The Kruskal-Wallis test was used to compare continuous data between groups when the normal distribution condition was unmet. Repeated-measures ANOVA and Bonferroni tests were used in the analysis of the repeated measurements of normally distributed variables. Pearson or Spearman correlation coefficients were calculated to evaluate relationships between changes in keratometry, visual acuity, and corneal thickness measurements. A value of $P < 0.05$ was considered statistically significant in all the tests.

Results

This study included 35 eyes of 27 patients with advanced keratoconus. The mean age was 31.2 ± 8.1 years (20–52 years), and 17 (63%) patients were male.

The visual and topographic outcomes preoperatively and at the first-year follow-up are given in Table 1. The mean UDVA improved significantly from 0.18 ± 0.16 (Snellen) preoperatively to 0.50 ± 0.26 at the 1-year follow-up ($P < 0.001$). Similarly, the mean CDVA increased from 0.29 ± 0.18 to 0.70 ± 0.24 ($P < 0.001$). The SE also showed a substantial reduction from −6.94 ± 4.32 D to −1.55 ± 4.44 D ($P < 0.001$). The mean spherical value improved from − 4.61 ± 3.99 D to − 0.05 ± 3.42 D ($P < 0.001$).

No statistically significant change was observed in the cylindrical error, which slightly increased from −4.24 ± 2.55 D to −4.82 ± 2.94 D (P = 0.455). The keratometric measurements indicated significant corneal flattening. The mean K1 decreased from 46.40 ± 4.42 D preoperatively to 42.44 ± 4.07 D at the 1-year follow-up (P = 0.001), and the mean K2 decreased from 50.33 ± 5.38 D to 46.83 ± 5.10 D (P = 0.018). Consequently, the mean keratometry (Kmean) reduced from 48.26 ± 4.78 D to 44.50 ± 4.42 D (P = 0.004). The maximum keratometry (Kmax) showed a reduction from 57.00 ± 6.81 D to 54.29 ± 5.61 D, although this change was not statistically significant (P = 0.124). Central corneal thickness (CCT) remained stable, with no significant difference between the preoperative and 1-year postoperative measurements (453.91 ± 47.65 µm vs. 452.00 ± 50.75 µm, P = 0.886).

Mild spaces adjacent to the allograft and thickening attributable to tissue edema in the allograft and recipient epithelium and stroma were detected only on day 1 post-surgery. The thickness of the mild spaces was not measured as they were not seen in the following examinations.

Table 1: Visual, refractive, and topographical results of the patients

	Preoperative	Postoperative 1st year	P
UDVA (Snellen)	0.18±0.16	0.50±0.26	**<0.001**
CDVA (Snellen)	0.29±0.18	0.70±0.24	**<0.001**
Sphere (D)	−4.61±3.99	−0.05±3.42	**<0.001**
Cylinder (D)	−4.24±2.55	−4.82±2.94	0.455
SE (D)	−6.94±4.32	−1.55±4.44	**<0.001**
K1 (D)	46.40±4.42	42.44±4.07	**0.001**
K2 (D)	50.33±5.38	46.83±5.10	**0.018**
Kmean (D)	48.26±4.78	44.50±4.42	**0.004**
Kmax (D)	57.00±6.81	54.29±5.61	0.124
CCT (µm)	453.91±47.65	452.00±50.75	0.886

SE: spherical equivalent, UDVA: uncorrected distance visual acuity, CDVA: corrected distance visual acuity, Kmean: mean keratometry, Kmax: maximum keratometry, CCT: central corneal thickness, D: diopters (statistically significant results are given in bold)

The mean ET, AST, ACRT, and PST measurements on the first day, first month, third month, sixth month, and first year are shown in Table 2.

The mean ET showed a decrease from 53.42 ± 8.21 µm on the first postoperative day to 46.92 ± 9.31 µm at 1 month, although this change did not reach statistical significance (P = 0.058). After the first month, the mean ET remained stable between the time intervals [Fig. 1a].

