Long-term outcomes after monocular corneal inlay implantation for the surgical compensation of presbyopia

Alois K. Dexl, MD, MSc, Gerlinde Jell, MD, Clemens Strohmaier, MD, Orang Seyeddain, MD, Wolfgang Riha, MD, Theresa Rückl, MD, Alexander Bachernegg, MD, Günther Grabner, MD

PURPOSE: To evaluate long-term outcomes of small-aperture corneal inlay implantation for the surgical compensation of presbyopia.

SETTING: Paracelsus Medical University, Salzburg, Austria.

DESIGN: Prospective interventional cohort study.

METHODS: Monocular implantation of a Kamra small-aperture inlay (model ACI7000) (1.6 mm central aperture) was performed in emmetropic presbyopic eyes. The preoperative and postoperative parameters included monocular and binocular uncorrected (UDVA) and corrected (CDVA) distance visual acuities, uncorrected intermediate visual acuity (UIVA), and uncorrected (UNVA) and corrected (CNVA) near visual acuities; refraction; patient satisfaction; and complications.

RESULTS: From September 4, 2006, to May 21, 2007, a small-aperture inlay (1.6 mm central aperture) was implanted in 32 emmetropic presbyopic eyes. The mean binocular uncorrected visual acuities improved as follows: UNVA from Jaeger (J) 6 $\pm$ 1.2 lines ($\sim$20/50) to J2 $\pm$ 1.8 lines ($\sim$20/25) ($P < .001$) and UIVA from 0.2 logMAR $\pm$ 1.3 lines ($\sim$20/32) to 0.1 logMAR $\pm$ 1.3 lines ($\sim$20/25) ($P = .04$). The UDVA decreased from -0.2 logMAR $\pm$ 0.2 lines ($\sim$20/12.5) to -0.1 logMAR $\pm$ 0.6 lines ($\sim$20/16) ($P < .001$). At 60 months, 74.2% of patients had a UNVA of J3 ($\sim$20/32) or better, 87.1% had a UIVA of 0.2 logMAR ($\sim$20/32) or better, and 93.5% had a UDVA of 0.0 logMAR ($\sim$20/20) or better. One inlay was removed after 36 months because of patient dissatisfaction with vision after a hyperopic shift in the surgical eye, with no loss of CDVA or CNVA 2 years after removal.

CONCLUSION: Long-term results of monocular corneal inlay implantation indicate increased UNVA and UIVA and slightly compromised UDVA in emmetropic presbyopic eyes.

Financial Disclosure: Dr. Grabner was reimbursed for travel expenses from Acufocus. Dr. Riha is a consultant to Acufocus. No other author has a financial or proprietary interest in any material or method mentioned.

J Cataract Refract Surg 2015; 41:566–575 © 2015 ASCRS and ESCRS

At present, there are more than 140 million people over the age of 40 years in the United States; it is projected that by 2020, there will be 2.1 billion presbyopic patients worldwide. These demographic trends drive a continuing interest in developing refractive surgical procedures to improve uncorrected near vision for these patients.[1] Corneal inlays have several advantages: They are additive and do not require tissue to be removed, they preserve future options for presbyopic correction, some of them can be used in the setting of pseudophakia and/or combined with laser refractive surgery, and they are removable.[1]

Currently, 3 types of corneal inlay are in various stages of development and commercial release for use in the surgical compensation of presbyopia. These inlays reshape the anterior curvature of the cornea to enhance near and intermediate vision (Raindrop Near Vision Inlay, Revision Optics, Inc.),[2] add

refractive power to the central cornea by implanting a refractive addition of +1.5 to +3.5 diopters (D) (Flexivue Microlens, Presbia Coöperatief U.A.),[3,4] or use small-aperture optics to increase the depth of focus (Kamra corneal inlay, Acufocus, Inc.).[5–7] Although these inlays are widely used in and outside of clinical trials, limited peer-reviewed data are available concerning their long-term results. Only 2 papers report on follow-up beyond 2 years.[6,7]

Mulet et al.[8] reported outcomes and complications of a hydrogel corneal inlay (Permavision, Anamed, Inc.) after 5 years of follow-up that show the importance of long-term evaluation of corneal inlays or implants. Although no cases of corneal vascularization or melting were seen, inlay removal was necessary in 20 (58.8%) of 34 eyes up to 6.1 years postoperatively because of intracorneal deposits in the visual axis, irregular astigmatism, reduced vision, severe corneal haze, implant decentration, or perilenticular opacity.[8]

This paper reports the visual acuity results, patient satisfaction, and postsurgical complications in cases followed for 60 months after monocular implantation of the ultrathin Kamra small-aperture corneal inlay (model ACI7000). To our knowledge, this is the longest follow-up reported in the ophthalmic literature for this type of corneal inlay.

PATIENTS AND METHODS

This single-center prospective interventional noncomparative cohort study evaluated eyes after monocular corneal inlay implantation at the Department of Ophthalmology of the Paracelsus Medical University Salzburg, Salzburg, Austria. This clinic participated in the U.S. Food and Drug Administration clinical trials with clinics in the U.S., Asia, and Europe. The Ethics Committee, County of Salzburg, approved the study protocol, and all patients provided written informed consent. The study was performed in accordance with the tenets of the Declaration of Helsinki.

Corresponding author: Alois K. Dexl, MD, MSc, Department of Ophthalmology, Paracelsus Medical University, Müllner Hauptstraße 48, A-5020 Salzburg, Austria. E-mail: a.dexl@salk.at.

Patients were included in the clinical trial if they were 45 to 55 years old, were naturally emmetropic and presbyopic, had a preoperative manifest refractive spherical equivalent (MRSE) of plano (defined as +0.50 to −0.75 D with no more than 0.75 D of refractive cylinder as determined by cycloplegic refraction), and had a corrected distance visual acuity (CDVA) of at least 0.0 logMAR ($\sim$20/20) in both eyes. In addition, the surgical eye had to have uncorrected near visual acuity (UNVA) of worse than Jaeger (J) 5 ($\sim$20/40), a central corneal thickness of 500 μm or more, a central endothelial cell count of 2000 cells/mm^2 or more, and a corneal power of 41.00 to 47.00 D in all meridians. Key exclusion criteria were previous ocular surgery, anterior or posterior segment disease or degeneration, and any type of immunosuppressive disorder. In addition, eyes with latent hyperopia (a difference of 1.00 D or more between the manifest and cycloplegic refractions) and patients using systemic medication with significant ocular side effects were excluded.

