Mathematician Edward Lorenz is famous for coining the term *butterfly effect*, the most common metaphorical example of chaos theory. This is the branch of mathematics that deals with complex systems whose behavior is highly sensitive to slight changes in conditions, so that small alterations can give rise to strikingly great consequences.

Case in point, the butterfly effect describes the effects of a butterfly flapping its wings on one side of the globe, setting into motion a tornado on the opposite side. The field of meteorology has developed advanced measurement tools and algorithms designed to predict future weather events in spite of the chaos that seems to control them. Even with the progress, inaccuracies occur, leading to ridicule of the meteorologist by the common man, who is unaware of the inherent challenges of the complex field.

The modern refractive cataract surgeon has some things in common with the poor weatherman. Despite sophisticated technologies including optical biometry, corneal topography, OCT, and high-powered mathematical formulas, most of us achieve refractive outcomes within ±0.50 D of intended target only 50% to 80% of the time.\(^1\) Chaos theory has not yet been mastered in our field. The butterfly wings flapping during cataract surgery may be the patient’s tear film quality at the time of testing, or the exact angle of approach we use when making the main incision, or perhaps the orientation of zonules affecting the effective lens position (ELP) of the IOL after implantation.

Regardless of the cause, we are frequently surprised by an imperfect refractive outcome—despite our most sincere efforts before, during, and after surgery. Unfortunately, patients who end up with these imperfect outcomes rarely have the capacity or perspective to understand why, and regardless of
all of our efforts (and in many cases their extra money spent), their metaphorical picnics have been rained upon. In essence, there is often a gap between the expectations of our patients and the realities achieved after surgery. The larger the gap, the greater the frustration, and we have but two choices: Either lower patient expectations or change their realities by achieving better postoperative outcomes.

Thankfully a new category of IOL technologies—adjustable and exchangeable lenses—is taking aim squarely at the latter through novel strategic designs that give doctors and patients better options for fine-tuning their vision after the initial cataract surgery.

**ADJUSTABLE IOLs**

**Light Adjustable Lens (RxLAL).** The three-piece silicone RxLAL (RxSight) is designed for in-the-bag placement. The material has a proprietary property technology that allows refractive changes to be induced by a UV light source (Light Delivery Device [LDD], RxSight). This adjustment is typically performed in the office after the refraction has stabilized. The RxLAL is the first of this new generation of adjustable IOLs to achieve FDA approval; the lens and LDD were approved in November 2017.1

Early clinical results showed that 91.8% of patients were within ±0.50 D of target refraction after LDD lock-in.1 The LDD is approved to correct up to 2.00 D of residual sphere and -0.75 to -2.00 D of residual astigmatism. The real-world results may be even better once we are able to correct lower levels of residual astigmatism (currently an off-label use).

The ability to noninvasively correct refractive error postoperatively is a distinct advantage of this technology. Being able to create customized monovision for patients is another application with a significant upside. The only downsides are the potential costs of the LDD and lens, along with ensuring that patients comply with UV light protection prior to the lock-in procedure. (Editor’s note: Phillips Kirk Labor, MD, FACS, FICS, ABES, provides further insights on the RxLAL in his accompanying sidebar.)

**THE RxLAL ▶ BY PHILLIPS KIRK LABOR, MD, FACS, FICS, ABES**

Despite advances in modern IOL designs and diagnostic technologies, cataract surgeons still have only one shot to get it right, and we remain limited by the ability to predict the postoperative status of the eye. A resulting lack of confidence in being able to satisfy demanding patients has clearly limited adoption of toric and presbyopia-correcting IOLs. LASIK far more consistently meets or exceeds patient expectations and is easily enhanced postoperatively; this increases confidence in pitching the technology.

This differential may soon change. The RxSight Light Adjustable Lens (RxLAL; RxSight), the first IOL designed to be noninvasively adjusted after implantation (Figure), received FDA approval in November 2017. The RxLAL is a foldable three-piece IOL made of photosensitive silicone that is implanted using routine preoperative and surgical techniques. Approximately 2 to 3 weeks after implantation, the patient returns to have his or her vision and refraction evaluated. If there is residual error, the surgeon enters the desired refractive change into the Light Delivery Device (LDD; RxSight), a UV light source also approved by the FDA in November. The UV light from the LDD is used to modify the shape and focusing characteristics of the lens.

