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Sterile Excimer Laser Shaped Allograft Corneal Inlay for Hyperopia: One-year Clinical Results in 28 Eyes

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ABSTRACT

Purpose: This study aimed to evaluate the one-year clinical results of an allograft corneal inlay (ACI) implantation in a case series of 28 hyperopic eyes of 16 patients.

Methods: Patients with manifest refraction spherical equivalent (MRSE) between +1.00 and +6.00 D and having a cylindrical refraction of less than 1 D were included in this prospective study. The refractive powers of excimer laser-shaped ACIs were determined based on the refractive error of the individual subject's eyes. After the creation of a femtosecond flap, the inlays were centered on the pupillary axis. Visual acuities, refractive results, and other clinical findings were reported for the 6- and 12-month follow-up exams.

Results: The mean age of the patients included in the study was 36.2 ± 12.4 years (range 22–65 years). The mean pre-operative MSRE of 3.6 ± 1.51 D decreased to 0.21 ± 0.56 D ($P < .001$). The uncorrected distance and near visual acuity increased from 0.33 ± 0.22 and 0.17 ± 0.13 to 0.75 ± 0.22 ($P < .001$) and 0.72 ± 0.19 ($P < .001$), respectively. The corrected distance visual acuity remained unchanged (pre-OP: 0.79 ± 0.22; post-OP: 0.80 ± 0.21; $P = .916$), and the corrected near visual acuity increased from 0.78 ± 0.22 to 0.84 ± 0.20 ($P = .003$). The mean K-value and central corneal thickness increased from 42.57 ± 0.81 D and 557.5 ± 43.0 µm to 44.8 ± 1.4 D ($P < .001$) and 597.1 ± 58.1 µm ($P < .001$), respectively. No significant postoperative complications such as diffuse lamellar keratitis, epithelial ingrowth, or decentralization were observed.

Conclusion: Excimer laser-shaped ACI offers an alternative treatment modality for patients with hyperopia. Acceptable visual results and similar regression rates were observed with ACI implantation compared with other laser refractive procedures.

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Allograft corneal inlay; hyperopia; laser; refractive surgery; corneal lenticule

Introduction

Laser refractive surgery can be challenging in hyperopic eyes.[1] For the treatment of hyperopia, laser refractive surgery offers a treatment option without the risks present in intraocular surgery. Photorefractive keratectomy (PRK) and laser-assisted in situ keratomileusis (LASIK) are the frequently preferred methods to correct hyperopia, with LASIK being the most common form of refractive surgery.[2]

Despite the technological advances in laser refractive surgery, post-LASIK regression of hyperopic LASIK is still observed. This result has important consequences on long-term visual performance and quality of life. The incidence of regression in patients undergoing refractive surgery can be difficult to accurately determine.[3] However, the incidence of regression following hyperopic LASIK is estimated to be around 30% in the first year after surgery. Therefore, a different treatment method that eliminates or reduces the amount of regression continues to be an unmet need in refractive surgery.[4–6] With the use of these current procedures, stromal thinning and steepening of the cornea is induced, which may potentially affect the structural integrity and stability of the cornea. In such cases, correction by laser ablation usually results in refractive regression more often than in laser correction driven by the epithelium remodeling in patients with myopia.[5] Here, the excimer laser photo ablation of the corneal stroma intends to create a relative steepness in the central part of the cornea. This procedure requires an annular ablation profile that causes more flattening around the corneal periphery, typically named the transition zone. Therefore, it is thought to be less predictable than myopic corrections that cause flattening in the corneal center area.[7,8]

Nowadays, another method methods of hyperopia treatment is treatment via small incision lenticule extraction (SMILE). The principle for the treatment of hyperopia in SMILE is similar to myopia. Some researchers have treated hyperopia with SMILE and reported its early results.[9–11] However, the long-term efficacy of SMILE for hyperopia correction remains unknown.

Another way to correct refractive errors is to place preformed biological (epikeratophakia) or synthetic (synthetic keratophakia) tissue material into the cornea.[12,13] Synthetic corneal inlays can correct hyperopia by increasing central corneal curvature.[13] Although synthetic inlays have been used frequently in the past, their use has gradually decreased due to biological compatibility problems.

Refractive lenticules made of human tissue implantation were enounced as a tissue additive method in 1966 by

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Barraquer,[14] but they have fallen out of favor because of the difficulties associated in the recovery of human donor tissue and the poor refractive predictability due to the lack of process control at that time.[12,15] Here, hyperopia tissue addition procedures steepen the anterior corneal surface and optical power of the cornea without creating a significant transition zone in the periphery known from laser ablation procedures.[16,17] Recently, some authors reported that femtosecond laser technology facilitates alternative solutions for tissue additive procedures. For example, the extracted lenticule in SMILE for myopia was implanted into an intrastromal layer in a patient with hyperopia to cause steepening of the anterior corneal curvature.[18] The postoperative refractive correction after allograft SMILE lenticule implantation remains unclear. Sun et al.[19] reported that transplanting an autologous lenticule by SMILE for hyperopia might be safe, effective, and stable, but the predictability of the procedure must be improved.

In the current prospective feasibility study, we used sterile allograft corneal inlays (ACIs) shaped for a refractive power by means of excimer lasers and transplanted them under a LASIK flap in patients with hyperopia to evaluate their safety, effectiveness, and predictability in hyperopia correction.

Materials and methods

Participants

Twenty-eight eyes of 16 subjects were included in this prospective study. A signed consent form was obtained from every patient after they were informed about the nature and possible results of the study. All implantations were performed between April 2018 and August 2018. This study followed the tenets of the Declaration of Helsinki. Ethics committee approval was obtained from the Institutional Review Board/Ethics Committee of Istanbul Medipol University (09.03.2018, 66291034–604.01.01-E.8430, approval number 08).

