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Intracorneal inlays showing positive outcomes

by Michelle Dalton EyeWorld Contributing Editor

While not yet on the U.S. market, clinical studies and longer-term outcomes in Europe indicate these have potential in treating presbyopia

***Editors' note**: This article discusses technologies that are under investigation in the U.S. and are not yet approved for marketing. Investigators for Revision Optics declined comment; information on that inlay is derived from a literature/abstract search.*

As the natural lens ages, its ability to accommodate begins to fail. The ability to return some of the near functions of our natural lens in its more youthful state—or some semblance thereof—is currently possible only through corneal or lenticular surgery. The options for presbyopia correction are LASIK (to create monovision), presby-LASIK, scleral segments, or premium IOLs. In the U.S., one other option—corneal inlays—is currently being investigated. The inlays are typically inserted under a LASIK flap or in a corneal pocket, attempting to improve near vision by creating a central myopic area or increasing the depth of focus. Three devices are under investigation in the U.S.—the Flexivue Microlens (Presbia, Los Angeles), the Kamra (AcuFocus, Irvine, Calif.), and the Vue+ (Revision Optics, Lake Forest, Calif.). All three are more widely available outside the U.S.; each has a different mechanism of action and is implanted in the non-dominant eye.

The Flexivue changes the central refractive index, the Kamra increases the depth of focus through the use of a pinhole, and the Vue+ reshapes the central cornea.

"Corneal inlays are a breakthrough for presbyopia surgery in emmetropic presbyopes of the pre-cataract age," said Ioannis Pallikaris, M.D., director, Institute of Vision and Optics, University of Crete, Heraklion, Greece, and medical advisory board chair, Presbia. "The use of the femtosecond laser will help advance the use of these inlays and make the procedure easier, more customizable, and more predictable."

How they work

"Synthetic keratophakia" was first described by José Barraquer in the 1940s; the concept has since evolved to products that have a small diameter, thin profile, and are highly permeable, said Vance Thompson, M.D., director of refractive surgery, Sanford Health, Sioux Falls, S.D.

"There's growing interest in corneal inlays because they blur distance vision less than monovision laser and can be removed or exchanged if the patient desires," he said during Cornea Day 2011, which preceded the ASCRS•ASOA Symposium & Congress in San Diego. For instance, the Kamra inlay is 5 microns thick, 3.8 mm in diameter, and has a 1.6 mm opening in the center surrounded by 8,400 laser etched microperforations (to allow nutrient flow) randomized between 5 and 11 microns wide (to minimize optical side effects), Dr. Thompson said. He said that the 1.6 mm central opening creates a pinhole effect providing for approximately 2.5 D of accommodative effect while blurring distance vision less than monovision laser.

"Following the creation of a superior-hinged flap in the non-dominant eye, the Kamra inlay is centered on the stroma based on the first Purkinje reflex, at a minimum depth of about 170 microns," said Günther Grabner, M.D., director, University Eye Clinic, Paracelsus Medical University of Salzburg, Austria.

The Flexivue Microlens is 3 mm in diameter and about 15 microns thick, Dr. Pallikaris said. After creating a corneal tunnel in the non-dominant eye, the device is placed about 280-300 microns deep.

"This is a 'modified monovision' technique," he said. "It's a procedure in the non-dominant eye to

improve near vision, but with two specific characteristics. First, it's reversible; second, it does not influence distance vision as would be expected with a classic monovision approach such as LASIK/PRK or monofocal lenses. I call this modified monovision 'smart monovision' since it is dependent upon the pupil diameter." For instance, when the pupil size is greater (distance vision), the inlay's effects are not as noticeable as when the pupil size is smaller (near vision).
The Vue+ is a 2 mm diameter hydrogel inlay implanted under a modified corneal flap (about 120-130 microns thick) in the non-dominant eye. The inlay creates a central steepening of about 2-3 mm, according to the literature. The inlay provides a central near add zone and a paracentral intermediate zone for both near and intermediate vision, reports say. A few years ago, the inlay underwent alterations to increase its diameter from 1.5 mm to 2 mm; the smaller size led subjects to complain that image area was small. A cosmetic advantage is that the Vue+ index of refraction is the same as the cornea, rendering it virtually invisible post-op.

