

PRESBYOPIA

PRESBYOPIA AND CORNEAL INLAYS

Corneal inlays discover new lease of life as potential presbyopic treatment

by Dermot McGrath



“

I think we need to keep an open mind and not rush to judgment on this promising technology

José Güell MD



“

Back in the early 1980s we saw several different attempts at corneal inlays for the presbyopic market that never really got off the ground for one reason or another

Daniel S Durrie MD



“

The versatility of the Kamra inlays makes them a great solution for presbyopia

Gunther Grabner MD

The past few years have seen a resurgence of interest in corneal inlays as a potential treatment for presbyopia. Some surgeons have hailed the latest generation of inlay technologies as a breakthrough in the search for a universally effective and universally applicable treatment for presbyopia.

Others warn that the marketing hype is running ahead of the clinical reality and that the inlay needs more hard data and longer follow-up to assess its credentials as a groundbreaking technology.

“I think we need to keep an open mind and not rush to judgment on this promising technology,” said José Güell MD, director of the Cornea and Refractive Surgery Unit at the Instituto de Microcirugía Ocular, Barcelona, Spain. “We need more scientific data on both the safety and efficacy of these inlays before we start recommending them systematically to our patients. If we are talking about inducing monovision optionally in an otherwise healthy eye just to slightly enhance near vision, then I don’t think the argument is strong enough to propose that to my patients right now. But it could certainly be an interesting addition to our surgical toolkit and merits close attention as more data becomes available,” he said.

Back to the future Given the current hype surrounding presbyopic inlays, it is perhaps easy to forget that the technology has actually been around for a long time, said Daniel S Durrie MD, clinical professor of ophthalmology, University of Kansas Medical Centre, and president, Durrie Vision, Kansas, US.

“Corneal inlays for improving vision are not a new concept. Back in the early 1980s we saw several different attempts at corneal inlays for the presbyopic market that never really got off the ground for one reason or another,” Dr Durrie told *EuroTimes*. “What we are seeing now is the maturing of this technology, which addresses a lot of the earlier issues with the inlays, and also more clinical data and commercial results are starting to filter through, so we are seeing a new excitement about it,” he said.

Dr Durrie identified three main types of inlay that have been used over the years to try to improve vision. The first approach tried to use inlays to change the corneal curvature, and in the process alter the corneal power.

“A lot of these early attempts used materials that were not very permeable to oxygen or glucose and were difficult to do because everybody’s corneal curvature is different and it just wasn’t very accurate. So

the inlays were eventually replaced by lasers which did the job more accurately,” he said.

The Vue+/PresbyLens inlay (ReVision Optics Inc), currently undergoing clinical trials in the US, uses a refined version of this approach, but changes the corneal curvature in the centre of the cornea only.

The second type of inlay sought to change the corneal power by putting a high index refraction inlay in the cornea.

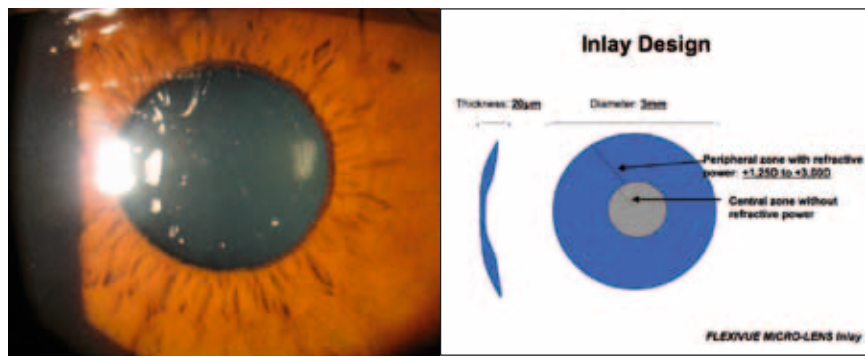
“They ended up not being very permeable and the cornea biologically did not tolerate them very well, so that too was abandoned,” said Dr Durrie.

This approach has since been re-visited by two inlays: the InVue corneal inlay (originally developed by BioVision AG, later acquired by Neoptics AG) which addressed the bio-compatibility issue by incorporating a pinhole in the centre of the lens that allowed nutrients to pass through, and the Flexivue Microlens (Presbia Inc.) corneal inlay which is placed in a self-sealing stromal pocket which holds the lens in place in the centre of the visual axis.