The inclusion criteria were as follows: stable refraction (manifest refraction spherical equivalent (MRSE) changing within 0.50 D in the previous 12 months in the treatment eye); central corneal thickness (CCT) greater than 500 μm; MRSE between +1.00 D and +6.00 D; and refractive cylinder of less than 1 D. The exclusion criteria were as follows: any ocular disease or a history of ophthalmic surgery in the treatment eye, topographic signs of keratoconus (or suspected keratoconus) or other ectatic disorders in either eye, distorted or unclear corneal mires on topography maps of the treatment eye, use of systemic medications with significant ocular side effects, and pregnancy. Contact lens wearers who participated in the study had to discontinue hard or rigid gas permeable lenses for at least 4 weeks, and soft lenses needed to be discontinued for at least 2 weeks prior to the baseline examination.

The pre-operative and postoperative examination included testing for MRSE, uncorrected distance and near visual acuity (UDVA and UNVA, respectively), corrected distance and near visual acuity (CDVA and CNVA, respectively), CCT, mean K-value, slit-lamp examination, and fundus examination. All visual acuity data are represented in the Snellen decimal system. Objective clinical measurements included corneal topography (Pentacam, Oculus, Germany) and anterior segment optical coherence tomography (OCT Spectralis, Heidelberg instruments, Germany).

Surgical procedure

After applying topical anesthesia (proparacaine hydrochloride 0.5%), a femtosecond-assisted flap was created (iFS 150kH, Intralase, Johnson&Johnson Vision, USA) with an intended flap thickness of 110 microns, a flap diameter of 8.8 mm, and a superior hinge of 70 degrees. The stromal interface was rinsed carefully with balanced salt solution during and after the opening of the flap. As a second surgical step, the corneal inlay was carefully transferred onto the exposed stromal bed by using a specially designed stainless steel loop and visually centered on the pupillary axis of the patients' eye using the surgical microscope of a clinical excimer laser (VISX S4, CustomVue S4IR, Johnson&Johnson Vision, USA). During the final surgical step, the surgeon assured the smoothness of the lenticule's edges, its centration, and its symmetry prior to replacing the flap by means of a cannula. After the flap was repositioned onto the stromal bed, a soft bandage contact lens (ACUVUE Oasys, Johnson & Johnson Vision Care Inc.) was placed onto the cornea. All implantations of the inlay (Transform, Allotex Inc. Boston, MA, USA) were performed by the same surgeon (AK). The ACI we used in our study had a diameter of 6.0 mm and its thickness varied according to the refractive status of the patient. These ACIs are prepared with the help of excimer laser after all virological and bacteriological tests are performed from human cornea by a certified eye bank. Each ACI comes sterile, in solution in a bottle and has a shelf life of 2 years.

The standard postoperative regimen consisted of 0.5% moxifloxacin hydrochloride ophthalmic solution five times a day, 0.1% fluorometholone ophthalmic solution five times a day, and a preservative-free tear supplement eight times a day for 1 month. The tear supplements were used up to 3 months as needed. The patients were examined for signs of dry eye syndrome, including conjunctival injection, punctate keratitis, reduced tear meniscus, tear film debris, abnormal tear breakup time and abnormal Schirmer test results. We attached importance of dry eye development. Therefore, the patients were treated with preservative-free artificial tears, and punctal plugs (Soft Plug, Extended Duration Plug by Oasis) were used for each patient for occlusion of the lacrimal drainage system and conservation of tears. Postoperative follow-up was performed on the 1st day, 1st week, and 1st, 3rd, 6th, and 12th months. Slit-lamp examination was performed at all follow-up visits to observe the corneal healing response and possible adverse events.

Statistical analysis

The primary outcome measure used to evaluate the efficacy of the procedure was the change in visual acuity from preoperation to the 12-month follow-up visit. Moreover, MRSE, mean K-value, and CCT changes were analyzed before and after surgery. For statistical analysis, SPSS (Statistical Package for Social Sciences, SPSS Inc., Chicago, IL, USA) version 20.0 was used. The Shapiro–Wilk test was used for normal distribution analysis. Analysis of variance (ANOVA) was used in the

analysis of the groups with normal distribution, and paired t-test was used as the post hoc test in these groups. In the groups not showing normal distribution, Friedman test was used, and Wilcoxon test was used as a post hoc test in these groups. *P* value below 0.016 was considered significant after Bonferroni correction.

Results

Patients and postoperative follow-up

The mean age of the patients included in the study was 36.2 ± 12.4 years (range 22–65 years). Of the 28 eyes operated, 15 were right eyes and 13 were left eyes. Among them, 11 of the patients were male (69%) and five were female (31%).

Refractive and corneal measurements

The mean pre-operative MSRE of 3.6 ± 1.51 D decreased to −0.22 ± 0.68 ($P < .001$) and 0.21 ± 0.56 D ($P < .001$) at the 6- and 12-month follow-up visits, respectively (Table 1). At the postoperative 12th month, MRSE was ± 1.50 D in 28 eyes (100%), ± 1.00 D in 25 eyes (89%), and ± 0.50 D in 16 eyes (57%; Figure 1). After the 6th month, approximately 0.44 ± 0.59 D ($P < .001$) regression was observed until the 12-month visit. Table 2 and Figure 2 show the stability assessment

Table 1. Statistical analysis of the results in the preoperative 6- and 12-months after surgery.

