AcuFocus Corneal Inlay to Correct Presbyopia Using Femto-LASIK. One Year Results of a Prospective Cohort Study

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AcuFocus Corneal Inlay to Correct Presbyopia Using Femto-LASIK. One Year Results of a Prospective Cohort Study

AcuFocus korneales Inlay zur Korrektur der Presbyopie mit Hilfe von Femto-Lasik. Ergebnisse einer prospektiven Kohortenstudie nach einem Jahr

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Key words
- intracorneal inlay
- KAMRA
- presbyopia
- Femto-Lasik

Schlüsselwörter
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- KAMRA
- Presbyopie
- Femto-Lasik

Abstract

Purpose: To evaluate the safety and efficacy of the AcuFocus small aperture corneal inlay (KAMRA) for the correction of presbyopia using femto-LASIK.

Patients and Methods: This is a prospective, non-randomised cohort study including 50 presbyopic patients with hyperopia, emmetropia or mild myopia. The intracorneal inlay was implanted in the non-dominant eye using a VisuMax femtosecond laser (Zeiss 500 kHz) to create a superior-hinged flap. The inlay was centred over the visual axis. Minimum postoperative follow-up was performed for a period of 12 months.

Results: Fifty intracorneal inlays were implanted. At one year follow-up, the median uncorrected near visual acuity significantly improved from Jaeger (J)8 to J2 ($p < 0.001$). 94% of patients could read J3 or better. The median uncorrected distance visual acuity also improved from 20/32 to 20/22 ($p < 0.001$). 92% of patients could see 20/32 or better. One implant had to be recentred at four weeks follow-up. One implant was removed six months after implantation due to insufficient uncorrected near and distance visual acuity as well as slight corneal haze, which resolved four weeks later under topical treatment with fluorometholone eye drops, without any loss of best corrected distance visual acuity. No other complications occurred during the postoperative follow-up period.

Conclusion: AutoFocus Corneal Inlay (ACI), also known as KAMRA, can provide a safe, effective and, most importantly, reversible treatment for presbyopia in hyperopic, myopic and emmetropic patients.

Zusammenfassung

Hintergrund: Evaluation der Sicherheit und Effektivität von AcuFocus KAMRA kornealem Inlay.

Patienten und Methoden: Monozentrische, nicht randomisierte prospektive Kohortenstudie mit 50 hyperopen, emmetropen und myopen Patienten mit Presbyopie. Das korneale Inlay wurde mit Hilfe von VisuMax Femto-Laser (500 kHz) in die Hornhaut des nicht dominanten Auges unter einen 200 Mikrometer dünnen Flap implantiert und über die Sehachse zentriert, nachdem die Fehlsichtigkeit mit einem Zeiss MEL 80 Excimer Laser korrigiert worden war. Nachuntersuchungen wurden für mindestens 12 Monate durchgeführt.

Ergebnisse: 50 korneale Inlays wurden implantiert. Ein Jahr nach der Implantation der Inlays hat sich der mediane unkorrigierte Nahvisus von präoperativ Jaeger (J)8 auf J2 signifikant verbessert ($P < 0.001$). 94% der Patienten lasen J3 oder besser. Der mediane unkorrigierte Fernvisus hat sich auch von präoperativ 20/32 auf 20/22 signifikant verbessert ($P < 0.001$). 92% der Patienten sahen 20/32 oder besser. Bei der Kontrolle vier Wochen postoperativ musste ein Inlay rezentriert werden. Sechs Monate nach der Implantation musste ein Inlay entfernt werden, da der unkorrigierte Nah- und Fernvisus nicht ausreichend war und eine leichte Hornhauttrübung vorlag. Die Hornhauttrübung war unter der Behandlung mit Fluorometholon Augentropfen 2-mal am Tag nach 4 Wochen regredient ohne Verlust von bestkorrigiertem Fernvisus. Keine weiteren Komplikationen traten während der Nachkontrollperiode auf.

Schlussfolgerung: AcuFocus korneales Inlay (KAMRA) konnte eine sichere, effektive und vor allem reversible Behandlung der Presbyopie darstellen.

