Long-term viability of allogenic donor stroma

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We report the clinical history and histopathology of the longest known postoperative course of a myopic cornea lenticule implanted via epikeratoplasty that also had been subjected to excimer laser and mitomycin. Despite the mechanical and photochemical processes the allogenic cornea stroma had sustained, it is notable that it retained structural integrity and clarity. This report affirms the potential long-term clarity and resilience of allogenic stromal cornea and supports its use as a potential stabilizing option in cornea allogenic intrastromal ring segments for keratoconus and variations thereof for other cornea disorders.

Key words: Allogenic cornea, epikeratophakia, epikeratoplasty, intrastromal implant, record-holding

A recently devised technique to treat keratoconus termed cornea allogenic intrastromal ring segments (CAIRS) has had great initial success.[1] By using allogenic donor corneal stroma, in a method similar to synthetic intrastromal ring segments, it avoids many of the issues of synthetic materials placed within corneal stroma, which include necrosis, migration, and extrusion.[2] As this newer procedure and variations of stroma use gain more world-wide use,[3] and would likely be used most often in young or middle aged patients, it is important to determine the long-term viability and clarity of modified allogenic cornea stroma, and how it may withstand possible mechanical, photochemical, and laser manipulations. One model for long-term use of allogenic cornea stroma is epikeratophakia (epikeratoplasty).

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Case Report

We describe herein the features of a case in which a myopic epikeratoplasty lenticule from a commercial source was implanted and removed after 30 years in-situ. What is unique to this case, besides what we believe is the longest reported postoperative interval for a myopic allogenic stromal lenticule, is that it also had been subjected to photorefractive keratectomy (PRK) and application of mitomycin.

Complete old records were not available, but based on the history and clinical appearance, the patient had bilateral sequential myopic epikeratoplasty for high myopia (-16 Diopters (D), spherical equivalent) in 1985, resulting in 20/30–40 vision. Over a decade vision regressed to <20/50 that improved with a small myopic correction from glasses, 14 years after the original surgery, the patient underwent PRK with mitomycin application (0.2 mg/ml, 60 s), which returned visual acuity to the initial post-epikeratoplasty of 20/30. The patient remained stable for 15 years, then developed a visually significant cataract.

In preparation for preoperative cataract surgery calculations, the lenticule was removed. The lenticule was removed because one of the author's (E.C.) prior experience with cataract surgery in similar patients found no difference in ability to obtain accurate IOL calculation and refractive results between those in whom the lenticule was left in-situ or removed. However, lenticule removal led to patients that were subjectively much happier. Preoperatively, the cornea OU to slit lamp view was clear with no central haze, scar, or striae, and no apparent interface irregularities. Both eyes had been virtually identical aside from PRK and mitomycin use in OS. This clinical information and the comparative densitometry with most significant decrease in

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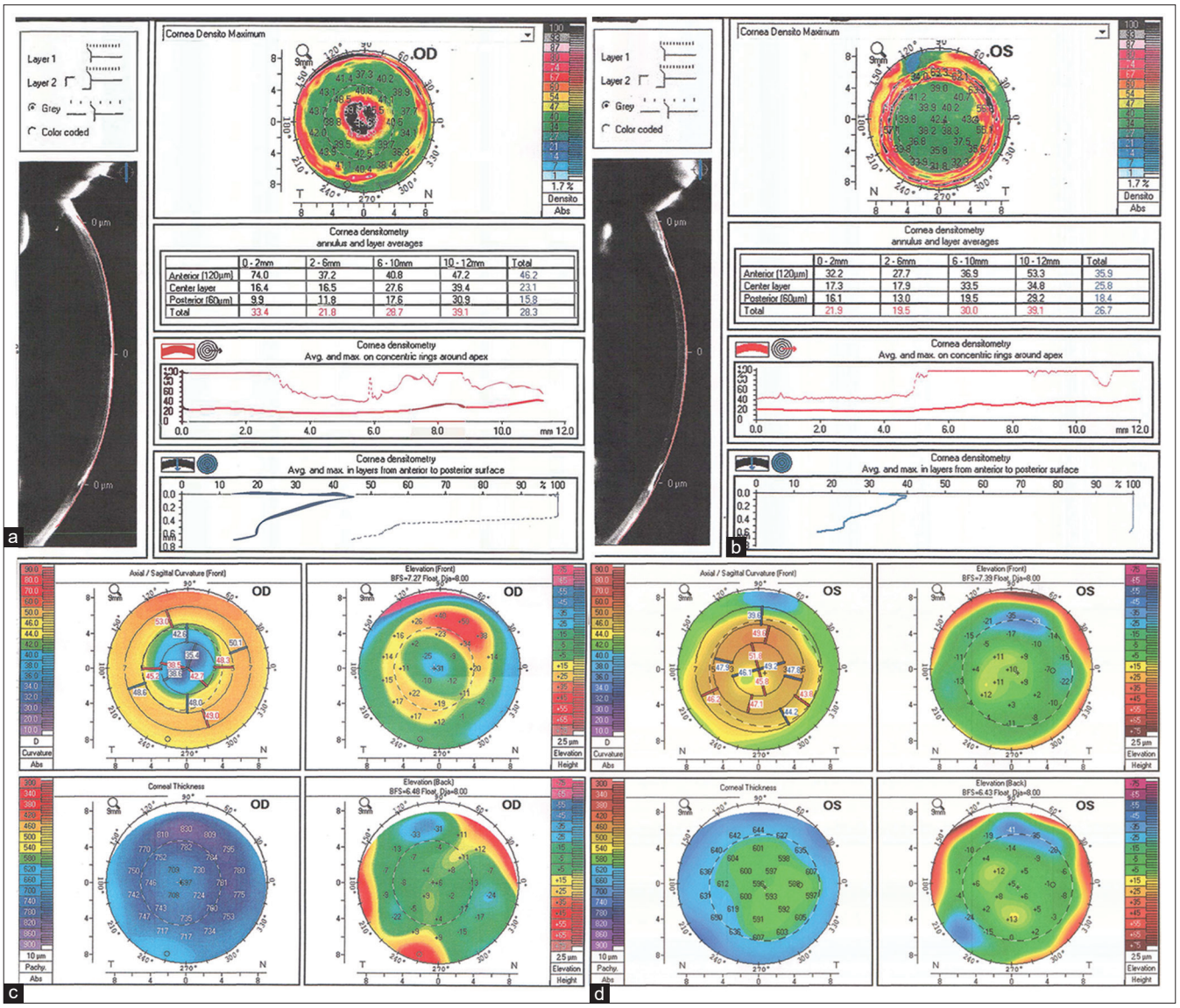