	Preoperative	Postoperative 6th months	Postoperative 12th months
MRSE (Diopter/mean±SD)	3.6 ± 1.51	−0.22 ± 0.68 $p = .000$ [b]	0.21 ± 0.56 $p = .000$ [b]
Mean K value (Diopter/mean±SD)	42.57 ± 0.81	46.02 ± 2.0 $p = .000$ [a]	44.8 ± 1.4 p = .000 [a]
CCT (µm/mean±SD)	557.5 ± 43.0	604.8 ± 60.1 $p = .000$ [a]	597.1 ± 58.1 $p = .000$ [a]
UDVA (Snellen decimal system/mean±SD)	0.33 ± 0.22	0.65 ± 0.18 $p = .000$ [b]	0.75 ± 0.22 $p = .000$ [b]
UNVA (Snellen decimal system/mean±SD)	0.17 ± 0.13	0.70 ± 0.21 $p = .000$ [b]	0.72 ± 0.19 $p = .000$ [b]
CDVA (Snellen decimal system/mean±SD)	0.79 ± 0.22	0.77 ± 0.20 $p = .202$ [b]	0.80 ± 0.21 $p = .916$ [b]
CNVA (Snellen decimal system/mean±SD)	0.78 ± 0.22	0.75 ± 0.19 $p = .094$ [b]	0.84 ± 0.20 $p = .003$ [b]

MRSE; Manifest refraction spherical equivalent, CCT; Central corneal thickness, UDVA; Uncorrected distance visual acuity, UNVA; Uncorrected near visual acuity, CDVA; Corrected distance visual acuity, CNVA; Corrected near visual acuity.
The *p* values given in Table 1 were obtained by comparing the 6th and 12th months results with the preoperative level.
[a]Paired T Test with Bonferroni correction.
[b]Wilcoxon Signed Ranks Test with Bonferroni correction.

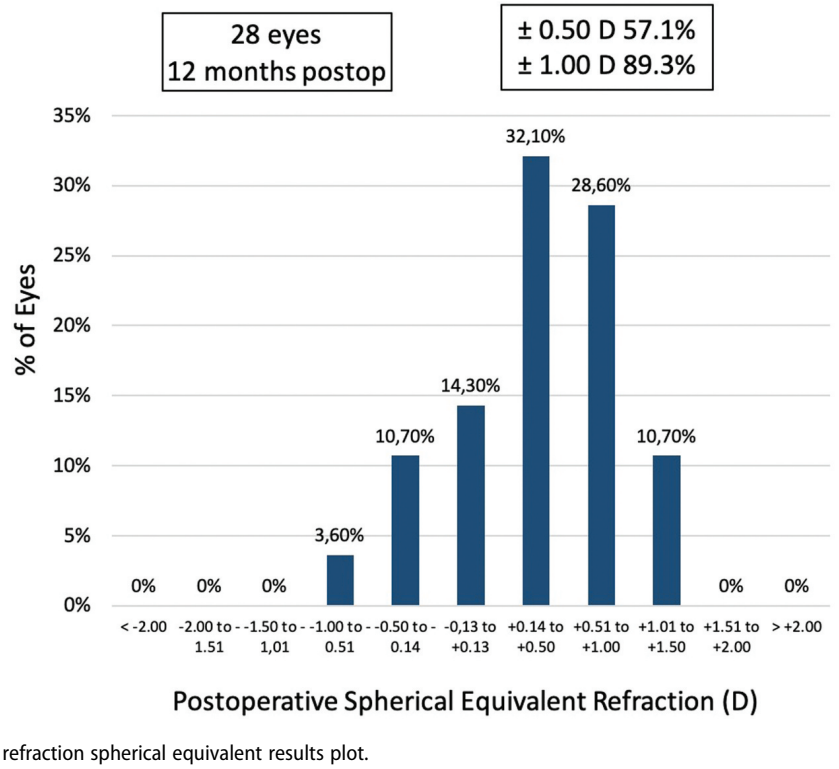

Figure 1. Postoperative manifest refraction spherical equivalent results plot.

Table 2. Stability assessment in terms of refractive values and visual outcomes between the 6- and 12-months after surgery.

	Postoperative 6th Month	Postoperative 12th Month	P
MRSE (Diopter/mean±SD)	−0.22 ± 0.68	0.21 ± 0.56	0.000[b]
Mean K value (Diopter/mean±SD)	46.02 ± 2.0	44.8 ± 1.4	0.000[a]
CCT (µm/mean±SD)	604.8 ± 60.1	597.1 ± 58.1	0.011[a]
UDVA (Snellen decimal system/mean±SD)	0.65 ± 0.18	0.75 ± 0.22	0.002[b]
UNVA (Snellen decimal system/mean±SD)	0.70 ± 0.21	0.72 ± 0.19	0.748[b]
CDVA (Snellen decimal system/mean±SD)	0.77 ± 0.20	0.80 ± 0.21	0.147[b]
CNVA (Snellen decimal system/mean±SD)	0.75 ± 0.19	0.84 ± 0.20	0.001[b]

MRSE; Manifest refraction spherical equivalent, CCT; Central corneal thickness, UDVA; Uncorrected distance visual acuity, UNVA; Uncorrected near visual acuity, CDVA; Corrected distance visual acuity, CNVA; Corrected near visual acuity
[a]Paired T Test with Bonferroni correction
[b]Wilcoxon Signed Ranks Test with Bonferroni correction