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Background

With advanced age, the crystalline lens gradually loses its flexibility, resulting in a limited ability to focus on close objects. This condition is called presbyopia and it progresses over time, thereby requiring some kind of near vision correction. Presbyopia can easily be corrected with spectacles or contact lenses, however in recent years more and more patients are interested in surgical correction of presbyopia. In the last decades several different surgical approaches to correct presbyopia at the level of cornea, crystalline lens or sclera have been developed. Corneal procedures for presbyopia correction include: monovision using microkeratome- or femto-lasik, presbyoptic-lasik, conductive keratoplasty (CK) and insertion of intracorneal inlays. At the level of crystalline lens, implantation of multifocal intraocular lenses in combination with cataract surgery or clear lens extraction is routinely performed. At the level of sclera, scleral expansion bands and anterior sclerotomy have also been reported. Although the presbyopic patients can benefit from all these procedures, none of these has been established as the ultimate solution because they all have major disadvantages.

Corneal inlays

The first attempt to correct hyperopia with an alloplastic inlay placed at the interface between the stromal bed and free corneal cap, was introduced in 1949 by Barraquer and was called keratophakia [1]. In recent years, great improvements in femtosecond laser technology and development of excellent biocompatible materials again significantly increased the interest in corneal inlays. Several new types of inlays have so far been developed. These inlays follow three different treatment approaches. First, to increase the central corneal curvature as in Raindrop Near Vision Inlay, formerly known as Vue+/PresbyLens inlay (ReVision Optics Inc., Lake Forest, CA, USA). Second, to change the corneal refractive power by placing a high index refractive corneal inlay in a stromal pocket in the center of the visual axis. The center of the lens has no refractive power thereby preserving distance vision. Near vision is corrected by the lens peripheral zone as in In-Vue corneal inlay (Biovision AG, Brüggs, Switzerland) or Flexivue Microlens (Presbia Coöperatief U.A.). The third principle is using small aperture optics to increase the depth of field as in KAMRA inlay [2] (ACI 7000 AcuFocus Inc., Bausch and Lomb, Rochester, NY, USA).

Patients and Methods

This is a prospective, non-randomized study conducted in the Eye Center Dr. Aus der Au in Freiburg/Switzerland in cooperation with the Department of Ophthalmology, Geneva University Hospitals HUG. The goal of the study was to evaluate the safety and efficacy of the AcuFocus Corneal Inlay (ACI) or KAMRA in presbyopic patients. Primary inclusion criteria for the study were the presence of presbyopia in patients between 43 and 65 years of age with uncorrected near visual acuity (UNVA) of Jaeger (J)3 or worse and distance visual acuity DVA correctable to 20/20 and a minimum central corneal thickness of ≥ 500 µm. Primary exclusion criteria were the presence of anterior or posterior segment ocular diseases and immunologic or immunosuppressive disorders. Fifty (n = 50) patients were included in the study (29 males and 21 females).

AcuFocus corneal inlay (ACI)

The new ACI or KAMRA is a 5 µm thin inlay with a 3.8 mm outer diameter and a 1.6 mm central aperture. The ACI is made of polyvinylidene fluoride (PVDF), an in vitro biocompatible material usually used in the haptics of IOLs [3]. This inlay contains 8400 small and random holes (5–11 µm) for sufficient oxygen and nutritional flow through the ACI to the stroma to maintain good corneal metabolism and prevent corneal thinning or epithelial decompensation [4] and is covered with a thin dark layer of nano-particles of carbon. The ACI uses the principle of small aperture optics to increase depth of focus and improve near visual acuity in presbyopic patients.

Pre- and postoperative examinations

Preoperatively, we performed an extensive eye examination on all patients including manifest refraction in miosis and mydriasis to identify patients with latent hyperopia, uncorrected near visual acuity (UNVA), uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), corneal topography with Pentacam (Zeiss, Jena, Germany), keratometry, intraocular pressure measurements with Goldmann applanation tonometry, detailed anterior and posterior segment examination including slit-lamp examination and optomap scaning laser of the retina (Optos plc, Scotland, United Kingdom). Eye dominance test was performed by having the patient fixate a distance object through a 2.5 cm hole in a card, asking the patient to bring the card toward his eyes, the eye that was looking through the hole on the object was chosen as dominant eye. We also performed a monovision test using soft highly gas permeable monthly contact lenses to correct the dominant eye for distance and non-dominant eye for near vision and let the patients perform their daily life. Most of the patients informed us after just one day if they were satisfied with monovision but few patients needed up to three or four days to decide. Follow-up examinations were scheduled for 1 day, 1 week, 1, 3, 6 and 12 months after implantation. Manifest refraction, UNVA, UDVA, CDVA and tonometry were obtained at all follow-up visits. The correct centration of the inlay was controlled immediately after the implantation as well as at all following visits. Postoperative subjective assessment of satisfaction was evaluated at 12-months visit.