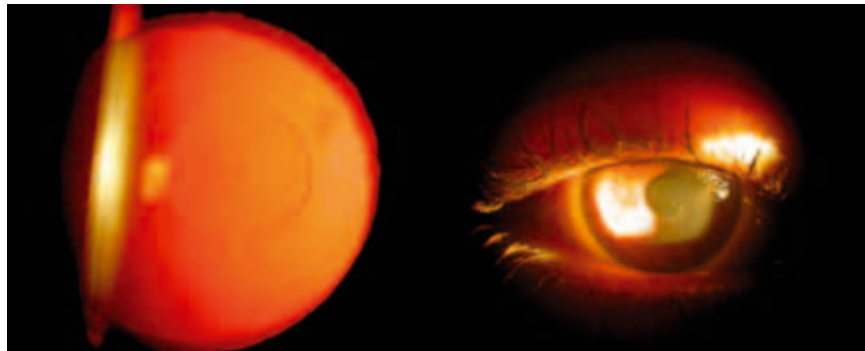
Changing the optical principles

The third strategy to improve vision for presbyopes eschews changing either the power or the curvature of the cornea, but instead seeks to alter the optical principles





Flexivue Micro-Lens Corneal Inlay (Presbia)



IntraCor technique

FLEXIVUE MICRO-LENS Inlay Characteristics:

- Acts changing the refractive index of the cornea
- Donut shape bifocal refractive power
- The lens is implanted into the stroma of the cornea on the non-dominant eye, inside a corneal tunnel created using femtosecond laser.
- The lens is “Invisible”
- Biocompatible hydrogel-based material with a central hole to increase more the nutrient flow.
- The refractive effect is pupil depended, increasing during near vision and decreasing during far vision, changing less the far vision in the operated eye than in a classic monovision procedure

Courtesy of Dimitris I Bouzoukis MD

of the cornea using small aperture optics.

This is the approach favoured by the Kamra inlay (previously the ACI 7000, AcuFocus Inc.), which is leading the inlay pack in terms of regulatory approval and clinical follow-up, with over 5,000 implants performed worldwide and four-year data from a Turkish centre now published¹.

“The versatility of the Kamra inlays makes them a great solution for presbyopia,” said Gunther Grabner MD, professor of ophthalmology and chairman of the University Eye Clinic at Paracelsus Medical University in Salzburg, Austria, noting that they have been implanted successfully in emmetropes, ametropes, monofocal pseudophakic patients and post-LASIK patients.

“In the United States clinical study of 507 patients who received the Kamra inlay, 18-month data showed that the inlay provided patients, on average, with J-2 uncorrected near acuity, 20/25 uncorrected intermediate acuity and 20/20 uncorrected distance acuity in their inlay implanted eye. Additionally, for the Kamra inlay, the mechanism of action using small aperture optics continues to work over several years without a reduction in acuity, as can happen with other power-based corneal inlays that need to be updated as the patient’s lens continues to lose accommodative function,” he said.

The inlays are also removable, allowing the patient to take advantage of future technologies for correcting presbyopia or cataract should the need arise, added Prof Grabner.

As a selling point for inlay technology, the implant’s reversibility should not be underestimated in a competitive market, according to Richard Lindstrom MD, founder of Minnesota Eye Centres, Minneapolis, US.

“The reversibility factor is certainly very attractive. If the patient doesn’t like them, they can be easily removed and no further procedure is required to restore them back to their original refractive status. I also appreciate the fact that the inlays always enhance near vision, with only a marginal loss of distance acuity depending on the inlay utilised. Because it is a monocular procedure, you always maintain quality distance vision in the other eye, which the patients seem to appreciate,” he said.

Target market In Dr Lindstrom’s view, the real target group for inlays are not so much early-stage presbyopes that occasionally need reading glasses, but rather the presbyopic population aged around 50-upwards who have become handicapped enough in their daily activities to consider alternatives to reading glasses.

While the initial expectation in the industry was that corneal inlays would hold most appeal for emmetropic presbyopes, the reality on the ground has been somewhat different, he said.

“Emmetropic presbyopes are certainly candidates but the largest number of patients who seem to ask for the surgery are presbyopes who are also myopic or hyperopic and may also have astigmatism. I see those patients in my practice every day, but understandably they don’t want to trade far glasses for near glasses. For these patients, the best solution is usually what we call SIM-LASIK, which is LASIK first to correct their ametropia and then the inlay to deal with their presbyopia,” he said.

While the demand for presbyopic treatments worldwide is on the increase, patients today are much better informed about the options open to them, said Cati Albou-Ganem MD, in practice at the Clinique de la Vision, Paris, France.

“There has been a definite shift in the age profile of the typical refractive surgery patient in recent years, from around 35 years about a decade ago to around 45 or 50 years-of-age today. These patients are looking for simple and effective solutions that can take care of their presbyopia, and I think corneal inlays will give us further options to offer more personalised solutions for these patients,” she said.