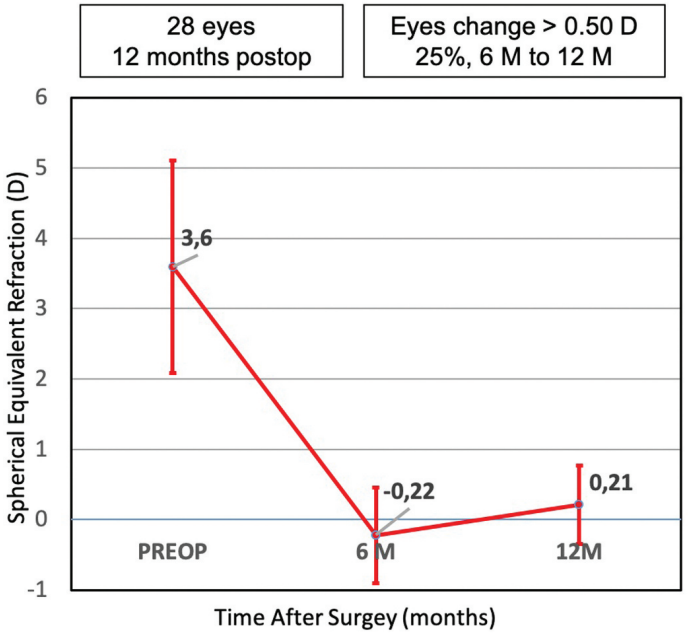

Figure 2. Stability assessment in terms of refractive values between 6- and 12-months after surgery.

in terms of refractive values between 6- and 12-months after surgery. Attempted spherical equivalent refraction versus achieved spherical equivalent refraction scatterplot is shown in Figure 3. According to the linear regression equation, the slope was calculated as 0.935 and the coefficient of determination (R^2) value was 0.863. Mean K-value and CCT increased from 42.57 ± 0.81 D and 557.5 ± 43.0 µm to 44.8 ± 1.4 D ($P < .001$) and 597.1 ± 58.1 µm ($P < .001$), respectively.

Visual acuity

Before the surgery, CDVA was 20/20 in 11 eyes, between 20/40 and 20/25 in 13 eyes, and 20/50 and below in four eyes. 17 eyes had different levels of amblyopia, because of hyperopia.

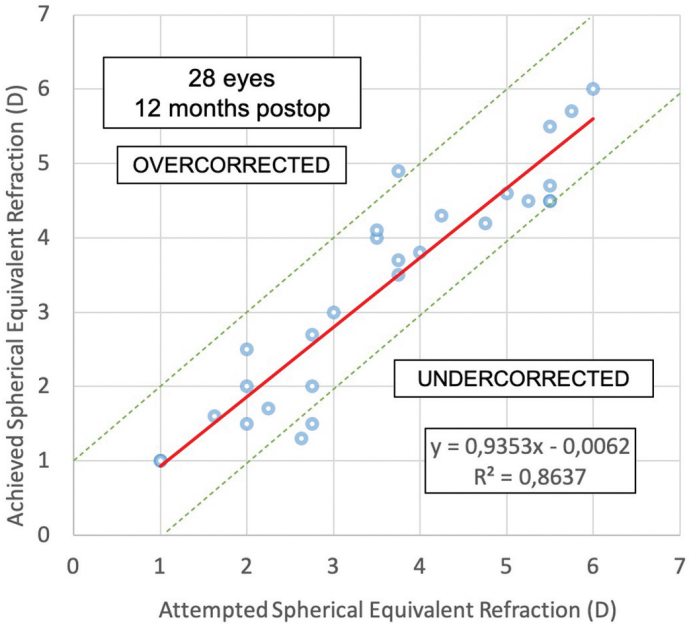

Figure 3. Attempted spherical equivalent refraction versus achieved spherical equivalent refraction scatterplot.

At the 12-month follow-up visit, UDVA and UNVA increased from 0.33 ± 0.22 and 0.17 ± 0.13 to 0.75 ± 0.22 ($P < .001$) and 0.72 ± 0.19 ($P < .001$), respectively. CDVA remained unchanged (pre-OP: 0.79 ± 0.22; post-OP: 0.80 ± 0.21; $P = .916$), and CNVA increased from 0.78 ± 0.22 to 0.84 ± 0.20 ($P = .003$). Table 1 shows the statistical analysis of the visual acuity results in the pre-operative, 6th, and 12th months after surgery. The results after 12 months of surgery revealed that UDVA did not decrease in any eyes, and one or more lines increased in all eyes. CDVA remained stable in 12 eyes (43%), one-line decreased in seven eyes (25%), and one-line increased in nine eyes (32%; Figure 4). UNVA increased by one or more lines in all eyes. CNVA remained stable in 17 eyes and increased by one or more lines in 11 eyes. In our study, the difference between the pre-operative CDVA and postoperative 12-month UDVA was not significant ($P = .087$). The pre-operative CDVA versus postoperative 12-month UDVA plot demonstrating the safety of the study is shown in Figure 5.

Slit-lamp examination

The common postoperative problem was clinically significant dry eye. Dry eye complaints were present in eight patients for up to 6 months. Two of these patients had a punctate epithelial defect that lasted up to the first 2 months. These patients were treated with preservative-free artificial tears (Artelac Advance®, Bausch&Lomb) for the first 6 months. Dry eye problem requiring treatment up to 12 months postoperatively was observed in one patient. Until the first postoperative year, none of the patients had clinically significant corneal haze. Lenticular rejection or decentralization was not seen in any patient. On slit-lamp examination, the lenticule was not visible in any patient at 6 months. There were no clinically relevant postoperative complications, such as diffuse lamellar keratitis, epithelium ingrowth, or decentralization.

