

History of Hydrogel Corneal Inlays

A modern approach aims to correct presbyopia along with refractive error.

BY ENRIQUE BARRAGAN, MD

The cornea is the most powerful refracting surface of the eye because of the large difference in the indexes of refraction between the air and the cornea. Large changes in the refractive power of the eye can be achieved by making small alterations to the anterior corneal curvature.

The concept of changing the cornea to improve vision has been with us for many decades. The excimer laser is able to reshape the cornea by removing tissue, pulse by pulse. Laser vision correction, particularly LASIK and PRK, has proven to be a clinical and commercial success. Millions of patients who have had refractive errors corrected now live spectacle-free lives.

The vast majority of patients who undergo laser vision correction are happy with their outcomes, often describing the event as life-changing. Complications can be serious, however. Ectasia can be induced by reducing the thickness of the cornea too greatly, with or without the mechanically destabilizing step of cutting a flap.

Such problems have kept the concept of keratophakia alive. The keratophakic principle can be thought of as laser vision correction in reverse. Material mimicking corneal tissue is introduced into the cornea, and the corneal shape is changed through addition rather than subtraction. This methodology offers the advantages of not compromising corneal strength through thinning and by allowing the opportunity to remove the implant to restore preoperative vision if required.

HISTORY OF KERATOPHAKIA

The field of refractive corneal surgery has been nurtured and refined by José Ignacio Barraquer, MD, of Bogotá, Colombia, since 1949. To perform keratophakia, Dr. Barraquer tried two approaches, first implanting donor corneal tissue obtained by shaping frozen donor tissue with a cryolathe and later using synthetic stromal inlays. These inlays were made of flint glass and plexiglass and caused anterior stromal necrosis followed by extrusion of the implant.

TAKE-HOME MESSAGE

- Early stromal inlays made of flint glass and plexiglass caused anterior stromal necrosis.
- About 20 years ago, manufacturers started making corneal inlays with hydrogels, but problems with biocompatibility and surgical difficulty remained.
- Newer designs may have solved the problems of implanting a hydrogel inlay in the cornea.

In 1961, Knowles¹ found that the cornea overlying a water-impermeable membrane thinned and often ulcerated. He determined that a water-impermeable intrastromal implant would prevent the movement of water and nutrients from aqueous to stroma and would result in excessive concentration of the tear film, stromal thinning anterior to the implant, and eventually epithelial and stromal breakdown. Therefore, it was important that any intrastromal implant be sufficiently permeable to water molecules, glucose, and lactate ions to permit the maintenance of normal corneal physiology.

Hydrogels offered a solution to the problem of water transport within the cornea. Hydrogels are networks of polymer chains that are hydrophilic and highly absorbent. They have the flexibility of natural human tissues, and their large pore sizes allow water and solutes to pass through in a manner similar to the stroma.

In 1967, Dohlman et al² implanted discs of glyceryl methacrylate hydrogel with an 88% water content and observed good corneal acceptance in rabbits and cats. Some necrosis was seen, possibly due to the thickness of the implants, some of which were more than 500 µm thick. Eventually, it was found that this particular hydrogel could be impregnated by proteins that render it opaque.³

In the years that followed, better hydrogels were developed, including hydroxyethyl methacrylate (HEMA).^{4,5} McCarey and colleagues⁵ performed a number of pri-

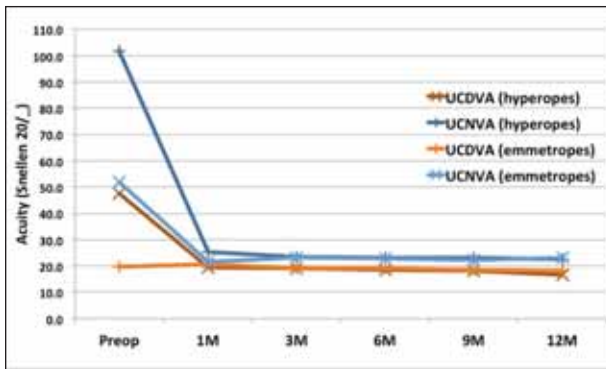


Figure 1. Near UCVA in treated eye in a recent study shown by cumulative percentages of patients with indicated Snellen acuity 1 week postoperative.

