Implantable inlay devices for presbyopia: the evidence to date

EM Arlt
EM Krall
S Moussa
G Grabner
AK Dexl

Department of Ophthalmology,
Paracelsus Medical University
Salzburg, Salzburg, Austria

Abstract: By 2020, it is estimated that 2.1 billion people will be presbyopic, and the demand for spectacle independence in this group is growing. This review article provides an overview of the three commercially available corneal inlays for the correction of presbyopia. Safety, efficacy, visual outcomes, and complications are analyzed for all three inlays according to published peer-reviewed data.

Keywords: corneal inlay, presbyopia, refractive surgery, small-aperture inlay, corneal reshaping inlay, refractive optic inlay

Introduction

Presbyopia is the most common refractive error, currently affecting approximately 2 billion people worldwide, with a steep predicted rise to 2.1 billion in 2020.[1,2] Presbyopia itself is defined as an age-related loss of accommodation of the crystalline lens. This condition typically manifests in people over the age of 40 years and can amount to a considerable decrease in the quality of life for many of those affected.[3,4] Therefore, the general demand for spectacle independence has been growing strongly in recent times, and has made the correction of presbyopia one of the most important last frontiers of refractive surgery.

Two basic principles are underlying all therapeutic options for presbyopia: one possibility is the enhancement of depth of focus; whereas the second option is restoration of accommodation.[5] Many surgical procedures have been studied over the years, and the issue has been tackled in different ways; corneal, lenticular, and scleral approaches were used to fight the pathology of presbyopia.

One of the early approaches for presbyopia correction was additive refractive keratoplasty, in which human donor material was added to corneal tissue to change the refraction.[6] Furthermore, Barraquer introduced the idea of corneal inlays in the late 1940s, initially as a treatment for aphakia and high myopia. These early inlays were made of flint glass or polymethyl methacrylate (PMMA) and succeeded in treating the refractive error, but to the cost of corneal necrosis and implant extrusion.[6,7]

Dohlman et al[8] introduced the use of hydrogel polymers as corneal inlays to improve nutrient and metabolic gradients in animals. Materials improved over the years, and finally Steinert introduced a well-biocompatible lens for aphakia: the Kerato-Gel lens (Allergan, Inc., Irvine, CA, USA), one of the precursors of modern corneal inlays.[9] At the moment, there are three different small-aperture intracorneal inlays commercially available: the Flexivue Microlens™ (Presbia Coöperatief U.A., Irvine, CA, USA); the Raindrop® Near Vision Inlay (ReVision Optics, Lake Forest, CA, USA); and the KAMRA™ inlay (AcuFocus Inc., Irvine, CA, USA) (Table 1).

Correspondence: Alois K Dexl
Department of Ophthalmology,
Paracelsus Medical University Salzburg,
Müllner Hauptstrasse 48, A 5020
Salzburg, Austria
Tel +43 662 4482 572 88
Fax +43 662 4482 3703
Email a.dexl@salk.at

Arlt et al

Dovepress

Clinical Ophthalmology downloaded from https://www.dovepress.com/ by 54.160.19.155 on 09-Aug-2020
For personal use only.

Table 1 Comparison of the three commercially available intracorneal inlays

	Flexivue Microlens	Raindrop inlay	KAMRA inlay
Material	Copolymer of hydroxyethyl methacrylate and methyl methacrylate, containing an ultraviolet blocker	Hydrogel	Polyvinylidene fluoride
Design and size	The central 1.8 mm diameter is plano; the annular peripheral zone has an add power	Positive meniscus-shaped, diameter of 2 mm, and a center thickness of 32 μm	5 μm thin microperforated artificial aperture, with a total diameter of 3.8 mm and a central aperture of 1.6 mm
Underlying principle	Corneal multifocality is the basic principle of the Flexivue Microlens inlay by changing the refractive power of the central cornea to improve near vision performance	Alters the eye's refractive power by increasing the central radius of curvature of the cornea overlying the implant	Increases depth of focus through the pinhole aperture
Implantation depth	280–300 μm	150 μm	170–200 μm
Possibility of combination with other refractive surgery	No peer-reviewed data available	Combination with LASIK possible, peer-reviewed data available	Combination with LASIK possible, peer-reviewed data available
Number of peer-reviewed studies available published until June 2014	1	2	21

Abbreviation: LASIK, laser in situ keratomileusis.

Besides inlays, corneal refractive surgery includes the creation of monovision in laser in situ keratomileusis (LASIK), which dates back long ago, and multifocal ablations (presbyLASIK).

Monovision initially became popular in the 1960s in contact lens wearers; a change of refraction in the nondominant eye to −1.0 up to −2.0 diopters (D) compared to 0 D was then a modern approach to treat presbyopia. This voluntary anisometropia can also be achieved permanently with the help of surgery and soon became a hot topic in the age of laser technology and LASIK.[10] Monovision is still a well-demanded option for presbyopia correction and is especially popular in the US.