Corneal Inlay

The Kamra corneal inlay (ACI7000, a model from 2006 to 2008) is a 10 μm thick artificial aperture with an outer diameter of 3.8 mm and a central aperture (inner diameter) of 1.6 mm. It is made of polyvinylidene fluoride that is pigmented with carbon nanoparticles for opacity; its 1600 randomly arranged microperforations (25 μm diameter) allow nutritional flow through to the stromal tissue.[A] These holes also allow an average of 7.1% light transmission through the inlay annulus.[A] This small-aperture optic is designed to increase the eye's depth of focus, improving near and intermediate visual acuity in presbyopic eyes while minimally affecting binocular distance vision.[A]

The model of the Kamra corneal inlay commercially available at present (ACI7000PDT) has design changes over the previous model used in this study. It is thinner (5 μm) and has 8400 smaller, pseudorandomly arranged microperforations (5 to 11 μm) that allow an average light transmission through the annulus of 6.7%.[A] These modifications diminish the visual symptoms experienced with use of the previous-generation inlay.[A] Currently, the corneal inlay is implanted within a corneal pocket to compensate for presbyopia in emmetropic eyes or within a corneal pocket after laser in situ keratomileusis (LASIK) in eyes with additional ametropia.[9]

Surgical Procedure

All surgeries were performed by the same experienced surgeon (G.G.) from September 4, 2006, to May 21, 2007. The surgical preparation and technique have been described in detail.[10] In brief, a superior hinged flap was created in the nondominant eye using a 60 kHz Intralase femtosecond laser (Abbott Medical Optics, Inc.) (8 μm × 8 μm spot/line separation, 0.9 μJ/pulse, 9.0 mm intended diameter). The intended depth from the corneal surface was 170 μm. The inlay was removed from the sterile package using a forceps and inspected under high magnification for defects. Centration was considered optimum when the first Purkinje reflex was in the center of the inner diameter of the inlay while the patient fixated on the microscope's light source.

Postoperative Regimen

The postoperative regimen included lomefloxacin hydrochloride 0.3% eyedrops (Okazin Augentropfen) 3 times daily

for 1 week, prednisolone acetate 0.5% eyedrops (Ultracortenol Augentropfen) 3 times daily for 1 week and then tapered over the next 2 weeks, and topical dry-eye therapy (sodium hyaluronate 1 mg/mL [Hylo-Comod Augentropfen]) 5 to 8 times daily for 1 month. Afterward, dry eye was treated with preservative-free hyaluronic acid eyedrops and corneal haze and hyperopic shifts were treated with topical steroids.

Outcomes

Postoperative examinations were scheduled for 1 day, 1 week, and 1, 3, 6, 9, 12, 18, 24, 30, 36, and 60 months. The primary parameters assessed were manifest refraction, visual acuity, patient satisfaction, and complications.

Manifest refraction and visual acuities were assessed preoperatively and postoperatively from 1 week to 60 months. Visual acuity measurements included monocular and binocular uncorrected distance visual acuity (UDVA) and CDVA (simulated for distance 20 feet [~6 m]), uncorrected intermediate visual acuity (UIVA) (simulated intermediate distance 32 inches [~80 cm]), and UNVA and corrected near visual acuity (CNVA) (test distance 16 inches [~40 cm]). All visual acuities were measured using the Optec 6500P Vision Tester (Stereo Optical Co., Inc.) by recording the number of correctly identified logarithmic Early Treatment of Diabetic Retinopathy Study (ETDRS) targets and deriving the corresponding logMAR, Snellen, and Jaeger equivalents.

Using a subjective questionnaire developed by the manufacturer of the corneal inlay to assess outcomes of the clinical trial, patients rated their postoperative need for reading glasses under different lighting conditions and their satisfaction with the procedure and with their UNVA.

Statistical Analysis

All data were analyzed on the basis of the ETDRS scores and then the logMAR, Snellen, and Jaeger equivalents. The results are given as mean $\pm$ standard deviation. Different timepoints were analyzed using 1-way repeated-measures analysis of variance (Sigmaplot 12, Systat Software), with a P level less than 0.05 considered statistically significant. Equal variance and normal distribution of the data were checked using the Shapiro-Wilks and Levene tests, respectively. All pairwise comparisons performed post hoc were adjusted using the Bonferroni method. Where appropriate, paired t tests were used to compare 2 timepoints.

RESULTS

The study cohort included 32 eyes of 32 patients with a mean age of 51.2 $\pm$ 2.2 years (range 48 to 55 years). Seven patients (21.9%) were women, and 25 (78.1%) were men. Of the 32 inlay eyes, 20 (62.5%) were left eyes and 12 (37.5%) were right eyes. Table 1 gives the preoperative parameters for the inlay eyes. All patients completed every scheduled follow-up examination; the inlay was removed from 1 eye after the 36-month follow-up, but that patient still attended the 60-month follow-up.

Refraction

In the surgical eyes, the mean MRSE changed from +0.19 D $\pm$ 0.22 (range −0.05 to +0.50 D)

preoperatively to −0.07 $\pm$ 0.47 D (range −1.75 to +1.38 D) at 12 months, remained stable until 36 months (0.00 $\pm$ 0.56 D, range −1.50 to +3.13 D), and was +0.40 $\pm$ 1.08 D (range −1.25 to +3.50 D) at 60 months. The change through the 5 years was not statistically significant (Figure 1). In the fellow eyes, a slight shift toward hyperopia also occurred, with the MRSE changing from +0.17 $\pm$ 0.27 D preoperatively to +0.45 $\pm$ 0.53 D at 60 months (P = .005). There was no statistically significant difference in the refraction between both sets of eyes at 60 months (P = .81) (Figure 1).