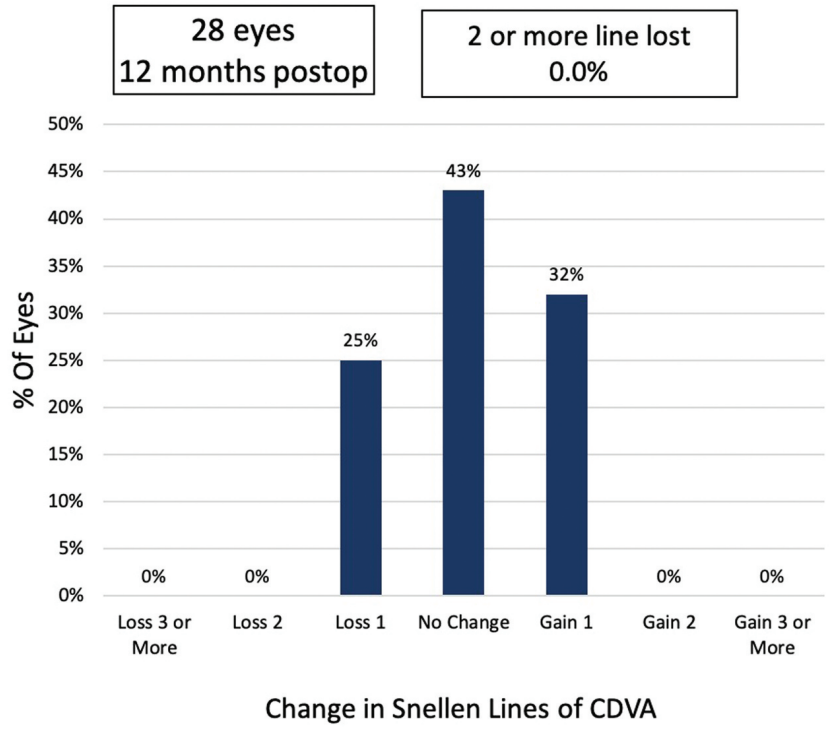

Figure 4. The post-operative corrected visual acuity change plot.

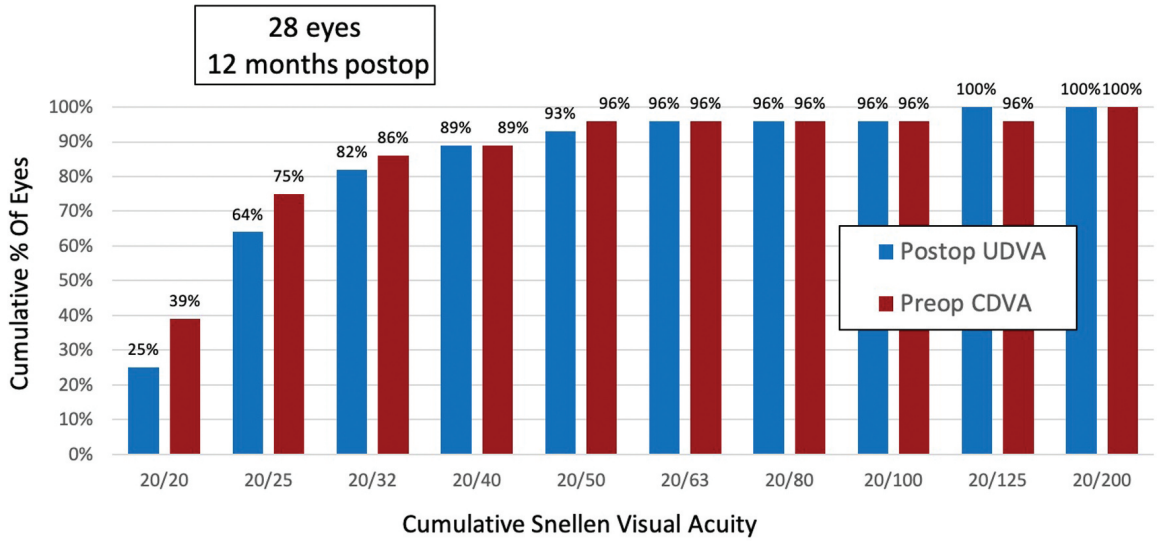

Figure 5. The pre-operative corrected visual acuity versus postoperative 12-month uncorrected visual acuity plot.

Discussion

In this prospective study, the results of excimer laser-shaped hyperopia corneal lenticules implanted under a standard LASIK flap were investigated. Results of the study showed that this surgical method was effective and safe in the refractive treatment of hyperopia. We found that uncorrected visual acuity levels increased significantly without a serious reduction in corrected visual acuity in the eyes. The unpredictability in the refractive results reported in the literature was shown to decrease in our study.

Hyperopic LASIK surgery has always been a challenge. The compensatory response of the corneal stroma and epithelial to hyperopic ablations often results in higher refractive regression than normally observed with myopic LASIK corrections.[20] During refractive surgery, cytokine-mediated wound healing cascades complete corneal stromal and epithelial cells that have been lost. Prolonged elevation of cytokine, which occurs instantaneously after laser ablation, can cause cellular proliferation events to overshoot the reestablishment of surface integrity and optical clarity, leading to regression after laser ablation. In addition, biochemical forces based in the collagen stromal network and instantaneous subtraction of tissues may lead to unwanted changes.[21] Current data showed no clear advantage between PRK and LASIK in the refractive correction

of hyperopia. Regression in patients treated with these methods has always been a problem for hyperopia laser refractive procedures.[2] Kanellopoulos[22] reported that the LASIK results performed in patients with hyperopia through topography-guided WaveLight 400 Hz excimer laser are quite effective and safe. Zadok et al.[23] reported that good results were obtained in patients with low and moderate hyperopia who underwent LASIK, whereas the results were poor in patients with high hyperopia. Biscevic et al.[24] showed acceptable results with LASIK in patients with hyperopia between 3.00 and 7.00 D. They reported that an average of 0.58 ± 0.56 D regression developed at the end of 1 year. After 1 year, UDVA was found to be better than baseline CDVA. In our study, we observed an average of 0.44 ± 0.59 D regression developed at the end of the 12 months. In this sense, we believe that ACI implantation applied to patients with hyperopia is an acceptable regression rate.

