Presbyopia Update 2012: New Technologies and Novel Treatments

BY MITCHELL C. SHULTZ, MD

The successful treatment of presbyopia is clearly the Holy Grail of refractive surgery. Although we ophthalmologists have made significant advances in the surgical management of presbyopia, the currently available technologies all have limitations we must consider during our preoperative decision-making process. IOL technologies are currently our main source for the preservation of patients' excellent binocular acuity for distance and near. Although some of us implant premium IOLs in 40% to 50% of eligible cataract patients, currently less than 10% of patients in the United States, and less than 4% of patients internationally, ultimately receives one of these lenses at the time of cataract surgery. Although financial considerations are a significant part of the equation, I believe that the surgeon's comfort level, concerns regarding adverse night vision symptoms, and the quality of postoperative near acuity are the foremost reasons why these technologies have achieved limited success. New IOL designs not currently commercially available in the United States appear to have promise for increasing the satisfaction of our patients and are reviewed in this article.

In addition to IOLs, intracorneal inlays have been under investigation for more than 20 years. Permeability to nutrient transport and the health of keratocytes anterior to these implants have been the major physiologic barriers to the long-term success of these technologies. However, recent improvements in material design and dimensions have increased the biocompatibility of these theoretically reversible technologies, which are likely to expand the marketplace for presbyopic correction. Three different strategies are currently being explored: (1) bifocal or refractive lens power (Flexivue; Presbia Coöperatief UA), (2) pinhole enhanced depth of focus (Kamra corneal inlay; Acufocus, Inc.), and (3) aspheric enhanced depth of focus (Vue+ corneal inlay, formerly PresbyLens; ReVision Optics, Inc.). Success with these technologies will likely require our critical attention to the implants' placement over the line of sight, which may be enhanced by the use of intraoperative aberrometry in the future.

Because the results of presby-LASIK using excimer lasers appear to be time limited, the procedure is less favored as a long-term solution. On the horizon and not yet ready for advanced human clinical trials are femtosecond laser technologies to perform intracorneal ablations and crystalline lens photodisruption, light-adjustable IOLs, and capsular refilling technologies.

I would like to welcome my new coeditor, Allon Barsam, MD, to Cataract & Refractive Surgery Today*'s "Peer Review" section. Dr. Barsam brings a European point of view to our study of the currently available peer-reviewed literature, and he has access to some of the technologies that are not yet available in the US marketplace. I look forward to working with Dr. Barsam, and I am confident he will bring a fresh perspective to the column.*

I hope you enjoy this installment of "Peer Review," and I encourage you to seek out and review the articles in their entirety at your convenience.

PRESBYOPIA-CORRECTING IOLs

Lichtinger and Rootman discussed the future direction of presbyopia-correcting IOLs. Some of the features they believe will help to improve the technology include lenses that will personalize the IOL to the patient's pupillary size, visual axis, corneal aberrations, and visual needs. A few of the technologies they discussed are the Synchrony accommodating IOL (Abbott Medical Optics Inc.), which consists of a foldable, one-piece, dual-optic system that features a high plus-powered anterior optic joined by a spring haptic to a minus-powered posterior optic. The ciliary body contracts on attempted accommodation, tension on the capsular bag and zonule is released, and the front optic moves forward, changing the eye's focus to intermediate or near vision. Tetraflex (Lenstec Inc.) is an acrylic, 5.75-mm single-optic lens that has two haptics and an anterior vault designed to move anteriorly with both vitreous pressure and ciliary swelling. The NuLens (Nulens Ltd.) changes

power through the alteration of lens curvature. The system consists of a small, rigid chamber containing silicone gel that is pressurized by a piston, actuated by the capsular diaphragm. The pressurized gel is displaced through a round hole to form a lens-shaped bulge that continuously changes its curvature in correlation with the ciliary muscle's movement. Other accommodating lenses under development include the 1CU (Human Optics AG), the FlexOptic (Quest Vision, Inc.), and the Smart Lens (Medennium, Inc.). Another promising technology is the Light Adjustable Lens (Calhoun Vision Inc.). The lens can be customized to the patient's visual axis and pupillary diameter by activation of the polymers with ultraviolet light irradiation. Finally, some ongoing developmental technologies include refractive index shaping in which in situ IOL power customization can be achieved. Specifically, focused 55-mW femtosecond laser pulses alter the refractive index of the lens, and the capsular bag is filled with a flexible polymer.[1]

