Corneal inlays are becoming a favored modality for treatment of presbyopia.\(^1\)\(^,\)\(^2\) These have an advantage over monovision LASIK and PresbyLASIK\(^3\)\(^-\)\(^7\) in being additive technologies, thereby preserving future options for presbyopia correction. However, all current inlays use synthetic material that is implanted into the cornea and may therefore be associated with complications such as inflammatory response, potential interference with glucose and ion diffusion into the anterior stroma above the implant, and peri-inlay deposits.\(^8\)\(^-\)\(^12\) We describe a new technique (PrEsbyopic Allogenic Refractive Lenticule [PEARL]) that uses an inlay obtained from a small incision lenticule extraction (SMILE) lenticule. This has been described by one of the authors (SJ).

**TECHNIQUE**

The study was approved by the institutional review board of Dr. Agarwal’s Eye Hospital and the procedure conformed to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients. Emmetropic presbyopic patients between the ages of 40 and 45 years were included. Patients with any ocular or systemic disease were not included.

**SMILE Lenticule Extraction**

SMILE\(^{13}\)\(^,\)\(^14\) was performed with the VisuMax 500-kHz femtosecond laser platform (Carl Zeiss Meditec, Jena, Germany) in healthy donors (donor age: 21 to 30 years) for myopic correction of between \(-2.50\) and \(-2.75\) diopters sphere, and the C

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anterior surface was marked for later identification. Serology testing was done for human immunodeficiency virus, hepatitis C virus, and hepatitis B virus surface antigen in all donors. Anterior surface marking was done with an inked Sinskey hook by making three horizontal lines—a single line above separated from two closely placed parallel marks below (Figure 1A). A flipped lenticule would therefore be identified when the two closely placed lines are seen above the single line. The lenticule was kept aside safely in corneal preservation medium (Cornisol; Aurolab, Tamil Nadu, India) for implantation in an emmetropic presbyopic patient.

**PEARL Inlay Preparation**

The anterior side of the stored SMILE lenticule was identified and it was spread out with the anterior side facing up, dried with a surgical sponge, and the center marked with the inked tip of a fine Sinskey hook (Figures 1B-1C). A 1-mm trephine was centered on the inked mark to fashion a small donor allogenic presbyopic corneal inlay (Figures 1D-1F).

**PEARL Inlay Implantation**

The light-constricted pupil of the nondominant eye of the emmetropic presbyopic patient was marked on the slit lamp over the first Purkinje reflex seen as the patient fixated coaxially. A pocket with a 295° hinge and 7.9-mm diameter was then created at 120-µm depth using the VisuMax 500-kHz femtosecond laser platform. A central 3.5- to 4-mm pocket was dissected and the PEARL inlay was inserted, aligned, and spread out in the pocket under the marked pupillary center. Intraoperative centration was achieved by gently pressing the center of the inlay while sliding it to the desired position (Figure 2). Retroillumination with the slit beam in the femtosecond laser platform was used to assess proper placement and absence of striae (Figure 2). Centration was further confirmed immediately on the slit lamp and by topography using the Orbscan II (Bausch & Lomb, Rochester, NY). A bandage contact lens was placed and the patient given instructions not to rub the eye. Postoperatively, topical ofloxacin with dexamethasone combination eye drops (OflacinDX; MicroVision, MicroLabs, Bangalore, India) was given six times a day for 1 month and then tapered to stop over the second month. Topical fluorometholone three times a day was then continued for an additional 2 months. All patients were also prescribed tear supplements for 2 months to prevent dryness associated with the femtosecond laser pocket creation (Video 1, available in the online version of this article).
RESULTS
Four emmetropic presbyopic patients underwent the procedure. The mean thickness of the SMILE lenticule used was 61.5 ± 3.32 µm. The average preoperative and postoperative refraction were +0.375 ± 0.25 and -0.125 ± 0.144 diopters sphere, respectively. Postoperative cycloplegic refraction was +0.78 ± 0.78. In the operated eye, uncorrected near visual acuity at 33 cm was J3 in one and J2 in three operated eyes. There was an improvement in all eyes of three to five lines. Uncorrected intermediate vision ranged between J3 and J5 at 67 cm and uncorrected distance visual acuity remained 20/20 in the operated eye and binocularly. There was no regression in near visual acuity over the 6-month follow-up period. Uncorrected distance visual acuity was also maintained during the entire period. Subjectively, the patients were comfortable and reported independence from glasses for near, intermediate, and distance for all of their routine visual tasks. There were no complaints of dysphotopsia or troublesome night glare/halos. Reading speed was better in the operated eye compared to the unoperated eye (Table 1). All patients reported satisfaction with the surgical procedure. The inlay was not visible on naked eye examination. Serial slit-lamp photography and anterior segment optical coherence tomography showed a well-centered inlay (Figure 3, Figure 4A) and inlay-induced complications such as opacification, extrusion, vascularization, or infection were not seen in any patient. Corneal topography showed an area of hyperprolateness in the central 3-mm zone (Figure 4B). The inlay did not interfere with fundus imaging or autoperimetry in any patient (Figure 4C).

