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A Novel Artificial Endothelial Replacement Membrane for the Treatment of Chronic Corneal Edema

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Purpose: The purpose of this study was to report the safety and efficacy results of an artificial lamellar implant for the treatment of chronic corneal edema.

Methods: The EndoArt (EyeYon Medical, Ness Ziona, Israel), an artificial endothelial replacement membrane designed to treat corneal edema, was implanted in 24 eyes of 24 patients with low-to-normal visual potential. We present the safety and efficacy results from a prospective, open-label, single-arm, multicenter study conducted over a 12-month period.

Results: Twenty-four patients were enrolled, with no device-related serious adverse events reported. Seventeen patients completed 12-month follow-up, showing a reduction in average central corneal thickness from 759 ± 116 μm to 613 ± 135 μm. Best-corrected distance visual acuity improved from 1.88 ± 0.79 logarithmic minimum angle of resolution (logMAR) to 1.34 ± 0.57 logMAR. Sixty percent gained at least 3 early treatment diabetic retinopathy study (ETDRS) lines. The EndoArt was removed in 5 cases due to incomplete attachment and replaced by corneal transplants; 1 patient was lost to follow-up, and 1 had a procedure failure. No device-related long-term complications, infections, or inflammations were reported. The implants remained transparent throughout the study.

Conclusions: The first-in-human results of EndoArt implantation demonstrated the device's potential to treat patients suffering from corneal edema with a favorable safety profile and effective edema reduction in most subjects, with no device-related serious adverse event. The EndoArt may offer a viable solution in regions facing a shortage of donor corneas, as well as for patients who have poor prognosis with human tissue.

Key Words: keratoprosthesis, corneal edema, endothelial keratoplasty, corneal implantation, EndoArt

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Endothelial keratoplasty (EK) is currently the preferred surgical option for treating refractory corneal edema, with Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK) offering good visual acuity (VA) and resolution of corneal edema.[1–4] However, these surgeries rely on human donor corneas, which are limited in availability and require carefully calibrated processing, transport, and storage conditions. As a result, millions of people with corneal blindness are left without a viable vision restoration solution.[5–7] In addition, EK is associated with reduced endothelial cell counts and graft rejections even when performed by experienced cornea specialists.[8–10] A comprehensive retrospective analysis of 30,600 eyes from the Intelligent Research in Sight registry investigating VA outcomes following EK procedures in the United States revealed that approximately 30% of the eyes did not achieve any visual improvement at the one-year mark after surgery. Moreover, approximately 15% of patients experience decreased VA when using human tissues. Notably, within this extensive cohort, postoperative rebubbling and repeat keratoplasties were identified as independent factors associated with poorer VA outcomes.[11] The success of human corneal graft transplantation is strongly dependent on the recipient's condition, as comorbidities such as glaucoma, prior trabeculectomy, and anterior chamber intraocular lens markedly lower graft retention.

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The data sets analyzed during the current study are not publicly available but are available from the corresponding author upon reasonable request.

O. Daphna is the inventor of EndoArt and cofounder of EyeYon Medical. O. Daphna, E. Gilboa, A. Lemze, and MD analyzed and interpreted the EndoArt FIH trial outcomes and wrote the manuscript. A. L. Marcovich is the cofounder of EyeYon Medical. A. L. Marcovich contributed to the writing of the manuscript. R. Lapid-Gortzak, S. Chaurasia, and G. U. Auffarth participated in the EndoArt FIH trial and contributed significantly to developing the implantation technique. All authors have read and approved the final manuscript.

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A synthetic device[12] that can alleviate corneal edema and serve as an alternative to the donor corneal lamella would benefit patients at high risk of human graft rejection and failure.[13,14] A synthetic device with a long shelf life is also readily available and may offer an additional option in regions with a shortage of human corneas.

The notion that a synthetic plate can substitute for the corneal endothelium and attenuate corneal edema came from clinical observations and literature reports of aphakic silicone oil-filled eyes, with silicone in the anterior chamber, after retinal detachment repair surgeries, which exhibited a clear cornea despite a low endothelial cell count, suggesting that the barrier mechanism of the silicone could substitute for the function of the corneal endothelium and attenuate corneal edema. After silicone oil removal, the corneas immediately became edematous, demonstrating the blocking function of the silicone oil and its potential for treating patients with corneal edema.[15–18] Huertas-Bello et al[19] demonstrated a similar phenomenon, where an air bubble in the anterior chamber obstructed the aqueous humor from reaching the cornea, leading to a significant reduction in central corneal thickness (CCT).

