Confocal Microscopy of Corneas With an Intracorneal Lens for Hyperopia

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ABSTRACT

PURPOSE: We evaluated short-term results and confocal microscopic corneal changes following intracorneal lens implantation.

METHODS: In six eyes of three patients with hyperopia between +3.00 and +6.00 diopters (D), an intrastromal hydrogel lens (Permavision, Anamed, Anaheim, Calif) was implanted. Mean baseline hyperopia was +3.90 D. Manifest refraction, uncorrected visual acuity, and spectacle-corrected visual acuity were evaluated. We also performed confocal real-time microscopy with a water immersion objective. Corneal optical sections were recorded and reviewed frame by frame. Examinations were done at months 3, 6, and 12 after intracorneal lens implantation.

RESULTS: After surgery, the spherical equivalent refraction was within ±0.50 D in 83% (five of six eyes) at 3 months and 100% (six eyes) at 6 and 12 months. Uncorrected visual acuity (UCVA) at 3 months was within 20/40 or better in 67% (four eyes) and in 100% (six eyes) at 6 and 12 months; no eyes had 20/20 or better UCVA at 3 and 6 months. One eye (17%) had 20/20 or better UCVA at 12 months. On confocal microscopy, one eye had an amorphous deposit adjacent to the lens and presumed fibroblastic activity in the same stromal area at 6 months, which was non-progressive up to 12 months.

CONCLUSION: Intracorneal lenses may be a treatment option for correction of spherical hyperopia. Predictability must be improved but results in these six eyes were stable up to 1 year. Confocal miscroscopy confirmed biocompatibility and showed no abnormal changes, except two spots of hypercellularity in one eye. [*J Refract Surg* 2004;20:778-782]

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José Ignacio Barraquer described the basis for most corneal refractive procedures that alter the anterior corneal curvature. He used the term keratophakia, originally working with donor corneal tissue.[1] Over three decades ago, he worked with nonpermeable plastics as inlays in the cornea but had problems with melting and necrosis of the anterior corneal cap and abandoned this procedure as a standard technique.[1] Nevertheless, synthetic material rather than corneal tissue was used; the lens required at the time of surgery can be manufactured in limitless quantities to precise specifications.[2] Several authors have used hyperopic implants in corneas of various animal models, observing that significant hyperopic refractive change (increasing the anterior corneal curvature) could be achieved.[3-6] In contrast to hydrogel material, polysulfone intracorneal implants affect the refractive properties of the cornea, not by changing its shape but by altering its refractive index.[7]

Watsky et al[8] and McCarey et al[9] started using water-permeable hydrogel materials for synthetic keratophakia. They modified the freehand pocket dissection approach by using the microkeratome to permit the anterior cornea to steepen over the hydrogel implant and thus correct hyperopic refractive errors. We report the initial refractive results in six eyes with a follow-up of 12 months and corneal confocal microscopic findings.

PATIENTS AND METHODS

We placed six intracorneal lenses (Permavision, Anamed, Anaheim, Calif) in six eyes with +3.00 to +6.00 diopters (D) of hyperopia (Table). Exclusion criteria included patients under 21 years of age, corneas steeper than 46.00 D or flatter than 41.00 D with thickness less than 430 µm, hyperopia greater

Table
Refractive Data and Lens Status in Six Eyes at 12 Months After Intracorneal Lens Implantation for Hyperopia

Eye No.	Spherical Equivalent Refraction (D)		Implant Power (D)	Uncorrected Visual Acuity		Best Spectacle-corrected Visual Acuity	
	Preop	Postop		Preop	Postop	Preop	Postop
1	+3.50	0.0	+3.50	20/200	20/20	20/20	20/20
2	+3.00	-0.12	+3.00	20/100	20/30	20/25	20/25
3	+3.20	-0.25	+3.50	20/400	20/40	20/25	20/30
4	+6.00	-0.37	+6.50	20/400	20/40	20/25	20/25
5	+3.50	-0.12	+3.50	20/200	20/30	20/20	20/20
6	+4.20	0.0	+4.50	20/400	20/30	20/25	20/25

than +6.20 D, and astigmatism greater than 1.00 D. All patients enrolled in the study provided written informed consent, and the study was conducted according to the principles of the Helsinki Declaration and good clinical practices.

