

Design Strategies for New Accommodating IOLs

A review of the available technologies and what is coming in the future.

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A number of diverse and ingenious strategies are under development for harnessing the accommodative forces generated by the ciliary muscle's contraction as the engine behind new accommodating IOL designs. According to Helmholtz's theory of accommodation, the ciliary muscle contracts in response to the effort of focusing on a near target. This forward and inward movement of the muscle relaxes the tractional outward counter forces habitually applied via the zonules to the lens capsule during disaccommodation. During accommodation, zonular slackening liberates the inherent contractile forces of the elastic lens capsule. The release of potential energy stored in the capsule, along with the vector forces of increased vitreous pressure, leads to an archetypal deformation of the flexible prepresbyopic crystalline lens. This change in shape is characterized by thickening of the crystalline lens, an increase in the anterior and posterior lens curvatures, and a decrease in the lens' diameter. The overall result is an increase in dioptric power.¹

Many muscles in the human body are paired as agonists and antagonists facilitating muscle movement back into their original position prior to contraction. In a liberal sense, the antagonist of the ciliary muscle can be construed as the elastic posterior attachment of the ciliary muscle, the posterior zonular fibers, and the choroid. During disaccommodation, these structures pull the ciliary muscle backward, which increases zonular tension and thereby conveys an outward equatorial vector force onto the lens capsule. Equatorial stretching increases the lens' diameter, flattens the anterior and posterior surfaces of the lens, and decreases the lens' thickness and dioptric power.²

Studies using capsular tension rings following phacoemulsification suggest that the diameter of the capsular bag initially averages about 10.5 mm in whites³ and around 11.3 mm in Asians.⁴ Then, over the course of 3 months, the bag contracts to between approximately

9.0 and 9.8 mm, respectively (ie, close to the average diameter of the crystalline lens). There is a weak but positive relationship between axial length and the capsular bag's diameter (ie, myopes generally have larger capsular bags than hyperopes). It is therefore essential that the potential functional impact of variations in the capsular bag's regional and overall dimensions and post-fibrotic changes be factored into accommodating IOL designs.

This article reviews the accommodating IOLs that are currently available, those that are in the pipeline, and what may be in the earliest stages of testing and development.

THREE BASIC APPROACHES TO ACCOMMODATING IOL DESIGNS

There are three basic approaches to accommodating IOL designs, which in theory can be combined. These approaches include a change in the axial position of a single or dual IOL optic, a change in the IOL optic's shape or curvature, and a dynamic change in the refractive index or power of a single- or dual-optic IOL. In addition, the near vision produced by accommodating IOLs benefits from the additive effect of pseudoaccommodative mechanisms (eg, instantaneous depth of focus [affected by pupillary size, ptotic eyelids, and squinting], low residual against-the-rule astigmatism, monochromatic higher-order aberrations [particularly spherical aberration and coma], chromatic aberration, and others).

SINGLE-OPTIC LENSES

Currently, the only accommodating IOLs approved by the FDA are the Crystalens 5-0 and Crystalens HD (both manufactured by Bausch & Lomb [Rochester, NY]). Other single-optic accommodating lenses include the Tetraflex (Lenstec, St. Petersburg, FL) and the HumanOptics 1CU (HumanOptics AG, Erlangen, Germany). There have been a number of mechanisms of action proposed for this group of lenses. The