The mean AST decreased significantly from 164.97 ± 21.60 µm on the first postoperative day to 147.57 ± 22.90 µm at 1 month (P = 0.040). After the first month, no statistically significant variations were observed in AST [Fig. 1b].

There was no statistically significant difference in the mean ACRT and PST measurements between the follow-up times [Fig. 1c and d].

The correlations between the changes in visual acuity, refractive error, and topographic parameters with the corneal thickness measurements at the 1-year follow-up are detailed in Table 3. Notably, there was a significant negative correlation between the change in SE and ET (r = −0.543, P = 0.023), as well as a significant negative correlation between K1 change and ACRT (r = −0.548, P = 0.008). 1st-year visual acuity, refractive, and topographical outcomes did not show a significant correlation between 1st year ET, AST, ACRT, and PST (P > 0.05) [Table 4]. Only 1st-year CCT showed a significant positive correlation between 1st-year graft thickness values (r = 0.482, P = 0.023).

Discussion

Visual rehabilitation in keratoconus patients can be provided by ICRS in moderate cases. Still, complications such as stromal thinning, segment migration, extrusion of the segment, and corneal melting can be seen in up to 30% of cases.[14,15] Deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty can be performed in advanced cases. These technically complex procedures have the risk of graft rejection. This study aimed to evaluate the corneal remodeling effects after CAIRS implantation for keratoconus by using AS-OCT to measure changes in epithelial and stromal thicknesses. The findings indicate that there were noticeable improvements in visual and topographic aspects after the surgery. However,

Table 2: Mean epithelial, stromal, and allograft corneal ring thickness measurements

	ET (µm)	AST (µm)	ACRT (µm)	PST (µm)
1st day	53.42±8.21	164.97±21.60	530.17±104.83	374.71±75.14
1st month	46.92±9.31 *0.058	147.57±22.90 ***0.040**	498.00±81.64 *0.856	346.92±80.59 *0.839
3rd month	45.07±9.67 *0.999 #0.310	146.92±18.68 *1.000 **#0.002**	502.60±94.93 *1.000 #0.055	361.68±78.60 *0.999 **#0.008**
6th month	45.63±7.96 *1.000 #0.998	144.06±18.87 *1.000 #1.000	480.17±90.08 *0.992 #0.965	342.41±76.11 *0.990 #0.954
1st year	47.76±6.29 *0.956 #0.937	142.11±23.28 *1.000 #0.996	466.92±90.11 *1.000 #0.985	342.07±60.17 *1.000 #1.000

ET: epithelial thickness, AST: anterior stromal thickness, ACRT: allograft corneal ring thickness, PST: posterior stromal thickness, *P values comparing the mean thickness measurement with the previous mean thickness measurement, #P values comparing the mean thickness differences with the previous time interval (statistically significant results are given in bold)