LASIK can also be used to create a multifocal cornea.[11,12] Profiles for corneal multifocal ablation in LASIK were developed by Alió et al[13] under the label presbyLASIK. More recently, Reinstein et al[14] presented the results of new aspheric ablation profiles and a micromonovision protocol showing promising results.

Both monovision and presbyLASIK share the negative side effects of reduced distance visual acuity, reduced stereopsis, reduced contrast sensitivity, and reduced quality of vision. Monovision patients even have a higher enhancement rate than patients who have standard LASIK correction.[10]

The lenticular approach to reverse the age-related phenomenon of presbyopia is either cataract surgery or, in early-stage cases with no lens opacifications, a refractive lens exchange. There is a variety of different intraocular lenses (IOLs) ranging from multifocal to monovision, and even accommodating IOLs.

Refractive lens exchange with implantation of multifocal or accommodating IOLs has shown to reduce the dependence on reading glasses, although one has to consider the relatively invasive procedure – ie, intraocular surgery with all associated risks (complications in lens exchange, biometric errors, photopic phenomena, reduced contrast sensitivity, loss of best-corrected vision and, finally, patient dissatisfaction) compared to other less-invasive procedures conducted in the early stages of presbyopia.[15]

Other procedures described for the treatment of presbyopia with little to no success at the cost of relatively high risks are scleral expansion and anterior sclerotomy techniques.[16,17]

Corneal inlays

One of the great achievements in the history of refractive surgery was the development and adaption of corneal inlays to treat presbyopia. The biggest advantage of corneal inlays is the fact that they are additive and do not remove tissue, and they therefore preserve future options for any kind of presbyopia correction.[1]

At present, there are three different types of corneal inlays commercially available. There is the group of refractive inlays that alters the index of refraction by the means of a bifocal optic (Flexivue Microlens), the group of reshaping inlays that makes changes in corneal curvature (Raindrop), and finally the third group of inlays that relies upon the principle of small-aperture optics to increase depth of focus (KAMRA).

130

submit your manuscript | www.dovepress.com

Dovepress

Clinical Ophthalmology 2015:9

Refractive optic inlays

Flexivue Microlens

Corneal multifocality is the basic principle of the Flexivue Microlens inlay by changing the refractive power of the central cornea to improve near vision performance. Similar to a multifocal design, the Microlens has a plano central zone to provide distance vision surrounded by rings of varying add power for intermediate and near vision.

The Flexivue Microlens is based on a precursor known as the InVue lens. On the Flexivue Microlens itself, only one peer-reviewed study is available.[18]

The Flexivue Microlens is a transparent, hydrogel-based, concave–convex disc made out of an optically clear copolymer of hydroxyethyl methacrylate and methyl methacrylate containing an ultraviolet blocker with a 3 mm diameter and ~15–20 µm thickness, depending on the additional power.[19]

The lens material has a refractive power of 1.4583 and a light transmission of 95% at a wavelength above 410 nm. The central 1.8 mm diameter is plano, and the annular peripheral zone has an add power. This inlay power ranges from +1.25 to +3.0 D in 0.25 D increments. At the center of the disc, a 0.15 mm hole facilitates the transfer of oxygen and nutrients into the cornea through the lens.[18]

For distance vision, rays that pass through the optically neutral zone of the implant (ie, the central zone) and the free peripheral corneal tissue without the lens-added refractive effect will be sharply focused on the retina. Rays passing through the refractive peripheral zone will be focused in front of the retina and are of no significance in distance vision. The opposite applies for near vision – rays passing through the peripheral refractive zone of the inlay will be focused on the retina, whereas rays passing through the central zone of the implant are out of focus behind the retina, and rays passing through the peripheral clear cornea will be blocked by the pupil.

The surgical procedure is performed under topical anesthesia. An intracorneal pocket is created using a femtosecond laser with the means of a full lamellar cut at a depth of 280 µm, a diameter of 9.0 mm, and with a line/spot separation of 2/2 µm. In this study, the tunnel was created from the temporal incision cut to the center of the cornea corresponding to the visual axis. Furthermore, a special injector was used to inject the implant into its pocket at the line of sight, which was determined previously with a microscope and a centration device of the excimer laser.[18]

In their study, Limnopoulou et al[18] showed the refractive outcome of 47 patients implanted with the Flexivue Microlens with a follow-up term of 12 months. One year postoperatively, the mean uncorrected near visual acuity (UNVA) significantly improved from 0.68±0.03 logarithm of the minimum angle of resolution (logMAR) to 0.14±0.9 logMAR in the operated eyes and from 0.53±0.13 logMAR preoperatively to 0.13±0.13 logMAR binocularly ($P<0.001$). UNVA of the operated eyes was 20/32 or better in 75% of patients 12 months after inlay implantation. The mean uncorrected distance visual acuity (UDVA) in operated eyes significantly decreased from 0.06±0.09 logMAR preoperatively to 0.38±0.15 logMAR, whereas it did not change significantly binocularly.

