

Ophthalmology Times

CUTTING-EDGE ADVANCEMENTS

CLINICAL DIAGNOSIS | SURGERY | DRUG THERAPY

Toward emmetropia: More advances, more improvements

Refractive, corneal surgery in 2016 saw gains in therapies for keratoconus, presbyopia

CROSSLINKING

“Crosslinking is probably the most meaningful advance of the year in the field of cornea, as well as the most clinically significant change in keratoconus management that we have had in many years,” said Peter Hersh, MD, clinical professor, and director, cornea and refractive surgery, Institute of Ophthalmology and Visual Science, both at Rutgers-New Jersey Medical School, Newark, NJ, and in private practice at the Cornea and Laser Eye Institute in Teaneck, NJ.

The procedure from Avedro was approved in April 2016 for treating progressive keratoconus and then in August 2016 for corneal ectasia, he pointed out. These approvals are the endpoints of 8 years of work beginning in 2008 in multicenter clinical trials carried out at 10 study sites.

FDA approval was based on the study results for progressive keratoconus (defined by changes in topography, refraction, etc.), in patients 14 years and older, or for patients with corneal ectasia, he explained.

“This is the first procedure that we have to decrease keratoconus progression, so it represents an important breakthrough,” Dr. Hersh said.

The clinical trials for keratoconus showed clinically meaningful results in more than 200 eyes in the U.S. clinical trial for keratoconus.

“We found that the average improvement in the keratoconus cone was about 1.6 D,” Dr. Hersh said. “In fact, about one-third of patients saw improvements of 2 D or more.”

Although actual topography improvement is not the goal of crosslinking in keratoconus, but rather stabilization of the disease progression, the results seen in the study clearly indicated that the procedure can effectively treat keratoconus with an excellent safety profile, he explained.

“Most patients stabilize, a good number improve, and a small percentage continues to have progression,” Dr. Hersh said.

Crosslinking also is effective in stabilizing progression of ectasia over time.

However, the actual topography improvement in these patients might not be as robust as that observed in patients with keratoconus, likely because of the steeper cones initially and more central cones in patients with keratoconus.

In other analyses performed by Dr. Hersh, he found that crosslinking patients with steeper cones tend to achieve more improvement; patients with a K reading of 54 or more were five or six times more likely to flatten by 2 D or more, and typically ectasia patients have less steep and more peripheral changes.

However, the actual stabilization of the cornea is effective with either keratoconus or ectasia, independent from the preoperative severity.

Crosslinking may ultimately eliminate the need for corneal transplantation in many patients. Dr. Hersh noted that in his practice patients have been stable for 8 years and in European studies, patients have been stable for 5 to 10 years after treatment.

CORNEAL INLAYS FOR KERATOCONUS

In line with keratoconus treatment, Dr. Hersh and colleagues have started a study of a new procedure that they have developed, called corneal tissue addition for keratoconus [CTAK] (Figure 1).



This novel procedure uses corneal inlays prepared from preserved corneal tissue. In a study of patients with keratoconus, he is performing the CTAK procedure, in which lenticules of this preserved tissue are shaped by a femtosecond laser and inlaid via a corneal pocket. (Image courtesy of Peter S. Hersh, MD)

This procedure is performed with the goal of restoring corneal tissue and thickness to severely ectatic keratoconus corneas that cannot

benefit from crosslinking and are unable to undergo any other procedures for visual rehabilitation short of corneal transplantation. CTAK may restore the cornea's viability for other procedures such as crosslinking or PRK.

This is a very early study, with only a few patients treated, but Dr. Hersh noted that the preserved corneal tissue can be shaped well and transplanted into a corneal pocket.

“The corneal tissue is clear in situ, causes no tissue reaction, healing is quick, and the corneas become clearer over time,” he said. “The tissue and thickness were restored in these early patients. The next steps are refinement of the procedure with possible adjunctive crosslinking and other interventions to improve the vision.”

ADJUNCTIVE THERAPIES TO CROSSLINKING

With approval of crosslinking, new recent consideration might be given to the use of Intacs (Oasis Medical) or potentially PRK.

“The use of Intacs is something that might gain in popularity in the future as surgeons become more comfortable with crosslinking,” Dr. Hersh said.