Uncorrected Near, Intermediate, and Distance Visual Acuities

The mean UNVA in the surgical eyes improved from J7/J8 $\pm$ 0.8 lines (~20/63; ~0.50 logMAR) preoperatively to J1 $\pm$ 1.4 lines (~20/20; ~0.00 logMAR) (P < .001) at 12 months, remained stable until 36 months (J1 $\pm$ 1.2 lines [~20/20; ~0.00 logMAR]), and decreased slightly at 60 months (J3 $\pm$ 2.0 lines [~20/32; ~0.20 logMAR]) (P < .001). At 60 months, 23 (74.2%) of 31 surgical eyes had achieved a UNVA of ≤ J3 (~20/32; ~0.20 logMAR) (Figure 2) versus in only 2 (6.5%) of the fellow eyes. The binocular UNVA showed the same pattern of stability until 36 months (J6 $\pm$ 1.2 lines [~ 20/50; ~0.50 logMAR] preoperatively, J1 $\pm$ 1.4 lines [~20/20; ~0.00 logMAR] at 12 months, and J1 $\pm$ 1.2 lines [~20/20; ~0.00 logMAR] at 36 months), and a decrease at 60 months to J2 $\pm$ 1.8 lines (~20/25; ~0.10 logMAR) (P < .001). At 60 months, 23 patients (74.2%) could read at or below J3 (~20/32; ~0.20 logMAR) binocularly, including 14 (45.2%) at or below J1 (~20/20; ~0.00 logMAR) (Figure 2).

The mean UIVA in the surgical eyes improved from 0.2 logMAR $\pm$ 1.6 lines (~20/32) preoperatively to 0.1 logMAR $\pm$ 1.2 lines (~20/25) (P < .001) at

Table 1. Preoperative parameters (N = 32).

Demographic	Mean ± SD	Range
MRSE (D)	+0.19 ± 0.22	−0.05, +0.50
UDVA*	−0.10 ± 0.06 (~20/16)	−0.20, 0.00
UIVA*	+0.20 ± 0.17 (~20/32)	−0.20, +0.50
UNVA†	+0.50 ± 0.08 (~J7/J8)	+0.40, +0.60
CDVA*	−0.10 ± 0.05 (~20/16)	−0.20, 0.00
CNVA†	−0.10 ± 0.06 (~J 1+)	−0.20, +0.00

CDVA = corrected distance visual acuity; CNVA = corrected near visual acuity; MRSE = manifest refraction spherical equivalent; UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity
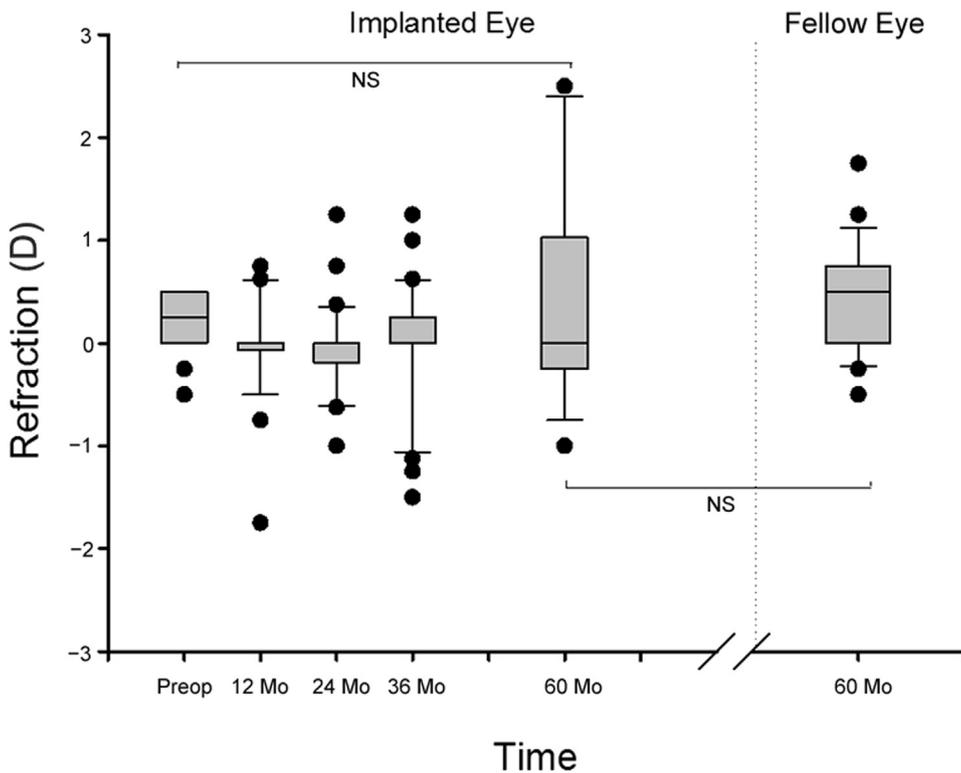*LogMAR (Snellen equivalent)
†LogMAR (Jaeger equivalent)

Figure 1. The spherical equivalents in the surgical eyes during the 60 months of follow-up and in the fellow eyes 60 months postsurgery (NS = not statistically significant).

12 months, remained stable until 36 months (0.0 logMAR ± 1.0 lines [~20/20]), and decreased slightly at 60 months (0.2 logMAR ± 1.5 lines [~20/32]). The binocular UIVA showed the same pattern of stability until 36 months (0.2 logMAR ± 1.3 lines [~20/32]) preoperatively, 0.0 logMAR ± 1.2 lines [~20/20] at 12 months, 0.0 logMAR ± 0.9 lines at 36 months), with a slight decrease (0.1 logMAR ± 1.3 lines [~20/25]) at 60 months ($P < .001$). At 60 months, the binocular UIVA was 0.20 logMAR (~20/32) or less in 27 patients (87.1%), including 16 (51.6%) with a binocular UIVA of 0.0 logMAR (~20/20) or less.