Figure 1: (a-d). a: Preoperative cataract surgery, myopic lenticule in-situ OD densitometry. Poor central 2 mm light transmission, reduced but dramatically improved in 2–6 mm annulus, and peripheral to this. b: Postoperative lenticule removal, cataract surgery, IOL OS densitometry showing uniformly relatively normal values. c: Axial map OD. Pre lenticule removal. Note extreme flattening and samall optical zone. d: Axial map OS. Post lenticule removal, cataract surgery and IOL. Note restored optical zone and steep keratometer values (there is no keratoconus)

light transmission in the central 2 mm OD with most dramatic improvement in the 2–6 mm annulus OD suggests central compressive-induced light scatter rather than alterations of the cornea stroma. The axial maps indicate that optical zone may play a role in visual performance as well [Fig. 1a-d].

Removal of the lenticule was relatively easy: The epithelium at the previously trephined edge was lysed with a Sinskey hook that was then employed to retract the lenticule centrally. Toothed forceps were used to grasp the lenticule edge for removal with movements akin to capsulorhexis, gently pulling and turning. Upon removal it was placed in formalin. The patient's central Bowman's layer appeared clear and clinically normal in the surgical microscope view. After cataract surgery with intraocular lens, the patient attained 20/25 vision.

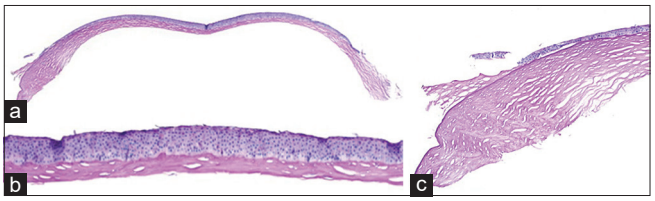

Figure 2: (a-c). Periodic acid-Schiff stain of the anterior corneal epikeratoplasty lenticule. (a) Low-power magnification demonstrates the thinner central stroma and thicker peripheral rim. (10×) (b) At higher power of the central area of the graft, the epithelium is intact and mildly thickened. Bowman's layer is absent, and there is fibrosis of the superficial stroma. (50×) (c) In the periphery of the graft, Bowman's layer remains intact and scattered keratocytes are seen in the deeper stroma. (20×)

Histopathologic examination of the lenticule revealed mildly thickened epithelium and patchy peripheral discontinuity. Bowman's layer is present in the periphery of the lenticule near the rim but absent centrally, consistent with the history of PRK. The central stroma is thin with thicker peripheral rim. There is superficial fibrosis of the subepithelial stroma. Stromal keratocytes are present and seen more densely in the deeper stroma [Fig. 2a-c].

Discussion

The use of allogenic cornea for optical disorders was introduced over 50 years ago by Jose Barraquer in his elegant and pioneering work employing a microkeratome and cryolathing in surgical techniques termed: Keratophakia, hyperopic/myopic keratomeliuesis.[4]

In order to make the general concept technically less demanding and available to a wide group of ophthalmic surgeons and their patients, epikeratoplasty was conceived and developed by Kaufman and others over 30 years ago as a reversible, lamellar onlay procedure to treat aphakia, myopia, hyperopia, and keratoconus.[5,6] Although fresh tissue alteration was possible and used, in its most efficient form a surgeon could obtain a previously altered corneal lenticule from a commercial source. Advantages to the "epi" techniques included a relatively simple and minimally invasive surgical technique, powerful refractive effects, reversibility, and little chance of rejection.

Several publications have described the long-term clarity and stability of epikeratoplasty for aphakia, myopia/hyperopia, and keratoconus variations.[7-10] One of which reported on a 28-year follow-up of epikeratophakia after congenital cataract surgery.[7] Clinical descriptions include uncorrected and corrected visual acuity and general appearance. Fan (2008) described alterations on a cellular level using in-vivo confocal biomicroscopy,[8] and McDonald (1986) attested to the effectiveness, stability, and safety of epikeratoplasty in keratoconus.[6] There have been prior published histopathologic reports,[7,8] but not in an optically clear myopic epikeratoplasty cornea with as long duration in-situ, that had also sustained a myopic PRK with mitomycin.

The three-decade life span of the allogenic stroma in the case reported herein included initial harvesting with a microkeratome, freezing, lathing, lyophilization (freeze drying), rehydration, and PRK with mitomycin. In addition to the donor cornea's longevity, it is notable that the allogenic donor cornea stroma, and host stroma, remained clear in slit lamp viewing and structurally intact subsequent to the mechanical, laser, and chemical processes to which it was subjected.

Conclusion

This case affirms the potential long-term clarity and resilience of allogenic stromal cornea and supports its use as a potential long-term stabilizing option in CAIRS for keratoconus and variations thereof for other cornea disorders.

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Conflicts of interest

There are no conflicts of interest.

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