A possible explanation for the barrier mechanism is that in a steady state, the relation between the inflow and outflow of fluids into and out of the cornea determines its thickness.[20] This process is regulated by both passive and active mechanisms. The passive component is formed by the intact endothelium and epithelium, where tight junctions restrict fluid influx into the cornea. The active mechanism involves endothelial Na+/K+ ATPase pumps, which facilitate fluid removal from the corneal stroma. Tear film evaporation also contributes to this fluid regulation, though to a lesser extent. When the endothelial cell density decreases, fluid outflow is compromised, disrupting the balance between inflow and outflow. This imbalance leads to increased stromal hydration and corneal thickening, resulting in corneal edema.[21–24] The EndoArt implant reinforces the passive barrier, by blocking the central portion of the posterior cornea and reducing inflow into the cornea, thus establishing a new steady state, resulting in a thinner cornea and alleviated corneal edema. The hypothesis suggested that the uncovered peripheral posterior surface of the cornea would facilitate sufficient fluid influx and nutrient transport, ensuring safe corneal physiology without adverse events such as corneal melting or perforation. Furthermore, considering the relatively broad range of corneal thicknesses within which the cornea remains transparent, EndoArt seeks to reduce corneal thickness to approximately 420 to 625 μm.[25] This range generally signifies a clear and viable cornea. The implant is composed of a transparent, flexible, water-impermeable, biocompatible synthetic material that can seal a part of the inner corneal surface to relieve corneal edema in the absence of a functioning endothelium (EndoArt, EyeYon Medical, Ness Ziona, Israel). Before human testing, EndoArt was tested and validated in porcine and leporine eyes with induced corneal edema.[12,26] The synthetic implant provided relief from edema and restored corneal transparency over a 12-month follow-up period, while the control eyes continued to suffer from persistent and severe corneal edema. In addition, compassionate implantation of the device in subjects who had previously failed multiple corneal transplantations has concluded that implantation of the EndoArt led to rapid corneal deturgescence and CCT restoration, presenting a possible option for patients with chronic corneal edema.[27]

The FIH study, completed in January 2023, focused primarily on evaluating the safety of EndoArt and refining both the design of the implant and its implantation technique.

MATERIALS AND METHODS

A multicenter, international, nonrandomized, open-label, prospective trial was conducted in Israel (Soroka Medical Center, Beer Sheva; Rambam Medical Center, Haifa; Sourasky Medical Center, Tel Aviv; Barzilai Medical Center, Ashkelon; and Assuta Medical Center, Tel Aviv), the Netherlands (UMC, Amsterdam), Spain (IMO, Barcelona), Germany (Universitäts-Augenklinik, Heidelberg), and India (LV Prasad, Hyderabad) and adhered to the Declaration of Helsinki. The institutional review board of each center approved the study, and subjects who met the eligibility criteria provided informed consent, including consent for the publication of results, before any study-related procedures were performed.

The primary safety end point was the frequency and severity of adverse events related to the EndoArt device documented during and up to 12 months after implantation. Adverse events of particular concern include corneal perforation, corneal melting, uncontrolled inflammation, and severe infection. The secondary efficacy end points were CCT and best-corrected distance visual acuity (BCDVA).

Subjects

The patients were required to be older than 40 years, pseudophakic, and have a stable posterior or anterior intraocular lens (IOL) with chronic corneal edema and a minimal CCT of 650 μm. A VA of 6/30 (0.70 logMAR) or worse was needed, with better VA recorded in the contralateral eye. Patients were excluded if they had any of the following: BCDVA of 6/30 (0.70 logMAR) or worse in the fellow eye, a history of ocular herpes simplex keratitis, a severely scarred cornea unsuitable for regular EK, irregular posterior cornea, current corneal infection, band keratopathy, limbal stem cell deficiency, clinically severe dry eye, phthisis or suspicion of phthisis, ocular hypotension of less than 6 mm Hg or ocular hypertension of more than 25 mm Hg, aphakia, significant iris defect that could compromise intraoperative anterior chamber stability, a history of corneal refractive surgery, glaucoma shunts (eg, Ahmed valve), neurotrophic keratopathy, a history of persistent corneal erosion, difficulties with epithelial growth (reepithelization), or participation in another investigational study within the past 60 days.

Device Description

The EndoArt implant is a transparent, foldable, and hydrophilic device composed of a copolymer of hydroxyethyl methacrylate and methyl methacrylate. This material is commonly used in the manufacturing of IOLs. The implants

used in this study had a diameter ranging from 5 to 6.5 mm, radius of curvature of 6.8 mm, thickness of 50 μm, and no optical power.