The mean UDVA in the surgical eyes decreased slightly from −0.1 logMAR ± 0.6 lines (~20/16) to 0.0 logMAR ± 1.1 lines (~20/20) at 12 months ($P < .001$), then was stable until 36 months (0.0 logMAR ± 1.1 lines [~20/20]) and decreased again at 60 months (0.1 logMAR ± 1.8 lines [~20/25]). At 60 months, 29 (93.5%) of 31 surgical eyes had a UDVA of 0.2 logMAR (~20/32) or less, 26 (83.9%) of 0.1 logMAR (~20/25) or less, and 14 (45.2%) of 0.0 logMAR (~20/20) or less (Figure 3). Preoperatively to 60 months, of 31 surgical eyes, 10 (32.3%) lost 1 line of monocular UDVA and 8 (25.8%) lost 2 or more lines. The decrease in binocular UDVA from
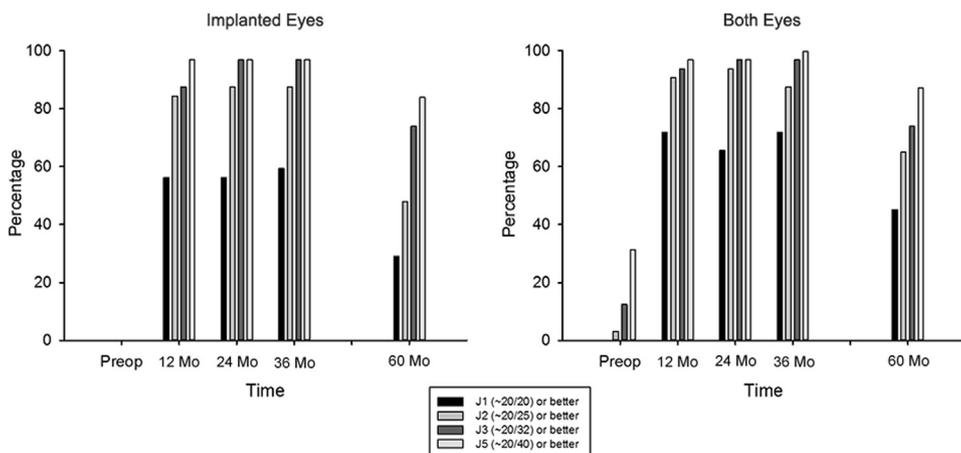

Figure 2. Uncorrected near visual acuities in surgical eyes and both eyes during the 60-month follow-up.
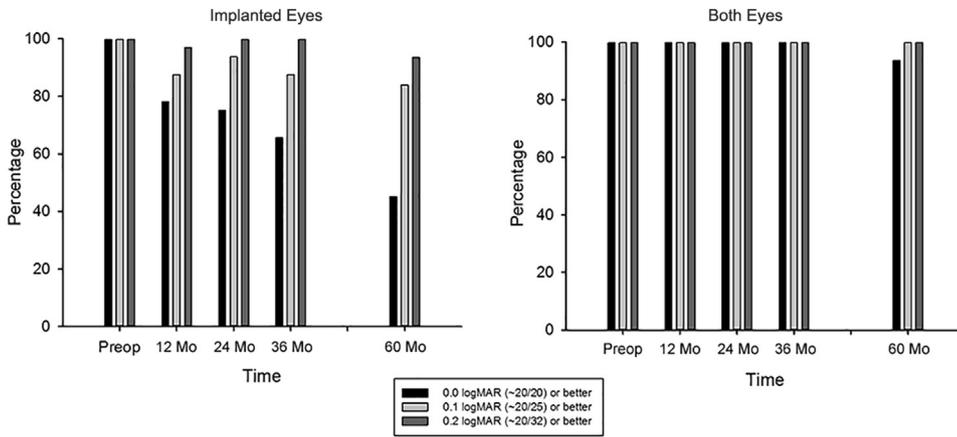
Figure 3. Uncorrected distance visual acuity in surgical eyes and both eyes during the 60-month follow-up.

36 months to 60 months was statistically significant ($P < .001$), although the mean binocular UDVA at 60 months was -0.1 logMAR $\pm$ 0.6 lines ($\sim 20/16$), with 29 eyes (93.5%) reaching 0.0 logMAR ($\sim 20/20$) or better (Figure 3). Binocularly, 10 (32.3%) of those 31 patients lost 1 line of UDVA and 1 (3.2%) lost 2 or more lines from preoperatively. However, the eyes were tested to -0.20 logMAR (20/12.5), so although this change might have been statistically significant, it was not clinically significant.

Corrected Distance Visual Acuity and Corrected Near Visual Acuity

In the surgical eyes, the mean CDVA was stable through 36 months (-0.1 logMAR $\pm$ 0.5 lines [$\sim 20/16$] preoperatively, -0.1 logMAR $\pm$ 0.7 lines [$\sim 20/16$] at 12 months, and -0.1 logMAR $\pm$ 1.0 lines [$\sim 20/16$] at 36 months) and decreased slightly at 60 months (0.0 logMAR $\pm$ 0.8 lines [$\sim 20/20$]) ($P < .001$). At 60 months, the mean CDVA in the surgical eyes was 0.0 logMAR ($\sim 20/20$) or less in 24 eyes

(77.4%), 0.1 logMAR ($\sim 20/25$) or less in 30 eyes (96.8%), and 0.20 logMAR ($\sim 20/32$) or less in 31 eyes (100%). Fourteen surgical eyes (45.2%) lost 1 line and 7 (22.6%) lost 2 or more lines (Figure 4). Binocular CDVA showed the same pattern of stability through 36 months (-0.2 logMAR $\pm$ 0.3 lines [$\sim 20/12.5$] preoperatively, -0.2 logMAR $\pm$ 0.4 lines [$\sim 20/12.5$] at 12 months, and -0.2 logMAR $\pm$ 0.3 lines [$\sim 20/12.5$] at 36 months), and decreased slightly at 60 months (-0.1 logMAR [$\sim 20/16$]) ($P < .001$). Until 36 months, no patient lost any lines of binocular CDVA. From 36 months to 60 months, 16 patients (51.6%) lost 1 line and 5 (16.1%) lost 2 or more lines (Figure 4).