The crosslinking procedure will provide the required stabilization, and the addition of Intacs can substantially improve the topography by upward of 10 to 15 D in some patients. Consideration may be given to both procedures in patients with keratoconus, since they address different aspects of the disease problem.

“In a clinical trial we have been performing, crosslinking and Intacs appear to be complementary,” he said.

The potential is also there for postoperative fitting of patients with keratoconus with scleral lenses and newer contact lens designs to aid in visual rehabilitation.

FEMTOSECOND LASER

Femtosecond laser-assisted transplants and the ability to use the femtosecond laser to perform more dependable deep anterior lamellar keratoplasty (DALK) in keratoconus are very helpful for patients with keratoconus, Dr. Hersh said.

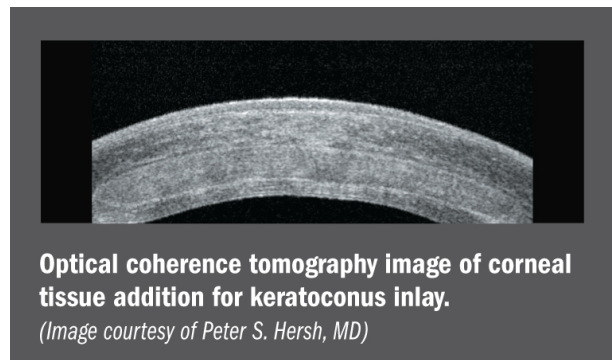
In his practice, most of the keratoconic transplants are done with the femtosecond laser.

A benefit of the femtosecond laser, he noted, is that the level of corneal astigmatism has been greatly reduced because of the good graft-host correspondences achieved.

Dr. Hersh noted he prefers the mushroom pattern, because it facilitates making a big bubble in the DALK procedure. In addition, the suturing is done peripherally, resulting in less astigmatism postoperatively and faster visual rehabilitation.
(Figure 2)

LASIK

Topography-guided LASIK was approved to treat patients with 8 D of myopia and 3 D of astigmatism. Dr. Hersh pointed out that ophthalmologists are beginning to incorporate this technology into their practices.



The clinical trial of topography-guided LASIK in normal corneas showed excellent results, he noted, with many patients achieving vision after LASIK that was better than their best-corrected spectacle vision before LASIK. This procedure is not approved for clinical use in the US for patients with unusual or irregular corneas that ophthalmologists might want to treat.

“This is an innovation that is one of the most exciting recent advances in LASIK,” he said. “It will be interesting to see the evolution of the procedure in clinical use in the United States as doctors become more experienced with it.”

He uses the technology in his practice and is pleased with the results.

The innovative VisuMax Femtosecond Laser for the small-incision lenticule extraction (SMILE) procedure (Carl Zeiss Meditec) was approved this year for treating patients with myopia.

“When the indication expands to treatment of astigmatism, I believe that we will see more surgeons performing SMILE in the United States,” Dr. Hersh said. “This is an exciting, new kind of technique.”

Presbyopia

Presbyopia has been the final frontier in the refractive arena for a while, and over the course of time, the approaches to correction of presbyopia have surpassed monovision in numbers and creativity.

However, in cataract and refractive surgery, the mainstay of presbyopia correction remains monovision, which requires careful patient selection, as well as considerations, such as previous corneal surgeries, thin corneas, signs of keratoconus, and ocular comorbidities that may be relative or absolute contraindications for monovision refractive surgery.

Monovision LASIK and monovision PRK procedures are easily successful in patients with myopia and astigmatism, according to Dimitri Azar, MD, but are more challenging in patients with hyperopia and the outcomes are less reliable.

Another surgical option for presbyopia correction is PresbyLASIK, which creates a multifocal corneal lens effect using three major techniques: multifocal transitional profile, central PresbyLASIK, and peripheral PresbyLASIK.

The success rates are relatively low, but Dr. Azar believes that the procedure has great potential.

Interestingly, Dr. Azar and two French collaborators, Damien Gatinel, MD, and Jacques Malet, MD, have hypothesized that the success of PresbyLASIK might be driven by the pupillary position during accommodation.

“When the patient accommodates, the lens power increases and the pupil decreases in size,” said Dr. Azar, Dean, College of Medicine, professor of ophthalmology, University of Illinois, Chicago. He and his collaborators are inventors on several patents for this technology, which is not yet in clinical practice.