Patient preparation and surgical technique

All femto-lasik corrections and following implantations of the KAMRA corneal inlays were performed by the same surgeon. Topical proparacaine ophthalmic solution 1 % (Alcaine, Alcon Laboratories, Inc. Fort Worth, Texas, U.S.A) was instilled shortly before the surgery. Lid and ocular adnexa were cleaned with disinfecting solution (Betaisodona, povidon-iodine, Mundipharma GmbH, Limburg, Germany). The eyes were prepared for surgery by placing a sterile drape on the eye. A lid speculum was placed to keep the eye wide open during the surgery, cornea and the fornices were irrigated with a balanced salt solution and wiped with a wet medical sponge. A superior-hinged 200 µm thick flap was created using a femtosecond laser (VisuMax Zeiss, Jena, Germany). The flap was carefully lifted and patient's defaults were corrected using a Mel 80 excimer laser (Zeiss). We have even corrected the latent hyperopia if the was over + 0.75 diopter. The inlay was carefully taken from the sterile package and was examined under the laser microscope for any possible damages. The inlay was placed on the stromal bed and the aperture of the inlay was centered based on the presurgical position of the Purkinje reflex, while the patient fixated the laser light. The inlay was

Demographic	Value
Age (y)	54.5 (range 43 to 65)
Sex (F/M, %)	42/58
Eye with inlay (R/L, n)	18/32
Median preoperative UDVA	20/32. (range 20/100 to 20/20)
Median preoperative UNVA	J8. (range J10 to J6)
Median preoperative SE	1.19D (range − 1.25 to + 2.75D)
Median preoperative spheric error	1.25D (range − 0.75 to + 3.0D)
Median preoperative cylinder error	− 0.5D (range − 0.25 to − 2.5D)
Median preoperative CDVA in none dominant eyes	20/20

Table 1 Demographics of 50 patients implanted with AcuFocus corneal inlay.

UDVA: uncorrected distance visual acuity, UNVA: uncorrected near visual acuity, CDVA: corrected distance visual acuity, SE: spherical equivalent refraction

placed on the visual axis. The preoperative Purkinje image is believed to be the best reference point to the visual axis [5], therefore the position of the Purkinje image to the centre of the pupil was preoperatively photographed with a special SMI device (SensoMotoric Instruments GmbH, Teltow, Germany). The flap was repositioned with lasik spatula and the interface was carefully irrigated paying attention not to change the position of the inlay, the position of the inlay was controlled immediately after the surgery and if the deviation was greater than 200 µm a recentration was performed. All inlays were implanted in the non-dominant eye. After the surgery was completed, Tobradex eye drops (tobramycin sulphate in combination with prednisolone acetate 1%, Alcon Laboratories) were prescribed 4 times a day for one week and were subsequently reduced to twice a day for another 5 weeks. Non-preserved artificial tears several times a day and dexpanthenol eye cream (Bepanthen, Bayer Pharmaceuticals, Leverkusen, Germany) for the night were also prescribed to keep the cornea well hydrated. In order to suppress a possible subtle immunoreaction, Fluorometholone eye drops (FML, Allergan, Inc., Irvine, CA, U.S.A) once a day for a period of at least 6 months was prescribed.

Results

A small-aperture corneal inlay was implanted in fifty presbyopic patients. 43 patients (86%) with hyperopia (range + 0.25 to + 3.0D), 4 patients (8%) with myopia (range − 0.25 to − 0.75 D) and three patients (6%) were emmetropic. None of the patients had astigmatism more than − 2.5D. 48 patients completed the 12-month examination. One inlay was removed after 6 months and one inlay had to be recentered 4 weeks after implantation.

Median preoperative UDVA was 20/32 (range 20/100 to 20/20). Median preoperative UNVA was J8 (range J10 to J3). Median preoperative SE refractive error was 1.19 D (range − 1.25 to + 2.75D). Median preoperative spheric error was 1.25D (range − 0.75 to + 3.0D). Median preoperative cylinder error was − 0.5D (range − 0.25 to − 2.5D) and median preoperative CDVA in non-dominant eyes was 20/20 (**Table 1**).

