Femtosecond Intrastromal Lenticule Implantation (FILI) for Management of Moderate to High Hyperopia: 5-Year Outcomes

Sheetal Brar, MS; Sri Ganesh, MS, DNB, FRCS; Skanda Samak Sriganesh, AS; Hemali Bhavsar, MS

ABSTRACT

PURPOSE: To report the long-term clinical experience following femtosecond intrastromal lenticule implantation (FILI) for the management of moderate to high hyperopia.

METHODS: Eligible patients who underwent FILI for moderate to high hyperopia from July 2013 to October 2020 were included. A donor small incision lenticule extraction lenticule, matched for refractive error, was implanted into the recipient's corneal pocket created using a femtosecond laser at 160 µm depth. Visual and refractive outcomes and long-term complications were evaluated at the end of a mean follow-up of 68 ± 17.28 months (5.6 years).

RESULTS: Forty-two eyes of 25 patients (mean age: 27.29 ± 5.52 years) were analyzed. The mean spherical equivalent reduced significantly from +5.50 ± 1.96 to +0.66 ± 1.17 diopters (D) at last follow-up visit. Thirty eyes (71%) were within ±1.00 D of spherical equivalent correction. Cumulative uncorrected distance visual acuity of 20/40 or better was achieved in 34 eyes (81%). Efficacy and safety indices were 0.86 ± 0.19 and 1.17 ± 0.39, respectively. There was a significant increase in mean keratometry (Kmean) anterior, central corneal thickness, Q-value, and corneal higher order aberrations and a decrease in Kmean posterior 2 weeks postoperatively, without any significant change in these parameters thereafter (P > .05). Four eyes of 3 patients underwent enhancement and another 4 eyes underwent explantation of the lenticule followed by exchange (2 eyes) and hyperopic laser in situ keratomileusis (2 eyes). No eye lost more than one line of CDVA.

CONCLUSIONS: At 5 years of follow-up, FILI for moderate to high hyperopia showed good safety, efficacy, and reversibility. Modification of nomograms and surgical planning may be employed for further refinement of the outcomes.

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In 1949, José Ignacio Barraquer laid the groundwork for the use of natural corneal tissue to change the refractive properties of the eye.[1,2] Subsequently, Pradhan et al[3] published a case report showing the feasibility of use of a myopic small incision lenticule extraction (SMILE) lenticule (endokeratophakia) for correction of aphakia. Following this, many researchers successfully reported the use of allogenic and autologous SMILE lenticules for management of conditions such as high hyperopia, keratoconus, presbyopia, and sealing corneal defects.[4-8]

In the technique of femtosecond intrastromal lenticule implantation (FILI), published by our group in 2014,[4] the cornea is made steeper by addition of a SMILE lenticule of known thickness and power into a pocket created in the recipient's cornea using a femtosecond laser. The concept was subsequently adopted by various authors, who reported their results with certain modifications in the technique.[5,9] Recently, Liu et al[10] published their 2-year results with SMILE lenticule implantation and suggested that allogenic

From Nethradhama Superspeciality Eye Hospital, Bangalore, India.

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Correspondence: Sheetal Brar, MS, Phaco and Refractive Department, Nethradhama Superspeciality Eye Hospital, Bangalore, Karnataka 560070, India. Email:brar_sheetal@yahoo.co.in

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lenticule transplantation may be a promising option for correcting moderate to high hyperopia.

We report 5 years of clinical experience with FILI for moderate to high hyperopia, including the visual and refractive results, safety and efficacy data, and outcomes of re-treatment cases. To our knowledge, this is the longest follow-up study reporting the long-term results of tissue addition using SMILE lenticules in the setting of moderate to high hyperopia.

PATIENTS AND METHODS

This retrospective study included eligible patients who underwent FILI for correction of moderate to high hyperopia from July 2013 to October 2020. The study was approved by the institutional review board of Nethradhama Superspeciality Eye Hospital, Bangalore, India, and adhered to the tenets of the Declaration of Helsinki. All patients provided written consent regarding the donor and recipient surgeries and using their data for analysis.

Inclusion criteria were: age 18 years or older, hyperopic refractive error between +3.00 and +11.00 diopters (D), stable refractive error (change of < 0.50 D within the past 12 months), preoperative corrected distance visual acuity (CDVA) of 0.6 logMAR or better, and a strong motivation for refractive correction. Exclusion criteria were: previous keratitis, severe dry eye disease, cataract, glaucoma, or vitreoretinal disorders, concomitant autoimmune diseases, pregnancy, and patients with unrealistic expectations.

Surgical Procedure

All of the primary FILI and subsequent procedures were performed by a single experienced refractive surgeon (SG) using the following standard techniques.

For FILI, the donor SMILE lenticules used were either cryopreserved or fresh (ie, the extracted lenticule was used either in the same sitting or within 48 hours, when stored in balanced salt solution). Briefly, the FILI procedure involved insertion of the donor SMILE lenticule into a femtosecond laser pocket created using the VisuMax FS Laser (Carl Zeiss Meditec) at a depth of 160 µm, as described earlier.[4]

For the enhancement procedure (Bowman membrane relaxation), a Hessburg-Barron trephine (Barron Precision Instruments) was used to trephine the Bowman membrane and part of the anterior stromal fibers. The technique has been explained in detail in a previously published study by our group.[11]

For the lenticule exchange procedure, a Sinskey hook was used to open the old incision and enter the corneal interface. A blunt spatula was then used to dissect the tissue above and below the implanted lenticule and separate it from the surrounding adhesions. The free lenticule was then grasped with a microforceps from its edge and extracted from the corneal pocket. The interface was washed with balanced salt solution, followed by which the fresh lenticule was implanted into the interface using the standard technique of FILI, described above. The postoperative regimen was similar to the one published earlier.[4]

TABLE 1
Patient Details

Parameter	Mean ± SD
Recipient	
Age (years)	27.04 ± 5.33
UDVA (logMAR)	1.03 ± 0.39
CDVA (logMAR)	0.22 ± 0.23
Sphere (D)	5.24 ± 1.96
Cylinder (D)	0.51 ± 0.48
SE (D)	5.50 ± 1.96
CCT (µm)	550.02 ± 29.68
Kmean anterior (D)	43.72 ± 1.55
Kmean posterior (D)	-6.30 ± 0.26
Q-value	-0.34 ± 0.09
HOA (RMS)	0.398 ± 0.15
Donor	
Age (years)	28 ± 5.33
SE treated (D)	-6.03 ± 1.99
Optical zone (µm)	6.50 ± 0.28
Lenticule thickness (µm)	114 ± 25.70
Length of cryopreservation (days)	61 ± 103.61

CCT = central corneal thickness; CDVA = corrected distance visual acuity, D = diopters; HOA = higher order aberration; Kmean = mean keratometry; RMS = root mean square; SE = spherical equivalent; UDVA = uncorrected distance visual acuity

Postoperative examinations were scheduled at 1 day, 2 weeks, 3 months, 6 months, and yearly thereafter. From postoperative 2 weeks on, the following assessments were performed: uncorrected distance visual acuity (UDVA), CDVA, manifest refraction, corneal tomography (Pentacam HR; Oculus Optikgeräte GmbH), anterior segment optical coherence tomography using the Optovue (Optovue, Inc) or MS-39 (CSO), and dilated clinical photography.