Implantation Procedure

The implantation of EndoArt is very similar to that of DSAEK. A peripheral corneal incision of approximately 2.4 mm was made to insert the device. The endothelial cell layer was either left untouched or removed (descemetorhexis) at the physician's discretion. The folded EndoArt device was placed into the anterior chamber through a peripheral corneal incision using an off-the-shelf injector or spatula. Once inside the eye, the device was allowed to unfold and was positioned centrally adjacent to the posterior surface of the cornea. To secure the device onto the posterior corneal surface, either an air bubble was introduced or through off-label applications, injections of 20% sulfur hexafluoride (SF_6) gas or 10% perfluoropropane (C_3F_8) gas were made into the anterior chamber, and according to the physician's discretion, a temporary fixating suture was placed at 12 o'clock. Immediately after the procedure, the patient was placed supine and faced up for 2.5 to 4 hours. The patient was either discharged after the procedure or hospitalized at the physician's discretion. As the study progressed, the implantation technique was refined to enhance device attachment. This evolution included the integration of descemetorhexis, a fixation suture, long-lasting gas (C_3F_8 or SF_6) injection, and iridectomy, into the standard implantation protocol. A video of the procedure is available in the Supplementary Video 1.

Visits and Procedure

Each patient underwent a comprehensive baseline evaluation, which included a BCDVA assessment using the ETDRS VA score, pachymetry measurement of CCT by optical coherence tomography (OCT), anterior and posterior segments examination using a slit lamp, endothelial cell count (if feasible), intraocular pressure (IOP) measurement (Goldman applanator), pain assessment using a visual analog scale (VAS, 0–100), and color photography of the cornea. Corneal clarity was evaluated using a slit lamp and graded as 0 (clear), 1 (clear iris details), 2 (obscured iris details), 3 (pupil barely visible), or 4 (pupil or iris details not visible). Ophthalmic assessments were conducted on days 1, 7, and 14, followed by assessments every 2 weeks for up to 3 months, monthly assessments for the first 6 months, and then every other month for up to 1 year after the procedure. Adverse events were monitored throughout the entire duration of the study period.

TABLE 1. Study Completion and Reasons for Dropout

Group		Number	Remarks
Enrolled		24	
Completed 1 yr of follow-up		17	
Dropout	Implant did not attach	5	Descemetorhexis was not performed
	Other	2	• Procedural failure: Non–device-related IOL dislocation • patientlost to follow-up

TABLE 2. Patients Demographics and Baseline Characteristics

Characteristic	
Age (yr), mean ± SD (range)	69.8 ± 9.6 (54–86)
Female sex, n (%)	10 (41.7)
Ophthalmic history, n (%)	
Cataract extraction	24 (100.0)
ACIOL	1 (4.2)
Glaucoma	4 (16.7)
Previous glaucoma-filtering surgery	2 (8.3)
Previous retinal detachment	3 (12.5)
Vitreal or retinal disease	5 (20.8)
Prior corneal surgery	
DMEK	2 (8.3)
DSAEK	2 (8.3)
DSO*	1 (4.2)

*Subject with low visual potential due to macular degeneration.
ACIOL, anterior chamber intraocular lens; DSO, Descemet stripping only.

Statistical Analysis

The Wilcoxon signed rank test was used to determine statistically significant changes from baseline. Calculations were performed using the stats.wilcoxon function in SciPy library in Python.

RESULTS

Twenty-four patients were enrolled, and 17 (71%) completed the 1-year follow-up (Table 1). Table 2 summarizes the characteristics of the study population. The mean age of the patients was 69.8 ± 9.6 years, and 41.7% of the patients were female. All subjects had a history of cataract extraction, and 5 had prior corneal surgeries. More than 30% of the subjects had a posterior segment comorbidity.

Primary Safety Results

Throughout the follow-up period, no serious device-related adverse events were reported (n = 24) nor were any

TABLE 3. Adverse Events

Adverse Event	Number of Subjects, n (%)	Comments
Eye pain	6 (25)	In 2 cases, the implant was not attached
Intraocular pressure increased	4 (16.7)	Perioperative due to gas bubble
Transient corneal epithelial defect/bullae	4 (16.7)	
Ocular discomfort	2 (8.3)	
Conjunctivitis	2 (8.3)	