In refractive surgery, low regression rates have been reported with wide stromal bed ablation in LASIK. Excimer laser, which is applied to this wide ablation zone, leads to increased corneal tissue loss.[3] Perhaps the most important advantage of inlay implantation is that patients do not undergo any loss of corneal stromal as with all other corneal refractive procedures. However, the increase in CCT values of patients leads to an increase in corneal tissue volume. Another advantage is that it is a surgical method that can be completely reversed. If there is an unexpected clinical problem due to the implant, the corneal flap can be reopened and the lenticule can be removed.

Current corneal lenticule implantation initially originated from SMILE, and promising results were obtained.[25–27] Williams et al.[26] showed that SMILE and lenticular implantation may be an alternative to LASIK in patients with low and moderate hyperopia. Damgaard et al.[25] reported that better refractive results were obtained in the 110 μm group in biological lenticule implantation performed under 110 and 160 μm corneal flaps ex vivo. In their study, the achieved correction was generally lower than the power of the implanted lenticule. Pradhan et al.[27] showed that implantation of an extracted myopic SMILE lenticule from a donor patient appears to be a viable procedure for correcting hyperopia on the cornea. Another study by Sun et al.[19] reported that CDVA increased in all five patients who underwent autologous lenticule implantation. In their study, they particularly emphasized the need for nomogram for lenticule implantation. The clinical outcomes after lenticule implantation and shape-changing inlay increased the central radius of curvature, resulting in a steep central cornea. However, these studies were mainly based on the implantation of lenticules obtained from myopic eyes into hyperopic eyes after SMILE. In these studies, this method can be used in refractive correction of patients with hyperopia, and the biggest problem is that postoperative outcomes are far from predictable. In the present study, we applied lenticule implantation using excimer laser-shaped ACI, which suitable for the refractive error of patients, and showed that predictable results could be obtained.

SMILE was recently modified, and peripheral lenticule was removed and started to be used in the treatment of hyperopia. First, Reinstein et al.[11] performed the first SMILE study for hyperopia correction. Improved refractive results were observed in 89% of patients at 3 months after surgery. It was found within ± 0.50 D in 59% eyes and within ± 1.00 D in 76% eyes. In CDVA, one-line loss was observed in 17% eyes and three-line loss was observed in 1.2% eyes; this patient recovered to one-line loss in at 9-month postoperatively. Wang et al.[28] reported that SMILE is more applicable and effective than LASIK in the correction of hyperopia. Pradhan et al.[29] reported that 53% of the eyes were within ± 0.50 D and 76% of the eyes were within ± 1 D after they performed hyperopic SMILE. Although one-line loss rate in CDVA was 16%, there was no loss of two lines or more. At the same time, Blum et al.[9] performed a prospective feasibility study with femtosecond lenticule extraction (ReLEx) in the treatment of hyperopia. In their study, at the postoperative 9th month, 38% of the treated eyes were within ± 0.50 D and 64% of eyes were within ± 1.00 D of target correction. Only one eye (2.1%) had >2 lines of CDVA loss. However, its stability was much worse than that of myopic ReLEx. Subsequently, they changed the lenticule design and used a large transition zone, which provided better refractive results than before. After 9 months, 33% were within ± 0.50 D and 78% were within ± 1.00 D of target correction. In this group, 33% eyes had one-line loss and 11% eyes had one-line gain in CDVA. When we compared our study with hyperopic SMILE and ReLEx, we found satisfactory results. In the literature, the most successful and satisfactory results were obtained among the series with lenticular implantation. In our study, two-line loss or more in CDVA was not observed in any of our patients. In the 12th month postoperatively, 89.3% of the eyes remained within ± 1 D. These findings showed that ACI implantation is safe and effective in the refractive treatment of hyperopia.

Another method of refractive treatment of hyperopia is clear intraocular lens exchange. Ferrer-Blasco et al.[30] reported that UDVA was 20/20 and above in 46.6% of patients with hyperopia implanted with AcrySof® ReSTOR® SN6AD3 intraocular lens (+ 4.00 D near addition). In their study, they reported that CDVA exhibited two-line loss in 7.6% of eyes and two-line gain in 11.5% of eyes. According to Alfonso et al.,[31] in low-moderate hyperopic eyes implanted with a trifocal intraocular lens, MRSE in the postoperative 6th month was within ± 0.5 D in 81% of eyes and within ± 1 D 99% of eyes. In the high hyperopic group, they found that MRSE was within ± 0.5 D in 78% of eyes and within ± 1 D in 95% of eyes. Although the results are quite acceptable with clear lens replacement in patients with hyperopia, the risks of intraocular surgery are not completely eliminated. For this reason, we believe that corneal surgical procedures that can have similar clinical results should be preferred in the treatment of hyperopia.