The mean CNVA in the surgical eyes was stable until 36 months ($J1^+ \pm 0.6$ lines [$\sim 20/16$] preoperatively, $J1^+ \pm 1.0$ lines [$\sim 20/16$] at 12 months; $J1^+ \pm 0.6$ lines [$\sim 20/16$] at 36 months) and then decreased slightly at 60 months ($J1 \pm 0.9$ lines [$\sim 20/20$]) ($P < .001$). Binocular CNVA values were also stable until 36 months ($J1^+ \pm 0.4$ lines [$\sim 20/16$] preoperatively, $J1^+ \pm 0.3$ lines [$\sim 20/12.5$] at 12 months; $J1^+ \pm 0.3$ lines [$\sim 20/12.5$] at 36 months) and at 60 months, decreased
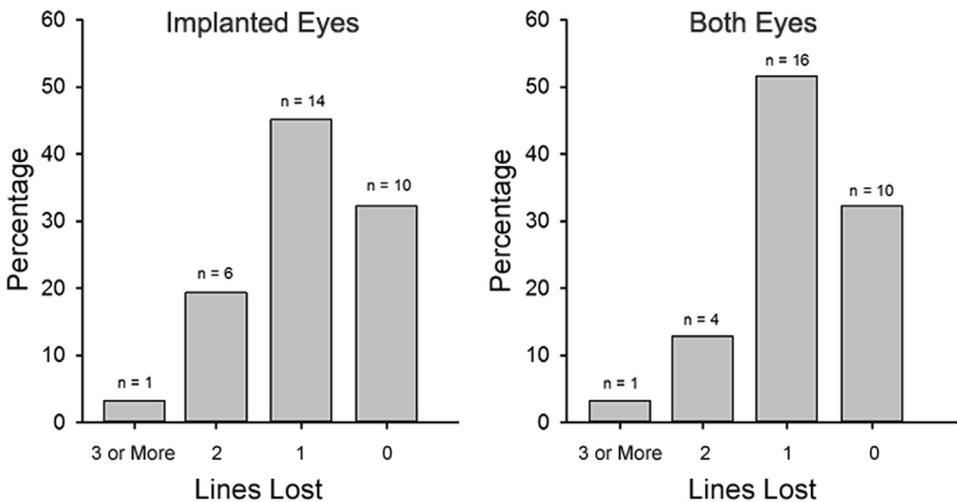

Figure 4. The change in CDVA in surgical eyes and in both eyes from baseline (preoperative) to 60 months.

Table 2. Refraction and monocular visual acuities in eyes with explanted corneal inlay.

Measurement	Preop	12 Mo Postop	36 Mo Postop (Preexplantation)	60 Mo Postop (2 Y Postexplantation)
MRSE (D)	0.00	+0.61	+2.25	+2.00
CDVA*	0.00 (~20/20)	−0.10 (~20/16)	−0.20 (~20/12.5)	−0.10 (~20/16)
CNVA[†]	−0.10 (~J1+)	−0.20 (~J1+)	−0.20 (~J1+)	−0.20 (~J1+)
UDVA*	0.00 (~20/20)	0.00 (~20/20)	+0.20 (~20/32)	0.00 (~20/20)
UIVA*	+0.20 (~20/32)	+0.20 (~20/32)	+0.60 (~20/80)	+0.40 (~20/50)
UNVA[†]	+0.40 (~J6)	+0.30 (~J5)	+0.50 (~J7/J8)	+0.50 (~J7/J8)

CDVA = corrected distance visual acuity; CNVA = corrected near visual acuity; MRSE = manifest refraction spherical equivalent; UDVA = uncorrected distance visual acuity; UIVA = uncorrected intermediate visual acuity; UNVA = uncorrected near visual acuity
*LogMAR (Snellen equivalent)
[†]LogMAR (Jaeger equivalent)

slightly to preoperative values (J1$^+$ ± 0.5 lines [~20/16]) (*P* < .001). At 60 months, 27 patients (87.1%) were able to read J1 or better (~20/20) monocularly, whereas all 31 patients were able to read J1 or better (~20/20) binocularly.

Complications

In 2 eyes, the inlays were recentered after 6 months because misplacement caused an insufficient increase in near and intermediate visual acuity and a decrease in UDVA. Because these eyes were among the first to have inlays implanted, late neural adaptation was initially assumed to be the reason for the lack of vision improvement. However, after 6 months with no improvement, the slightly decentered inlays were recentered and visual acuity increased significantly in the eyes of both patients. In addition, 1 patient developed flap striae after 1 month, requiring lifting and smoothing of the flap. At 3 months, interface epithelial ingrowth was observed, requiring a repeat flap lift and debridement of the epithelial cells in the interface. After a second recurrence of epithelial ingrowth, 3 10-0 nylon sutures were placed at the flap margin and removed 2 months later. No further epithelial ingrowth was observed.

During the follow-up, no inflammatory reactions were observed in the surgical eyes. There was no evidence of stromal deposits in the interface or around the inlay. However, at 36 months, corneal epithelial iron deposits developed in 18 eyes (56.3%). These appeared as central, spot-like iron deposits (similar to deposits after epikeratophakia) in a half-moon shape in the inferior cornea, parallel to the outer margin of the inlay, or in a ring formation (similar to a Fleischer ring and to iron lines reported after radial keratotomy) in 1 or both areas. The location of the iron deposits was positively correlated with characteristic postoperative topographic changes; corneal topography showed corneal flattening in the areas of the eyes where iron

deposits formed. No additional patients developed iron deposits from 36 to 60 months postoperatively.

The inlay was removed from 1 eye after the 36-month follow-up because of the patient's dissatisfaction with vision after a hyperopic shift occurred. Table 2 shows the eye's refraction and visual acuities before and 24 months after removal of the inlay. Figure 5 shows cumulative images of 2 eyes without refractive shift (*A* and *B*) and 2 eyes with the highest hyperopic shift (*C* and *D*; +3.5 D and +3.75 D, respectively). Images *A1–D1* are from preoperative topography, and *A2–D2* and *A3–D3* are from the slitlamp examination at 60 months. The topographic images show that the elevation above the inlay is more pronounced in hyperopic-shift patients, but even in patients without refractive shift, the topographic red ring is a typical finding in eyes with this earlier Kamra model and implantation technique.

Patient Satisfaction

Table 3 shows the mean preoperative and 60-month postoperative patient satisfaction. Asked whether they would have the procedure again, 26 patients (83.9%) said yes, 3 (9.7%) were undecided, and 2 (6.4%) said no. Unsatisfied patients (undecided or said no) showed a pattern of hyperopic shift (mean MRSE +1.65 D) and inferior binocular UNVA (mean binocular UNVA of J5).

DISCUSSION

This prospective nonrandomized cohort study evaluated the visual acuities, complications, and patient satisfaction after implantation of an early-generation Kamra corneal inlay (model ACI7000) in nondominant eyes to surgically compensate for plano and near-plano presbyopia.