TABLE 4. Implantation Technique and Rebubbling

	Implantation Technique	n/N* (%)	Rebubbling Rate (%)	Average Rebubbling Procedures per Subject
I	1) Endothelium intact 2) No fixating suture	4/22 (18)	100	3.3
II	1) Endothelium intact 2) With a fixating suture	2/22 (9)	100	5.0
III	1) Endothelium removed 2) No fixating suture	7/22 (32)	100	3.0
IV	1) Endothelium removed 2) With a fixating suture	9/22 (41)	56	2.0
IV.1	1) Endothelium removed 2) With a fixating suture 3) Air	3/22 (14)	67	2.3
IV.2	1) Endothelium removed 2) With a fixating suture 3) long-lasting gas	6/22 (27)	50	1.8

*Analysis on 22/24 subjects. One procedure failure and 1 lost to follow-up were excluded.

chronic inflammatory reactions observed in the treated eyes. No device-related irritation, infection, uncontrolled IOP, or corneal melting was observed. One procedure-related serious adverse event was reported, where the EndoArt was inverted and required repositioning. One patient demonstrated herpetic epithelial and stromal keratitis, with melting and thinning, which healed with topical acyclovir and systemic steroids without EndoArt removal. Transient eye pain was reported in 6 patients (25%) mainly due to dry eye or transient bullae. Four patients experienced perioperative IOP elevation, all occurring following gas bubble injection. In 3 of these patients, paracentesis was necessary for resolution. Transient corneal epithelial defects/bullae were reported in 4 cases and treated with contact lenses (Table 3). Increase in lacrimation, dry eye, ptosis, and macular edema was each reported in 1 patient.

Rebubbling Procedure

A rebubbling procedure was performed when a complete or clinically significant partial detachment of the EndoArt implant was identified. Throughout the trial, an average rebubbling rate of 2.9 ± 2.0 procedures per patient was documented. During the study, an improved attachment technique was established, including an obligatory descemetorhexis, a temporary fixation suture, and the utilization of a long-lasting gas. Among subjects who had undergone both descemetorhexis and implant suturing to the cornea (n = 9), the rebubbling rate decreased to 56% compared with 100% in subjects in whom at least 1 of these steps was not performed. The use of long-lasting gas also seemed to have a positive effect on device attachment (Table 4). Iridotomy/iridectomy was performed in 17% of implantations with air tamponade versus 67% of implantations where a long-lasting gas was used.

First-in-Human Dropout

Six EndoArt implants (25.0%) were explanted. In 5 patients, the devices were explanted due to attachment failure despite repeated rebubbling and replaced with DSAEK. In all those patients, descemetorhexis was not performed. In 1 patient, the IOL was dislocated during the procedure, which

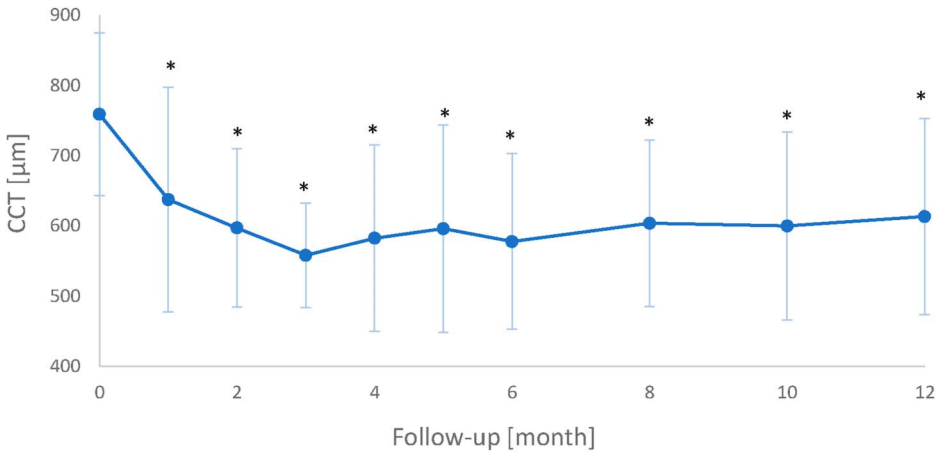

FIGURE 1. CCT after EndoArt implantation. The mean ± SD CCT over time is displayed. A significant improvement from the baseline CCT was observed at the 1-month follow-up, and the CCT remained stable throughout the 12-month follow-up (n = 17). *$P < 0.05$. (The full color version of this figure is available at www.corneajrnl.com.)