“When this occurs, if the pupillary position is traced in the accommodative and non-accommodative positions, the positions are not concentric,” he said. “If this information is known for a particular patient, we might be able to design the multifocal corneal shape to consider the pupillary position in the unaccommodated state versus that in the accommodated state and, therefore, in principle, improve the likelihood of success of PresbyLASIK.”

Another interesting method is the use of concentric femtosecond laser treatments to achieve multifocality in the cornea. This procedure, INTRACOR (Technolas Perfect Vision GmbH), which is under investigation, is performed intrastromally to reshape the corneal tissue.

A fourth approach uses corneal inlays for presbyopia, which is currently gaining more and more acceptance, and some devices have received FDA approval for presbyopia. These devices have different designs, i.e., an intracorneal aperture, a high index of refraction lenticule in the center of the cornea, and a central lenticule to change the cornea curvature causing multifocality.

The recently approved RainDrop Near Vision Inlay from ReVision Optics received the FDA go-ahead in 2016 and joined the KAMRA inlay (AcuFocus) as another option for patients with presbyopia.

Multifocal IOLs and pseudoaccommodating IOLs are approved and also rapidly gaining acceptance for use during cataract surgery to treat presbyopia. The major issues associated with these are glare and halos. Dr. Azar pointed out that the designs are improving, and he predicts that the popularity will increase when the visual issues are addressed.

“In the future, IOLs will be approved that combine correction of astigmatism and multifocality, that is, astigmatic lenses that are multifocal,” he commented.

Many of these lenses are already approved in Europe.

Accommodating IOLs that change shape in the eye in response to accommodation are not yet approved in the United States. Dr. Azar believes that the Smart Lenses from Alcon Laboratories and Google Verily is the final frontier in this area.

“These lenses can be in the form of a smart contact or IOL with a battery inside the lens, computer chip, means to adjust the lens power, and a sensor to know where the eye is focused,” Dr. Azar said. “At near the lens power increases and at distance the power returns to baseline. Regardless of whether the lens is a contact lens or an IOL, they can provide true accommodation.”

He is optimistic about this technology. The first such contact lens is scheduled for clinical testing soon. Dr. Azar holds multiple patents for this technology. The Smart Lens builds on the technologies developed by Google Verily lens for tear glucose measurements in diabetes.

THE QUEST FOR EMMETROPIA

[One ophthalmologist views the burgeoning technologies as a continued escalation to his full spectrum of kerato-lenticulo-refractive surgery from a specific vantage point.](#)

“With the recent approval of the new technologies for premium lens implants, crosslinking, extended application of femtosecond lasers and presbyopic inlay options along with dry eye therapy, we seem to be seeing a much-awaited scenario that I have envisioned for the last two decades—i.e., Corneoplastique, a super specialty that involves the art of utilizing all these technologies in a holistic and symbiotic manner to custom-design each patient’s vision outcomes,” said Arun C. Gulani, MD.

“Using this ever-expanding armamentarium of tools, we can help patients become candidates for surgery who were not candidates previously, said Dr. Gulani, founding director and chief surgeon, Gulani Vision Institute, Jacksonville, FL. “With each approval of a new technology ranging from diagnostic to interventional, there is one additional tool that has been added to my already overflowing toolbox to plan, perform, and improve each patient’s vision.”

Dr. Gulani has used many of these technologies abroad before the FDA approval this year and was predictably impressed with the rapid adaptation of these new technologies by surgeons in the United States who were awaiting their approval.

Notable among these advancements were the approvals of crosslinking (Avedro), two presbyopic corneal inlays (KAMRA and RainDrop), newer premium lens implants like the Symphony IOL (Tecnis, Abbott) for cataract surgery and more indications for laser cataract technologies that will be added to an already wide array of currently available advances to help achieve the best vision possible in the safest and most predictable fashion.

Other new tools introduced in 2016 were ocular surface therapeutics, which included medications for dry eye, technologies to evaluate dry eye, diagnostic criteria, and ocular sealants like ReSure (Ocular Therapeutix, Inc.) and surface tissue, the use of which allow patients to become candidates for refractive surgery.

