

## **Ophthalmology Times – December 2006** 2006 saw the fine-tuning of existing technologies Emerging innovations show promise

By Lynda Charters

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New options for patients, such as multifocal IOLs; refinements in surgery, such as Descemet's stripping automated endothelial keratoplasty (DSAEK); and encouraging results from technology in the pipeline, such as intracorneal inlays, which would provide another new avenue for patients with presbyopia to explore; as well as high marks received by the femtosecond laser (IntraLase FS, IntraLase Corp.) for cutting flaps – these are but a few of the high points of 2006 cited by ophthalmic surgeons.

Generally speaking, ophthalmologists are perceiving the past year as one of continuation and refinements of trends, new procedures, and devices that previously were available, said Jonathan H. Talamo, MD, an associate clinical professor of ophthalmology at Harvard Medical School, Boston, and the founder of Talamo Laser Eye Consultants.

“Specifically, we are seeing a merger of corneal and lens-based refractive surgery to a degree that I have not observed in my nearly 20 years of practice,” he said. “Up until now, there has been a philosophical division between the refractive surgeons, who performed primarily corneal procedures such as LASIK, and cataract surgeons, many of whom until recently did not focus on achieving emmetropic refractive results as carefully as they are now.”

“The stimuli for this paradigm shift are two-fold: 1) the explosion of newly approved IOL designs for presbyopia, and 2) advances such as laser interferometry (IOL Master, Carl Zeiss Systems) and immersion A-scan ultrasound, which allow improved ease and precision of axial length measurement,” Dr. Talamo said. “These advances have spawned the growing acceptance of the phakic IOLs and bioptics, the combination of lens-based and corneal refractive surgery to achieve better vision.”

## **Laser procedures**

“Year 2006 was one of fine-tuning, especially of custom excimer procedures,” said Peter S. Hersh, director, Cornea and Laser Eye Institute - Hersh Vision Group, clinical professor of ophthalmology, and chief, Cornea and Refractive Surgery, University of Medicine and Dentistry-New Jersey Medical School, Newark, NJ. “This includes iris registration, new FDA approvals for higher corrections for some mixed astigmatisms,” and approval of lasers for custom treatments (Allegretto Wave Eye-Q, Wavelight) and quicker treatments (LADARVision 6000, Alcon Inc.), he said. “These advances account for the slow, steady improvements in outcome that we now see in these procedures.”

Although Dr. Talamo said he does not use either excimer laser system, he described surgeons’ reactions to both as positive. The former laser is one of the better, faster excimer lasers to arrive on the scene this year, facilitating treatment times that are a fraction of the time required by other available lasers, he said. It has “improved the excimer arsenal available to surgeons,” Dr. Talamo said. “Most of the surgeons who use this system use wavefront-optimized rather than wavefront-guided ablations. This system allows surgeons to use either approach.”

Regarding refractive surface procedures, both Dr. Hersh and Dr. Talamo said they see a trend of surgeons performing them. Dr. Hersh cited the greater comfort and the expanded indications for the surface procedures, which are encouraging more surgeons to avoid creating LASIK flaps, and the expanded group of patients.

“Surgeons are becoming less and less likely to try to preserve the epithelium when doing these procedures,” Dr. Hersh said. “There is no preferred way to remove the epithelium, and surgeons generally are using alcohol or a microkeratome. In my practice, about 30% of the procedures are surface procedures, and about 70% beneath the flaps,” he said.

Dr. Talamo credited the increase in surface procedures in part to the use of antimetabolites. “I think the widespread acceptance of prophylactic antimetabolites in surface ablation has allowed resurgence in the number of these procedures performed,” he said.

In 1991, Dr. Talamo was the first to suggest the use of antimetabolites for excimer surface ablation in a manuscript published in Archives of Ophthalmology (1991;109:1141-1146). “There was widespread acknowledgement that something had to be done to modulate corneal wound healing. Steroids did not seem to work,” he said. “Despite concerns about toxicity, single-dose intraoperative mitomycin C has proven very effective in improving refractive results.”