The surgery was performed according to the following technique. First, the eye was cleaned and draped similarly to any other anterior segment surgical procedure, and topical anesthesia was applied. The suction ring of a manual microkeratome (LSX One; Moria/Microtech, Antony, France), with a redesigned head (200 µm) was placed at the limbus and centered on the geometric center of the cornea. The suction pump was activated to standardize intraocular pressure to approximately 70 mmHg, as evidenced by pupillary dilation and verified with digital pressure. The microkeratome head was then placed into the groove of the suction ring (slightly pulled up to check for correct suction). We tried to obtain a flap between 180 and 200 µm thick and a diameter between 7.5 and 8.0 mm, to theoretically achieve better implant stability and adequate physiological function of the anterior cornea. Several drops of balanced salt solution (BSS) were applied on the corneal surface and the flap was dissected. Once suction was released, the microkeratome head and suction ring were removed together. The corneal flap was then lifted with a flap spatula, exposing the underlying corneal stroma (at this point it is important to keep the stroma clean and dry to allow better adherence and avoid postoperative displacement of the lens). We centered the lens at the midpoint between the projected pupil center and the fixation point reflex over the cornea. The flap was then gently replaced with a spatula, trying to avoid striae—important with the dry technique that we use. Adherence was verified by smoothly passing a sponge over the corneal flap for approximately 1 minute.

All intracorneal lenses were manufactured by Permavision, which originally manufactured five different diameters: 4.4, 5.0, 5.5, 6.0, and 6.5 mm, with an edge thickness of 10 µm, and with power ranging from +1.00 to +6.00 D. In our series of six eyes, we used a new lens design that offers a diameter of 5.00 mm, an edge beveled to a thickness between 6 and 10 µm, with a base curve of 7.35 mm and a power range from +1.00 to +6.50 D. The water-permeable implant is made from Nutrapore (micro-porous hydrogel) with 78% water content and a refractive index of 1.376.

In this study we evaluated, before and after surgery, spherical equivalent refraction under cycloplegia, uncorrected visual acuity, spectacle-corrected visual acuity, slit-lamp examination, Placido ring topography (EyeSys 2000, Houston, Tex), and confocal microscopy at 3, 6, and 12 months.

Confocal Microscopy

All six eyes were reviewed with white-light tandem slit-scanning confocal microscopy (Confoscan P4; Tomey, Erlangen, Germany). The microscope objective used was a 40x water immersion objective (Achroplan, 40/0.75; Zeiss, Aalen, Germany). A cooled thixotropic carbomer gel (Viscotears; Ciba Vision, Barcelona, Spain) was used as immersion fluid. Corneas were examined centrally and at midperiphery (3 mm from the center of the intracorneal lens). First, the endothelium was imaged to ensure exact alignment within the frontal plane. After that, several passes from epithelium to the endothelium were done, although images were mainly focused in the anterior stroma, the surrounding intracorneal lens area, and the posterior stroma. The examination was recorded in real-time on an S-VHS videotape. Picture sequences were reviewed frame by frame at 3, 6, and 12 months after surgery.

RESULTS

After surgery, spherical equivalent refraction was within ±0.50 D in 83% (five eyes) at 3 months, and 100% (six eyes) at 6 and 12 months. Uncorrected