Medications to improve pupillary dilation, new tools and technologies to quantify surgical procedures including intraoperative IOL calculations and also means to perform consistent capsulorrhexis, expand the iris, and stabilization of anterior chamber also were introduced.

Dr. Gulani cited Descemet’s membrane endothelial keratoplasty as a technique that was further refined and applied to enhance surgical outcomes to achieve enhanced predictability and vision beyond correcting just the pathology, thus exuding his much beloved refractive-outcome concept to every corneal surgery.

Patients with keratoconus can have surgeries planned from lasers to microsegment inserts, including intraocular manipulation including toric, phakic, and piggyback IOLs, and now include crosslinking as a permanizing end-stage surgery to move patients with keratoconus and LASIK ectasia to excellent refractive outcomes, he explained.

In addition, patients who previously could not undergo LASIK because of thin corneas can undergo the SMILE procedure or enhanced laser PRK with improved drug modulation and have a pain-free experience and even combine this with corneal inlay surgery to address presbyopia.

Patients with complicated presentations resulting from their pathologies and complications from previous surgeries such as radial keratotomy can have more accurate intraocular measurements using newly approved devices to measure lens implant powers resulting in

emmetropia without any refractive surprises. Patients with ocular surface inadequacies can be diagnosed and treated with new modalities (chemical and visual diagnostics) to prepare the patients for a refractive procedure.

“When we consider all the approvals, increased indications, and enhanced technologies and add them to our relentless pursuit of striving for visual acuity over 20/20 in all cases, more patients can become surgical candidates, complex cases can be simplified, and less predictable situations can become more predictable,” Dr. Gulani said.

He expressed excitement about using more of these tools in his practice that has a worldwide referral base with a global clientele of complex and complicated cases and applying them in single or staged combinations to achieve perfect vision.

“My dream of turning every patient into a refractive candidate is becoming a reality,” Dr. Gulani said.

A year of ocular surface therapeutics taking shape

The year 2016 was notable for new ocular surface therapeutics, including medication for dry eye, such as lifitegrast ophthalmic solution (Xiidra, Shire), the first prescription eye drop approved to treat both the signs/symptoms of dry eye disease; technologies to evaluate and manage different aspects of dry eye disease, including products ranging from mechanical lid cleansers to pharmaceutical interventions, and also biologic corneal bandage devices (Prokera family, TissueTech).

Arun C. Gulani, MD, uses the biologic corneal bandage in his clinical practice to promote rehabilitation in complex refractive surgical cases.

The product is “a welcome addition to our corneal armamentarium for in-office management of multiple situations for which I have used it in cases ranging from implantation of Intacs [Addition Technology/Oasis Medical] to aggressive cases of pterygium postoperatively to complicated LASIK cases to radial keratotomy (RK) corrections and epithelial remodeling conditions,” said Dr. Gulani, founding director and chief surgeon, Gulani Vision Institute, Jacksonville, FL.

“In my practice, in which I see a large population of complex cataract surgical candidates, I have used ocular sealants [such as ReSure Sealant, Ocular Therapeutix], especially during cataract surgery in patients who had undergone a previous RK to seal sutureless corneal incisions and also provide security to patients who must travel to return home postoperatively with con-

junctival closure over their scleral incisions,” he said. “I have since applied this in LASIK epithelial ingrowth corrections, lamellar corneal cases, and pterygium surgery, among others.”

Intraocular innovations and approvals, such as phenylephrine and ketorolac injection 1%/0.3% (Omidria, Omeros Corp.), to improve dilation of pupils in difficult eyes have been introduced to decrease the complexity and increase the surgical predictability and safety in many cases in which visibility with a larger pupil was the Achilles' heel of that case in taking such patients from ordinary to excellent visual outcomes.

In addition, new tools and technologies to quantify surgical procedures ranging from measurement of the capsulorrhexis to IOL implant calculations especially in post-refractive surgical candidates and also stabilization of the anterior chamber to ensure increased safety and predictability that was not previously ensured, Dr. Gulani explained.

“Many of the previously mentioned products have not only increased our efficacy and predictability along with safety in regular cases, but also have significantly increased the indications to help patients who were not candidates to become candidates for vision corrective/enhanced kerato-lenticulo-refractive surgery,” he said. ■

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