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ESCRS 2006: London Calling

Last month, over 5,500 delegates attended the European Society of Cataract and Refractive Surgeons (ESCRS) meeting in London. This year we had to choose between the ESCRS and American Society of Retina Specialists (ASRS), conveniently scheduled on the exact same dates on opposite sides of the English Channel. Since Genentech seems to have the AMD market well in-hand at this point, we opted for the fast-growing ESCRS, which each year provides a look into the future of refractive surgery.

In this report, we highlight the latest developments in the surgical presbyopia correction market, including:

- Multifocal and accommodating IOLs that primarily address older presbyopes with cataracts or those at high risk for cataracts, as well as younger "refractive lens exchange" patients
- Corneal solutions primarily for younger, pre-cataract presbyopes, including multifocal LASIK, CK, and corneal inlays
- Solutions involving scleral surgery.

We also provide updates regarding LASIK products and technologies, including excimer and femtosecond lasers, and emerging devices to treat glaucoma. **Q**

Presby-IOLs: The Clash of the "Fab Four," a Debate Worthy of Parliament

The emerging market for presbyopia-correcting IOLs was, not surprisingly, a major topic of conversation once again at ESCRS. Podium presentations and off-line conversations focused on clinical outcomes and relative merits of each of the three approved lenses, and the pros and cons of mix/match strategies versus bilateral implantation of the same lens. As a reminder, the three FDA-approved presbyopia-correcting IOLs are:

- ReSTOR diffractive multifocal IOL from Alcon
- ReZoom refractive multifocal IOL from AMO
- crystalens accommodating IOL from eyeonics

AMO's Tecnis Multifocal diffractive IOL, which is approved in Europe and in clinical trials in the US, was also widely discussed. Because the characteristics, advantages, and disadvantages of each of these lenses are fairly well understood at this point, the mix/match debate grabbed much of the attention. Also, because crystalens usage in Europe is modest, the competing multifocal IOLs received much more attention on the podium.

The early uptake of presbyopia-correcting IOLs has been disappointing relative to initial guidance provided by both Alcon and AMO, and both companies have had to lower their 2006 revenue guidance for these IOLs in recent months. Our conversations with surgeons at ESCRS suggest some reasons behind this:

Continued on next page

Presby-IOLs from Page 1

- $4,000-5,000 additional out-of-pocket expense for the average Medicare cataract patient is a significant sum.
- The required chair time, for patient education and management of expectations, has been greater than initially expected, particularly for cataract surgeons that have not had active refractive practices in recent years.
- All three of the FDA approved lenses involve some level of visual compromise, which contributes further to the chair-time issue.

The major arguments for and against mixing and matching presby-IOLs are summarized in the table on the next page. Our take right now is that mix/match strategies make sense for patients that are less than fully satisfied with their first presby-IOL, and it appears that many cataract/refractive surgeons are coming to the same conclusion.

Early mix/match case series are generally reporting good adaptation by patients, higher patient satisfaction versus strict bilateral strategies, reduced spectacle dependence, fewer problems with glare and halos, and better binocular visual acuity at all distances. Anecdotally, rather than the combination of different types of optics creating problems for patients, the opposite appears to be true. In the case of the ReSTOR/ReZoom combination, the lenses are also complementary in terms of functional vision in different lighting conditions, since ReSTOR is near-dominant in bright light and the opposite is true for ReZoom.

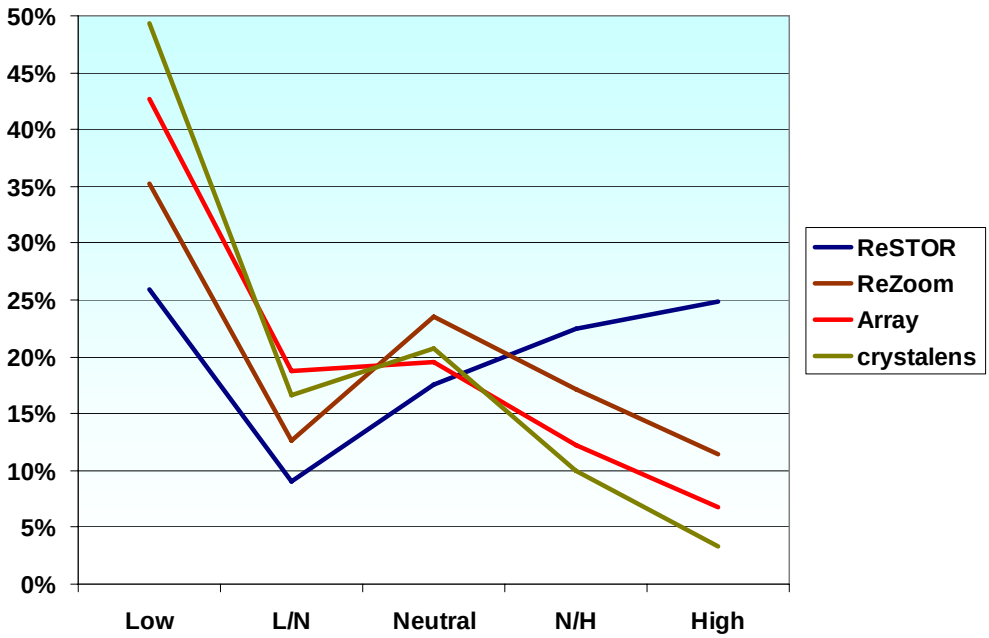
A study presented at ESCRS by Con Moshegov, MD of Australia showed superior results with bilateral ReSTOR versus a ReSTOR/ReZoom combination. However, in the mix/match patients, ReSTOR was implanted in the dominated eye, which is not the usual approach.