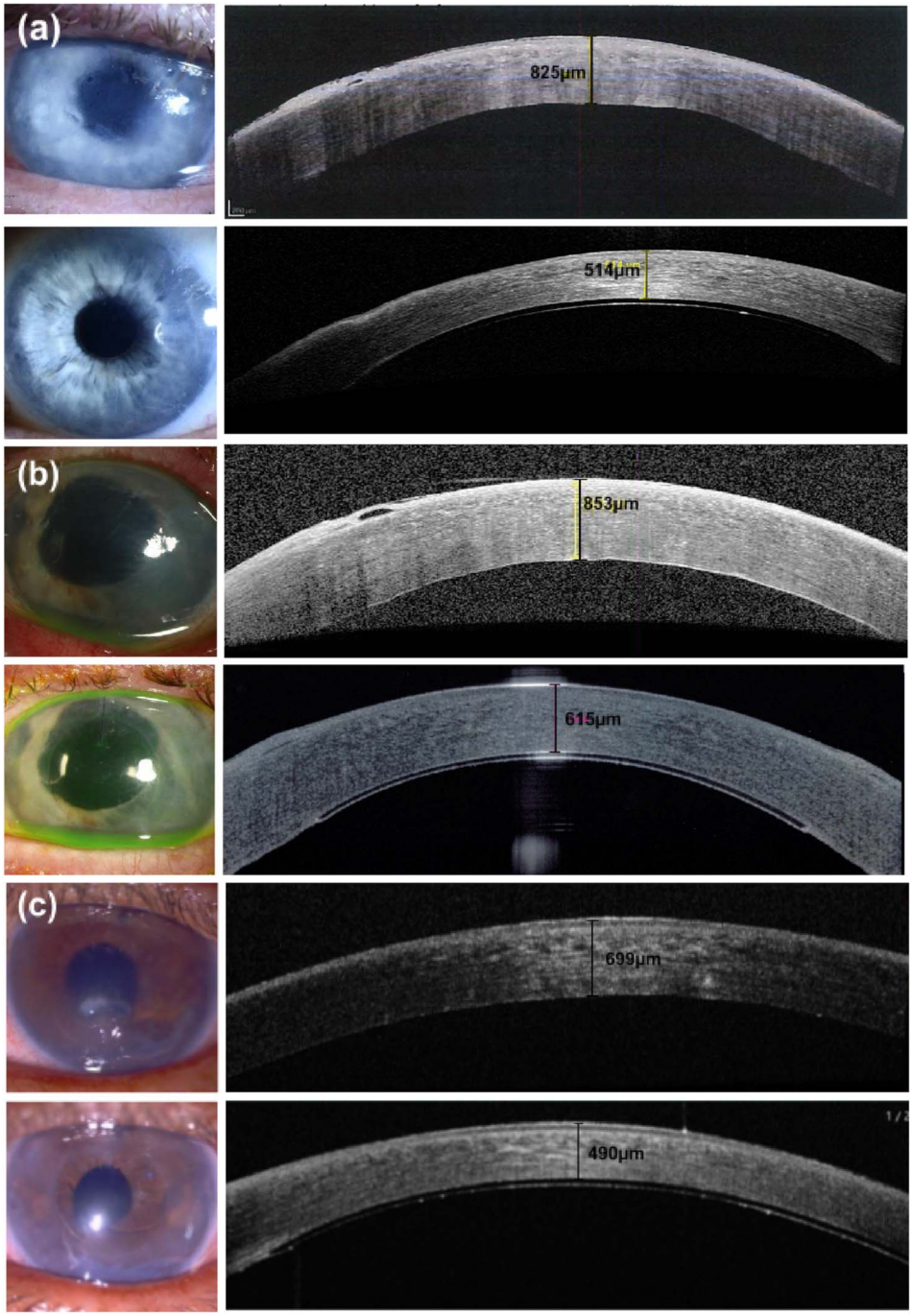

FIGURE 2. Changes in clarity and CCT. Slit-lamp color photography and OCT images at baseline (upper images) and 12 months (lower images) after EndoArt implantation into the eye of (A) a 67-year-old male, pseudophakic, myopic, with macular degeneration, after failed Descemet stripping only; (B) an 80-year-old male, pseudophakic, after glaucoma-filtering surgery; and (C) a 60-year-old male, pseudophakic (anterior chamber intraocular lens), with a macular scar. (The full color version of this figure is available at www.corneajrnl.com.)

led to an inability to create an effective air bubble and was converted to penetrating keratoplasty. The removal of all devices was straightforward, without any complications.

Secondary Efficacy Results

Central Corneal Thickness

The CCT decreased from an average baseline measurement of 759 ± 116 µm to 613 ± 135 µm (n = 17) at 12 months. Significant improvement was noted in the first month after implantation (Fig. 1) and remained stable throughout the follow-up. In 4 patients, the CCT did not show improvement. Among them, 3 patints faced insufficient implant attachment, while 1 patient experienced subepithelial fibrosis. Figure 2 shows the improvement in CCT once EndoArt is fully attached using OCT and slit-lamp images of 3 patients at baseline and 12 months after implantation.