RESULTS

FILI was performed on 42 eyes of 25 patients. **Table 1** provides the preoperative demographic and baseline data of all recipient patients, as well as the donors whose lenticules were used for implantation. Mean follow-up was 68 ± 17.28 months (range: 12 to

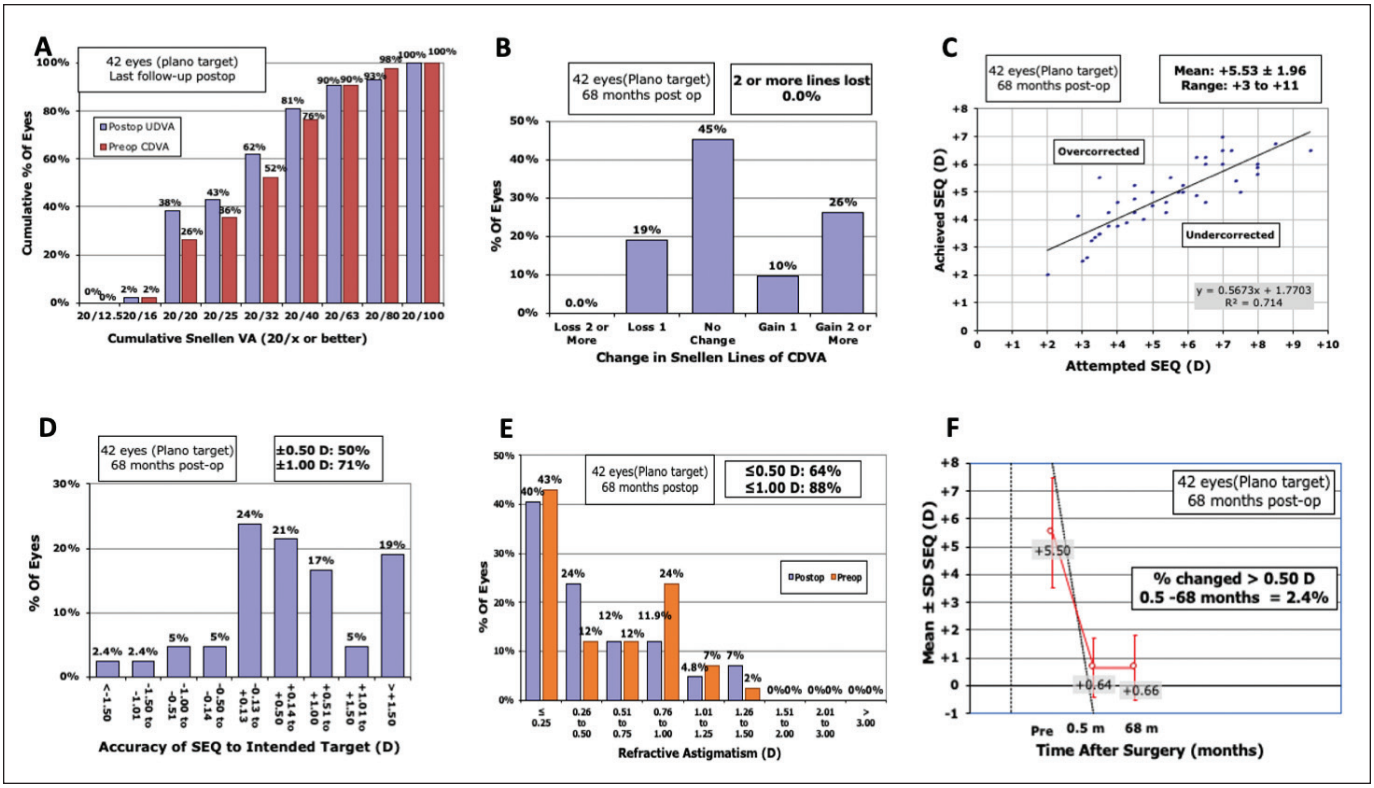

Figure 1. Standard graphs for 42 eyes treated with femtosecond intrastromal lenticule implantation in the series. CDVA = corrected distance visual acuity; D = diopters; SEQ = spherical equivalent; UDVA = uncorrected distance visual acuity

84 months) and median follow-up was 72 months. **Table A** (available in the online version of this article) shows the postoperative visual and refractive results at 2 weeks and at the end of the mean follow-up.

Efficacy

At last follow-up visit, the mean efficacy index was 0.86 ± 0.19 (range: 0.39 to 1.0). The postoperative mean UDVA was 0.25 ± 0.22 logMAR (range: -0.12 to 0.6 logMAR). Cumulative UDVA of 20/20 or better and 20/40 or better was seen in 38% (n = 16) and 81% (n = 34) of eyes, respectively (**Figure 1A**).

Safety

The mean safety index was 1.17 ± 0.39 (range: 0.63 to 2.54). Thirty-six percent of eyes (n = 15) gained one or more lines, 45% (n = 19) had no change, and 19% (n = 8) lost one line of CDVA. No eye lost more than two lines of CDVA (**Figure 1B**).

Spherical Equivalent and Astigmatism Accuracy

The accuracy of spherical equivalent (SE) refraction within ±0.50 D was observed in 50% of eyes (n = 21), but 71% (n = 30) of the treated eyes were within ±1.00 D of SE correction. A coefficient of determination value of 0.71 was obtained on the predictability curve (**Figures 1C-1D**). Sixty-four percent of eyes (n = 29) were within ±0.50 D of astigmatism, whereas 88% of eyes (n = 37) were within ±1.00 D of astigmatism (**Figure 1E**).

Stability

The mean residual refraction at 2 weeks postoperatively was 0.64 ± 1.05 D, which showed a non-significant increase to 0.66 ± 1.17 D at last postoperative visit ($P = .95$) (**Figure 1F**).

Changes in Anterior and Posterior Keratometry, Central Corneal Thickness, Q-value, and Corneal Higher Order Aberrations

There was a significant increase in the mean keratometry (Kmean) anterior, central corneal thickness, Q-value, and corneal higher order aberrations 2 weeks postoperatively compared to the preoperative values ($P < .05$) (**Table B**, available in the online version of this article). However, no significant change was observed in these parameters at the last follow-up visit, when compared to 2 weeks ($P > .05$) (**Table B**). On the other hand, Kmean posterior values showed a significant change from -6.30 ± 0.26 to -6.13 ± 0.34 D ($P = .02$) (ie, becoming more positive) 2 weeks after FILI, which did not change significantly thereafter ($P = .23$, 2 weeks vs last follow-up visit).