mate studies that validated the use of hydrogels in the cornea as well as substantial modeling of nutrient flow to determine the viability of these materials from a theoretical angle. Over 8 years of observation in nonhuman primates, Werblin et al⁶ demonstrated that hydrogel lenses had excellent tissue biocompatibility based on persistent corneal clarity, lack of inflammatory reaction, absence of vascularization, stable epithelium, and normal appearance of endothelium.

McDonald et al⁷ also found that high-water-content hydrogel intracorneal lenses were well tolerated in primates for up to 5 years. Steinert et al⁸ continued this work by using implants with a thickness of 300 μm . These implants showed excellent biocompatibility in human trials, but surgery was difficult because LASIK and the surgical instrumentation to enable it had still not been popularized.

Commercialization of inlays continues to be a goal that is pursued vigorously. Anamed, Inc. (Lake Forest, California), developed Nutrapore, a hydrogel material, and introduced the PermaVision keratophakia lens to correct hyperopia. Early results were encouraging,⁹ but these inlays had thicknesses that measured in the hundreds of microns and diameters of 5 mm. The product was unsuccessful due to the high percentage of patients in whom the inlay caused an intrastromal epithelial reaction that reduced BCVA.¹⁰

PRESBYLENS

ReVision Optics, Inc. (Lake Forest, California), recently developed the PresbyLens, a hydrogel corneal inlay for the correction of presbyopia. Arturo S. Chayet, MD, of Tijuana, Mexico, and I performed early trials of the implant in Mexico. Currently the device is undergoing trials in the United States and commercialization in Europe. This lens was recently renamed the Vue+ Corneal Inlay, and Dr. Chayet and

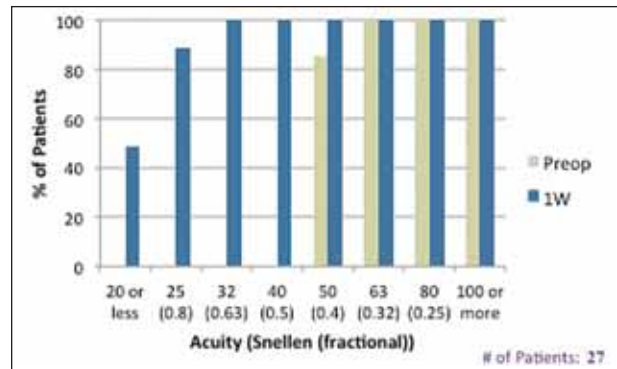


Figure 2. Mean near and distance UCVA as a function of time for two recent studies of emmetropes and concurrent LASIK patients.

I are now working on combining the inlay with LASIK.

The Vue+ differs considerably from previous inlay designs; it is very small, with a diameter less than half that of the Anamed inlays and a thickness of a few tens of microns, making it much less intrusive. The Vue+ has demonstrated excellent biocompatibility in several hundred surgeries performed in Mexico. The inlay's small diameter (1.5 mm) results in a region of corneal shape change that is centered on the pupil to produce a multifocal effect for presbyopic patients. The hydrogel material has the same refractive index as the cornea, so the center of the cornea provides near vision and the periphery remains focused for distance vision.

PATIENT SELECTION, SURGICAL TECHNIQUE

Patients who are treated with the Vue+ typically have a preoperative refraction between -0.50 and 1.00 D and monocular distance vision better than 20/32. Between the ages of 45 and 60 years, such patients usually have poor near vision preoperatively, but near vision improves to approximately 20/20 or 20/25 within 1 week of surgery (Figure 1). Distance visual acuity drops slightly to approximately 20/32 in the treated eye, but, as only the nondominant eye is treated, distance visual function is little affected and patients are happy with their vision at all distances.