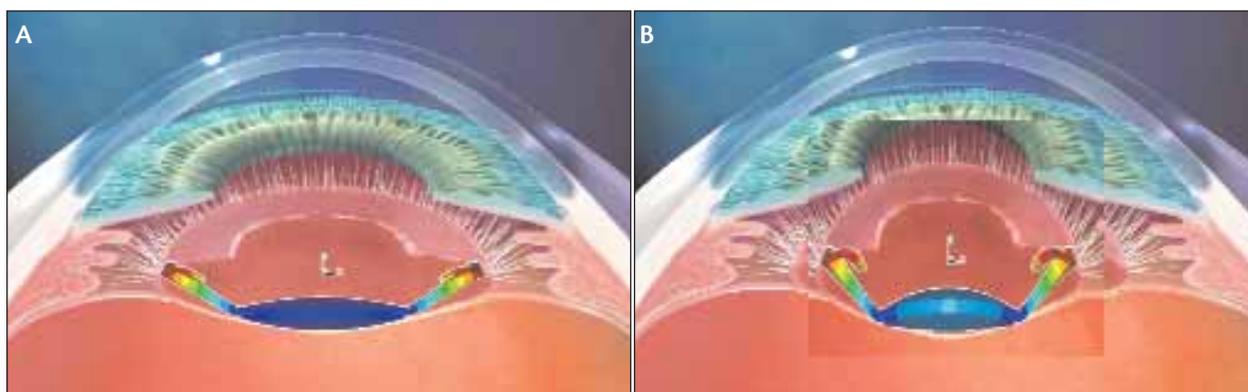


Figure 1. Finite element analysis demonstrates the mechanism of accommodative arching with the Crystalens. Note the change in the shape of the optic between disaccommodation (A) and accommodation (B).

increased near vision reported in studies of these IOLs cannot be produced solely by a change in the axial position of the lens optic. If it could, then one would expect hyperopes to obtain better near vision than myopes with these lenses, because comparable movement of a higher-powered IOL in hyperopes would more effectively produce near vision than the same movement of a lower-powered IOL implanted in myopes. This has not been the case. Studies using a variety of measuring devices and techniques have all shown less than 1.00 mm of anterior movement (approximately 0.35 mm on average) by these IOLs' optics following the instillation of pilocarpine and, in some cases, have demonstrated posterior movement of the optic.⁵ Assuming an average axial length and effective lens position, ray tracing studies predict that a single-optic 20.00 D IOL will produce only 0.80 to 1.85 D of accommodation with 1.00 mm of anterior axial movement, depending on individual keratometry.²

If small amounts of anterior axial movement cannot fully account for the increased near vision measured with single-optic accommodating IOLs, what other mechanisms may play a role? Finite element analysis of the Crystalens 5-0 predicts that the ciliary muscle's contraction produces a transfer of energy exerted through the haptics, along with forces from increased vitreous pressure, that causes the lens' optic to arch (Figure 1). This arching induces positive spherical aberration, with a resulting increase in depth of field as well as anterior movement of the best plane of focus (ie, in the myopic direction). This effect is accentuated by the aspheric modification of the central optic of the Crystalens HD. This 3- to 5- μm central thickening of the Crystalens HD has a very small optical zone and further extends the depth of field. Similarly, iTrace (Tracey Technologies, Houston, TX) studies, which are not yet published, of the Tetraflex lens during accommodation and disaccommodation (Figure 2) demonstrated a statistically significant increase in total and



Figure 2. A comparison of changes in total and specific higher-order aberrations in eyes implanted with the Tetraflex lens and monofocal controls between disaccommodation and accommodation. These results reflect 129 valid Tetraflex examinations and 47 valid monofocal control examinations.

selected higher-order aberrations relative to monofocal controls that theoretically would contribute to an increase in depth of field. Better near vision with single-optic accommodating IOLs therefore may represent the combined effect of multiple mechanisms.

DUAL-OPTIC ACCOMMODATING IOL

The design of the Synchrony dual-optic accommodating IOL (Visiogen, Inc. Irvine, CA) has a moving +32.00 D front optic connected by spring haptics to a posterior optic of variable negative power,⁶ which is individualized for each patient using a proprietary IOL power calculation formula (Figure 3). During disaccommodation, radial tension on the capsular bag compresses the optics closer together, thus generating strain energy in the connecting haptics. In response to the ciliary muscle's contraction during accommodation, the zonules relax and release tension on the capsular bag. The subsequent release of the stored strain energy produces forward movement of the front optic. Optical modeling suggests that 1.5-mm of movement by the