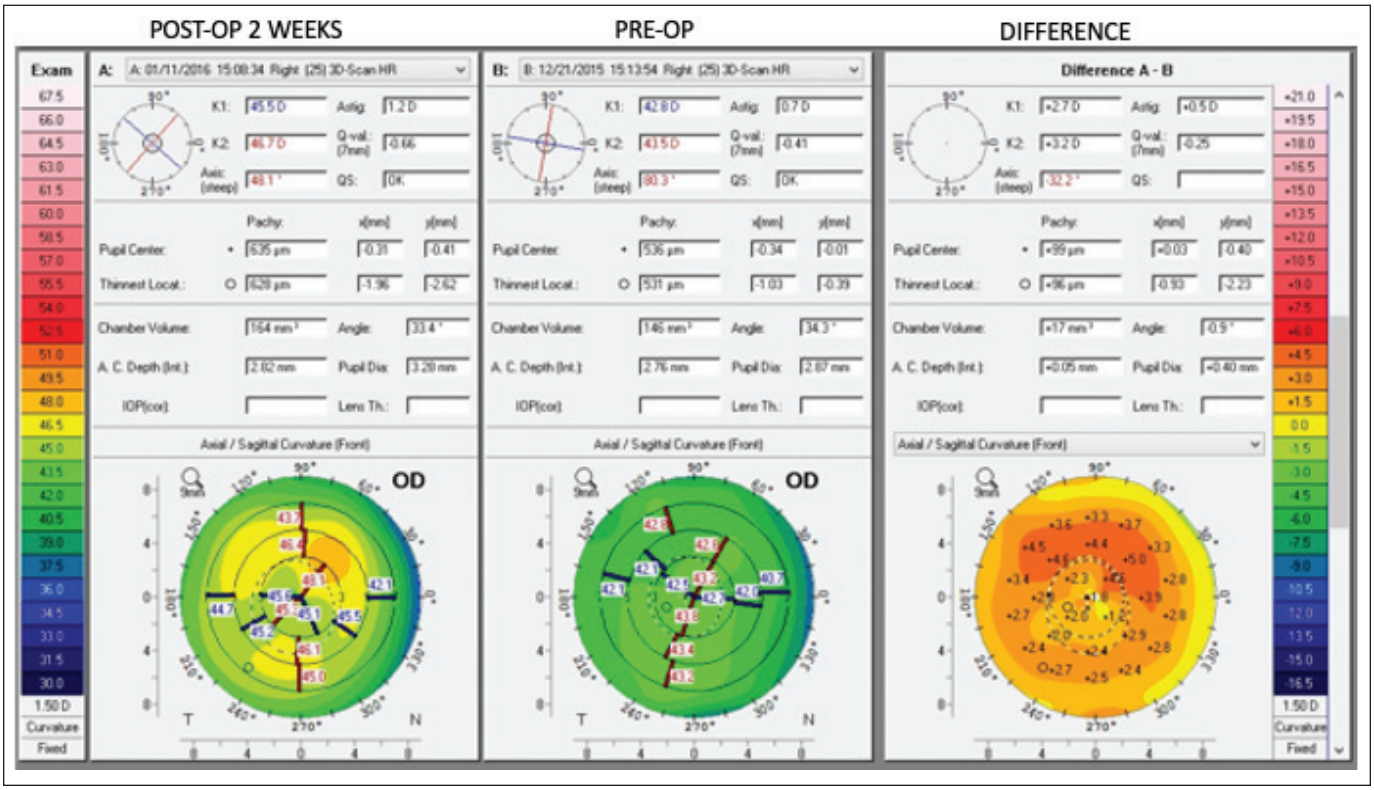

Figure 2. Two-week postoperative versus preoperative difference maps of the right eye of a 29-year-old patient who underwent femtosecond intrastromal lenticule implantation for hyperopic refractive error of +6.50 diopters (D).

Figure 2 and **Figure A** (available in the online version of this article), respectively, show the 2 weeks versus preoperative difference maps of both eyes of a 29-year-old man who underwent FILI for high hyperopia of +6.50 and +7.00 D in the right and left eyes, respectively. Compared to preoperative values, an increase in steep and flat keratometry and thinnest pachymetry by 2.70 D, 3.20 D, and 96 µm, respectively, was observed at 2 weeks in the right eye (**Figure 2**). Similar changes were observed in the left eye of the patient, wherein the steep and flat keratometry and thinnest pachymetry increased by 3.00 D, 4.10 D, and 77 µm, respectively (**Figure A**). **Figures B-C** (available in the online version of this article) show the difference maps of both eyes of the same patient at a long follow-up of 5.8 years versus 2 weeks after FILI. A mild steepening in steep and flat keratometry (0.90 and 0.40 D in the right eye and 0.40 and 1.10 D in the left eye) was noted in both eyes at 5.8 years when compared to 2 weeks postoperatively. **Figure D** (available in the online version of this article) (A1 and B1) shows clinical photographs of both eyes of the same patient at 2 weeks postoperatively, showing the implanted lenticule in situ. Note that, in a freshly implanted lenticule, the borders are well defined and mild folds in the tissue can be observed. However, at 5.8 years of follow-up (**Figure D**, A2 and B2), the borders of the lenticules are merged with the surrounding host tissue and a faint boundary of the lenticule is visible. The lenticule is relatively clear and does not have any folds or interface haze of any kind. **Figure E** (available in the online version of this article) demonstrates the corresponding anterior segment optical coherence tomography scans with clear and well-centered lenticules in situ.

ENHANCEMENT

Four eyes of 3 patients underwent enhancement with Bowman membrane relaxation for a significant residual refractive error. **Table C** (available in the online version of this article) lists the visual and refractive outcomes of these eyes following enhancement.

COMPLICATIONS

Four eyes of 2 patients underwent explantation of the lenticule due to suspected stromal rejection. All lenticules used in these eyes were cryopreserved. For one patient, the lenticules were exchanged with fresh lenticules. **Figure F** (available in the online version of this article) shows the dilated clinical photographs of the left eye of this patient at 1.5 years postoperatively, showing interface haze due to diffuse lenticule scar-

ring. After the exchange, the lenticules remained clear with full recovery of visual acuity (**Table D**, available in the online version of this article). For the second patient, lenticules were explanted 3 years after the FILI procedure, after which hyperopic laser in situ keratomileusis (LASIK) was performed 2 months later (**Table D**).

DISCUSSION

In the current study, we evaluated the long-term clinical outcomes of FILI for the treatment of moderate to high hyperopia in 42 eyes treated with this technique. At a mean follow-up of 68 months (5.6 years), our results were fairly accurate and stable, showing reduction of SE from +5.54 to +0.64 D at 2 weeks and +0.66 D at last follow-up visit. When compared to the long-term results of hyperopic LASIK reported by Dave et al,[12] the mean SE in their study reduced from +3.74 to +0.84 D at a comparable follow-up of 5 years. This may support the previously proposed mechanisms described in relation to tissue addition, such as lesser epithelial response, fewer induced aberrations and less dry eye, and better biomechanical stability, potentially improving CDVA and thus favoring this technique over excimer laser procedures for higher degrees of hyperopia.[4,11]

SMILE as a treatment modality for hyperopia was explored by Pradhan et al,[13] who reported a relative change in SE from +5.61 to -0.19 D at 12 months of follow-up. However, they reported an 11% loss of follow-up at the last visit. The authors suggested SMILE to be a promising modality for high hyperopia, but a longer follow-up is necessary to assess the long-term stability following this procedure.