Alcon is still aggressively selling against mix/match approaches, which is understandable given that the company does not currently have an intermediate-dominant accommodating or refractive IOL. We suspect that R&D efforts are underway at Alcon to address this product gap, with either a refractive multifocal IOL or a diffractive IOL with less add-power ("ReSTOR Lite"), which we understand would not be a trivial development task.

European experience with AMO's Tecnis Multifocal IOL has been favorable. Studies seem to indicate that this lens is slightly more intermediate-dominant, and performs somewhat better overall, than ReSTOR. However, we expect that the introduction of an aspheric version (ReSTOR IQ) will narrow or close this gap.

Results of the 2005 survey of ESCRS members regarding presby-IOL preferences, conducted and presented by David Leaming, MD of Palm Springs, came as no surprise given Alcon's strong market-leading share in cataract surgery (see chart below). European surgeons expressed the highest level of interest in ReSTOR, followed by ReZoom, Array, and crystalens, in that order. For reference, of the 715 respondents, over 90% perform cataract surgery but only about 30% perform refractive surgery. The countries represented most in the survey are the UK (19%), Netherlands (11%), and Germany (10%). **Q**

Survey of ESCRS Members, 2005: Level of Interest in Presbyopia-Correcting IOLs



Source: David Leaming, MD, www.leamingsurveys.com

crystalens Continues to Grow, at Least Back in the Colonies

Privately-held eyeonics, inc. announced in July that more than 50,000 crystalens IOLs have been implanted to date worldwide, and that during the second quarter of 2006 both revenues and implants were up about 30% versus the same period in 2005. August was another record month for the company. According to John Doane, MD, there are now more than 400 credentialed crystalens surgeons in the United States.

The company currently does very little business in Europe, due to initial surgeon experience that did not live up to expectations following the European launch several years ago. Because of limited interest among European surgeons, little new clinical data on crystalens was presented at ESCRS. eyeonics will likely take another run at the European market once it is ready to launch its next-generation accommodating IOL. **Q**

Key Arguments For and Against Presby-IOL Mix/Match Strategies

FOR

- Just as monovision treats eyes differently (one for distance, one for near) and allows the brain to resolve the images to create good functional vision, a mix/match strategy places lenses with different characteristics in each eye to create a good overall functional result for the patient.
- Mix/match exposes patients to strengths of different lenses: good distance and near vision for diffractive IOLs (ReSTOR and Tecnis MF), good distance and intermediate for refractive (ReZoom) and accommodating (crystalens) IOLs, good quality of vision for accommodating IOLs (crystalens)
- Conversely, mix/match reduces the impact of the compromises inherent in each of the current lenses: insufficient intermediate vision for diffractive IOLs, insufficient near vision for refractive and accommodating IOLs, glare/halos/reduced contrast sensitivity for diffractive and refractive multifocals.

AGAINST

- Off label usage; medical/legal risk.
- Limited amount of supporting clinical data, and lack of understanding of visual side effects and unanticipated problems resulting from mix/match.
- Mix/match creates a form of monovision, and not everyone tolerates monovision well.
- Bilateral implantation of ReSTOR results in "bilateral visual summation," neural adaptation that improves with time, and a high level of spectacle independence.
- Lack of intermediate vision with diffractive multifocal IOLs should be managed through pre-op education and proper patient selection.

Arguments “against” compiled from reports by James P. McCulley, MD, Richard J. Mackool, MD, and Kerry D. Solomon, MD

Next in the Queue: Synchrony Dual-Optic IOL from Visiogen

Because each of the three currently FDA-approved presbyopia correcting IOLs comes with some level of visual compromise, interest is building in next-generation solutions that will provide a broader range of functional vision while avoiding visual side effects.

The next important accommodating IOL in the development pipeline is the Synchrony dual-optic lens from privately-held Visiogen. This single-piece silicone IOL consists of 5.5 mm and 6.0 mm optics connected at the periphery by spring-like haptics. The lens comes in a pre-loaded injector, is inserted through a 3.6-3.8 mm clear corneal incision, and is designed to completely fill the capsular bag. The pre-loaded injector is an important product feature, given the relatively large size of the Synchrony IOL

and the importance of minimizing incision size. CEO Reza Zadno came to Visiogen from the cardiology device sector, where he says that companies wouldn't consider introducing a new device without the appropriate delivery system.