In this study, no intraoperative or postoperative complications were encountered, and no removal or replacement of the inlay was performed. However, only this study has been conducted on the current commercially available Flexivue Microlens (comprising 47 patients), and no long-term follow-up results are yet available.

ICOLENS

Similar to the Flexivue Microlens design, the ICOLENS™ (Neoptics AG, Hünenberg, Switzerland) is a hydrogel microlens with a central zone for distance vision and a peripheral zone for near vision correction. There have been reports at professional meetings from clinical trials in Europe, but no publications are yet available in the peer-reviewed literature.[20]

Cornea reshaping inlays

The Raindrop inlay

The Raindrop corneal inlay is a clear, permeable, positive meniscus-shaped hydrogel implant. It has a diameter of 2 mm, a center thickness of 32 µm, and approximately the same refractive index as the cornea.

Therefore, the inlay has no intrinsic refractive power itself, but it alters the eye's refractive power by increasing the central radius of curvature of the cornea overlaying the implant. Because the inlay is thinner at the edge than in the center, the increase in anterior corneal height transitions from the region anterior to the inlay diameter through an intermediate region and back to the unaltered cornea.[21] It thus creates a hyperprolate corneal shape, resulting in a multifocal cornea. The hydrogel material used for the implant is highly permeable and allows for the free passage of oxygen and nutrients, therefore ensuring stable corneal conditions. As it is the case for the other inlays, the Raindrop is implanted in the nondominant eye, but relatively shallowly in the cornea (130–150 µm).[21,22] At the moment, there are two peer-reviewed articles on the Raindrop inlay that have reported on the use and results following implantation of the Raindrop.[21,22]

Garza et al[21] and Chayet et al[22] used keratotomy according to their standard clinical procedures and created a flap with a diameter greater than 8 mm and a depth of 130–150 μm using a femtosecond laser. The Raindrop inlay was placed in the stromal bed by the inserter provided by the manufacturer and correctly positioned over the center of the pupil. Finally, the flap was replaced over the inlay on the corneal bed.[21,22]

Garza et al[21] reported their results 12 months after implanting the device in 19 presbyopic emmetropes. One hundred percent of patients achieved UNVA of 0.2 logMAR or better in the operated eye. The mean UNVA was better than 0.1 logMAR at all visits, including the final follow-up after 12 months. One hundred percent of patients achieved a binocular UNVA of 0.18 logMAR or better. By 1 month postoperatively, mean binocular UDVA was 0.01 logMAR and remained at this level or better until the last postoperative visit.[21]

The mean photopic contrast sensitivity in the implanted eye was similar to the preoperative levels both at the 6-month and 12-month follow-up visits. The mean change in contrast sensitivity was <0.3 log units at all frequencies. The authors suggest that there is no clinical significance to this mean change of contrast sensitivity in the study group, but they point to the trend to significance in a larger group.[21] However, postoperative sensitivity values were within the normal range of phakic eyes.[21,23,24]

In this study, a patient questionnaire concerning spectacle wear and satisfaction was completed by all patients. After 12 months, 95% of patients reported that they were satisfied or very satisfied with their near and intermediate vision. All patients reported that they were very satisfied with their distance vision and the overall visual outcome. Eighty-four percent of patients stated that they used glasses rarely, if ever.

Two adverse events occurred in this study: one patient was not satisfied with the postoperative distance vision, and the device was removed after 6 months. Another patient required recentration. Both patients were satisfied after the correcting procedure.

Chayet et al[22] presented the results of 16 hyperopic presbyopic patients implanted with the Raindrop inlay immediately after the laser corneal correction of the hyperopia. The mean UNVA in the implanted eye was 20/21 (Snellen) ±0.04 (logMAR) after 12 months. The mean uncorrected intermediate visual acuity (UIVA) was 20/26±0.07 and the UDVA was 20/31±0.14 after 12 months. The mean binocular UNVA was 20/21±0.03 after 12 months. The mean binocular UIVA was 20/26±0.08, and the mean UDVA was 20/19±0.11 after 12 months.

Patient satisfaction questionnaires were completed by the patients in this study as well. Fourteen out of 16 patients reported being satisfied or very satisfied with their near, distance, and overall vision. Reports of halos and glare, which can be problematic for post-LASIK patients,[25] were minimal in this study.[22]

In one patient, the device was explanted due to recurrent haze after 9 months. After 12 months, no adverse sequelae were reported in this patient. Neither contrast sensitivity nor corneal stability measured by endothelial cell count was examined or tested in this study.