Liu et al[10] recently reported their 2-year clinical experience of treating 14 eyes with implantation of an allogenic SMILE lenticule for moderate to high hyperopia. All of their lenticule implantation procedures were scheduled on the same day as SMILE in the myopic donor eye. In our series, 24 eyes were implanted with cryopreserved SMILE lenticules, whereas the remaining 18 eyes received fresh lenticules. Contrary to our results, Liu et al noted a slight overcorrection with the preoperative SE decreasing from +5.53 to -0.60 D at 2 years postoperatively. This may be explained by the fact that the depth of the femtosecond laser pocket at which the donor lenticule was implanted in their study was set at 100 µm compared to 160 µm in our study, which may have maximized the refractive effect by mainly changing the anterior corneal curvature, without significantly influencing the posterior curvature. Moshirfar et al[14] reported a case of high hyperopia of +6.00 -1.00 × 40° managed with lenticule intrastromal keratoplasty using a thick corneal lenticule of 157 µm (+7.00 D), implanted under a flap at a depth of 100 µm. At 6 months postoperatively, manifest refraction reduced to 0.00 -1.25 × 71°, without any noticeable change in the posterior curvature (0.20-D change in steep keratometry). Damgaard et al[15] evaluated changes in corneal tomography after stromal lenticule implantation ex vivo, using a combination of two implantation depths (110 and 160 µm) and two lenticule thicknesses (95 µm = 4.00 D, 150 µm = 8.00 D). For the front curvature, a 110-µm implantation depth induced significantly more steepening than a 160-µm depth in all groups. These observations may suggest that a relatively superficial implantation of the lenticule may result in more pronounced anterior curvature changes. In addition, they also observed the relative correction achieved at 160 µm was up to 50%. However, in our study we noticed an 88% achieved correction when the lenticules were implanted at 160-µm depth. These differences may be explained by the ex vivo nature of their study, wherein the total corneal refractive power was measured before and after lenticule implantation by imaging the corneas mounted on an artificial chamber, the pressure of which was adjusted with an attached column of organ culture media and monitored with a pressure monitor. This experimental set-up may have led to variability in the results, which may not be applicable to the in vivo ocular conditions.

In terms of the changes in front keratometry, corneal thickness, and Q-value, we noted a significant increase in these parameters after FILI at 2 weeks, similar to the results of Liu et al[10] obtained at 1 month after allogenic lenticule implantation. However, they observed a significant decrease in the anterior keratometry at 2 years when compared to 3-month values (-0.36 D, $P < .001$). No significant corresponding change in the SE was reported. On the contrary, we did not observe any significant change in either anterior keratometry or SE values at last follow-up visit versus 2 weeks postoperatively. This may indicate that our results were comparatively more stable at a longer follow-up of 5.6 years when compared to the maximum follow-up of 2 years in their study. It may be possible that the mild flattening observed in their study at 2 years may continue over time, and result in some amount of regression at a comparable follow-up of 5.6 years. The anterior placement of the lenticule (at 100 µm) may result in an acute and exaggerated change in the anterior corneal curvature and Q-value, thus making the cornea more prone to regression due to the resulting epithelial response. On the other hand, it may be hypothesized that, when the lenticule is implanted at a

deeper depth of 160 µm, the anterior curvature changes observed for the same amount of tissue may be more gradual, possibly resulting in less epithelial response and better refractive stability.

The ideal depth at which the lenticule must be implanted for accurate results and long-term stability after tissue addition for hyperopia is debatable. Based on the observations and discussions of the aforementioned studies, it may be proposed that the lenticule be implanted at 120 to 130 µm to achieve the desired effect on the anterior curvature, without inducing much posterior change. Significant overcorrections and undercorrections may also be avoided by potentially improving the refractive predictability.

Tissue additive procedures for high hyperopia may involve insertion of natural corneal tissue or SMILE lenticule under a LASIK flap (lenticule intrastromal keratoplasty)[16] or inside a corneal pocket created using a femtosecond laser (FILI and small-incision lenticule intrastromal keratoplasty).[4,9] The creation of a flap for tissue addition poses challenges such as increased risk of dry eye, diffuse lamellar keratitis, weakening of biomechanics, poor adhesion, and dislocation of the flap edge, and epithelial ingrowth that may not be present when the tissue is implanted inside a pocket.[9] Moshirfar et al[14] reported a case of moderate flap necrosis with epithelial ingrowth following lenticule intrastromal keratoplasty for high hyperopia, presenting at 1 month postoperatively. The case was managed with scraping of the epithelial ingrowth, suturing, and application of glue at the necrotic flap edge, but the incidence of such complications may be minimized by implanting the tissue in a stromal pocket because the incision is small and the amount of surgical manipulation is less.

Liu et al[10] reported a good safety profile with 14.3% of eyes gaining one line, 78.6% showing no change, and 7.1% losing one line of CDVA at 2 years postoperatively. In our study, 45% of eyes had no change, 36% of eyes gained one line or more, and 19% of eyes lost one line of CDVA. No eye lost two or more lines of CDVA in either study. However, 4 eyes in our series required lenticule explantation due to suspected stromal rejection diagnosed at a mean period of 2.25 years. A common factor in these 4 eyes was the use of cryopreserved tissue, compared to their study, wherein all lenticules were harvested and implanted on the same day. The cryopreservation process may alter the physical properties of the stromal collagen and keratocytes, making them susceptible to necrosis, possibly due to a relative lack of cell membrane protection by cryoprotectants used.[17] However, the cases wherein fresh lenticules were used may still need to be followed up due to the potential risk of late stromal rejection that remains. Pretreatment with gamma radiation has been suggested to deantigenize the donor tissue and prevent future rejection.[18,19] However, the feasibility of this option needs to be explored. It may be noteworthy to mention that all 4 eyes for which the lenticules were explanted achieved complete visual recovery following reimplantation of fresh lenticules (2 eyes) and subsequent excimer treatment (2 eyes), suggesting full reversibility of the procedure.

Moshirfar et al[9] and Ganesh et al[20] suggested use of CIRCLE software and the side cut–only technique to convert the cap into a LASIK flap for the purpose of enhancement after small-incision lenticule intrastromal keratoplasty procedure for high hyperopia. We achieved satisfactory outcomes using the Bowman membrane relaxation technique for treating residual refractive error after FILI by potentially reversing the posterior corneal curvature changes.[11]

Our tissue addition technique of FILI resulted in satisfactory visual and refractive outcomes with good safety, efficacy, and stability of achieved correction. The truly reversible nature of the procedure could be verified by successful re-treatments resulting in complete restoration of visual acuity in eyes requiring explantation of the lenticules. Enhancements with Bowman membrane relaxation resulted in improved refractive accuracy. However, predictability of refractive results may be further improved by suitable nomograms and modifications in surgical planning and techniques. Future research is suggested in the areas of biomechanical changes, epithelial and stromal remodeling, tissue treatments, and preservation to prevent rejection following this procedure. To the best of our knowledge, this study reports the longest follow-up data of the largest series of patients with moderate to high hyperopia treated with SMILE-derived lenticule implantation. This is also the first time that the outcomes of re-treatments following lenticule explantation after FILI are being reported.