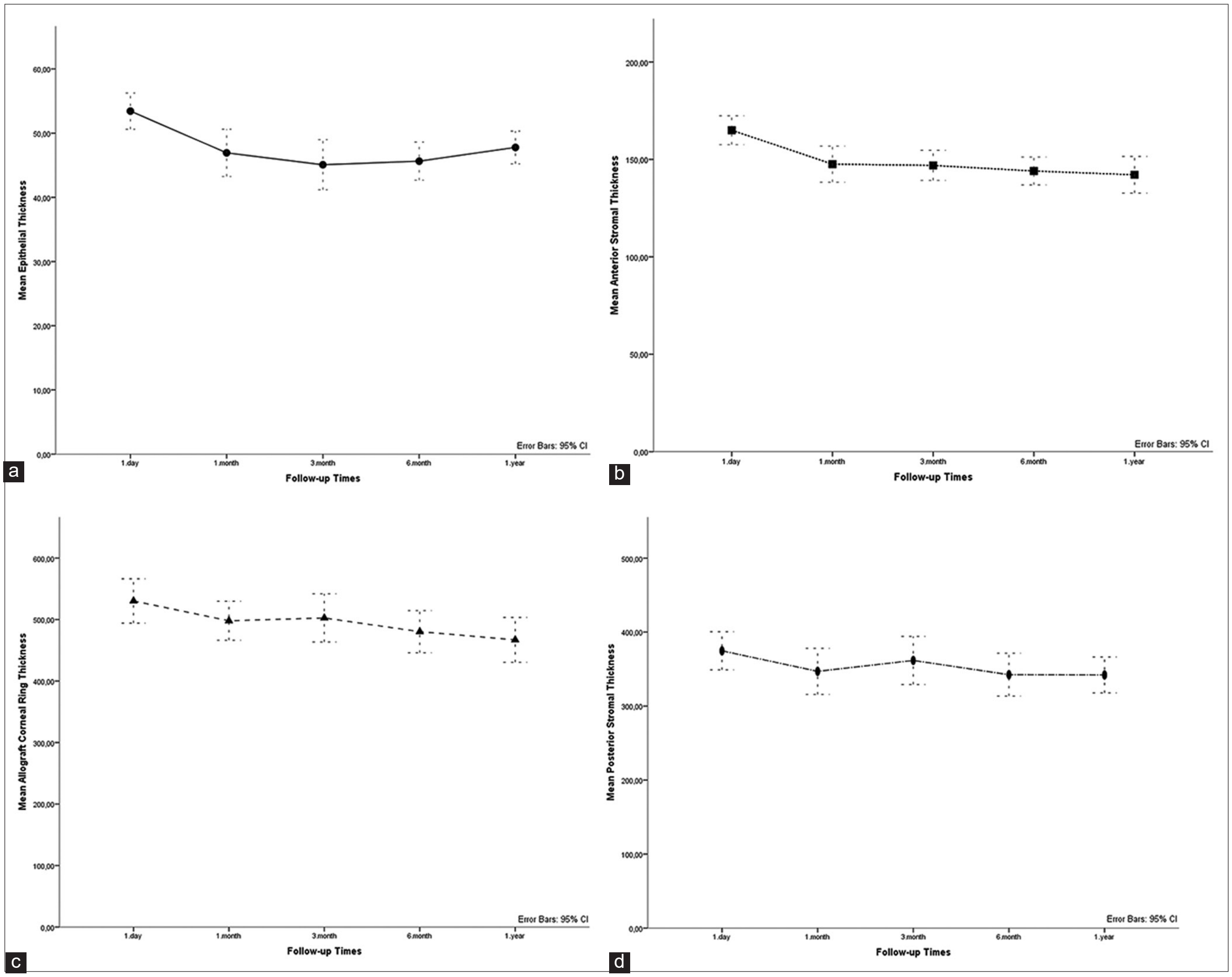

Figure 1: Mean Corneal Thickness Changes during the 1-year follow-up. (a) mean epithelial thickness change, (b) mean anterior stromal thickness change, (c) mean allograft corneal ring thickness change, (d) mean posterior stromal thickness change

corneal thickness measurements, specifically the thickness of the outermost layer and the front part of the cornea, remained consistent after the first month. This suggests that the cornea underwent successful remodeling without any significant ongoing alterations.

Some studies in the literature have presented the effects of lenticule addition surgeries for keratoconus treatment. Some of these studies have used femtosecond-assisted small-incision lenticule, and the results showed improvements in CDVA and flattening in K1, K2, and Kmean.[16,17] Alio *et al*.[18] implanted autologous adipose-derived adult stem cells and decellularized donor cornea to 14 advanced keratoconus patients and obtained an increase in visual acuity and an improvement in refractive and keratometry measurements. In a previous study, Jacob *et al*.[7] utilized a surgical procedure called CAIRS to treat keratoconus. They observed that this treatment led to improvements in UDVA and CDVA (by −0.14 D and −0.19 D, respectively), a reduction in SE (by −4.07 D), and a flattening of the steepest and maximum keratometry (by 2.78 D and 1.70 D, respectively). The utilization of sterile allograft materials, such as KeraNatural, signifies a notable progression in the treatment of keratoconus. These materials provide improved biocompatibility and lower rates of complications when compared to synthetic options. The long-term results presented by Keskin Perk *et al*.[9] further support the durability and safety of these allografts, reinforcing the potential of CAIRS to become a standard treatment option for keratoconus patients.

