Trends-in-Medicine

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SUMMARY

Use of premium IOLs is increasing, but almost exclusively for cataract patients. ♦ Alcon's ReStor dominates the U.S. multifocal IOL market, but interest in Advanced Medical Optics' ReZoom is growing, and doctors increasingly believe that mixing and matching these two lenses in the same patient may be the best approach. ♦ The data on Eyeonics' accommodating IOL, Crystalens, continued to build, but it appeared to be somewhat lost in the noise of mixing and matching multifocal IOLs. ♦ Competition in the femtosecond laser market is heating up, with FDA approval of Ziemer's mobile Da Vinci laser. ♦ LASIK volume and pricing are flat in 1Q06 vs. 1Q05 and the outlook is for 2006 to mirror 2005 – even with many surgeons planning an increase in advertising.

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AMERICAN SOCIETY OF CATARACT AND REFRACTIVE SURGERY (ASCRS)

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While LASIK remains the bread and butter of refractive surgeons, the theme of this year's ASCRS meeting was the convergence of cataract and refractive surgery. Premium IOLs – a new term referring to both multifocal and accommodating IOLs – are blurring the line between cataract and refractive surgeons, even though they are primarily being used for cataract patients. Thirty cataract and/or refractive surgeons plus industry experts and company officials were interviewed about trends in refractive surgery.

A speaker urged doctors to "get into the game" (refractive surgery) themselves. "Don't stand on the sidelines waiting for someone else to tell you," he urged, adding, "These (multifocal and accommodating lenses) are not yet perfected. While each technology has potential pitfalls, it has far more positive attributes. I believe lens removal will become a procedure most commonly performed on patients under age 65. The government will save money as lens removal will occur before patients reach Medicare age."

Barriers to adoption of new technology by ophthalmologists were described as:

- **Distrust** – of manufacturers who are perceived as only concerned with their self-interests and of opinion leaders who are suspected of shilling on behalf of industry.
- **Lack of knowledge** – of what and how to tell patients about the new technology. A speaker said, "Cataract surgery has been so successful that the prospect of spending a lot of chair time with patients may not look attractive."
- **Confusion** – over too few studies but too many observations as well.

PREMIUM (MULTIFOCAL AND ACCOMMODATING) IOLS

Currently, accommodating IOLs are being used for both cataract patients and some presbyopes. Multifocal IOLs are being used primarily for cataract patients, and that is not expected to change significantly in the near future. However, those cataract patients are starting to get younger, and their cataracts less severe. This may help to make refractive lens exchange (RLE) appealing to more people, especially pre-cataract patients. The price of premium IOLs appears to be holding steady; no sources reported any price cutting.

About 80% of doctors questioned are using premium IOLs, and they estimated they are using them for an average of 20% of their cataract patients and <5% of RLE patients. Dave Harmon of ***Market Scope*** estimated that ~100,000-120,000

premium IOLs were implanted in the U.S. during 2005, and he predicted that number will more than double in 2006 to ~250,000-300,000, or about 10% of cataract procedures. He said, "I expect premium IOL market share to continue to grow in the near term, but to stall in the range of 20%-30% of U.S. cataract patients."

Several speakers noted that the visual measures being used may be misleading. A speaker commented, "It's a myth that patients need to be 20/20 to read the newspaper…Newspaper print is J5, stock quotes are J3, so we don't need to be J1 to read the newspaper for daily functional vision." Another speaker pointed out that there aren't 5-zone IOLs, though patients need 5 zones for a full range of vision. He said, "The average person wants Zone 1 and Zone 2…Presbyopes want both Zone 1 and Zone 2…Therefore, binocular blending (mix-match) is becoming important…The disadvantage is that there is no commercial payoff for industry (to mix-match)."

The cataract market for premium IOLs started to take off in May 2005 when CMS ruled that doctors can charge Medicare patients more for multifocal vs. conventional lenses. A speaker said, "That ushered in a convergence of cataract and refractive surgery." A Georgia doctor said, "I've been a cataract surgeon for 26 years, and I missed the first two refractive surgery waves, but I plan to catch this one…When Medicare allowed reimbursement last May, that helped push the wave, so now there is no disincentive."

Premium IOL use in Europe is taking off much slower because their government health plans do not cover them. Several European experts said they are working to try to get some coverage for premium IOLs, but they were not optimistic. A German doctor said, "We are trying, but we haven't had any success yet. It is very difficult. Even in my country there are 22 different regions that have to be convinced one at a time. There is no national decision process (on premium IOLs)." An Italian doctor said, "We are trying to get reimbursement increased, but it is very difficult to convince the government to pay more or to let patients pay themselves."

Are patients better able to get rid of their spectacle (glasses) use with one premium IOL than another? The answer is not clear, but probably not. The answer may depend more on matching the lenses to a patient's visual needs than which lens is used. A ReStor user said that, in his experience, 67% of patients never require glasses, 27% sometimes need them, and 6% always need them. Another ReStor user said 65% never wore glasses after surgery. A third ReStor user said all of his patients so far have been glasses-free, but he is very selective about the patients he does. A Pennsylvania doctor said, "80% of my patients are completely glasses-free, depending on what they want to do. A computer screen at 21 inches is a weak area; those are the glasses patients – and maybe people who want to drive a lot at night. Multifocals are not for truck drivers." A ReZoom user said 53% of his patients did not wear glasses after getting multifocal IOLs.

The disadvantages of multifocal lenses include: decreased contrast sensitivity, halos and glare at night, pupil size dependence, and decreased visual acuity in some patients for intermediate or near tasks, depending on the lens used. However, a speaker commented, "These lenses are very successful when patients are properly selected…Patient satisfaction is often better at the end of one year than it is after a few weeks because our brain's neural adaptation process takes time." Dr. Kevin Waltz of Indiana warned doctors to expect their cataract patients to do slightly worse than refractive lens exchange patients, "The expectations are different, cataract patients are older, and more things are wrong with their eyes, so RLE patients do a little better in all categories."

Features of Several of the Premium IOLs

Alcon ReStor	AMO ReZoom	Eyeonics Crystalens	AMO Tecnis multifocal
Diffractive	Refractive	Accommodative	Diffractive
Best with small pupils	Best with large pupils	N/A	Pupil independent
Best at near vision	Best at intermediate and distance vision	Best at intermediate and distance vision	Best at near vision
Some halos and glare at night	Some halos and glare at night	None or minimal halos and glare at night	Some halos and glare at night
Good for readers	Good for computer users	Good for computer users and night drivers	Good for readers
97% never or only sometimes require glasses	92% never or only sometimes require glasses	N/A	N/A

Fitting IOLs to Patient Needs

Visual feature	Experts' choice of lens
Near vision (reading) most important	ReStor or Tecnis
Intermediate vision (computer) most important	ReZoom, Tecnis, or Crystalens
Distance vision (golf) most important	Crystalens
Night driving	Crystalens

Matching Patient Focus Zones and IOLs

Zone 1	Zone 2	Zone 3	Zone 4	Zone 5
Sewing	Menus	TV	Daytime driving	Night driving
Stocks	Labels		Golf	Theater
	Cell phone			Aviation
ReStor	**ReZoom or Crystalens**			

Comparison of Cataract and RLE Patients

Measurement	Cataract patients	RLE patients
Age	70-80s	49-62
Pre-operative vision	Poorly corrected	Well corrected
Expectations	Pay less, expect less	Pay more, expect more
Activity level	Less active	More active
Litigiousness	Less litigious	More litigious

From 1%-15% of patients getting a premium IOL require an explant, a lens repositioning, or a post-IOL touch-up or enhancement (usually LASIK). A ReStor user warned doctors to expect a 5%-10% enhancement rate. Another ReStor user put his enhancement rate at 28.7%. Another ReStor user said, "I haven't had any explants yet because I've been very patient-selective. I don't do people who drive at night or have AMD, and I only do cataract patients. I turn away patients who would complain."

Glare is an issue for many patients getting premium IOLs. A speaker said, "I think the biggest problem from glare comes from dry eye and not the lenses. All multifocal lenses impose higher aberrations on the eye…The system will tolerate a certain amount of aberrations, and add a bit of dry eye or astigmatism, and then the glare gets much worse…So, I strongly urge people to get adept at treating dry eye and a lot of glare symptoms will go away." Another speaker said, "Hyperopic patients are more satisfied...They experienced glare and halos already. So they can't distinguish new glare from multifocals…And over time their complaints decrease."

Other speakers noted that near vision can be measured at different distances, and some of the distances are not clinically relevant. For instance, people don't generally read at 12 inches, so J1 at 12 inches isn't clinically relevant.

The marketing wars were in full swing at ASCRS, with each manufacturer trying to convince doctors that their lens was superior. One expert estimated that Alcon's ReStor has about 70% share of the premium IOL market, Advanced Medical Optics' (AMO's) ReZoom 16%, and Eyeonics' Crystalens 14%. An expert described Alcon as in a "steady growth mode, while AMO is in an early momentum mode…In 2-3 years, Alcon will have 60%-65% share."

How did doctors at ASCRS think ReStor and ReZoom compare? Most agreed that ReStor has better near vision, and ReZoom has better intermediate vision.

- *Texas:* "There are more night symptoms with ReStor, and Crystalens has better distance vision with good intermediate vision."
- *California #1:* "I was using ReZoom, and then I tried ReStor, but I'm going back to ReZoom because it has better intermediate vision. ReStor needs more light for reading up close."
- "I've done ReStor/Crystalens, and Crystalens works well, too. There are no issues with that…There have been no complaints of gray haze."
- *Nebraska:* "I use ReZoom for patients more interested in intermediate distance or who have a large pupil, and I use ReStor for small people with closer vision needs. Overall, I use 40% ReStor and 60% ReZoom. My success rate…Patient satisfaction depends on how good a candidate they are. Hyperopic patients get a more 'Wow' effect. Myopic patients appreciate the surgery, but they don't realize as much benefit unless they have a significant cataract…If a patient wants all three distances – near, far, and intermediate – I would consider a mix-match of ReStor and ReZoom."
- *California #2:* "ReStor has a problem with 'glistening' of the lenses. The lenses develop little opacities over time (years), and you can't predict who will get it. They have to address that problem. There is a lot of anger that Alcon appears to be ignoring this and pooh-poohing it. But it is not visually significant yet in any patients, but if you are considering ReStor for RLE in younger patients, it is an issue." However, a Georgia doctor said he's only seen one or two cases of glistening and does not consider it a major issue.

A German ophthalmologist, Dr. Ulrich Klemen, also compared four different multifocal IOLs in 40 patients with 80 eyes at four weeks. He recommended choosing a lens based on the subjective expectations of patients.

German Head-to-Head Comparison of Multifocal IOLs

Measurement	AMO Array	Acri.Tec AcriTwin	AMO ReZoom	AMO Tecnis
Near UCVA				
400 cm	0.6	0.4	0.8	0.5
200 cm	0.3	0.5	0.45	0.4
60 cm	0.4	0.4	0.3	0.5
40 cm	0.5	0.7	0.6	0.8
Intermediate UCVA				
100 cm	0.3	0.5	0.45	0.40
60 cm	0.4	0.4	0.3	0.5
Contrast sensitivity				
Pre-op	1.35	1.35	1.35	1.5
Post-op	1.5	1.65	1.5	1.65
Subjective measures				
Halos	3%	2%	2%	1%

When choosing an IOL, Dr. Warren Hill of Arizona urged surgeons to maintain as many options as possible. His recommendations for monofocal IOL choice ***after keratorefractive surgery*** are summarized in this chart.