Inlays with small-aperture optics
The KAMRA inlay
The KAMRA inlay is the one inlay that has been studied the most among its class. There are reports on its implantation in natural emmetropes, post-LASIK emmetropes, in conjunction with LASIK correction as a simultaneous or two-step procedure, and pseudophakes after implantation of a monofocal IOL.[2,4,22,25–30] The KAMRA inlay is approved in 50 countries outside the US with nearly 20,000 inlays implanted today worldwide.[1,31]

The current generation of the inlay (model ACI7000PDT) is a 5 μm thin microperforated artificial aperture, with a total diameter of 3.8 mm and a central aperture of 1.6 mm made of polyvinylidene fluoride with incorporated nanoparticles of carbon. The opaque permeable material has a light transmission of 6.7%; it further features a pseudorandom microperforation pattern consisting of 8,400 holes ranging in size from 5–11 μm in diameter to allow water and nutrition flow in order to prevent corneal thinning and epithelial decompensation.

Based on the pinhole effect, the inlay increases depth of focus and consequently improves near and intermediate visual acuity. The KAMRA does not split light between near, intermediate, and distance focal points. The patient, therefore, maintains his binocular summation despite the monocular implantation in the nondominant eye.[32] The inlay is – as is the case for its other inlay companions – implanted in the nondominant eye to improve near and intermediate visual acuity with minimal compromise to distance vision.

Inlay implantation is now usually performed in a lamellar pocket that is 220 μm or deeper, created with a full-spectrum laser using a 6×6 spot/line separation or the equivalent. It used to be inserted under a shallower flap (170–180 μm). If the procedure is combined with LASIK, a dual interface technique is used. First, the excimer laser correction is performed under a thin flap; secondly, the inlay is implanted

at least 100 µm below in a pocket interface. The inlay is always inserted directly in the line of sight.

Making a pocket interface by femtosecond laser minimizes the impact on the corneal nerves when compared to creating a flap, in which more nerve-fiber bundles are cut; as a result, the risk of dry eye disease is higher and this might affect outcomes. Interface thickness is another important factor as well; one study recommended using a thicker flap for intracorneal inlay implantation to avoid flap complications.[33]

Another factor is using a femtosecond laser rather than a microkeratome to optimize intrastromal pockets. Femtosecond lasers are known to provide more predictable flap thickness, lower incidence of LASIK-induced dry eye, quicker visual recovery, and better UDVA results than mechanical mikrokeratomes.[34–36]

Tabernero and Artal suggest – using a theoretical eye model – that the best depth of focus in KAMRA patients can be obtained with small residual myopia (−0.75 D to −1.0 D) in the inlay eye and a plano refraction in the fellow eye.[37] The manufacturer recommends this strategy as well, and some authors report successful use of this scheme.[2,4,26]

The inlay's safety has been well-documented in animal and human studies. Corneal inflammation was studied in rabbit eyes implanted with the KAMRA inlay. An early increase in stromal cell death and inflammation was shown 48 hours after surgery in eyes that underwent a femtosecond laser pocket creation and KAMRA insertion compared to eyes with pocket formation only. The difference disappeared by 6 weeks after surgery.[38]

In long-term follow-up studies in humans, no inflammatory reactions or ulcerations, no stromal fibrosis, and no significant change in endothelial cell count were described.[26,28] No stromal deposits were reported, as seen in patients with other corneal implants, including hydrogel intracorneal inlays and intracorneal ring segments.[6,30,39,40]

However, epithelial change in the form of central and peripheral iron deposits in more than 56% of eyes in a study with the ACI7000 corneal inlay, the first-generation design of the KAMRA, were described after 3 years of follow-up.[26] These changes were not associated with visual or refractive outcomes. With the new design of the KAMRA inlay, only one out of 20 patients showed these deposits without any changes in vision or refraction. The study authors assumed that the new and thinner design – as well as the now deeper implantation compared to the previous study group – further induced only minor topographic changes in the cornea.[2]

Tomita et al[4,25] have published the two largest reported series with any presbyopia correcting inlay to date. In one study, 223 eyes were implanted with the current version of the KAMRA inlay (all eyes had received LASIK treatment before).[4] In an earlier study comprising 360 eyes (180 patients), simultaneous corneal inlay implantation and LASIK were performed for presbyopia in patients with hyperopia, myopia, or emmetropia.[25]

The first study enrolled 223 eyes (223 patients) with a mean age of 53.6 years (range: 44–65 years) and a mean manifest spherical equivalent of −0.18 D (range: −1.00 to +0.50 D). The mean UDVA in the operated eye decreased one line from 20/16 preoperatively to 20/20 6 months postoperatively (*P*<0.001). The mean UNVA improved four lines from Jaeger (J) 8–J2 (*P*<0.001). At 6 months, significant improvements were observed in patient dependence on reading glasses and patient satisfaction with vision without reading glasses.[4]

The purpose of the earlier study was to evaluate the safety and efficacy of simultaneous KAMRA corneal inlay implantation and LASIK for the treatment of presbyopia in emmetropic, hyperopic, or myopic patients. Preoperative UDVA and UNVA were significantly different between the three groups of patients, whereas at 6 months postoperatively, no significant difference was detected.