The light treatments take place in an office setting and last around 90 seconds; they can be performed multiple times, as needed. Once the desired vision is achieved, the custom prescription is permanently locked in. Until the refractive change is permanent, patients must wear special UV-protective glasses to prevent exposure of the IOL’s photosensitive silicone material to UV light.

In patients implanted with the RxLAL, the LDD can be used to treat postoperative manifest cylinder from -0.75 to -2.00 D and manifest sphere from -2.00 to 2.00 D.1

In the pivotal study that led to approval of the IOL and LDD, 91.8% of eyes achieved a result within ±0.50 D of target manifest refraction spherical equivalent,1 which is similar to the refractive accuracy seen in recent LASIK studies.2 This level of accuracy will clearly benefit distance vision and astigmatism and monovision refractive corrections. Postoperative adjustability may also have great utility in eyes that have undergone previous corneal refractive surgery, and future technology advances are likely to provide additional presbyopic solutions.

**EASY TO USE**

As one of the investigators in the 17-site US clinical trial, I implanted and adjusted a significant number of RxLALs. The presurgical and surgical experiences did not require any additional skills beyond what a cataract surgeon is familiar with. Postoperatively, the LDD was easy for me to use and comfortable and painless for patients. The protective UV glasses were not difficult for patients to use.
Advances in femtosecond laser technology at the turn of 21st century helped to improve the precision and safety of LASIK. Further innovation in femtosecond technology with the introduction of the small-incision lenticule extraction (SMILE) technique marked another milestone in corneal refractive surgery. The biggest limiting factor with corneal refractive surgery now lies in the limitations of the cornea itself.

Today, the femtosecond laser is poised to carve out a new role for itself in IOL surgery. Experimental work by Sahler et al has shown that it is possible to create a negative refractive index change in a hydrophobic acrylic material by exposing the material to water and low energy light from a femtosecond laser at 520 nm wavelength. This approach, known as refractive index shaping, is an exciting new technology being developed by Perfect Lens.

In the event of residual refractive error or postoperative refractive surprise after IOL implantation, the refractive index shaping device could be used to change the IOL power to correct the refractive error postoperatively. This technology could minimize the need for lens explantation or additional touchup corneal refractive procedures due to unsatisfactory refractive results of cataract surgery.

Power changes of up to 4.00 D have been successfully accomplished in bench testing and animal studies. The technology could also potentially be used in complex cases to treat limited amounts of higher-order aberrations.

The treatment area is a disc-shaped segment within the IOL optic with a diameter of at least 4 mm and depth of 50 µm. Treatment algorithms direct the laser via scanning movements to create a disc of refractive index gradient to modify up to 4.00 D of positive or negative sphere and 3.00 D of astigmatism (Figure). A rabbit study showed an average of 3.60 D change could be achieved with error of less than 0.10 D and standard deviation of 0.03 D. Another experimental study found that the technology could be used to accurately adjust dioptric power in a commercially available hydrophobic acrylic IOL without significantly altering the qualities of the IOL, including modulation transfer function, light transmission, and light scattering.

The startup company Perfect Lens is developing a femtosecond laser technology to noninvasively change the optical power of any acrylic lens. Using a concept called phase wrapping, the laser creates a change in the refractive index of an acrylic IOL in vivo. Sphere, cylinder, and even multifocality can be either induced or reversed using this process in dioptric ranges that would perhaps place all but the most extreme cases within its capabilities.

This approach to postoperative power adjustment has potential advantages over other IOL power-adjustable technologies because it could be applied to many commercially available acrylic IOLs. Additionally, it does not depend on a special IOL material, and there would be no time restrictions regarding when it can be done postoperatively. It would be a minimally invasive laser treatment that potentially could be performed in a doctor’s office under topical anesthesia.

The ability to customize sphero-cylindrical treatment and to place or remove multifocality would create a paradigm shift in how surgeons address their patients’ lens choices. True customization of refractive outcomes with IOL technology could be achieved. Wound healing and corneal limitations might no longer be a factor in the postoperative adjustment of refractive errors. This would give patients a true choice of customization and surgeons a tool to correct potentially unwanted visual side effects that patients cannot neurally adapt to with no time period limitation.

In vivo clinical studies of the Perfect Lens are under way.