IOL Recommendations

Surgery	IOL
Hyperopic LASIK	B&L's LI61AO
Wavefront LASIK	B&L's LI61AO
<β-incision RK	Alcon's IQ
Non-wavefront LASIK	Alcon's IQ or AMO's Tecnis
>β-incision RK	AMO's Tecnis

Dr. Ivan Ossma-Gomez of Colombia presented the results of his randomized clinical trial of bilateral ReZoom vs. bilateral ReStor vs. bilateral monofocal lenses in cataract patients over age 40. He found that ReStor outperformed ReZoom in near vision (p=.04), and intermediate vision trended better with ReZoom (p=.06). Contrast sensitivity decreased with both lenses.

Dr. Giuseppe Ravalico of Italy offered a comparison of four IOLs in 168 patients getting bilateral cataract surgery.

Italian Head-to-Head Comparison of Multifocal IOLs

Measurement	AMO Tecnis n=17	AMO ReZoom n=17	Alcon ReStor n=10	AMO Array n=124
BCDVA	1.02	1.02	1.0	1.02
BCNVA	2.5	3.1	3.0	2.33
Depth of focus (20/40)	5.57	4.11	4.83	4.88
Near vision analysis (words per minute)	78.3	77.6	63.9	71.8
VF-7: satisfaction	98%	98%	100%	91%
VF-7: traffic signs	96%	99%	98%	97%
VF-7: precise handling	100%	88%	96%	92%

Among other comments on premium IOLs were:

- *California:* "People in my area can't afford multifocal lenses. And the results are not as good (in clinical practice) as in the clinical trials, especially Crystalens. In Europe, they are getting totally different results."
- *Missouri:* "I've only done a handful of ReStor and no ReZoom, but I'm starting Crystalens. ReStor has been very good for reading, but distance is not so hot. Patients are happy, but I'm just not happy."

AMO Tecnis monofocal IOL and Tecnis multifocal IOL

Currently, only the Tecnis monofocal is approved in the U.S., but both the monofocal and the multifocal Tecnis are available in Europe. Experts gave high marks to this silicone, bifocal, three-piece, aspheric lens, which is approved in Europe but is not expected to get FDA approval until late 2007 or early 2008. The pivotal study is fully enrolled and 12-month follow-up is underway.

In January 2006, CMS gave a new technology incentive for use of Tecnis, making it the only NT-IOL. Thus, an ambulatory surgery center (ASC) that uses Tecnis gets a $50 incentive (bonus payment). Doctors said this has had little or no influence – at least yet – on their choice of lens. A Midwest doctor said, "I don't own an ambulatory surgery center, so it has no bearing on me. But a lot of ASCs will let me use Tecnis now if I want it. It makes getting Tecnis in the door of the ASC easier." A West Coast doctor said, "I own the ASC, so it definitely makes a difference to me." A Florida doctor said, "I own part of my ASC, and the new technology incentive has not made me change to Tecnis, but I'm looking into it."

Experts equated the Tecnis to Alcon's ReStor, describing Tecnis as fairly similar to ReStor. Sources predicted Tecnis would compete more with ReStor than ReZoom, allowing AMO to market a mix-match combination that is all AMO.

Among the experts who discussed their Tecnis experience were:

➢ **Dr. Han-Bor Fam of Singapore** described his experience with Tecnis in 24 eyes in 20 patients, and compared that to a pre-LASIK population of 50 eyes in 50 patients. He found both monofocal and multifocal Tecnis statistically significantly reduced spherical aberration compared to pre-LASIK patients – 0.022 with Tecnis multifocal, 0.016 with Tecnis monofocal, and 0.086 in pre-LASIK patients. He also noted that Tecnis multifocal reduced patients' dependence on glasses.

➢ **Turkish ophthalmologist Dr. Baha Toygar** described his experience with the Tecnis multifocal lens for RLE in 49 eyes of 25 patients with high myopia or hyperopia who are not suitable for LASIK or phakic IOLs. At three months, 79.6% had ≥J1, 83.7% ≥J2, and 93.9% ≥J3. He reported no surgical complications, and no YAG capsulotomies. He concluded, "Tecnis corrects far, intermediate, and near vision. Predictability is comparable to LASIK, depending on the choice of biometry technique and formula…It is independent of pupil size, and patient satisfaction is good."

Turkish Experience with Tecnis Multifocal Lenses

Measurement	Results at 3 months
≥J1	79.6%
≥J2	83.7%
≥J3	93.9%
Glare	27%
Moderate-to-severe glare	19.9%
Moderate-to-severe halos	19.9%
Night vision problems	6.7%
Patients very satisfied with their vision	93.4%
If given the opportunity would get the same IOLs	80%
Never wear glasses	93.4%
Could not see colors very well	1 patient

➢ **Dr. Ana Fonseca of Portugal** also discussed her experience with Tecnis multifocals. At six months, all patients had mean near VA of J1. She said Tecnis produced good refractive results and "remarkable" near VA.

➢ **Dr. G. Bakeoff of France** described his experience with Tecnis multifocal for RLE in 27 eyes of 15 patients with a mean age of 57. He said, "Hyperopes are good patients. They don't see at distance or near." He said patients only complained of halos if questioned about them and only occasionally needed glasses in dim light. He said the best indication for Tecnis is very demanding hyperopes.

➢ **Dr. Frank Goes of Belgium** presented his results with Tecnis multifocal lenses in 84 RLE eyes. He said "not one patient" considered explantation, and 40 of the 42 patients were glasses-free (two needed glasses for specific activities). However, 14 required post-Tecnis LASIK.

➢ **Dr. Con Moshegov of Australia** said that, based on his experience with Tecnis and ReZoom multifocals, "ReZoom gives only a tad more intermediate vision than Tecnis…The rule of 20 applies – 20% will complain of night vision, 20% will complain of halos, and 20% will say they are more sensitive to light." Among his patients, 60% said they saw halos if they were asked specifically about them, and two required explants – one a myope dissatisfied with intermediate vision, and one due to poor image quality/halos. His prediction: "The next big American name will be Tecnis."

➢ **Dr. Johann Kruger of South Africa** said that his experience with 50 Tecnis patients, all were spectacle-independent for near and far, 100% had >20/40 for near and distance, 95.7% had 20/30 or better UCNVA, and 34.8% had better than 20/20 for UCNVA. He said, "Tecnis is more suited for patients who read a lot…It is not suited for patients doing a lot of computer work…Average intermediate vision was 0.25 at 60 cm, which is not very good…Therefore, combining Tecnis with a ReZoom in the dominant eye is being investigated."

➢ **Dr. Mark Packer of Oregon**, during a presentation at the AMO booth, stressed that flying an airplane or driving at night requires good contrast sensitivity, claiming Tecnis has improved contrast sensitivity. He explained, "Contrast sensitivity function is the gold standard measurement of quality of vision. Seeing is a lot like hearing. Loudness in sound is the same as contrast in vision. Sound frequency equates with spatial frequency, and an audiogram equates to contrast sensitivity function…Contrast sensitivity predicts how well you can fly an airplane or drive at night…Contrast sensitivity declines with each decade of life, even in absence of ocular disease…In a night driving simulation, Tecnis provided 45 feet increased driving detection distance (to avoid a pedestrian)."

Dr. Packer estimated that <1% of patients would benefit from a spherical IOL, ~5% of patients would benefit from Bausch & Lomb's Advanced Optic, ~20% would benefit most from Alcon's AcrySof IQ, and ~two-thirds would benefit most from Tecnis. He said, "You could stratify patients by pre-operative spherical aberration."

➢ **Dr. Michael Woodock of Maryland,** also at the AMO booth, claimed spherical aberration is the single most important high order aberration in the human cornea. He claimed Tecnis "outperforms" all other lenses. He said, "Where you really see a difference is in 5 mm pupils; there Tecnis significantly outperforms all other lenses. If there is a pinhole pupil, it doesn't matter which lens you put in, but with a larger pupil, there is significant improvement in contrast sensitivity with Tecnis over the other available lenses." He said with approximately 6,000 Tecnis implants, he has observed no clinically significant tilt or decentration.

➢ **Dr. Y. Ralph Chu of Minnesota,** again at the AMO booth, said what's exciting about the Tecnis monofocal is that "now we can tell patients we are offering the same wavefront technology from LASIK with IOL correction…What was important to me was a survey of 55-75-year-old people in which 88% said they are extremely or very concerned with not being able to drive at night…When I started using Tecnis, I noticed anecdotally that more patients were seeing 20/20 and 20/25 on Day 1...Will people see a difference? I think you do. You see a trend and data that people do see a little bit of a difference…The take-home message is that Tecnis is designed for the general population…In the future there may be more choices, and we may choose based on spherical aberration, but right now, if I were just picking one lens, I think Tecnis is the one to cover you for most patients in a safe way."

Other comments on Tecnis include:

- *Midwest:* "I don't think it surpasses (Alcon's) AcrySof, but it is a strong competitor."
- *Florida:* "I think the Tecnis multifocal has a lot of potential. We offer the Tecnis monofocal now."
- *Indiana:* "Tecnis will kill ReStor when it comes out. I would mix it with ReZoom."

Mix-match

Of the patients getting multifocal IOLs, sources estimated that ~15%-20% are getting mix-match lenses. About 40% of sources have either started to mix-match or plan to do so in the near future, another 40% are using only one brand of multifocal in an individual patient, and the other 20% are not using multifocals. Thus, mix-match may account for <10% of all cataract patients.

Alcon's ReStor multifocal lens has dominated the market, but it appears that AMO's ReZoom is gaining ground. Numerous surgeons who have been using ReStor exclusively said that they have recently started or plan to start trying some ReZoom lenses. It was clear at ASCRS that each lens has its advocates, but an increasing number of surgeons are deciding to use both lenses, and even to mix and match them in the same patient.

The take-home messages from ASCRS for many doctors were that (1) it's time to try premium IOLs if they aren't already, and (2) different brands of premium IOLs can be mixed and matched – and may give better outcomes than bilateral use of the same IOL.

The preferred mix-match appears to be ReZoom in the dominant eye for distance, and ReStor in the non-dominant eye for near vision. In fact, some experts reported that this combination seemed to produce a synergistic effect on intermediate vision, giving better intermediate vision than either lens alone. Crystalens for the dominant eye plus ReStor for the non-dominant eye is also a good option, but doctors

appeared to want to deal with multifocal lens mix-match before factoring another kind of lens, so Crystalens is likely to take a back seat for a while among doctors just starting with mix-match.

An ophthalmologist with mix-match lenses (ReStor/ReZoom) described his experience several times at the meeting, and he was very enthusiastic about it. He said, "It was a great decision for me. I had a ReStor two years ago, and my biggest complaint was that I could read 20/20 at 12 inches – but that is not where you read the newspaper – there was no contrast sensitivity, and I never neuroadapted...I ended up with ReZoom in the second eye because there was more positive input (from colleagues) on that. This was done six days ago in my left eye. At distance I see much better and crisper with ReZoom…And my overall acuity up close is out to about 15 inches, where ReStor is still 12 inches."