AS-OCT imaging has been shown to be useful in understanding intracorneal changes following patients with ectatic disorders and in patients who have undergone refractive surgery.[19] AS-OCT (Heidelberg Engineering, Germany) has been previously used for corneal pachymetry measurements in keratoconic corneas and to determine the demarcation line after corneal crosslinking.[20,21] In this study, AS-OCT sections were used to evaluate corneal epithelial and stromal regional thickness changes over time. Mild spaces adjacent to the allograft and thickening attributable to tissue edema in the allograft and recipient epithelium and stroma were detected only on day 1 post-surgery, and then the OCT scans confirmed minimal morphological changes over the 1-year follow-up period. The changes in the mean ET, AST, ACRT, and PST between time intervals are shown in Fig. 2; after 1 month, the change in all measurements decreased.

ET and AST measurements were higher on the first postoperative day than at the end of the first month, and after the first month, they remained stable. On the first day after surgery, there would be tissue edema adjacent to the allograft ring segment. Nubile *et al*.[22] evaluated the epithelial and stromal remodeling after femtosecond laser-assisted stromal lenticule addition keratoplasty for keratoconus treatment and did not analyze the first-week measurements because some transient stromal edema had been observed with confocal microscopy in their previous study.[23]

Table 3: Correlations of visual, refractive, and topographic changes among 1st-year corneal thickness measurements

	AST 1st year	ACRT 1st year	PST 1st year	ET 1st year
SE change	0.172	0.158	**0.013**	**0.023**
	−0.318	0.328	**−0.543**	**−0.504**
Spheric change	0.645	0.492	**0.037**	0.862
	−0.117	0.173	**−0.494**	0.044
Cylinder change	0.064	0.781	0.319	0.054
	−0.446	−0.071	−0.249	−0.462
UDVA change	0.983	0.122	0.483	0.443
	−0.005	0.358	0.167	−0.182
CDVA change	0.762	0.638	0.702	0.978
	−0.072	0.112	0.091	0.007
K1 change	0.373	**0.008**	0.877	0.227
	0.200	**−0.548**	0.035	0.269
K2 change	0.116	0.054	0.678	**0.024**
	0.345	−0.417	0.094	**0.479**
Kmean change	0.949	0.213	0.851	0.992
	−0.015	0.276	−0.042	−0.002
Kmax change	0.170	0.473	0.877	0.122
	0.303	0.161	0.035	0.340
CCT change	0.843	0.560	0.494	0.909
	−0.045	0.131	−0.154	0.026

SE: spherical equivalent, UDVA: uncorrected distance visual acuity, CDVA: corrected distance visual acuity, Kmean: mean keratometry, Kmax: maximum keratometry, CCT: central corneal thickness (the rows include the changes from preoperative to 1st-year outcomes), ET: epithelial thickness, AST: anterior stromal thickness, ACRT: allograft corneal ring thickness, PST: posterior stromal thickness (the columns include the 1st-year final outcomes). The first line indicates the *P* values, and the second line gives the *r* values (statistically significant results are shown in bold)