## **Iris registration**

Out of those aforementioned technologies, by far one of the most noteworthy technologies to become available to ophthalmic surgeons, according to Eric D. Donnenfeld, MD, is iris registration.

“My results with iris registration are so much better than they were with just conventional custom ablation,” said Dr. Donnenfeld, an associate professor of ophthalmology, New York University Medical Center, New York, and a founding partner of Ophthalmic Consultants of Long Island, Rockville Centre, NY, and Connecticut. “I think controlling for centroid shift, pupillary movement, and cyclotorsion between the wavefront and the ablation is imperative for achieving good outcomes with custom ablation. Iris registration is the most important advance that I have seen in years in the quality of our ablations,” he emphasized.

Because of the addition of iris registration to the refractive surgery procedure, 20/20 or better vision and better contrast sensitivity are being achieved in more patients, he said.

Also of note, he said, is that irregular corneas that were previously untreatable are now treatable.

“I am able to treat patients who had undergone previous ablations that were problematic and patients with forme fruste keratoconus,” Dr. Donnenfeld said. “Iris registration can capture these irregular corneas and allow the ablation to be applied precisely to the appropriate area to achieve the desired results.

“This technology has been a quantum leap forward in the quality of excimer laser ablations,” he said, adding that the technology is especially important when treating normal corneas to avoid inducing aberrations. The average movement of the pupil is 0.3 mm, which will induce aberrations in many patients, he said.

## **Femtosecond laser**

Another trend noted this year was the increased incorporation of the femtosecond laser into refractive practices. Dr. Talamo pinpointed the last 12 to 18 months as the period during which the femtosecond laser was accepted as a microkeratome.

“About one-third of the US market is now all-laser LASIK, which has translated into explosive growth for [the femtosecond laser] worldwide. This growth has been driven by the rapid dissemination of the 60-kHz technology. Now the femtosecond laser can create a flap in 18 to 40 seconds, which is almost comparable to a mechanical microkeratome,” Dr. Talamo said.

When he introduced the femtosecond laser into New England 4 years ago, Dr. Talamo said, he believed the device had a quantitative and qualitative benefit of safety and precision. Because of this belief, he has been using the femtosecond laser for all of his LASIK cases. In a report published in the *Journal of Refractive Surgery* (2006;22:556-561), he and his associates found a statistical difference in the precision with which flaps were created using the older 15-kHz femtosecond technology compared with widely used mechanical microkeratomes.

“The importance of precision in the creation of LASIK flaps is underscored by the growing recognition of the potential for development of corneal ectasia in patients who are at risk, and the role that excessively thick flaps may play in the development of this complication,” Dr. Talamo said. Another important consideration, he said, is the planar shape of the flap created by the femtosecond laser, which he said he considers a better flap, compared with the meniscus flap of the mechanical microkeratome. In addition, complications associated with mechanical microkeratomes, such as button-hole flaps, intraoperative bleeding, epithelial sloughing, and epithelial ingrowth, are very rare with the use of the femtosecond laser, he said.

Improvements in the femtosecond laser have been sufficiently impressive enough over the past year that Dr. Donnenfeld purchased the instrument and uses it in about 80% of his ablative procedures.

“In the past I thought the femtosecond laser was an interesting tool, but the smoothness of the bed and the associated complications kept me from using it routinely, especially with the inflammation it produced,” he said. “Now, however, the real advance in [the femtosecond laser] has been in the smoothness of the bed, which gives better visual results. The ability to have a smooth bed with a planar flap and very small standard deviations in the flap thickness provides surgeons with more security when making flaps.”