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testing, this technology could become the refractive cataract surgeon’s best friend. No longer would we need to spend hours preoperatively counseling patients and finding out which IOL they would like to have implanted. Imagine a day when every patient receives a standard IOL, and the upgrade conversation happens postoperatively, when the patient is no longer contending with the cataract and is in a better position to make a decision that is right for his or her lifestyle. Plus, if the patient chooses a multifocal IOL and is unable to adapt, the multifocality could be erased without a lens exchange (bit.ly/waring0518).

Harvard Business School Professor Clayton Christensen defined disruptive innovation as a process by which a product or service takes root

THE GEMINI REFRACTIVE CAPSULE ▶ BY WILLIAM F. WILEY, MD

Over the past decade and more, cataract surgeons have noticed a shift in patient expectations and demands, with patients more often requesting spectacle independence and maximal acuity across their entire range of vision. As more technologies become available and more resources are accessible to our patients, these expectations will continue to increase.

The current mindset of technology consumers is that a product’s lifespan is only about 1 to 2 years. After that, it is time to upgrade to the next latest-and-greatest technology. As the younger generations start to develop cataracts, they will undoubtedly expect the same potential for upgradability of their lens technology. That is why, in my opinion, exchangeable and adjustable IOLs are the way of the future.

IT STARTS NOW

With current IOL technology, whatever the patient opts for at the time of cataract surgery is a lifetime lens. But even today, some patients ask questions like, “If I get a multifocal IOL now and something better becomes available in the future, could I upgrade my lens?” or “I can’t afford a multifocal IOL right now, but could I exchange it for one in the future?”

Unfortunately, we have to tell these patients no. Because the patient’s lens selection is permanent, it can influence presbyopia-correcting IOL conversion rates. However, if surgeons had the ability to easily exchange a lens—say, when a new technology became available or when the patient was unhappy with his or her vision after surgery—I think it would give them more confidence to offer premium lens technologies and patients more confidence to opt for them.

A NEW SOLUTION

Several adjustable and exchangeable lens technologies are in the pipeline, including the Gemini Refractive Capsule (Omega Ophthalmics; Figure 1), which I intend to try in the near future. The defined plane in the middle of this implant securely holds a separate IOL in place. The open space could also be used for drug delivery and biometric sensors.

I envision pairing the Gemini with both traditional and premium lens technologies. I might suggest starting with a monofocal IOL within the Gemini in patients who are not yet ready to invest in a premium lens and then, over time, as their visual or financial status changes, upgrade them to a more advanced IOL. Alternatively, in patients who express a desire for spectacle independence or crisp vision at all distances, I might start with a multifocal IOL now and upgrade to a trifocal IOL technology once one becomes available in the United States.

Another interesting scenario with the Gemini Refractive Capsule is that I could implant the RxLAL (RxSight) now to give the patient the highest quality distance vision, but in the future exchange that for a light adjustable lens with extended depth of focus.

CLINICAL RESULTS

Gabriel Quesada, MD, recently reported the first human experience with the Gemini Refractive Capsule.1 In the study, the capsule was implanted into the eyes of eight patients at the time of cataract/IOL surgery. Postoperative exams were performed on day 1 and at 1, 3, and 6 months. In all cases, a mild anterior surface iris trauma was noticeable between the pupil and the incision. The anterior chamber depth and shape was normal in all eyes and at all postoperative visits, and Dr. Quesada noted that implantation of the Gemini was technically straightforward.

At 1, 3, and 6 months postoperative, mean distance BCVA was 0.1 logMAR. At 6 months postoperative, four of the eight patients with residual refractive errors

Harvard Business School Professor Clayton Christensen defined disruptive innovation as a process by which a product or service takes root

By keeping the anterior capsule open with the Gemini Refractive Capsule, we are essentially providing our patients with the opportunity to later upgrade to lens technologies beyond the refractive technology we have available today.

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initially in simple applications at the bottom of a market and then relentlessly moves upmarket, eventually displacing established competitors. If the Perfect Lens technology is eventually approved, it could render all other lenses obsolete. With any intervention, however, the possibility of risk is present. It will be interesting to see clinical results with this technology to allow us to evaluate it in a better light. (Editor’s note: Dan B. Tran, MD, provides further insights on the Perfect Lens in his accompanying sidebar.)