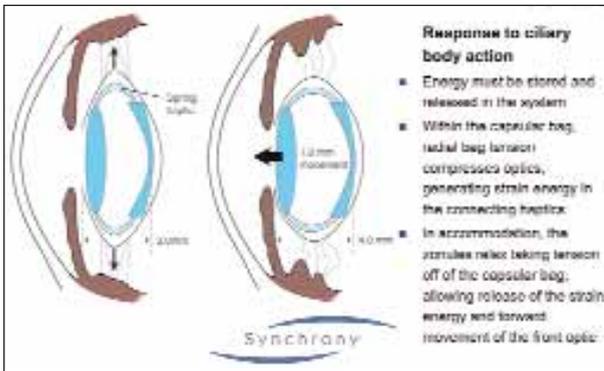


Figure 3. The Synchrony dual-optic accommodating IOL works by anterior movement of the high-powered front optic during accommodation.

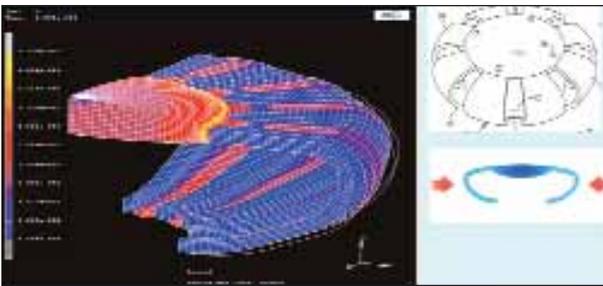


Figure 5. The haptics of the Flex Optic IOL compress the optic and change the optic's radius of curvature and power. The forces changing the shape of the optic during accommodation are demonstrated, here using a finite element model.

high-powered anterior optic should result in approximately 3.50 D of accommodation. One benefit to this dual-optic design is that the moving optic is always +32.00 D, which means that the accommodative amplitude is consistent across all lens sizes and does not diminish with net lens power. Using defocus curves, a recent pilot study⁷ found a statistically significant difference in mean accommodative range between 26 eyes implanted with the Synchrony lens and 10 eyes that received the monofocal control (ie, Synchrony 3.22 ±0.88 D [range, 1.00 to 5.00 D] vs monofocal 1.65 ±0.58 D [range, 1.00 to 2.50 D]). Another key feature of the Synchrony lens is its three-dimensional structure, which is designed to preserve the physiologic geometry of the natural crystalline lens. This conservation of geometric form may facilitate increased movement of the lens optic as well as contribute to the free flow of aqueous, which may be an important factor resulting in the extremely low levels of posterior capsular opacification.⁶ Another modification specific to the Synchrony lens' design is two posterior wings that facilitate the IOL's centration, compensate for variations in the capsular



Figure 4. Features of the Synchrony dual-optic design are highlighted in red.

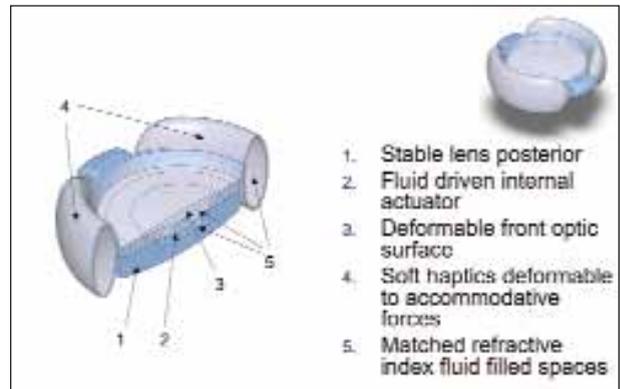


Figure 6. The Power Vision Fluid Vision IOL uses fluid to change the shape of the front surface of a deformable optic. This process produces a dioptric power change with accommodative effort.

bag's size, and ensure posterior fixation. The IOL also features spacers to prevent interoptic lens adhesions and aqueous channels to facilitate fluid exchange between the dual optics (Figure 4). This lens has obtained CE Marking in Europe and is completing phase 3 clinical trials in the United States.

IOLs THAT CHANGE IN SHAPE OR CURVATURE

A number of new lenses in various stages of development are designed to change shape or curvature with accommodative effort. The Flex Optic IOL (Advanced Medical Optics, Inc. Irvine, CA) is a single-optic IOL. During accommodation, the optic is compressed by the haptic, thus reducing its diameter and changing the radius of curvature of its front and back surfaces (Figure 5). This steepening of the curvature of the lens optic upon contraction of the ciliary muscle thereby increases its total dioptric power.