Comparing groups, hyperopic presbyopic patients had an improvement in UDVA of three lines and in UNVA of seven lines at 6 months. Emmetropic presbyopic patients had an improvement of one line and six lines, respectively, and myopic patients, ten lines and two lines. The two-line gain in myopic patients was due to the relatively good preoperative near vision in these patients. Patient satisfaction concerning spectacle independence and overall vision was significantly increased in hyperopic and emmetropic patients postoperatively, though not in myopic patients, who had good UNVA preoperatively. Most patients in this study were complaining of dry eye disease preoperatively, as well as glare, halos, and night vision disturbances preoperatively, and the data did not change significantly 6 months postoperative.[25]

In regard to long-term results, Yilmaz et al[28] published data on a 4-year follow-up on 39 patients, Seyeddain et al[26] published 3-year follow-up data in 32 patients, and Dexl et al[41] published 5-year follow-up results in 32 patients. All these patients had an earlier version of the KAMRA inlay (model ACI7000) and, therefore, did not have the benefits of recent improvements in surgical techniques (ie, the pocket implantation technique and advancement of the device itself) (Table 2).

Table 2 Peer-reviewed data on the three commercially available intracorneal inlays

Inlay type	Author/study	Patients/eyes	Follow-up	UNVA (mean values [Snellen equivalent])		UIVA (mean values [Snellen equivalent])		UDVA (mean values [Snellen equivalent])	
				Monocular (implanted eye)	Binocular	Monocular (implanted eye)	Binocular	Monocular (implanted eye)	Binocular
Flexivue Microlens	Limnopoulou et al[18]	47 emmetropic presbyopes (47 eyes)	1 year	0.14 logMAR (~20/28)	0.13 logMAR (~20/26)	Not reported	Not reported	0.38 logMAR (~20/48)	Not reported
Raindrop inlay	Garza et al[21]	20 emmetropic presbyopes (20 eyes)	1 year	<0.1 logMAR (<~20/25)	<0.1 logMAR (<~20/25)	<0.2 logMAR (<~20/32)	Not reported	<0.2 logMAR (<~20/32)	<0.1 logMAR (<~20/25)
	Chayet et al[22]	16 hyperopic emmetropic (32 eyes: LASIK in 32 eyes; implantation of the inlay in 16 eyes) eyes	1 year	20/21	20/21	20/26	20/26	20/31	20/19
KAMRA inlay	Dexl et al[32]	24 patients (24 eyes)	1 year	20/25	20/25	20/25	20/20	20/20	20/16
	Dexl et al[42]	24 patients (24 eyes)	2 years	Mean reading acuity at best distance improved significantly from 0.33 logRAD to 0.23 logRAD		Not applicable	Not applicable	20/20	20/16
	Dexl et al[41]	32 patients (32 eyes)	5 years	J3 (~20/30)	J2 (~20/25)	0.2 logMAR (~20/32)	0.1 logMAR (~20/25)	0.1 logMAR (~20/25)	−0.1 logMAR (~20/16)
	Huseynova et al[30]	13 patients (13 eyes)	3 months	J4 (~20/32)	Not reported	Not reported	Not reported	Mean: 20/20	Not reported
	Seyeddain et al[2]	24 patients (24 eyes)	2 years	20/25	20/25	20/25	20/20	20/20	20/16
	Seyeddain et al[27]	32 patients (32 eyes)	2 years	J2 (~20/25)	J1 (~20/20)	20/25	20/20	20/20	20/16
	Seyeddain et al[26]	32 patients (32 eyes)	3 years	J1 (~20/20)	J1 (~20/20)	20/25	20/20	20/20	20/16
	Tomita et al[4]	223 patients (223 eyes)	6 months	J2 (~20/25)	J2 (~20/25)	Not reported	Not reported	20/20	20/12.5
	Tomita et al[25]	180 patients (360 eyes: LASIK in 360 eyes; implantation of the inlay in 180 eyes)	6 months	Hyperopic group: 0.18 logMAR; (~20/30) Emmetropic group: 0.10 logMAR; (~20/25) Myopic group 0.12 logMAR (~20/26)	Not reported	Not reported	Not reported	Hyperopic group: −0.04 logMAR; (~20/18) Emmetropic group: −0.07 logMAR; (~20/17) Myopic group: −0.01 logMAR (~20/20)	All hyperopic patients ≤0.0 logMAR; (~20/20) All emmetropic patients ≤0.0 logMAR; (~20/20) All myopic patients: ≤0.0 logMAR (~20/20)
	Yilmaz et al[28]	39 patients (39 eyes)	4 years	Not reported	20/20	Not reported	Not reported	Not reported	20/25

Abbreviations: UNVA, uncorrected near visual acuity (if specified in studies at 16 inches); UIVA, uncorrected intermediate visual acuity (if specified in studies at 32 inches); UDVA, uncorrected distance visual acuity; logMAR, logarithm of the minimum angle of resolution; LASIK, laser in situ keratomileusis; logRAD, logarithm of reading acuity determination; J, Jaeger.