AUTHOR CONTRIBUTIONS

Study concept and design (SG); data collection (HB); analysis and interpretation of data (SB, SSS); writing the manuscript (SB); critical revision of the manuscript (SG, SSS, HB); statistical expertise (SB, HB); administrative, technical, or material support (SG); supervision (SG)

REFERENCES

1. Barraquer JI. *Queratomileusis y queratofakia*. Instituto Barraquer de America; 1980:342.
2. Barraquer JI. Refractive corneal surgery: experience and considerations. *An Inst Barraquer*. 1993;24:113-118.

3. 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):777-782. https://doi.org/10.3928/1081597X-20131021-07 PMID:24203809

4. Ganesh S, Brar S, Rao PA. Cryopreservation of extracted corneal lenticules after small incision lenticule extraction for potential use in human subjects. *Cornea*. 2014;33(12):1355-1362. https://doi.org/10.1097/ICO.0000000000000276 PMID:25343698

5. Sun L, Yao P, Li M, Shen Y, Zhao J, Zhou X. The safety and predictability of implanting autologous lenticule obtained by SMILE for hyperopia. *J Refract Surg*. 2015;31(6):374-379. https://doi.org/10.3928/1081597X-20150521-03 PMID:26046703

6. Ganesh S, Brar S. Femtosecond intrastromal lenticular implantation combined with accelerated collagen cross-linking for the treatment of keratoconus: initial clinical result in 6 eyes. *Cornea*. 2015;34(10):1331-1339. https://doi.org/10.1097/ICO.0000000000000539 PMID:26252741

7. Jacob S, Kumar DA, Agarwal A, Agarwal A, Aravind R, Saijimol AI. Preliminary evidence of successful near vision enhancement with a new technique: PrEsbyopic Allogenic Refractive Lenticule (PEARL) corneal inlay using a SMILE lenticule. *J Refract Surg*. 2017;33(4):224-229. https://doi.org/10.3928/1081597X-20170111-03 PMID:28407161

8. Bhandari V, Ganesh S, Brar S, Pandey R. Application of the SMILE-derived glued lenticule patch graft in microperforations and partial-thickness corneal defects. *Cornea*. 2016;35(3):408-412. PMID:26764882 https://doi.org/10.1097/ICO.0000000000000741 PMID:26764882

9. Moshirfar M, Shah TJ, Masud M, et al. A modified small-incision lenticule intrastromal keratoplasty (sLIKE) for the correction of high hyperopia: a description of a new surgical technique and comparison to lenticule intrastromal keratoplasty (LIKE). *Med Hypothesis Discov Innov Ophthalmol*. 2018;7(2):48-56. PMID:30250852

10. Liu S, Wei R, Choi J, Li M, Zhou X. Visual outcomes after implantation of allogenic lenticule in a 100-μm pocket for moderate to high hyperopia: 2-year results. *J Refract Surg*. 2021;37(11):734-740. PMID:34756142 https://doi.org/10.3928/1081597X-20210730-02 PMID:34756142

11. Brar S, Ganesh S, Sriganesh SS, Dorennavar L. Long-term outcomes of Bowman's membrane relaxation for enhancement of femtosecond intrastromal lenticule implantation performed for the management of high hyperopia. *J Refract Surg*. 2022;38(2):134-141. https://doi.org/10.3928/1081597X-20211215-01 PMID:35156459

12. Dave R, O'Brart DP, Wagh VK, et al. Sixteen-year follow-up of hyperopic laser in situ keratomileusis. *J Cataract Refract Surg*. 2016;42(5):717-724. PMID:27255248 https://doi.org/10.1016/j.jcrs.2016.03.028 PMID:27255248

13. 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):442-450. PMID:31298724 https://doi.org/10.3928/1081597X-20190529-01 PMID:31298724

14. Moshirfar M, Hopping GC, Somani AN, et al. Human allograft refractive lenticular implantation for high hyperopic correction. *J Cataract Refract Surg*. 2020;46(2):305-311. doi:10.1097/j.jcrs.0000000000000011

15. 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):245-252. https://doi.org/10.3928/1081597X-20180206-01 PMID:29634839

16. Jankov M, Mrochen M, Seiler T. Laser intrastromal keratoplasty: case report. *J Refract Surg*. 2004;20(1):79-84. https://doi.org/10.3928/1081-597X-20040101-14 PMID:14763476

17. Borderie VM, Laroche L. Ultrastructure of cultured and cryopreserved human corneal keratocytes. *Cornea*. 1999;18(5):589-594. PMID:10487434 https://doi.org/10.1097/00003226-199909000-00012 PMID:10487434

18. Stevenson W, Cheng SF, Emami-Naeini P, et al. Gamma-irradiation reduces the allogenicity of donor corneas. *Invest Ophthalmol Vis Sci*. 2012;53(11):7151-7158. https://doi.org/10.1167/iovs.12-9609 PMID:22991417

19. Utine CA, Tzu JH, Akpek EK. Lamellar keratoplasty using gamma-irradiated corneal lenticules. *Am J Ophthalmol*. 2011;151(1):170-174.e1. https://doi.org/10.1016/j.ajo.2010.08.007 PMID:21145036

20. Ganesh S, Brar S, K v M. CIRCLE software for the management of retained lenticule tissue following complicated SMILE surgery. *J Refract Surg*. 2019;35(1):60-65. PMID:30633789 https://doi.org/10.3928/1081597X-20181120-01 PMID:30633789