The Synchrony IOL has been implanted in over 350 subjects in seven countries over the past four years. The pivotal FDA clinical trial began enrolling in the US last November, following approval of the injector. On June 23, the company announced that it had received a CE Mark designation for the product. Visiogen does not plan a commercial launch in Europe at this time, but will instead use the CE Mark to facilitate the expansion of post-marketing research activities.

Clinical data presented at past meetings has shown that the Synchrony IOL has monocular accommodative amplitude of over 2.75D, resulting from relative movement of the optics of nearly 1 mm. Synchrony provides quality of vision similar to that of a monofocal IOL, and is associated with low PCO rates. IOL power calculations are inherently more complicated with a dual optic lens system, but uncorrected visual acuity outcomes have steadily improved as investigators have gained additional experience with the product.

The Synchrony IOL was the subject of a number of presentations at ESCRS. Iván L. Ossma, MD of Colombia presented functional vision outcomes of bilateral implantation in 27 patients, with 12-26 month follow-up:

- At six months, 96%, 93%, and 100% of patients achieved uncorrected 20/40 and J3 or better at distance, intermediate, and near, respectively.
- At six months, with best distance correction in place, 100% of patients achieved 20/40 and J3 or better at all three distances; 93% achieved J2 or better near, and 81% achieved J1 or better.
- Surgically-induced astigmatism was reduced from 1.5D to 0.67D with the transition from forceps insertion (4.5-5.5 mm incision) to the pre-loaded injector (3.6-3.8 mm incision).

Victor Bohorquez, MD, also from Colombia, presented results of a pilot study evaluating subjective and objective accommodative amplitude. In measurements of subjective accommodation using push-up/push-down tests, Synchrony eyes on average demonstrated about 2D more accommodative amplitude than did eyes with monofocal IOLs. Dr. Bohorquez noted that three dimensional movement of the high powered font lens also results in a refraction gradient across the optic, which may lead to an increase in depth of focus that further improves near vision.

Ricardo Alarcon, MD, from the same institution in Bogotá, presented data from 32 binocular synchrony patients, with follow up from 3-24 months. With distance correction in place, 100% of patients achieved 20/25 or better intermediate VA. At near, 81% of patients achieved 20/32 or better, and 88% achieved 20/40 or better.

George Beiko, BM, BCh of Canada presented data on 14 patients implanted monocularly that had reached six month follow-up. In his study population, 71% of patients are within 0.5D of emmetropia, and 86% of eyes achieve 20/40 or better distance-corrected near VA (similar to outcomes reported from Colombia). Importantly, Dr. Beiko and other investigators have noted that the Synchrony IOL is quiet in the eye: even at one year post implantation, the capsule has not significantly changed from day one, and the lens maintains its ability to move. **Q**

Multifocal/Presby-LASIK: So Far, Not Surgeons' Cup of Tea

Multifocal LASIK continues to be a major topic of conversation at refractive surgery meetings, with updated data presentations from Canadian and US clinical trials and case reports from Europe and elsewhere. Some surgeons express interest in this emerging presbyopia treatment, but we still sense overall caution. AMO-VISX, the company that is furthest along the path toward US regulatory approval, is keeping the hype and promotion to a minimum, and is marketing multifocal LASIK in a very measured way in regions where it is approved.

With regard to attitudes toward multifocal LASIK, many surgeons express discomfort with the idea of intentional ablation of a significant higher order aberration onto the cornea. On a more practical level, there are concerns regarding high rates of post-operative spectacle wear in early series, tissue loss from revision/reversal, and the burning of future surgical bridges.

Most cataract and refractive surgeons are reporting explant rates for the new presbyopia-correcting IOLs in the low single digits, with some reporting rates closer to 10%. While this is not an ideal scenario for either surgeon or patient, IOL exchange in the early post-op period is relatively straightforward. However, surgeons are telling us that if the percentage of presby-LASIK patients that demand reversal of their treatment is as high as 2-5%, this will create a major barrier to adoption. In theory, multifocal LASIK is reversible; although we have not seen clinical data regarding outcomes post-reversal, some of the early pioneers say that they have successfully performed reversal ablations. However, such patients will be left without presbyopia correction, and with significantly less corneal tissue than they started with.

In addition, as IOL-based solutions continue to evolve and improve, younger pre-cataract patients will want corneal solutions that do not preclude the use of the latest accommodating IOLs once cataract removal becomes necessary. As such, removable/reversible approaches, such as intracorneal inlays (see Page 6), hold promise.

Clinical Data Updates

At ESCRS, W. Bruce Jackson, MD of Ottawa presented 12-month results from his large Canadian study of "aspherical" treatment of hyperopic presbyopes. The 12-month results include 20 patients that received bilateral treatment, plus an additional 19 patients with unilateral treatment (59 eyes total). Visual acuity outcomes at 12 months were good, with 20/20 or better uncorrected distance vision in 70% of eyes, and binocularly in 90% of bilateral treated patients. At near, J1 or better was achieved in 63% of uncorrected eyes and in 56% of distance-corrected eyes. At 12 months, all 20 bilateral subjects achieved both 20/25 distance and J3 near or better binocularly; 85% achieved 20/25 and J1.