DISCUSSION
The PEARL inlay acts as a shape-changing inlay by increasing the central radius of curvature and resulting in a hyperprolate corneal shape. Unlike the synthetic implants, there is unhindered passage of oxygen and nutrients because the PEARL inlay is made of allogenic cornea, thus ensuring stable corneal conditions and decreasing the risk for corneal necrosis and melt. The use of allogenic tissue provides biocompatibility and good integration into the cornea, thus avoiding problems such as inflammation related to insertion of synthetic material into the cornea. As with synthetic corneal inlays, it has the advantages of reversibility and adjustability. Our results showed improved near vision with no loss of corrected distance visual acuity or other complications. All patients were satisfied with their surgical outcome and none reported troublesome night vision or other dysphotopsic symptoms. Preservation of good uncorrected distance visual acuity and no loss of lines in the operated eye was possible due to the use of a small (1-mm) inlay that covered only a small area of the pupillary zone (Figure 3). This is an advantage over currently available synthetic inlays, most of which are at least 2 mm in diameter.1

Refractive lenticule reimplantation has already been performed in animal models15,16 and also in human stud-
ies for hypermetropia, 17-19 aphakia, 17,19 and keratoconus, 20 with favorable results and safety profile. LASIK for inducing monovision following reversal of myopic SMILE through refractive lenticule reimplantation has been reported in an experimental rabbit model. 21 The use of these inlays for the correction of presbyopia is a natural logical...
extension. However, to the best of our knowledge, allogenic corneal inlay implantation has not been reported in human subjects for the treatment of presbyopia.

A disadvantage of this technique is the lack of easy availability of SMILE lenticules of the desired thickness. However, cryopreservation of SMILE lenticules is possible, which in the future would allow storage and transportation of these lenticules over long periods. Eye bank involvement in the manufacture and distribution of PEARL inlays can also make availability easier.

Although the risk of complications is low with allogenic tissue, a potential disadvantage is the risk of stromal rejection from donor tissue. However, this was not seen in any of our patients. It is possible that being only 58 to 66 μm (mean: 61.5 ± 3.32 μm) at its thickest point, the antigenic load was too small to provoke a reaction in the immunologically privileged cornea. Compared with deep anterior lamellar keratoplasty (DALK), where the volume of tissue transfer in a donor button of approximately 7.5-mm diameter and 500-μm thickness is 22.1 mm$^3$, the volume of tissue transfer in the PEARL inlay implantation was 0.048 mm$^3$ (less by a factor of 460 times compared to DALK). The immunogenicity is decreased even further because only stromal transfer (without the more antigenic donor epithelium and endothelium) is performed in the PEARL inlay implantation and because repopulation of the small lenticule by the patient’s own keratocytes can occur from all sides and therefore is likely to occur faster. In addition, previous reports of use of the larger allogenic implants for aphakia, hyperopia, and keratoconus point to its safety. Treatment of the donor lenticule prior to use with gamma irradiation to deantigenize it further may be possible in the future.

This preliminary report shows the feasibility of an allogenic presbyopic inlay and has shown safety and efficacy in our small case series. This is only an initial report with a limited number of patients and serves to lay a foundation for a larger study with a longer follow-up. Further studies are recommended to determine long-term safety and efficacy.

**AUTHOR CONTRIBUTIONS**

Study concept and design (SJ); data collection (DAK, AR, AIS); analysis and interpretation of data (SJ, DAK, Amar Agarwal, Athiya Agarwal, AR); writing the manuscript (SJ, DAK); critical revision of the manuscript (SJ, Amar Agarwal, Athiya Agarwal, AR, AIS); statistical expertise (DAK); administrative, technical, or material support (Amar Agarwal); supervision (SJ)

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