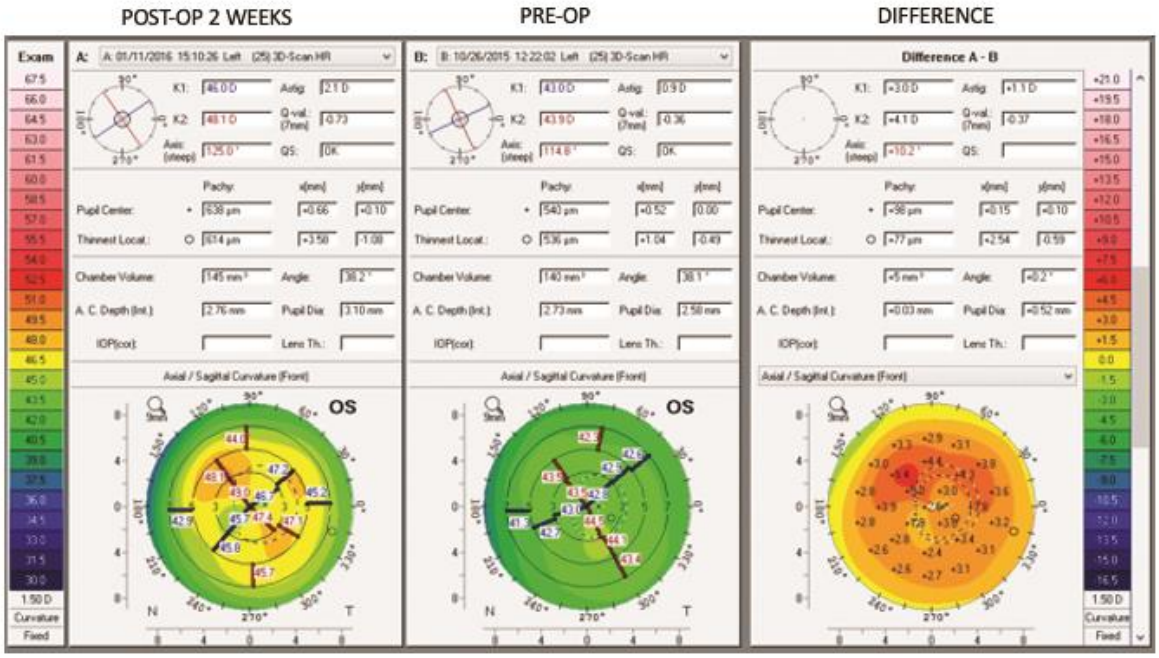

Figure A. Two weeks versus preoperative difference maps of the left eye of a 29-year-old patient who underwent femtosecond intrastromal lenticule implantation for hyperopic refractive error of +7.00 diopters.

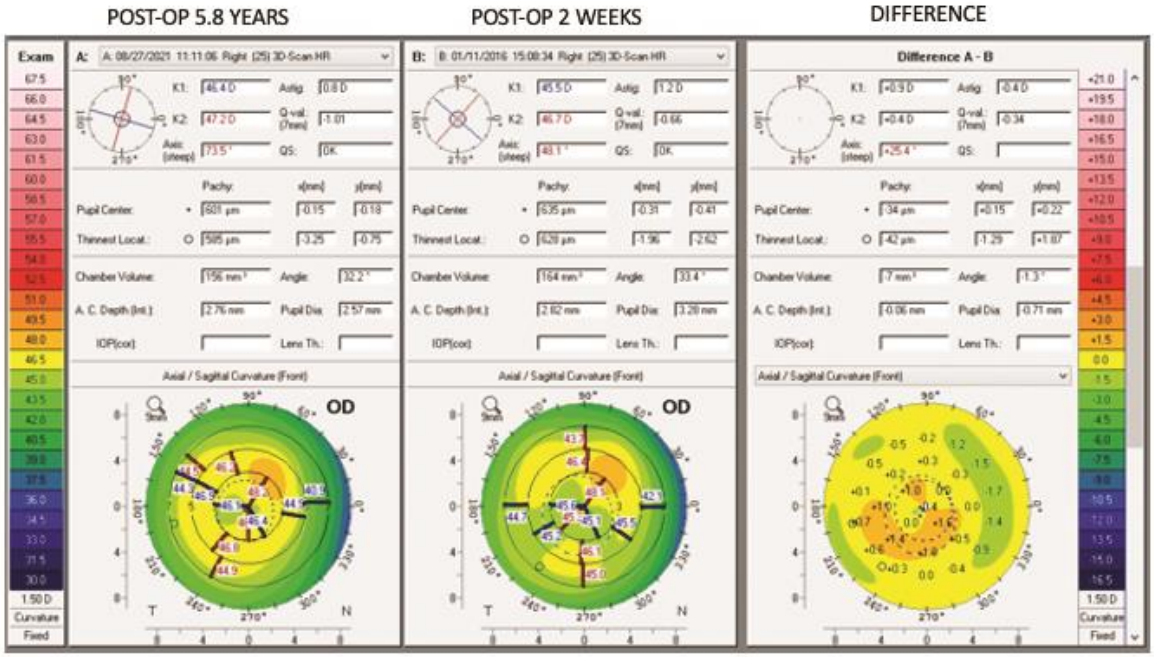

Figure B. Right eye difference map of 5.8 years versus 2 weeks after femtosecond intrastromal lenticule implantation of the same patient.

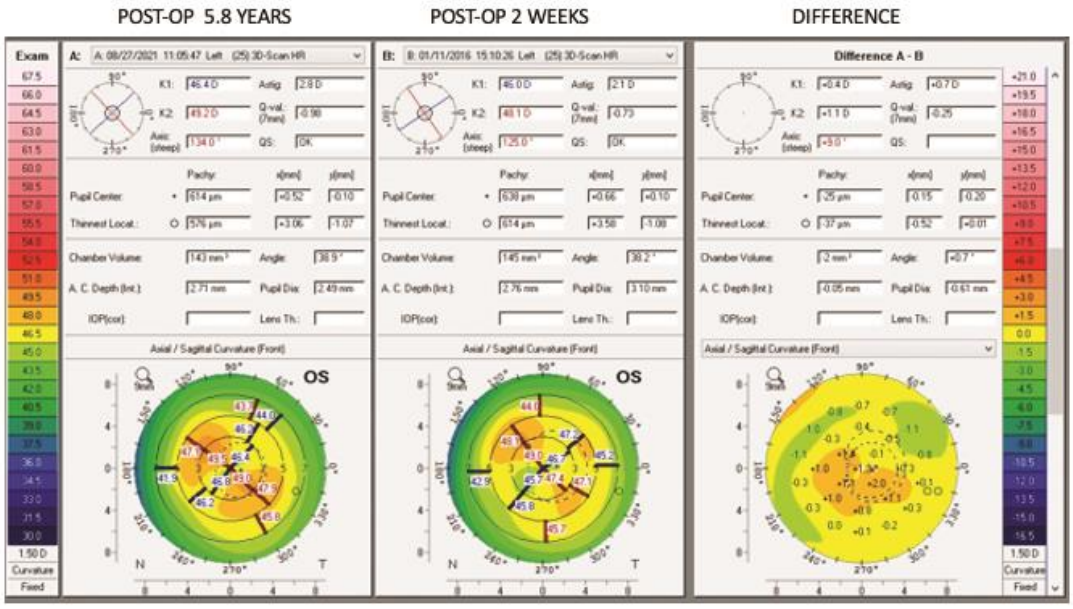

Figure C. Left difference map of 5.8 years versus 2 weeks after femtosecond intrastromal lenticule implantation of the same patient.