Dr. Henry Milne of South Carolina described his experience with mix-match lenses. He said he has no connection to either Alcon or AMO, with one of his two ambulatory surgery centers using Alcon lenses and the other using AMO lenses. His premium lens use is 85% cataract surgery and 15% RLE. He reported on at least six-month results with 23 patients who got ReStor + ReStor and 28 who got ReZoom + ReStor. His conclusion: "Mix-match is working very well, and it is now my procedure of choice…In cataract patients, I put the ReZoom in first, and do the ReStor in the other eye. In RLE patients, I put the ReZoom in the dominant eye, and the ReStor in the second eye…I started with bilateral ReStor, and the patients were unhappy…I know some people who do bilateral ReZoom, but I don't do that."

U.S. Experience with Mix-Match Multifocal Lenses

Measurement	ReStor + ReStor n=23	ReZoom + ReStor n=28
Patient overall satisfaction		
Satisfied	74%	96%
Neutral	0	4%
Dissatisfied	26%	0
Patient near vision satisfaction		
Satisfied or very satisfied	83%	96%
Neutral	0	4%
Dissatisfied	17%	0
Other subjective responses		
Would not have the surgery again	30%	30%
Would recommend the surgery to a friend/family	64%	96%
Complete spectacle independence	65%	94%
Halos during the day	43%	18%
Halos at night	86%	72%
Objective findings		
Average VA	---	20/30
Each eye average near VA	---	J2
Explants	3 patients	0

After this, Dr. Milne said he moved to 100% mix-match with ReStor/ReZoom. He said, "I tried (mix-matching with) ReStor in the first eye and had three patients who wouldn't let me do the second eye until I fixed the ReStor eye, so now I do the ReZoom eye first."

Brazilian ophthalmologist Dr. Patrick Tzelikis described his experience with mix-matched ReStor/ReZoom in 44 eyes in 22 patients, with ≥3 month follow-up. He said the first IOL was chosen according to patient characteristics, and two weeks later the other IOL was chosen, with a mix-match used if the patient had complaints with the first IOL. If the patient was pleased with the first IOL, the same IOL was implanted in the fellow eye, and the patient was eliminated from the study. He reported that all patients became spectacle independent for near, intermediate, and far; none required explants, and 50% of patients noticed a difference between both eyes during the first three months.

Brazilian Experience with Mix-Match Multifocal Lenses

Measurement	ReStor	ReZoom
UCDVA at Month 1	0.9	0.9
UCDVA at Month 3	0.83	0.82
≥20/25 at Month 3	82.8%	68.1%
UCNVA at 3 months (J1)	91%	50%
UCIVA at 60 cm at 3 months	45% (≥J5)	59% (≥J4)

Italian surgeon Dr. Pietro Giardindi described his experience combining an AMO Tecnis multifocal and a ReZoom in eight patients. Tecnis was placed in the dominant eye, and ReZoom in the other eye. He reported that the combination was well tolerated in all patients, patient satisfaction was very high, and all patients were glasses-free for near and intermediate vision, though one patient needed readers "due to hyperopic error." He also commented that using Tecnis in the dominant eye produced better results.

Dr. Frank Bucci of Pennsylvania reported on his mix-match experience. He said he initially implanted 55 ReStor/ReStor (bilateral ReStor) lenses before starting to combine ReStor/ReZoom. Fourteen of these patients complained about their intermediate vision without being asked about it. They could read J1.0 near and J3.8 intermediate.

Dr. Bucci has now done 39 ReStor/ReZoom mix-matches. He has become convinced, he said, that ReZoom in the dominant eye and ReStor in the fellow eye is the best approach. These patients read an average of J1.09 near and J2.39 intermediate. He commented, "Why are we mixing technologies? Because it works…My opinion of ReStor is going down, so now I put ReZoom in the dominant eye…I did ReZoom in the non-dominant eye, and I got complaints, but I don't get complaints if I put ReStor in the non-dominant eye...ReZoom/ReZoom is a viable option…If ReStor didn't exist, that (ReZoom/ ReZoom) would be my first choice…But ReStor addresses the two minor weakness of ReZoom – a little less near vision and more halos…I have noticed distance problems with ReStor,

but when you put ReZoom in, that seems to go away. It seems ReZoom is rescuing ReStor instead of the other way around."

Another expert said, "I do the same thing – ReStor in the non-dominant eye, and ReZoom in the dominate eye…I don't get any complaints (with that)…It definitely widens the range of intermediate and near vision. No patients complain that one eye is better than the other because they know the eyes are doing different things for them."

Anecdotal reports like these have convinced many doctors to start mixing-matching, but the data on mix-match are limited, and that is keeping other doctors from trying it. A speaker said, "We have data on bilateral implantation of these lenses...but no one has vast experience on mix-match…We just don't have the numbers yet, and we need to be very conservative with these patients. I'd still rather use the best lens bilaterally...If there were good data to support mix-match, I'm not opposed to it…My other concern is…I really think patients do better with binocular implantation…and it is very difficult to sort out patients after the first lens…I would worry about doing worse with the second lens."

Another argument against mix-match is that the brain might have trouble choosing the appropriate image if it had multiple choices to make. Monovision works, that argument went, because the brain only has to choose between distant and near vision at any given point. With the multiple vision options provided with the two technologies (ReStor/ReZoom) together, the brain might not be able to process information as well. A Florida doctor said, "I'm just starting ReStor, and I won't do mix-match. The brain is not good at sorting out two technologies…It is best to have the same kind of lens in both eyes."

However, other doctors who have tried ReStor/ReZoom reported good results and didn't have any patients with "processing" problems. An expert said, "With refractive multifocal IOLs (e.g., ReZoom), we have 3-4 images… Diffractive lenses (e.g., ReStor) present only two images – far and near. A diffractive lens is technically a true bifocal IOL. In the beginning, I was sure a small number – but still more than two – were necessary for achieving good multifocality. Now, I am convinced that the bifocal presentation given by a diffractive IOL is better. Our brain enhances images. The brain has to choose between fewer choices. If there are only two images – far and near – it can enhance the edges and utilize the best."

General comments about mixing and matching premium IOLs or the choice among ReStor, ReZoom, and Crystalens included:

- "I think mix-match will make more and more sense."
- "We combine a diffractive and a refractive lens…because most of our patients ask about intermediate vision and want to read…In the last six months, I've combined dominant eye ReZoom with ReStor or Tecnis (monofocal) in the other eye, and I have really very happy patients… Patients also see fewer halos with that combination, and I don't know why."
- *Pennsylvania:* "I'm only using ReStor, no mix-match. The jury is still out on mix-match."
- "I've been doing ReStor/ReZoom for six months and am very happy."
- "I've only done Crystalens with ReZoom, and there is no gray haze – because both are mid-range dominant…I did have a gray, muddy effect in ReStor eyes."
- "I would mix-match…with a refractive lens (e.g., ReZoom) in the dominant eye and a diffractive lens (e.g., ReStor, Tecnis) in the non-dominant eye…Tecnis sounds good to me."
- "I prefer a monofocal lens...Obtaining a little myopia in the non-dominant eye is better than perfect vision for far and near."
- "I would stick with ReStor bilaterally, though the jury is still out."
- "I would probably go with ReStor if pressed to do multifocals…I am not convinced of mix-match yet."
- *California:* "I haven't used any ReStor yet, but I'm looking into ReZoom. I've heard complaints from both doctors and patients that they are not satisfied…I am not mixing and matching. There are no data, and I'm not convinced multifocals are really better or that I would want a multifocal in my own eye."
- *Florida #1:* "I've only used ReStor, but I will start mixing it with ReZoom…I like the idea of mixing…For patients who never read, I'll use bilateral ReZoom. Otherwise, I'll use a ReZoom in the dominant eye, and a ReStor in the non-dominant eye. For a seamstress, I'd use bilateral ReStor."
- *Georgia:* "I'm not doing multifocals yet, but the more aggressive guys are doing it, and marketing it. I plan to use Crystalens for the dominant eye, and ReStor for the non-dominant eye. I'll start with cataract patients and then move to presbyopes…People over age 72 don't want to pony up the extra money for multifocals. Age 60-65 is the sweet spot…At first I would not do patients with presbyopia and no cataracts. There is a 'Wow!' factor with multifocals in cataract patients."
- *Texas:* "I've been doing both ReStor and Crystalens, but I don't mix them. I'm interested in ReZoom, and I may mix that (with ReStor) because the intermediate distance is a little better. ReStor would be good for the non-dominant eye, and ReZoom for the dominant eye, but patient selection is extremely important."
- *Florida #2:* "I haven't done any mix-matches, but I'm considering doing ReStor/ReZoom. If the results are good, I'll do that for all my patients. I'm happy with ReStor, but I'm not 100% satisfied."

- *Nebraska:* "I would consider a mix-match of ReStor and ReZoom."
- *Florida #3:* "I've only used ReStor, but I'm preparing to start ReZoom. I like the advantage of intermediate vision. I want to see if it is as good as I hear…And I'm receptive to the idea of mix-match…I'm not excited about Crystalens because of the prolonged rehabilitation and the cycloplegia. Best VA can take six months with Crystalens."
- *Florida #4:* "I just started ReZoom – because I feel it has more potential. I may do mix-match down the road, but I want to do 50-100 ReZoom only first."
- *Oregon:* "I use premium IOLs for 20% of my cataract patients, but I'm not doing any mix-match because I tend to do surgery (on the fellow eye) a day apart, so it doesn't fit my practice style to wait two weeks between surgeries. I use ReStor/ReStor for ~25% of multifocal patients, ReZoom/ReZoom for 50%, and Crystalens/Crystalens for 25%."

EYEONICS' Crystalens, an accommodating IOL

Several speakers discussed potential mechanisms of action for Crystalens. Dr. Steven Dell of Texas said Crystalens patients are seeing better up close than expected, and he suggested the optic itself is flexing, not just moving back and forth. Dr. Dell said that he finds a "significant improvement in reliability and the magnitude of outcome" by orienting the Crystalens using pre-operative wavefront. He also said that there is subtle improvement in vision from years 1-3, minimal improvement from years 3-4, and almost none from years 4-5 – but no degradation of effect.

Another speaker said he developed a series of special books to help Crystalens patients exercise their eyes, saying reading routine materials may not be a good exercise. The booklet helps ensure that patients concentrate and focus on progressively smaller font sizes. He said, "Patients can see they are making progress, the booklets keep them busy while they recover, they don't whine as much, and they look forward to finishing each book because it means they are getting better."

The original Crystalens has a tapered edge, but the newest version has a square edge. Dr. Jason Stahl of Kansas compared Crystalens and Alcon's ReStor in 20 patients. He said, "Binocular near vision is better than monocular… Combining (Crystalens and ReStor) increases the rate of intermediate and near vision…I do this routinely with ReStor and ReZoom…Patients are very happy with intermediate vision (with Crystalens)…There is a little bit of want for more near vision (with Crystalens), and just the opposite for ReStor, where patients are happy with their near vision, but intermediate is not quite as good. Certainly, it is better with binocular (mix-match) vision, and that is why I think combining the lenses may make sense…but the predictability of a ReStor/ReZoom mix-match is better, so that is what I'm doing."