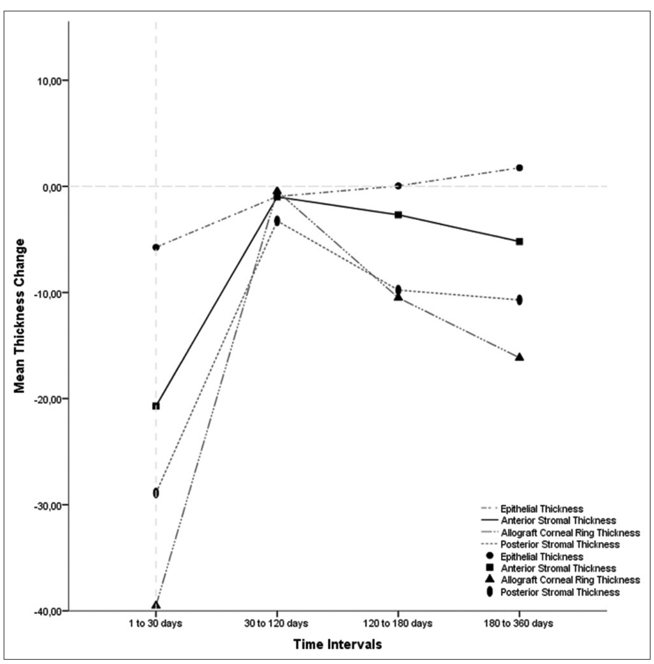

Figure 2: Mean Thickness Changes according to Time Intervals

In the current study, corneal epithelium thickness in the middle of the allograft ring segment was 46.92 ± 9.31 at 1 month postoperatively and 47.76 ± 6.29 at 1 year postoperatively. In a study by Nubile *et al*.,[22] the corneal epithelium at the apex of the cone increased 1 month after surgery compared to preoperative measurements, and it was stated that remodeling might plateau sometime between 1 and 3 months. Furthermore, corneal flattening after small-incision lenticule extraction is considered to induce a significant increase in ET.[24] In a recent study concerning a comprehensive segmental tomography evaluation after CAIRS, Bteich *et al*.[25] concluded that epithelial remodeling flattens the recipient cornea by decreasing the difference in ET between the cone and the site of ring insertion. It stabilizes at approximately 1 month postoperatively. In the current study, the thickest ET was measured on the first day, and the modifications were consistent with the epithelial turnover. However, as the patients did not have preoperative OCT measurements, comparisons could not be made.

Table 4: Correlations of 1st-year visual, refractive, and topographic outcomes among 1st-year corneal thickness measurements

	AST 1st year	Graft 1st year	PST 1st year	ET 1st year
SE 1st year	0.581	0.189	0.699	0.499
	0.131	0.306	0.092	−0.161
Spheric 1st year	0.088	0.745	0.339	0.187
	0.413	0.082	0.239	0.326
Cylinder 1st year	0.936	0.313	0.400	0.603
	0.020	0.252	0.211	−0.131
UDVA 1st year	0.777	0.515	0.294	0.647
	0.068	0.154	0.247	−0.109
CDVA 1st year	0.543	0.245	0.281	0.963
	0.145	0.272	0.253	0.011
K1 1st year	0.912	0.619	0.357	0.903
	−0.025	−0.112	−0.206	−0.028
K2 1st year	0.908	0.547	0.190	0.938
	−0.026	−0.136	−0.290	0.018
Kmean 1st year	0.913	0.196	0.791	0.950
	−0.025	0.287	−0.060	−0.014
Kmax 1st year	0.891	0.674	0.220	0.976
	0.031	−0.095	−0.273	0.007
Pachymetry 1st year	0.876	0.497	0.023	0.606
	−0.035	0.153	0.482	0.116

SE: Spherical equivalent, UDVA: Uncorrected distance visual acuity, CDVA: Corrected distance visual acuity, Kmean: Mean keratometry, Kmax: maximum keratometry, CCT: Central corneal thickness (the rows include the 1st-year outcomes), ET: Epithelial thickness, AST: Anterior stromal thickness, ACRT: Allograft corneal ring thickness, PST: Posterior stromal thickness (the columns include the 1st-year outcomes). The first line indicates the *P* values, and the second line gives the r values