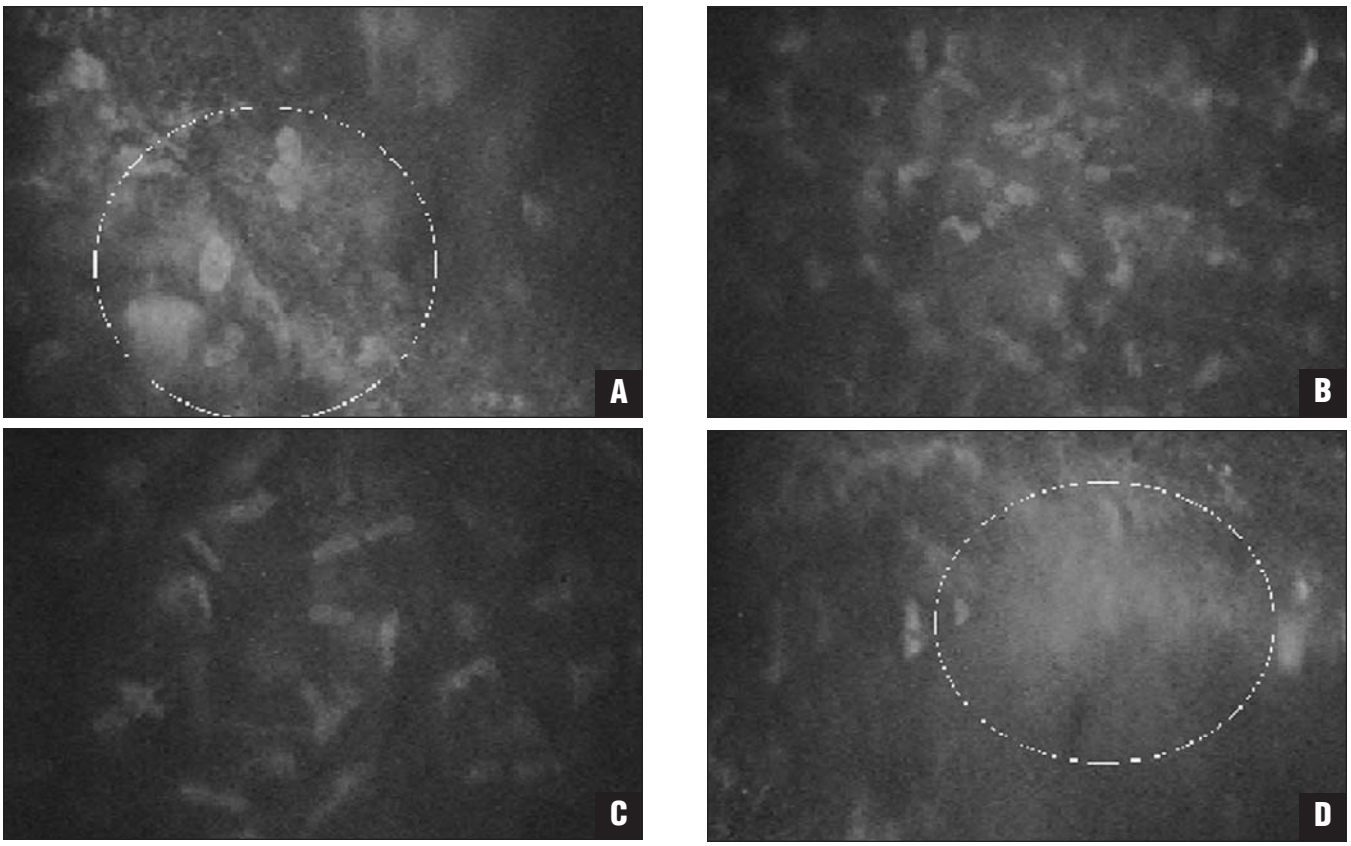

Figure 1. A) Deposits of amorphous material and highly reflective irregular keratocytes at mid-periphery immediately above the intracorneal lens; **B)** Normal appearance of the anterior stroma in an eye implanted with an intracorneal lens; **C)** Normal appearance of the posterior stroma in an eye implanted with an intracorneal lens; **D)** Scant haze in the anterior corneal stroma in an eye implanted with an intracorneal lens.

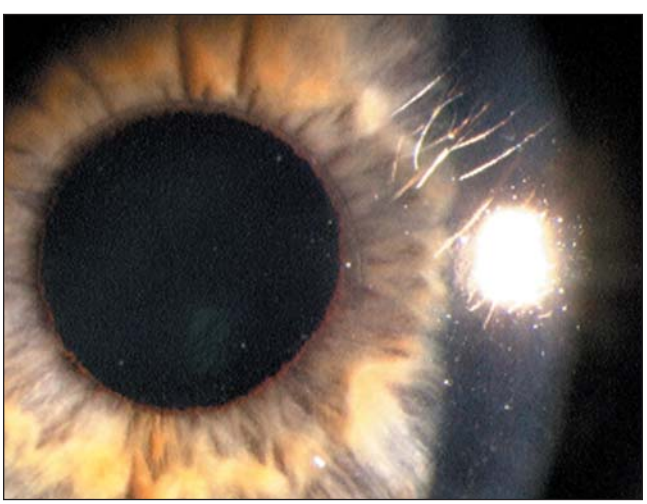

Figure 2. Slit-lamp microscopy 16 months after placement of the hydrogel intracorneal lens shows a well-centered lens with diffuse light haze.