Compared to approaches such as PresbyLASIK or IntraCor, corneal inlays offer a minimally invasive, safe, reversible surgical technique for presbyopes, said Dimitris I Bouzoukis MD, Institute of Vision and Optics, University of Crete, Greece

“There is no steep learning curve for the surgeon and the surgery can be performed without changing or adding new equipment or software in a modern refractive surgery theatre equipped with a femtosecond laser,” he said.

Downsides to inlay technology

But even the best technology has its downsides – and corneal inlays are no exception.

“The main disadvantage is that the inlay is a reasonable but not a perfect solution for presbyopia, as only one eye is corrected,” said António Limão Oliveira MD, Instituto Microcirurgia Ocular in Lisbon, Portugal, who has been involved with the European multicentre trial of the Vue+ corneal inlay. “With this approach, binocularity is disturbed, at least at near, and patients become independent but not completely free of glasses for near vision,” he said. In Dr Oliveira’s view, the best candidates for inlays are emmetropic presbyopes with a clear lens, 20/20 uncorrected distance vision and a near add of about +2.00 D.

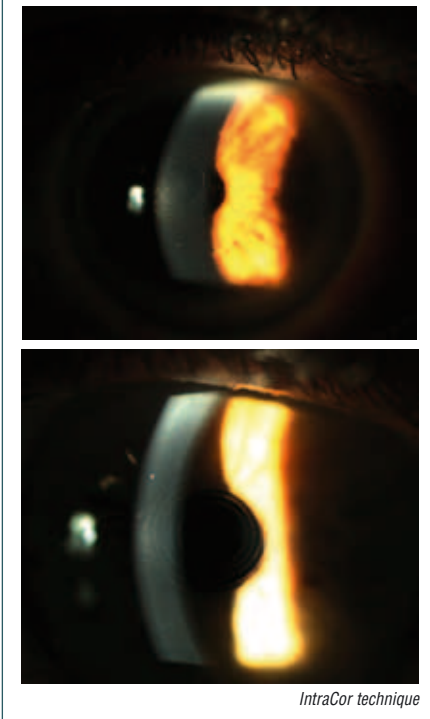
“The most important exclusion criteria for the Vue+ corneal inlay is dry eye, any kind of corneal pathology, central corneal thickness inferior to 500 microns, and monovision intolerance,” he said.

Inlays may also be unsuitable for patients with very high expectations, said Dr Bouzoukis. “As with all bifocal or multifocal corrections, retinal image contrast may be reduced in eyes implanted with the Flexivue and Vue+ devices and retinal illuminance may be markedly reduced with the Kamra implant. Effects on contrast sensitivity and stereopsis have yet to be adequately explored. Regarding reversibility and safety, more studies are needed to demonstrate if the technique is really reversible with no changes to the preoperative emmetropic status of these patients, or if they are just removable, and to demonstrate that after a long follow-up they are not creating corneal alterations,” he said.

Prof Grabner said that in his clinical experience with the Kamra inlay, there was no significant reduction found in retinal illuminance for patients implanted with the inlay, and he believes that the five-year follow-up data speaks volumes for the long-term safety of the device.

“We tested the inlay and found that there was only a very slight reduction in the mean deviation visual field of 2 dB. We now have up to five years’ follow-up in the first series – a time frame that seems quite reasonable to postulate that they are very safe,” he said.

Another potential problem is that not all patients adapt quickly to their post-inlay vision, said Dr Albou-Ganem. “I recently



IntraCor technique



“The reversibility factor is certainly very attractive. If the patient doesn’t like them, they can be easily removed and no further procedure is required to restore them back to their original refractive status

Richard Lindstrom MD



“There has been a definite shift in the age profile of the typical refractive surgery patient in recent years, from around 35 years about a decade ago to around 45 or 50 years-of-age today

Cati Albou-Ganem MD

PRESBYOPIA

contacts

José Güell - guell@imo.es
 Daniel Durrie - ddurrie@durrievision.com
 Gunther Grabner - g.grabner@salk.at
 Richard Lindstrom - rliindstrom@mneye.com
 Cati Albou-Ganem - cati.ganem@wanadoo.fr
 Dimitris Bouzoukis - Dbouzoukis@hotmail.com
 António Limão Oliveira - antoniolimao@imo.pt



“

There is no steep learning curve for the surgeon and the surgery can be performed without changing or adding new equipment or software in a modern refractive surgery theatre equipped with a femtosecond laser