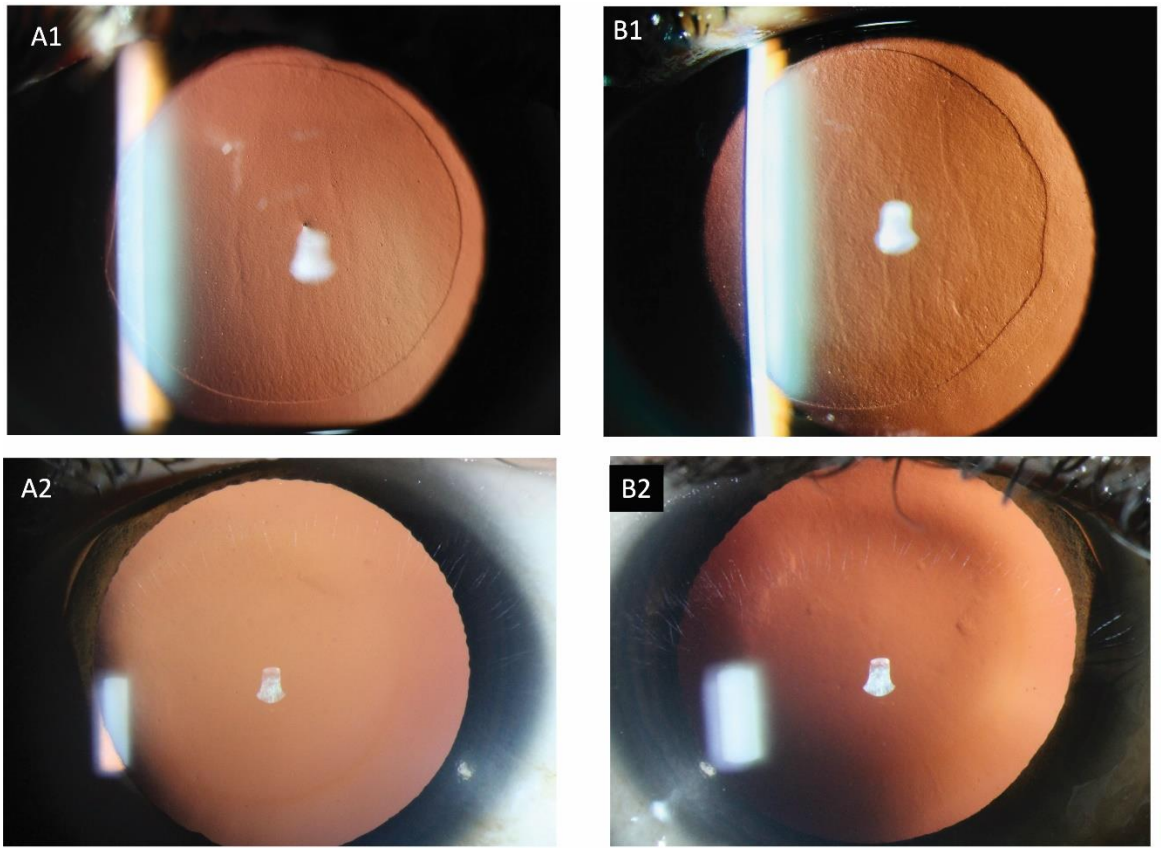

Figure D. Clinical photographs of the same patient. A1 and B1: 2 weeks postoperatively and A2 and B2: 5.8 years postoperatively, for the right and left eyes, respectively.

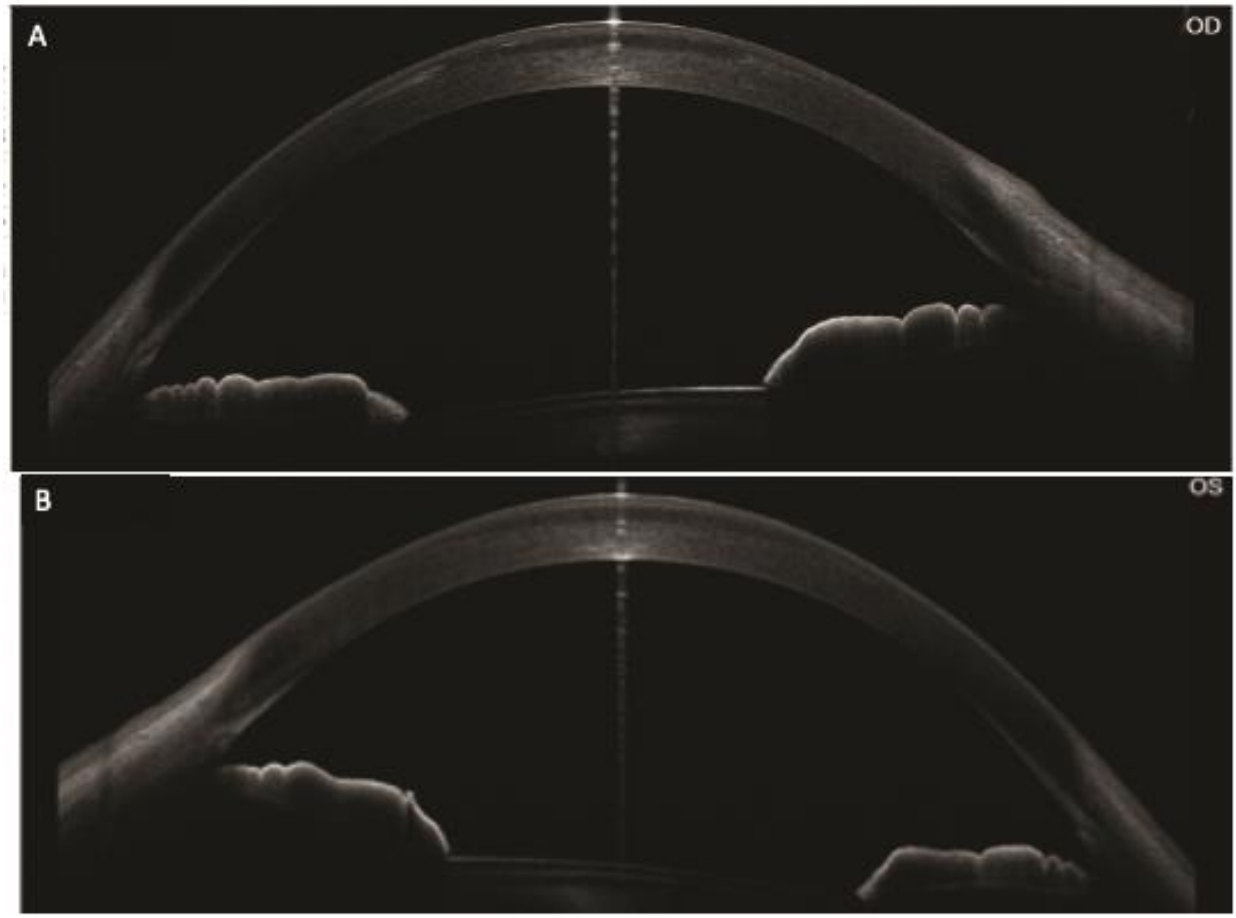

Figure E. Anterior segment optical coherence tomography of both eyes of the same patient at 5.8 years of follow-up, with clear and well-centered lenticules in situ.