This previous version of the KAMRA inlay (ACI7000) differs from the now commercially available KAMRA inlay (ACI7000PDT). The commercially available version is thinner (5 μm versus 10 μm) and has several smaller laser-etched porosity holes (8,400 holes ranging in diameter from 5–10 μm versus 1,600 with a diameter of 25 μm), with an average light transmission through the annulus of the inlay of 6.7% versus 7.5%. These changes reduce visual symptoms experienced by patients implanted with the earlier device.

However, all three studies showed safe and good results for the prior generation of the KAMRA inlay. Mean UNVA in the 3-year and 4-year follow-up studies was J1 with 96%–97% of treated eyes seeing J3 or better. Preoperative and postoperative binocular UDVA did not change significantly. Intermediate visual acuity was found to be satisfactory with this device, with 91% of patients being able to see at least 20/32.[26,28]

The 5-year follow-up shows the following results: mean UNVA and UIVA in the surgical eye improved significantly after 1 year; remained stable for 36 months; and decreased slightly until the last follow-up. The same pattern was seen for both binocular UNVA and UIVA. Mean UDVA in the surgical eye showed a slight decrease at 1 year, remained stable until the 3-year follow-up as well, and showed an additional slight decrease until the last follow-up. In the 5-year follow-up time interval, four adverse events occurred. One patient was dissatisfied with his or her vision after a hyperopic shift and required removal of the implant. Two other inlays were recentered 6 months after implantation. Another patient developed epithelial ingrowth soon after implantation; this issue was solved by performing a flap lift and positioning a nylon suture at the flap margin for 2 months. In conclusion, the 5-year long-term follow-up showed increased monocular and binocular UNVA and UIVA, while slightly compromising monocular and binocular UDVA in emmetropic presbyopic patients.[41]

The ability to perform common daily tasks without glasses might be – at least from the patient's point of view – a better indicator of functional success than actual visual acuity. Dexl et al[42] evaluated the change in reading performance parameters after monocular KAMRA inlay (ACI7000PDT) implantation in 24 naturally presbyopic emmetropic patients over 2 years. The following parameters were evaluated using the Salzburg Reading Desk™ (SRD Vision, LLC, Little Neck, NY, USA): bilateral uncorrected reading acuity; reading distance; mean and maximum reading speed; and the smallest log-scaled print size.

Reading distance decreased significantly, whereas mean reading acuity at best distance improved significantly, and the smallest print size improved significantly. Reading speed metrics showed a slight increase, but this was not statistically significant.

Seyeddain et al[2] found a statistically significant reduction in contrast sensitivity after 24 months in the surgical eye. These findings were measured under photopic conditions at higher spatial frequencies. Contrast sensitivity was also reduced binocularly under mesopic conditions at the highest measured spatial frequency. One has to point to the fact, though, that these postoperative contrast sensitivity scores remained within the range of the normal population at all frequencies postoperatively. Thus, implantation of the inlay does not appear to cause any localized changes or scotomas in the visual field.[1]

Discussion

Increasing experience and evolving technology in corneal inlays and their implantation has made them a favorable therapeutic option in presbyopic patients. Above all, the patient selection for an appropriate procedure and counseling is important. Data on the Flexivue Microlens and KAMRA inlay have shown that the thinner the inlay the better and, furthermore, that a deep placement in the cornea is best. For the KAMRA inlay, more and smaller fenestrations were introduced to ensure better nutrition and to limit unwanted rays of defocused light through the opaque device.

For all three known corneal inlays, exact positioning and centration is essential to achieve the best refractive results. Decentration of small-aperture inlays of as little as 0.5 mm can reduce image quality. Recentration can be easily and successfully accomplished with improvements in vision.[25,26,43]

None of the published studies on these corneal inlays published data on serious or sight-threatening complications. Only a few cases of epithelial ingrowth and complaints of glare, halo, dry eye, or night vision problems were named. Ingrowth was either resolved in all cases and/or did not affect the visual axis. The complaints were described by patients as being mostly mild-to-moderate, and they happened to be the same complications as those encountered after LASIK.

Only a few small-aperture intracorneal inlays were explanted due to various complications like dissatisfaction with visual outcomes; visual problems including glare, halo, and night vision problems; flap problems; or refractive shift.[25,26,28] Removal of the device is usually easily done, and problems after explantation are resolved. Yilmaz et al[28] reported in their long-term follow-up study that patients returned to within ±1 D

of their preoperative refraction after inlay removal. Furthermore, Alió et al[44] presented their data evaluating the safety of corneal inlay removal of the various types of KAMRA inlays. According to the results of this study, removal of the KAMRA inlay is safe, and this results in a good recovery of corneal topography and corneal aberrometry.[44] One of the biggest advantages of corneal inlays versus other means of presbyopic surgery, therefore, is the fact that they are additive and do not remove tissue. Future options for presbyopic correction either in the setting of pseudophakia and/or combined with laser refractive surgery is preserved.