Dr. Hersh, who has used the femtosecond laser in place of a mechanical microkeratome for all of his procedures, also pointed to this trend. “Clearly, more and more flaps are being created with the femtosecond laser. Surgeons are becoming increasingly aware of the advantages offered by this instrument. It will be curious to see over the next year whether the femtosecond laser will be used for other corneal procedures, in particular, if there is a benefit when implanting [prescription corneal inserts] (Intacs, Addition Technology Inc.) used to treat keratoconus and ectasia,” he said.

In his practice, Dr. Hersh treats a large number of patients with keratoconus, and he said he has noted the better results that are being achieved when the femtosecond laser is used to implant the corneal inserts.

Dr. Talamo concurred. Having implanted the corneal inserts in patients with keratoconus and post-LASIK corneal ectasia for 7 years, he said he believes that

the use of the femtosecond laser as a channeling device adds precision to the procedure. With the addition of therapeutic software released this year, femtosecond technology is capable of creating channels that are deeper within the corneal stroma than the 400 µm previously allowed, which should further improve results.

Dr. Donnenfeld said he also thinks that the femtosecond laser should be used for lamellar dissections and penetrating keratoplasty, where the technology will be a major advance in corneal surgery.

### **Multifocal IOLs and nonsteroidal drugs**

Multifocal IOLs “are excellent for patients who want good near and distance visual acuity after cataract surgery,” Dr. Donnenfeld said. “I learned this year that mixing and matching of IOLs is a very good way to optimize visual outcomes for these patients.”

Previously, he said, he had been concerned about using two different multifocal IOLs and had implanted either two AcrySof ReSTOR (Alcon Inc.) or two ReZoom (Advanced Medical Optics Inc.) IOLs, which provided the patients with good distance vision. The former lens provided a close focal point, and the latter lens provided an intermediate focal point, he said.

Dr. Donnenfeld said he found, however, that the visual results achieved when he implants IOLs of two different strengths have been exceptional. “By using two different lenses, the patients have a full range of vision, and they have been happier with this combination,” he said. “This approach is not the best choice for all patients, but this has been a big change in how I use multifocal IOLs in my practice.”

The best news with this approach to post-cataract refraction, Dr. Donnenfeld said, is that almost 99% of his patients are spectacle free—a substantial jump from about 87% when patients received the same lenses in both eyes.

In conjunction with multifocal IOLs, Dr. Donnenfeld emphasized the importance of using nonsteroidal drugs when performing cataract surgery in general and when implanting multifocal IOLs especially. He and his colleagues reported in the *Journal of Cataract and Refractive Surgery* (2006;32:1474-1482) on the importance of using nonsteroidal drugs in routine cataract surgery, in this case ketorolac tromethamine 0.4% (Acular LS, Allergan Inc.). They found that 3-day and 1-day dosing of ketorolac reduced surgical time, phacoemulsification time, and energy, as well as endothelial cell loss and improved visual acuity in the immediate postoperative period, compared with 1-hour predosing and a placebo. Also, in another study reported at the 2006 meeting of the American Society of Cataract and Refractive Surgery (ASCRS), he found that contrast sensitivity improved after ketorolac was administered four times daily in patients in whom

ReSTOR lenses were implanted, compared with the patients who were not treated with ketorolac.

“The patients treated with the nonsteroidal drug had substantially better contrast sensitivity than those not treated with the drug because of the absence of macular thickening,” he said.

### **Phakic IOLs**

The widespread acceptance of phakic IOLs might have been slower than expected, Dr. Hersh said. “Thus far, these IOLs may not have been adopted at the rate that originally was anticipated when they reached the market,” he said. “The reasons for this may be that these IOLs require elective intraocular surgery, the subset of patients needing an IOL is small compared with [the subset needing] LASIK, and the surgery carries inherent risks different from corneal procedures. These factors may have impeded the wide adoption of the IOLs so far.

“In contrast,” he said, “LASIK is an in-office procedure performed on the cornea, and although patients are fearful, they are less so. Intraocular surgery performed in an operating room starts to be a big barrier for adoption of a technology.”