EXCHANGEABLE IOLs

*Gemini Refractive Capsule.* The Gemini Refractive Capsule (Omega Ophthalmics) takes an open-source approach to providing the option of exchangeability to any modern lens design while also stabilizing ELP. The product is an implant that lines the circumference of the capsular bag and provides a defined plane in the middle of the capsule to securely exchange any modern lens.

**THE HARMONI SYSTEM**

Many modern cataract surgery patients have a low tolerance for imperfect postoperative refractive outcomes and resultant dependence on eyeglasses. Therefore, the need for innovation in postoperative refractive adjustment is greater than ever. A modular IOL system, in which the optic component could be exchanged during a simple surgery while the base remains in place, could have significant applications in this setting.

With such a lens system, the diopter power of the optic could be adjusted at any time throughout the life of the patient, allowing corrections related to the changing refractive status of pediatric eyes, changes in effective lens position due to capsular fibrosis and contraction, and even upgrades to new IOL optic technology as it becomes available. A toric optic could be easily rotated and aligned to the appropriate axis within the stable base component. Also, if a multifocal optic was implanted and the patient could not neurally adapt to it, the optic could be easily exchanged for a monofocal one.

**THE HARMONI SYSTEM**

The Harmoni Modular IOL System (ClarVista Medical) consists of a hydrophobic acrylic base component and a hydrophobic acrylic optic component (Figure). The anterior rim of the base component is blue to facilitate identification of the rim during attachment of the optic component to the base. We have evaluated this modular system in preclinical studies in our laboratory at the Moran Eye Center using a rabbit model.2-4

Stability and capsular and uveal biocompatibility were evaluated in short- (6 weeks)2 and longer-term (6 months)4 studies. Stability in the capsular bag and uveal biocompatibility of the system were excellent for up to 6 months in the rabbit model. Due to the design of the base component featuring long loops and peripheral anterior and posterior square edges, the lens appeared to prevent overall capsular bag opacification.

We performed another study specifically designed to evaluate the ease of replacement of the optic of this modular system in comparison with replacement of a standard, commercially available one-piece hydrophobic acrylic lens. A replacement procedure was performed at 2 weeks after implantation, and then an explantation procedure was performed at 6 weeks postoperatively. At both times, explantation and replacement of the optic of the test lens was found to be easier than the control using only standard instruments. More manipulation of the capsular bag—which may result in zonular stress—was needed to free the haptics of the control lenses, especially at the 6-week explantation.

In patients with previous Nd:YAG laser capsulotomies, exchange procedures of standard IOLs can be challenging, sometimes requiring additional vitreoretinal surgery. IOL exchange in these cases would be less likely to result in vitreous leakage, however, if the base component of the IOL did not have to be removed during the procedure.

**CLINICAL TRIAL UNDER WAY**

Clinical trials of this modular system are currently under way in several locations outside the United States, and US pivotal trials are being planned. The first US pivotal trial is projected to start during the second half of 2019.


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**Figure.** Schematic drawings show the base component (left), the optic component (center), and the assembled Harmoni Modular IOL System (right).
The holy grail of cataract surgery is to match the accuracy of laser refractive surgery and allow patients to attain maximal postoperative visual outcomes. However, a recent report including more than 200,000 eyes found that only about three in four were within ±0.50 D of predicted spherical equivalent after cataract surgery. Roberts and coworkers reported similar results using advanced IOL calculation formulas. These results indicate a need for technological improvements in the area of cataract surgery refractive outcomes.

A new generation of modular and multicomponent IOLs has the potential to accurately and safely resolve these postoperative refractive issues. One such multicomponent IOL is the Precisight system (InfiniteVision Optics). It consists of two refractive lenses (Figure 1), a front and base lens, which are preassembled outside the eye (Figure 2). This assembled complex is then injected into the capsular bag through a 2.2-mm clear corneal incision. Together, both lenses provide the refractive power needed by the eye (Figure 3).

In the event of a refractive surprise or other optical issues, the front lens can be removed and exchanged for a new front lens with a different refractive power in a 5-minute surgical procedure (Figure 4). A major advantage of this system lies in the ease of implantation during the primary procedure, similar to that of conventional IOL implantation. The workflow in the OR is thereby unaltered.

**CLINICAL EXPERIENCE**

I have performed more than 50 front lens exchanges with the Precisight at 3 to 7 months after primary surgery. After the enhancement, UCVA in 100% of these eyes has been 20/25 or better. The mean manifest refraction spherical equivalent of 1.39 D before enhancement decreased to 0.09 D after enhancement. The lens position is predictable, and there is excellent rotational stability.