However, the patient satisfaction and spectacle independence results do not seem match the visual acuity outcomes. While 81% of subjects were "satisfied/very satisfied" with overall visual sharpness and clarity, 15% were "somewhat/very dissatisfied." 22% of subjects report dissatisfaction with uncorrected near vision in bright light, versus only 11% pre-op with correction. Satisfaction with night vision improves after surgery, but the dissatisfaction rate still stands at 11% at one year. Regarding spectacle independence, only 0-2% of bilateral subjects report using spectacles for driving or recreational activities, but 38% report using spectacles for computer use, and 57% use spectacles for reading. According to Dr. Jackson, some patients express interest in greater reading vision, but not at the expense of distance acuity.

Keith Williams, MD of Vancouver reported six month results on 52 eyes of 26 patients using the VISX multifocal algorithm in a surface ablation approach. Visual acuity outcomes were very similar to those reported by Dr. Jackson, although subjective/questionnaire results were somewhat more positive.

- At six months, monocular uncorrected distance visual acuity (UCDVA) was 20/20 or better in 44% of eyes, and binocularly in 85% of subjects (versus 53% and 82% respectively at six months in the Jackson study).
- Uncorrected near visual acuity (UCNVA) was J1 or better in 67% of eyes (versus 66% for Jackson), and binocularly in 85% of subjects.
- Distance corrected near visual acuity (DCNVA) was J1 or better in 60% of eyes (versus 65% for Jackson).
- Questionnaire results: at six months, 8% of subjects were somewhat/very dissatisfied with uncorrected distance vision, and 15% were "not sure." This compares with 13% dissatisfied and 12% not sure at six months in the Jackson study.
- Regarding near vision, 8% were unsatisfied and a 12% were not sure; this compares with 16% unsatisfied and 7% not sure in the Jackson study.
- With respect to overall vision, no subjects expressed dissatisfaction and 15% were not sure. **Q**

Corneal Inlays: Important New Tools for the Presbyopia Surgery Arsenal

Corneal inlays represent an attractive future option for presbyopia correction surgery for a number of reasons: (1) they are additive procedures that do not rely on corneal ablation or tissue removal; (2) they are removable at the slit lamp and adjustable; (3) they can be implanted during simple, safe, minimally invasive surgical procedures; and (4) they are compatible with concurrent and prior LASIK, both myopic and hyperopic.

The highest profile entrants in this category are the PresbyLens from ReVision Optics, the AcuFocus pinhole inlay, the Invue inlay from Biovision, and a corneal onlay in early stage development from CooperVision.

The AcuFocus inlay was not the subject of a formal presentation at this year's ESCRS, although anecdotal feedback from surgeons that are knowledgeable about this product is that the US FDA Phase II clinical study is progressing well, and that patients treated previously in Turkey are also doing well.

The BioVision Invue inlay was the subject of one presentation at ESCRS. This inlay is 3 mm in diameter and 20µm thick. Francisco Sanchez León, M.D. of Mexico presented 12-18 month results that indicated good near visual acuity, although distance visual acuity was not reported.

PresbyLens Moves Front and Center

The PresbyLens corneal inlay from privately-held ReVision Optics was the subject of three papers at ESCRS. This inlay is very small, measuring 1.5 mm in diameter, 24-40µm center thickness, and 10µm in edge thickness. The inlay alters the anterior curvature of the cornea, providing a center near add with an additional corneal draping effect that provides improved intermediate vision. The PresbyLens is made from a proprietary biocompatible material: a larger, 5 mm hyperopic design has shown excellent biocompatibility and no visually significant haze in 32 patients with up to three years of follow-up. The material has the same index of refraction as the cornea, minimizing or eliminating any edge effect.

Stephen Slade, MD of Houston presented initial short-term results from a Mexican pilot study of PresbyLens in one eye of 18 presbyopic subjects undergoing concurrent myopic LASIK.

- Implanted eyes sacrificed some distance VA (mean VA of 20/40 versus 20/20 for LASIK-only eyes), but had somewhat better intermediate VA (20/25 versus 20/32) and significantly better near VA versus LASIK-only eyes (mean of 20/32 versus 20/80).
- 94% of PresbyLens eyes were 20/40 or better at near, versus only 28% of LASIK-only eyes.
- All patients are spectacle-free for distance and intermediate tasks, and 89% are spectacle-free for near tasks.

John Doane, MD of Kansas City presented initial outcomes for three prior LASIK patients implanted with PresbyLens monocularly. In these subjects, not only was near vision improved as expected (from a range of 20/63-20/100 to a range of 20/25-20/32), but distance vision was also the same or better post implant, which is an unexpected result. Patients report spectacle independence and improved functionality at distance, intermediate and near.

According to a presentation authored by Jon Dishler, MD of Denver and presented by Dr. Slade, PresbyLens provides 1.5-2.0D of near-add, while affecting distance visual acuity less than similar levels of monovision. While only 7% of monovision eyes with +1.5D add have distance VA of 20/40 or better, 86% of PresbyLens eyes achieve this result.