The most clinical experience and the greatest amount of published data are on the KAMRA inlay. Also, long-term follow-up data are only available for the KAMRA inlay, which is especially important to ensure the safety and efficiency of a device. In the longest follow-up term of 5 years, the KAMRA intracorneal inlay shows very good biocompatibility. No stromal deposits as seen in other intracorneal implants, including hydrogel intracorneal inlays and intracorneal rings, were reported.[39,40]

However, the development of epithelial iron deposits was reported, although the presence of these deposits situated near Bowman's layer do not influence visual acuity at any distance. These changes seem to happen less often in patients implanted with the commercially available KAMRA design (ACI7000PDT); in addition, changes in the corneal topography seem to be more rare with this design. The reduced inlay thickness and the modified implantation technique seem to be the key factors associated with less biomechanical changes.[2] This design provides significantly increased near and intermediate vision, whereas monocular and binocular UDVA are only slightly compromised in emmetropic presbyopic patients.

Conclusion

Corneal inlays are favorable options in correcting presbyopia, with significant increases in near and intermediate vision, and only a slight decrease in distance vision. Comparing the three commercially available inlays is difficult due to the fact that there is only little data on the Flexivue Microlens and the Raindrop inlay compared to the comparatively large studies and long-term studies on the KAMRA inlay.

Disclosure

References

1. Lindstrom RL, Macrae SM, Pepose JS, Hoopes PC. Corneal inlays for presbyopia correction. *Curr Opin Ophthalmol*. 2013;24(4):281–287.
2. Seyeddain O, Bacherneg A, Riha W, et al. Femtosecond laser-assisted small-aperture corneal inlay implantation for corneal compensation of presbyopia: two-year follow-up. *J Cataract Refract Surg*. 2013; 39(2):234–241.
3. McDonnell PJ, Lee P, Spritzer K, Lindblad AS, Hays RD. Associations of presbyopia with vision-targeted health-related quality of life. *Arch Ophthalmol*. 2003;121(11):1577–1581.
4. Tomita M, Kanamori T, Waring GO, Nakamura T, Yukawa S. Small-aperture corneal inlay implantation to treat presbyopia after laser in situ keratomileusis. *J Cataract Refract Surg*. 2013;39(6):898–905.
5. Baumeister M, Kohnen T. [Accommodation and presbyopia: part 2: surgical procedures for the correction of presbyopia]. *Ophthalmologe*. 2008;105(11):1059–1073; quiz 74. German.
6. Barraquer JI. Modification of refraction by means of intracorneal inclusions. *Int Ophthalmol Clin*. 1966;6(1):53–78.
7. Choyce DP. The correction of refractive errors with polysulfone corneal inlays. A new frontier to be explored? *Trans Ophthalmol Soc U K*. 1985; 104(Pt 3):332–342.
8. Dohlman CH, Refojo MF, Rose J. Synthetic polymers in corneal surgery. I. Glyceryl methacrylate. *Arch Ophthalmol*. 1967;77(2):252–257.
9. Steinert RF, Storie B, Smith P, et al. Hydrogel intracorneal lenses in aphakic eyes. *Arch Ophthalmol*. 1996;114(2):135–141.
10. Braun EH, Lee J, Steinert RF. Monovision in LASIK. *Ophthalmology*. 2008;115(7):1196–1202.
11. Jackson WB, Tuan KM, Mintsioulis G. Aspheric wavefront-guided LASIK to treat hyperopic presbyopia: 12-month results with the VISX platform. *J Refract Surg*. 2011;27(7):519–529.
12. Pinelli R, Ortiz D, Simonetto A, Bacchi C, Sala E, Alió JL. Correction of presbyopia in hyperopia with a center-distance, paracentral-near technique using the Technolas 217z platform. *J Refract Surg*. 2008;24(5): 494–500.
13. Alió JL, Chaubard JJ, Caliz A, Sala E, Patel S. Correction of presbyopia by technovision central multifocal LASIK (presbyLASIK). *J Refract Surg*. 2006;22(5):453–460.
14. Reinstein DZ, Carp GI, Archer TJ, Gobbe M. LASIK for presbyopia correction in emmetropic patients using aspheric ablation profiles and a micro-monovision protocol with the Carl Zeiss Meditec MEL 80 and VisuMax. *J Refract Surg*. 2012;28(8):531–541.
15. Maxwell WA, Waycaster CR, D'Souza AO, Meissner BL, Hileman K. A United States cost-benefit comparison of an apodized, diffractive, presbyopia-correcting, multifocal intraocular lens and a conventional monofocal lens. *J Cataract Refract Surg*. 2008;34(11): 1855–1861.
16. Hamilton DR, Davidorf JM, Maloney RK. Anterior ciliary sclerotomy for treatment of presbyopia: a prospective controlled study. *Ophthalmology*. 2002;109(11):1970–1976; discussion 1976–1977.
17. Qazi MA, Pepose JS, Shuster JJ. Implantation of scleral expansion band segments for the treatment of presbyopia. *Am J Ophthalmol*. 2002;134(6):808–815.
18. Limnopoulou AN, Bouzoukis DI, Kymionis GD, et al. Visual outcomes and safety of a refractive corneal inlay for presbyopia using femtosecond laser. *J Refract Surg*. 2013;29(1):12–18.
19. Bouzoukis DI, Kymionis GD, Panagopoulou SI, et al. Visual outcomes and safety of a small diameter intrastromal refractive inlay for the corneal compensation of presbyopia. *J Refract Surg*. 2012;28(3):168–173.
20. Neoptics [homepage on the Internet]. Neoptics ICOLENS™ – an adaptable surgical solution for presbyopia. Huenenberg, Switzerland: Neoptics AG; 2013. Available from: www.neoptics.ch. Accessed.