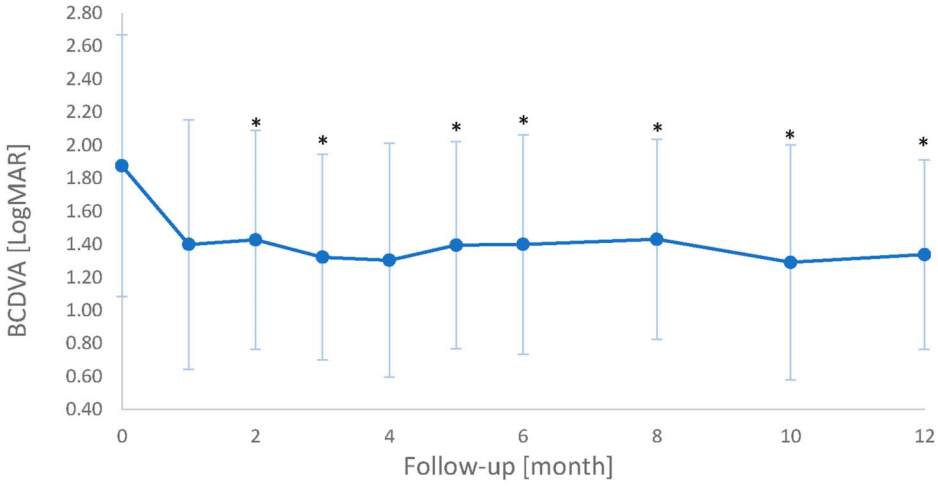

FIGURE 3. BCDVA after EndoArt implantation in patients with low-to-normal visual potential. The mean ± SD BCDVA over time after EndoArt implantation is displayed. A clinically significant improvement from baseline was observed (n = 15). *$P < 0.05$. (The full color version of this figure is available at www.corneajrnl.com.)

Corneal Clarity

A significant improvement in central corneal clarity was observed within 2 weeks of surgery, and the degree of improvement remained stable during the 12-month follow-up period. The average clarity improved from 3.2 ± 0.6 at baseline to 1.1 ± 1.1 at the 12-month follow-up.

Best-Corrected Distance Visual Acuity

Of the 17 patients who reached the 12-month follow-up assessment, 2 had no vision due to optic neuropathy and were therefore not assessed for VA throughout the study.

Despite low visual potential in 10 of the remaining 15 patients, attributed to ocular conditions such as retinal detachment, macular scarring, amblyopia, and cystoid macular edema, there was a significant improvement in average VA. VA improved from a baseline logMAR score of 1.88 ± 0.79 to 1.34 ± 0.57 at 12-month follow-up (Fig. 3). Notably, 60% of the patients (9 out of 15) improved at least 3 lines of ETDRS. The most remarkable improvement in VA was from FC to 0.6 logMAR (6/24).

Pain Score

The average VAS (0–100) score significantly decreased from 32 ± 30 at baseline to 2 ± 8 12 months after EndoArt implantation (Fig. 4). All patients who complained of pain (VAS ≠ 0) at baseline (11 out of 17) experienced pain relief.

DISCUSSION

The FIH study proved the concept of reducing corneal edema through a barrier mechanism rather than solely relying on endothelial function. As the study progressed, it became apparent that the performance of EndoArt was closely tied to its attachment quality to the posterior cornea. Factors influencing this attachment, such as the omission of descemetorhexis, were scrutinized during the study. Indeed, in 5 cases where descemetorhexis was not performed, the implant could not achieve attachment and had to be explanted. Surgical steps promoting attachment were identified and consolidated into a protocol. This protocol included a 7.0 to 7.5 mm descemetorhexis, a single fixation suture, and 10% C_3F_8 gas for all implantations. Integrating these steps into the EndoArt implantation technique showed a trend toward