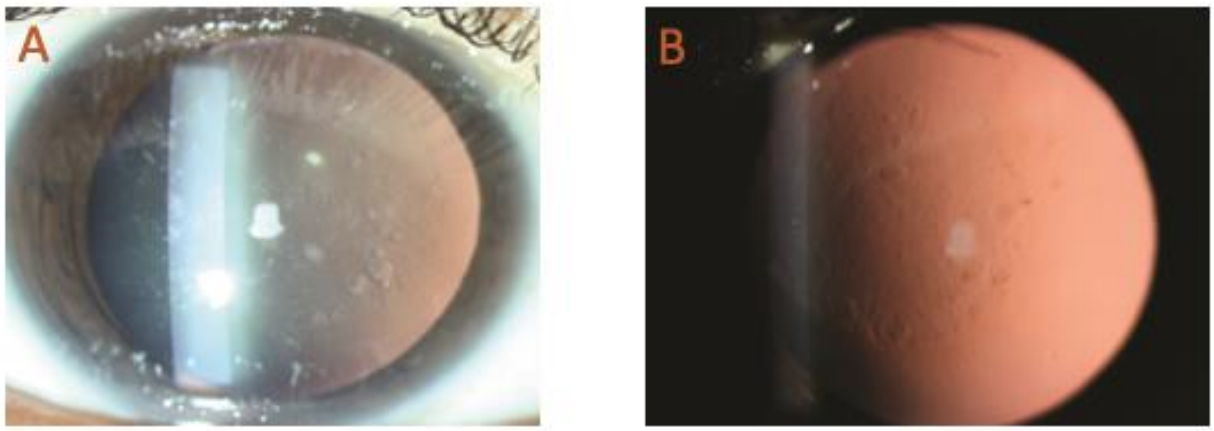

Figure F. Dilated clinical photographs (A) oblique illumination and (B) retroillumination of the left eye of a patient at 1.5 years postoperatively, showing interface haze due to diffuse lenticule scarring. The hazy lenticule was explanted and exchanged with a fresh lenticule 2 weeks later, which remained clear over a follow-up of 6 years.

Table A

Visual and Refractive Results After FILI (n = 42 eyes) at 2 Weeks and Last Follow-up Visit

Parameter	Preop, Mean ± SD (Range)	2 Weeks, Mean ± SD (Range)	*P* (Preop vs 2 Weeks)	Last Follow-up, Mean ± SD (Range)	*P* (2 Weeks vs Last Follow-up)
UDVA (logMAR)	1.03 ± 0.39 (0.22 to 1.78)	0.21 ± 0.23 (-0.10 to 0.80)	< .001	0.25 ± 0.23 (-0.10 to 0.60)	.36
CDVA (logMAR)	0.22 ± 0.23 (-0.10 to 0.80)	0.19 ± 0.20 (-0.10 to 0.70)	.51	0.19 ± 0.21 (-0.20 to 0.60)	.88
Sphere (D)	5.24 ± 1.96 (+3 to +11)	0.57 ± 0.82 (0 to +2.25)	< .001	0.56 ± 0.94 (-1.50 to +2.25)	.95
Cylinder (D)	0.51 ± 0.48 (0 to +1.50)	0.14 ± 0.65 (-1.50 to +1.50)	< .001	0.19 ± 0.67 (-1.25 to +1.50)	.71
SE (D)	5.54 ± 1.96 (+3 to +11)	0.64 ± 1.05 (-0.625 to +4.50)	< .001	0.66 ± 1.18 (-2.00 to +2.375)	.95

CDVA = corrected distance visual acuity, D = diopters; FILI = femtosecond intrastromal lenticule implantation; SD = standard deviation; SE = spherical equivalent, UDVA = uncorrected distance visual acuity

Table B

Changes in Kmean Anterior, Kmean Posterior, CCT, Q-value and Corneal HOAs at 2 Weeks and Last Follow-up Visit

Parameter	Preop, Mean ± SD (Range)	2 Weeks, Mean ± SD (Range)	*P* (Preop vs 2 Weeks)	Last Follow-up, Mean ± SD (Range)	*P* (2 Weeks vs Last Follow-up)
Km Anterior (D)	43.72 ± 1.55 (41.50 to 46.20)	47.45 ± 1.75 (44.20 to 50.30)	< .001	47.48 ± 2.02 (44.30 to 50.90)	.94
Km Posterior (D)	-6.30 ± 0.26 (-5.70 to -6.80)	-6.13 ± 0.34 (-5.37 to -6.60)	.02	-6.19 ± 0.31 (-5.50 to -6.70)	.23
CCT (µm)	550.02 ± 29.68 (494 to 596)	631.59 ± 37.72 (546 to 717)	< .001	625.76 ± 41.69 (530 to 720)	.50
Q-value	-0.34 ± 0.09 (-0.13 to -0.55)	-0.89 ± 0.23 (-0.43 to -1.69)	< .001	-0.95 ± 0.28 (-0.40 to 1.94)	.29
HOAs (RMS)	0.39 ± 0.15 (0.07 to 0.97)	0.83 ± 0.34 (0.13 to 1.62)	< .001	0.96 ± 0.34 (0.41 to 1.94)	.10

CCT = central corneal thickness; D = diopters; HOAs = higher order aberrations; Km = mean keratometry; RMS = root mean square; SD = standard deviation

Table C

Visual and Refractive Results of Eyes Enhanced With Bowman Membrane Relaxation

Parameter	Pre-FILI, Mean (Range)	Pre-Enhancement, Mean (Range)	Post-Enhancement, Mean (Range)
UDVA (logMAR)	0.80 (0.50 to 1.00)	0.55 (0.5 to 0.6)	0.33 (0.3 to 0.4)
Sphere (D)	+6.88 (+6.50 to +7.00)	+1.50 (+1.00 to +2.50)	+0.25 (0.00 to +0.50)
Cylinder (D)	+0.69 (+0.50 to +1.00)	+1.50 (+0.50 to +3.00)	+0.12 (-1.50 to +1.25)
SE (D)	+7.22 (+6.75 to +7.50)	+2.25 (+1.75 to +2.50)	+0.31 (-0.50 to +1.125)
CDVA (logMAR)	0.30 (0.2 to 0.4)	0.35 (0.3 to 0.4)	0.30 (0.2 to 0.4)

CDVA = corrected distance visual acuity; D = diopters; FILI = femtosecond intrastromal lenticule implantation; SE = spherical equivalent; UDVA = uncorrected distance visual acuity

Table D

Details of Eyes for Which Lenticules Were Explanted

Patient	Eye	Pre-FILI SE (D)	Pre-FILI CDVA (logMAR)	Follow-up Duration at Rejection (Years)	CDVA at Time of Rejection (logMAR)	Treatment Done	CDVA After 2nd Surgery (logMAR)	Follow-up After 2nd Surgery (Years)
1	Right	3.50	0.00	1.5	0.22	Lenticule exchange	0.00	6
1	Left	3.50	0.00	1.5	0.22	Lenticule exchange	0.00	6
2	Right	3.12	0.10	3	0.22	Hyperopic LASIK	0.10	1
2	Left	2.87	0.10	3	0.22	Hyperopic LASIK	0.10	1

CDVA = corrected distance visual acuity; D = diopters; FILI = femtosecond intrastromal lenticule implantation; LASIK = laser in situ keratomileusis; SE = spherical equivalent