Corneal Onlay: Likely to be More Challenging

W. Bruce Jackson, MD of Ottawa took a break from presby-LASIK to present information regarding a tissue-engineered corneal onlay that is being developed by CooperVision. Unlike the intrastromal corneal inlays described above, this device is placed more superficially, between Bowman's layer and the corneal epithelium. At this point the developers appear to be looking beyond just presbyopia correction, and hope to be able to correct up to +/-6D of refractive error with up to 3D of cylinder. The first implanted patient was a 28 year-old with keratoconus.

The onlay is made from collagen plus synthetic materials, with cellular components coming from the host, where possible. The onlay is significantly larger than the corneal inlays under development: 7.5 mm in diameter, with center thickness of 50-140µm. A sub-epithelial pocket is created using a device developed by Gebauer of Germany. Tests show that the epithelial flaps are not viable long-term, and healing depends upon formation of new epithelial cells. Challenges include handling/insertion, centration, maintaining the onlay in place during healing, and long-term stability. **Q**

CK: Exploring the Realm of the Post-LASIK Presbyope

Privately-held Refractec is currently focusing its efforts on the application of conductive keratoplasty (CK) for post-LASIK presbyopes. At ESCRS, Daniel S. Durrie, MD of Kansas City presented results of a multicenter study of CK to improve near vision in presbyopic emmetropes with prior LASIK. Dr. Durrie presented a progress report on 55 eyes, out of a total study population consisting of 150 eyes of 150 patients. The treatment approach is relatively conservative, with intended near-add of +1.25D and actual achieved mean effect so far of +1.39D. At three months, 68% of eyes have achieved J1 or better, and 95% have achieved J3 or better. 60% of subjects can read fine print, and about 77% can read a newspaper. CK-treated eyes regress about 0.15D on average between years one and three, which is similar to the progression of spherical equivalent observed in non-treated eyes.

Dr. Durrie says that his post-LASIK patients tend to choose CK over a LASIK monovision touch-up, because of safety (not having to lift the flap) and less loss of distance visual acuity. **Q**

Scleral Approaches: Ready to go Underground?

Scleral approaches to presbyopia correction have some appeal because they aim to re-establish accommodative ability without operating directly in the optical zone of the eye. However, surgeon interest in scleral approaches has been limited up to this point, due to minimal accommodative effect and/or regression of effect, and the fact that these tend to be bloody surgical procedures, particularly in comparison to other refractive surgical approaches.

Boris Malyugin, MD of Moscow presented long-term follow-up of sclerotomy with T-shaped implants for presbyopia. Twenty-five eyes of 19 patients each received four implants and were followed for 2.5-3.5 years. During the early follow-up period (1 week - 3 months), UCNVA improved in 23 of 25 eyes, and amplitude of accommodation increased by 2D. However, by 18 months, mean UCNVA and mean accommodative amplitude had both returned to pre-op levels. Over time, the implants tend to migrate toward the superficial scleral layers and conjunctiva.

Another recent report regarding scleral implants for presbyopia, and their lack of efficacy, was presented at ARVO in May by Jay Pepose, MD of St. Louis. We did not highlight this poster in our ARVO recap (EyeQ Report No. 6) due to our focus on AMD therapeutics. The purpose of this study was to measure accommodation subjectively (using a "push" technique) and objectively in 29 scleral expansion segment (SES) patients and in unimplanted control eyes, in a Phase I multicenter trial. Accommodation results for the treated and control groups were almost identical, with zero mean objective accommodation in both groups. Dr. Pepose concluded, "There is no objective evidence of restoration of accommodation with SES in the patients tested."

Back at ESCRS, Stefano Pintucci, MD of Rome described laser presbyopia reversal ("LAPR") using the SurgiLight Erbium:YAG laser. The procedure involves multiple 4.5 mm scleral incisions, and Dr. Pintucci reports an increase in accommodation immediately post-op of 2D. Another laser-based scleral approach, LaserACE from Ace Vision Group, was shown on the ESCRS exhibit floor. This approach utilizes an Er:YAG laser to ablate a spot pattern in the sclera, which is intended to relieve the compression load in the sclera and restore dynamic accommodation to the eye. **Q**

Excimer Laser Update: Which of the VISX Crown Jewels is Most Valuable?

As Julian Stevens, MD of Moorfields Eye Hospital in London pointed out during the opening symposium on wavefront-driven LASIK, excimer laser technology is reaching the point of diminishing returns. Outcomes are so good at present, with over 90% of patients achieving 20/20 or better vision, that optical errors are smaller than what optometrists can measure, and each new feature that is added to the lasers contributes incrementally less to visual outcomes. The precision that is incorporated into excimer laser ablation patterns is reaching the limits of the corneal cells ability to perfectly mirror those ablation patterns.