Intracorneal inlays may be an option to treat hyperopia. The hydrogel inlays were generally well tolerated in short-term studies of complications in monkeys[32] and humans,[33] post the emergence of synthetic corneal inlay due to substantial problems with the nutrition diffusion. Several studies reported lipid deposits around the inlays, epithelial opacification, and necrosis of the central corneal anterior layer.[33,34] Mulet et al.[35] evaluated safety and efficacy of an intracorneal inlay (Permavision, Anamed Inc., Lake Forest, CA, USA) for the

correction of hyperopia. There was a loss of > 2 lines best-corrected distant visual acuity (BCDVA) in 35% of the eyes at 2 years post procedure and a loss of > 2 lines in 55.5 of the eyes at 5 years. In this study, refractive predictability was poor, and ± 3.00 D emmetropia was observed in 60% of the eyes. Decentralization was seen in the inlay in 29.4% of the eyes, progressive peri-lenticular deposits were observed in 88.2%, a haze was seen in 73.5%, and the inlay was explanted in 58.8% of the eyes. They reported that inlays caused significant visual loss and scarring and had to be explanted in the majority of cases after hydrogel intracorneal inlay implantation to correct hyperopia. All current corneal inlays contain synthetic material which is implanted into the cornea. Therefore, this technique may be associated with complications, such as inflammatory response, potential interference with substrate diffusion into the anterior stroma above the implant, and peri-inlay deposits.[33–35] Alternatively, the use of allogenic tissue provides biocompatibility and good integration into the cornea. Given the low tissue alteration, "tissue addition-based" alternative techniques can be performed to treat hyperopia.[25]

The limitations of this study were that it was performed with a small group of patients and lacked long-term results. Moreover, there was no precisely adjusted nomogram for refractive correction.

In summary, refractive correction of patients with hyperopia does not yield the desired results in the long-term for various reasons. Therefore, new treatment models should be studied in this group of patients. In summary, we found predictable refractive results, satisfactory visual results, and acceptable rates of regression with ACI implantation. This method is not perfect but seems promising in this patient group. We believe that the refractive treatment of patients with hyperopia can be performed with ACI in the future. For the development of this method, it is necessary to publish long-term results in larger series.

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Disclosure statement

The authors declare that they have no conflict of interest.

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Ethical approval

Ethics committee approval was received from the Istanbul Medipol University Ethics Committee on 25/01/2018 with the number 10840098-604.01.01-E-2703 for this study.

Informed consent

Informed consent form was taken from all patients for this study.

References

1. Sher NA. Hyperopic refractive surgery. Curr Opin Ophthalmol. 2001;12(4):304–08. doi:10.1097/00055735-200108000-00011.
2. Settas G, Settas C, Minos E, Yeung IY. Photorefractive keratectomy (PRK) versus laser assisted in situ keratomileusis (LASIK) for hyperopia correction. Cochrane Database Syst Rev. 2012 Jun 13;2012(6):CD007112.
3. Yan MK, Chang JS, Chan TC. Refractive regression after laser in situ keratomileusis. Clin Exp Ophthalmol. 2018;46(8):934–44. doi:10.1111/ceo.13315.
4. Albietz JM, Lenton LM, McLennan SG. Effect of laser in situ keratomileusis for hyperopia on tear film and ocular surface. J Refract Surg. 2002;18:113–23.
5. Plaza-Puche AB, Yebana P, Arba-Mosquera S, Alió JL. Three-year follow-up of hyperopic LASIK using a 500-Hz excimer laser system. J Refract Surg. 2015;31(10):674–82. doi:10.3928/1081597X-20150928-06.
6. Waring GO 3rd, Fant B, Stevens G, Phillips S, Fischer J, Tanchel N, Schanzer C, Narvaez J, Chayet A. Laser in situ keratomileusis for spherical hyperopia and hyperopic astigmatism using the NIDEK EC-5000 excimer laser. J Refract Surg. 2008 Feb;24(2):123–36. doi:10.3928/1081597X-20080201-02.
7. Suarez E, Torres F, Duplessie M. LASIK for correction of hyperopia and hyperopia with astigmatism. Int O Phthalmol Clin. 1996;36(4):65–72. doi:10.1097/00004397-199603640-00010.
8. Reinstein DZ, Archer TJ, Gobbe M, Silverman RH, Coleman DJ. Epithelial thickness after hyperopic LASIK: three-dimensional display with Artemis very high-frequency digital ultrasound. J Refract Surg. 2010;26(8):555–64. doi:10.3928/1081597X-20091105-02.
9. Blum M, Kunert KS, Voßmerbäumer U, Sekundo W. Femtosecond lenticule extraction (ReLEx) for correction of hyperopia - first results. Graefes Arch Clin Exp Ophthalmol. 2013;251(1):349–55. doi:10.1007/s00417-012-2064-y.
10. Sekundo W, Reinstein DZ, Blum M. Improved lenticule shape for hyperopic femtosecond lenticule extraction (ReLEx FLEx): a pilot study. Lasers Med Sci. 2016;31(4):659–64. doi:10.1007/s10103-016-1902-2.
11. Reinstein DZ, Pradhan KR, Carp GI, Archer TJ, Day AC, Sekundo W, Dhungana P. Small incision lenticule extraction for hyperopia: 3-month refractive and visual outcomes. J Refract Surg. 2019;35(1):24–30. doi:10.3928/1081597X-20181025-01.
12. Busin M, Spitznas M, Hockwin O. Evaluation of functional and morphologic parameters of the cornea after epikeratophakia using prelathed, lyophilized tissue. Ophthalmology. 1990;97(3):330–33. doi:10.1016/S0161-6420(90)32585-X.
13. Binder PS, Lin L, van de Pol C. Intracorneal inlays for the correction of ametropias. Eye Contact Lens. 2015;41(4):197–203. doi:10.1097/ICL.0000000000000128.
14. Barraquer JI. Modification of refraction by means of intracorneal inclusions. Int Ophthalmol Clin. 1966;6:53–78. doi:10.1097/00004397-196606010-00004.
15. Cahill M, Condon P, O'Keefe M. Long-term outcome of epikeratophakia. J Cataract Refract Surg. 1999;25(4):500–07. doi:10.1016/S0886-3350(99)80046-7.
16. Busin M, Schmidt J, Koch J. Physiologic analysis of corneal healing after epikeratophakia. Ophthalmology. 1992;99(3):415–17. doi:10.1016/S0161-6420(92)31959-1.
17. American academy of Ophthalmology. Epikeratoplasty: ophthalmic procedure assessment. Ophthalmology. 1996; 103:983–91.
18. Li M, Li M, Sun L, Ni K, Zhou X. Predictive formula for refraction of autologous lenticule implantation for hyperopia correction. J Refract Surg. 2017;33(12):827–33. doi:10.3928/1081597X-20171016-01.
19. Sun L, Yao P, Li M, Shen Y, Zhao J, The Safety ZX. Predictability of implanting autologous lenticule obtained by SMILE for hyperopia.