The FluidVision Lens (PowerVision Inc., Belmont, CA)

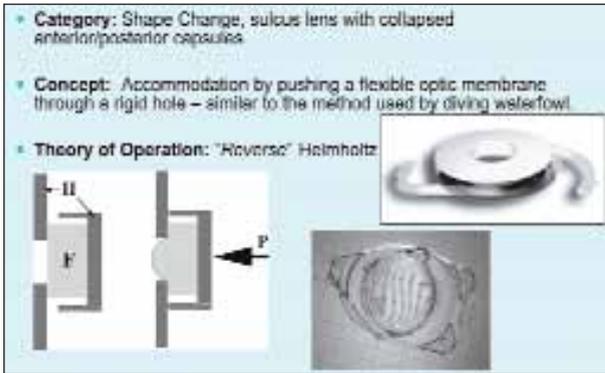


Figure 7. The NuLens sulcus-fixated accommodating IOL relies on the collapse of the anterior and posterior capsules to push a flexible optical membrane through a rigid orifice, which changes the optic's anterior curvature.

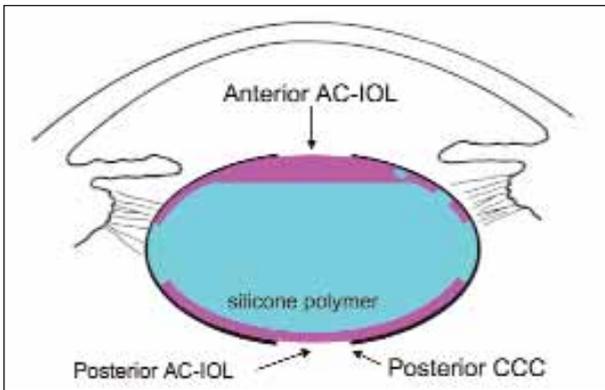


Figure 9. Dr. Nishi and colleagues developed a bag-filling technique using two silicone lenses and an injectable silicone polymer that is injected via a hole in the anterior lens haptic.

drives fluid of a polymer-matched refractive index from the soft haptics through channels to a fluid-driven internal activator. This action produces an accommodation-driven increase in the anterior curvature of the deformable optic's anterior surface (Figure 6).⁸ Preliminary studies in five blind eyes with end-stage glaucoma showed a pilocarpine-induced accommodative change in the lens' curvature of up to 8.00 D for the 3-month study period. Studies in sighted eyes are planned for the near future.

The NuLens (NuLens Ltd. Herzliya Pituah, Israel) is a sulcus-based accommodating IOL. This lens is designed for implantation in front of collapsed anterior and posterior lens capsules, which serve as a zonular/capsular diaphragm. In a reverse of the Helmholtz principle, during disaccommodation, the tightened capsular diaphragm pushes a flexible optic forward through a rigid hole, thereby significantly increasing the optic's anterior curvature (Figure 7).⁹ The transfer of force from the capsular diaphragm to the optic is accomplished via

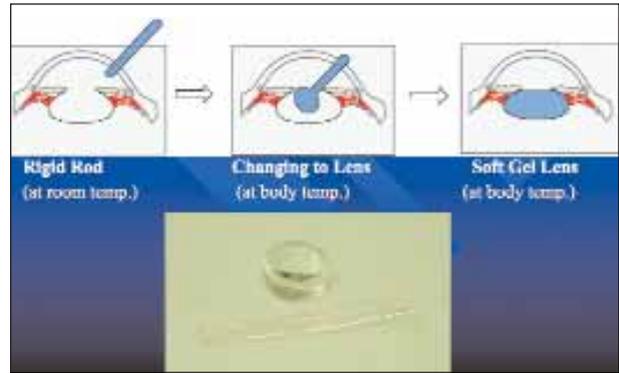


Figure 8. The Medennium SmartIOL relies on a proprietary material with unique thermodynamic properties that changes shape from a solid rod at room temperature to a gel-like lens-shaped polymer at body temperature.