This sentiment was echoed by another London ophthalmologist, John Marshall, MD, who pointed out that the major hurdle remaining in correlating theoretical and actual laser vision correction outcomes is corneal cell biology. As Mr. Marshall put it, "cells do not read physics textbooks." He also noted that most of the published research on corneal wound healing deals with rabbits and monkeys, not humans, and that issues regarding corneal biomechanics further complicate matters.

Given this backdrop, the next generation of excimer laser systems (AMO-VISX Star S6, Alcon LADAR8000) will likely focus on improvements in areas such as ease of use, surgeon workflow, systems integration, and service related issues.

AMO/VISX continues to promote the benefits of its CustomVue system on its STAR S4 IR excimer laser platform, which incorporates VSS (variable spot scanning), VRR (variable rep rate), and iris registration (with compensation for cyclotorsional movement and pupil centroid shift). Outside the US, VISX is marketing "Advanced CustomVue for Presbyopia" in a measured, targeted rollout.

In a very interesting analysis, Douglas C. Koch, MD of Houston examined which is the more important feature of iris registration: compensation for cyclotorsional rotation or adjustment for pupil centroid shift. In a study of 58 eyes, he measured mean cyclotorsional rotation of 2.5° and mean pupil centroid shift of 0.29 mm. Dr. Koch concluded that pupil centroid shift is significantly more impactful in terms of visual benefit (total RMS and HOA), with the only exception being eyes with high degrees of astigmatism.

Updates from WaveLight, Bausch, and Alcon

On August 28, WaveLight AG of Germany announced US FDA approval of the company's wavefront-guided (WFG) procedure using the ALLEGRETTO WAVE excimer laser, for myopes with up to -7D spherical equivalent, with up to -7D of spherical component and up to 3D of cylindrical component. Previously, WaveLight offered only wavefront-optimized (WFO) treatment. The company plans to maintain equivalent procedure pricing for the two treatments.

According to Karl G. Stonecipher, MD of Greensboro, NC, who presented final one-year results from the FDA clinical trial, European physicians that have access to both WaveLight algorithms (WFO and WFG) still treat most of their patients with WFO. Those who benefit most from WFG are the 20-25% of patients with high pre-operative HOA. Results of the FDA clinical study demonstrated equivalence between WaveLight's WFO and WFG treatments. Because of the benefits of WFO treatment over conventional LASIK, WaveLight's WFG treatment outcomes were less differentiated from the control-group than has been seen in previous studies comparing WFG-LASIK to standard/ conventional LASIK.

At ESCRS, Bausch & Lomb highlighted two recent improvements to its Zyoptix system that have been launched recently in Europe. The Zyoptix APT (Advanced Personalized Technologies) system represents a major software upgrade that significantly speeds patient flow through faster data analysis and patient work-up time, increased data storage, and reduced need for pupil dilation. The new Zyoptix Aspheric treatment reduces surgically-induced spherical aberration and higher order aberrations by taking into account each eye's individual Q-values (corneal asphericity) and K-values (corneal curvature).

Alcon continues the rollout of its LADAR6000 system, which offers a number of improvements over the LADARVision 4000 system in the areas of ergonomics, efficiency, speed, and serviceability. **Q**

Changing of the Guard: Femtosecond Technology Continues to Penetrate LASIK Market

Femtosecond laser technology for LASIK flap creation is earlier in its life cycle than is excimer laser technology, and its adoption is driving improved visual outcomes and better corneal biomechanics, while making LASIK safer intra-operatively. As a newer technology, the current rate of improvement is rapid, with two meaningful upgrades from IntraLase over the past two years and new systems in the works from several competitors.

ESCRS was yet another positive meeting for IntraLase. It helps, of course, that this is an international meeting and the company is performing very well internationally, with a majority of new lasers this year expected to be placed outside the US. In fact, company management believes that by 2008-2009, >50% of company revenues will come from international markets. Currently, international sites account for 39% of the IntraLase installed base (182 out of 471).

Customers continue to respond favorably to the product upgrades that IntraLase has introduced over the past two years, which have taken the speed of the system from 15 to 30 to 60KHz. This transition has resulted in faster flap-cutting times (from >1 minute to 15-20 sec.), fewer complications (DLK and transient light sensitivity), greater flap thickness accuracy, faster visual recovery, and smoother stromal beds.

We noted after ASCRS in March that IntraLase adoption in the US is becoming less "offensive" and more "defensive." That is, surgeons have lower expectations regarding additional money that they will make with the femtosecond laser, and are adopting the technology in order to keep pace with the local competition and to provide the best outcomes for their patients. Anecdotally, we heard that a number of relatively low-volume European refractive practices are acquiring the technology.

Growing European interest in IntraLase was reflected in the results of the 2005 Leaming Survey of ESCRS members. Regarding current practice, only 2.6% of respondents said that they use IntraLase for most of their LASIK flaps, which tied the product for #8 on the list, behind seven bladed microkeratomes. However, when asked which microkeratome they would like to use/acquire, IntraLase drew 37% of responses, topping the #2 choice (AMO Amadeus) by a 2:1 margin.