Study outcomes

During the 2011 ASCRS Annual Meeting, several surgeons presented results to date on the Kamra lens. Kevin L. Waltz, M.D., Eye Surgeons of Indiana, Indianapolis, reported on 407 patients with follow-up through month 6. In the non-dominant eye, 17.9% achieved 20/20 uncorrected near vision, 67.3% were at 20/32, and 83% were 20/40; 93.4% were 20/32 in distance vision, and 97.1% achieved 20/40 or better distance vision. The Snellen distance vision improves over time, he said, but remains "essentially unchanged." Dr. Thompson said in his arm of the U.S. study, "there was a slight reduction in contrast sensitivity in the inlay eye; these patients read quite well with their reading eye and their distance vision in that same eye was still often 20/20 … it is a different 20/20, but still quite a bit more comfortable than the distance blur created with monovision laser to achieve the same near functioning." He said patients reported a high rate of satisfaction. With results out to 36 months, Dr. Grabner said 90% had J3 or better and none had a loss of distance vision.
"The inlay had to be centered for good near vision," he told
EyeWorld. "It's not as important for distance vision. In our earlier studies, we did not realize centration was so important."
Dr. Pallikaris's latest study includes the femtosecond laser for flap creation; the current study evaluated 20 patients.
"After surgery, uncorrected near visual acuity was 20/25 or better in 77%," he said. "A full 92% did not use reading glasses and 8% used reading glasses for less than half of their near activities." Of those with 15 months follow-up, 77% were 20/16 in near vision, he said. He added that the implanted eye tended to show a slight decrease in distance vision.
An earlier study using the microkeratome has results out to 3 years, Dr. Pallikaris said. Results with the femtosecond are "very similar" to those with the microkeratome. There have been no adverse events reported that have affected the inlay's performance, he said. In the original cohort, presbyopia progressed in two patients, and the inlays had to be replaced. During the early learning curve, "there were some patients who had epithelial ingrowth because we had mistakenly put some cells in the tunnel," he said.
Initial data presented on the Vue+ seems encouraging as well, with subjects averaging five-line improvements in near vision with no more than two lines lost in distance vision. At 3 months (N=30), all subjects achieved 20/25 uncorrected near vision and 20/20 distance vision binocularly. All implanted eyes were 20/40 or better. At the 2010 ASCRS Annual Meeting, Enrique Barragan presented on the PresbyLens (the previous name for the Vue+). At 6 months (n=34), the mean uncorrected near vision in the implanted eye was J1, 20/25, which corresponded to a four-line improvement. Intermediate vision improved by a mean of two lines, and distance vision decreased by a mean of one and a half lines. Binocularly, however, no patient was worse than 20/25.
Although biocompatibility seemed to be an issue in the earliest studies dating back to the 1960s, Dr. Pallikaris says that's no longer an issue.
"The materials that have been developed and are used by all the inlays—even if they are different materials—are very friendly to the cornea," he said. With 4 years of follow-up on the Flexivue,

"using confocal microscopy we have demonstrated that even after years there are not any inlay-associated degenerative issues to the cornea."
However, as recently as 2009, there was a report of one patient who developed late-onset ulceration after implantation of the Revision Optics' device for the treatment of hyperopia, which "most likely represents a neurotrophic melt," the authors wrote.1 Another complication was reported in 2004, epithelial perilenticular opacity, and again, the subjects had undergone intracorneal inlay implantation for the correction of hyperopia.2
Dr. Thompson said all corneal inlays have the potential for complications, with a similar incidence of LASIK-type complications, including thin flaps, epithelial ingrowth, striae, and surgical corneal abrasion. Conversely, studies to date have shown the inlays "typically blur distance less than monovision," he said. "The corneal correction of presbyopia is an exercise in compromise. The question the patient has to address is what he/she is willing to give up at distance to help with near vision."

What the future holds

Dr. Pallikaris said researchers learned from those earlier mistakes, and "presbyopia treatment selection is closely related to patient selection," he said. "That means one of the most important steps of the surgery is to understand the necessities of your patient for near vision." He added this should include which eye to operate on, what type of surgery the eye should receive, what material will be placed in the eye, "and even the possibility of avoiding surgery."
Dr. Grabner prefers to use the inlays on hyperopes (up to 1.5 D) without spectacle correction; a new diagnostic tool (AcuTarget,
AcuFocus) has significantly improved centration capabilities.
"Emmetropic presbyopes are the most difficult patients to please," Dr. Waltz said. "In my opinion, the only other treatment that can compete with the inlay is monovision." Dr. Thompson said for ametropic presbyopes, he would combine the inlay with LASIK. He added, "in the 88 patients I treated in the clinical trial I removed three. That is a great track record compared to the amount of monovision LASIK patients that come back to me and want the near eye brought closer to distance. I believe corneal inlay technology will play a large role in lessening patients' dependence on reading glasses until they have cataract surgery with a premium implant to help their near."
As long as there is no definitive surgical preference for the treatment of presbyopia, corneal inlays will continue to be investigated and used, according to the experts.
"I believe in this technique even though some surgeons are skeptical; I believe it has a great future," Dr. Pallikaris said, adding, "someone must believe" and buck the system for true innovation and science to progress.

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Editors' note*: Dr. Grabner has no financial interests related to his comments, but has received travel support in the past. Drs. Thompson and Waltz have financial interests with AcuFocus. Dr. Pallikaris has a financial interest with Presbia.*

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