The ideal synthetic material for intracorneal use should be permeable enough to allow sufficient nutrient flow through the cornea because virtually
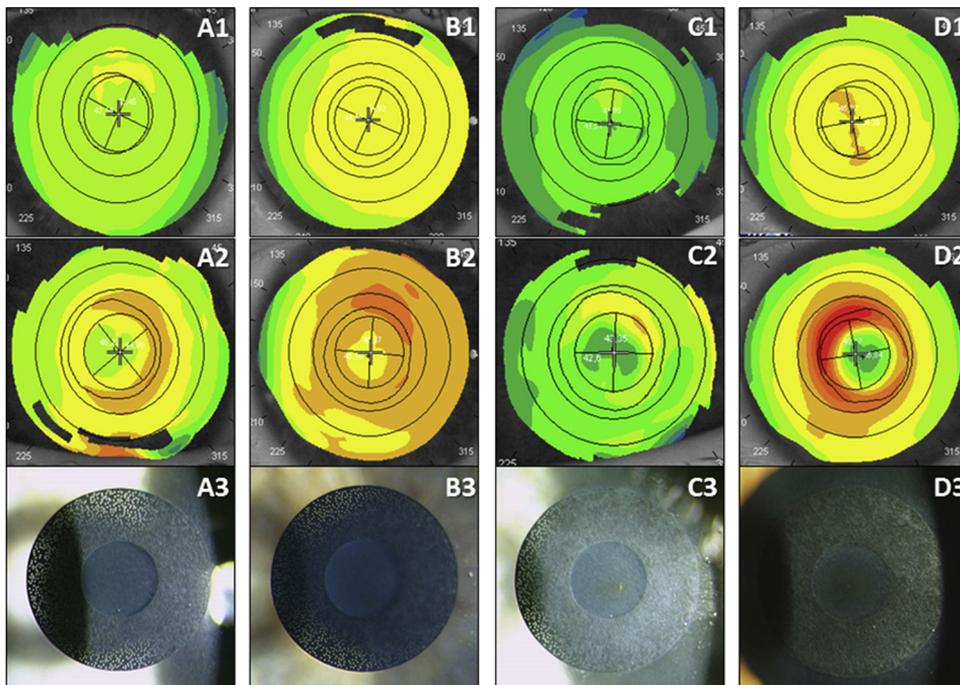
Figure 5. Topography and slitlamp images for eyes of 2 patients without refractive shift (*A* and *B*) and for eyes of 2 patients with the highest hyperopic shift (+3.50 D and +3.75 D) (*C* and *D*, respectively). Row 1 contains preoperative topography, row 2 contains 60-month topography, and row 3 contains 60-month slitlamp images. Patients with significant hyperopic shift show more pronounced elevation above the inlay as well as more haze.

all corneal nutrients come from the aqueous humor. Interrupting this flow can cause corneal thinning, transparency loss, and corneal epithelial and stromal decompensation and melt.[7] To date, we have seen no evidence of biocompatibility concerns with this type of inlay; the microperforations in the annulus seem to allow the necessary nutritional flow of glucose and other metabolic substances. Although in a study of rabbit eyes, an early increase in stromal cell death and inflammation occurred in eyes that had femtosecond laser pocket creation and Kamra inlay insertion, compared to a control group with the pocket only, no significant difference was noted between the inlay group and the control group in stromal cell death or inflammation 6 weeks after surgery.[11] In the present study, within 60 months, we saw no stromal deposits in the interface or around the inlay such as have occurred with other corneal implants, including hydrogel corneal inlays[8] and intrastromal corneal ring segments.[12]

The development of epithelial corneal iron deposits after corneal surgery is common. In such cases, confocal microscopy shows clusters of iron deposits near Bowman layer and individual dots of iron deposits in the rest of the epithelium.[13] Previous studies[13,14] reported the appearance of central and paracentral corneal iron deposits and suggested that contributing factors for these deposits might be alterations in tear-film thickness and possibly its composition and corneal epithelial basal cell storage (as a result of minute changes in corneal

topography). These deposits did not affect visual acuities, and no additional eyes developed deposits between 36 months and 60 months. With implantation of the commercially available Kamra design (ACI7000PDT), corneal topography changes and corneal epithelial iron deposition occurred less often, in 4% of eyes with this model versus in 56% with the inlay model evaluated here.[14] The inlay thinness (5 μm versus 10 μm for the earlier model), the greater number of nutritional pores (8400 microperforations versus 1600), and the modified implantation technique (insertion into a deep lamellar pocket versus under a shallow LASIK flap) seem

Table 3. Patient satisfaction.

Parameter	Mean Score* ± SD	
	Preop	60 Mo
Near tasks		
Reading small text (map)	9.4 ± 1.0	5.3 ± 3.1
Reading a book or newspaper	8.8 ± 1.5	2.6 ± 2.2
Doing fine handwork (sewing)	9.3 ± 1.0	5.5 ± 2.8
Intermediate task		
Reading the computer screen	4.9 ± 2.5	3.0 ± 2.5
Distance tasks		
Watching a movie	0.1 ± 0.4	0.9 ± 1.2
Driving at night	0.6 ± 0.8	3.8 ± 2.8

*Scale: 0 = no problem; 7 = severe problems

to be contributing factors in the difference in observed biomechanical changes.[14]

Using monovision is simple and effective and is the most common approach to alleviating presbyopia.[15] Durrie[16] reported that UNVA in the eye corrected for near vision improved with increased contact lens power, achieving a mean UNVA of 0.29 logMAR (~20/39) using a +1.50 D lens and of 0.11 logMAR (~20/26) using a +2.50 D lens. Concomitantly, the UDVA in the eye corrected for near vision decreased with increasing lens power and became worse than 0.6 logMAR (~20/80) when using a +2.50 D lens. Stereopsis is one of the functions of binocular vision that can be seriously compromised by applying monovision. Unlike monovision, the Kamra corneal inlay uses small-aperture optics to increase the eye's depth of focus by allowing only central collinear light rays to reach the retina. As a result, distance vision in the treated eye does not decrease as much as in eyes treated with monovision or modified monovision. Fernández et al.[15] also showed that a monocular small aperture can yield stereoacuity values similar to those attained under normal binocular vision in photopic conditions.

Unlike other surgical treatments for presbyopia, a corneal inlay can be removed easily if necessary. In a long-term follow-up of inlay removal, Yilmaz et al.[6] reported that all patients returned to within ±1.00 D of their preoperative refraction with no loss of corrected visual acuity. In our study cohort, 1 inlay was removed after 36 months, with no loss of CDVA and CNVA in the eye (Table 2).