On this topic, Dr. Talamo said he sees slow but steady growth in the use of phakic lenses, primarily for younger to middle-aged patients with high myopia who are high-risk candidates for clear lensectomy because of the risk of retinal detachment and who still have a substantial capacity for accommodation.

Because fine-tuning of the correction with corneal refractive procedures often is necessary, the surgeons adopting this technology are those who are comfortable performing both laser vision correction and intraocular (ie, cataract) surgery, he said. “As this group of surgeons grows, I believe we will see growth in procedure volumes,” Dr. Talamo said.

### **Options for presbyopia**

Dr. Donnenfeld said he continues to view accommodative IOLs as the Holy Grail after cataract surgery. “We have the crystalens (eyeonics Inc.), and there are new IOLs entering the marketplace. The Synchrony dual-optic accommodating IOL (Visiogen Inc.) is in FDA trials and appears to provide additional accommodation. Lenses with deformable optics will be a very exciting addition to this area in the future,” he said.

Another approach to presbyopia, Dr. Donnenfeld said, is an intracorneal inlay (ACI 7000, AcuFocus Inc.) that also is in FDA trials. This technology involves a small, thin disc placed under a LASIK flap. The inlay, according to Dr. Hersh,

resembles a pinhole that enhances the patient's depth of field. "One study done in Turkey has reported encouraging results," he said.

Dr. Donnenfeld said he finds this approach to treating presbyopia to be promising. "The results thus far are interesting, and this device may have a place in the treatment of presbyopia in the future," he said. He is participating in the trials of the inlay, which in a small number of patients has provided uncorrected distance visual acuity of 20/20 and J1 near visual acuity. The procedure is reversible.

"In the future, we will be able to treat refractive errors and provide patients with good reading acuity in the nondominant eye," Dr. Donnenfeld said.

Other inlays are emerging and use different methodologies to either induce multifocality or induce enhanced depth of field for patients who are presbyopic, he said, noting that inlays that induce multifocality are very small central plus lenses that cause a center surround type of phenomenon. Other corneal inlay models try to steepen the central cornea, he said.

Dr. Hersh has noticed a trend toward more conductive keratoplasty (CK) procedures being performed to treat presbyopia over the past year. "In my practice," he said, "we have participated in two CK protocols, one using the Light Touch technique (Refractec Inc.) for presbyopia, with which we have had quite good results and notably better results than with the original procedure. This has improved predictability of results compared with the original procedure and is probably the result of being able to achieve more effect using larger optical zones.

"The early CK procedures used a 6-mm optical zone. We now do not go smaller than a 7-mm optical zone," he explained. "With the larger zones and the different methodology of the procedure, we are getting more dependable outcomes and more effect, and less astigmatism and better optical results because of the larger optical zones."

In a study of the optics of CK, Dr. Hersh and his colleagues found good topography that can be notable for its inherent multifocality. In particular, his group found a consistent postoperative prolate configuration of the cornea after CK. This study was published in *Transactions of the American Ophthalmologic Society* (2005;103:412-456).

The use of CK also has expanded to the treatment of patients who have previously undergone LASIK for myopia, Dr. Hersh said. As part of a multicenter study, he and his colleagues conducted a trial, the data from which are still being compiled. All patients were treated with one ring at 8 mm for a large optical zone.

“While we still don’t know the exact results, my feeling is that the procedure did quite well. For presbyopes who have undergone LASIK and continue to become more presbyopic, across the board the effects of CK were good because of the use of the large optical zone,” he said. “The patients undergo the procedure with knowledge of refractive surgery and know what to expect.”

In addition, Dr. Hersh said he has found CK to be very useful as a “rescue” procedure after some cases of complicated LASIK (Hersh PS, Fry KL, Chandrashekar R, Fikaris DS, Steinert RF, Ashrafzadeh A, Hersh PS. Conductive keratoplasty to treat complications of LASIK and photorefractive keratectomy. *Ophthalmology* 2005;112:1941-1947).