visual acuity achieved at 3 months was 20/40 or better in 67% (four eyes) and in 100% (six eyes) at 6 and 12 months, but no eyes had 20/20 or better visual acuity at 3 and 6 months; only one eye (17%) had 20/20 or better visual acuity at 12 months. Spectacle-corrected visual acuity at 1 month was 20/40 or better in 67% (four eyes) and improved in 100% (six eyes) at 6 and 12 months (Table). Safety analysis of this technique showed a vision loss of 1 line in 17% (one eye); 83% maintained the same spectacle-corrected visual acuity at 12 months. One eye had inferior displacement of the intracorneal lens, which was subsequently replaced. At slit-lamp examination, a scant haze was evident in both anterior and posterior surfaces of all the lenses between months 6 and 12 (Fig 1); its appearance was not progressive. Corneal topography was centered, and the findings in one eye are shown in Figure 2.

Confocal Microscopy Evaluation

We examined changes in each layer of the cornea with confocal microscopy at 3, 6, and 12 months after surgery. In all eyes at 3 months after surgery, no apparent changes were found; the epithelium was regular, anterior stroma, posterior stroma, and surrounding area of the intracorneal lens did not show changes with respect to cellular morphology,

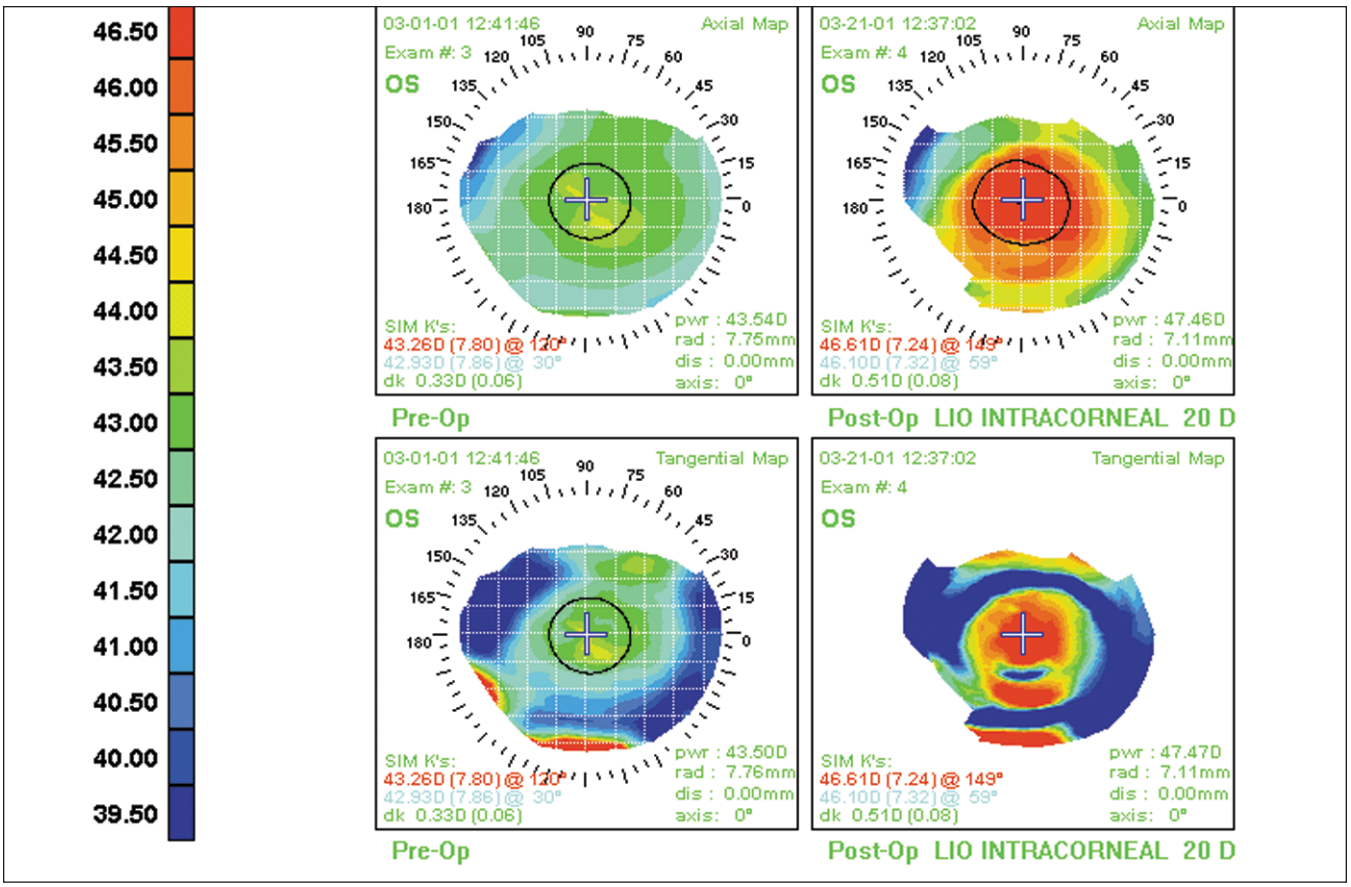

Figure 3. Corneal topographic change (well-centered steepening, slightly inferior) induced by intracorneal lens.

cellular distribution, signs of keratocyte activity, deposits, or any material with high reflectivity. The endothelium showed normal appearance. We also verified these findings with slit-lamp examination, and demonstrated transparency of the cornea. At 6 months, in five eyes all layers appeared similar to those observed at the 3-month examination (Fig 3). Nevertheless, in eye number 4, a deposit of amorphous material and numerous highly reflective, irregularly shaped keratocyte nuclei clustered at 3 mm from the center were observed. These were found immediately above the intracorneal lens, corresponding to a slight haze surrounding the lens at the slit-lamp and probably revealing local fibroblastic activity.[10,11] Posterior stroma was not affected, and the changes in the remaining corneal layers were inconspicuous. We did not observe any progression between the 6- and 12-month follow-up examinations.

DISCUSSION