Comparison of Crystalens and ReStor

Measurement	Crystalens	ReStor
UCDVA 20/25 at 1 month	45%	88%
UCDVA 20/25 at 3 months	55%	65%
UCNVA J3 at 3 months	55%	100%
Mean spherical equivalent at 1 month	-0.71 D	+0.21 D
Mean spherical equivalent at 3 months	-0.54 D	+0.39 D
Strengths	More intermediate dominant	Strong near vision

Other comments of interest about ReStor, ReZoom, Tecnis, or Crystalens premium IOLs include:

- *On AMO's ReZoom:* "Even at one week ReZoom performs better than Array at six months in nearly all visual categories."
- *On Alcon's ReStor:* "Patient satisfaction has been very good…Approximately 89% of my patients are not using reading glasses, and those who are use them in dim light, and an occasional person is using glasses for intermediate vision."
- *On Crystalens:*
  - "The data are bearing out that this is probably a better intermediate and distance option."
  - "Crystalens accommodation is 1.25-1.5 diopters…It is clear Crystalens works, but it is not clear what the mechanism of action is."
  - *Florida:* "I won't put a Crystalens in. It defies everything we've evolved from. The present IOL shape goes in the wrong direction – and I've seen a couple by other doctors with complications."

Other companies with premium IOLs include:

ACRI.TEC'S AcriTwin, a diffractive/refractive lens. A speaker said this lens had very good distance and near visual acuity as well as "sufficient" intermediate visual acuity. Contrast sensitivity is improved, but halos are still present.

ADVANCED OCULAR SYSTEMS. This Australian company, which merged with Regenera, has a Phase III trial underway and is planning a 2008 launch.

CALHOUN VISION'S Light Adjustable Lens (LAL) accommodating IOL. This three-piece photosensitive adjustable silicone IOL has a lens that moves within the eye when fine-tuned via a low intensity beam of near ultraviolet light. Human clinical trials are expected to start this year outside the U.S.

LENSTEC'S Tetraflex, a one-piece accommodating IOL with a 5-degree anterior angulance that allows the lens to move forward during the accommodating process.

NuLens' NuLens, an accommodating IOL. This was described by a speaker as "the first lens that truly accommodates and changes power rather than changes position in the eye. Primates implanted measure up to 40 diopters of change in anterior curvature power."

Visiogen's Synchrony, an accommodating IOL. This silicone dual-optic system is not expected to be available in the U.S. until late 2008 or early 2009. Asked how the company plans to sell Synchrony, an official said, "That is still to be determined, but we could do it with an independent sales force, a 'boutique-type' sales organization." A Canadian surgeon said he has implanted 15 Synchrony lenses since September 2005, and his patients have been very satisfied, with no reports of glare or halo. Another Synchrony researcher called it "an interesting alternative for presbyopia reversal."

Phakic IOLs

The advantages of phakic IOLs, a speaker said, are: better quality of vision compared to LASIK, more stability, reversibility, and patient perception, with no significant difference in predictability or adjustability.

Staar Surgical's Visian. A Florida doctor said, "Visian is good. It's superior to (Ophtec's) Artisan or iris fixation." An Ohio doctor said, "I love it. It's great for people outside the range of LASIK and too young for clear lens exchange."

AMO's Verisyse. A speaker said, "This is the one I prefer. It is easy and foldable, so I can introduce it through a small incision."

Miscellaneous Topics

Surface Ablation

Surface ablation has been seeing a resurgence of interest. Dr. Richard Yee of Texas said, "Advanced surface ablation procedures may have short-term complications – e.g., flap-related complications – and these probably are under-reported. If you do two million cases a year, that means 6,000 patients with a buttonhole flap. If you do advanced surface ablation, you have zero chance of that complication…Surface ablation will take over because we can treat haze and modulate the pain (with autologous serum)."

Lower ultrasonic energy for refractive cataract surgery

- **AMO's Whitestar** technology was described as the "pioneer."
- **Alcon's AquaLase** was described as "ideal" for refractive lens exchange. A fluid pulse is propelled from the tip at up to 50 pps, with no mechanical motions of the tip in the eye. A speaker said it is best utilized with softer lenses.
- **Torsional phacoemulsification**, which is 10% the normal ultrasound speed. The nuclear material stays attracted to the tip, and there is greatly reduced chatter.

LASIK

For the first three months of 2006, sources described their LASIK volume as flat compared to the same period last year, and they predicted that volume for all of 2006 is likely to be flat vs. 2005. Many said they plan to do more advertising over the next few months, but that is not expected to lead to increased volume, just to help maintain current volume levels.

Refractive surgery is different from other surgical procedures, and speakers urged doctors to keep this in mind. One speaker said, "Refractive surgery is patient-driven…It is elective, self-pay – and we are all happy it is self-pay – and volume follows the consumer confidence index…It is a sociological phenomenon spread by word of mouth…75%-80% of my patients come from previous patients or some kind of word of mouth, not so much by marketing."

LASIK pricing appears to be holding steady. Low-price centers and discounters are not eroding physician prices for LASIK, surgeons insisted.

Ophthalmologists were fairly positive about the merger of Advanced Medical Optics (AMO) and Visx. Most agreed that it has gone smoothly, with little impact on them or their practice. Service and support does not appear to have been affected, except in rare cases. One of those exceptions was a California surgeon who said, "Service has not been as good, and we're not getting the same treatment we used to get." A Florida doctor was much more positive, "It was a great deal for AMO. They've been transparent, and service is still there. I haven't had any problems." A Midwest doctor said, "The merger makes sense from a business standpoint. Cataract and refractive surgery are getting more blended, so it makes sense to have a company with a full spectrum." A Texas surgeon said, "The transition has been fairly smooth. All the Visx people seem happy." An Illinois doctor said, "The merger is a very good thing for both companies."

Dr. George Waring III of Atlanta argued that lamellar surgery will not be replaced by multifocal IOLs, that patients still perceive LASIK as more high-tech and acceptable than multifocal IOLs, "There is a perception in the minds of patients that a lamellar procedure is great, miraculous, and quick and easy, and that anything else we have may not be as nice…We are getting better at picking (LASIK) patients. Things are looking up…The biggest need we have for lamellar surgery is long-term follow-up data. We don't have it. We've done hundreds of thousands of cases without published five-year data. And we need to differentiate desirable from undesirable aberrations…Lamellar surgery is the most flexible, most desired by patients. It will lead in the future."

Patient View of LASIK vs. Multifocal IOLs

LASIK	Multifocal IOLs
Common	Rare surgery
Quick and easy	Complex and difficult
Rapid recovery	Slow recovery
Laser appears invisible and miraculous to patients	Lens implant is viewed by patients as "something in my eye"
Patients have friends who had LASIK	Patients ask – A what?

In addition, from 10%-15% of multifocal IOL patients require an enhancement or "touch-up," often LASIK. And surgeons have to pay a per-procedure fee for doing these enhancements, so it costs them money. However, surgeons are divided on how they charge for this enhancement. Some are raising the global fee to include it, and others are charging patients an additional $500-$800. One sources said, "I charge a global fee, nothing extra for enhancements." Another expert said, "I charge $1,800 (additional) for cataract patients and $4,000 for RLE patients, and I charge an extra $790 for post-multifocal AK." A Midwest doctor said, "I charge patients an additional $500 for enhancements."

Flap Creation: Mechanical Microkeratome or Femtosecond Laser?

For the past couple of years, the debate has been between whether a mechanical microkeratome or a femtosecond laser is better for creating LASIK flaps. IntraLase's FS femtosecond laser has had a monopoly on the femtosecond market, and the company estimates that its device is used in ~25% of LASIK procedures in the U.S. today.

A speaker presented a comparison of IntraLase and AMO's mechanical Amadeus microkeratome. He concluded there are "superior" outcomes with IntraLase and "impressive" outcomes with the Amadeus. He said there was less variability at three months with IntraLase.

Comparison of IntraLase and Amadeus

Measurement	IntraLase	Amadeus
VA 20/20		
Day 1	60%	70%
Week 1	66%	80%
Month 1	77%	82%
% with 0.5 D spherical equivalent		
Month 1	95%	88%
Month 3	100%	92%
Post-op astigmatism		
Month 1	0.12 (p<.02)	0.21
Month 3	0.02 (p<.07)	0.22

Another study – a randomized clinical trial – looked at 100 eyes in 50 patients using Visx CustomVue, with the first eye done with an IntraLase and the fellow eye with a Bausch & Lomb Hansatome microkeratome. The researcher concluded:

- Both flap methods had excellent visual outcomes.
- UCVA was better from Week 1 to Month 6 with IntraLase.
- IntraLase produced a more accurate and reproducible flap.
- Both methods had similar refractive stability.
- Patients preferred IntraLase at both Month 1 and Month 3. Contrast sensitivity may account for the preference for the IntraLase.

Comparison of IntraLase and Hansatome

Measurement	IntraLase n=50	Hansatome n=50
Complications	1 narrow hinge	0
UCVA D1	Nss difference	
Residual cylinder at 3 months	0.19	0.29
Residual cylinder at 6 months	Nss difference	
Contrast sensitivity at 3 months	0.15	0.18
Contrast sensitivity at 6 months	Nss difference	

Asked about their plans for an IntraLase, most sources said they were holding back because they didn't have the volume to justify the expense.

- *California:* "I have the money for one, but I'm waiting for the volume to pay for maintenance."
- *Florida #1:* "It is a good thing but so expensive that I can't justify it. And I haven't had a bad flap in two years. A year ago I was on the fence. I didn't buy it, and now I don't think it is that big a deal, although it is good for doctors who do one or two surgeries a month."
- *Nebraska:* "We'd get an IntraLase if I could justify the cost with volume, but the IntraLase is not mobile."
- *New York:* "I'm looking at it and talking to them. Some surgeons said they would bring all their cases to us if we got an IntraLase, but we need to be ***sure*** of that to justify the expense. I can count on one hand the patients who ever asked about it."
- *Pennsylvania:* "I'm really looking into IntraLase. I'd like my TLC Center to get it – for marketing. I'm not sure there is a clinical advantage."
- *Texas:* "I have an IntraLase, and I love it. I charge extra for it, and I use it in ~90% of cases. Patients love it, and there is high acceptance. In 3-5 years, most flaps will be IntraLase. I didn't get it just for marketing. There was the safety factor and visual results."
- *Florida #2:* "I don't have an IntraLase, but I have access to one. Patients find it appealing."

- *Florida #3:* "I'm not using IntraLase, but I feel pressured to do so because I have two competitors using it. The science just ***slightly*** favors IntraLase, but the marketing favors it."

However, there are now two other femtosecond lasers with FDA 510(k) approval, and at least one of these may give IntraLase a run for its money. 20/10 Perfect Vision received FDA approval for its Femtec femtosecond laser in late 2005 as a laser microkeratome for flap creation, but it has not started selling it in the U.S. yet. A 20/10 Perfect Vision official claimed "double digit" sales of its Femtec laser workstation in Asia and Europe, where it has a C.E. Mark for flaps and a variety of therapeutic applications, including keratoplasty. The company is seeking expanded indications and is amending the 510(k) to include a newer system that operates at a higher frequency, and this is expected to be done in 2006, but the company has not said when it will start taking orders in the U.S.

In March 2006, just before ASCRS, Ziemer received 510(k) approval for its Da Vinci femto-second laser. Ziemer's Da Vinci was attracting a lot of attention at ASCRS. Ziemer officials said they would like a strong partner in the U.S. Ziemer is continuing to talk with AMO, but Ziemer wants to keep its name on the product this time (which they didn't do with Amadeus), and that appears to be a stumbling block. The company also needs to do clinical validation studies, and the first two IRB approvals are in Switzerland.