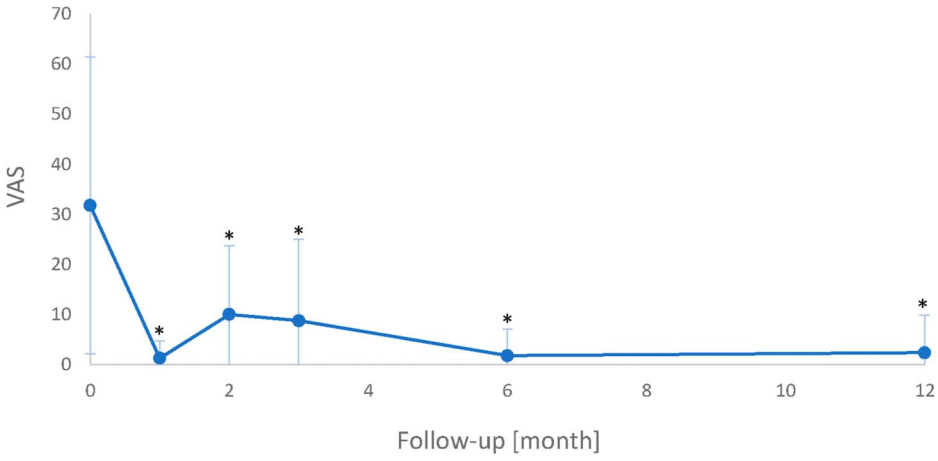

FIGURE 4. Pain score in VAS after EndoArt implantation. The mean ± SD pain score was measured using a visual analog scale. Significant pain relief was noted at all time points (n = 17). *$P < 0.05$. (The full color version of this figure is available at www.corneajrnl.com.)

minimizing the need for rebubbling, ultimately resulting in successful attachment in the last 2 patients without requiring additional rebubbling. Further details on implementing this modified implantation technique will be provided in upcoming publications of a more extensive cohort study.

The main concerns surrounding potential adverse events associated with keratoprostheses were corneal melting and perforation, both consequences of insufficient corneal nutrition; however, none of the 24 implanted patients presented any signs of corneal nutrients depletion. Concerns regarding uncontrolled inflammation and severe infection were also refuted, as none of the patients exhibited a prolonged inflammatory response. No serious device-related adverse events were reported during the 12-month follow-up. The main adverse events involved ocular pain and discomfort, all resolving during the follow-up period, as well as elevated IOP resulting from gas bubble injection. The latter required paracentesis to relieve the high IOP in 3 cases. To mitigate the risk of postoperative pupillary block, iridectomy was introduced as a mandatory procedural step.

Over the 12-month follow-up period, a clinically significant decrease in the average CCT was observed in the 17 patients who completed the study. This decrease in CCT correlated with improved central corneal clarity, as anticipated. As corneal clarity improved, VA enhanced, even among patients deemed to have low visual potential due to comorbidities. Notably, despite most patients having low visual potential, 60% of all patients exhibited improvements of at least 3 lines in VA at the 12-month follow-up, with the best 12-month VA reaching 0.6 logMAR (6/24).

Similar results were reported in another case series[28] involving 5 patients with prior EK failures who were implanted with EndoArt. Corneal clarity and VA showed improvement, with the most significant 6-month improvement in VA recorded from 1.3 logMAR at baseline to 0.2 logMAR (6/9.5). Furthermore, all patients who reported pain at baseline experienced substantial pain relief after EndoArt implantation. Importantly, no significant complications, such as corneal melting, chronic inflammation, or related infections, were observed during the follow-up period.

It is important to acknowledge the study's limitations, including the evolving method of EndoArt implantation over the trial period and difficulties with the early learning curve. In the future, the results of a more extended follow-up period should be reported.

This FIH study provides evidence supporting the concept that EndoArt may act as a passive barrier, effectively reducing corneal edema and enhancing vision while demonstrating a relatively safe profile with no device-related serious adverse events. The reported outcomes highlight its potential utility in treating chronic corneal edema, particularly in high-risk patients with a history of graft rejection, for which the nonrejection nature of EndoArt is a key feature, or in patients with low visual potential as a treatment of pain. Furthermore, EndoArt may be an available, ready-to-use option in geographic regions with a limited supply of donor corneas. The observed detachment rate, possibly due to the initial learning curve, requires attention for improvement. A more extensive follow-up period and larger cohort are essential to ascertain the precise role of EndoArt as a therapeutic tool in managing patients with corneal edema.