Previous morphological studies with intrastromal implants have revealed a variety of results. Watsky et al[8] found minimal keratocyte activity at the junction of the hydrogel-stromal interface in a rabbit model. Sendele et al[12] found that high water content hydroxymethylmethacrylate (Permalens, Anamed Inc) hydrogel implants were well tolerated within the rabbit corneal stroma, and no signs of inflammation, ulceration, or neovascularization were found. Zavala et al[13] developed an in vitro model for keratocyte interaction with hydrogel materials, and observed the growth of baboon stromal keratocytes on the surface of various hydrogel materials, demonstrating that a hydrogel lens with 55% of hydration was free of keratocyte attachment or activation. Ismail[14] reported excellent tolerance of hydrogel lens in corneas of rabbits and no signs of keratocytic activity or intrastromal fibrosis.

A limitation of our study is the lack of preoperative confocal microscopy data. Nevertheless, findings with respect to the amorphous material and the fibroblastic activity observed in one cornea are of unknown etiology. They may have been derived from disturbances in access to nutritional factors or a stress related to mechanical forces, although these

findings remain uncertain; this change occurred in the patient with the highest correction (+6.00 D). Our results were stable and nonprogressive, similar to those observed in corneas after intracorneal ring segment implantation.[15,16] In fact, a successful intrastromal implant must, in terms of biocompatibility, be sufficiently permeable to nutrients and water, and thus be able to sustain normal corneal physiology. Chemically pure polymers rarely demonstrate chemical toxicity.[2] The Permalens implant seems to overcome most of these problems.

Barraquer and Gomez[17] and Steinert et al[18] evaluated the efficacy and safety of a hydrogel intracorneal lens for correction of spherical ametropia in aphakic eyes. They demonstrated that hydrogel intracorneal lenses were well tolerated and the refractive results were stable, although they did not use confocal microscopy.

Our visual acuity results improved over time during the first 12 months after surgery; they were suboptimal and similar to those of other published ablational techniques (laser in situ keratomileusis or photorefractive keratectomy).[19-21]

Intracorneal lens implants may be a treatment option in the correction of spherical hyperopia. However, predictability must be improved and long-term safety established in a larger number of eyes. Intracorneal implants have the theoretical advantage of reversibility, but currently no data are available to demonstrate reversibility. In our experience, the main limitations of this technique are its limited adjustability, the actual limitation of cylinder correction, the low range of correction (eg, not valid for most aphakic eyes), and also the small optical zone of the lens (probably a limitation for visual quality performance).

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