During the enhancement procedure, the front lens tabs are easily separated from the base lens using simple instruments. IOL forceps are then used to pull the front lens out of the eye through the original main incision site. A new front lens is inserted into the position of the extracted front lens.

With conventional IOLs, there is a race against time for IOL exchange because capsular fibrosis can complicate the exchange process. However, with the Precisight, the enhancement procedure is unaffected by capsular fibrosis and time elapsed after primary surgery.

**UTILITY AND APPLICATION**

Multicomponent IOLs such as the Precisight will be helpful for patients with high visual expectations or for those with a high likelihood of refractive surprise, such as eyes with previous refractive surgery, corneal transplantation, or extreme ocular dimensions. Further, surgeons will be able to easily exchange a multifocal IOL for a monofocal if patients experience poor tolerance or visual disturbances. The exchange can be performed without time limit, providing patients with the maximal period for neural adaptation. The Precisight also provides the opportunity for long-term enhancements when a change in refraction occurs. The Precisight has received the CE Mark and is commercially available in Europe.


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“There is often a gap between the expectations of our patients and the realities achieved after surgery. We have but two choices: either lower patient expectations or change their realities by achieving better postoperative outcomes.”

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hold a traditional IOL in place. The company is also developing a proprietary hydrophobic acrylic optic that could be used in conjunction with the Gemini Refractive Capsule, either alone or in combination with traditional IOLs, to create new optical systems for low-vision patients or simply to fine-tune refractive outcomes.

Additionally, by keeping the capsular bag open, the Gemini Refractive Capsule has been shown to dramatically reduce posterior capsular opacification (PCO). Other nonrefractive devices, such as biometric sensors, are also being developed to fit inside the real estate that is protected by the Gemini Refractive Capsule. With a protected environment inside the capsule, adding or exchanging lenses or other technologies would become a simple proposition without the traditional risks of damage to zonules or the natural capsule. Human trials demonstrating the implantation of the Omega Gemini plus an additional IOL were first presented at the OIS ASCRS meeting in 2017. While the intent of the device has remained constant, the design has evolved since then and was shown to be safe and effective through another human trial presented in April of this year. An expanded human trial is currently being scheduled in El Salvador. (Editor’s note: William F. Wiley, MD, provides further insights on the Gemini in his accompanying sidebar.)

Harmoni Modular IOL System. The Harmoni Modular IOL System (ClarVista Medical) is a two-part hydrophobic acrylic lens system that sits inside the capsular bag. This well-designed technology uniquely solves the problem of lens exchange. On an annual basis, the most common reason for IOL exchange is implantation of an IOL with the wrong power. As we know, lens exchanges become more complicated once the anterior and posterior capsules fuse. With the Harmoni system, the optic is separate from the haptic and base, and late exchange of the optic component would theoretically be easier than a full IOL exchange, should the patient desire a change.

With a proprietary clip-in optic, the worries over complications from an optic exchange are greatly mitigated. There have also been reports of dramatic PCO reduction, which is an added bonus. Bench and animal study results have been published, and clinical trials are said to be under way. (Editor’s note: Liliana Werner, MD, PhD, provides further insights on the Harmoni in her accompanying sidebar.)

Precisight IOL. Originally designed by ophthalmologist Theodore P. Werblin, MD, PhD, the Precisight lens (InfinityVision Optics) was conceived well ahead of its time. This two-piece hydrophobic acrylic lens system is designed to have a posterior lens with a plate-style haptic that sits in the capsular bag and an anterior lens component that is connected to the posterior component through the capsulorrhexis but that resides in the ciliary sulcus.

This system also nicely solves the problem of lens exchange by eliminating the need to remove haptics that have become fixated by a fibrosed capsule. The front lens can be exchanged while the posterior lens remains in place. This lens has received the CE Mark and is commercially available in Europe. (Editor’s note: Harvey Siy Uy, MD, provides further insights on the Precisight in his accompanying sidebar.)

ON TO NIRVANA
As we have seen, there are multiple technologies in development that promise to assist in conquering the chaos theory of refractive cataract surgery. May we all someday find ourselves together in the nirvana of routine exceeding patient expectations and being properly recognized for the hard work and effort we apply to helping our patients.


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