Doctors were signing up for the off-site wet lab, and some were even negotiating purchases, though it won't be shipped until at least June 2006.

IntraLase has the advantages of first-to-market, experience, faster speed, Z axis, etc., but sources believe that Ziemer poses a significant threat to IntraLase. Doctors were particularly excited to see competitors enter the market, and they hope that, over time, this will drive the price of femtosecond lasers down. They also liked the ergonomics of the Da Vinci and the mobility – it can be configured as a roll-on/roll-off mobile laser.

The Da Vinci laser, which officials said is priced competitively with IntraLase, is small, works with all of the current excimer laser systems, and can be used without moving the patient intraoperatively. Ziemer also has experience in flaps with a product well-known to refractive surgeons; it developed the Amadeus mechanical microkeratome that AMO sells, giving it experience in microkeratomes and a well-known and accepted product on the market. Ziemer also plans to increase the speed, add a Z axis to its next generation femtosecond laser, and add a method for doing side cuts.

Comparison of Femtosecond Lasers with FDA Approval

Measurement	IntraLase FS60	Ziemer Da Vinci	20/10 Perfect Vision Femtec
Speed	60 kHz	N/A	500-800 femtoseconds
Axis	X, Y, and Z	Currently only X and Y	X, Y, and Z
Flap procedure time	~15-20 seconds	~45-60 seconds	~30-60 seconds
Experience	Extensive human experience and data	First human clinical trials about to start	In use in Europe and Asia
Availability	Now	Taking orders now and expects to start shipping in June 2006	Not available until at least late 2006
Portability	No	Yes, fully mobile	No
Type of cut	Planar	Meniscus	Spherical

IntraLase introduced its fourth-generation FS laser at ASCRS, and it is twice as fast as the previous version. A company official said they recently got approval in China, and have already placed systems in Korea, Japan (12), and Australia (6).

Yet, with all the excitement over femtosecond lasers, microkeratomes are not dead. Dr. George Waring III of Atlanta defended mechanical microkeratomes, saying, "They are getting better…Modern mechanical keratomes are getting a standard deviation of 0.2 µm, which is close to what you can get with a femtosecond laser."

Looking further down the road, femtosecond lasers may be used for a lot more than flap creation. A speaker suggested that femtosecond lasers may replace excimer lasers for LASIK. She said, "Nanosecond lasers have an elevation of temperature, a lot of collateral damage due to the shock wave effect which…decreases as the cube of the distance, and the level of optical breakdown is variable from one laser to another…With femtosecond pulses, thermal diffusion is suppressed, so a minimum volume is ablated. We get no collateral damage, and the pulse is so fast that water has no time to realize that it should boil."

Other potential femtosecond laser uses include:

- **Glaucoma treatment.** So far, this has only been tested in rabbits.
- **Anterior capsulotomy.** This also has not been tested in humans yet.
- **Cataract removal.** This has been tried in animals and cadavers but not live humans.

DRY EYE

Allergan's Restasis (cyclosporine) is the most commonly used prescription dry eye drug, and it has become the standard-of-care prescription medication for dry eye. A speaker said 50% show a good response, and maybe 10% of these won't keep taking it, "Very few stop because they don't tolerate (Restasis). The ones who do stop, do it because it is not working or can't afford it…It's important to tell patients that it takes cyclosporine some time to work." A Florida doctor said,

"Restasis is wonderful, but it doesn't work on all patients, and it can take a long time to get an effect."

Another speaker noted that prednisone can be used short-term but has unacceptable side effects long-term, and pulse IV steroids can be a useful alternative, especially when patient non-compliance is a concern. Oral methotrexate 15 mg QW, Cytoxan (cyclophosphamide), and chlorambucil are alternatives.

The TNF inhibitors also can be valuable for ocular inflammation, but they are very expensive, and payors may be resistant, a speaker warned, advising doctors to turn to them when methotrexate is ineffective or not well-tolerated. He reviewed anti-TNFs and other options:

- **Johnson & Johnson's Remicade** (infliximab) is an excellent first choice. "It is extremely effective for scleritis and ulcerative keratitis regardless of the underlying cause."
- **Amgen's Enbrel** (etanercept) is more convenient but seems not as effective as Remicade in treating ocular manifestations.
- **Abbott's Humira** (adalimumab).
- **Sanofi-Aventis's Plaquenil** (hydroxychloroquine) has little or no value in eye disease.
- **Roche's Zenapax** (daclizumab).
- **Biogen Idec's Rituxan** (rituximab). He said there is growing evidence this will be useful, especially for peripheral ulcers and keratitis.

Doctors also recommend non-prescription dry eye treatments. Everyone who was asked about Alcon's Systane praised it. A Florida doctor said, "I use Systane. It is a lot more chemically balanced, but I'm not sure about the osmolity." An Illinois doctor said, "It works wonderfully. Most thick drops cause significant blurred vision, and blurred vision with Systane only lasts ~30 seconds." Another Florida doctor said, "It's great. I use a ton of it."

AMO also has a dry eye therapy in development and is supposed to introduce it in late 2006 or early 2007. Sources said this will be a new use for an existing product – Blink contact lens wetting solution. Non-AMO sources said that getting a dry eye label for Blink would require either:

1. Convincing the FDA that the preservative is an inactive agent, so it could be approved without a clinical trial.
2. Clinical trial data.

Comments on dry eye therapies included:

- "I use non-preserved artificial tears…By the time someone comes to us, they shouldn't be using preserved tears. Almost all should be on non-preserved tears. Then, it is a choice between gel and ointment…Allergan's ReFresh Liquigel and Novartis's GenTeal gel thread the needle between lasting long enough and not causing too much blur. I think they are underutilized."
- "Many of us still pick the tear the last drug rep left in the office…I start with a preserved tear, based on symptoms. Then, I get more aggressive with symptoms…But if the patient is using a lot of preserved tears, then you have to switch to non-preserved tears. Drug companies do not like head-to-head studies because they are expensive, and the results usually are not very good. You should have two or three things you like best and stay with those."
- "It's very important to educate patients on how tear therapy works…They think a single drop will solve the problem…They need to understand it is tear therapy that will solve the problems."

DRUGS

Anti-bacterials

Bausch & Lomb's Zylet (loteprednol etabonate 0.5% and tobramycin 0.3%) was approved by the FDA in December 2004. Sales reportedly have been disappointing, even though it is less expensive than Alcon's TobraDex (tobramycin 0.3%), and sources suggested this is because B&L has done a poor job of marketing Zylet. Zylet cannot even be found on the B&L website more than a year after approval. A doctor said, "I started using Zylet, and it works pretty well, but TobraDex is a more potent steroid, and I rarely see the B&L sales rep."

NSAIDs

The FDA approved Alcon's Nevanac (nepafenac 0.1%), an NSAID for post-cataract surgery pain and inflammation, in August 2005. Doctors at ASCRS said they liked it for inflammation but ***not*** for pain. However, sources agreed that Nevanac is not helping sales of Alcon's Vigamox (moxifloxacin, 0.5%) or its surgical kits. A California doctor said, "It may be good for inflammation but not pain. I've had referrals from people who used it in the wrong situation." An Illinois doctor said, "It isn't for pain but for macular edema in cataract surgery. It works well but it has to be given TID, and Xibrom (Ista Pharmaceuticals, bromfenac) is BID."

REGULATORY PERSPECTIVE

Two FDA officials – **Dr. Malvina Eydelman**, a senior medical advisor in the FDA's Center for Devices and Radiological Health (CDRH), Division of Ophthalmic and ENT Devices, and **Dr. William Boyd**, an FDA ophthalmology medical officer – addressed some of the key issues of concern to ASCRS members. Perhaps the biggest question was off-label use of Genentech's Avastin (bevacizumab) in wet AMD, and the FDA officials avoided answering this directly. The take-away message was that doctors can use Avastin off-label

for AMD, but they can't study it without FDA permission – by submitting an investigational new drug (IND) application.

This exchange was interesting:

A Midwest doctor in the audience: "We use Avastin, which is an off-label use of an approved drug. What we are finding is that there are some not-so-veiled threats from the manufacturer to try to restrict access – because of economic concerns. The question is how much control does the FDA have over a manufacturer restricting access to physicians using something off-label?

FDA official: (Non-responsive answer) – "Manufacturers may not promote off-label use."

Midwest doctor: "Can a manufacturer restrict the ability of physicians to use a drug off-label by restricting access? Is that an FDA issue?"

FDA official: "It is not an FDA issue."

QUESTION 1 – Premium IOLs. A 45 year-old male presented with an interest in laser eye surgery. Preliminary testing shows the patient is not a good candidate but could benefit from RLE using an accommodative or multifocal IOL. However these lenses are only FDA-approved for use in cataract surgery.

a. **Can I still inform the patient about these new lenses? Yes**

b. **If so, can we use the lenses "off-label"? Yes**

Dr. Eydelman said that doctors can use premium IOLs off-label, and they can promote the medical procedure, but neither they nor the manufacturers can promote off-label use of ***specific*** lenses. An attorney added, "Promotion of these off-label devices not only raises FDA questions but also liability issues. You need to have in your informed consent that you are using something off-label…On the promotion side, you need to be careful not to mention a specific device in ads, radio/TV, or on your website."

QUESTION 2 – Avastin. A new drug for metastatic colorectal cancer (CRC) recently entered the market. Several of your colleagues have started using this new drug "off-label" to treat patients with AMD. You are considering this as an option for your patients as well.

a. **Is this allowed? Yes**

b. **What does the patient need to be informed about before using this new drug off-label?**

The caveat is that if the drug is being studied in some sort of human trial, an IND is required. Dr. Boyd said, "If you are going to conduct a trial in humans, you need an IND to take the drug across state lines…The distinction is a study in humans, not use for an individual patient. If you have 30 patients come in, you can treat 30 individually, but if you plan to collect that information in the form of a clinical study, you need an IND…If you are not planning to conduct a trial, you do not need an IND; you can get Avastin and use it. If you are conducting a trial, you need an IND. It is not just the drug that is regulated but the components of the drug."

If a physician submits an IND, the FDA must respond in 30 days and, in urgent situations, the Agency can respond by telephone much quicker. Asked what qualifies as a "study," Dr. Boyd said, "The law is somewhat less than specific, and the definition of what is an adequate trial varies as well…For the most part, we are talking of a prospective trial, whether or not patients are randomized or there is an adequate control." Dr. Eydelman added, "The law doesn't have a clear definition of what is a study and what isn't…If it were a case series of 20 subjects, no one would say much about it, but if you set up a larger study with different sites and 2,000 patients, we would probably ask for an IDE."

An IND is required when studies in humans are conducted for:

- Off-label indications.
- Unapproved drugs.
- Changes in formulation.
- Change in route of administration.