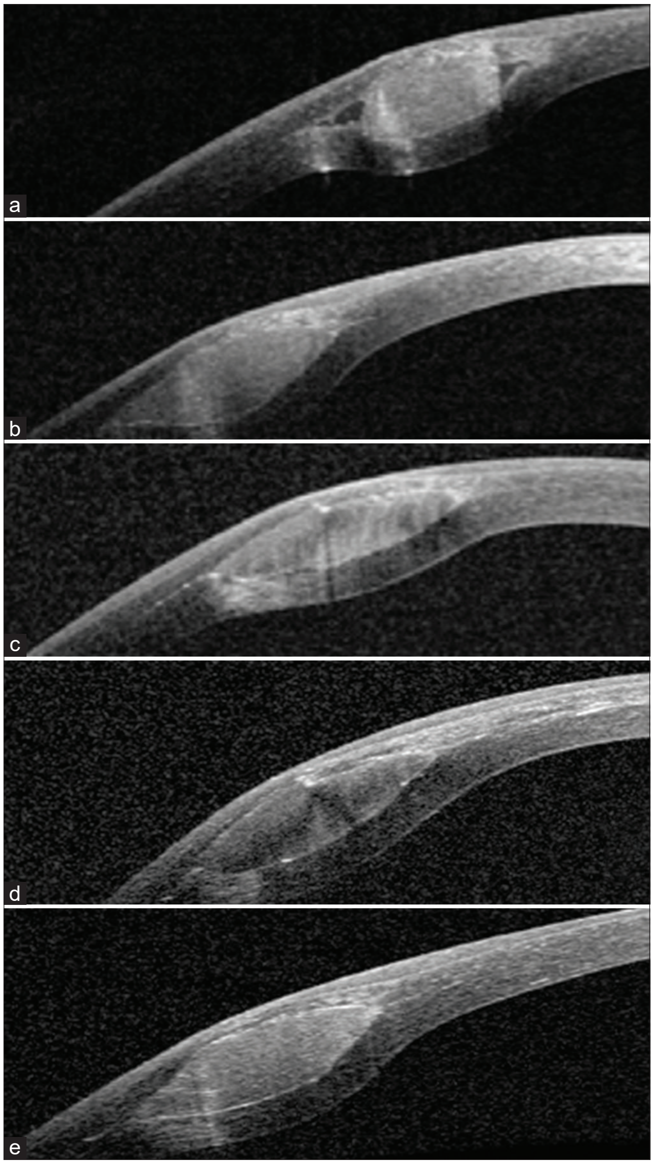

Figure 3: B-scan OCT images*. a: One day after allograft corneal ring segment implantation, b: One month after allograft corneal ring segment implantation, c: Three months after allograft corneal ring segment implantation, d: Six months after allograft corneal ring segment implantation, e: One year after allograft corneal ring segment implantation, *: All images are on the same scan

There is only one previous study on corneal remodeling in ICRS surgery. In that study, only ET changes were evaluated in patients who underwent ICRS with different arc lengths.[26] Although the results of that study showed that the ET thickened in the cone region during the 6-month follow-up period, no information was provided on whether there was any change in AST, which may be important, especially in terms of the risk of extrusion of the ring segment. A critical discovery from this study is that no additional substantial alterations in AST were found within the first month after the surgery throughout the whole 1-year monitoring period. The continued stability observed in AST after the initial month suggests a low risk of complications such as allograft extrusion, which is a concern in surgeries involving synthetic ICRS.

The AS-OCT B-scan images of a patient are shown in Fig. 3. On the first day after surgery, there are spaces near the allograft ring segment, and the graft is thicker. The allograft ring segment fills the spaces from the first month and becomes thinner. According to the results of this study, it can be said that after the first postoperative month, reshaping of the allograft and remodeling of the recipient cornea remained stable.

The correlation analysis conducted in this study revealed essential associations between corneal thickness parameters and visual outcomes. Specifically, a significant negative correlation was found between the change in SE from preoperative to 1s^t year and 1s^t year ET outcomes (r = −0.543, *P* = 0.023), indicating that greater improvements in SE are associated with thinner epithelial layers. This finding implies that the restructuring process occurring within the epithelium plays a role in the overall improvement of vision acquired after surgery. Furthermore, a significant negative correlation was observed between the change in K1 from preoperative to 1s^t year and 1s^{t-}year ACRT measurements (r = −0.548, *P* = 0.008). This correlation emphasizes the significance of the implanted allograft in achieving corneal flattening as thinner ACRT seems to be associated with improvements in keratometry.