J Refract Surg. 2015;31(6):374–79. doi:10.3928/1081597X-20150521-03.
20. Moshirfar M, Desautels JD, Walker BD, Murri MS, Birdsong OC, Hoopes PCS. Mechanisms of optical regression following corneal laser refractive surgery: epithelial and stromal responses. Med Hypothesis Discov Innov Ophthalmol. 2018;7:1–9.
21. Wilson SE, Mohan RR, Hong JW, Lee JS, Choi R, Mohan RR. The wound healing response after laser in situ keratomileusis and photorefractive keratectomy: elusive control of biological variability and effect on custom laser vision correction. Arch Ophthalmol. 2001;119(6):889–96. doi:10.1001/archopht.119.6.889.
22. Kanellopoulos AJ. Topography-guided hyperopic and hyperopic astigmatism femtosecond laser-assisted LASIK: long-term experience with the 400 Hz eye-Q excimer platform. Clin Ophthalmol. 2012;6:895–901. doi:10.2147/OPTH.S23573.
23. Zadok D, Raifkup F, Landau D, Frucht-Pery J. Long-term evaluation of hyperopic laser in situ keratomileusis. J Cataract Refract Surg. 2003;29(11):2181–88. doi:10.1016/S0886-3350(03)00416-4.
24. Biscevic A, Pidro A, Pjano MA, Grisevic S, Ziga N, Bohac M. Lasik as a solution for high hypermetropia. Med Arch. 2019;73(3):191–94. doi:10.5455/medarh.2019.73.191-194.
25. Damgaard IB, Ivarsen A, Hjortdal J. Biological lenticule implantation for correction of hyperopia: an ex vivo study in human corneas. J Refract Surg. 2018;34(4):245–52. doi:10.3928/1081597X-20180206-01.
26. Williams GP, Wu B, Liu YC, Teo E, Nyein CL, Peh G, Tan DT, Mehta JS. Hyperopic refractive correction by LASIK, SMILE or lenticule reimplantation in a non-human primate model. PLoS One. 2018;13(3):e0194209. doi:10.1371/journal.pone.0194209.
27. Pradhan KR, Reinstein DZ, Carp GI, Archer TJ, Gobbe M, Gurung R. Femtosecond laser-assisted keyhole endokeratophakia: correction of hyperopia by implantation of an allogeneic lenticule obtained by SMILE from a myopic donor. J Refract Surg. 2013;29(11):777–82. doi:10.3928/1081597X-20131021-07.
28. Wang Y, Ma J. Future developments in SMILE: higher degree of myopia and hyperopia. Asia Pac J Ophthalmol (Phila). 2019;8(5):412–16. doi:10.1097/01.APO.0000580128.27272.bb.
29. Pradhan KR, Reinstein DZ, Carp GI, Archer TJ, Dhungana P. Small incision lenticule extraction (SMILE) for hyperopia: 12-month refractive and visual outcomes. J Refract Surg. 2019;35(7):442–50. doi:10.3928/1081597X-20190529-01.
30. Ferrer-Blasco T, García-Lázaro S, Albarrán-Diego C, Belda-Salmerón L, Montés-Micó R. Refractive lens exchange with a multifocal diffractive aspheric intraocular lens. Arq Bras Oftalmol. 2012;75(3):192–96. doi:10.1590/S0004-27492012000300009.
31. Alfonso JF, Fernández-Vega-Cueto A, Alfonso-Bartolozzi B, Rodríguez-Uña I, Montés-Micó R. Visual and refractive outcomes in hyperopic pseudophakic patients implanted with a trifocal intraocular lens. Clin Ophthalmol. 2019;13:2261–68. doi:10.2147/OPTH.S229228.
32. McDonald MB, McCarey BE, Storie B, Beuerman RW, Salmeron B, van Rij G, Knight PM. Assessment of the long-term corneal response to hydrogel intrastromal lenses implanted in monkey eyes for up to five years. J Cataract Refract Surg. 1993;19(2):213–22. doi:10.1016/S0886-3350(13)80945-5.
33. Ismail MM. Correction of hyperopia by intracorneal lenses: two-year follow-up. J Cataract Refract Surg. 2006;32(10):1657–60. doi:10.1016/j.jcrs.2005.08.057.
34. Alió JL, Mulet ME, Zapata LF, Vidal MT, De Rojas V, Javaloy J. Intracorneal inlay complicated by intrastromal epithelial opacification. Arch Ophthalmol. 2004;122(10):1441–46. doi:10.1001/archopht.122.10.1441.
35. Mulet ME, Alio JL, Knorz MC. Hydrogel intracorneal inlays for the correction of hyperopia: outcomes and complications after 5 years of follow-up. Ophthalmology. 2009;116(8):1455–60, 1460.e1. doi:10.1016/j.ophtha.2009.05.019.