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REFERENCES

1. Vasiliauskaite I, Oellerich S, Ham LI, et al. Descemet membrane endothelial keratoplasty: ten-year graft survival and clinical outcomes. *Am J Ophthalmol*. 2020;217:114–120.
2. Price DA, Kelley M, Price FW, Price MO. Five-year graft survival of Descemet membrane endothelial keratoplasty (EK) versus Descemet stripping EK and the effect of donor sex matching. *Ophthalmology*. 2018;125:1508–1514.
3. Hamzaoglu EC, Straiko MD, Mayko ZM, et al. The first 100 eyes of standardized Descemet stripping automated endothelial keratoplasty versus standardized Descemet membrane endothelial keratoplasty. *Ophthalmology*. 2015;122:2193–2199.
4. Dickman MM, Peeters JMPWU, van den Biggelaar FJHM et al. Changing practice patterns and long-term outcomes of endothelial versus penetrating keratoplasty: a prospective Dutch registry study. *Am J Ophthalmol*. 2016;170:133–142.
5. Gain P, Jullienne R, He ZP, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol*. 2016;134:167–173.
6. Keane MC, Coffey VJ, Jones VJ, et al. The Australian corneal graft registry 2021/22 report; 2022.
7. Singh R, Gupta N, Vanathi M, et al. Corneal transplantation in the modern era. *Indian J Med Res*. 2019;150:7–22.
8. Moura-Coelho N, Manero F, Elies DN, et al. Repeat Descemet membrane endothelial keratoplasty for failed primary Descemet membrane endothelial keratoplasty at a referral center for keratoplasty in Spain: DIMOEK study. *Am J Ophthalmol*. 2020;215:49–55.
9. Shahnazaryan D, Hajjar Sese A, Hollick EJ, et al. Endothelial cell loss after Descemet's membrane endothelial keratoplasty for fuchs' endothelial dystrophy: DMEK compared to triple DMEK. *Am J Ophthalmol*. 2020;218:1–6.
10. Coster DJ, Lowe MT, Keane MC, et al. A comparison of lamellar and penetrating keratoplasty outcomes: a registry study. *Ophthalmology*. 2014;121:979–987.
11. Srikumaran D, Son HS, Li C, et al. Disparities in visual acuity outcomes after endothelial keratoplasty: an intelligent Research in Sight registry analysis. *Ophthalmology*. 2022;129:912–922.
12. Ofer Daphna . Treating corneal edema with artificial corneal endothelial implant: first human experience and 4-year animal study; 2018. ASCRS. Available at: https://ascrs.org/clinical-education/abstracts/2018/treating-corneal-edema-with-artificial-corneal-endothelial-implant-first-human-experience-and-4year
13. Colby KA, Koo EB. Expanding indications for the Boston keratoprosthesis. *Curr Opin Ophthalmol*. 2011;22:267–273.
14. Aravena C, Yu F, Aldave AJ. Long-term visual outcomes, complications, and retention of the Boston type I keratoprosthesis. *Cornea*. 2017;37:3–10.
15. Dohlman CH, Brown SI, Martola EL. Replacement of the endothelium with alloplastic material: a new technique in corneal surgery. *Ophthalmology*. 1966;71:851–864.
16. Brown SI, Dohlman CH, A buried corneal implant serving as a barrier to fluid. *Arch Ophthalmol (Chicago, IL, 1960)*. 1965;73:635–639.
17. Miller D, Dohlman CH. Optical properties of buried corneal silicone prostheses. *Am J Ophthalmol*. 1968;66:633–640.
18. Gurelik G, Safak N, Koksal M, et al. Acute corneal decompensation after silicone oil removal. *Int Ophthalmol*. 1999;23:131–135.

19. Huertas-Bello M, Seery CW, Sem KM, et al. Effect of anterior chamber air on central corneal thickness in human donor eyes. *Cornea*. 2024;43:1355–1360.
20. Klyce SD. 12. Endothelial pump and barrier function. *Exp Eye Res*. 2020; 198:108068.
21. Edelhauser HF. The balance between corneal transparency and edema: the proctor lecture. *Invest Ophthalmol Vis Sci*. 2006;47:1754–1767.
22. Srinivas SP. Cell signaling in regulation of the barrier integrity of the corneal endothelium. *Exp Eye Res*. 2012;95:8–15.
23. Bonanno JA. Identity and regulation of ion transport mechanisms in the corneal endothelium. *Prog Retin Eye Res*. 2003;22:69–94.
24. Feizi S. Corneal endothelial cell dysfunction: etiologies and management. *Ther Adv Ophthalmol*. 2018;10:2515841418815802.
25. Camburu G, Zemba M, Tataru CP, et al. The measurement of central corneal thickness. *Rom J Ophthalmol*. 2023;67:168–174.
26. Doyle S. Artificial corneal endothelial implant in animal models. ASCRS, Los Angeles; 2017. Available at: https://ascrs.org/clinical-education/abstracts/2017/artificial-corneal-endothelial-implant-in-animal-models.
27. Auffarth GU, Son HS, Koch MGU, et al. Implantation of an artificial endothelial layer for treatment of chronic corneal edema. *Cornea*. 2021; 40:1633–1638.
28. Fontana L, di Geronimo N, Cennamo ML, et al. Early outcomes of an artificial endothelial replacement membrane implantation after failed repeat endothelial keratoplasty. *Cornea*. 2023;43:1088–1094.