Dimitris I Bouzoukis MD



“

The main disadvantage is that the inlay is a reasonable but not a perfect solution for presbyopia, as only one eye is corrected

António Limão Oliveira MD



(1) Slit lamp photo of a Vue+ inlay well centred in the pupil (2,3) Animated eye representing the Vue+ inlay

Courtesy of António Limão Oliveira MD

did a LASIK procedure followed by Kamra implantation in the non-dominant eye of a myopic patient but after several days the patient was still not very comfortable with it. However, I always urge these patients to give it time because there is a process of neuro-adaptation with the inlay. It is a little bit like the IntraCor procedure in this respect – some patients have immediate results after the surgery, but sometimes it takes a few weeks for other patients to adapt to their new vision,” she said.

Centration is another potential issue with inlays, said Dr Lindstrom, and some concerns have also been raised about long-term bio-compatibility. “There can be some mild interface reaction that occurs between the implant and the cornea. I have seen some earlier generation hydrogel inlays 20 years after implantation and they look good with no visually significant scarring. But if you remove the inlay and look very carefully you can see where the implant was placed. That occurs with the Kamra inlay as well, although it does not cause visually significant light scatter or other symptoms,” he said.

Dr Durrie agrees that centration is critical for optimal functioning of the inlay,

but believes that an electronic alignment system such as that recently introduced for the Kamra inlay, effectively deals with this issue and will become the norm for optimal placement of these types of implant.

Using latest-generation femtosecond laser technology will also help to reduce variations in wound healing, said Dr Durrie.

“We found that creating the femtosecond pocket or flap atraumatically using the latest laser models resulted in faster visual rehabilitation. The key is making sure that you are using modern equipment for a smooth ablation and then there is less variability in the wound healing,” he said.

For optimal outcomes with the Presbylens/Vue+ inlay, Dr Oliveira advised using disposable instruments, with careful delivery of the inlay in the centre of the pupil, without tearing it, and keeping the flap hydrated to avoid microstriae, he said.

Prof Grabner highlighted the importance of managing patient expectations and advised careful and aggressive management of dry eye pre- and postoperatively, as this population tends to have drier eyes. “Other tips to get the best from the Kamra inlay are to ensure that patients follow the post-operative medication regimen precisely, to target

for a little residual myopia in the inlay eye and use the AcuTarget-System to place the Kamra inlay with great precision,” he said.

Massive market potential While corneal inlays are still only in the early phases of adoption for most ophthalmic practices, that picture could change rapidly as more clinical trial data becomes available and demand for the inlays gathers momentum.

“From a business aspect, this appears to be one of those rare products that turns out to be a win-win-win situation for the patient, the doctor and the company producing it,” said Dr Durrie. “It is relatively straightforward for the company to produce, and patients tend not to mind spending a bit more money on it in order to get what they consider to be a top-of-the-line product. As doctors, we are often introduced to technologies that just increase the cost of what we are doing without really increasing the value, which is definitely not the case with corneal inlays,” he said.

[1] Ömer F. Yilmaz, et al. *Journal of Cataract & Refractive Surgery* Vol. 37, Issue 7, Pages 1275-128.

INLAY	COMPANY	PHYSICAL PROPERTIES	MECHANISM OF ACTION	REGULATORY SITUATION
Kamra	AcuFocus Inc.	3.8mm diameter, opaque biocompatible polymer material, a 1.6 mm centre aperture and 8,400 random holes for oxygen and nutrition flow. Implant placed under corneal flap or in corneal pocket using proprietary guidance system	The inlay's 1.6mm centre aperture creates a pinhole effect which is designed to improve depth of focus, allowing the eye to see near and intermediate objects more clearly	CE mark. FDA trials nearing completion
InVue	BioVision AG	3.0mm diameter and 15 µm to 20 µm thick microlens made of hydrophilic acrylic material	The centre of the lens has no power, but features a pinhole for nutritional purposes. Near vision is corrected by the lens' outer rim	Technology acquired by Neoptics AG. Trials currently under way in Europe
Vue+	ReVision Optics Inc.	2.0mm diameter bio-engineered, micro-porous, hydrogel material	Adds a microscopic change in curvature to the centre of the cornea of non-dominant eye to add near and intermediate focusing power	CE mark. FDA trials currently under way in the United States
Flexivue Microlens	Presbia Cooperatief U.A.	3.0mm diameter refractive hydrophilic polymer lens placed in a corneal stromal pocket using FS laser	The lens' central zone is free of refractive power with a standard positive refractive power in the peripheral zone	CE mark

©Eurotimes. Data compiled from industry sources

Don't miss *Paediatric Ophthalmology*, see page 37