At 12 months-visit median postoperative UDVA was 20/22 (range 20/63 to 20/20). Median UNVA was J2 (range J6 to J1). Median SE refractive error was 0.0D (range − 1.5 to 2.0D). Median spheric error was 0.25D (range − 1.0 to + 2.5D). Median cylinder error was − 0.5D (range 0.0 to − 1.5D) and median CDVA was 20/20 (range 20/32 to 20/20). Our statistical analysis revealed that there was a significant difference between all pre- and postoperative values ($p < 0.001$).

Efficacy

The median postoperative UNVA in the eyes with the inlay improved from J8 to J2 at 4 weeks visit and was maintained the same throughout the 12-months study. The median UDVA in eyes with inlay improved from 20/32 to 20/22 at 12-months visit. The median SE refractive error shifted from + 1.19D at baseline visit to 0.0D at 12-months visit. These differences were statistically significant ($p < 0.001$).

Safety

At 12-months visit, one patient (2.1%) lost one line of UDVA and 3 patients (6.3%) lost 2 lines. At the same visit, 4 patients (8.4%) lost 1 line of CDVA and two patients (4.2%) lost two lines. The lowest measured UDVA was 20/32. In one patient the inlay was removed at 6-months visit because of insufficient UNVA (J5), UDVA (20/40), a hyperopic shift of + 1D and CDVA of 20/32 due to mild corneal haze. Four weeks after inlay explantation the UDVA improved to 20/32 with no loss of CDVA, UNVA was reduced to J10. In one patient the inlay had to be recentered after 4 weeks (**Figs. 1** and **2**).

Discussion

We have evaluated the safety and efficacy of the AcuFocus corneal inlay (KAMRA) for treatment of presbyopia in a prospective non-randomized clinical study and are reporting our one-year postoperative results. A small-aperture corneal inlay was implanted in fifty presbyopic patients. The inlay was placed between the stromal bed and the flap on the visual axis of the non-dominant eye. We have combined this procedure successfully with the usual femtosecond lasik operation in one single session in hyperopic, emmetropic and myopic patients. At 4 weeks visit one inlay had to be recentered. After recenteration both distance and near visual acuity significantly improved. In one patient the inlay was removed at 6 months visit due to insufficient UNVA of J5, UDVA of 20/40 and reduced CDVA of 20/32. The patient was a 65-year old man with a preoperative hyperopia of + 2.25D. A hyperopic regression of + 1D and slight corneal haze were noticed at this visit. Four weeks after inlay explanation UDVA improved to 20/32 with no loss of CDVA, UNVA reduced to J10 and corneal haze disappeared under the topical treatment with fluorometholone eye drops twice a day. Since we implanted KAMRA only in patients who tolerated monovision well, we were able to offer this patient the option to perform a monovision with laser three month later. We implanted KAMRA even in patients over 60 years of age since this is a relatively non-invasive and reversible operation only performed in one eye compared to a bi-

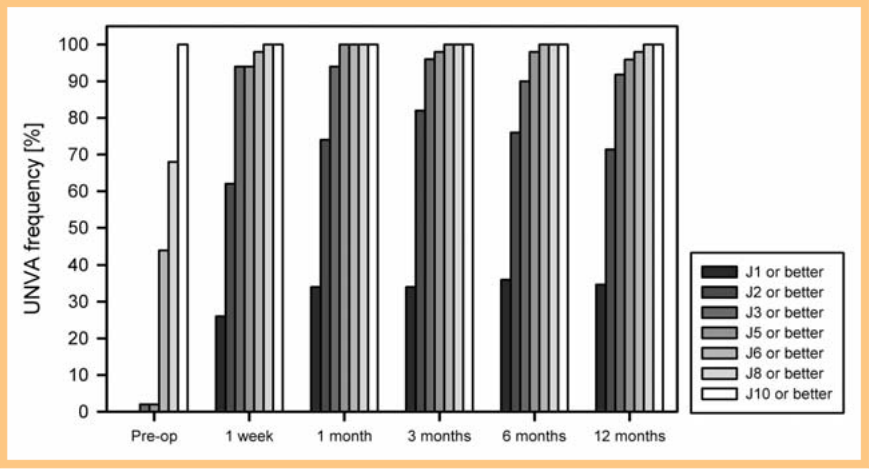

Fig. 1 Uncorrected near visual acuity (UNVA) frequency in 48 eyes implanted with AcuFocus corneal inlay. (J: Jaeger)