For patients who are ametropic preoperatively, the ReVision Optics device can be combined with LASIK. Dr. Chayet and I have performed a series of 38 hyperopic patients who had a preoperative manifest refraction between 1.00 and 3.00 D. Results have been excellent, although not all patients have completed 1-year follow-up in this study. Acuities at all distances are similar to those with the inlay alone (Figure 2), and satisfaction scores are better than for emmetropes treated with the inlay.

The surgical technique is straightforward. The inlay, although tiny and transparent, can be seen through a stan-

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REFRACTIVE SURGERY **BONUS FEATURE**

ward operating microscope. Delivery is accomplished via a titanium inserter that has a small horizontal slit at its tip. The inlay is held in this space by the surface tension of the balanced saline solution in which it is stored. After creation of a LASIK flap, the inlay is released onto the stromal bed via a vertical notch in the inserter. A stripping spatula is used to gently hold the inlay onto the stromal bed, and the inserter is pulled away. The inlay can then be easily slid into position. After approximately 1 minute, the inlay dries and adheres to the cornea, preventing further motion. The flap is then positioned back over the inlay. The length of the procedure is similar to that of a standard LASIK surgery.

COMPLICATIONS

Corneal inlay technology moved in the direction of hydrogels more than 20 years ago, but problems with corneal biocompatibility and surgical difficulty caused earlier efforts to be unsuccessful. Corneal reaction to the ReVision Optics Vue+ inlay is either absent or mild. About 10% of patients develop a light haze over the inlay about 6 months after implantation. In some cases, this effect gradually disappears by itself, but in others a second round of steroids quickly clears the cornea, and the haze rarely returns.

CONCLUSION

The ReVision Optics intrastromal corneal inlay seems to have solved the problem of using a hydrogel device to produce consistently good visual results without inducing undue corneal reaction. As a result of the success that Dr. Chayet and I have observed with monocular implantation of the PresbyLens (now Vue+), we are investigating the possibility of binocular implantation. So far we have had very good results. ■

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1. Knowles WF. Effect of intralaminar plastic membranes on corneal physiology. *Am J Ophthalmol*. 1961;51:1146-1156.
2. Dohlman CH, Refojo MF, Rose J. Synthetic polymers in corneal surgery. I. Glyceryl methacrylate. *Arch Ophthalmol*. 1967;77(2):252-257.
3. Dohlman CH, D'Amico DJ. Can an eye in phthisis be rehabilitated? A case of improved vision with 1-year follow-up. *Arch Ophthalmol*. 1999;117:123-124.
4. Mester U, Heiming D, Dardenne MU. Measurement and calculation of refraction in experimental keratophakia with hydrophilic lenses. *Ophthalmic Res*. 1976;8:111-116.
5. McCarey BE, Andrews DM. Refractive keratoplasty with intrastromal hydrogel lenticular implants. *Invest Ophthalmol Vis Sci*. 1981;21(1):107-115.
6. Werblin TP, Peiffer RL, Binder PS, McCarey BE, Patel AS. Eight years experience with Permalens intracorneal lenses in nonhuman primates. *Refract Corneal Surg*. 1992;8(1):12-22.
7. McDonald MB, McCarey BE, Storie B, et al. 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(3):213-222.
8. Steinert RF, Storie B, Smith Pet al. Hydrogel intracorneal lenses in aphakic eyes. *Arch Ophthalmol*. 1996;114(2):135-141.
9. O h'Eineachin R. New synthetic lenticule produces good results in hyperopic patients. *EuroTimes*. 2000;5(6):53.
10. Alio JL, Mulet E, Zapata LF, Vidal T, De Rojas V, Javaloy J. Intracorneal inlay complicated by intrastromal epithelial opacification. *Arch Ophthalmol*. 2004;122:1441-1446.