21. 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(3):166–172.

22. Chayet A, Barragan Garza E. Combined hydrogel inlay and laser in situ keratomileusis to compensate for presbyopia in hyperopic patients: one-year safety and efficacy. *J Cataract Refract Surg*. 2013; 39(11):1713–1721.

23. Hohberger B, Laemmer R, Adler W, Juenemann AG, Horn FK. Measuring contrast sensitivity in normal subjects with OPTEC 6500: influence of age and glare. *Graefes Arch Clin Exp Ophthalmol*. 2007;245(12):1805–1814.

24. Pomerance GN, Evans DW. Test-retest reliability of the CSV-1000 contrast test and its relationship to glaucoma therapy. *Invest Ophthalmol Vis Sci*. 1994;35(9):3357–3361.

25. Tomita M, Kanamori T, Waring GO, et al. 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(3):495–506.

26. Seyeddain O, Hohensinn M, Riha W, et al. Small-aperture corneal inlay for the correction of presbyopia: 3-year follow-up. *J Cataract Refract Surg*. 2012;38(1):35–45.

27. 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(10):707–715.

28. Yilmaz OF, Alagöz N, Pekel G, et al. Intracorneal inlay to correct presbyopia: Long-term results. *J Cataract Refract Surg*. 2011;37(7): 1275–1281.

29. Yilmaz OF, 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(11):1921–1927.

30. Huseynova T, Kanamori T, Waring GO, Tomita M. Small-aperture corneal inlay in presbyopic patients with prior phakic intraocular lens implantation surgery: 3-month results. *Clin Ophthalmol*. 2013;7: 1683–1686.

31. AcuFocus™ [homepage on the Internet]. AcuFocus™: The Intra-Corneal Company™. Irvine, CA: AcuFocus, Inc.; 2014. Available from: www.acufocus.com. Accessed.

32. Dexl AK, Seyeddain O, Riha W, et al. 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(2):262–269.

33. Ismail MM. Correction of hyperopia by intracorneal lenses: two-year follow-up. *J Cataract Refract Surg*. 2006;32(10):1657–1660.

34. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. *J Cataract Refract Surg*. 2004;30(4):804–811.

35. Salomão MQ, Ambrósio R Jr, Wilson SE. Dry eye associated with laser in situ keratomileusis: Mechanical microkeratome versus femtosecond laser. *J Cataract Refract Surg*. 2009;35(10):1756–1760.

36. Tanna M, Schallhorn SC, Hettinger KA. Femtosecond laser versus mechanical microkeratome: a retrospective comparison of visual outcomes at 3 months. *J Refract Surg*. 2009;25(7 Suppl):S668–S671.

37. 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(2):270–277.

38. 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(2):144–149.

39. Mulet ME, Alió JL, Knorz MC. Hydrogel intracorneal inlays for the correction of hyperopia: outcomes and complications after 5 years of follow-up. *Ophthalmology*. 2009;116(8):1455–60, 1460.e1.

40. Ruckhofer J, Twa MD, Schanzlin DJ. Clinical characteristics of lamellar channel deposits after implantation of intacs. *J Cataract Refract Surg*. 2000;26(10):1473–1479.

41. Dexl AK, Jell G, Strohmaier C, et al. Long-term outcomes after monocular corneal inlay implantation for the surgical compensation of presbyopia. *J Cataract Refract Surg*. In press 2014.

42. Dexl AK, Seyeddain O, Riha W, Hohensinn M, Hitzl W, Grabner G. Reading performance after implantation of a small-aperture corneal inlay for the surgical correction of presbyopia: Two-year follow-up. *J Cataract Refract Surg*. 2011;37(3):525–531.

43. Gatinel D, El Danasoury A, Rajchles S, Saad A. Recentration of a small-aperture corneal inlay. *J Cataract Refract Surg*. 2012;38(12): 2186–2191.

44. Alió JL, Abbouda A, Huseynli S, Knorz MC, Homs ME, Durrie DS. Removability of a small aperture intracorneal inlay for presbyopia correction. *J Refract Surg*. 2013;29(8):550–556.