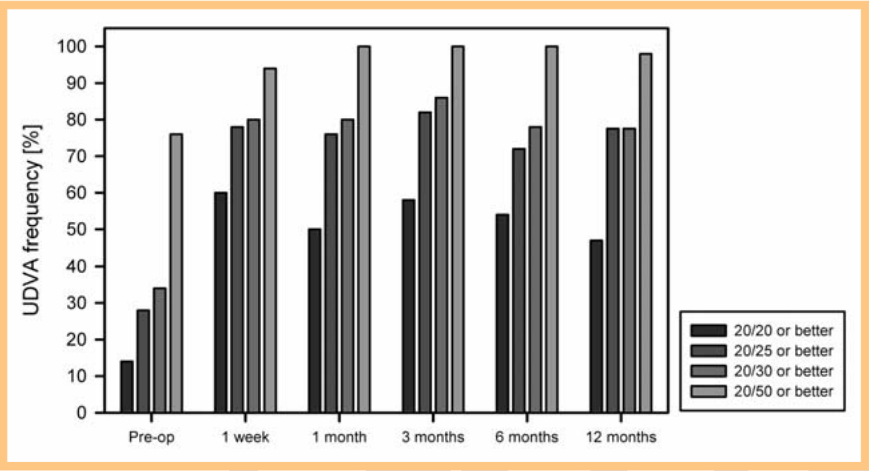

Fig. 2 Uncorrected distance visual acuity frequency in 48 eyes implanted with AcuFocus corneal inlay. (Snellen/feet)

lateral clear lens extraction with implantation of multifocal lenses. Our results revealed that although in this age group emmetropic patients performed as well as younger patients, patients with hyperopia over +1.75 Diopters tended to do worse, with a median improvement of UNVA preoperative from J10 to only J6 at 12 months visit. This was mainly due to slight regression of hyperopia. In our opinion in this group early cataract operation or clear lens extraction and multifocal IOL implantation could be a better option.

We have included only one patient with UNVA of J3 before KAMRA implantation in this study. He was a 50 years old patient with a manifest refraction of − 0.75 spheric. Therefore we decided not to correct his refractive error. After implantation his UDVA improved from 0.4 to 0.8 and his UNVA improved from J3 to J1.

Our results for postoperative UNVA are equal and for UDVA are slightly lower than some other investigators [6–11]. In our opinion it is mainly due to the fact that we have also treated older patients (up to 65 years) with high ametropia, hyperopia up to +3D and astigmatism up to − 2.5D and we combined the femtosecond lasik correction and inlay implantation in one single session. We think this is the best strategy in a clinical, patient oriented setting.

In this study we have demonstrated that ACI (KAMRA) could significantly improve the near vision in presbyopic patients under good photopic condition and reduce their dependency on reading glasses. At one-year visit a total of 98% of the patients gained two or more lines of UNVA, one patient (2.1%) lost one and 4 patients (8.4%) lost 2 lines of UDVA. The reduction in uncorrected distance visual acuity was mainly due to slight regression of hyperopia and astigmatism. At this visit 4 patients (8.4%) lost one and two patients (4.2%) lost two lines of CDVA. The loss of CDVA was due to slight corneal haze and was successfully treated with fluorometholone eye drops two to three times a day within 4 weeks. In this study 83.3% of patients were satisfied with their near and distance vision and were able to perform their daily activities without reading glasses but only 68.7% stated that they would undergo this treatment again. The main reasons were extensive postoperative treatment because of dry eye (58%), difficulty in reading in dim light (52%), appearance of halos and glare particularly under scotopic condition (42%) and slight blurred vision (31%). The subjective patient questionnaire was in accordance with the objective visual acuity results obtained at one-year visit. Our results demonstrate that the ACI could be considered a safe and effective treatment of presbyopia in hyperopic, emmetropic and myopic patients. In our opinion further studies with more patients and longer follow-up period are required.

Author contributions: Study design, data collection, Statistical Analysis, interpretation and writing the paper (Shahrokh Jalali, MD); Surgeon (Walter Aus der Au, MD); revision of the paper (Tarek Shaarawy MD).

Conflict of Interest

No author has a financial or proprietary interest in any material or method mentioned in this study.

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