FDA officials also warned doctors about these ***potential*** dangers of off-label Avastin use in AMD, urging them to use it within six hours of opening a vial:

- Unknown aggregation/interaction with the syringe. There is a potential for Avastin to form aggregates during transfer to the syringe.
- Unknown potency.
- Potential concern of Avastin sticking to the syringe.
- Unknown sterility. There is a potential for microbial growth if it not used within 6 hours after opening. The label in CRC says to use it within 8 hours, but Dr. Boyd pointed out that this is when it is diluted in an IV solution, not injected into the eye directly as it comes out of the vial, "The minute the sterile vial is broken, we know from past experience that you have six hours to have a fairly good certainty of sterility."
- Particulate matter in products intended for IV administration can be several hundred-fold greater than products approved for ophthalmic use.

The ASCRS lawyer warned, "I'm stressing that the liability issues of using a new drug for an unapproved indication are pretty substantial. You are taking some serious risk…You have to clearly put this in your informed consent…Until there is some IND process, you are stepping outside the boundary of comfort. You do it at your own peril."

QUESTION 3 – Reporting IOL defects. After years of implanting a couple of your favorite IOL models, you decided to venture out and try a new one. After your first few cases, you realize that there is a significant problem with this lens. What do you do? Whom do you call? The FDA

Physician reporting to the FDA's MedWatch is generally voluntary, but there are mandatory reporting requirements for hospitals and ambulatory surgery centers (ASCs). Physicians who are owners or partial owners in an ASC need to keep the mandatory reporting requirement in mind. The ASCRS attorney warned, "Literally, any time a device is in the room, and there is a bad outcome leading to a serious injury, there is a mandatory reporting requirement. There are very serious penalties for not reporting." An FDA official explained that whistleblowers help the agency know if adverse events are being reported, "I don't encourage anonymous reporting…but I see a tremendous number of adverse events reported by people other than physicians, and there are many anonymous reports."

QUESTION 4 – Use of unapproved drugs. On a recent trip to Europe, you note colleagues prescribing a new anti-infective not available in the U.S. If you bring a supply of the drug home and want to dispense it to a select number of your patients, is this acceptable? No

Dr. Boyd said, "To bring an unapproved drug product into the country, you need an IND unless you are using the drug yourself. You can't dispense it to patients."

QUESTION 5 – Informed consent for LASIK enhancements. After a LASIK procedure, my patient has complaints of glare and haloes at night and shows significant spherical aberration on his wavefront map. I would like to perform a wavefront LASIK enhancement. What do you recommend be included in the informed consent for this patient? Informed consent prior to retreatment was the only response.

QUESTION 6. For OTC drugs, do you need an IND? Probably not.

Dr. Boyd said, "Typically, you do not need an IND (for an OTC drug) unless you are doing something very unusual – and that is hard to describe. For example, if you are using an OTC artificial tear and plan to study that for a claim beyond the OTC claim, then, yes, you need an IND. That sounds excessive, but you don't want to run a 300-patient study where you think the OTC drop will be demonstrated to have this effect without FDA input because you are technically exposing patients to a risk."

QUESTION 7 – Use of investigational drug outside of a clinical trial. There is an ongoing Phase III clinical trial evaluating a new therapy for wet ARMD. I am not participating in the trial, but I have a patient who may benefit from the drug under study. My patient does not meet all the entry criteria for the ongoing clinical trial, but I would like to treat this patient with the new therapy. Can I do that? Yes, if you can get the drug.

Dr. Boyd said, "You could get a single patient IND exemption for one person, or you could start a trial yourself if you can get the drug from the company."

COMPANY INTERVIEWS

Executives from 17 companies were interviewed at ASCRS about what's new and what's ahead for their companies.

20/10 PERFECT VISION: Selling the Femtec femtosecond laser in Europe and Asia but not in the U.S. (despite FDA approval) until the newer, faster generation is approved

CEO Reinhard Mueller-Spaeth said that sales of its Femtec femtosecond laser workstation are "in the double digits" in Asia and Europe, where it has a C.E. Mark for flaps and a variety of therapeutic applications, including keratoplasties. The systems are now in routine use, according to Mueller-Spaeth. He said that Femtec is not yet launched in the U.S.: "We have U.S. approval for flaps and are now expanding the indications…Also, our new system operates at a higher frequency, so we are amending the 510(k). We expect to be done this year."

Mueller-Spaeth said the company has not decided when to start taking orders in the U.S., adding, "We are also looking at therapeutics in applications like keratoplasty for the U.S. as well – but that is only an amendment to the 510(k)…At this point our product is approved in the U.S. as a laser microkeratome."

To make a LASIK flap with the Femtec, the laser spot is moved inside the cornea in a spiral pattern, creating a bladeless cut following stromal lamellae at the pre-programmed depth. Once the flap bed is formed, the mean is moved in arc-shaped patterns along the circumference of the flap, while the focal depth is gradually reduced. A perfectly defined edge of the flap is created, leaving a hinge at its user-defined position. Mueller-Spaeth said, "Flattening of the cornea is not required as we work with a spherical PI."

A.R.C. LASER: Introduction of the new, small, and portable Fox laser for dentists, dermatologists, and vets

Robert Hofler, international sales coordinator, talked about the debut of his company's Fox portable diode laser system, which is powered by a lithium battery that can last four hours. He said, "This is brand new. It weighs two kilograms and is very small. We say that we have reduced the size, not the power." He explained that the laser system can be used in the

dental, dermatology, and veterinary fields: "For example, koi (fish) are very expensive in Europe and can be worth up to €20,000. If they have a disease, a skin fungus, normally they have to be taken to the doctor, and it's very stressful for the fish. Here, the doctor goes to the patient." The laser, which is not sold in the U.S., costs €3,750.

Other veterinary medicine applications include wound healing, surgery, treatment of cartilage, and regeneration of nerves, tendons and ligament damage, pain therapy, and oral surgery. Dermatology applications include skin alterations, vascular lesions, coagulation, and endovascular. Dental/ear, nose, and throat (ENT)/oral and maxillofacial surgeon (OMS) surgical applications include endonasal surgery, dacryocystorhinostomy (DCR), and oropharynx procedures and excisions.

A.R.C. Laser also makes the Q-Las 10, Classic G, and TrabecuLas. The company does not sell in the U.S.; its market is in Europe and the Middle East.

ELLEX: Introduction of Integre Duo, the first red and green solid-state photocoagulator, an intense focus on rebranding the company, and moving the headquarters to California

CEO Peter Falzon said, "The main news today is our rebranding. The rebranding is our message to the ophthalmic marketplace that we are ***the*** ophthalmic laser company, dedicated only to ophthalmic lasers, and that we have a full product line that customers expect from ***the*** ophthalmic laser provider. Why I think that's important is that customers have been telling us that they want to buy their laser from a laser company and the laser specialist. The exit from the market of what was the recognized laser specialist, Coherent, three years ago gave an opportunity for someone to come in. We saw the opportunity to replace Coherent in that space."

Falzon said the company invested up to 20% of its revenue in R&D over the past three years: "Normally, the companies that are R&D-focused invest 10% of their revenues in R&D, and the average is 8%. We went outside the boundaries to fill up our product line and get to the point where we can present ourselves as laser specialists. The other hallmark of the best laser company is service, so we invested in our U.S. office in Minneapolis and in increasing our service capabilities there and our network of service engineers around the country. If a doctor's laser ever goes down, we can respond immediately and guarantee they will be back in service in 24 hours."

The company headquarters is moving to San Francisco, although engineering and manufacturing will remain in Australia. Falzon said, "We want to be closer to the customer …Global headquarters will be supporting our U.S. subsidiary based in Minneapolis. We have a Japanese subsidiary in Osaka, and our European office is in France. Ellex is listed on the Australian stock exchange."

Ellex introduced its Integre Duo, the world's first red and green solid-state photocoagulator, at ASCRS. Falzon said he expects it to receive FDA approval soon and hopes to begin shipping in July 2006. It is already approved in Japan, where the first units are scheduled to be installed in April 2006. He said, "Integre Duo is the product that we are introducing today. It's the unique product for ophthalmologists because it's the first solid-state red and green photocoagulator. What doctors will relate to is there are a lot of argon-krypton ion lasers that are in use, and doctors use them because of clinical versatility, but they're almost the size of this room and require ten gallons of flowing water per minute. It's not a major part of a modern clinic to have an installation like that, so the market moved away from these big ion lasers to solid-state lasers in the past eight to 10 years, but no company has engineered an argon-krypton solid-state. We know doctors love the clinical utility of having a red and green laser, and they want it delivered in a nice compact package."

Falzon said that Integre Duo has no competitors: "There is no other red and green solid-state. Doctors' choices today – if they want to buy a retinal laser – are either compromising down to a single green laser, which is still the workhorse for photocoagulation, and which can get them through most procedures, or, if they want more utility, there are two competitors that make three-color systems – green, red, and yellow. Green lasers are in the $30,000 range, and three-colors are more than $100,000. Lumenis and Nidek (lasers) are for a clinic or for most hospitals; they're basically over-designed and out of reach, so they're not an option for the majority of ophthalmologists. We want to offer something that's more practical; a more compact, nicer design; actually appropriate for a clinic; and that gives you some of the utility of a second color without the complexity and cost – compared to some of the other options out there today. Physicians have told us that you can do almost every procedure with green and red. In some cases where you're going to work right in the macula…you should use yellow, and there is a very small percentage of retinal specialists who will use red in the macula. In the U.S. you can probably count them on two hands. I wouldn't be telling them the Integre Duo is for them, but, outside of that, having a two-color system (is sufficient)."

Asked what's ahead for Ellex, Falzon said, "Right now the horizon for this company is more products in retina. We talked about yellow (lasers). We don't have any product announcements, but to be the leading ophthalmic company in this market. If we can innovate the design of the yellow product to get away from what's offered today, then, yes, we'll announce that. The downside is that these products are extremely complicated designs. There was the old style, where you have a huge tower with optical fiber to the slit lamp. You can see the space constraints we have. And if we can innovate and put yellow in a nice, integrated package, that would be good."

Falzon said that he wants Ellex to be viewed as the place for one-stop shopping for treating diseases with lasers. He said,

"We spend 1% of revenue, as a policy, on advanced research, which is aimed at trying to make better-designed photo-coagulators. We're doing research with leading researchers around the world who have ideas for new treatments for diseases using lasers, and it's the collaboration between our engineers and those doctors with what might seem like out-of-the box ideas that results in new laser therapies. Some examples in recent years include the introduction of SLT, which came out of a collaboration like this."

Falzon said that his company is "aggressively transitioning away from being an OEM supplier to other companies and into the Ellex brand. He explained, "Historically, as much as two-thirds of our business has been supplying Coherent (now Lumenis) and Alcon, and we made a strategic decision three years ago, after Coherent became Lumenis, to move away from that relationship and to market our products ourselves. March (2006) ends our OEM relationship with Lumenis and signifies the complete focus on our own brand. Alcon remains our OEM customer, and we like that relationship, and they like that relationship, and that will continue long-term. Many accounts are Alcon accounts, so we want to put our energy in Alcon accounts…Sales of Ellex branded products grew 73% over the previous year. I believe that no one else's brand of lasers is growing anywhere near that fast, so it shows that the investment we made in the new products is being well received. Two-thirds of that revenue came from products we didn't have three years ago, which include the Ultra Q (photodisrupter), Solitaire (photocoagulator), Solo SLT laser, the Tango SLT and photodisrupter combination, and now the Integre Duo. And 78% of our revenue was from our own brand of products."