Once again, SM^2 Consulting (www.sm2consulting.com) has collected and analyzed user data for IntraLase, this time from international users (78 customers in seven markets). Some highlights:

- In six of the seven markets (excluding Japan), IntraLase users increased price per procedure by 19-40% (weighted average 30%).
- In these same six markets, volume in IntraLase practices grew by 2-37% (weighted average 11%).
- In Japan, an underdeveloped LVC market, several providers have attempted to kick-start adoption by significantly reducing price. In Japan, IntraLase users reported price declines of 37% and volume increases of 182%.
- Overall, for all seven markets, mean LASIK revenue for IntraLase surgeons increased 28-92% (weighted average 45%).
- Across these seven markets, conversion to IntraLase within enabled practices averaged 84% of procedures.

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IntraLase from Page 9

The subject of corneal biomechanical stability was clearly a hot topic at this year's ESCRS, further contributing to the buzz around femtosecond technology. Much of the key research in this field is being conducted and published by John Marshall, MD and his colleagues at St. Thomas' Hospital in London. In recent years, there has been a resurgence of interest in surface ablation (PRK, LASEK, Epi-LASIK), despite the drawbacks of greater postoperative pain and slower visual recovery, driven by a desire to avoid flap-related risks and corneal biomechanical issues associated with LASIK. With recent advances in femtosecond laser technology, some of the perceived benefits of surface ablation over LASIK are diminishing.

Nathaniel Knox Cartwright, MD and Philip Jaycock, MD, who work with Mr. Marshall in London, presented findings from a finite element analysis of corneal weakening after the cutting of LASIK flaps. They note that their model is consistent with clinically observed results, and conclude that the cornea weakens exponentially with increasing flap depth. A150µm flap results in 27% weakening of the cornea, while a 300µm flap results in 77% weakening. These sorts of findings are leading to increased interest in thinner LASIK flaps, and suggest that the ultimate goal may be a sub-Bowman's LASIK flap created using femtosecond laser technology. Such a flap would entirely avoid both stromal interruption and epithelial injury.

Therapeutic applications, such as penetrating keratoplasty for corneal transplants, are turning out to be a more important business driver for IntraLase than we anticipated when the company went public two years ago this week. Although few surgeons, even in Europe, expect to use femtosecond lasers for more therapeutic procedures than refractive procedures, the ability to perform therapeutic procedures is becoming an increasingly important purchasing consideration. This is particularly true outside the US, where ophthalmic surgeons tend to have more diversified practices. In IntraLase's 2005 international customer survey, 60% expressed interest in performing therapeutic procedures.

The company has branded its therapeutic technology as IntraLase-Enabled Keratoplasty (IEK). Corneal transplants that are performed with the femtosecond laser (to cut both host and donor corneas) have a much more precise fit, form more hermetic would seals, deliver better optical results (i.e., significantly less astigmatism), and enable suture removal in less than six months versus one year using the standard trephine technique.

IEK is just getting started, with only 62 cases (27 in Europe) performed so far by 16 surgeons. Starting in 2007, all new IntraLase lasers will be IEK-enabled with a list price of $425,000. Upgrading earlier models for IEK capability will cost $50,000, and IEK procedure kits will be priced at $700 ($350 each for donor and recipient corneas). Company management estimates that there are currently about 110,000 corneal transplants performed each year worldwide. **Q**

Look Right! New Femtosecond Competitors Coming, but Mind the Gap

DA VINCI System from Ziemer

Ziemer Ophthalmic Systems of Switzerland introduced its DA VINCI Femtosecond Surgical Laser at the AAO meeting in Chicago last fall, and received CE Mark designation and FDA clearance last winter. At ESCRS, Ziemer reported its first sighted-eye treatments and provided updated information regarding its global launch. As of mid-September, about 100 sighted eyes had been treated in Switzerland, Germany, and the UK.

Ziemer is currently ramping up production of the DA VINCI system, and plans to begin rolling out machines this month. We would expect the company to gain greater initial traction in Europe than in the US, where it enjoys some "home-field advantage." Ziemer is currently in negotiations with potential marketing partners in the US and other regions.

Although the DA VINCI system will be entering a market segment in which IntraLase has already established a strong foothold, Ziemer plans to employ a marketing strategy based on premium/differentiated technology, and intends to price its product similarly to IntraLase. Ziemer has had previous success employing a premium technology strategy (along with marketing partner AMO) with its Amadeus microkeratome.

The primary differentiating feature of the DA VINCI system is its small footprint and ability to use directly

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under the excimer laser, which could improve patient flow. Ziemer will also highlight the low per-spot energy delivered by its system, which should minimize corneal heating and provide smooth stromal beds. With respect to flap cutting time, a group of Swiss surgeons at ESCRS reported 20-25 second cutting time (competitive with IntraLase 60kHz) during its initial clinical experience, and a group of German surgeons reported 45 second cutting time (competitive with IntraLase 30kHz). One disadvantage of the DA VINCI system that has been noted by some surgeons is the inability to see the cornea during the flap cutting process. The greatest barrier to adoption, at least over the near term, is likely to be reluctance on the part of refractive surgeons to make such a significant investment (about $400,000, similar to the hardware cost for IntraLase) on a system with very limited clinical usage to date.