Figure 10. The AkkoLens relies on accommodative forces to move two overriding cubic optical elements in opposite directions, thereby dynamically changing the refractive power of the IOL.

a piston-like element that is part of the lens. The principle of this optomechanical system is similar to the accommodative mechanism utilized in the eyes of waterfowl, which have a rigid muscular iris and flexible crystalline lens and require a very high accommodative range during underwater dives. In theory, the NuLens' deformable optic could produce up to 10.00 D of accommodation. The lens has undergone preliminary human trials in partially sighted individuals with macular degeneration. The IOL currently requires a large incision for implantation.¹⁰ Newer designs may reduce this requirement and also incorporate a spring-like element to reverse the driving mechanism so that the increase in

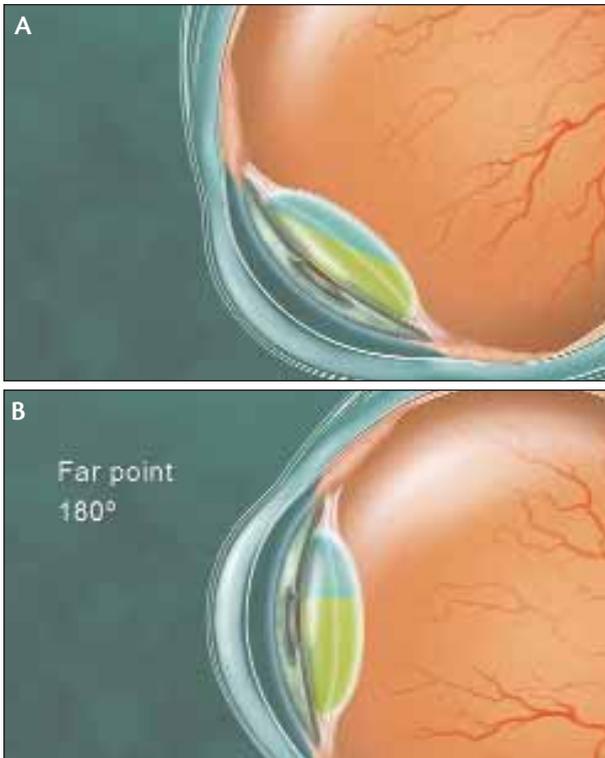


Figure 11. The LiquiLens harbors two immiscible liquids of differing refractive indices. The IOL relies on the effect of gravitational forces during downgaze (A). The dynamic interplay of these fluids on downgaze changes the composite refractive index through the line of sight versus looking straight ahead (B).

the anterior lens' curvature occurs during accommodative effort, rather than during disaccommodation. Both options are being studied.

Another shape-changing lens under development is HumanOptics' Superior Accommodating IOL. This lens has a soft, gel-like internal kernel surrounded by a highly elastic capsule designed to mimic the behavior of the natural presbyopic crystalline lens.

LENS-FILLING TECHNIQUES

For many years, investigators have been studying the concept of endocapsular surgery followed by lens replacement with a soft gel or polymer that would allow changes in accommodative shape. Research dates back to the pioneering work of Kessler¹¹ in 1964, and the approach has been referred to by some investigators as Phaco-Ersatz.¹² The most significant challenges are the high incidence of capsular opacification, leakage of the polymer during or after the procedure, how to adjust the volume of the injected material and remove the material after polymerization (if needed), and the

development of a polymer with viscoelastic qualities that is amenable to deformation. The polymer must allow accurate targeting to emmetropia during disaccommodation, return to its resting shape during accommodation, and produce minimal aberrations throughout accommodation and disaccommodation.

“When examining the pipeline, it is important to realize that developmental times vary according to the challenges that each one of these lenses will face.”

Several novel IOL designs merit discussion. The Medennium SmartLens IOL (Medennium, Inc., Irvine, CA) represents an innovative approach that utilizes a proprietary “smart” hydrophobic acrylic material with unique thermodynamic properties. The material starts out as a solid rod at room temperature that can be inserted into the eye through a 3.0- to 3.5-mm incision. When placed in the eye, body temperature transforms the material into a gel-like polymer that takes the natural shape of a lens, after which it is implanted in the capsular bag (Figure 8). This IOL solves an anatomic problem in that a 3.0-mm diameter rod can be gradually transformed into a 9.5-mm lens.