### **Ectasia**

Collagen cross-linking trials are about to begin in the United States, and this treatment should be a major benefit to patients with this dreaded complication, said Dr. Donnemfeld.

### **Tear film in refractive surgery**

The importance of tear film in refractive surgery also became more apparent in 2006, Dr. Donnemfeld said. Administration of cyclosporine (Restasis, Allergan Inc.) after refractive surgery has improved visual outcomes, he added, pointing to a study by George Salib, MD, and Marguerite McDonald, MD, in the *Journal of Cataract and Refractive Surgery* (2006;32:772-778). An unpublished study to be presented at the 2007 meeting of ASCRS by Dr. Donnemfeld also showed better outcomes in patients with multifocal IOLs because of the improved quality of the tear film as a result of cyclosporine application.

### **Descemet’s stripping endothelial keratoplasty**

Ophthalmologists are viewing DSAEK as the corneal highlight of the year. Kazuo Tsubota, MD, chairman and professor of ophthalmology, Department of Ophthalmology, Tokyo Dental College, Chiba, Japan, cited the procedure, which is performed to replace the endothelium to treat bullous keratopathy.

“The regular treatment approach for bullous keratopathy is, of course, corneal transplantation,” he said. “Corneal transplantation, however, changes the total corneal curvature as well as the refractive conditions. But with [DSAEK], the corneal curvature does not change because the ocular surface is in fact not touched while the procedure is performed. Descemet’s membrane is removed and replaced with the new donor-derived Descemet’s membrane with live endothelial tissue,” Dr. Tsubota said.

“The number of patients who have undergone this surgery is not large, but the impact is very big for the corneal refractive surgeon,” he said.

Dr. Donnenfeld said he began performing this surgery during the past year and believes that it provides more rapid visual rehabilitation with better refractive results in patients with Fuchs' dystrophy and bullous keratopathy.

"This is a major step forward in our treatment of corneal disease," he said, noting the contributions of Mark Terry, MD, and Frank Price, MD, to advancing this procedure in the United States.

DSAEK probably will dramatically change corneal transplantation to treat endothelial types of problems, Dr. Hersh predicted, adding that the procedure should change how surgeons deal with Fuchs' dystrophy and bullous keratopathy.

"The primary problem with corneal transplantations, especially in the older patients with suboptimal endothelium, is that these patients can have surprise refractions such as -5.0 D of myopia and 3 D of astigmatism postoperatively," he said. "Many patients are elderly and cannot tolerate contact lenses.

"Before the advent of DSAEK, my inclination was to do photorefractive keratectomy to improve their vision," Dr. Hersh said. "DSAEK, however, should improve their situation greatly. If DSAEK becomes a dependable procedure, it should surpass penetrating keratoplasty (PK)."

Dr. Talamo echoed those sentiments and said he believes DSAEK will open the surgery to a whole class of patients who previously might not have been candidates as the result of co-morbidities that eliminated PK, or whose vision was high enough for them to undergo a full-thickness procedure.

"If we can improve our results with DSAEK to surpass the 20/30 to 20/40 best-corrected outcomes often achieved now," Dr. Talamo said, "then the procedure will allow transplantation and visual rehabilitation earlier than had been considered previously when we were limited to PK."

Another development in corneal transplantation is the shaping of penetrating and lamellar grafts using the femtosecond laser. "The early results with penetrating grafts, whether using a zig-zag Christmas tree or a top-hat dissection shape, suggest that by matching the donor and recipient tissues very precisely, the astigmatic results will be better," he said.

Dr. Donnenfeld is a consultant for Allergan Inc. and Advanced Medical Optics Inc. Dr. Hersh is a consultant for Refractec Inc. and Alcon Inc. Dr. Tsubota has no proprietary interest related to any aspect of this report. Dr. Talamo is a consultant for IntraLase Corp.