In a prospective, nonrandomized study, 2-year postoperative follow-up data were presented by Bohórquez and Alarcon after bilateral implantation of the Synchrony dual-optic accommodating IOL. Patients' reading speed had improved at 2 years compared with 1-year follow-up results for print sizes of 0.3 to 0.1 logMAR (20/40 to 20/20 Snellen equivalent). However, there was no difference in reading speed at 0.4 logMAR (20/50 Snellen equivalent or newspaper print), with patients' achieving 180.5 words per minute at 1 year and 184.2 words per minute at 2 years (P = .90, paired t-test). When patients' subjective accommodation was tested, the mean accommodative amplitude in patients with the dual-optic accommodating IOL was 2.00 D greater than in those with a monofocal IOL. Mild posterior and anterior capsular opacification was seen in four patients at 1 year and 2 years postoperatively; none required a neodymium:YAG capsulotomy. Furthermore, no eye had regenerative or proliferative capsular fibrotic material between the two IOL optics.[2]

CORNEAL INLAYS

Waring recently discussed results of the Kamra small-aperture corneal inlay to improve near vision in emmetropic presbyopes. The inlay is 5-µm thick and 3.8 mm in total diameter, with a 1.6-mm central aperture that increases depth of focus and improves near visual acuity by restricting bent light rays from entering the eye similar to the f-stop in a camera. A small corneal pocket or flap is created in the nondominant eye by a femtosecond laser or a mechanical keratome, and the inlay is placed on the stromal bed (n = 507). Waring evaluated results for up to 18 months after implantation. Subjects' mean age was 52.87 ±3.64 years. Monocular mean near UCVA was J8 preoperatively, J3 at 1 month (n = 506), and J2 at 18 months (n = 99). Mean intermediate UCVA was 20/35 preoperatively and 20/26 at 18 months (P < .0001). Mean distance UCVA declined slightly to 20/20 at 18 months (P < .0001), and photopic and mesopic contrast sensitivities were within the range of the normal population at 1 year.[3]

In a study with 4-year follow-up on the Kamra lens by Yilmaz et al, the mean final near UCVA was J1, with 98% of patients (n = 22) reading J3 or better. Patients in this study had all undergone placement of the inlay under a flap created with a mechanical microkeratome. Four patients underwent explantation—two for flap-related complications and two for refractive shifts. None of these patients lost BCVA after explantation compared with their preoperative BCVA.[4]

In a recent volume of *International Ophthalmic Clinics*, Waring and Klyce presented an overview of corneal inlays for the treatment of presbyopia. In addition to a discussion of the Kamra inlay, they provided a comprehensive history of the topic as well as an update on other corneal inlays currently under investigation, including the Vue+ and the Flexivue. Of extreme importance to this technology is the principle that it must be semipermeable to allow oxygen from the nearby tear film and glucose from the aqueous humor to nourish vital corneal cells and to permit catabolic waste to return to the aqueous humor. The Vue+ corneal inlay differs from the Kamra inlay: the former's design is based on the creation of a hyperprolate cornea. The most current design includes a 2.0-mm near optical zone. The inlay is 24- to 40-µm thick centrally and 10-µm thick at the periphery. Distance acuity is minimally affected, because light rays paracentral to the 2-mm inlay remain primarily focused on the retina. In the first phase of FDA investigations, all eyes with the implant retained 20/32 or better near UCVA 2 years postoperatively. The mean gain in near UCVA was 3.6 lines with a binocular mesopic distance UCVA of 20/25 or better in all patients. The Flexivue differs in that it is the only corneal inlay in development that uses a refractive add power. The Flexivue is composed of a hydrophilic acrylic polymer measuring 3 mm in diameter with an edge thickness of 20 µm. This inlay functions as a bifocal refractive interface with separate distance and near focal points. The central zone is free of power, with the peripheral zone that generates +1.25 to +3.00 D of add power. Waring and Klyce related data from an unpublished study by Pallikaris et al in which 93% of 43 patients achieved a near UCVA of J2 or better.[5]