Perhaps the most significant recent advances in the treatment of presbyopia via lens filling surgery have been made by Nishi et al,¹³ who address two of the main obstacles previously limiting the success of this procedure: capsular opacification and leakage of the injected silicone polymer. Following standard phacoemulsification through a 3.5- to 4.0-mm capsulorhexis, the surgeon creates a small posterior continuous curvilinear capsulorhexis. As shown in Figure 9, a foldable disk-shaped silicone IOL with sharp edges is placed posteriorly in the capsular bag. Then, an anterior foldable accommodating IOL that serves as both a lens optic and plug is injected anteriorly in the bag in piggyback fashion. This anterior lens has both a positioning pocket near the edge of the optic and an injection hole within the haptic’s rim. Using a Sinsky hook, the surgeon can displace the anterior optic such that the injection hole comes close to the edge of the continuous curvilinear capsulorhexis, thus allowing the injection of a silicone polymer that polymerizes in around 2 hours. Although questions remain regarding this technique, Nishi et al have demonstrated the technical feasibility of an accommodating lens filling method and the potential for future clinical application.

IOLs WITH DYNAMIC CHANGES IN REFRACTIVE INDEX OR POWER

Two lens designs in development rely on dynamic changes in refractive index or power to accomplish changes in near vision. The AkkoLens variable focus IOL (AkkoLens International BV, Berda, The Netherlands) has two partially overlapping optics, which are compressed and move centripetally (in opposite directions) during the ciliary muscle’s contraction (Figure 10). The anterior element combines a spherical lens for refractive power and a cubic surface for the varifocal effect. The posterior optic has only a cubic surface. The focal length of the IOL changes as the superimposed refractive elements shift in opposite directions in a plane perpendicular to the optical axis.¹⁴ Bench testing of a prototypic lens demonstrated 4.00 D of accommodation with 0.75 mm of lateral displacement of the optical elements.

The second IOL design in this category is the LiquiLens IOL (Vision Solutions Technology, Rockville, MD), developed by Alan Glazier, OD. This IOL contains two immiscible fluids of different refractive indices that are axially juxtaposed when the patient lowers his head to read, but not when he looks into the distance (Figure 11). Rather than rely on Helmholtz-based accommodative mechanisms, this gravity-dependent IOL depends completely on the interplay of fluids upon downward gaze: it changes the focal length by altering the indices of refraction that occur through the line of sight. Given the lens’ higher variable range of power, the initial concept was directed more toward patients with age-related macular degeneration, but there are plans to develop the LiquiLens as an accommodating IOL as well.

CONCLUSION

Increased near vision can be accomplished via a variety of accommodative and pseudoaccommodative mechanisms that can be combined. The vast majority of these utilize the ciliary muscle as an engine to drive the process.

When examining the pipeline (from concept to prototypes and initial implants in blind eyes), it is important to realize that developmental times vary according to the challenges that each one of these lenses will face. Factors like improving the ease of implantation (ie, developing an adequate delivery system), achieving long-term capsular stability (eg, addressing variations in the capsular bag’s size, contraction, fibrosis, and opacification), and enhancing refractive predictability and accuracy without introducing unwanted aberrations all cumulatively impact the expected clinical availability. After meeting these challenges, if the prototype is

robust enough to undergo an FDA study, it then generally takes between 4 and 6 years from the first lens implanted in a human to approval. Add-ons like post-operative modification of the IOL's refractive properties (ie, light adaptable IOLs) may prove to be advantageous in tackling some of these issues.

Given the number of diverse approaches to the surgical treatment of presbyopia and the inherent advantage of an IOL that does not split light to provide vision at all distances, the future of accommodating IOLs looks bright. Recent formidable advances in stem cell research and regenerative biology, however, could mean that the ultimate future goal is to regenerate the crystalline lens via the lens epithelium. ■

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