Notably, while the study observed significant changes in AST and correlations with SE and K1, there were no significant correlations between the 1-year visual, refractive, and topographic outcomes with 1-year ET, AST, ACRT, and PST measurements. This suggests that after the initial postoperative period, the remodeling of the cornea becomes stable, and further alterations in these parameters do not substantially impact long-term visual results.

This study had some limitations, primarily the relatively small sample size and limiting enrolment of patients with non-central asymmetric cone forms of keratoconus. As this is a new surgical method, patient selection was limited to patients who would derive maximum benefit. Another limitation was the lack of preoperative OCT evaluations of the patients. It would have been beneficial to compare the preoperative and postoperative ET at the cone location for a more comprehensive interpretation of the epithelial remodeling. Future studies with larger cohorts and extended follow-up periods are necessary to confirm these findings and further elucidate the mechanisms underlying the corneal remodeling observed after CAIRS implantation.

Conclusion

CAIRS is an effective and safe treatment for keratoconus, resulting in notable visual acuity and corneal topography enhancements without causing significant alterations in graft thickness or recipient corneal epithelial and stromal thicknesses during the 1-year follow-up period. The correlations identified between corneal thickness changes and visual outcomes offer valuable insights into the remodeling processes, which support the ongoing use of CAIRS in clinical practice.

Financial support and sponsorship: This study was funded by the authors and did not receive any grant from finance agencies in the public or commercial sectors. (N/A for the award/grant number.).

Conflicts of interest: There are no conflicts of interest.