Because only 1 eye had a CDVA of 0.2 logMAR (~20/32), we also checked that eye's CDVA using a conventional 4 m chart. Surprisingly, the CDVA at 4 m was 0.0 logMAR (~20/20). We repeated the measurements with the test-up setting of the Optec 6500P Vision Tester using different available trial frames, but were unable to achieve better CDVA results in this eye.

Yilmaz et al.[6] reported 4-year follow-up data for 39 naturally and post-LASIK emmetropic eyes in Istanbul, Turkey. All of the eyes in that long-term study had the same corneal inlay (ACI7000) implanted as in the present study, and so we did not have the benefit of recent improvements to the inlay (redesign) and the surgical technique (implantation in a corneal pocket instead of a flap). The postoperative mean binocular UNVA in the Istanbul trial was J1, with 96% of treated eyes seeing J3 or better and no significant loss of binocular UDVA.

In the present study, intermediate visual acuity with this small-aperture inlay was very good, with 87.1% seeing at least 20/32 binocularly at intermediate distance after 60 months and with significant reported improvements in the ability to perform intermediate tasks without correction.[9,17] For presbyopic eyes, this is a major advantage over multifocal options, which typically provide relatively poor intermediate visual acuity.[1]

Clinical experience and optical modeling indicate that overall binocular visual acuity with a small-aperture inlay is optimized by leaving some residual myopia in the implanted eye.[1] Having −0.75 D of myopia results in an average depth of focus of 2.50 D and a near visual acuity of J1 or better; in perfect emmetropic eyes, the resultant depth of focus decreases to approximately 1.75 D.[18] Although small-aperture inlays are forgiving of astigmatism and higher-order aberrations, correcting astigmatism of more than 0.50 D will also improve performance.[18]

There are many peer-reviewed articles about the Kamra inlay,[1,5–7,9–11,13–15,17–19] but only a few regarding the other available inlay technologies.[2,4] Yilmaz et al.[6] reported safely performing cataract surgery using small-incision phacoemulsification steps, including capsulorhexis with intraocular lens (IOL) implantation in the capsular bag in 2 corneal inlay patients. Both cataract eyes had a final UNVA of 20/20 or better, indicating the inlay remained effective after surgery. They concluded that pseudophakic eyes after implantation of a monofocal IOL might be good candidates for a small-aperture corneal inlay to compensate for the loss of near visual acuity.[6] Recent papers indicate this technique also can be performed safely in post-LASIK emmetropic eyes in conjunction with a LASIK correction as a simultaneous or 2-step procedure.[5,6,9,19]

Only 1 peer-reviewed article about a clinical trial involving the Flexivue Microlens has been published.[4] In that trial, this refractive optic inlay in was implanted in the nondominant eye in 47 emmetropic presbyopic patients 45 to 60 years old; the patients were followed for 12 months. After this bifocal optic was implanted, the MRSE changed from +0.66 ± 0.35 D to −1.95 ± 1.32 D, improving the binocular UNVA from 0.53 ± 0.13 logMAR (~20/60) to 0.13 ± 0.13 logMAR (~20/25). However, this refractive shift also decreased the monocular UDVA from 0.06 ± 0.09 logMAR (~20/25) to 0.38 ± 0.15 logMAR (~20/50), representing a mean loss of 3 lines. Thirty-seven percent of patients lost 1 line of monocular CDVA, and no patient lost 2 or more lines. The binocular UDVA and CDVA were not affected by the procedure. Twelve months after implantation, 93.75% of patients were spectacle independent; however, 12.50% experienced halos and 12.50% experienced glare.

Only 1 peer-reviewed clinical trial is currently available about the Raindrop inlay that reshapes the

corneal surface. Barragan Garza et al.[2] reported 1-year results of 20 emmetropic and presbyopic patients (48 to 55 years of age) after monocular implantation in the nondominant eye. Twelve months after implantation, the mean monocular and binocular UNVA were 0.1 logMAR (~20/25) or better and the mean monocular UDVA was 0.2 logMAR (~20/32) or better. A minimal mean CDVA and CNVA loss of 0.02 logMAR occurred, and no patient lost 2 or more lines. One patient required inlay removal because of poor UDVA (0.4 logMAR; ~20/50). One month after removal, the UDVA returned to 0.0 logMAR (~20/20). At 1 year, 16 of the remaining 19 patients seldom or never wore glasses and all 19 were satisfied or very satisfied with their overall vision.

Although in the present study, results regarding improvement in UNVA and UIVA and preservation of UDVA remained stable until 36 months, a statistically significant decrease in UNVA, UIVA, and UDVA occurred between 36 months and 60 months. We concluded that these changes were caused by a natural age-related hyperopic shift over the 60-month follow-up that was evident in the inlay eyes and in the untreated fellow eyes. Hyperopic shifts in this age group are known from epidemiological trials in the Beaver Dam Eye Study,[20] which reported a mean change in refraction of +0.48 D within 10 years of follow-up in eyes of patients aged 43 to 59 years, and the Liwan Eye Study,[21] which showed that the MRSE tends to become hyperopic at 60 years of age and then shifts toward myopia at 75 years.

There is no published literature about wound-healing response or foreign-body reaction after Kamra inlay implantation. All patients heal differently, and some patients might experience a more aggressive response than others. When implanting a device in the cornea, a healing response should be anticipated, although the incidence of such is low, as evidenced by our study. In a wound-healing response, what typically occurs is stromal thickening over the inlay annulus. This thickening translates forward to the corneal surface and causes central flattening over the inlay aperture, which results in a hyperopic refractive shift. In this study, the inlay was thicker, implanted under a flap, and not as deeply implanted in the cornea than what is currently practiced. All 3 factors affect topography. Also, corneal haze might form (Figure 5).

In this clinical trial, topical steroids were used to treat 3 eyes with hyperopic shifts and corneal haze formation. We know now that a small subset of patients might be unresponsive to or might rebound after the first round of steroid therapy. In our clinical trial, the guidance was to continue steroids to try to keep the inlay in the eye. However, now we would recommend early removal of the inlay[A] because the eyes of such

patients will likely never adapt to it. Further evaluation of the wound-healing response using the current, state-of-the-art procedure is needed. As they become available, long-term results of the current (corneal pocket) implantation technique and the new inlay design will yield additional important information.