ENDOOPTIKS: Highlighting a study on the benefits of ECP

Dr. Martin Uram, who invented EndoOptiks' ECP (endo-scopic cyclophotocoagulation) devices, said, "We have something big…We use it to treat glaucoma, but the most common use of this technology in the U.S. is combining ECP with phacoemulsification at the time of cataract surgery in the setting of medically-controlled glaucoma. People getting their cataracts out are also on glaucoma medications, even though the glaucoma is not out of control. There are compliance issues, expense, and so the party line has been, 'If you do ECP at the time of phaco, you can get patients off of some or all of their medication.' The opposing argument was, 'When you take out a cataract, the pressure is going down anyway, so the treatment doesn't do anything.' That's where it's been an argument for a long time. But like any treatment in medicine – whether surgical or medical – if you do that treatment, people know whether it works or it doesn't, but how do you prove to others that it works?"

Dr. Stanley Berke, a glaucoma specialist in New York, and colleagues presented a study at the last National Glaucoma Society meeting. Dr. Uram described that study: "It was a very large comparative study with long-term follow-up that pretty much unequivocally bears out what we've been saying.

ECP at the Time of Phacoemulsification vs. Phaco Alone

Measurement	Phaco + ECP n=626	Phaco alone n=81
Mean IOP over time		
Pre-op	19.08	18.16
6 months	16.03	17.62
12 months	16.14	16.28
24 months	16.09	16.87
36 months	16.03	18.93
Medication usage		
No change	27%	77%
Increase	5%	12%
Decrease	68%	11%
Safety		
Serious adverse events	0	0
CME	1 patient	1 patient

The study compared patients with phaco alone and patients with ECP added to phaco…I'd say it's a watershed study that changes the paradigm of how we treat our patients. The study shows it's not okay to use phaco alone, and if you have phaco patients, you're doing them a disservice because not only aren't you lowering the pressure, but you're condemning them to more medications…So this is a really pivotal study for us…and dispels the mythology associated with ECP. It's been clearly demonstrated in unequivocal terms that adding ECP to phaco is better than doing phaco alone in this huge group of patients who pop up in everybody's practice all the time. Now, all ophthalmologists have to change what they're doing in order to give their patients the best care, even though it means learning a new technique, which costs some money." He added that the learning curve for the procedure is "about a day. We make everyone do a wet lab and get certified before they do any people. They have to take a course, and they have to do a wet lab."

Dr. Uram said that a medication analysis, using retail prices, showed that patients with phaco and ECP spent $1,500 dollars a year less than the phaco-only group. He added, "Two and a half million Americans a year get cataract surgery, and 500,000 are also on glaucoma medications. If you were going to project what this would mean if everyone had an ECP, then almost a billion dollars fewer glaucoma medications would be purchased. The point is that if these two lines wound up in the same place pressure-wise, then you might say, 'Well, who cares if they use lower medications, their pressure is still okay. The reality is that when you add ECP to it, you get both – lower meds and lower pressure and a not insignificant benefit to the patients, if not a medical benefit to them."

According to Dr. Uram, the cost breakdown for ECP added to phaco is about $250 for the facility fee, $220-$250 device cost, and a $220-$250 increment for the surgeon. "Society saves the first year, not the first six months," he explained. "For the first time this proves, with a huge long-term study,

that there's no question ECP with phaco is better than doing nothing. The other thing is that the complication rates between the treatment group and the control group are the same, so it doesn't add any risk to the procedures."

Dr. Uram described the process: "When you laser the ciliary body from outside the eye, that does huge damage, and there is a 60% chance of vision loss. It doesn't work very well…and it's a brutal treatment, so it's reserved for end-stage eyes. But with ECP it's the opposite." He said that the device is "mostly for the general ophthalmologist, and that's who we made it for. We made it so the general ophthalmologist can treat most of his glaucoma patients from mildest to most severe." Dr. Uram said that ECP also can be used with multifocal IOLs.

INTRALASE: A faster femtosecond laser and a new indication for corneal transplants

Marketing manager Eric Weinberg said the big buzz at ASCRS was his company's fourth-generation femtosecond laser, which runs at 60 kHz. He said, "The second objective is the launching of keratoplasty for corneal transplants."

The laser's procedure speed "doubled from the previous version," Weinberg said. "More than that, not only is it faster, but it's a better clinical product, and our physicians have learned that from its use and are going out there touting the benefits. From the doctors' perspective, it's a tremendous improvement in technology…A reasonably high percentage of the premium IOLs require LASIK to refine the outcomes, so there is no better play for IntraLase – for anyone doing LASIK. We make LASIK better, and that's how we participate in that." Weinberg added that IntraLase will "do our millionth eye this year."

Asked about response to IntraLase at ASCRS, Weinberg said, "We saw tremendous activity at the booth (about the speed). Clearly, surgeons understand the benefit of this, and the booth traffic was phenomenal…It's like our campaign says – 'no more excuses.' We deliver all of the clinical benefits that we achieved with the 30 kHz laser we launched nine months ago, and now with the benefits of half the procedure time to help get the procedure done faster and cleaner and better. There's a sense of urgency among refractive surgeons. The technology's ready for us today…We've launched a consumer website: **www.intralasefacts.com**. That's to get out the right information to consumers about the differences among lasers…We think that will have a benefit not only to our customers but to the industry…We are constantly innovating. The goals for this year are to launch the 60 kHz (at ASCRS), and there is a full plan to upgrade our entire installed base and to take our customers to the next level."

IRIDEX: The big news will be at the American Academy of Ophthalmology (AAO) meeting in November

President/CEO Barry Caldwell said, "ASCRS is not a big meeting for us because we're more of a retina company. We're not a big player with the refractive and cataract guys; our strength is on the retina side. Our international distributors have a strong presence here. On the anterior side, we can present the green laser…We've got at least one new laser device – and maybe two – that we plan to introduce at AAO. It's an area in which we don't compete today, so its additive. We are also working on several new probes for retinal surgery. About 60% of the time, they need a laser… They also have a disposable problem, so we're working on several new versions of probes, and we'll be introducing those at the Academy."

LCA-VISION: Small booth, no news, but business on track and new centers being added

The most senior person at the LCA-Vision booth, Scott Kirk, a professional services vice president, said, "Business is doing very well. We reported 4Q05 earnings, and we've had a pretty good run for quite some time in terms of volume growth. Hopefully there will be more of the same – additional growth …We're on schedule to open 10-12 centers this year."

LIGI TECNOLOGIE MEDICALI SPA: American doctors get a look at a popular European custom laser

Ligi's business consultant Dr. Charles Stewart described the company's 1 kHz excimer laser system, which performs both custom refractive and custom therapeutic surgeries. He said, "We have a C.E. Mark and installed systems in Europe, which is our initial primary market, and we have signed a distribution agreement for China…We are in the process of completing our FDA strategy."

He said that Ligi's laser differs from other excimer lasers, "We were designed from the ground up to do custom surgery rather than applying a lens onto the cornea. Secondly, we have therapeutic applications, specifically for (certain) keratoplasties that are performed by the laser. It can treat a broad range of problems other than just nearsightedness and farsightedness. The applications I've described are quite new, and to date we are the only company that is providing this therapeutic application…To create a bed for a therapeutic lamellar keratoplasty we reference the posterior sections of the cornea, leaving a uniform thickness receiving bed as opposed to the keratome or femtosecond lasers, which run the anterior surface, leaving a mirror of the irregularities still on the cornea. So, we remove those using a differential thickness map as the data source."

LUMENIS: Doctors see eight products launched last fall

Lumenis' director of ophthalmology, Dennis Dowell, said, "At the American Academy of Ophthalmology meeting (in October 2005), we released eight new products." He described the company's new Selecta family of products for glaucoma and cataract treatment: "Selecta is a platform that would allow the doctor to expand from a standard YAG laser all the way up through a photocoagulator and SLT, or any

combination. We have a stand-alone YAG, and we have the Selecta Duet, which is a YAG and SLT, and the Selecta Duo is a YAG and a photocoagulator. The Selecta Trio is all three: YAG, SLT, and photocoagulator. The doctor can choose and pick whatever level platform he wants, and all of them are upgradable. What makes it unique is that it's very customizable to the doctor's specific situation. It also has portability and is compact." Dowell added that Lumenis also released a laser indirect ophthalmoscope: "It's a three-color laser, and it's the world's lightest coaxial three-color LIO (laser indirect ophthalmoscope)."

NIDEK: Touting the advantages of combining a YAG and a green light laser

Executive director of sales and marketing Gary Pehrson said, "We have a combination system YAG and 532 green light, and there is no compromise when you put the two systems together. The only other combination system is the Zeiss system, and there are compromises there. For example, you can't obtain a red reflex with Zeiss when doing capsulotomies and iridotomies; you have to go at an angle. The other thing is that it has a moving filter for the 532 and a split prism assembly which is much more like a standable system. It's no compromise by putting the two systems together, and if you buy either one, you can hook the other system to it. It is cost-saving and space-saving. It's called the Nidek combo. We sell 70% of the combos in the U.S."

Pehrson said the company is still waiting for a hyperopia indication with its excimer laser: "It's something that we expect sometime this year (2006)."

Nidek's consolidation of products from Nidek Technologies America, in Greensboro NC, officially took place on April 1, 2006. Pehrson said, "The products from Nidek Technology are the ConFoScan 4, the MP-1 maculate performance testing unit, and the Magellan corneal topographer."

As for future products, Pehrson said, "Nidek continues to introduce new products every year; we'll have a couple of new products this year." Marketing manager Frank Wood added, "We're leaders in what I call 'trends of vision performance.' We're always working on ways to fix glaucoma and cataracts, but what's exciting to me is, because we're international, we're taking it one step further. If we were only in the U.S., we'd be very limited by what we could do. But a lot of our R&D happens overseas, where they're always looking for the cutting edge of what we can do."

NORWOOD ABBEY: New patent protection

COO Jeff Bell claimed the safety of his company's Epi-LASIK procedure makes it superior to other procedures. He said, "We just had some patents granted making it the only IP (intellectual property) in the space and giving us an extremely strong position to market our product, which is current generation. There is no cutting through the eye; it is a completely bladeless procedure, whereas with other procedures the LASIK flap never heals." He added that his company is working on the next generation of the device.

Bell said that "anyone can use this device," and proved it by allowing a reporter to try out the machine.

Epi-LASIK, which is a surgical modality for the advanced surface ablation treatment of myopia and hyperopia, uses a mechanical device called an epikeratome. Before photoablation, the corneal epithelium is gently separated using a customized epikeratome that features a unique-non-sharp separator. Separation is created mechanically without the use of alcohol. Once the photoablation treatment is accomplished, the epithelial sheet is replaced onto the ablated cornea and protected by a bandage contact lens.

QUANTEL: A new green laser is available

Sanford Lane, CEO of Quantel Group's U.S. division, Quantel Medical, said that his company is redesigning all of its laser equipment, "We have a green laser called a Viridis, and we've redesigned that and all of our green lasers with a new internal laser mechanism." Lane is most excited about his company's new Vitra solid-state, portable green laser for photocoagulation. He said, "It's a new little device the size of a shoebox and weighing about 10 pounds. It's a fully functional green laser with memory on board for memorizing up to 60 different settings and delivery systems. We just brought it out. We showed it at a meeting four months ago, and now it's actually available – working and all deliverable. We have a full line of accessories, including motorized filters, slit lamp adapters…So that's the new product." The company also has a YAG laser, but it is still only available in Europe.