References

1. Gomes JA, Tan D, Rapuano CJ, Belin MW, Ambrosio R Jr, Guell JL, *et al*. Global consensus on keratoconus and ectatic diseases. Cornea 2015;34:359-69.
2. Parker JS, van Dijk K, Melles GR. Treatment options for advanced keratoconus: A review. Surv Ophthalmol 2015;60:459-80.
3. Sakellaris D, Balidis M, Gorou O, Szentmary N, Alexoudis A, Grieshaber MC, *et al*. Intracorneal ring segment implantation in the management of keratoconus: An evidence-based approach. Ophthalmol Ther 2019;8(Suppl 1):5-14.
4. Riau AK, Lwin NC, Gelfand L, Hu H, Liedberg B, Chodosh J, *et al*. Surface modification of corneal prosthesis with nano-hydroxyapatite to enhance *in vivo* biointegration. Acta Biomater 2020;107:299-312.
5. Arnalich-Montiel F, Alio Del Barrio JL, Alio JL. Corneal surgery in keratoconus: Which type, which technique, which outcomes? Eye Vis (Lond) 2016;3:2.
6. Luengo-Gimeno F, Tan DT, Mehta JS. Evolution of deep anterior lamellar keratoplasty (DALK). Ocul Surf 2011;9:98-110.
7. Jacob S, Patel SR, Agarwal A, Ramalingam A, Saijimol AI, Raj JM. Corneal allogenic intrastromal ring segments (CAIRS) combined with corneal cross-linking for keratoconus. J Refract Surg 2018;34:296-303.
8. Haciagaoglu S, Tanriverdi C, Keskin FFN, Tran KD, Kilic A. Allograft corneal ring segment for keratoconus management: Istanbul nomogram clinical results. Eur J Ophthalmol 2022:11206721221142995. doi: 10.1177/11206721221142995.
9. Keskin Perk FFN, Tanriverdi C, Karaca ZY, Tran KD, Kilic A. Long-term results of sterile corneal allograft ring segments implantation in keratoconus treatment. Cornea 2024. doi: 10.1097/ICO.0000000000003592.
10. Kanellopoulos AJ. Comparison of corneal epithelial remodeling over 2 years in LASIK versus SMILE: A contralateral eye study. Cornea 2019;38:290-6.
11. Hwang ES, Schallhorn JM, Randleman JB. Utility of regional epithelial thickness measurements in corneal evaluations. Surv Ophthalmol 2020;65:187-204.
12. Reinstein DZ, Archer TJ, Urs R, Gobbe M, RoyChoudhury A, Silverman RH. Detection of keratoconus in clinically and algorithmically topographically normal fellow eyes using epithelial thickness analysis. J Refract Surg 2015;31:736-44.
13. Rocha KM, Perez-Straziota CE, Stulting RD, Randleman JB. Epithelial and stromal remodeling after corneal collagen cross-linking evaluated by spectral-domain OCT. J Refract Surg 2014;30:122-7.
14. Kanellopoulos AJ, Pe LH, Perry HD, Donnenfeld ED. Modified intracorneal ring segment implantations (INTACS) for the management of moderate to advanced keratoconus: Efficacy and complications. Cornea 2006;25:29-33.
15. Coskunseven E, Kymionis GD, Tsiklis NS, Atun S, Arslan E, Siganos CS, *et al*. Complications of intrastromal corneal ring segment implantation using a femtosecond laser for channel creation: A survey of 850 eyes with keratoconus. Acta Ophthalmol 2011;89:54-7.
16. Mastropasqua L, Nubile M, Salgari N, Mastropasqua R. Femtosecond laser-assisted stromal lenticule addition keratoplasty for the treatment of advanced keratoconus: A preliminary study. J Refract Surg 2018;34:36-44.
17. Wei Q, Ding H, Nie K, Jin H, Zhong T, Yu H, *et al*. Long-term clinical outcomes of small-incision femtosecond laser-assisted intracorneal concave lenticule implantation in patients with keratoconus. J Ophthalmol 2022;2022:9774448.
18. Alio JL, Alio Del Barrio JL, El Zarif M, Azaar A, Makdissy N, Khalil C, *et al*. Regenerative surgery of the corneal stroma for advanced keratoconus: 1-year outcomes. Am J Ophthalmol 2019;203:53-68.
19. Yip H, Chan E. Optical coherence tomography imaging in keratoconus. Clin Exp Optom 2019;102:218-23.
20. Bonnel S, Berguiga M, De Rivoyre B, Bedubourg G, Sendon D, Froussart-Maille F, *et al*. Demarcation line evaluation of iontophoresis-assisted transepithelial corneal collagen cross-linking for keratoconus. J Refract Surg 2015;31:36-40.
21. David K, Mandana HZ, Niklas P, Peter W, Matthias F. Reproducibility and reliability of central corneal thickness determination in more and less profound corneal edema using ultrasound pachymetry, a Scheimpflug camera and anterior segment OCT. Graefes Arch Clin Exp Ophthalmol 2020;258:351-8.
22. Nubile M, Salgari N, Mehta JS, Calienno R, Erroi E, Bondi J, *et al*. Epithelial and stromal remodelling following femtosecond laser-assisted stromal lenticule addition keratoplasty (SLAK) for keratoconus. Sci Rep 2021;11:2293.
23. Mastropasqua L, Salgari N, D'Ugo E, Lanzini M, Alio Del Barrio JL, Alio JL, *et al*. *In vivo* confocal microscopy of stromal lenticule addition keratoplasty for advanced keratoconus. J Refract Surg 2020;36:544-50.
24. Luft N, Ring MH, Dirisamer M, Mursch-Edlmayr AS, Kreutzer TC, Pretzl J, *et al*. Corneal epithelial remodeling induced by small incision lenticule extraction (SMILE). Invest Ophthalmol Vis Sci 2016;57:OCT176-83.
25. Bteich Y, Assaf JF, Mrad AA, Jacob S, Hafezi F, Awwad ST. Corneal allogenic intrastromal ring segments (CAIRS) for corneal ectasia: A comprehensive segmental tomography evaluation. J Refract Surg 2023;39:767-76.
26. David C, Reinstein DZ, Archer TJ, Kallel S, Vida RS, Goemaere I, *et al*. Postoperative corneal epithelial remodeling after intracorneal ring segment procedures for keratoconus: An optical coherence tomography study. J Refract Surg 2021;37:404-13.