From the long-term data in this study, we conclude that Kamra corneal inlay implantation is an effective and safe method for the surgical compensation of plano and near-plano presbyopia.

WHAT WAS KNOWN
- Monocular implantation of a small-aperture optic in the cornea of the nondominant eye safely and effectively compensates for presbyopia by increasing the depth of focus.

WHAT THIS PAPER ADDS
- The small-aperture corneal inlay safely and effectively compensated for plano and near-plano presbyopia by increasing the depth of focus.
- Although improvement of UNVA and UIVA and preservation of UDVA were stable until the 36-month follow-up, a statistically significant decrease in UNVA, UIVA, and UDVA occurred between 36 months and 60 months in response to normal age-related hyperopic changes.

REFERENCES

1. Lindstrom RL, MacRae SM, Pepose JS, Hoopes PC Sr. Corneal inlays for presbyopia correction. Curr Opin Ophthalmol 2013; 24:281–287
2. Barragan Garza EB, Gomez S, Chayet A, Dishler J. One-year safety and efficacy results of a hydrogel inlay to improve near vision in patients with emmetropic presbyopia. J Refract Surg 2013; 29:166–172
3. Bouzoukis DI, Kymionis GD, Limnopoulou AN, Kounis GA, Pallikaris IG. Femtosecond laser-assisted corneal pocket creation using a mask for inlay implantation. J Refract Surg 2011; 27:818–820
4. Limnopoulou AN, Bouzoukis DI, Kymionis GD, Panagopoulou SI, Plainis S, Pallikaris AI, Feingold V, Pallikaris IG. Visual outcomes and safety of a refractive corneal inlay for presbyopia using femtosecond laser. J Refract Surg 2013; 29:12–28
5. Yilmaz ÖF, Bayraktar S, Agca A, Yilmaz B, McDonald MB, van de Pol C. Intracorneal inlay for the surgical correction of presbyopia. J Cataract Refract Surg 2008; 34:1921–1927
6. Yilmaz ÖF, Alagöz N, Pekel G, Azman E, Aksoy EF, Çakır H, Bozkurt E, Demirok A. Intracorneal inlay to correct presbyopia: long-term results. J Cataract Refract Surg 2011; 37:1275–1281
7. Seyeddain O, Hohensinn M, Riha W, Nix G, Rückl T, Grabner G, Dexl AK. Small-aperture corneal inlay for the correction of presbyopia: 3-year follow-up. J Cataract Refract Surg 2012; 38:35–45

8. Mulet ME, Alio JL, Knorz MC. Hydrogel intracorneal inlays for the correction of hyperopia; outcomes and complications after 5 years of follow-up. Ophthalmology 2009; 116:1455–1460

9. Tomita M, Kanamori T, Waring GO IV, Yukawa S, Yamamoto T, Sekiya K, Tsuru T. Simultaneous corneal inlay implantation and laser in situ keratomileusis for presbyopia in patients with hyperopia, myopia, or emmetropia: six-month results. J Cataract Refract Surg 2012; 38:495–506

10. Seyeddain O, Riha W, Hohensinn M, Nix G, Dexl AK, Grabner G. Refractive surgical correction of presbyopia with the AcuFocus small aperture corneal inlay: two-year follow-up. J Refract Surg 2010; 26:707–715

11. Santhiago MR, Barbosa FL, Agrawal V, Binder PS, Christie B, Wilson SE. Short-term cell death and inflammation after intracorneal inlay implantation in rabbits. J Refract Surg 2012; 28:144–149

12. Ruckhofer J, Twa MD, Schanzlin DJ. Clinical characteristics of lamellar channel deposits after implantation of Intacs. J Cataract Refract Surg 2000; 26:1473–1479

13. Dexl AK, Ruckhofer J, Riha W, Hohensinn M, Rueckl T, Messmer EM, Grabner G, Seyeddain O. Central and peripheral corneal iron deposits after implantation of a small-aperture corneal inlay for correction of presbyopia. J Refract Surg 2011; 27:876–880

14. Dexl AK, Seyeddain O, Grabner G. Follow-up to "central and peripheral corneal iron deposits after implantation of a small-aperture corneal inlay for correction of presbyopia" [letter]. J Refract Surg 2011; 27:856–857

15. Fernández EJ, Schwarz C, Prieto PM, Manzanera S, Artal P. Impact on stereo-acuity of two presbyopia correction approaches: monovision and small aperture inlay. Biomed Opt Express 2013; 4:822–830. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3675862/pdf/822.pdf. Accessed October 19, 2014

16. Durrie DS. The effect of different monovision contact lens powers on the visual function of emmetropic presbyopic patients (an American Ophthalmological Society thesis). Trans Am Ophthalmol Soc 2006; 104:366–401. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1809906/pdf/1545-6110_v104_p366.pdf. Accessed October 19, 2014

17. Dexl AK, Seyeddain O, Riha W, Hohensinn M, Rückl T, Reischl V, Grabner G. One-year visual outcomes and patient satisfaction after surgical correction of presbyopia with an intracorneal inlay of a new design. J Cataract Refract Surg 2012; 38:262–269

18. Tabernero J, Artal P. Optical modeling of a corneal inlay in real eyes to increase depth of focus: optimum centration and residual defocus. J Cataract Refract Surg 2012; 38:270–277

19. Tomita M, Kanamori T, Waring GO IV, Nakamura T, Yukawa S. Small-aperture corneal inlay implantation to treat presbyopia after laser in situ keratomileusis. J Cataract Refract Surg 2013; 39:898–905

20. Lee KE, Klein BEK, Klein R, Wong TY. Changes in refraction over 10 years in an adult population: the Beaver Dam Eye Study. Invest Ophthalmol Vis Sci 2002; 43:2566–2571. Available at: http://www.iovs.org/content/43/8/2566.full.pdf. Accessed October 19, 2014

21. He M, Huang W, Li Y, Zheng Y, Yin Q, Foster PJ. Refractive error and biometry in older Chinese adults: the Liwan Eye Study. Invest Ophthalmol Vis Sci 2009; 50:5130–5136. Available at: http://www.iovs.org/content/50/11/5130.full.pdf. Accessed October 19, 2014

OTHER CITED MATERIAL

A. Data on file. Acufocus, Inc., Irvine, California, USA

First author:
Alois K. Dexl, MD, MSc

Department of Ophthalmology, Paracelsus Medical University, Salzburg, Austria