SCHWIND EYE-TECH-SOLUTIONS: Building relationships, previewing new software, and stressing quality and relationships

Rolf Schwind, president/CEO, said that his company is entering the U.S. market with its Carriazo-Pendular microkeratome. He said that his company's excimer laser does not yet have FDA approval, but the company may try to get approval with its next generation model. He said Schwind was at ASCRS because "it's important for (U.S. doctors) to see us here and build up relationships. We have a new workstation, diagnostics, and information about new software…A new software version will be released in about two months… We have 510(k) approval for the microkeratome, and we are in the main markets in Europe and also in Southeast Asia. We are also strong in South America."

Asked about the possible threat from femtosecond lasers, Schwind said, "I think many people are using it as a marketing instrument…It might work as a competitor to the excimer laser, but nobody knows this. It may be the case, but it may also not be the case. It is something we are watching." He said that his company is thinking about working on a femto-

second laser, not by copying the existing systems, but with another approach.

Schwind said that his company, a private, family-owned firm, is not interested in going public, "Companies in the stock market are mainly interested in how to make the prices go up. That is not relevant for us. We can work with our customers on the long-term strategic view. I think quality in this field is a goal for everyone…We are a small company with 80 people, and we make all the decisions. I can make a decision quickly. We have no hierarchical system, so we can adapt when anything changes, very quickly. We also see our clients as part of the family, and they have direct access to me."

SOLX: Approval in Europe and progress in the U.S. on an innovative shunt and a new laser for glaucoma

SOLX's DeepLight 790 titanium sapphire laser for glaucoma has a C.E. Mark in Europe, according to co-inventor Joseph Lowery. DeepLight uses near infrared 790 nm. He said, "We're approaching treating 1,000 patients with the laser… We have lasers all over Europe and Canada (<50). We're in a trial here in the U.S., and we're close to completing our IDE. The trial has been going on for more than two years. There have been 100 eyes treated in the trial out of 160 that we're approved to do. At the completion of the trial, we'll submit the results to the FDA, and that could be the second half of this year (2006). We hope we're done with enrollment by the end of this year. We're following patients up to 12 months after treatment with the laser." Lowery said the randomized trial puts the SOLX laser head-to-head against argon laser trabeculoplasty. He said, "We're going against the 30-year-old gold standard, and interim results show we appear to be equivalent." The system costs $65,000 in Europe.

SOLX's other product is a gold microshunt, which also has a C.E. Mark. Lowery said, "It's novel for a few reasons. It's a glaucoma implant, and it's made out of pure gold for compatibility. The head of the shunt is in the anterior chamber and, fairly unique to all implants, the tail goes into the superchoroidal space – a natural drainage passage not like trabeculoplasty. We're keeping it inside the eye, and it acts as an assist to move that fluid down…We're also in clinical trials with the FDA on this device (comparing it to the Ahmed valve). It's unique – much smaller than anything else (6 mm by about 2.5 mm by only 50 microns). Inside the shunt are channels – holes at top and holes at the bottom."

Lowery said there has been "extensive" interest in the shunt: "The FDA granted us 10 clinical trial sites, and we've had to turn down many more requests to be an investigator than we have sites for…We hope that enthusiasm continues when we receive FDA approval."

Asked what lies ahead for SOLX, Lowery said, "One could envision someday a shunt that would go in the eye with, say, 6 holes at the tip, and you would get a pressure read down to some baseline. You could then envision going in two months later – imagine the pressure drops to a certain level and the surgeon wanted a little more – and the laser can create additional holes in the head of the shunt to help titrate the pressure down from 15 to 11, if that's better for the patient."

Lowery added, "We're not looking to replace shunts. We're looking to replace trabeculoplasty. One of the most singular things we're hearing is: avoid the bleb. That carries with it a lot of complications. The glaucoma surgeons don't necessarily enjoy dealing with it, and (our products) would avoid all those complications. For example, we heard one speaker at this meeting say that he does a lot of trabeculoplasties during the week and spends his weekends tending to complications related to them."

WAVELIGHT: An innovative, wavefront-optomized excimer laser for Europe and perhaps in the future the U.S.

One of the Allegretto excimer laser's most innovative features is the way it uses wavefront-optimized technology to automatically compensate for the curvature of the cornea, WaveLight global marketing manager Katrin Teigeler explained. She said, "(The) Allegretto Wave sends extra pulses to the peripheral cornea area in order to compensate for the angle of the laser beam, preserving the cornea's aspherical shape…While wavefront-guided procedures customize laser treatments based on the individual characteristics of the eye being corrected, the term wavefront-optimized refers to laser treatment software that has been designed with certain corrections pre-programmed, although a true and customized wavefront plan is not employed." She said that the "official" price of the Allegretto is $495,000.

She said of the conference, "We want doctors to take home the message that we're proud of being the innovation leader in the refractive industry for the past seven years since we got into the market, and we have introduced the latest, newest standards since we came to market…That started with wavefront tech-nology. We were the first to introduce aspheric ablations, then we were first with a standing spot laser system…We want to continue down that path. We recently engaged topography- guided LASIK trials, which are in the final stages of development. The trials will begin as soon as we have submitted final protocols to the FDA…We have a topography-guided laser and we also have the premium Concerto laser system. We are the only company that offers a variety of laser systems, not just one…Internationally, we have the 400 system and the Concerto…The Concerto is premium. It is built on-demand only. It comes in any color you want…It's an interesting product that we put out there."

Teigeler said that the Concerto costs €1 million. It is not available in the U.S., but the company is considering entering the U.S. market.

Teigeler said that WaveLight also is working on its own femtosecond laser system. She said, "We're developing a

femtosecond laser, and we plan to show the prototype this year, most likely…That's our plan, and then we have to go through extensive clinical trials and make sure it's tested, validated, and retested."

CARL ZEISS MEDITEC: New OCT and fundus camera introduced at ASCRS, IOL Master proving useful with premium IOLs, and watch for announcements later this year about their new excimer laser and new femtosecond laser

Director of refractive lasers, Stefan Kaiser, said that Zeiss is working on a femtosecond laser. He said, "That's the big thing we're working on. We're in a stage where we cannot disclose many details; that will come later this year. But our intention is to give some more visibility with the project, plus really to show the community that we're not just thinking in terms of excimer lasers, but we are planning the next big step. Also, we want to show our commitment as a company to refractive laser surgery. This is completely our own project."

Kaiser said he is expecting FDA approval for the Zeiss excimer laser "within this fiscal year, which ends in September. This is the other milestone for us, and then we enter the U.S. market."

Director of marketing Christine Randle said Zeiss introduced several new products at ASCRS: "Our strategy is to target major ophthalmic conditions and provide standard-of-care instruments in all of these areas. In the cataract and refractive area, the new product is the Visante OCT, which we are introducing at ASCRS. The first shipments in the U.S. are starting. OCT technology is a cross-section of the eye, which is breakthrough technology. The Stratus is now the standard of care in retinal practices. It is used to detect AMD and monitor response to therapy. We've taken this technology and made similar images of the anterior segment. This is important at ASCRS because it helps physicians evaluate patient suitability for phakic IOL surgery and determine whether there is adequate stromal bed thickness for LASIK enhancements. (OCT technology helps in) surgical planning, assessment of post-operative results, and for diagnosing tumors and other anterior segment disease. (The Visante) also has a glaucoma application to see how wide the angle is between the iris and the cornea…This is a way a doctor can detect closed angle glaucoma. Another thing that is new is that this is non-contact; this can also be technician-operated."

Zeiss also has a new fundus camera, the Visucam, which is a non-mydriatic solution for fundus imaging. Randle said, "We have a rich history of fundus photography. This camera does not require that the eyes be dilated. In today's market, patients don't want to be dilated, so a new market has emerged …The reason our product is effective is that it combines all the computerized data and archiving functions as well as photographic functions in one sleek package. It is incredibly easy to use, so technicians can use it. The images are incredibly high quality, and it's designed with workflow in mind. It has been very well-received, and it's being shipped now, too."

Randle continued, "The other news we have is our IOL Master, and that's for measuring the length of the eye prior to cataract surgery. This year the procedure will be the most-used method of determining (eye length). It is one of the ways you can ensure a good result because patient expectations are higher, and this is the gold standard. That's our strategy, to make our products provide exceptional clinical benefits and workflow efficiency, so that they become standard-of-care in ophthalmologic and optometric practices."

Asked what message she wants doctors to take away from ASCRS, Randle said, "We want doctors to think that Zeiss is their trusted partner in providing clinically-validated, practical solutions to allow them to make confident medical decisions."

ZIEMER OPHTHALMIC SYSTEMS: Newly approved femtosecond laser generating interest and orders but only first step in company's laser plans

President Frank Ziemer described his company's rollout plan for its Da Vinci femtosecond surgical laser system, which received FDA approval on March 13, 2006, and a C.E. Mark the week before that. He said, "We are ramping up just at the moment. We started to ramp up production, and the plan is that we can roll out machines starting in July (2006)." He said the company has about 10-15 European orders: "The rollout plan is also from June (2006) on, and I have heard that there is a lot of interest."

Ziemer explained how the femtosecond laser differs from other machines: "First of all, we have laser physics which create minor cavitations. That means hardly any tissue bridges, and there are hardly any gas bubbles. As soon as you lift the flap, the gas bubbles are gone. Also, patient input is not slowed down. Our patient throughput is more or less the same as a traditional mechanical microkeratome. You can use this mobile – unique feature – directly and you don't have to move the patient. And you use it directly, with the handpiece. It is directly applied on the patient's eye, which is a completely different machine concept in comparison to the IntraLase. So, the whole application, the whole process, is very easy and straightforward, and you don't lose time."

Pricing for the Da Vinci was described as "more or less the same" as that of the IntraLase. Ziemer said, "It's a high-tech machine and the most modern laser technology. We have to say that IntraLase started six years ago, and I have a lot of respect for IntraLase, with its laser technology, but it is not the most modern technology…So it's a quality strategy, and we don't want to compete with price." He added that the Da Vinci is a Swiss-engineered and -manufactured device.

Ziemer said that the company does not have a marketing partner but is working on getting one. Asked who is interested, he said, "All the major companies who are really

focusing on refractive surgery, of course. There is a lot of interest." Ziemer developed the Amadeus microkeratome which is sold by AMO, so the company has experience in flap creation.

Ziemer said the company already is working on its next generation femtosecond laser, "The next generation will have a lot of new features. Our strategy is to deliver to the refractive market every one and a half or two years the most modern femtotechnology. One has to understand that femtotechnology is changing quickly. You have to imagine that six to seven years ago there was no femtosecond laser, and the technology is changing every year, so we have to come up with new femtotechnology and implement it in the machine and offer that to the ophthalmic market. We see also that the femtosecond laser has a great potential in corneal surgery, not only for refractive surgery, but, even more than corneal surgery, we see that femtotechnology could play a role in glaucoma surgery. At the end of the day, and it's too early today, there is also possible potential in retinal surgery. It (a femtosecond laser) is a great tool for ophthalmology. We decided four years ago that to move into femtotechnology we had to bring together a lot of technology, and our strategy for the coming years is just to go ahead with it and not stop…We want to keep growing. The next generation is the so-called 3-D handpiece, where you can change the handpiece and do whatever you want, such as keratoplasty."

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