Ziemer has not yet introduced systems capable of therapeutic applications such as penetrating keratoplasty, although the company says that such applications simply require modified handpieces and updated software, which are under development.

FEMTEC Laser from 20/10

20/10 PERFECT VISION of Germany has had FDA 510 (k) clearance to market its FEMTEC femtosecond laser since February 2004, although the company has not yet launched its product in the US. According to company management, this may change in the near future, although they are not ready to announce US launch plans, and Europe and Asia are likely to remain the primary focus. Like Ziemer, 20/10 has priced its system in the same ballpark as IntraLase. A key differentiating feature of the FEMTEC system is the spherically-shaped patient interface, which significantly reduces flattening (applanation) of the cornea.

At recent meetings, 20/10 has downplayed the LASIK flap application and focused on therapeutic uses of its technology. Recent upgrades to the FEMTEC laser have increased the speed from 15kHz to 40kHZ, reducing flap-cutting time to about 30 seconds and making the system more competitive for LASIK. 20/10 has also introduced improved optics, a tighter spot pattern, a 50% lower energy profile, and new interface/control software. All installed lasers have been upgraded with these features, which are awaiting 510(k) approval in the US.

Other Potential Competitors: Zeiss and WaveLight

Carl Zeiss Meditec of Germany plans to disclose more information regarding its new femtosecond laser at AAO in November, and intends to launch the system in mid-2007. The Zeiss femtosecond laser will not be incorporated with its MEL-80 excimer laser in a single hardware unit, but the two lasers will enable some level of system integration, and Zeiss will likely bundle these two products from a sales and marketing standpoint.

WaveLight AG announced nearly one year ago that it had plans to introduce a femtosecond laser sometime during 2006, but the company has not provided any updated information regarding its potential entry in this category. **Q**

Glaucoma: SOLX Launches a Gilded Alternative to the Tube

On September 1, 2006, OccuLogix completed its acquisition of SOLX, Inc., which is developing novel technologies to treat glaucoma. While OccuLogix continues to work with the FDA to re-launch its clinical trial program for its RHEO procedure (therapeutic apheresis) for dry AMD, the company is focusing increasing attention on its new glaucoma franchise. ESCRS marked the European launch of the SOLX product line.

The company's DeepLight System consists of two components, both of which have CE Mark approval in Europe and are under evaluation in randomized multi-center trials in the US. The DeepLight 790 Titanium Sapphire Laser, which utilizes a near-infrared 790nm wavelength that penetrates deeper into the trabecular meshwork than the blue/green light delivered by other lasers, provides a new alternative for laser trabeculoplasty. The short laser pulses should minimize thermal damage and allow for re-treatment. Recently published results of an ongoing randomized study showed 31% mean IOP reduction at one year (from about 26 to 18mm Hg), versus 19% for argon laser trabeculoplasty (ALT).

Enrollment of the US laser trial began in June 2004. The study will include 180 eyes at up to 10 sites, with one-year follow-up. The study is randomized against ALT, and results will be used to support a 510(k) submission.

The DeepLight Gold Micro-Shunt (GMS) is one of a number of new glaucoma shunts/stents under development that drain fluid from the anterior chamber to another location within the eye, avoiding the bleb-related complications that plague current glaucoma shunts. The product is a 24 karat gold ultra-thin (45µm) flat plate implant, measuring approximately 2.5 mm x 5mm, that rests permanently in the supra-choroidal space. It contains multiple channels that shunt fluid from the anterior chamber to the supra-choroidal space.

In a pilot clinical study of 94 patients with refractory glaucoma, mean IOP was reduced by at least 30% at all time points out to two years, from 28 mm Hg baseline down to 17-20 mm Hg. In the current FDA clinical trial, the DeepLight GMS is randomized against the Ahmed Glaucoma Valve. Enrollment began in December 2005. The study will include 145 eyes at up to 10 sites, with one-year follow-up, although a 510(k) submission may be possible with six month data. The endpoint is equivalency or superiority to the Ahmed Valve.

An advanced version of the GMS, currently under development, is a photo-titratable device in which the DeepLight laser is used to open additional channels in the shunt to further reduce IOP.

iScience Surgical Prepares for Launch at AAO

iScience Surgical plans to introduce its new device for glaucoma/IOP reduction at the AAO meeting in November. The company has received an FDA 510(k) clearance, although the labeled indication will likely include infusion and aspiration of Schlemm's canal, not glaucoma/ IOP reduction directly. A CE Mark in Europe is pending.

The iScience technique involves cannulation of the canal and passing of a 10-0 Prolene suture 360° around the canal. Placement of the suture is facilitated using the company's illuminated microcannula and high resolution ultrasound system. The suture is tied, placing it in tension and keeping the canal patent. We have not seen the product in use, but suspect that the technique may be challenging and require a relatively long learning curve for physicians. **Q**

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