EXCIMER LASERS AND MULTIFOCAL CORNEAL ABLATIONS

Alarcón et al evaluated different theoretical models of a multifocal cornea for the correction of presbyopia by laser ablation using ray tracings. Because the pupil's size decreases

with accommodation, the investigators preferred the central model to obtain optimal multifocality with the achievement of a 2.4-mm central zone diameter to the peripheral model with a 2.9-mm central zone. It should be noted that, although near vision is better, the quality of distance vision provided by these models is worse than that of a presbyopic emmetropic eye.[6]

In a prospective, nonrandomized clinical trial, Jackson et al presented 12-month results of aspheric wavefront-guided LASIK to treat hyperopic presbyopia. They treated 66 eyes of 33 patients using the Visx Star S4 IR (Abbott Medical Optics Inc.). Six months postoperatively, mean corrected distance visual acuity was 20/20+1, and distance-corrected near visual acuity was 2.7 ±1.7, with a maximum of a 6-line improvement in near vision. At 12 months, 100% of patients achieved a binocular simultaneous UCVA of 20/25 or better and J3. Negative spherical aberration highly correlated with a postoperative improvement in distance-corrected near visual acuity. In their conclusions, the researchers stated that patients who had a larger amount of preoperative hyperopia or a greater decrease in preoperative distance-corrected near visual acuity were more likely to have overall satisfaction.[7]

Gordon performed a single-surgeon retrospective chart review of 178 consecutive patients who underwent bilateral presby-LASIK (or progressive multifocal LASIK) using the WaveLight Allegretto excimer laser (Alcon Laboratories, Inc.). The patients had a preoperative refractive error of emmetropia, myopia of up to -5.00 D, or hyperopia of up to +3.00 D and no more than 3.00 D of astigmatism. Of 102 patients with at least 3 months' postoperative follow-up, 81% had a binocular distance UCVA of 20/20 or better, and 98% saw 20/25 or better. Additionally, 44% achieved J1 binocular near acuity, 60% J2, and 96% J3 or better.[8]

FEMTOSECOND LASERS

In a prospective, nonrandomized trial, Holzer et al presented early outcomes of Intracor femtosecond laser treatment for presbyopia. The investigators treated the nondominant eye of 25 patients using the Technolas Perfect Vision femtosecond laser (Technolas Perfect Vision GmbH). The procedure involves the creation of five consecutive intrastromal rings around the line of sight. Treatment times were approximately 20 seconds. The mean gain in UCVA was 4.42 lines, with a range of 0 to 9 lines of improvement. The mean loss of distance BCVA was -0.46 ±0.83.[9] Similarly, Ruiz et al evaluated 83 eyes of 45 patients with 6- to 12-month follow-up. Of the 83 eyes, 89.2% achieved both J2 and 20/25 or better, and 69.9% achieved a near UCVA of J1. This technology has the advantage of being minimally invasive, with a rapid effect manifesting within minutes to several hours. Further investigation of long-term stability is ongoing.[10]

Reggiani et al recently presented an overview of femtosecond laser photodisruption of the crystalline lens for restoring accommodation. They related data from a safety study performed in the Philippines by Harvey S. Uy, MD. Fourteen patients were between 45 and 60 years of age with 20/40 or better BCVA, had no greater than grade 2 cataracts, and had originally consented to cataract surgery. All underwent unilateral treatment with the option to proceed to cataract surgery after 1 month of follow-up. Early results showed no progressive cataract formation at 1 month.[11]

CAPSULAR BAG REFILLING

Hao et al recently introduced data on injectable in situ curable accommodating IOLs. Using functionalized polysiloxane macromonomers, they were able to refill the empty lens capsular bag via an injection. To prevent leakage from the capsular bag, the investigators performed in situ cross-linking of polysiloxane gel using blue light (wavelength, 400-500 nm) at an intensity of 70 mW/cm^2. A 3-month in vivo biocompatibility study was performed in rabbits. No iritis, uveitis, retinal detachment. or corneal decompensation was observed.[12] ■

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